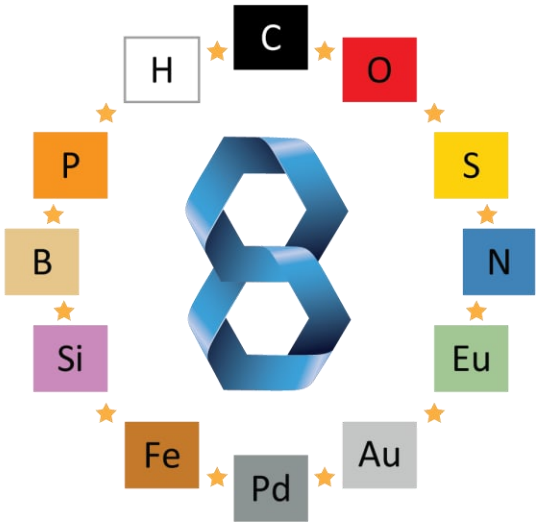

EuChemS

Chemistry Congress

28 August to 1 September

2022 · LISBON.PT

Detailed programme

8th EuChemS Chemistry Congress

Lisbon Congress Centre, Lisbon (Portugal)

This is a working copy of the Book of Abstracts. The definite edition with ISBN and DOI will be made available to all participants on the ECC8 webpage shortly after the congress.

Editors

Artur M. S. Silva

Adelino M. Galvão

Bruno F. Machado

Joaquim L. Faria

Edition

Sociedade Portuguesa de Química

This book of abstracts was produced from the works submitted directly by the authors. Only minor editing changes were introduced, which in no way altered the scientific content. The final online version was established for the 8th EuChemS Chemistry Congress according to the published template. The authors are responsible for the scientific content of their abstracts.

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PREFACE

Dear friends and colleagues,



It gives me an immense pleasure to welcome you on behalf of the Executive Board of the European Chemical Society to the 8th EuChemS Chemistry Congress. We all have been looking forward to this event for a long time and we are really pleased that it will be finally possible again to meet with friends and discuss chemistry with participants from all over Europe and beyond.

I wish to acknowledge Artur Silva and his crew for the tremendous efforts that they have dedicated to organizing this conference essentially twice after it was postponed due to COVID two years ago. Jointly with the Scientific Committee, headed by Luisa de Cola, a wonderful programme has been put together, containing not only high-level chemical science, but also broader elements such as discussions on societally relevant challenges where chemists can contribute to finding solutions. To mention some elements in particular, the conference features two EuChemS Gold Medal awardees, topical parallel sessions covering the full width of the chemical sciences, lectures by young talented researchers aiming for the European Young Chemists' Award, and a programme organized by the European Young Chemists' Network (EYCN).

I also would like to acknowledge the Institute of Chemistry of Ireland (ICI), the host of the 9th EuChemS Chemistry Congress (ECC9), initially scheduled for this year in Dublin along with their centennial, and then postponed to the summer of 2024. Congratulations to ICI with reaching the 100th anniversary!

Finally, I want to thank you, all the participants, for coming to Lisbon and contributing to making this conference a success. We have seen in the past two years that many things can be done online, but certainly not everything. Brainstorming about new scientific ideas, having lively discussions, drawing chemical structures, speculating about mechanisms, none of this is possible through Zoom. Neither is it possible to personally interact with other people, to make new friends, or have a glass of wine over a good dinner. That is why we go to conferences and why the EuChemS Chemistry Congress is organized for.

I wish you a very pleasant stay in Lisbon, but most of all enjoy the conference!

Floris Rutjes

President of the European Chemical Society

Dear friends and colleagues,

EuChemS, the Sociedade Portuguesa de Química and the Sociedade Portuguesa de Electroquímica have the pleasure to welcome you to the 8th Chemistry Congress (ECC) in Lisbon from 28 August until 1 September 2022. The conference, first scheduled for 2020 and postponed to 2022 because of the pandemic situation, wishes to continue a tradition of excellence in general chemistry meetings in Europe, started in Budapest in 2006.

With the theme "Chemistry the Central Science", the congress aims to emphasize the central role of chemistry at the interfaces with biology, materials science and environmental sciences, both for the sake of science progress and for the solution of important problems that our society is facing. The discussions on different aspects of the chemical science will take place over five days that are filled with plenary lectures, oral and poster communications, and many activities that should stimulate interactions, imagination and promote knowledge in the broadest possible context. During the lunch period, there will be tutorials where chemistry interfaces with art, cinema and astronomy are discussed, broadening our perspectives in a stimulating way.

In this edition three transversal topics were introduced: Molecules in Motion, Energy, Environment and Sustainability, and Imaging that will be tackled from different aspects to highlight the importance of different scientific contributions for the understanding of a complex problem.

In addition, young scientist sessions with oral talks will show the new emerging directions of chemistry.

Awards of the European Chemistry Gold Medals, to recognize the achievement of two scientists working in the field of chemistry in Europe and from the Gesellschaft Deutscher Chemiker (GDCh; German Chemical Society) will be presented.

The presence of more than 25 countries and an excellent gender balance reflect that science has no barriers and speak a single language that everyone can understand and use to communicate, like music.

We hope that all the participants will have the opportunity to enjoy Lisbon, one of the oldest European capitals, a city full of charm with more than 3000 years of history and combining many cultural influences.

Science is a peaceful international endeavour for the benefit of all humanity, and we will have another EuChemS conference based on a science and a friendship with no borders.

We look forward to meeting you in Lisbon at the EuChemS ECC8





Luisa De Cola

Berberan Santos

Dear friends and colleagues,

The Portuguese Chemical Society (SPQ), with the support of the Portuguese Electrochemical Society (SPE), is very proud and happy to be the host organisation for the 8th EuChemS Chemistry Congress (ECC8), and, as its President, I welcome you warmly to Lisbon.

Under the general and unifying theme of Chemistry the Central Science, the ECC8 will have an exciting scientific programme led by renowned international experts. It will focus on the central role of chemistry in solving fundamental problems of modern societies at the interface of biology, material and environmental sciences, among others, both for the progress of humankind and for the solution of fundamental problems of modern societies.

After the difficulties and uncertainties felt in 2020 due to COVID 19 that led us to postpone the ECC8 to 2022, the accumulation of scientific congresses competing for the same period of the year and some with overlapping dates, we managed to put together an excellent program. Given the current situation and the fears that some colleagues still have, the number of participants that will exceed 1200 is not what was expected when we proposed to organise ECC8 in 2020. However, it is a good result considering our current situation in August 2022. This face-to-face meeting will be the appropriate environment to share and discuss novel ideas and to showcase the most recent advances in chemical sciences of Europe and around the world, but also for the young scientist to discuss with more experienced ones, which was not possible in the last two years.

The Portuguese Chemical Society (SPQ) serves more than 1000 members internationally with the purpose of promoting, cultivating and developing in Portugal the research, teaching and application of Chemistry and its close connected Sciences. SPQ works diary to create opportunities for chemists to meet through the organisation of national and international meetings.

Lisbon is a historic capital full of charm, where more than three centuries of cultural influences blend with modern trends and lifestyles. It is, therefore, the perfect place to receive you all and engage in a fruitful scientific discussion.

As actively engaged members of EuChemS, we are very honoured to have worked hard with many talented people and various organisations to bring this congress to all of you.

I would like to sincerely thank everyone who contributed to building this excellent scientific event, namely, the chairs of the congress, Luisa De Cola and Mário Berberan Santos, our brilliant scientific and organising committees, session conveners, participants, sponsors and exhibitors, and not forgetting the SPQ secretariat.

I hope these five days of congress will be a great opportunity to share knowledge, make friends and establish scientific collaborations, overcoming the barriers that sometimes appear in our lives and the world we live in. I hope you are happy and have a very successful and productive week in Lisbon.



Artur Silva

SCIENTIFIC COMMITTEE

Luisa De Cola, Italy – Chair – Materials

Mário N. Berberan Santos, Portugal – Co-Chair – Spectroscopy/Physical Chemistry

Artur M. S. Silva, Portugal – SPQ – Organic Chemistry/Synthesis

Alice Solda, Italy - European Young Chemists´ Network

Katharina M. Fromm, Switzerland – Inorganic Chemistry and Solids

Piotr Stepnowski, Poland – Analytical & Environmental Chemistry

Maria Lucia Curri, Italy – Nanostructured and Multifunctional Materials

Paolo Melchiorre, Spain – Catalysis and Photocatalysis

Oren Scherman, United Kingdom – Dynamic Supramolecular Assemblies

John Cassidy, Ireland - Analytical Chemistry and Instrumentation

Johan Hofkens, Belgium – Spectroscopy and Imaging

ORGANIZING COMMITTEE

Adelino Galvão, SPQ General Secretariat, IST, Universidade de Lisboa

Ana Isabel Ricardo, FCT, Universidade Nova de Lisboa

Antonio M. Rodríguez García, Spain - European Young Chemists´ Network

Eckart Ruehl, Freie Universität Berlin, Treasurer and Member of EuChemS Executive Board

Fernanda Proença, Universidade do Minho

Joaquim L. Faria, SPQ Vice-President, FEUP, Universidade do Porto

Luísa Martins, SPE, IST, Universidade de Lisboa

Manuel Minas da Piedade, FCUL, Universidade de Lisboa

Maria José Calhorda, FCUL, Universidade de Lisboa

Rui Fausto, FCT, Universidade de Coimbra

Tito Trindade, Universidade de Aveiro

Vítor Freitas, FCUP, Universidade do Porto

ORGANIZERS







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O Presidente da República

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With a global community of more than 150,000 in over 140 countries, ACS accomplishes this through 32 technical division, 26 international chapters, and hundreds of ways to engage with professionals across the globe who share your passion for chemistry and the chemical sciences.

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NOVARTIS

EXHIBITORS

The European Chemical Society (EuChemS) aims to nurture a platform for scientific discussion and provide a single, unbiased European voice on key policy issues in chemistry and related fields.

Active since 1970, EuChemS represents more than 160,000 chemists from more than 51 member societies and other chemistry related organisations.

The American Chemical Society is the largest scientific society in the world, providing authoritative, comprehensive information and resources to chemistry professionals around the globe. Discover the latest scientific advances and chemistry related information through ACS Publications' 75+ peer-reviewed journals, and reveal unseen connections with CAS scientific information solutions, including CAS SciFinder-n.

With 16 Chemical societies from 15 European countries behind Chemistry Europe, we are dedicated to publish the highest quality of research across all chemistry disciplines. Within our publications we support researchers at every stage of their careers by providing the ideal platforms for the international dissemination of their results.



The Portuguese Chemical Society (SPQ) is one of the largest, most active and oldest Portuguese scientific societies, having been founded on 28 December 1911. SPQ promotes, cultivates and develops research, teaching and application of Chemistry and Science, with which it is more directly related.



Founded in 2004, Magritek is the global leader in manufacturing cryogen-free benchtop Nuclear Magnetic Resonance (NMR) spectrometers for the analytical instrument market. Magritek's revolutionary 90 MHz, 80 MHz, and 60 MHz Spinsolve family of benchtop NMR models offer the highest sensitivity and resolution available in the market.



Thieme Chemistry publishes highly evaluated information about synthetic and general chemistry for professional chemists and advanced students since 1909. Our portfolio includes the journals SYNFACTS, SYNLETT, SYNTHESIS and SynOpen, the synthetic methodology reference work Science of Synthesis, the German chemical encyclopedia RÖMPP, and monographs in electronic and printed format.



Fluorochem is the UK's largest Independent Research Chemical Supplier, offering an extensive range of intermediates, reagents, building blocks and deuterated solvents, spanning over 16500 scaffold groups.

In order to help customers search our sizable catalogue, we launched the Doug Discovery platform. The website uses a novel method to search by functional and structural groups, reducing the time spent finding chemicals and therefore allowing the chemist to spend more time on research.



The Gesellschaft Deutscher Chemiker (GDCh – German Chemical Society) brings together people working in chemistry and the molecular sciences and supports their striving for positive, sustainable scientific advance, for the good of humankind and the environment. The GDCh supports chemistry in education, research and application and promotes the understanding of chemistry in the public.



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Our journals publish a range of content across the chemical sciences.

We offer high quality peer review, open access and open peer review options; promotion by a dedicated press office; and broad dissemination to an international audience. To find out more, come and see us at our booth.

We are an international organisation connecting chemical scientists with each other, with other scientists, and with society as a whole. Founded in 1841, we have an international membership of over 50,000 and exist to give everyone in the chemical sciences the resources, connections and inspiration to shape the future of chemistry and our world.

The independent academic publisher, De Gruyter, has been on the market for the past 270 years, releases 1300 new books each year, has more than 650 journals and a variety of digital media. The STM team provides content on materials sciences, polymer science, and nanotechnology, among others.

Springer Nature advances discovery by publishing robust and insightful research, supporting the development of new areas of knowledge, making ideas and information accessible around the world, and leading the way on open access. Our journals, eBooks, databases and solutions make sure that researchers, students, teachers and professionals have access to important research.

"Research in Germany" is an initiative of the Federal Ministry of Education and Research. It presents Germany as a country of research and innovation and creates a forum for international exchange and cooperation. It also provides information on the German research landscape and on career and funding opportunities for researchers.

Reaxys speaks the language of chemistry. Reaxys is a highly-curated, easy-to-use chemical information solution built on validated data. It harnesses the power of machine learning to help researchers, teachers and students to find, connect and utilize chemistry literature, property and reaction data, patents and experimental procedures.

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VENUE & LOGISTICS

Lisbon Congress Centre (LCC)

The Congress centre is located close to the river Tagus and the historical and cultural heritage of Belem, just a few minutes from the city centre.

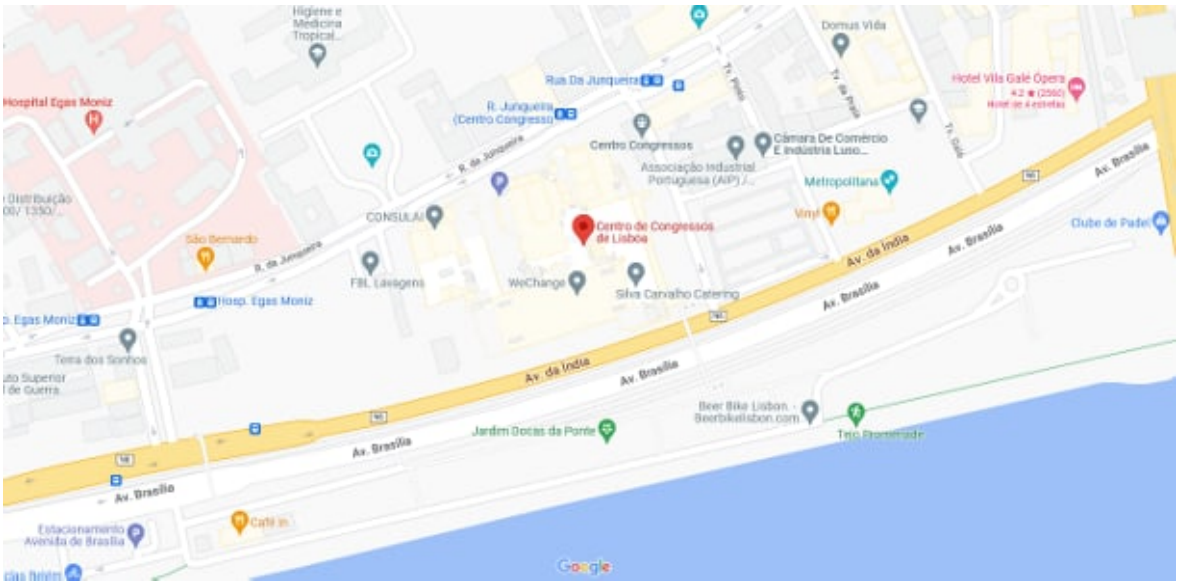
Registration opening times

Sunday:	14h00 – 17h00
Monday:	09h00 – 17h00
Tuesday:	09h00 – 17h00
Wednesday:	09h00 – 17h00
Thursday:	09h00 – 12h00

Contact:
Praça das Indústrias
1300-307 Lisboa – Portugal
Tel. (+351) 218 921 420
Fax (+351) 218 921 499
Email: lisboacc@ccl.fil.pt

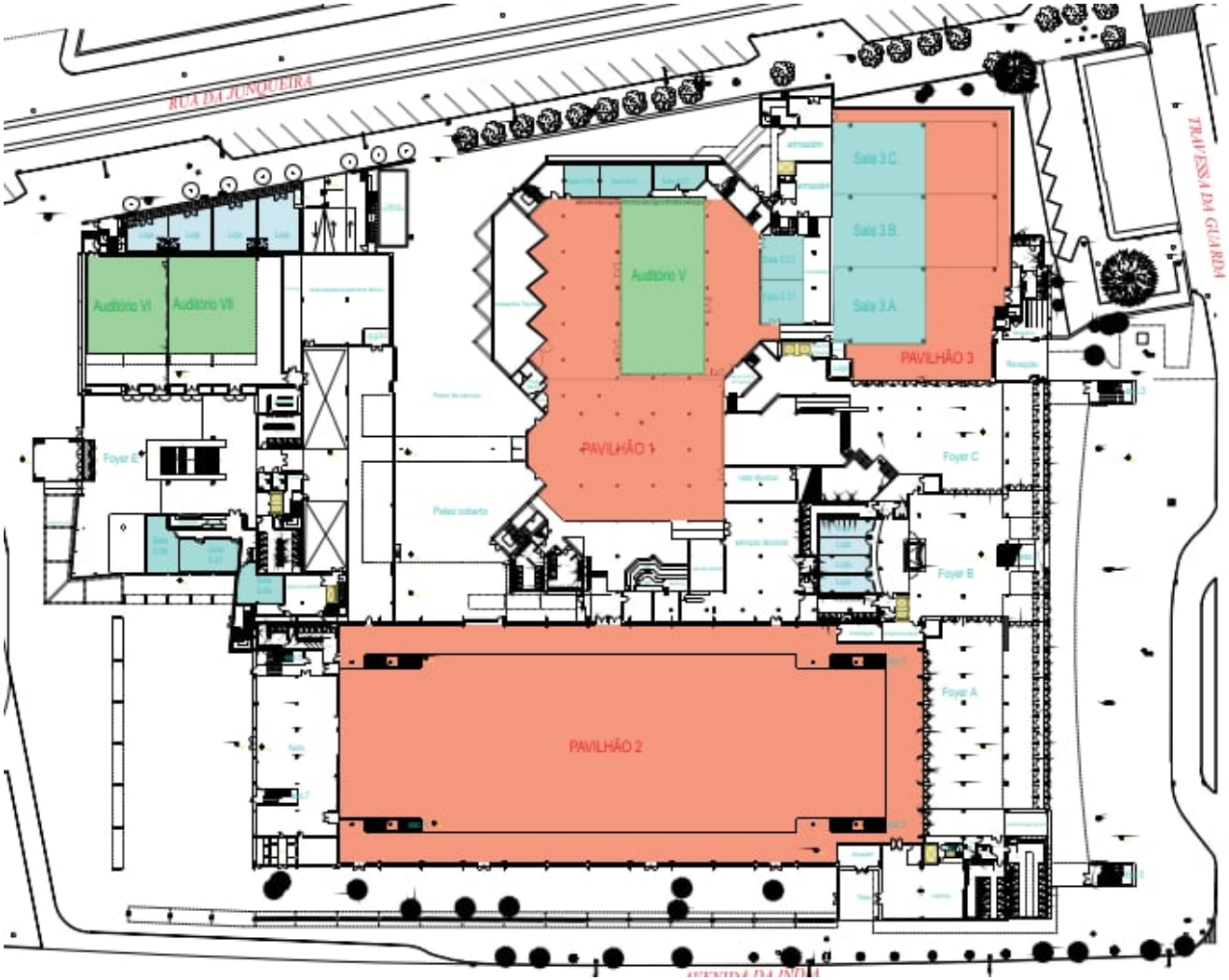
GPS: Latitude – 38°41'57.80"N – Longitude – 9°10'57.00"W





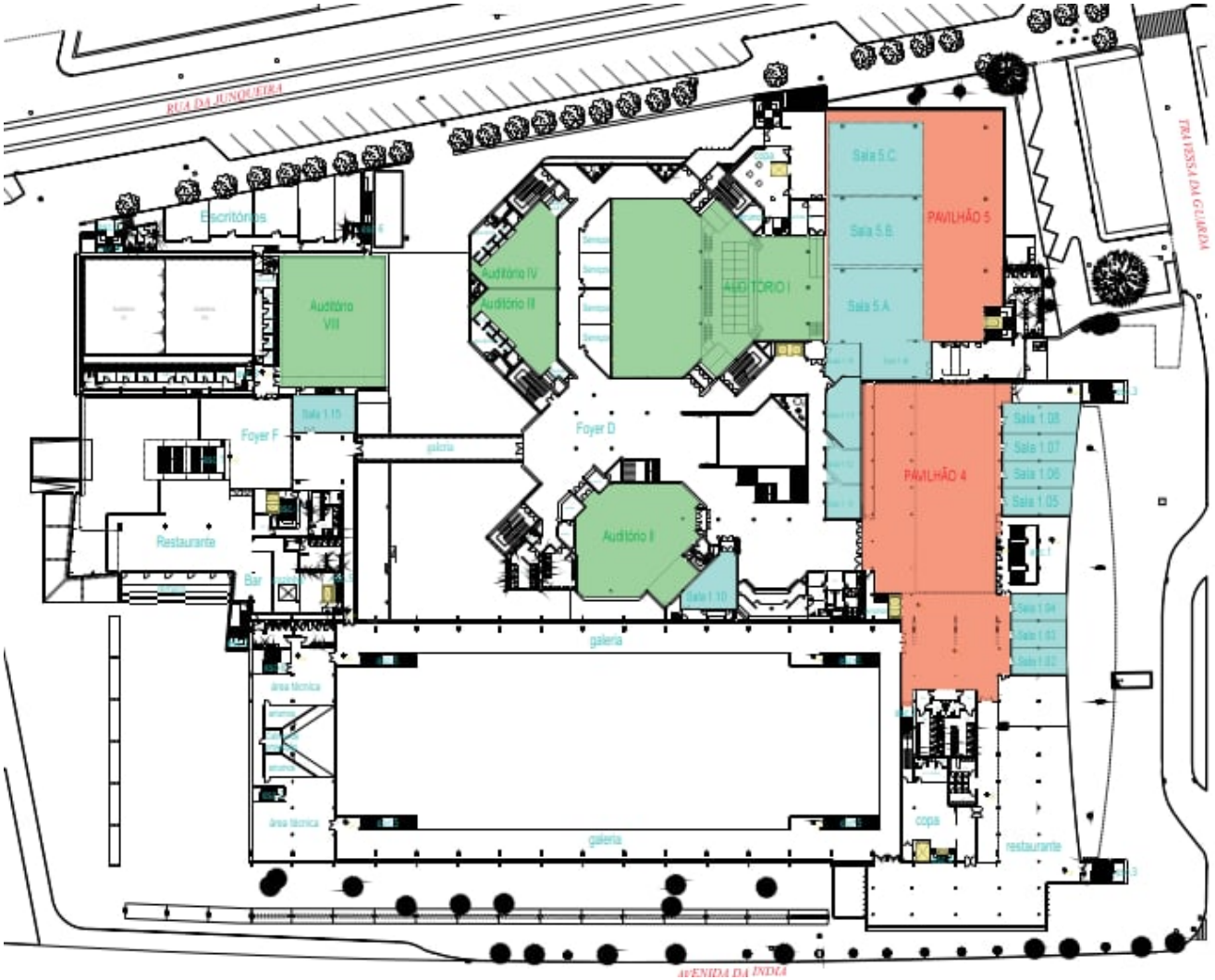
LCC - Ground Floor

Pavilions | Auditoriums | Rooms | Elevators | Stores

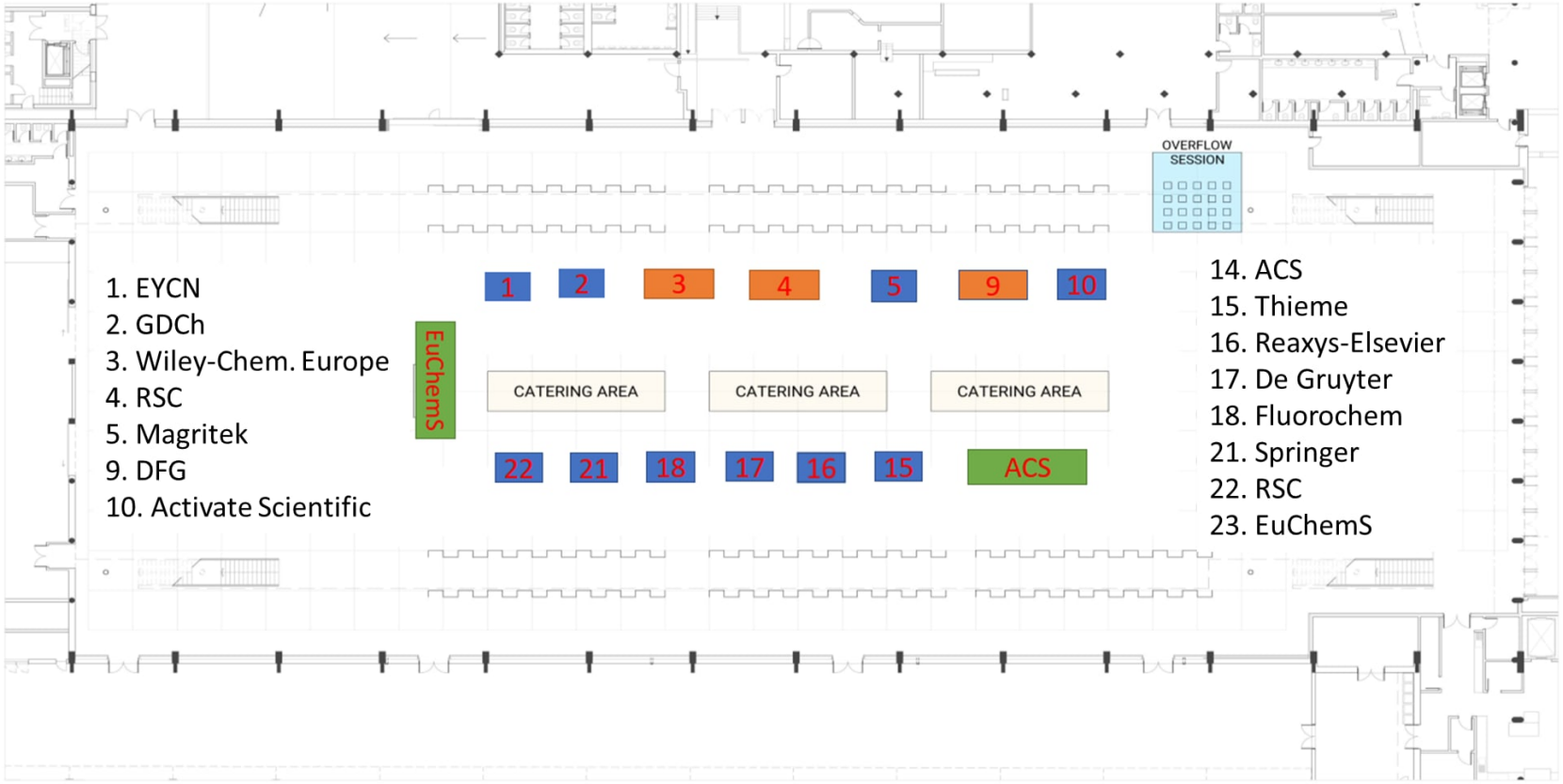


Pavilions Auditoriums Rooms Elevators Stores

LCC - First Floor



Details for Pavilion #2 | Ground Floor



PROGRAM – TYPE OF PRESENTATION

In 8ECC will be presented Plenary Lectures, Invited Lectures, ERC communications, Oral Communications and Poster Communications.
Please find below important information and carefully read the one that applies to your presentation mode.

PLENARY LECTURES (PL)

Plenary Speakers will have **40 min** for a complete presentation comprising any discussion time (questions and answers, Q&A) if desired.

INVITED LECTURES (IL)

Keynote Speakers will have **30 min** for presentation, including 5 min for Q&A.

ORAL COMMUNICATIONS (OC)

Oral communications will be **15 min**, meaning 12 min of presentation and 3 min of Q&A.

ERC COMMUNICATIONS (ERC)

ERC communications will be **10 min** for presentation.

POSTER COMMUNICATIONS (PC)

Posters should be a maximum size of **0.9 m x 1.2 m** (width x height).
The participants are asked to hang their posters from the registration opening on the 28th of August (or at least in the morning of 29th of August) and leave them in the exhibition through the congress days untill the 1st of September. During the poster session, each author must stand near the poster so other interested participants, including prize assessors, may find the author and discuss the topics of interest.

All spoken presentations must be uploaded, tested, and submitted to **Master View Room.**
Opening and closing hours of the Master View Room – 08h00-18h00. Here, the speakers must deliver the presentation file at least **3 h before the afternoon session** or the **day before the morning sessions** (no later than 18h00).

The conference rooms will be equipped with **MS PowerPoint 2016** laptops.
Using your own laptop is not allowed. **Apple platform is not supported**; ensure your files are PC compatible. Before the start of your session, visit the conference room to check your presentation, familiarise yourself with the audio-visual equipment and meet the chairperson. You will easily find your presentation at the pulpit according to the scheduled session, date, hour and speaker. Using the laptop podium, you will be able to control your presentation. There are no individual microphones.

MS PowerPoint Presentations Specifications

All spoken presentations must be uploaded, tested, and submitted to **Master View Room.**

1. Videos and pictures must be in the same folder as the MS PowerPoint presentation. Moreover, they must be copied into the folder before being inserted into the presentation. Videos included in the presentation shall have the following extensions: “.avi”, “.mpeg”, “.mov,” or “.wmv”

2. JPG, GIF, and BMP compressed images are the preferred file format for inserted images (other types of extensions will also be accepted, provided that they are recognized by MS PowerPoint 2016).

3. Use Microsoft Windows 10 default system font. Otherwise, please provide a font package for later installation.

4. Please use Microsoft PowerPoint 2016 (*.ppt) to guarantee your presentation will open successfully on an on-site PC. Save your presentation with the extension ".ppt," or ".pptx".

5. For MAC-Users: Export your Keynote presentation to PowerPoint for Mac or export your keynote presentation to a movie (iMovie, QuickTime video with "Playback Uses" settings) or export it to PDF. Be aware of the need to edit/reformat the presentation - fonts, images and charts – especially when exporting to PowerPoint for Mac. For embedded movies, please use the possibility of "Quicktime" to save the movie in "*.mpeg 1(2)" or "*.avi" format. Please try out the proper functionality of your presentation as soon as possible in the Master View Room.

6. Presentations must be designed in 16:9 format

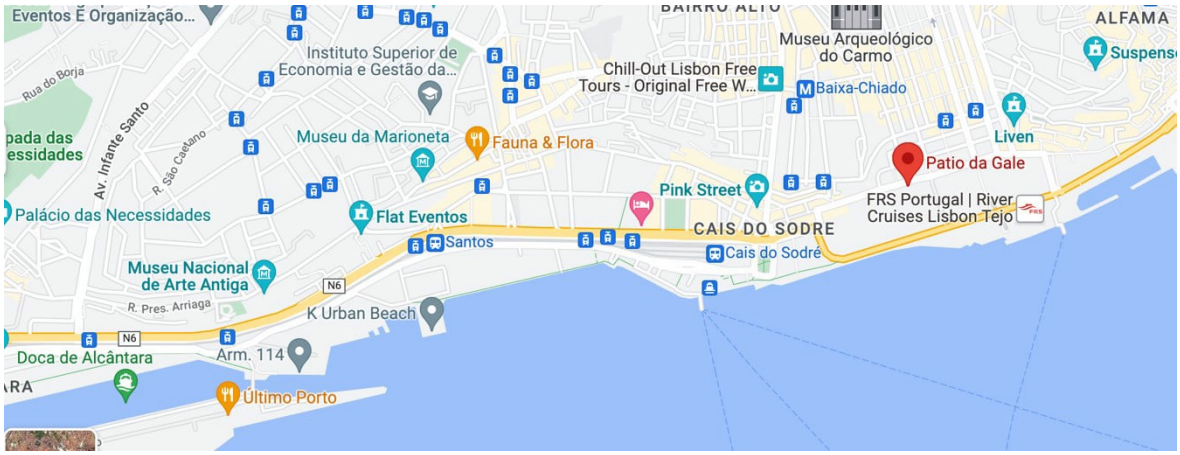
7. Presentations using Prezi must be delivered at least 3 h before the session and should be delivered in a portable format. For more details, please follow the link: https://support.prezi.com/hc/en-us/articles/360003478454-Presenting-and-viewing-a-downloaded-presentation-portable-presentation

8. Specify file name as "first-name_last-name_conference-name", e.g., "Joaquim_Faria_8ECC.ppt";

9. HDD and USB-Memory (Stick) are supported data media for downloading presentations.

CONGRESS DINNER

The Congress Dinner will take place on the evening of **Wednesday 31 August** at the **Pátio da Galé** (casadomarques.pt/patio-da-gale) **at 20h00**. The conference dinner venue is easily reachable from the hotels or the Lisbon Congress Centre. Directions will be provided during the congress, and the staff will be glad to help the participants. To attend the Congress Diner, you must have pre-purchased your attendance.

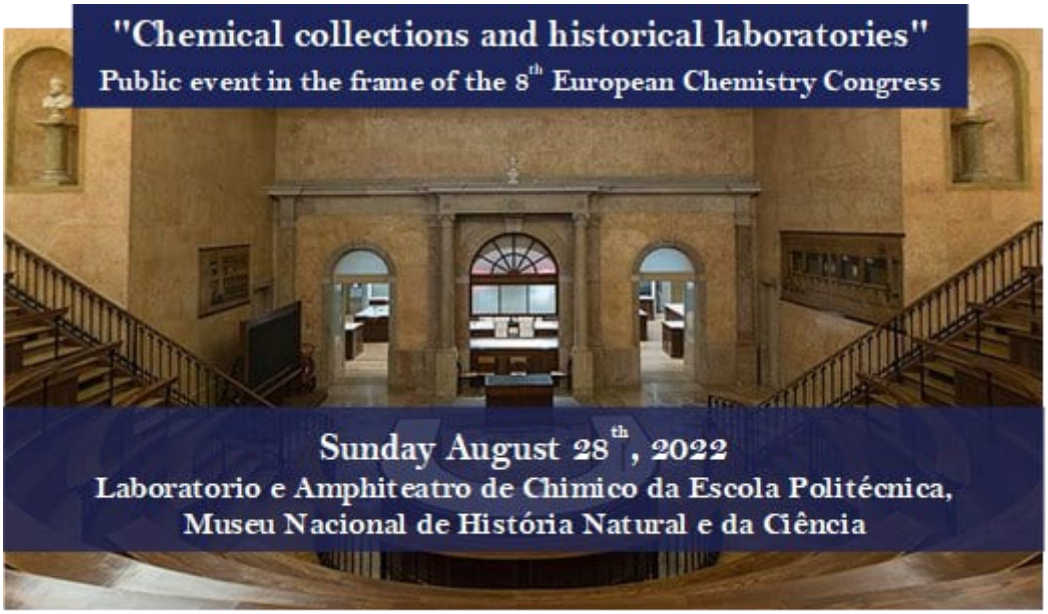


Pátio da Galé, inaugurated in 2011, **is located in the west wing of Terreiro do Paço**, where, at the time of the earthquake of 1755, the Royal Palace and the House of India were located.

PARALLEL PROGRAMME

Chemical Collections and Historical Laboratories

Sunday, August 28th, 2022



14h00 **Judite Alves**, deputy director (Museum of Natural History and Science)
Welcome

14h05 **Brigitte Van Tiggelen** (Science History Institute)
"EuChemS Historical Landmarks: chemists and their past"

Collections of chemical instruments and artefacts

14h15 **Slađana Savić** (University of Belgrade)
"The chemical collection of the University of Belgrade"

14h25 **Isabel Malaquias** (University of Aveiro)
"Collections of didactic instruments from Portuguese secondary schools"

14h35 **Duccio Tatini** and **Pierandrea Lo Nostro** (University of Florence/*Substantia*)
"Ugo Schiff collection at the University of Florence and an Italian initiative for chemical collections"

14h45 Discussion

Historical laboratories and sites of chemistry

14h55 **Gilberto Pereira** (Science Museum of the University of Coimbra)
"The historical laboratory of Coimbra: 250 years of History"

15h05 **Yoshiyuki Kikuchi** (Aichi Prefectural University)
"Historical Chemical Theaters and Laboratories in Aichi and Kumamoto Prefectures, Japan"

15h15 **Marisa Monteiro** (Natural History and Science Museum of the University of Porto)
"An historical chemistry laboratory at the University of Porto"

15h25 Discussion

Visit

15h35 **Maria do Carmo Elvas** (Museum of Natural History and Science)
"Laboratorio e Amphiteatro Chimico – introduction to the visit"

15h45 Visit and free time

All ECC8 attendees are welcome!

Register by writing to vantiggelen@memosciences.be

Getting there

Rua da Escola Politécnica 56/58, 1250-102 Lisboa

Bus from/to the Congress Center: 727 stop at Largo do Rato (300 m from Museum), 25/30 min

Other public transportation connections to the Museum:

- Bus 58, 773 stop and tramcar route 24 in front of the Museum
- Bus 92 and 790 stop at Príncipe Real (200 m from the Museum)
- Tube: Rato Station (Yellow Line)

During the ECC8 you have free access to the Museum with your conference badge

Kindly made possible by

Chemistry Europe Symposium

Monday, August 29th, 2022

Chair: Francesca Rita Novara (ChemistryOpen)

9h15-9h30 **Haymo Ross**
"Chemistry Europe"

9h30-10h00 **Anat Milo** (Department of Chemistry, Ben-Gurion University of the Negev, Israel)
"Learning from nature the hard way: Secondary-Sphere Modification in Organocatalysis"

10h00-10h30 **Ramón Martinez Mañez** (School of Industrial Engineering, Universitat Politècnica de Valencia, Spain)
"Gated materials for drug delivery and biomedical applications"

Chair: Jonathan Faiz (ChemPlusChem)

11h00-11h30 **Celia Fonseca-Guerra** (Department of Theoretical Chemistry, Vrije Universiteit Amsterdam, The Netherlands)
"Discovering in silico the uniqueness of hydrogen bonding"

11h30-12h00 **Francesco Ricci** (Chemistry Department, University of Rome, Italy)
"Reorganization of self-assembled DNA-based polymers in higher ordered structures"

12h00-12h30 ChemistryViews - **Javier García Martínez** (President of IUPAC)
"Chemistry Entrepreneurship: Transforming Chemistry Discoveries into Chemistry Solutions"

EuChemS Program

Tuesday, August 30th, 2022 | 09h15-10h30

Chemists' contributions to the global approach for tackling pollution

In this panel discussion, we will discuss how can chemistry contribute to Sustainable Development Goals.

On 2 March 2022, the 5th UN Environment Assembly concluded with 14 resolutions to strengthen actions for nature to achieve the Sustainable Development Goals. Most of them require contributions from Chemistry community, especially:

- Resolution L13: End Plastic Pollution – by developing a new legally binding instrument
- Resolution L14: Science Policy Panel to support the sound management of chemicals and waste to prevent pollution

This moderated panel discussion, which is one of many activities of EuChemS on topics of global concern to which science shall proactively contribute, focuses on the L14 resolution.

The session will feature prestigious panelists from the international chemistry community, including representatives from the Royal Society of Chemistry (RSC), the American Chemical Society (ASC), the German Chemical Society (GDCh), and last, but not least, the European Chemical Society (EuChemS):

Moderator: Camilla Alexander-White (RSC, Lead Policy Advisor)

Panelists:

- **Nineta Hrastelj** (EuChemS, Secretary-General)
- **Floris Rutjes** (EuChemS, President)
- **Carla Seidel** (GDCh, Senior Past-President)
- **Tom Welton** (RSC, President)
- **Angela Wilson**, (ACS, President)

Tuesday, August 30th, 2022 | 10h30-12h00

Culture and Policy in Science

In this session, we invite the scientific community to take a step back, and indulge in a different perspective on natural sciences, and the people who work with them.

Every community has its own habits, language, behaviour, – its own culture – and the scientific community is no exception. But no community exists in a vacuum. The products of the scientific community will spread beyond its borders. Innovation is adopted by the public, science will influence policy, and the human beings from other communities will be informed by and engage with scientists.

Our speakers, coming from anthropology and political sciences backgrounds, will use the tools of social sciences to introduce the unique oddities of the culture of science and its community, and demonstrate how policymaking and the scientific process works together.

While some of the discussed topics may invite you to look at the scientific process with a certain sense of irony, this is not to criticize or diminish the importance of natural science, rather, to help cross-disciplinary understanding, and to build bridges between communities.

Moderator: Nineta Hrastelj (EuChemS, Secretary-General)

Panelists:

- **Marton Kottmayer** (Science Communication and Policy Officer)
- **Bruno Vilela** (Public Affairs Consultant)

OutReach ACS Chemistry for Life

Tuesday, August 30th, 2022 | 16h00-17h45

Plan Effective Interactive Chemistry Experiences for the Public

Many chemists communicate chemistry's value through science outreach and interactive chemistry events. Research demonstrates that these events and similar experiences can increase positive participant attitudes towards chemistry. Using this research, we present practical guidance in how to format, select content, and facilitate effective interactive chemistry activities. Basic information will be provided about various developmental levels to help you reach participants of different ages, whether within a school or at a standalone event.

This course is designed for both new and experienced outreach event organizers and other engaged volunteers who would like to engage the public in learning and doing chemistry.

ACS/EuChemS Industry Kickstarter Workshop

The **Industry Kickstarter Workshop** is a three-part interactive career development workshop designed to teach graduate students and postdoctoral scholars about different industry career options that span from working for large to small organizations. This workshop will prepare them for the industry job application process and touch on how to start their own business. During this workshop participants will receive the necessary knowledge and tools that would otherwise require weeks of individual effort to obtain.

The interactive workshop includes:

Monday, August 29th, 2022 | 14h00-15h30

Part 1: How to Develop a Satisfying Career?

A key aspect to finding a satisfying career path is to be intentional and informed during the decision-making process. Attendees will learn how to use the individual development plan framework to examine the intersection of core skills, values and opportunities and use it to make informed career choices.

Wednesday, August 31st, 2022 | 09h15-10h30

Part 2: Is an Industry Career a Good Fit for You?

This section addresses this by providing an overview of different careers in industry and current industry trends, as well as resources for participants to determine if a career in industry would be a satisfying career path.

Wednesday, August 31st, 2022 | 11h00-12h30

Part 3: How to Successfully Transition into a Career in Industry?

Transitioning from academia into industry requires proficiency in a wide range of professional skills. In this section, participants will learn how to leverage connection building, effective communication and leadership in the academic to industry transition. Additionally, a 45-minute panel with chemists who have recently transitioned into different industry roles, will provide first-hand and current experience on the transition to industry positions.

EYCN Program

Monday, August 29th, 2022

Bonding for Impact | Chair: Antonio M. Rodríguez García (EYCN)

09h15-09h35 **Maximilian Menche** (EYCN)

09h35-09h55 **Nineta Hrastelj** (EuChemS)

09h55-10h15 **Javier Garcia** (IUPAC)

10h15-10h30 **João Borges** (IYCN)

10h30-10h55 "CR awards" - OPEN DISCUSSION

Science Policy in Europe: Open Science | Chair: Maximilian Menche (EYCN)

11h00-11h15 **Floris Rutjes** (EuChemS)

11h15-11h30 **Alina-Maria Tomoiaga** (ERC)

11h30-11h45 **Laura Fisher** (RSC)

11h45-12h00 **Wolfram Koch** (GDCh)

12h00-12h30 OPEN DISCUSSION

Assessing CV: Academia vs Industry | Chair: Alice Soldà (EYCN/DB) / Federico Bella (POLITO)

14h00-14h20 **Federico Bella** (POLITO)
"Academic CV: what to do (and not do)"

14h20-14h30 **Alice Soldá** (EYCN/DB)
"How to convert an academic CV for industry positions"

14h30-15h00 Company Challenge presentations
Amorim, Symeres and Dynamic Biosensors

15h00-15h30 Panel Discussion with all the Speakers

Tuesday, August 30th, 2022

EYCA Competition

09h15-12h30 EYCA Competition
PhD students (6 x 10 min each)

09h15-10h30 EYCA Competition
Postdoctoral fellow (6 x 15min each)

Diversity and Gender balance | Chair: Claudia Bonfio (EYCN)

14h00-14h30 **Jan Mehlich** (EuChemS), **Ale Palermo** (RSC), **Pilar Goya** (EuChemS), **Marta Da Pian** (SCI), and **Marie Perrin** (ETH Zürich)

Small address from Speakers

14h30-15h30 OPEN DISCUSSION

Wednesday, August 31st, 2022

MSCA Training Workshop | Chair: Liva Dzene (EYCN)

09h15-09h40: **David Marçal** (MSCA-NCP Portugal)

09h40-10h00: Reviewing MSCA and Fellows (Marco Carlotti, etc…)

10h00-10h30: OPEN DISCUSSION

ERC Training Workshop | Chair: Alina Maria TOMOIAGA (ECC)

11h00-11h30 **Alina-Maria Tomoiaga + ERC grantees**

11h30-12h30 OPEN DISCUSSION

Science Communication | Chair: Fernando Gomollón-Bel (Agata Communications - Cambridge, UK)

14h00-14h10 Introduction: **Fernando Gomollón-Bel**

14h10-14h30 Science outreach: **Laura Howes** (C&Eng Mag)

14h30-14h50 Science journalism: **Barbara Pinho**

14h50-15h10 Science divulgation: **Carmen Bretón** (Vaya Elementos, UR)

15h10-15h30 PANEL CLOSURE & DISCUSSION

Thursday, September 1st, 2022

Company Challenge pitches | Chair: Alice Soldà (EYCN/DB)

9h15-12h30

For the 8th edition of the **EuChemS Chemistry Congress**, the main goal of the **European Young Chemists' Network (EYCN)**, the early career division of the European Chemical Society (EuChemS) is to strengthen the collaboration with the chemical Industries, and enhance the interactivity with companies. The EYCN is organizing a **Company challenge for students**, as well as **early-stage researchers** to train them and highlight the importance of teamwork, creativity, innovation, communication, resilience and problem solving, while also sharing ideas and fostering fruitful collaborations and discussions.

For the 'Company challenge', **3 companies** (**Amorim Cork, Symeres and Dynamic Biosensors**) will propose one challenge or problem to be solved by the young attendees. The presentation of the companies and of the challenge will take place during the EYCN CV session on August 29th (14h00-15h30). The participants can participate as a team or single person, and they will be supported by one (or more) person (people) from the company that proposed the challenge during the entire congress. Suggested meeting point: every day at the coffee break 15h30-16h00. However, the participants of the challenge are highly encouraged to work during the whole week according to their own schedule, for the development and validation of their ideas through hypothesis and creation, where possible, of a prototype. Once they have found a good solution for the challenge, they have to create a pitch (TEDx format - video, demonstrator, or presentation) that must be presented (5 min max each) in front of a committee on September 1st from 9h00 to 12h00. The committee will announce the winner of each challenge and give the Industry prizes.

Companies:

1. **Amorim Cork** has been the world leading company for 150 years dedicated to the production of cork stoppers for still wines, sparkling wines, and spirits, producing 5.8 billion corks annually. Amorim Cork Research provides R&D services for the Amorim Group towards more natural and sustainable solutions for the wine industry and all applications involving cork composites.

2. **Symeres** is the leading mid-sized European Contract Research Organization for your drug discovery and development needs. With over 600 scientists at six locations, we offer best-in-class solutions for drug discovery and drug development for small molecules and beyond. Our services span from early-stage hit finding all the way to the delivery of your early clinical drug substance API. We blend a deep scientific knowledge base with creativity to deliver the quality results your project needs. We Make Molecules Matter. Together.

3. **Dynamic Biosensors** is a provider of instruments, consumables, and services in the field of analytical systems for the characterization of biomolecules and molecular interactions. The company commercializes switch SENSE®, a groundbreaking platform technology for the analysis of biomolecules with applications in R&D and drug development.

SCIENTIFIC PROGRAMME

	Sunday, 28 August
14h-	**Registration - Congress Center** **Public event "Chemical collections and historical laboratories"**
17.30-18.00h	**Auditorium I**
	Opening Ceremony
	Chair: Floris Rutjes, EuChemS President
18.00-18.40h	PL - 1: Michele Parrinello (EuChemS Gold Medal 2020)
18.40-19.20h	PL - 2: Dame Carol Robinson (EuChemS Gold Medal 2022)
19.30-21.00h	Welcome Reception
	Monday, 29 August
08.30-09.10h	**Auditorium I**
	Chair: Artur Silva, President of SPQ, University of Aveiro, Portugal PL - 3: Lutz Ackermann, Institute for Organic and Biomolecular Chemistry, Georg-August-University Göttingen, Germany

	Monday, 29 August								
08.30-09.10h	**Auditorium I**								
	Chair: Artur Silva, President of SPQ, University of Aveiro, Portugal PL - 3: Lutz Ackermann, Institute for Organic and Biomolecular Chemistry, Georg-August-University Göttingen, Germany								
	Auditorium VII	**Room 5A+5B**	**Auditorium II**	**Room 3A+3B**	**Auditorium VIII**	**Auditorium I**	**Auditorium VI**	**Room 5C**	**Room 3C**
	Theme A	Theme B	Theme C	Theme D	Theme E	Theme F	Theme G	EYCN	Other
09.15-10.30h	Chair: Fabio Juliá, ICIQ, Tarragona, Spain	Chair: Reiner Anwander, Eberhard Karls Universität Tübingen, Germany	Chair: Marina Rubini, University College Dublin, Ireland	Chair: M. Lucia Curri, University of Bari "A. Moro" and CNR IPCF, Bari, Italy	Chair: Holger Stephan, Helmholtz-Zentrum Dresden-Rossendorf, Germany; and Avi Schröder, Technion Israel Institute of Technology, Israel	Chair: John F. Bower, University of Liverpool, UK	Chair: Roberta D'Agata, University of Catania, Italy	Chair: Antonio M. Rodríguez García (EYCN)	Chair: Francesca Rita Novara, ChemistryOpen
	A1-New Synthetic Methodologies in Organic Chemistry II.A1.1; 30 min OC.A1.1-OC.A1.3 15 min x 3	B1-Organometallic chemistry II.B1.1 - 30 min OC.B1.1-OC.B1.3 15 min x 3	C1-Chemical Biology II.C1.1 - 30 min OC.C1.1-OC.C1.3 15 min x 3	D2-Nanomaterials and Nanostructures II.D2.1 - 30 min OC.D2.1-OC.D2.3 15 min x 3	E1-Drug Design and Discovery II.E1.1 - 30 min OC.E1.1-OE.C1.3 15 min x 3	F1-Organo and Metal Homogeneous Catalysis II.F1.1 - 30 min OC.F1.1-OF.F1.3 15 min x 3	G1-New Developments and Methods II.G1.1 - 30 min OC.G1.1-OG.C1.3 15 min x 3	Bonding for Impact	Chemistry Europe Symposium 15 + 2 x 30 min
10.30-11.00h	Coffee break								
11.00-12.30h	Chair: Jiwoong Lee, University of Copenhagen, Denmark	Chair: Emma Gallo, University of Milan and ICCOM-CNR, Fiorentino, Italy	Chair: Wiktor Szymanski, University of Groningen, The Netherlands	Chair: M. Lucia Curri, University of Bari "A. Moro" and CNR IPCF, Bari, Italy	Chair: Anne Duhme-Klair, University of York, UK	Chair: Jose L. Vicario, University of the Basque Country, Bilbao, Spain	Chair: Pavel Jelinek, Institute of Physics, CAS, Czech Republic	Chair: Maximilian Menche (EYCN)	Chair: Jonathan Faiz, ChemPlusChem
	A1-New Synthetic Methodologies in Organic Chemistry II.A1.2-II.A1.3 2x 30 min OC.A1.4-OC.A1.5 15 min x 2	B1-Organometallic chemistry II.B1.2-II.b1.3 2 x 30 min OC.B1.4-OC-B1.5 15 min x 2	C1-Chemical Biology II.C1.2-II.C1.3 2 x 30 min OC.C1.4-OC.C1.5 15 min x 2	D2-Nanomaterials and Nanostructures II.D2.2-II.D2.3 2 x 30 min OC.D2.4-OC.D2.5 15 min x 2	E1-Drug Design and Discovery II.E1.2-II.E1.3 2 x 30 min E3-Metals in Medicine II.E3.1 - 30 min	F1-Organo and Metal Homogeneous Catalysis II.F1.2-II.F1.3 2 x 30 min OC.F1.4-OC.F1.5 15 min x 2	G1-New Developments and Methods II.G1.2-II.G1.3 2 x 30 min OC.G1.4-OC.G1.5 15 min x 2	Science Policy in Europe: Open Science	Chemistry Europe Symposium 3 x 30 min
12.30-14.00h	**Lunch** **Auditorium I** **Chair:** Artur Silva, President of SPQ, University of Aveiro, Portugal **Masterclass Chemistry in Space:** Daniel Glavin, Astrobiology Analytical Laboratory at NASA, USA								

	Monday, 29 August								
	Auditorium VII	**Room 5A+5B**	**Auditorium II**	**Room 3A+3B**	**Auditorium VIII**	**Auditorium I**	**Auditorium VI**	**Room 5C**	**Room 3C**
	Theme A	Theme B	Theme C	Theme D	Theme E	Theme F	Theme G	EYCN	Other
14.00-15.30h	Chair: Martin Kotora, Charles University, Praha, Czech Republic A1-New Synthetic Methodologies in Organic Chemistry OC.A1.6-OC.A1.11 15 min x 6	Chair: Cláudia Silva, FEUP, University of Porto F1-Organo and Metal Homogeneous Catalysis OC.F1.6-OC.F1.11 15 min x 6	Chair: Erica Del Grosso, University of Rome Tor Vergata, C3-Biomolecules: Synthesis and applications OC.C3.1-OC.C3.6 15 min x 6	Chair: Silvia Gross, University of Padova, Italy D5-Nanoparticles: synthesis and applications OC.D5.1-OC.D5.6 15 min x 6	Chair: Gilles Gasser, PSL University, CNRS, Paris, France E1-Drug Design and Discovery OC.E1.4-OC.E1.8 15 min x 5	Chair: Joaquim Faria, FEUP, University of Porto F2-Heterogeneous and Supported Catalysis OC.F2.1-OC.F2.6 15 min x 6	Chair: Boris Mizaikoff, Ulm University, Germany G1-New Developments and Methods OC.G1.6-OC.G1.11 15 min x 6	Chair: Alice Soldà (EYCN/DB) / Federico Bella (POLITO) Assessing CV: Academia vs Industry	EuChemS / ACS EuChemS/ACS Industry Kickstarter workshop Part 1: How to Develop a Satisfying Career?
15.30-16.00h	Coffee break								
	Auditorium I								
16.00-17.45h	**Chair:** Johan Hofkens, KU Leuven, Belgium Imaging II.Imag.1-II.Imag.2 - 2 x 30 min OC.Imag.1-OC.Imag.3 - 15 min x 3								
17.45-18.25h	**Chair**: Katharina M. Fromm, University of Fribourg, Switzerland PL - 4: Cristina Nevado, University of Zurich, Zurich, Switzerland								
18.30-19.10h	ERC.1 - ERC.4								
19.15-21.00h	Poster Session 1								

	Tuesday, 30 August								
08.30-09.10h	**Auditorium I** **Chair**: João Rocha, University of Aveiro, Portugal PL - 5: Clément Sanchez, Collège de France and Institute of Advanced Studies of Strasbourg, France								
	Auditorium VII	**Room 5A+5B**	**Auditorium II**	**Room 3A+3B**	**Auditorium VIII**	**Auditorium I**	**Auditorium VI**	**Room 5C**	**Room 3C**
	Theme A	Theme B	Theme C	Theme D	Theme E	Theme F	Theme G	EYCN	Other
09.15-10.30h	Chair: Norbert Krause, Dortmund University of Technology, Germany	Chair: Carlos Salgueiro, FCT-NOVA, New University of Lisbon; Portugal	Chair: Manuel Aureliano, Universidade do Algarve, Faro, Portugal	Chair: Carlos Lodeiro, FTC-NOVA, NOVA University Lisbon, Portugal	Chair: Takashi Hayashita, Sophia University, Tokyo, Japan	Chair: Bert F Sels, KU Leuven, Belgium	Chair: David Robinson, Nottingham Trent University, UK	Chair: Angela Agostiano	Moderator: Camilla Alexander-White, RSC, Lead Policy Advisor
	A2-Green chemistry II.A2.1 - 30 min OC.A2.1-OC.A2.3 15 min x 3	B3-Molecular Magnets II.B3.1 - 30 min OC.B3.1-OC.B3.3 15 min x 3	C3-Biomolecules: Synthesis and applications II.C3.1 - 30 min OC.C3.7-OC.C3.9 15 min x 3	D4-Organic-Inorganic Hybrids II.D4.1 - 30 min OC.D4.1-OC.D4.3 15 min x 3	E6-Molecular Sensors II.E6.1 - 30 min OC.E6.1-OC.E6.3 15 min x 3	F2-Heterogeneous and Supported Catalysis II.F2.1 - 30 min OC.F2.7-OC.F2.9 15 min x 3	G4-Surface Processes and Analysis II.G4.1 - 30 min OC.G4.1-OC.G4.3 15 min x 3	EYCA Competition	Chemists' contributions to the global approach for tackling pollution Nineta Hrastelj, EuChemS, Secretary-General Floris Rutjes, EuChemS, President Carla Seidel, GDCh, Senior Past-President Tom Welton, RSC, President Angela Wilson, ACS, President
10.30-11.00h	Coffee break								
11.00-12.30h	Chair: Anat Milo, Ben-Gurion University of the Negev, Israel	Chair: Richard Winpenny, The University of Manchester, UK	Chair Boris Vauzeilles, Université Paris-Saclay, Gif-sur-Yvette, France	Chair: Carlos Lodeiro, FTC-NOVA, NOVA University Lisbon, Portugal	Chair: Veronica Dodero, Bielefeld University, Germany	Chair: Michael Schnürch, TU Wien, Vienna,Austria	Chair: Bernhard Lendl, TU Wein, Austria	Chair: Angela Agostiano	Chair: Nineta Hrastelj, EuChemS, Secretary-General
	A3-Reaction mechanisms II.A3.1-II.A3.2 2x 30 min OC.A3.1-OC.A3.2 15 min x 2	B2-Multimetallic systems II.B2.1-II.B2.2 2x 30 min OC.B2.1-OC.B2.2 15 min x 2	C3-Biomolecules: Synthesis and applications II.C3.2-II.C3.3 2x 30 min OC.C3.10-OC.C3.11 15 min x 2	D4-Organic-Inorganic Hybrids II.D4.2-II.D4.3 2x 30 min OC.D4.4-OC.D4.5 15 min x 2	E2-Drug Delivery II.E2.1-II.E2.2 2x 30 min OC.E2.1-OC.E2.2 15 min x 2	F4-Photo and Electrocatalysis II.F4.1-II.F4.3 3 x 30 min OC.F4.1 - 15 min	G4-Surface Processes and Analysis II.G4.2-II.G4.3 2 x 30 min OC.G4.4-OC.G4.5 15 min x 2	EYCA Competition	Culture and Policy In Science Marton Kottmayer, Science Communication and Policy Officer and Bruno Vilela, Public Affairs Consultant
12.30-14.00h	**Lunch** **Auditorium I** **Chair**: Luisa De Cola, Università degli Studi di Milano, Italy **Put Some Movie Wow! in Your Chemistry Classroom**, Mark Griep, University of Nebraska–Lincoln, Lincoln, USA								**Reaxys Workshop**: Predictive Retrosynthesis in the Classroom

	Tuesday, 30 August								
	Auditorium VII	**Room 5A+5B**	**Auditorium II**	**Room 3A+3B**	**Auditorium VIII**	**Auditorium I**	**Auditorium VI**	**Room 5C**	**Room 3C**
	Theme A	Theme B	Theme C	Theme D	Theme E	Theme F	Theme G	EYCN	Other
	Chair: Pedro M. P. Gois, Universidade de Lisboa, Portugal	Chair: Bert F Sels, KU Leuven, Belgium	Chair: Cristina M. Cordas, FCT NOVA, Universidade NOVA de Lisboa, Portugal	Chair: Silvia Gross, University of Padova, Italy	Chair: Jeremy Luterbacher, École Polytechnique Fédérale de Lausanne (EPFL), Switzerland	Chair: Sami Lakhdar, CNRS/Université Paul Sabatier, Toulouse, France	Chair: Tia Keyes, Dublin City University, Ireland	Chair: Claudia Bonfio (EYCN)	Chair: Adelino Galvão, IST, University of Lisbon, Portugal
14.00-15.30h	A3-Reaction mechanisms OC.A3.3-OC.A3.8 15 min x 6	F1-Organo and Metal Homogeneous Catalysis OC.F1.12-OC.F1.17 15 min x 6	C3-Biomolecules: Synthesis and applications OC.C3.12-OC.C3.17 15 min x 6	D5-Nanoparticles: synthesis and applications OC.D5.7-OC.D5.12 15 min x 6	F2-Heterogeneous and Supported Catalysis OC.F2.10-OC.F2.15 15 min x 6	F4-Photo and Electrocatalysis OC.F4.2-OC.F4.8 15 min x 7	G5-Applied Physical Chemistry OC.G5.1-OC.G5.6 15 min x 6	Diversity and Gender balance	OTS2.3 – Chemistry and Heritage: preserving and sharing II.OTS2.3.1-II.OTS2.3.1 2 x 30 min OC.OTS2.3.1-OC.OTS2.3.2 15 min x 2
15.30-16.00h	Coffee break								
	Auditorium I								
16.00-17.45h	**Chair:** Luis C. Branco, Universidade Nova de Lisboa, Portugal; and Wojciech Bury, University of Wroclaw, Poland Energy, Environment and Sustainability II.EES.1-EES.2 - 2 x 30 min OC.EES.1-OC.EES.3 - 15 min x 3								OutReach ACS Chemistry for Life Plan Effective Interactive Chemistry Experiences for the Public
17.45-18.25h	**Chair**: Luisa De Cola, Università degli Studi di Milano, Italy PL - 6: João Rocha, University of Aveiro, CICECO-Aveiro Institute of Materials, Department of Chemistry, Aveiro, Portugal								
18.30-19.10h	ERC.5-ERC.8								
19.15-21.00h	Poster Session 2								

	Wednesday, 31 August								
	Auditorium I								
08.30-09.10h	**Chair**: Ana Isabel Ricardo, NOVA-FCT, NOVA University of Lisbon, Portugal PL - 7: Hanadi Sleiman, Department of Chemistry, McGill University, Montreal, Canada								
	Auditorium VII	**Room 5A+5B**	**Auditorium II**	**Room 3A+3B**	**Auditorium VIII**	**Auditorium I**	**Auditorium VI**	**Room 5C**	**Room 3C**
	Theme A	Theme B	Theme C	Theme D	Theme E	Theme F	Theme G	EYCN	Other
09.15-10.30h	Chair: Carlos Afonso, University of Lisbon, Portugal	Chair: Michael Zaworotko, University of Limerick, Ireland	Chair: Jalila Simaan, CNRS, Aix Marseille Université, France	Chair: Ana Isabel Ricardo, NOVA-FCT, NOVA University of Lisbon, Portugal	Chair: Christoph Hagemeyer, Monash University, Victoria, Australia	Chair: David Écija, IMDEA Nanoscience, Madrid, Spain	Chair: Luca Prodi, Università di Bologna, Italy	Chair: Liva Dzene (EYCN)	EuChemS / ACS
	A2-Green chemistry II.A2.2 - 30 min OC.A2.4-OC.A2.6 15 min x 3	B5-Porous Materials II.B5.1 - 30 min OC.B5.1-OC.B5.3 15 min x 3	C4-Bioinorganic Chemistry II.C4.1 - 30 min OC.C4.1-OC.C4.3 15 min x 3	D1-Assemblies, Aggregates and Interfaces II.D1.2-II.D1.3 2 x 30 min OC.D1.4-OC.D1.5 15 min x 2	E4-Biopolymers, Hydrogels and Processing II.E4.1 - 30 min OC.E4.1-OC.E4.3 15 min x 3	OTS1.1-Carbon-based Materials II.OTS1.1 - 30 min OC.OTS1.1.1-OC.OTS1.1.3 15 min x 3	G3-Electrochemistry II.G3.1 - 30 min OC.G3.1-OC.G3.3 15 min x 3	MSCA Training Workshop	EuChemS/ACS Industry Kickstarter workshop Part 2: Is an Industry Career a Good Fit for You?
10.30-11.00h	Coffee break								
11.00-12.30h	Chair: Sophie Beeren, Technical University of Denmark, Kongens Lyngby, Denmark	Chair: Christian Serre, ESPCI Paris, PSL University, France	Chair: P. Klahn, Technische Univ Braunschweig, Germany; Univ Gothenburg, Sweden	Chair: Ana Isabel Ricardo, NOVA-FCT, NOVA University of Lisbon, Portugal	Chair: Dirk-Peter Herten, University of Birmingham, UK	Chair: Diego Peña, CiQUS), Universidade de Santiago de Compostela, Spain	Chair: Ivana Nikšić-Franjić, Ruđer Bošković Inst., Zagreb, Croatia	Chair: Alina Maria TOMOIAGA (ECC)	EuChemS / ACS
	A4-Supramolecular Chemistry II.A4.1-II.A4.2 2 x 30 min OC.A4.1-OCA4.2 15 min x 2	B5-Porous Materials II.B5.2-II.B5.3 2 x 30 min OC.B5.4-OC.B5.5 15 min x 2	C2-Sensors and Diagnostic II.C2.1-II.C2.2 2 x 30 min OC.C2.1-OC.C2.2 15 min x 2	D1-Assemblies, Aggregates and Interfaces II.D1.2-II.C1.3 2 x 30 min OC.D1.4-OC.D1.5 15 min x 2	E4-Biopolymers, Hydrogels and Processing II.E4.2-II.E4.3 2 x 30 min OC.E4.4-OC.E4.5 15 min x 2	OTS1.2-Organic Electronics II.OTS1.2 - 30 min OC.OTS1.2.1-OC.OTS1.2.4 15 min x 4	G2-Light and Matters II.G2.1 - 30 min G6-Photochemistry and Photophysics II.G6.1-II.G6.2 30 min x 2	ERC Training Workshop	EuChemS/ACS Industry Kickstarter workshop Part 3: How to Successfully Transition into a Career in Industry?
12.30-14.00h	**Lunch** **Auditorium I** **Chair**: Victor Freitas, Faculty of Sciences, University of Porto, Portugal **Masterclass Chemistry in Arts** - The perfect medieval hand-writing: hands-on workshop; Maria João Melo, Marcia Vilarigues and Paula Nabais, NOVA-FCT, Nova University of Lisbon; Natércia Teixeira, Faculty of Sciences, University of Porto, Portugal; Antonio Sgamellotti, Università degli Studi di Perugia, Italy; Cristina Barrocas Dias and Ana Manhita, Universidade de Évora, Portugal								

	Wednesday, 31 August								
	Auditorium VII	**Room 5A+5B**	**Auditorium II**	**Room 3A+3B**	**Auditorium VIII**	**Auditorium I**	**Auditorium VI**	**Room 5C**	**Room 3C**
	Theme A	Theme B	Theme C	Theme D	Theme E	Theme F	Theme G	EYCN	Other
14.00-15.30h	Chair: Tibor Kudernac, University of Groningen, The Netherlands	Chair: Kasper Moth Poulsen, Chalmers Univ of Technology, Sweden	Chair: Matthew Baker, Maastricht University, Netherlands	Chair: Ana Rita C. Duarte, FCT NOVA, NOVA University of Lisbon, Portugal	Chair: Teresa Pellegrino, Istituto Italiano di Tecnologia, Genova, Italy	Chair: Joaquim Faria, FEUP, University of Porto	Chair: Alan Ryder, National University of Ireland, Galway	Chair: Fernando Gomollón-Bel (Agata Communications - Cambridge, UK)	Chair: Rachel Mamlok-Naaman, Weizmann Institute of Science, Israel
	A4-Supramolecular Chemistry OC.A4.3-OC.A4.8 15 min x 6	OTS1.3-Polymers and devices II.OTS1.3 - 30 min OC.OTS1.3.1-OC.OTS1.3.4 15 min x 4	C1-Chemical Biology OC.C1.6-OC.C1.11 15 min x 6	D1-Assemblies, Aggregates and Interfaces OC.D1.6-OC.D1.11 15 min x 6	E5-Diagnostics and Nanotherapeutics OC.E5.1-OC.E5.6 15 min x 6	F1-Organo and Metal Homogeneous Catalysis OC.F1.18-OC.F1.19 15 min x 2 F3-Bio and Biomimetic Catalysis OC.F3.1-OC.F3.3	G6-Photochemistry and Photophysics OC.G6.1-OC.G6.6 15 min x 6	Science Communication	OTS2.2 – New Tools for Learning II.OTS2.2.1-II.OTS2.2.2 2 x 30 min OC.OTS2.2.1-OC.OTS2.2.2 15 min x 2
15.30-16.00h	Coffee Break								
	Auditorium I								CAS
16.00-17.45h	Chair: Adelino Galvão, IST, University of Lisbon, Portugal Molecules in Motion II.MM.1-II.MM.2 - 2x 30 min OC.MM.1-OC.MM.3 - 15 min x 3								SciFinder-n: A World of Difference
17.45-18.25h	**Chair**: Mário Berberan e Santos, IST, Universidade de Lisboa, Portugal PL - 8: Nicola Armaroli, National Research Council – Institute for Organic Synthesis and Photoreactivity (CNR-ISOF), Bologna, Italy								
18.30-19.10h	ERC.9-ERC.12								
20.00h	Congress Dinner								

	Thursday, 1 September								
	Auditorium I								
08.30-09.10h	**Chair**: M. Fernanda Proença, Universidade do Minho, Braga, Portugal PL - 9: Nazario Martín, Dpto de Química Orgánica, Facultad de Química, Universidad Complutense, Madrid, Spain; IMDEA-Nanociencia, Madrid, Spain								
	Auditorium VII	**Room 5A+5B**	**Auditorium II**	**Room 3A+3B**	**Auditorium VIII**	**Auditorium I**	**Auditorium VI**	**Room 5C**	**Room 3C**
	Theme A	Theme B	Theme C	Theme D	Theme E	Theme F	Theme G	EYCN	Other
09.15-10.30h	Chair: Jose L. Vicario, University of the Basque Country, Bilbao, Spain	Chair: Maria del Carmen Gimenez Lopez, CiQUS, University of Santiago de Compostela, Spain	Chair: Claudia Bonfio, Institut de Science et d'Ingénierie Supramoléculaires (ISIS), Strasbourg, France	Chair: A.J. Stasyuk, Universitat de Girona, Spain; University of Warsaw, Poland	Chair: Joao Mano, University of Aveiro, Portugal	Chair: Bruno Machado, FEUP, University of Porto	Chair: Nils Metzler-Nolte, Ruhr University Bochum, Bochum, Germany	Challenges Organization	Deutsche Forschungsgemeinschaft (German Research Foundation)
	A5-Asymmetric Synthesis and natural products II.A5.1 - 30 min OC.A5.1-OC.A5.3 15 min x 3	B4-Inorganic Interfaces II.B4.1 - 30 min OC.B4.1-OC.B4.3 15 min x 3	C3-Biomolecules: Synthesis and applications OC.C3.18-OC.C3.22 15 min x 5	D3-Theory meets experiments-predicting properties of materials II.D3.1 - 30 min OC.D3.1-OC.D3.3 15 min x 3	E5-Diagnostics and Nanotherapeutics II.E5.1 - 30 min OC.E5.7-OC.D5.8 15 min x 2	F2-Heterogeneous and Supported Catalysis OC.F2.16-OC.F2.20 15 min x 5	E3-Metals in Medicine II.E3.2 - 30 min B5-Porous Materials OC.B5.6 G3-Electrochemistry OC1.G3.4 G6-Photochemistry and Photophysics OC1.G6.7 15 min x 3	Company Challenge pitches	"Research in Germany" Science Breakfast
10.30-11.00h	Coffee break								
11.00-12.30h	Chair: Patrícia Rijo, Universidade Lusófona de Humanidades e Tecnologias, Lisboa, Portugal	Chair: Steven De Feyter, KU Leuven, Department of Chemistry, Belgium	Chair: Hannes Mikula, TU Wien, Austria	Chair: A.J. Stasyuk, Universitat de Girona, Spain; University of Warsaw, Poland	Chair: Silvia Osuna, IQCC, Univ Girona, Spain	Chair: Arianna Quintavalla, Univ of Bologna, Bologna, Italy	Chair: Federico Bella, Politecnico di Torino, Italy	Challenges Organization	Chair: Silvija Markic, Ludwig-Maximilians-University Munich, Germany
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	Thursday, 1 September
	Auditorium I
14.00-15.30h	**Chair:** Floris Rutjes, EuChemS President and Hans-Peter Luehti, International Award Committee for the EuChemS Lecture Award
	PL - 10: EuChemS Lecture Award 2020 - Victor Mougel (45 min) PL - 11: EuChemS Lecture Award 2021 - Silvia Osuna (45 min)
15.30-16.30h	**Chair:** Karsten Danielmeier, GDCh President
	PL - 12 and PL - 13: 9th GDCh – Prize August-Wilhelm-von-Hofmann-Denkmünze: Paul Anastas and John C. Warner (60 min)
16.30h-...	**Chair:** Floris Rutjes, EuChemS President; Pilay Goya, EuChemS Past-President and Angela Agostiano, University of Bari, Italy
	EYCA awards + Service Awards (Antonio Lagana, Livia Sarkadi, Keinan Ehud and Jan Mehlich) Next meeting - Dublin 2024 - Pat Guiry **Closing Ceremony**

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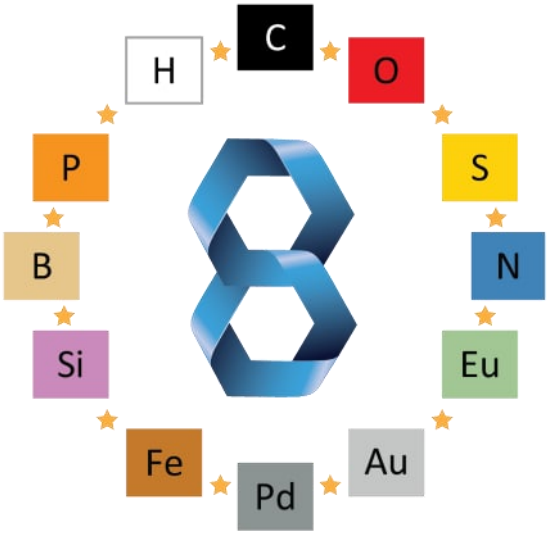

PLENARY LECTURES (PL)

Ammonia Decomposition on Lithium Imide Surfaces: a new paradigm in heterogeneous catalysis

Prof. Dr. Michele Parrinello

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The industrial production of commodity chemicals often requires extreme conditions of temperature and pressure. Yet, the catalyst remains active for long time, notwithstanding the harsh operating conditions. This challenges the static picture of catalytic process. To explain the long-term stability of industrial catalysts we invoke instead a dynamical scenario.

We illustrate this concept with a state of the art simulation of the Li2 NH catalyzed decomposition of ammonia at T = 750 K, a process has been intensively studied for its possible use in a hydrogen-based economy.

We show that, when exposed to the reactants an ionic liquid-like dynamical fluctuating steady state is set up at the Li2 NH surface. In this environment a series of reactions that eventually leads to the release of N_2 and H_2 molecules become possible.

A new phase for structural biology

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While cryo-EM has transformed our view of the structures of protein assemblies, behind the scenes gas phase structural biology has been emerging. Over a number of decades mass spectrometrists have revealed that the folding and topology of protein complexes can be retained in the gas phase, if appropriate experimental parameters are applied. These discoveries led to early compelling studies of antibody-antigen complexes, viruses, ribosomes and molecular chaperones. More recently 'snapshots' of membrane protein complexes in the gas phase have been particularly enlightening. Widely considered the most challenging of protein complexes, but yet the most important given their physiological roles, the gas phase turns out to be an excellent medium in which to interrogate hydrophobic membrane proteins. When encased in detergent micelles, or other membrane mimetics, the effects of lipids on stability, conformational change, dynamics and protein interactions are revealed. As such, mass spectrometry is informing membrane embedded efflux pumps (often implicated in antibiotic resistance mechanisms) assembly of membrane protein interfaces (primarily in solute carriers) and receptor mediated signalling pathways (typically of GPCRs). In this lecture I will trace the history of these developments using selected highlights to illustrate progress made to date. Finally, I will describe exciting future developments - soon to be realised.

Metallaelectro-Catalyzed Bond Activations

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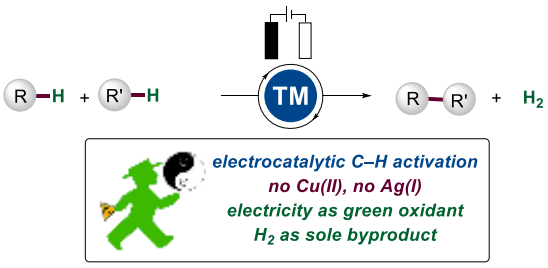
Oxidative C–H activation has emerged as an increasingly powerful tool in molecular syntheses.[1] Despite major progress towards atom and step economy, these transformations largely rely on precious metal catalysts and stoichiometric amounts of toxic metal oxidants, compromising the overall sustainability of the C–H activation strategy. In contrast, employing electrooxidation *in lieu* of reactive chemical oxidants prevents undesired waste formation through oxidant economy and offers efficient use of renewable energies from sustainable sources for chemical bond formation.[2] Inexpensive Earth-abundant 3d metal[3] cobaltaelectrocatalysis set the stage for molecular syntheses at a unique level of resource economy.[4] Our studies towards metallaelectrocatalytic C–H and C–C activation will be discussed, with a topical focus on sustainable base metals.[5]



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Activating σ and π bonds with transition metals: mechanistic insights and asymmetric variants

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Alkylidenecyclopropanes (ACPs) and cyclobutenes (CBs) are readily accessible motifs that have found widespread application in organic synthesis. A highly strained ring and a C–C double bond makes these structures especially reactive in the presence of suitable transition metal complexes. Here we will present the effect of coordinating groups in the activation of otherwise inert C-C bonds in the presence of gold salts [1,2]. On the other hand, multicomponent reactions involving alkenes have been the focus of substantial efforts in our group. Specifically, radical-mediated processes have been implemented enabling the construction of complex molecular blueprints by careful design of the corresponding alkene acceptors. Our more recent progress in this area, with special focus on newly developed asymmetric variants of these transformations, will be presented here [3-5].

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Nature Inspired Integrative Materials Chemistry

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For millions of years, high-performance natural materials have been produced using highly selected structures such as those found in magnetotactic bacteria, ferritin, the teeth of certain molluscs, crustacean shells, diatom frustules, byssus, some plants or flowers etc ....In fact, natural materials are often highly integrated intelligent hybrid systems that know how to compromise between different functions: mechanical behavior (flexibility vs. rigidity), density, controlled permeability, color, hydrophobicity ...). Integration has two positive aspects: miniaturization, which aims to house a very large number of elementary functions in a small volume, and hybridization, in particular between mineral and organic components, which enriches the whole by association of functions selected in the best of both worlds. Hybrid inorganic-organic materials can be broadly defined as synthetic materials with organic and inorganic components which are intimately mixed. They can be either homogeneous systems derived from monomers and miscible organic and inorganic components, or heterogeneous and phase-separated systems where at least one of the components' domains has a dimension ranging from a few Å to several nanometers. Hybrid phases can also be used to nanostructure or texture new inorganic nanomaterials (porous or non porous). The versatile and soft bottom-up synthetic conditions can also be bio-inspired. The tunable processing temperatures and solvents and the adjustable rheology of the colloidal state allow for the mixing of the organic and inorganic components at the nanometer scale in virtually any ratio. These features, and the advancement of organometallic and polymer chemistries and sol-gel processing, make possible a high degree of control over both composition and structure (including nanostructure) of these materials, which present tunable structure-property relationships. This, in turn, makes it possible to tailor and fine-tune properties (mechanical, optical, electronic, thermal, chemical…) in very broad ranges, and to design specific systems for applications. Hybrid materials can be processed as gels, monoliths, thin films, fibers, particles or powders or can be intermediates to design inorganic materials having complex shapes or hierarchical structures. The seemingly unlimited variety, unique structure-property control, and the compositional and shaping flexibility give these materials a high potential in sensing, membranes, catalysis, bio-catalysis, photocatalysis, nanomedicine, the tailoring of smart functional surfaces etc…. This lecture will describe some recent advances on this integrative materials chemistry that allows via a chemistry-process coupling to tailor made nanostructured and hierarchically structured functional inorganic and hybrid materials. Some of their properties will also be discussed. For more information see few recent reviews:

0. **History of Organic–Inorganic Hybrid Materials: Prehistory, Art, Science, and Advanced Applications,** M Faustini, L Nicole, E Ruiz-Hitzky, C Sanchez, *Advanced Functional Materials*, 1704158 (2018)
1. **Aerosol processing: a wind of innovation in the field of advanced heterogeneous catalysts**, DP Debecker**,** S Le Bras, C Boissière, A Chaumonnot, C Sanchez, *Chemical Society Reviews* 47 (11), 4112-4155
2. ***Optical Properties of Hybrid Organic-Inorganic Materials and their Applications,*** Parola S., Julián-López B., Carlos L. D., Sanchez C. (2016). *Advanced Functional Materials*, 26(36):6506-6544.
3. ***The core contribution of transmission electron microscopy to functional nanomaterials engineering***, Carenco S, Moldovan S., Roiban L., Florea I., Portehault D., Valle K., Belleville P., Boissière C., Rozes L., Mézailles N., Drillon M., Sanchez C., Ersen O., (2016). *Nanoscale*, 8(3):1260-1279.
4. ***"Chimie douce": A land of opportunities for the designed construction of functional inorganic and hybrid organic-inorganic nanomaterials,*** C. Sanchez, L. Rozes, F. Ribot, C. Laberty-Robert, D. Grosso, C. Sassoye, C. Boissiere and L. Nicole, *Comptes Rendus Chimie*, 13, 3, (2010)
5. **Hybrid materials science: a promised land for the integrative design of multifunctional materials,** Lionel Nicole Christel Laberty-Robert, Laurence Rozes[a] and Clément Sanchez, *Nanoscale* , 2014,**6**, 6267-6292

6. ***Mesoscopically structured nanocrystalline metal oxide thin films***, A. Carretero-Genevrier; G. L. Drisko; D. Grosso; C. Boissiere; C. Sanchez, *Nanoscale*, 6, 14025, (2014)
7. **Molecular Engineering of Functional Inorganic and Hybrid Materials,** C. *Sanchez*, C. Boissiere, S. Cassaignon, C. Chaneac, O. *Durupthy*, M. Faustini, D. Grosso, C. Laberty-Robert, L. Nicole, D. Portehault, F. Ribot, L. Rozes, and C. Sassoye. *Chemistry of Materials 2014* 26 (1), 221-238
8. **Nanoscaled Metal Borides and Phosphides: Recent Developments and Perspectives,** Sophie Carenco, David Portehault, Cédric Boissière, Nicolas Mézailles, Clément Sanchez. *Chemical Reviews* 2013 113 (10), 7981-8065
9. **Aerosol Route to Functional Nanostructured Inorganic and Hybrid Porous Materials**, Boissiere, Cedric; Grosso, David; Chaumonnot, Alexandra; C. Sanchez. *Advanced Materials***,** Volume: 23 Issue: 5 Pages: 599-623 , 2011
10. **Applications of advanced hybrid organic-inorganic nanomaterials: from laboratory to market,** Sanchez, Clement; Belleville, Philippe; Popall, Michael; et al. *Chemical society Reviews* Volume: 40 Issue: 2 Pages: 696-753, 2011
11. **Molecular and supramolecular dynamics of hybrid organic-inorganic interfaces for the rational construction of advanced hybrid nanomaterials**, Grosso, David; Ribot, Francois; Boissiere, Cedric; et al. *Chemical society Reviews* Volume: 40 Issue: 2 Pages: 829-848 2011
12. **Design and properties of functional hybrid organic-inorganic membranes for fuel cells**, Laberty-Robert, C.; Valle, K.; Pereira, F.; et al. *Chemical society Reviews* Volume: 40 Issue: 2 Pages: 961-1005 2011
13. **Titanium oxo-clusters: precursors for a Lego-like construction of nanostructured hybrid materials**, Rozes, Laurence; Sanchez, Clement *Chemical society Reviews* Volume: 40 Issue: 2 Pages: 1006-1030 2011
14. **Bio-inspired synthetic pathways and beyond: integrative chemistry**, Prouzet, Eric; Ravaine, Serge; Sanchez, Clement; et al. *New Journal of Chemistry* Volume: 32 Issue: 8 Pages: 1284-1299 2008
15. **Design, synthesis, and properties of inorganic and hybrid thin films having periodically organized nanoporosity**, Sanchez, Clement; Boissiere, Cedric; Grosso, David; et al. *Chemistry of Materials***,** Volume: 20 Issue: 3 Pages: 682-737 2008
16. **Inorganic and hybrid nanofibrous materials templated with organogelators**, Llusar, Mario; Sanchez, Clement *Chemistry of Materials* Volume: 20 Issue: 3 Pages: 782-820 2008
17. **Photonic and nanobiophotonic properties of luminescent lanthanide-doped hybrid organic- inorganic materials**, Escribano, Purificacion; Julian-Lopez, Beatriz; Planelles-Arago, Jose; et al. *Journal of Materials Chemistry* Volume: 18 Issue: 1 Pages: 23-40 2008
18. **Biomimetism and bioinspiration as tools for the design of innovative materials and systems**, Sanchez, C; Arribart, H; Giraud-Guille, MM, *Nature Materials***,** Volume: 4 Issue: 4 Pages: 277-288 2005



Bio-inspired hybrid materials synthesized via " Chimie Douce": A cornucopia where creativity of chemists can be expressed at best

The importance of being porous: silicates and organic-inorganic hybrid materials

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For decades, there has been much interest in crystalline materials with frameworks exhibiting channels and cavities ('pores') of small-molecule dimensions. Zeolites, the archetypal microporous solids, are crystalline hydrated aluminosilicates with open framework structures assembled from $[SiO_4]^{4-}$ and $[AlO_4]^{5-}$ tetrahedral units interconnected by sharing all the oxygen atoms. The frameworks' negative charge is balanced by extra-framework, exchangeable, cations. Zeolites have found real-world applications, particularly in catalysis, gas sorption and separation, and ion-exchange. An outstanding feature of zeolites is that their frameworks are based on tetrahedral (Si, Al) building units. However, microporous silicate solids built from heteropolyhedra, such as tetrahedra, pentahedra, and octahedra are also known, even if much less studied. These (so-called OPT) materials contain transition metals, *e.g.*, titanium and zirconium, or lanthanides and, in addition to the conventional zeolite properties, exhibit features, such as magnetism and light emission, enabling a range of new applications. This talk presents examples of applications of OPT materials developed in my laboratory in light emission devices [1] and in the treatment of the medical condition hyperkalemia (excess K^+ in serum), with a new drug now on the market [2,3]. New challenges, such as greener OPT synthesis routes will also be briefly addressed [4].

Metal Organic Frameworks (MOFs) are crystalline organic–inorganic hybrid materials with nanoporous frameworks built by linking polyatomic metal clusters entirely by strong covalent interactions. While zeolite-like silicates are highly (thermally and chemically) robust systems, allowing applications in relatively harsh conditions, it is very challenging to synthesise the desired architectures and to modify them post-synthesis. In contrast, MOFs operate in milder conditions and often lack robustness, but they are much more amenable to 'rational synthesis' and post-synthetic modification using the conventional methods of organic synthesis. Zeolitic materials and MOFs, thus, complement each other. In this talk I shall present some examples of my groups' research on MOFs, encompassing temperature sensing via light emission [5], anti-mosquito textile nets [6] and uranyl ion capture from waters [7].

The talk will draw to an end presenting our recent work on photoresponsive organic−inorganic hybrid molecular ferroelectrics, towards multiple-state ferroelectric memories and optical switches [8].

Acknowledgements. This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, Grants UIDB/50011/2020, UIDP/50011/2020 and LA/P/0006/2020, financed by national funds through FCT/MEC (PIDDAC).

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DNA nanostructures: Design and biological properties

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DNA nanotechnology can assemble materials on the nanoscale with exceptional predictability and programmability. In a sense, this field has reduced the self-assembly space into a simple 'language' composed of four letters (A, T, G, C). Nature, on the other hand, relies on many more supramolecular interactions or 'languages' to build its functional structures. Over the last 50 years, supramolecular chemistry has taken advantage of these interactions to assemble materials with highly diverse structures and functions.

This talk will describe our efforts to merge the field of supramolecular chemistry with DNA nanotechnology. This approach results in new motifs and functionalities that are unavailable with base-pairing alone. Starting from a minimum number of DNA components, we create 3D-DNA host structures, such as cages, nanotubes, and DNA-polymer nanostructures that are promising for targeted drug delivery. These can encapsulate and selectively release drugs and accomplish anisotropic 3D-organization. We find that they resist nuclease degradation, silence gene expression, and have a favorable in vivo distribution profile. We will also discuss the ability of small molecules to reprogram the assembly of DNA, away from Watson-Crick base-pairing into new motifs.

A complex energy transition. The big picture from a chemical perspective

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The transition from fossil fuels to renewable energy is the key tool to fight climate change and avert catastrophic effects on human civilization. The targets set by the European Union for the reduction of greenhouse emissions for 2030 and 2050 highlight the need to act very quickly. Humankind has been in energy transition for over 200 years, but previous transitions in some parts of the world (e.g., from biomass to coal in Europe) lasted about one century. Unfortunately, we do not have that much time and the whole world should get carbon neutral by 2050. An epochal energy transition to be completed in less than thirty years is a huge technological, economic and societal challenge and the next ten years will be crucial. An analysis of the many technical bottlenecks along the way will be made. The points discussed include the perspectives of electrification of final energy uses and related storage needs, the feasibility of a hydrogen economy and the availability of mineral resources to manufacture converters and accumulators of renewable energy fluxes. The global picture evidences enormous opportunities for scientific and technological advancement, particularly for the chemical sciences. But it also suggests that we have a narrow path towards a just and sustainable transition, in a world with old and new tensions, with limited resources, and already suffering climate change.

Acknowledgements. The European Commission (GA 101006839, H2020 RIA, CONDOR). CNR (PHEEL; CNR-CNRS joint lab D10-GREEN; RIPRESA; Decarbonizzazione e CCU - Capitale Naturale e Risorse per il Futuro dell'Italia) are gratefully acknowledged for financial support.

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Synthetic Chiral Molecular Nanographenes

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Chirality is an important and fascinating concept which has not been properly addressed in nanocarbons science [1]. We have previously reported the first inherently chiral bilayer nanographene with a helicene linker, both as the racemate and the M isomer [2]. By extending precedented [6]helicene starting material, we obtained an unprecedented chiral nanographene comprised of two hexa-peri-hexabenzocoronene layers fused to a [10]helicene . Furthermore, we have also described a bottom-up synthesis of structurally well-defined curved nanographenes from corannulene, affording inherent helicenes in the resulting molecular nanographene [3]. These nanographenes are appealing systems for the study of further chemical reactions including supramolecular interactions [4] and redox reactions [5]. In this presentation, the recent findings on nanographenes as well as their less known photophysical properties will be discussed.



The authors acknowledge support from the Spanish Ministry of Science and Innovation MCINN (Projects, PID2020-114653RB-I00, RED2018-102815-T, Centro de Excelencia Severo Ochoa SEV-2016-0686.

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Bio-inspired strategies across multiple scales: application to overall CO_2 reduction

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Selective electrochemical reduction of CO_2 into energy-dense organic compounds is a promising strategy for using CO_2 as a carbon source. However, efficient and selective earth abundant metal catalysts for the two reactions typically required for efficient overall CO_2 electrolysis, namely the oxygen evolution reaction (OER) and CO_2 reduction, are still scarce. We will present here an array of strategies inspired from biological systems to promote these reactions with high selectivity and efficiency. The importance of tackling these challenging reaction at multiple scale will be illustrated by a series of molecular and heterogeneous catalysts replicating enzymatic features, from their active sites including secondary features such as hydrophilic and hydrophobic domains to the overall shape of organs involved in gas trapping.[1-7]

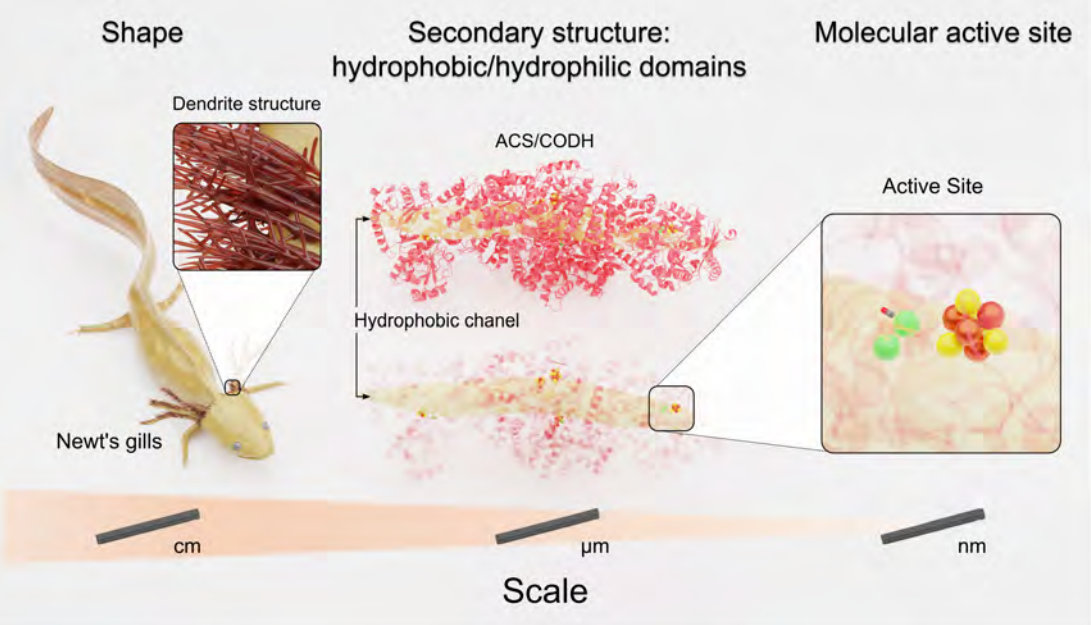

Figure 1: Multi-scale bio-inspired approach mimicking the shape, secondary structure, and active sites of living and enzymatic systems.

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CAN WE RATIONALLY DESIGN EFFICIENT ENZYMES?

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Life could not be sustained without the presence of enzymes, which are responsible for accelerating the chemical reactions in a biologically compatible timescale. Enzymes present additional advantageous features such as high specificity and selectivity, plus they operate under very mild biological conditions. Inspired by these extraordinary characteristics, many scientists wondered about the possibility of designing new enzymes for industrially-relevant targets.

Enzymes exist as an ensemble of conformational states, whose populations can be shifted by substrate binding, allosteric interactions, but also by introducing mutations to their sequence. Tuning the populations of the enzyme conformational states through mutation enables evolution towards novel activity.[1] A common feature observed in many laboratory-evolved enzymes, is the introduction of remote mutations from the catalytic center, which often have a profound effect in the enzyme catalytic activity. [2] As it happens in allosterically regulated enzymes, distal mutations regulate the enzyme activity by stabilizing pre-existing catalytically important conformational states. In this talk, the rational enzyme design approaches our group has developed based on inter-residue correlations from microsecond time-scale Molecular Dynamics (MD) simulations and enhanced sampling techniques will be presented. Our work along the years in many different enzyme systems evidences that the current challenge of distal active site prediction for enhanced function in computational enzyme design can be ultimately addressed.[3]

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Green Chemistry: The Molecular Mechanisms of Sustainability

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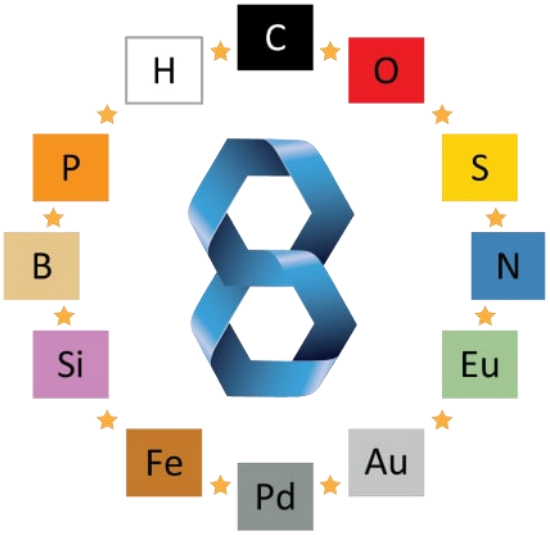
2) Teresa and H. John Heinz III Professor in the Practice of Chemistry for the Environment, School of Environment, Department of Chemistry, and the Department of Chemical & Environmental Engineering and Director of the Center for Green Chemistry and Green Engineering, Yale University, New Heaven, CT, USA

If chemistry is to genuinely advance sustainability it will begin through basic research that allows for an understanding of fundamental mechanisms and intermolecular interactions that then proceed through design, discovery, invention, innovation and scaling for positive impact. For a quarter of a century, a global community of green chemists has been recognizing that by working at the molecular level, great cascading achievements in sustainability can be made in everything that chemistry touches: food, medicine, energy, transportation, materials, and so much more. A review of the successes of green chemistry will be provided as well as a forward-looking framework for the future. This presentation will include comments from the two presenters related to current and future sustainability issues facing the chemistry enterprises and how to address them.



ERC

LECTURES (ERC)

Enzyme-mediated dynamic combinatorial chemistry with cyclodextrins

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Dynamic combinatorial chemistry (DCC) is a well-established methodology for the templated synthesis of complex molecular architectures, wherein molecular building blocks are linked together using reversible reactions to give dynamic mixtures of oligomers under thermodynamic control [1]. While a range of reversible covalent reactions have been examined for DCC, enzyme-catalysed reactions have been little explored in this context. In this talk I will present *Enzyme-Mediated Dynamic Combinatorial Chemistry*, wherein an enzyme is employed to take seemingly stable (bio)molecules and turn them into a dynamic mixture of interconverting (bio)-oligomers.

Cyclodextrins (CDs) are macrocycles formed from α-1,4-linked glucopyranose units. Cyclodextrins with 6, 7, and 8 glucose units (α- β- and γ-CD) are important hosts for the encapsulation of hydrophobic molecules and are widely utilised in the food, pharmaceutical and cosmetics industries. I will discuss how dynamic mixtures of interconverting cyclodextrins can be generated by the action of *cyclodextrin glucanotransferase* (CGTase) [2]. Templates can then be used to direct the selective synthesis of specific cyclodextrins, including modified cyclodextrins and large-ring cyclodextrins with more than 8 glucose units [3]. By using stimuli-responsive templates, we can control the outcome of this enzymatic reaction by means of light [4], pH change [5] and redox chemistry.

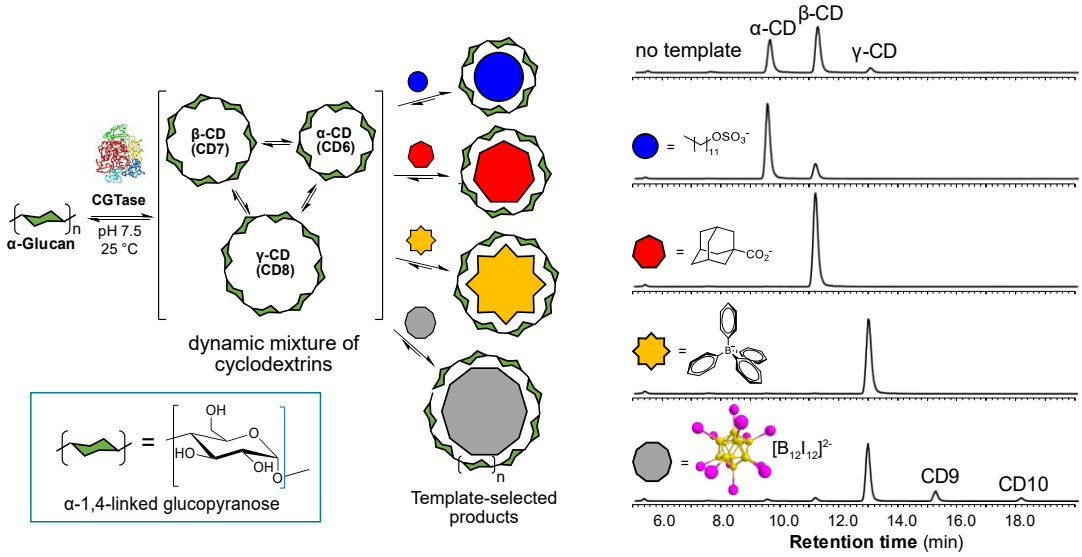

Figure 1. Cyclodextrin glucanotransferase (CGTase) converts cyclodextrins from static molecules into a dynamic mixture of interconverting cyclic and linear oligosaccharides. Templates (guest molecules) can be added to control which cyclodextrin products are formed.

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Synthetic Biology-inspired Approaches for Engineering Optical Nanosensors

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The vast expansion of available synthetic biology tools has led to explosive developments in the field of materials science. No longer confined to engineering just synthetic materials, the increased accessibility of these tools has pushed the frontier of materials science into the field of engineering biological and even living materials. This presentation highlights specific applications in optical biomedical sensing that exploit the synergistic coupling of nanobio-hybrid materials. We discuss the development of bio-conjugated single-walled carbon nanotubes (SWCNTs) for near-infrared fluorescence sensing and the application of these nanobioptic sensors for continuous measurements in living cells and organisms.

Bioinspired 3D Micro-Structures and Micro-vehicles – Design, Fabrication and Function

Larisa Florea, Colm Delaney, Alexa Ennis, Annael Sort-Montenegro, Jason Delente, Srikanth Kolagatla, Amrutha Augustine, Luisa Lavelle

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Researchers have long been inspired by the precision and sophistication of biological systems. This is reflected in recent activities surrounding the creation of synthetic analogues which can mimic specific aspects of biological behaviour, albeit often at a much simpler level of development. Recently, significant advances in additive manufacturing, such as direct laser writing (DLW) by two-photon polymerization (2PP), has enabled significant advances in the realization of bio-inspired micro-structures and surfaces due to its sub-micron resolution, and its compatibility with a wide range of materials and photoresists. This has allowed for the realization of smart actuators such as photo-responsive micro-walkers [1], magnetic micro-swimmers [2, 3], photonic structures and sensors [4], and a multitude of stimuli-responsive micro-actuators [5]. The incorporation of responsive units at the molecular level, combined with precise and sophisticated design brought by 2PP has enabled precise and controllable 4D movement and function akin to that found in nature.

My research focuses on the development of responsive materials that can switch between different states upon exposure to external stimuli. Stimulation of these materials using light, temperature, electrochemical potential, or variation of the local chemical environment, can result in changes in local charge, polarity or molecular conformation. When incorporated in polymeric networks or liquid compartments (e.g. micro-droplets), such changes can enable functions such as movement, transport, and sensing.

During this talk I will give several illustrations of stimuli-responsive behaviour, including programmed movement of droplets that can perform pre-programmed functions at specific locations, and bio-inspired 4D structures fabricated by 2PP, for movement and sensing at the micro-scale. 3D micro-fabrication by 2PP coupled with intrinsic (molecular) alignment will also be demonstrated for the realization of dual-responsive soft polymer micro-structures.

Acknowledgments: This research is supported by the European Research Council (ERC) Starting Grant (project number 802929-ChemLife), Science Foundation Ireland (SFI), and European Regional Development Fund (ERDF) under grant number 12/RC/2278_P2.

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Dynamic Covalent Chemistry with Azines

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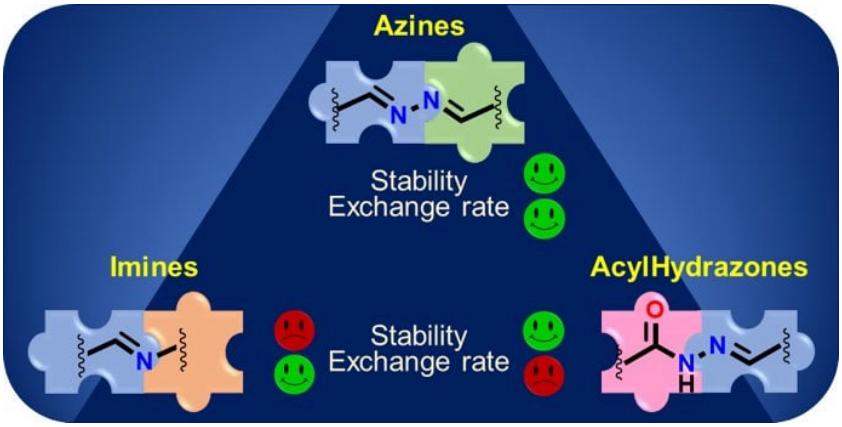
Dynamic covalent chemistry is used in many applications that require both the stability of covalent bonds and the possibility to exchange building blocks [1-3]. Acylhydrazones and imines are commonly used, despite their drawbacks: acylhydrazones are rather stable and exchange only slowly, while imines exchange much faster, but hydrolyse in the presence of water [1].

We will present azines as a dynamic covalent functional group that combines the best characteristics of imines and acylhydrazones. We show that azines are much more stable than imines and show only minimal hydrolysis in presence of water. Additionally, azines are dynamic and can exchange to form dynamic combinatorial libraries in the presence of a Brønsted or Lewis acid in various solvents. Equilibration of libraries can be obtained in less than an hour. Furthermore, the libraries can be frozen by the addition of base. This pH-dependent on/off switching of exchange enables the use of azines in orthogonal dynamic covalent chemistry. The great stability of azines and versatility of their exchange conditions open the way to many applications ranging from bioconjugation to materials chemistry.



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Towards Supramolecular Systems for Small-Molecule Diagnostics in Biofluids

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Supramolecular systems hold great promises for future use in molecular diagnostics applications due to their potentially superior robustness, cost-efficiency, and response time compared to biosensors.[1] New technologies that allow for targeted detection of small biomarkers such as metabolites are of particular interest, as their detection is often not possible with antibody-based sensors and cumbersome with chromatographic methods. However, major challenges remain to be solved before the use of synthetic supramolecular systems can become a general option for molecular diagnostics. Simply speaking, current synthetic receptors, nanosensors, and probes still display significant shortcomings both in terms of binding strength and selectivity for small molecule analytes such as amino acids, biogenic amines, or neurotransmitters.

We show here novel supramolecular systems, including macrocyclic chemosensors and hybrid-material nanozeolites (**Fig. 1**) that offer new ways to address the binding affinity- and analyte-distinction challenges.[2-4] Moreover, proof-of-concept examples for the detection of metabolites and drugs at a physiologically relevant concentration range in biofluids such as human urine, saliva, or blood are showcased. Finally, we would also like to invite the community to contribute to the open-access SupraBank repository, that makes both structures and physicochemical properties of non-covalent systems accessible and findable in a machine-readable format.[5]

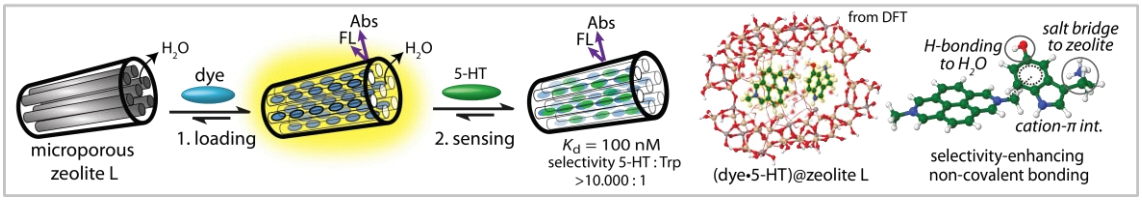

Figure 1. Showcase of a hybrid organic-inorganic nanosensor that displays protein receptor-like binding affinities and selectivity for the neurotransmitter serotonin (5-HT). Despite its simplicity, it is operational in biofluids.

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Mechanistic investigations in light-driven synthetic chemistry
Making predictable the unpredictable

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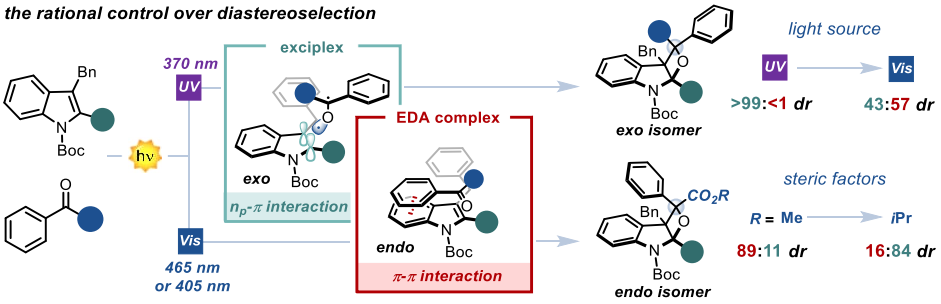
I herein report how we resolve the puzzling mechanistic scenario of light-driven [2+2] heterocycloadditions (Paternò-Büchi reactions) making use of in-depth spectroscopical investigations.[1] We have evaluated the impact of the light-source variation and the electronic and steric factors on the diastereoselectivity of the reaction between indoles and aromatic ketones.[2] Specifically, ground-state UV-Vis absorption and state-of-the-art transient absorption spectroscopy (TAS) were used to identify the elusive exciplex and an electron donor acceptor (EDA) complex, as the key intermediates in these light-driven processes.



When moving from 370 to 456 nm irradiation, the EDA complex is increasingly favored and the diastereomeric ratio dr (*endo:exo*) passes from >99:<1 up to 47:53. On the other hand, a simple Methyl-to-iPropyl switch in the starting material hampers the EDA complex formation favoring the exciplex and reversing the dr from 89:11 to 16:84. These findings were supported by DFT calculations and extended to structurally diverse ketones and indoles.[2,3]

Our study shows how light and steric parameters can be rationally exploited to gain control over the diastereoselectivity of synthetically relevant photo-reactions, opening new mechanistic avenues to previously inaccessible stereochemical variants.

[1] *Submitted manuscript*

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Squaramide-based supramolecular biomaterials

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The application of adaptive materials in areas from medicine to electronics has invigorated the development of new supramolecular materials with specific function. These polymers show great potential thanks to the non-covalent interactions that hold them together and enable their easy preparation with tailorable compositions, environmental responsiveness, self-healing upon damage, and recyclability. In the biomaterials field, their straightforward processing permits the mixing of monomers functionalized with biomolecules such as peptides, and their responsiveness to different stimuli opens the door to designer materials for applications in drug delivery or tissue engineering. In order to realize these end-stage applications, there is a need for structurally simple monomers that can be easily prepared and robustly self-assemble into polymeric architectures in the presence of complex molecular cargo. Squaramides, structurally simple ditopic hydrogen-bonding units, show tremendous potential in this regard due to their high synthetic accessibility starting from commercially available precursors and capacity to engage in strong non-covalent interactions. In this talk, I will share our exploration of the squaramide synthon as a building block for supramolecular polymers and their introduction into nanoparticles for drug delivery and hydrogel materials in 3D cell culture applications.

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Tailoring spin waves in single-layer CrSBr by strain engineering

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The recent isolation of two-dimensional (2D) magnets offers tantalizing opportunities for spintronics and magnonics at the limit of miniaturization. [1, 2] One of the key advantages of atomically-thin materials is their outstanding deformation capacity, which provides an exciting avenue to control their properties by strain engineering. Herein, we investigate the magnetic properties, magnon dispersion and spin dynamics of the air-stable 2D magnetic semiconductor CrSBr (T_C = 146 K) [3] under mechanical strain using first-principles calculations. [4] Our results provide a deep microscopic analysis of the competing interactions that stabilize the long-range ferromagnetic order and the orientation of the spin in the monolayer [5]. We showcase that the magnon dynamics of CrSBr can be modified selectively along the two main crystallographic directions as a function of applied strain, probing the potential of this quasi-1D electronic system for magnon straintronics applications. Moreover, we predict a strain-driven enhancement of T_C by ~30%, allowing the propagation of spin waves at higher temperatures.

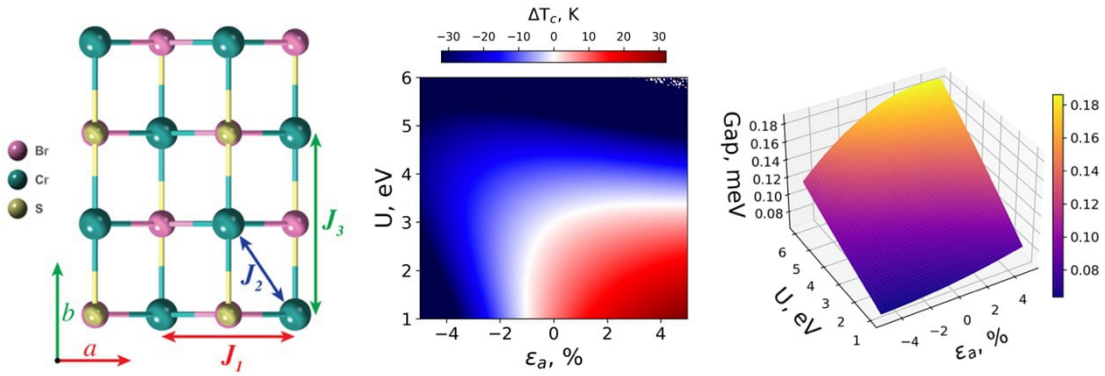

Figure 1. From left to right: (i) chemical structure indicating exchange interactions up to third neighbors, tuning of the (ii) Curie temperature and (iii) gap at Γ-point of the magnon dispersion by uniaxial strain in *a* axis and Coulomb screening.

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From molecular machines to chemical engines

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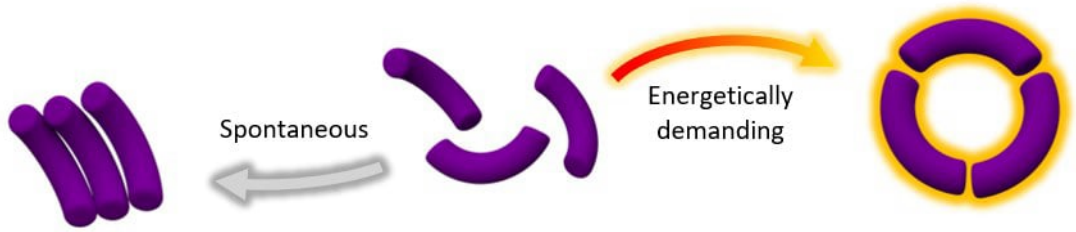
How can we exploit the operating principles of molecular machines besides motion?

Since molecular motors can perform work, mastering their operating principles may enable energy-demanding (endergonic) processes, that seemingly overcome thermodynamic barriers.[1,2]

Experimental efforts will serve as a basis to discuss how energy can be exploited to drive molecular motion and the assembly of high-energy structures, revealing common underlying principles.[3-5]

As a young principal investigator, I will take this opportunity to present how my research background is evolving into future directions. The overarching goal of my group's research is contributing to unravel how energy sources can drive non-equilibrium processes at the molecular level.



Epitomic example. Suitably engineered monomers (middle) can spontaneously assemble into ordered low-energy structures (left). This process is reasonably well controlled by chemists. On the other hand, exploiting an energy source to induce the assembly of an energy-demanding structure (right) is far from trivial. The talk will illustrate how the principles at the basis of molecular motion can be exploited to obtain high-energy assemblies and drive other non-equilibrium processes.

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From Reversible Photoinduced Electron Transfer to Energy Storage

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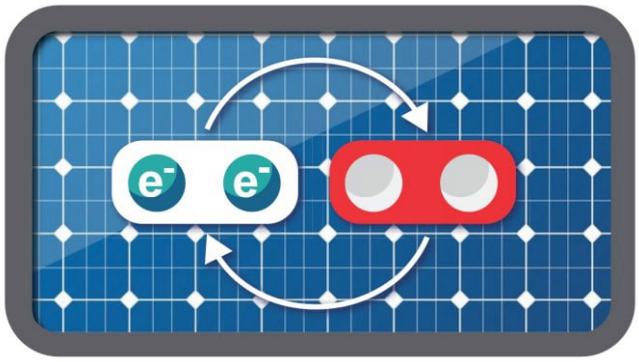
Photoinduced electron transfer is one of the essential processes in light-driven systems in Nature. Upon excitation, molecules have simultaneously higher reduction and oxidation potential, which enables to transfer electrons between partners that would otherwise not react in the ground state. The formed charge-separated state is often metastable, and a back electron transfer leads to its rapid quenching. The charge-separated state becomes thermodynamically stable if a photoinduced electron transfer is coupled with a fast follow-up process that stabilizes the formed radical ions. We study systems for reversible bidirectional photoinduced electron transfer based on redox switches [1] and triarylamine donors [2] capable of single- and double-electron redox processes. Our long-term goal is to bring this unique property to energy-storing organic materials that combine the properties of secondary batteries with organic solar cells.



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A TrojaNanoHorse to fight cancer with stimuli-responsive, biomimetic and theranostic nanoparticles

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The role of nanomedicine in the fight of cancer is increasing steadily, as cancer itself is still the second major death cause worldwide, even superior to Covid-19 related deaths. Many investigations are actually related to the role of nanomaterials in biological fluids, their drug adsorption and release capabilities, their ability to respond to intrinsic cues or external stimulations for exploiting therapeutic or imaging purposes: all these aspects are hot topics towards the development of smart theranostic nanosystems.

In this lecture, the role of nanomaterials, especially metal oxide nanocrystals, will be thoroughly discussed in terms of biological identity and strategies to improve their biocompatible and even biomimetic properties.

Zinc oxide nanocrystals are particularly interesting, having a rich plethora of possible doping with transition metals, surface modifications with chemical and biological entities, as well as intriguing properties (semiconducting, piezoelectric, and even magnetic properties). The final aim is to enable such nanocrystals being responsive to stimuli activations, such as magnetic fields, light or ultrasound irradiations and allow their use as nano-sized contrast agents for high-resolution and site-selective imaging or exploit an antitumor action against selected cancer cell. Thereafter, strategies to increase their colloidal stability, improve their biomimetism and biocompatibility towards living cells will be shown. Approaches to impart a selectivity towards cancer cells will be proposed, as site-selective targeting by means of functional peptides and antibodies. Finally stimuli-responsive treatments and drug delivery to different cancer cells will be highlighted together with their role in bioimaging.

Fundings: This work has received funding from the European Research Council (ERC) under Horizon 2020 programme (GA678151—'TROJANANOHORSE'—ERC StG; GA957563—XtraUS'—ERC PoC; GA842964-MINT-H2020-MSCA-IF-2018).

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Understanding CO_2 capture mechanisms in porous adsorbents via solid state NMR spectroscopy

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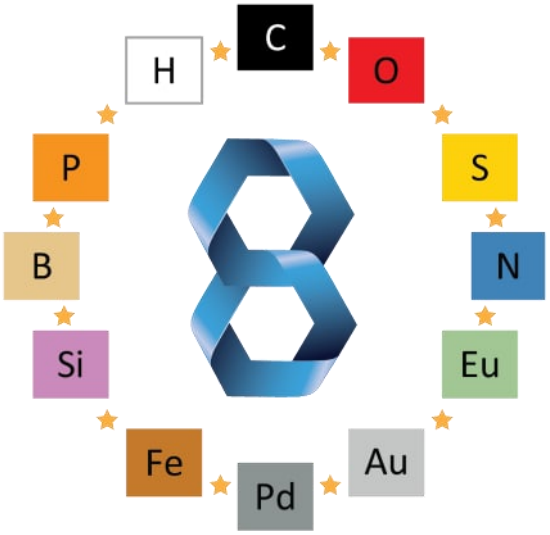
The nature of CO_2 species interacting with porous surfaces determines the gas sorption capacity/kinetics, selectivity and cyclic stability of a given adsorbent material. However, an atomic-level understanding of the CO_2 sorption process remains elusive, hindering our ability to design improved sorbents. The lack of advanced spectroscopic studies, tailored to elucidate the structure of adsorbed gas species, has also been a major bottleneck for further progresses in understanding the physical chemistry of gas-solid interfaces. This presentation highlights the most recent advances from our team, demonstrating that solid-state (ss) NMR spectroscopy is a unique site-selective technique to study the structure and the dynamics of CO_2 species adsorbed at porous CO_2-adsorbent materials. Strategies combining ssNMR and computational methods to study CO_2 speciation in porous materials are showcased.



INVITED LECTURES (IL)

Catalytic Carbyne Transfer in Organic Synthesis

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The art of organic synthesis and reaction discovery relies on logic-guided thought processes that often involve hypovalent carbon reactive species and their corresponding stabilized equivalent forms. However, not all of the possible carbon reactive intermediates and their reactivity rules have attracted the same attention by the synthetic community. This is mainly because of the perception of the lack of synthetic utility and importantly, because of the challenges associated with controlling its extreme reactivity and lack of efficient sources.

In this lecture, I will show how the catalytic generation of conceptually-novel carbyne equivalents, enabled the discovery of new carbon reactivity towards C–H and C–C bonds. The metal or photocatalytic activation of tailored carbyne sources revealed new reactivity rules at carbon that have been under-appreciated, not only in the design and discovery of new chemical reactions, but also in their use to build molecular complexity through unexplored disconnection approaches. Our catalytic carbyne transfer platform has demonstrated to be an effective and unique option in the construction of chiral centers using C–H and C–C double bonds as functional groups, and that has found applications in the late-stage functionalization of medically relevant agents. [1], [2]

European Research Council (ERC-CoG 2019, 865554), Agencia Estatal de Investigación (AEI) of the Ministerio de Ciencia e Innovación (PID2019-104101GB-I00, PDC2021-121180-I00, Severo Ochoa Excellence Accreditation 2020–2023 -CEX2019-000925-S), ICIQ Foundation, the CERCA Programme (Generalitat de Catalunya) and Marie Skłodowska-Curie Actions are gratefully acknowledged for financial support.

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Bio-inspired synthesis of spherical containers and bambusuril anion transporters

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Self-assembly of twelve pentatopic tectons, which can be linked using either digonal or trigonal connectors, represents the optimal synthetic strategy to achieve spherical objects, such as the spherical viral capsids. This process requires conditions that secure uninterrupted equilibria of binding and self-correction en route to the global energy minimum.[1] We demonstrated this concept by synthesizing a highly soluble, deca-hetero-substituted corannulene[2] that bears five terpyridine ligands.[3] Spontaneous self-assembly of twelve such tectons with 30 Cd(II) cations produces a giant icosahedral capsid as a thermodynamically stable single product in high yield. This spherical capsid has an external diameter of nearly 6 nm and shell thickness of 1 nm, in agreement with molecular modeling. NMR and liquid chromatography evidences imply that chiral self-sorting complexation generates a racemic mixture of homochiral capsids.

Synthetic anion carriers are essential for studying natural ion transporters and channels and for useful applications, such as treatment of channelopathies, supramolecular architecture, anion sensing and catalysis. Driven by the hypothesis that replacing oxygen atoms in bambusurils (BUs) with other heteroatoms could significantly modify their anion binding properties, we calculated their molecular electrostatic potential, and found a general trend of anion-affinity: S>O>NH. Later, we confirmed these predictions experimentally by synthesizing semithio- and semiaza-BUs and studying their binding and transport properties.[4,5,6] Although all analogs are excellent anion binders, semithio-bambus[6]uril is the most effective transmembrane transporter capable of polarizing lipid membranes through selective anion uniport.[7] Semiaza-BUs exhibit simultaneous accommodation of three anions, linearly positioned along the main symmetry axis.[8] These cavitands were found to be anion-specific transmembrane transporters.[9]

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Synthetic transformations under flow conditions

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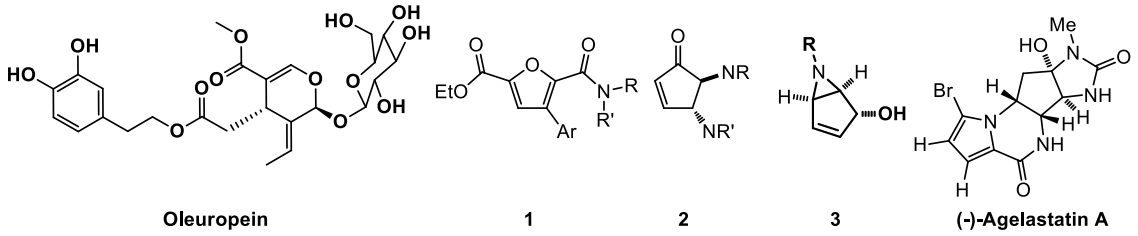
Performing reactions under continuous processes, using either high scale or microflow devices, provides valuable benefits in terms of productivity, purity and safety derived from efficient reagent mixing, heat transfer and pressure control, when compared to batch processes.[1] This laboratory has been involved on the development of some synthetic methodologies based on functional groups transformations under batch conditions. In this line, will be presented some examples on the application of flow chemistry to some studied transformations under batch conditions such as enzymatic resolution, oleuropein methanolysis,[2] chemoselective modification of 5-hydroxymethylfurfural (HMF) derivatives (**1**),[3] heterogeneous catalyzed transformation of furfural to *trans*-4,5-diaminocyclopent-2-enones (**2**),[4] and sequential photochemical rearrangement and hydration of *N*-alkyl pyridinium salts to bicyclic aziridines (**3**) [5] as the starting building block to the total synthesis of (-)-Agelastatin A.



We thank Fundação para a Ciência e Tecnologia (PTDC/QUI-QOR/32008/2017 UIDB/04138/2020 and UIDP/04138/2020) for financial support. The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951996.

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Atom-efficient diarylations through metal-free cascade reactions

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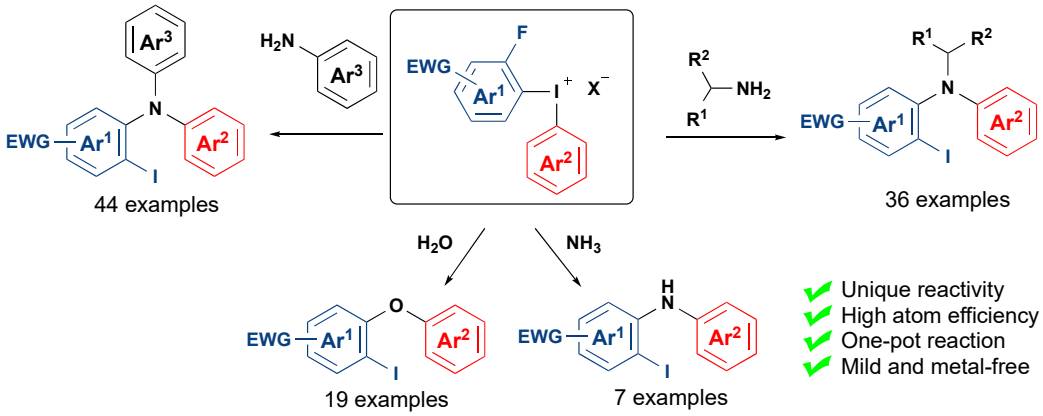
Hypervalent iodine compounds have recently gained considerable interest in synthetic chemistry due to their attractive features as reactive, selective and sustainable reagents. We have developed several one-pot syntheses of diaryliodonium salts from commercially available starting materials,[1] and demonstrated their efficiency as electrophilic arylation reagents with various heteroatom and carbon nucleophiles under mild and metal-free conditions,[2] e.g. in the *N*-arylation of aliphatic amines.[3]

This lecture will focus on our most recently developed arylation methodology, in which both aryl groups in diaryliodonium salts are efficiently transferred to a variety of nucleophiles under mild and transition metal-free conditions.[4] The reaction in made possible through a novel mechanistic pathway, where the first arylation proceeds through nucleophilic aromatic substitution, rather than the ligand coupling that is generally seen with these arylation reagents. A subsequent intramolecular aryl transfer delivers diaryl ethers, diarylamines and triarylamines with excellent atom economy.



In memory of Prof. Kilian Muñiz.

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CO_2-Mediated Processes

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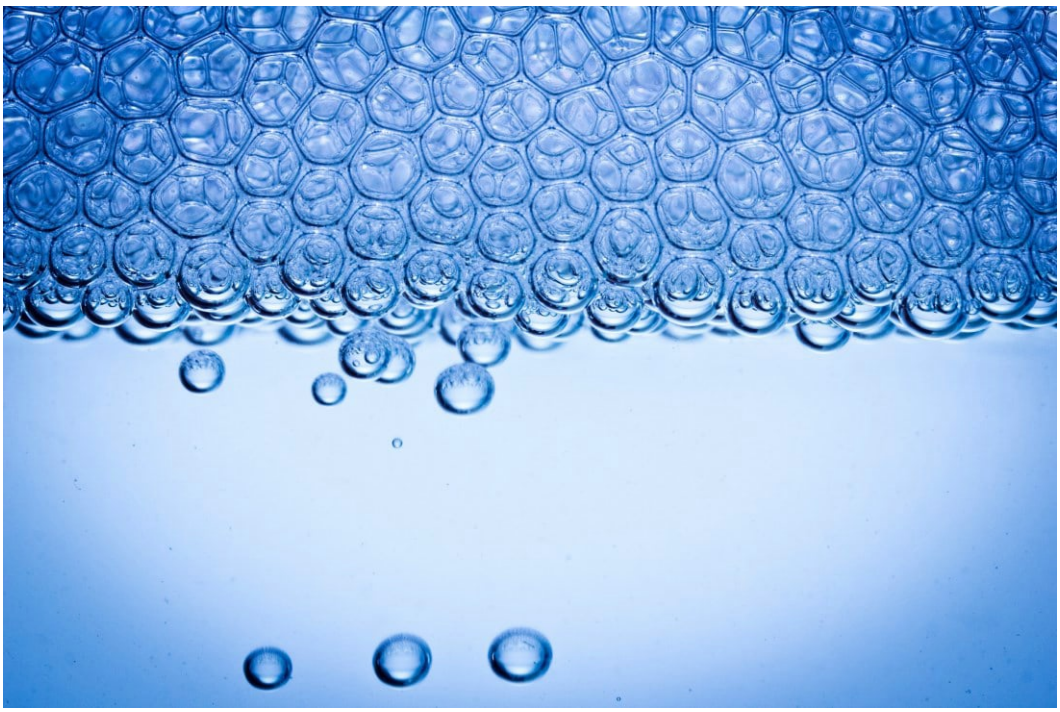
Currently, more than 40 gigatonnes of CO_2 are released annually into the atmosphere as a result of fossil fuel combustion, causing ocean acidification and climate unpredictability. Anthropogenic CO_2 emission is seemingly hard to diminish in the near future and, therefore, CO_2-capture and sequestration or CO_2-functionalization can be viable solutions to address this issue. To use CO_2 as a chemical feedstock, namely as a C1 building block, it is essential to equip the process with a nucleophilic catalyst or a highly active reagent, as exemplified by Grignard carboxylation reactions and some recent progress in metal-catalyzed reactions. In this seminar, I will display how we can utilize CO_2 not only as a chemical feedstock and a catalyst but also as a stimulus for unprecedented processes. The obtained knowledge in CO_2 activation and desalination will be beneficial in supramolecular chemistry, biology, CO_2 functionalization catalysis and CO_2 sequestration processes.



Multi-Step Domino Reactions: Access to Versatile Compounds for Material and Life Sciences

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The domino process is a powerful tool to economically and sustainably build up complex molecular architectures which drastically reduces the number of work-up and purification steps. Recently we developed new metal-free multi-step domino reactions and one-pot processes for the waste-reducing and cost-effective preparation of versatile frameworks, which otherwise are difficult to access via traditional methods. The developed new methods engage malononitrile and other simple and readily available compounds in a wide range of domino reactions to construct e.g., azabicycles, fluorescent quinazolines, 2,6-dicyanoanilines, o-terphenyls and hexaarylbenzenes of interest for medicinal chemistry and materials science [1-4].



The in vitro tests against P. falciparum 3D7 strains and human cytomegalovirus (HCMV) revealed the selected domino products and corresponding artemisinin-containing hybrid compounds as highly active agents, outperforming the clinical reference drugs. Remarkably, these hybrid compounds show also highly improved potencies against multidrug-resistant P. falciparum strains (Dd2 and K1) compared to approved drug chloroquine and strongly suppressing parasitemia in experimental malaria [5].

These recent results will be discussed in the talk.

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Rational approaches to design selective transition metal catalysts using supramolecular chemistry

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Transition metal catalysis has been developed over the past decades as a central technology for organic synthesis and chemical processes. Based on numerous fundamental studies, detailed insight in reaction mechanism have been obtained. Despite the knowledge, and availability of a plethora of different ligands, there are still many challenges that mainly involve the control of the selectivity of the reaction. Over the years we have demonstrated that the implementation of supramolecular strategies in catalyst design provides additional powerful tools to gain control over the selectivity of a reaction. In this presentation I will elaborate on supramolecular strategies to control activity and selectivity in transition metal catalysis, using designed catalysts based on the reaction mechanism. For substrates with functional groups we use substrate orientation effects to control selectivity. We demonstrate this for asymmetric hydrogenation, regioselective hydroformylation and C-H borylation reactions. DFT calculations demonstrate that in some examples the catalyst centers adapt after substrate coordination, similar to what is observed in some enzymes. The lecture will focus on our most recent (unpublished) results.



Figure *Flow chart of design by substrate orientation and an example of rhodium complex in which the substrate is fixed by hydrogen bonds.*

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The Chaotropic Effect as an Assembly Motif in Supramolecular Chemistry

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Following up on scattered reports on interactions of conventional chaotropic ions (e.g., I^-, SCN^-, ClO_4^-) with macrocyclic host molecules, biomolecules, and hydrophobic neutral surfaces in aqueous solution, the chaotropic effect has recently emerged as a generic driving force for supramolecular assembly, orthogonal to the hydrophobic effect. The chaotropic effect becomes most effective for very large ions that extend beyond the classical Hofmeister scale, and that can be referred to as superchaotropic ions (e.g., borate clusters and polyoxometalates). In this contribution [1], we present a continuous scale of water-solute interactions (Figure 1) which includes the solvation of kosmotropic, chaotropic, and hydrophobic solutes, as well as the creation of void space (cavitation). Recent examples for the soft-matter association of chaotropic anions to hydrophobic synthetic [2-5] and biological binding sites, lipid bilayers, colloids [6], and surfaces are discussed, and a new application that introduces the use of superchaotropic anions in biology is reported.

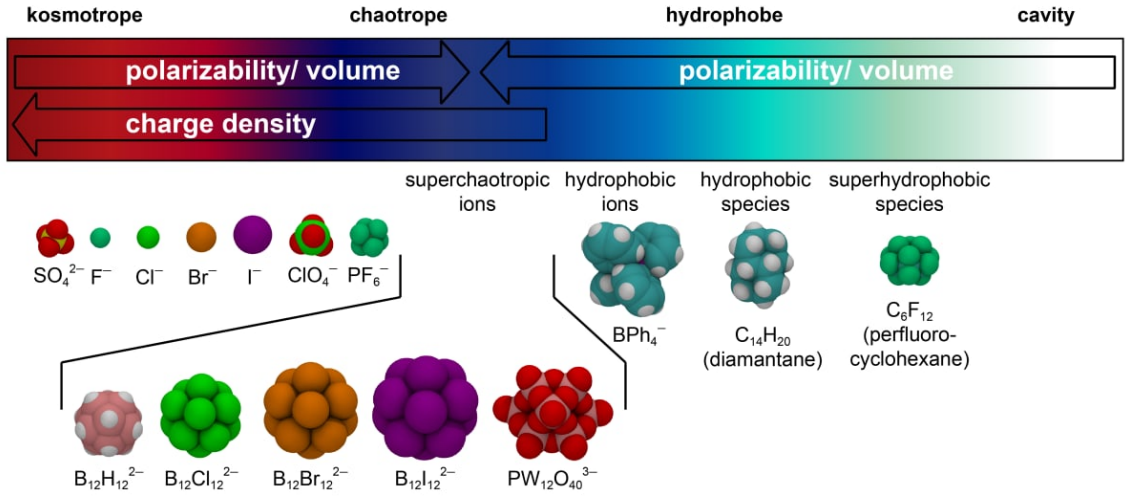

Figure 1: Extended Hofmeister scale with specification of the superchaotropic, hydrophobic ionic, and superhydrophobic regions.

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Synthetic Information Molecules

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The encoded recognition properties of nucleic acids are currently unrivalled in any other material. High fidelity sequence selective duplex formation is the molecular basis for replication of the genetic information encoded by DNA and is finding widespread applications in the programmed assembly of complex nucleic acid nanostructures. We have been investigating the sequence-selective duplex formation properties of synthetic recognition-encoded oligomers that bear no resemblance to the natural system [1].

The basic blueprint shown in Figure 1 tolerates a wide range of different base-pairing motifs, backbone architectures and coupling chemistry used for the synthesis of oligomers. This talk will describe examples of different molecular designs developed in our laboratory, highlighting the key supramolecular design principles that govern high fidelity sequence-selective duplex formation in synthetic recognition-encoded oligomers.

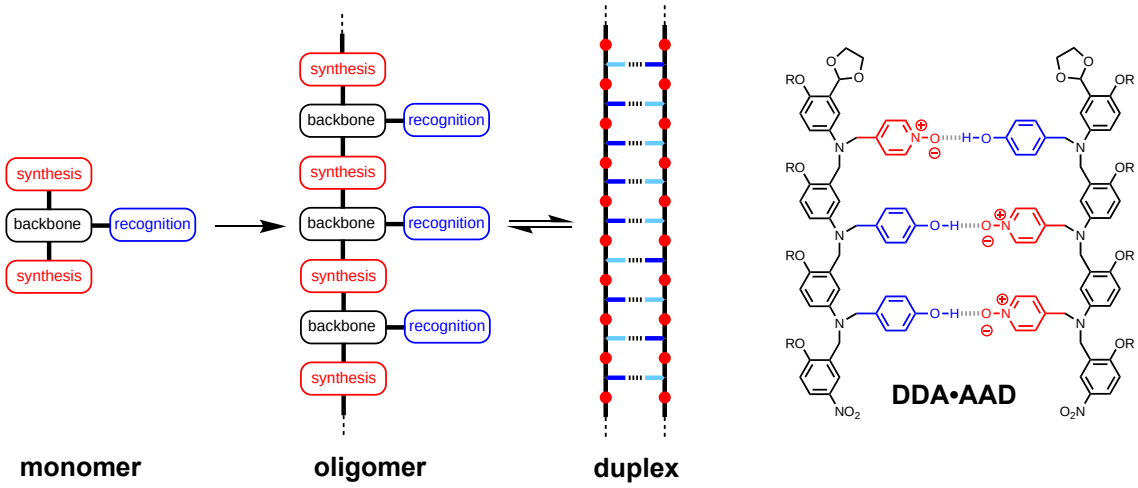

Figure 1. Blueprint for assembly of a polymer that forms a duplex with sequence selectivity.

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Ring Construction via Palladium(0)-Catalyzed C–H Activation

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Intense research efforts from our group in the past couple of decades have been dedicated to the functionalization of non-activated C(sp^3)-H and C(sp^2)-H bonds using catalysis by palladium(0) complexes.[1]



This lecture will present some of the most recent aspects of this chemistry, for instance enantioselective reactions using different types of chiral catalysts,[2] remote bond formation using the 1,4-Pd shift strategy,[3] and applications in natural product synthesis.[4]

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Development of New Photocatalytic Reactions

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Photo-induced transformations have been at the forefront of chemical research for many years, yet lately they have received enormous interest. The basis for modern photocatalytic methodologies is set on the transmission of photons to a specific molecule - a photosensitizer, which can be parlayed into the population of the molecule's excited state. This energy can then be transferred to other substrates via energy or electron transfer, wherein the pairing of excited-state energies and of redox potentials, respectively, of the sensitizer and the reactive substrate is crucial for a successful outcome in photochemical reactions. Very recently, our group has started a new research line concerning the use of photochemistry for different reactions, such as thiol-ene/oxidation tandem reactions,[1] asymmetric alkylation of imines[2] and ring opening cyclopropane expansions.[3] More recently, we have found that the rupture of C-O bonds is possible and can be used for further transformations.[4] In this communication, the latest results of our group will be also presented.[5]

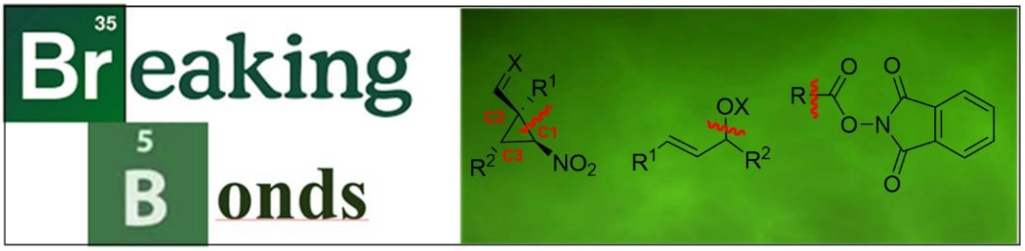

Figure 1. *Some of the breaking bonds for the development of new reactions.*

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Power of transition metals
Functionalization and construction heterocycles

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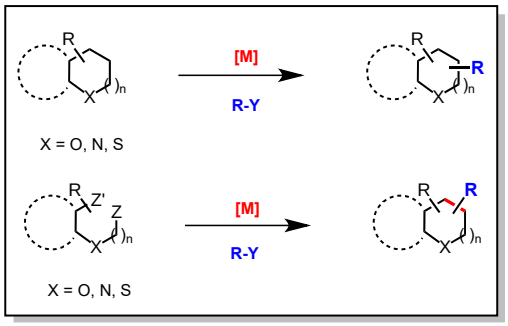
Heterocycles are present in a great diversity of natural products and/or bioactive compounds. They are also present in ligands, dyes, materials, etc. It is worth mentioning that, in the literature, two third of the publications are related to heterocycles. Due to the importance of the heterocycles, the development of chemoselective, efficient and versatile methods is one of our main area of research.

In this lecture, different methods will be presented to acess functionalized heterocycles containing oxygen and nitrogen. We will show that transition metals such as gold, iron, cobalt, nickel and rhodium are appropriate to realize the functionalization and the construction of heterocycles (Scheme).



Scheme: General scheme

Synthesis of heterocyclic compounds promoted by porphyrin-based catalytic systems

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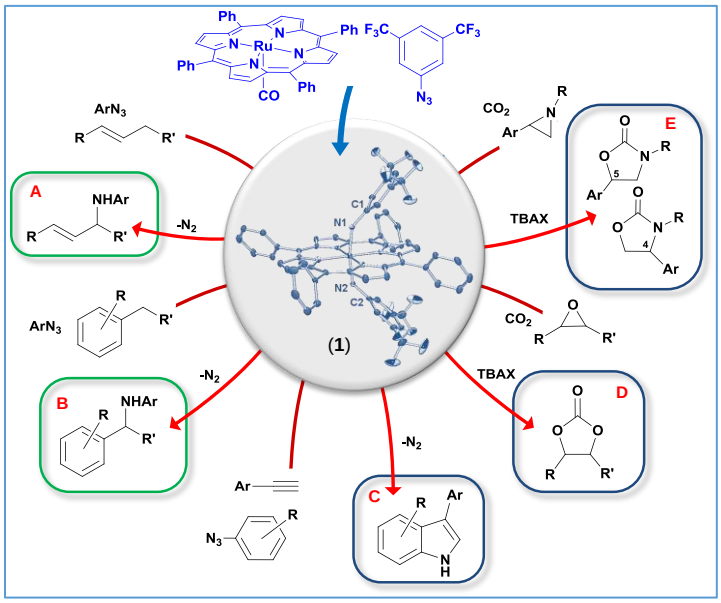
During our ongoing studies on the catalytic activity of ruthenium porphyrin complexes to promote nitrene transfer reactions by using aryl azides as 'ArN' sources, we isolated and characterized by X-ray spectroscopy a ruthenium *bis*-imido porphyrin complex [1], which is the *active intermediate* in this class of reactions and appears to have a perfect equilibrium between stability and reactivity. Besides the synthesis of allylic (**A**) and benzylic (**B**) amines [2], the complex Ru(TPP)$(NAr')_2$ (**1**) (TPP = dianion of tetraphenyl porphyrin; Ar' = 3,5$(CF_3)_2C_6H_3$) efficiently promoted the reaction of ArN_3 with triple bonds forming indoles [3] (**C**), rather that triazoles, as well as the cycloaddition of CO_2 to epoxides and aziridines yielding cyclic carbonates (**D**) [4] and oxazolidinones (**E**) [5], respectively. It should be noted that the atomy economy of the synthesis of heterocycles **C**, **D** and **E** was very high producing either molecular nitrogen or nothing as the by-product of the cyclization reaction.

The *one-pot* formation of indoles (**C**) performed well in the presence of differently substituted aryl azides and terminal aromatic alkynes. The catalytic mechanism was investigated by applying a symbiotic experimental/theoretical approach. The study was fundamental for shedding light on the nature of possible catalytic intermediates as well as optimizing reaction performances.



Complex **1** also mediated very well the synthesis of cyclic carbonates **D** and oxazolidinones **E** in the presence of a tetrabutyl ammonium salt (TBAX) as the co-catalyst. In addition, we discovered that the reaction between CO_2 and aziridines [6] or epoxides [7] was very well mediated by a free-base porphyrin/TBAX binary system, and the presence of a transition metal promoter was not required. In view of the general applicability of the Ru(porphyrin)CO-based catalytic methodology in the synthesis of *N*-aryl aziridines, we also studied a *catalytic tandem reaction*, in which aziridines were first synthesized and then reacted with CO_2 without being isolated nor purified [8].

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New Horizons in Metal-Methyl Chemistry

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Metal-methyl complexes and even more so homoleptic derivatives $[M(CH_3)_x]$ are archetypal organometallics and as such have remained in the focus of interest since Frankland´s report on dimethylzinc in 1849 [1]. Subsequent major milestones of this research area comprise $[LiCH_3]_n$ (*s*-Block) [2], $[Al(CH_3)_3]_2$ (*p*-block) [3], $W(CH_3)_6$ (*d*-block) [4], and $[Ho(CH_3)_3]_n$ (*f*-Block) [5]. Notwithstanding these seminal discoveries, the synthesis, isolation, and clear characterization of ionic or thermally labile derivatives presents still a particular challenge, and has been driving us lately. In the meantime, the elaboration and implementation of new synthesis protocols have given us access to single-crystalline $[Mg(CH_3)_2]_n$ [6] as well as X-ray amorphous $[Ca(CH_3)_2]_n$ [7], $[Sc(CH_3)_3]_n$ [8], and $[Yb(CH_3)_2]_n$ [7]. The talk will provide an overview of the synthesis, reactivity, and derivatization of such metal-methyl complexes.

Thanks to the German Science Foundation (An 238/14-2 and An 238/15-2) for generous support.

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Bioactive Metal-Organic Networks for Antimicrobial Applications

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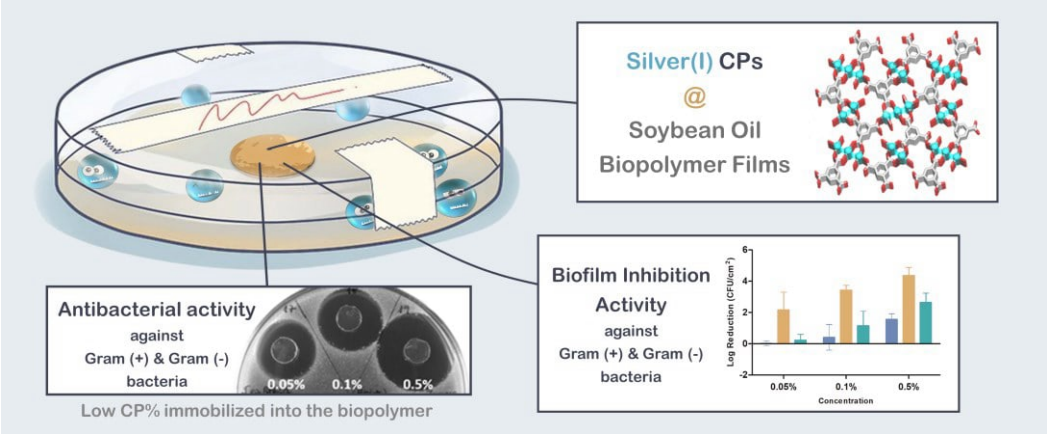
This presentation will highlight our recent research on the self-assembly synthesis, crystallization methods, structural features and applications of a wide diversity of functional metal-organic architectures, including bioactive metal-organic frameworks (bioMOFs), coordination polymers (bioCPs) and derived materials with potent antimicrobial properties [1,2]. The following topics will be discussed:

(1) Self-assembly generation and structural diversity of silver(I) and copper(II) coordination polymers derived from carboxylic acids and aminoalcohols.
(2) Application of these compounds as efficient antimicrobials against different types of Gram-positive and Gram-negative bacteria, and bacterial biofilms.
(3) Design of bioCP-doped polymer films, based on epoxidized soybean oil acrylate (ESOA) or potato starch (PS) as model biopolymer materials.
(4) Antibacterial and biofilm inhibition activity of the obtained biopolymer films as a function of bioCP dopant type and loading, biopolymer matrix, and metal ion release rates (Fig. 1).

This multidisciplinary study expands antimicrobial use of bioactive coordination polymers [3] and hybrid biopolymer materials obtained from renewable biofeedstocks such as soybean oil and potato starch.



All the coauthors of the cited references are gratefully acknowledged. Financial support is provided by the FCT (PTDC/QUI-QIN/29697/2017, LA/P/0056/2020, UIDB/00100/2020, Portugal).

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Modulation of the iron properties in multiheme cytochromes for sustainable green-energy alternatives

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Multiheme cytochromes are abundant in exoelectrogenic microorganisms, particularly in *Geobacter* bacteria. These bacteria have unique redox biological features and transfer electrons to the cell's exterior, converting highly toxic compounds into non-hazardous forms [1]. In addition, they can also grow on electrode surfaces and produce electric current in distinct microbial fuel cells [1]. These metabolic features opened new avenues for *Geobacter*-based practical applications in the fields of bioremediation and bioenergy production. Yet, these applications are still far from being economically viable and several strategies can be explored to improve them. One conceivable strategy relies on the manipulation of the redox properties of *Geobacter*'s proteins engaged in extracellular electron transfer (EET) pathways. These pathways are highly dependent on a multitude of multiheme cytochromes. Multiheme cytochromes are, therefore, the logical targets for rational protein engineering to improve current generation, either by increasing the bacterium's biomass production or by optimizing their EET mechanisms. Mutated forms of multiheme cytochromes from *Geobacter sulfurreducens* and *Geobacter metallireducens* were designed to explore different chemical properties, including the heme's solvent exposure and network of interactions, such as surrounding hydrogen bonds and ionizable residues. The characterization of these mutants revealed how the individual redox properties of each heme, and the global protein's functional behavior, including working functional range of the proteins can be rational engineered [3,4]. This approach lays the path for development of cytochromes with rationally designed redox properties, that ultimately might contribute for improvement of EET efficiency for various biotechnological applications.

Acknowledgments: This work was supported by research grants PTDC/BIA-BQM/31981/2017, PTDC/BIA-BQM/4967/2020, 2020.04717.BD (FCT Portugal); UIDP/04378/2020, UIDB/04378/2020(UCIBIO).

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Search Strategy for Novel Superionic Solid-State Lithium-Ion Conductors – Lithium-Phosphido Trielates and Tetrelates

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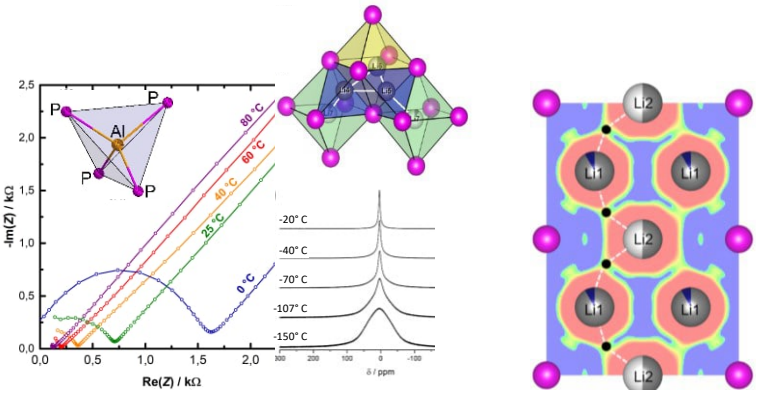
Superionic conductors as a solid-state electrolyte materials are essential for the use for all-solid-state lithium ion batteries. Whereas intensive research on oxide and sulfide based lithium ion conductors resulted in optimized materials which reach ionic conductivities up to 25 $mScm^{-1}$ other compound classes are disregarded. Design principles for fabricating new superionic conductors follows the idea of increasing the carrier densities, changing the diffusion pathways of the mobile species, creating vacancies or increasing structural defects, and including anions that are more polarizable. For example to increase the carrier density the aliovalent substitution of cations is chosen by formal substitution from "P^{5+}" to "Ge^{4+}" in pristine Li_3PS_4 arising in $Li_{3.25}Ge_{0.25}P_{0.75}S_4$ with a four times higher ionic conductivity.

We introduce here phosphide-based materials as ionic conductors that result in principle from the aliovalent substitution of $[TtS_4]^{4-}$ tetrahedra, which are an important key building block in sulfide-based electrolytes, by $[TtP_4]^{8-}$ (*Tt* = tetrel = Si, Ge, Sn) and $[TrP_4]^{9-}$ (*Tr* = triel = Al, In, Ga) leading to analogous tetrahedral anions. The resulting higher charge of the tetrahedra allows for more than twice the number of lithium ions per formula unit for charge compensation if compared to $[TtS_4]^{4-}$ and in addition, the more negatively charged P^{3-} is more polarizable than S^{2-}. In this context we discovered a new family of compounds such as Li_8SiP_4 [1] and $Li_{14}SiP_6$ [2] Li_9AlP_4 [3] α- and β-Li_8SnP_4 [4] and many others with conductivities for the pristine materials up to 3 $mScm^{-1}$ at a very low theoretical density.



We give here an overview on the recent development in this material class and report on the synthesis and structures, the lithium ion mobility by means of temperature dependent NMR and electrochemical impedance spectroscopy, analyze lithium diffusion pathways by temperature-dependent powder neutron diffraction measurements in combination with maximum entropy method (MEM) and DFT calculations. The role of lithium occupation in the various tetrahedral and octahedral sites that occur in those compounds on the lithium ion diffusion is highlighted.

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From Rings to Nanostructures

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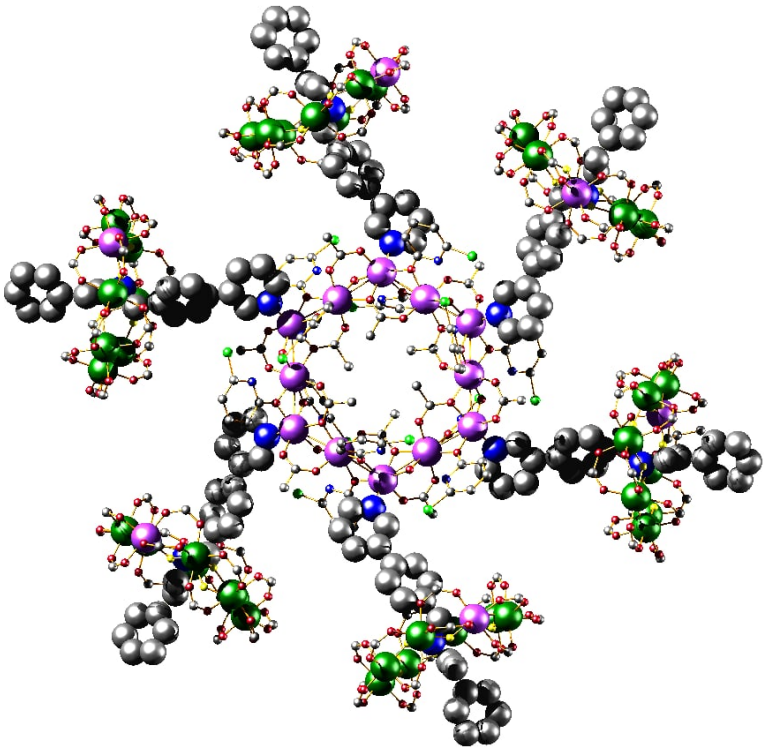
Around twenty years ago it was proposed that molecular magnets could be used as qubits for quantum information processing [1,2]. The most studied targets involve preparation of two level systems as possible qubits [2] – either $S = 1/2$ molecules or by using the ground m_I doublets of a lanthanide centre. We are pursuing chemistry to link together heterometallic rings to make large supramolecular structures that bring together multiple such potential qubits. In some cases we can include switchable units that allow us to propose strategies to implement entangling gates such as the CNOT or the $\sqrt{\text{iSWAP}}$ gate [3] and possibly to incorporate quantum error corrections [4]. Routes to much larger structures will also be described which involve heterometallic rings as parts of hybrid *n*[rotaxanes] [5].

We have also found that the rings and assemblies of the rings are excellent resist materials for electron beam lithography [6]. New results in this area will also be discussed.



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Controlling self-assembly and reactivity on surfaces

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In the first part, we will focus on the formation of self-assembled molecular networks at the liquid-solid interface on small areas on covalently functionalized graphite and graphene surfaces, leading to confinement effects. Several strategies will be demonstrated to realize two-dimensional lateral confinement, all based on the covalent modification of the surface, making use of bottom-up approaches or a combination of bottom-up and top-down approaches. The impact of these various types of confinement on the formation of self-assembled molecular networks will be discussed, including aspects such as nucleation and growth, directional self-assembly, on-surface chirality, polymorphism, and reactivity.

In a second part, we will focus on the formation of porous two-dimensional covalent organic frameworks at the liquid-solid interface, and reveal various interesting aspects at the molecular level such as nucleation and growth mechanisms, and the impact local electric fields may have on (de)polymerization processes.

The relevance and importance of scanning probe microscopes to investigate (and control) self-assembly and reactivity on surfaces will be illustrated.

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Bone biomineralization studies by X-ray diffraction based 2D and 3D imaging

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Bone has a complex hierarchical structure. It is a composite whose main components are nanocrystalline apatite-like mineral, collagen type I and water, which are accompanied by a several additional minor components. The complexity of bone structure has made the understanding of bone elusive. One approach to addressing this problem is to use X-ray diffraction, small angle scattering or fluorescence to map, respectively, crystalline components, nanostructure or chemical elements. To resolve the hierarchical structure, this must be done in a position resolved manner to build images. It is even possible to do so in 3D using tomographic reconstruction [1]. I will present how these techniques afford new insights into bone biomineralization also when combined with multiscale X-ray imaging [2]. X-ray diffraction computed tomography with sub-µm X-ray beams revealed that the crystallographic properties of bone biomineral depends on location within human bone in a manner that was hypothesized to result from effects of mineralization inhibiting proteins [3]. support for this hypothesis was obtained by mouse models lacking the ability to process such proteins correctly, which results in localized unmineralized spaces in bone [4]. Moving towards the nanoscale, we harnessed X-ray nanobeams to establish X-ray diffraction computed tomography with better than 120 nm 3D resolution on bone [5]. Such nanobeams further revealed that bone close to bone cells, called osteocytes, surprisingly present crystallographic properties that depend on orientation so that lattice constants and nanostructure effects vary on the few-hundred nm length scale in an orientation dependent manner.

Orientation of nanostructure and mineral can be obtained by tensor tomography, where the scattering and diffraction signals provide orientation information when collected for various orientations and tilts of the sample [6]. Such results suggest that human lamellar bone may contain localized biomineral components not aligned with collagen fibrils.

These results suggest that while our understanding of bone has increased drastically over the past few decades, much still remains to be learned.

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Advanced Energy Materials for Sustainable Future

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Electrocatalyst materials that drive fuels cells and other fossil fuel-free energy technologies have shown to play an important role on the production of clean and sustainable energy. However, those electrocatalysts containing precious metals, such as Pt, are currently hindered by their short-term durability. Recyclability and re-use of highly active nanocatalysts is still an outstanding global challenge of increasing importance in energy conversion and heterogeneous catalysis[1]. As these precious elements are rapidly diminishing, the research community is forced to urgently address this major issue until more abundant efficient electrocatalysts are put forward. In this respect, hollow carbon nanostructures can provide an excellent mean for the fabrication of highly durable electrocatalyst materials through nanocatalyst confinement [2-4], allowing their sustainable use in a whole variety of electrochemical processes. Thus, these hybrid nanocatalysts have shown performance comparable to commercial electrocatalysts (Pt/carbon black), but most importantly they exhibit outstanding durability, retaining most of the electrocatalytic activity even after 50,000 and 30,000 cycles of the ORR and HER, and thus significantly outperforming all existing electrocatalytic systems under these conditions. The observed behaviours are directly linked to interactions between the metal nanoparticles and the graphitic step-edges within the carbon nanoelectrodes. These surprising and remarkable properties of the reported hybrid electrocatalyst materials have opened up a new strategy for the sustainable use of precious metals in electrocatalysis and other technological applications that require stabilization of metal nanoparticles under harsh conditions (Figure 1).

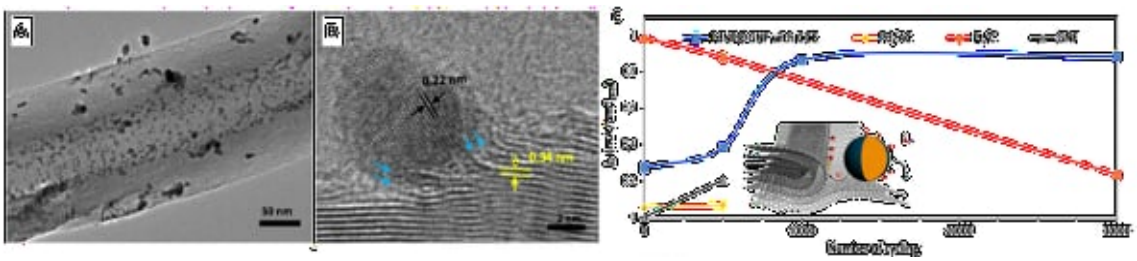

Figure 1. A HRTEM image (A) of the internal cavity of an electrocatalytic nanoelectrode with nanoparticles positioned predominantly at the graphitic step-edges (B) and its increasing HER activity (C) during potential cycling [4].

This work has received financial support from the Ministry of Science of Spain (RYC-2016-20258, RTI2018-101097-A-100 and EIN2019-103246 for M.G-L), the European Research Council (ERC) (Starting Grant (NANOCOMP-679124, ZABCAT-966743) for M.G-L) and the Xunta de Galicia (ED431B 2021/13).

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Towards green synthesis and applications of robust MOFs

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Metal-organic frameworks (MOFs) are highly tunable crystalline hybrid porous materials due the almost infinite choice of metal, ligands leading to thousands of micro or meso-porous architectures bearing different functionalities (flexible or rigid frameworks, polar or apolar groups, open metal sites etc…). This has been associated to date with a large range of potential applications from gas sorption, separation, heat reallocation, sensing, catalysis or in biomedicine etc...

Until recently most MOF synthesis routes have relied on the use of corrosive or toxic chemicals under high temperature conditions preventing from an economically viable large scale production, a prerequisite for their integration into real applications. However recently an increasing interest has been dedicated to find alternative ways to produce these materials under greener more economically friendly conditions.[1] In our laboratory, during the past decade, we have devoted a particular effort to optimize the synthesis and scale-up of robust high valence benchmark MOFs including in some cases the technico-economic evaluation of their production at industrial scale.[2,3] Here we will report several very recent examples of successful green strategies to produce several benchmark MOFs or their related composites[4-7], in a view of their fascinating properties related to potential applications such as gas phase separation, volatile organic compounds removal, heat reallocation or the catalytic conversion of small molecules.

Acknowledgements
CS would like to acknowledge the European Community Horizon 2020 Program (H2020-NMBP-2017-two-stage) under Grant Agreement No. 760801-2 (project Nemosine).

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Coordination polymers as toolbox for a panoply of applications: from antimicrobial properties via clay-like behavior to detection, sensing and separation

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The dimensionality of coordination polymers can be tuned depending on the preferred coordination number of the used metal ions, leading e.g. to one-dimensional chains (1D), two-dimensional sheets (2D) or three-dimensional networks (3D) [1]. The size, chemical functionality, physical properties and structural flexibility of the ligands convey important properties to the overall assembly. In this presentation, several examples will be given with different possible applications.

For instance, silver coordination polymers possess antimicrobial properties and can be used as antimicrobial and biocompatible coatings for implants if the ligands are well chosen [2]. Such compounds can also reversibly swell and shrink as a function of the solvent or change structure over time, forming first nanowires and later bulk crystals [3,4].

Tuning the size of the ligand, making it longer, introducing aromatic entities such as anthracene, conveying intersting optical properties, may lead to chemical sensors. Indeed, using e.g. zinc as metal ion and anthracene derived donors, coordination polymers with large pores can be obtained, which are able to sense guest molecules. We have thus shown that e.g. nitro explosives can be detected just as some pesticides and even the cork taint in wine [5].

One of the more recent applications is the use of porous metal-organic frameworks for the separation of different sizes of fullerenes, allowing thus a smooth purification process of the latter [6].

KMF thanks the University of Fribourg, the National Center of Competence in Research “Bioinspired Materials” as well as the Swiss National Science Foundation for generous support of different projects.

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The "Chemistree" of porous solids

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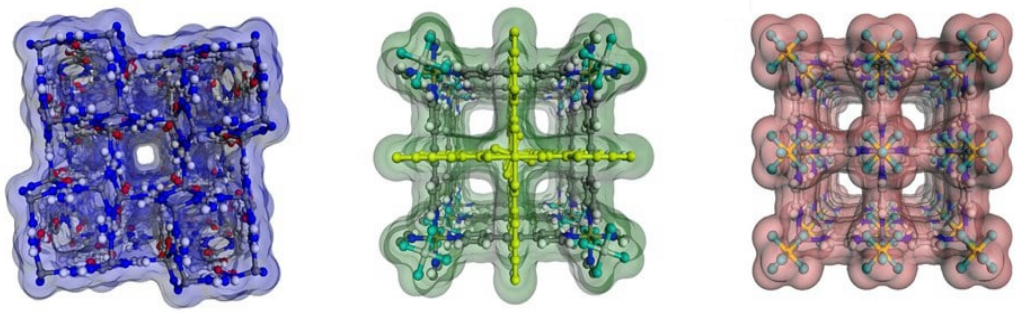
That composition and structure profoundly impact the properties of crystalline solids has provided impetus for exponential growth in the field of *crystal engineering* over the past 30 years. Crystal engineering has evolved from structure design (form) to control over bulk properties (function). Today, when coupled with molecular modelling, crystal engineering can offer a paradigm shift from the more random, high-throughput methods that have traditionally been utilized in materials discovery and development. Custom-design of the right crystalline material for the right application could therefore be at hand.

Porous crystalline materials exemplify this situation. Whereas purely inorganic materials (e.g. zeolites) and those based upon coordination chemistry (e.g. Metal-Organic Frameworks, MOFs, and Porous Coordination Polymers, PCPs) are well studied and offer great promise for separations, storage and catalysis, they are often handicapped by cost or performance (e.g. poor chemical stability, interference from water vapour, low selectivity) limitations. In this contribution, we will present an overview of the "chemistree" (taxonomy) of porous coordination networks and address why their amenability to crystal engineering is critical to enable the creation of platforms of related materials that are ideal for study of structure-function relationships. Two classes of functional porous materials will be highlighted:

1. Ultramicroporous Materials, *UMs*, are built from metal or metal cluster "nodes" and combinations of organic and inorganic "linkers"; their pore chemistry and size (< 0.7 nm) can overcome some of the weaknesses of existing classes of porous material. Three families (platforms) of UMs will be detailed and their performance with respect to important gas separation (e.g. CO_2 capture [1], C_2H_2 capture [2]) and water purification applications will be discussed. Most recently, we have shown that UMs can function synergistically to address complex gas mixtures [3] (Figure 1) or capture trace levels of CO_2 even in the presence of humidity [4].

2. Materials that switch between non-porous (closed) and porous (open) phases can exhibit isotherms that, perhaps counterintuitively, are advantageous in terms of working capacity vs. rigid porous materials. Examples of 2D [5] and 3D [6] switching materials that offer excellent gas storage performance will be presented.



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Live cell labelling of proteins and carbohydrates by templated chemistry

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Fluorescence labelling is key to enable the microscopic imaging of (glyco)protein localization and function in live cells. Particularly useful are methods that allow the on-demand introduction of reporter groups on specific (glyco)protein targets. The labelling agents are typically directed to unique microenvironments provided by intrinsic features of the target or, if these features are unknown, by genetically encoded tags.[1] Specificity of labelling is the paramount challenge. In this presentation, I will present templated chemistries that provide high target specificity.

Templates align functional groups in defined 3D arrangements, and it is this spatial arrangement that provides specificity of molecular recognition. For example, we developed a labeling reaction, which allows the introduction of virtually any reporter group, requires only small tag sequences (max 23 aa), occurs with high tag specificity and proceeds within 1-5 minutes.[2] The labeling reaction is based on the interaction between two peptides that form a coiled coil. The label-accepting tag coil peptide has an N-terminal cysteine, the label donor coil peptide contains a reporter group linked via a thioester structure. Templating via coiled coil formation enhances aligns the cysteine and the thioester. The increase of effective molarity and triggers a rapid transfer reaction. We used the method to label different GPCRs including the human neuropeptide Y receptors 1, 2, 4, 5, the neuropeptide FF receptors 1 and 2, and the dopamine receptor 1.[3,4] Demonstrating the versatility of the labeling reaction, we tagged membrane proteins with peptide nucleic acids (PNA).[5] PNA conjugation provides new, fascinating opportunities for barcoding, ultrabright labeling and hybridization-based control of homo- and heterooligomerization of membrane proteins. I will discuss the use of PNA tagging for enabling an erasable imaging of the epidermal growth factor receptor (EGFR), which facilitates the analysis of EGFR internalization. The combined use of orthogonal coiled coils enables a rapid covalent labeling of two distinct membrane proteins such as EGFR and Her2 or with PNA barcodes.[6] Orthogonal peptide-templated labeling elucidated the lateral proximity between endothelin receptors A and B (ET_AR and ET_BR).[7]

In a second example, I will present unpublished work, in which we use peptide templating to probe physical properties around cell surface carbohydrates. Here, our interest pertains to the hydrogel formed by glycoproteins in mucus and the glycocalix. To allow a hydrogel-specific positioning, dyes are equipped with boronic acid-based functional modules that allow recognition of carbohydrates. The modules are comprised of peptide structures that arrange up to four different boronates in defined distances. Variations of valency, boronate-boronate distances and the nature of the peptide scaffold decide about properties of the labeling agent. Perhaps surprisingly, not only is it possible to achieve high affinity for cell surfaces, but structural variations also enable the design of peptide conjugates that confer cellular delivery even at submicromolar concentrations.

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Macromolecular design for 3D hydrogel biomaterials

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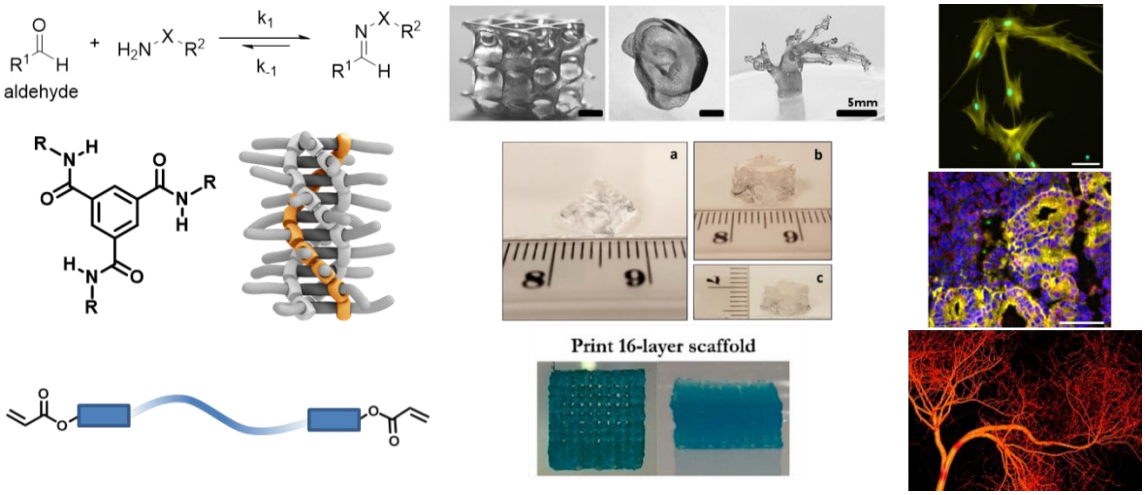
Tissue engineering and regenerative medicine have the potential to transform the way we treat the human body. However, the ability to recapitulate the 3D environment of tissues and cells remains a major bottleneck for the field. From mimicking the complex extracelluar matrix (ECM) to positioning cells in the right place at the right time, the spatiotemporal control of cells and their environment remain crucial for tissue growth. In order to tackle this problem, our lab designs new materials to enable customizable and life-like tissue constructs. Via (macro)molecular design, we aim to control the rheological properties of hydrogels for bioprinting, create new resins for 3D printing, and probe fundamental cell-biomaterial interactions. Relying heavily on dynamic interactions (dynamic covalent, supramolecular), these materials have remarkable control over the dynamic and temporal aspects of artificial extracellular matrices. We aim to push forward our ability to create more life-like tissue engineering constructs combining the power of macromolecular design, with cell culture, and biofabrication technologies.



Chemical Probes enabling Drug Discovery

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Ed is Professor of Chemical Biology at Imperial College London, and a Group Leader at the Francis Crick Institute. His lab is particularly interested in the chemical biology of post-translational modifications (PTMs) and the enzymes which modulate them, leading to the development of a wide range of chemical probes and tools for PTM discovery and target validation. Recent highlights include the first cell-active activity-based probes for deubiquitinases, new tools for the analysis of secreted proteases and de novo discovery of proteases undertaking specific pathogenic cleavage events, and the first comprehensive maps of specific classes of protein lipidation through chemical proteomics. His work extends into drug discovery and new modalities, including one of the first reports of targeted antibody-PROTAC conjugates, discovery of picomolar inhibitors of lipid transferase enzymes, and the foundation Myricx Pharma, a spinout which is developing discoveries in his lab towards clinical applications. Research by his group has also been recognised with a number of awards, most recently the 2019 Sir David Cooksey Translation Prize and the 2020 Corday-Morgan Prize of the Royal Society of Chemistry.

Representative publications:

- "Structure, mechanism, and inhibition of Hedgehog acyltransferase", *Mol Cell* 2021, 5025, doi: 10.1016/j.molcel.2021.11.018.
- "Substrate-biased activity-based probes identify proteases that cleave receptor CDCP1", *Nat Chem Biol* 2021, **17**, 776, doi: 10.1038/s41589-021-00783-w
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- "Photochemical probe identification of a small-molecule inhibitor binding site in Hedgehog acyltransferase (HHAT)", *Angew Chemie* 2021, **60**, 13542, 10.1002/anie.202014457.
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- "AWZ1066S, a highly specific anti-Wolbachia drug candidate for a short-course treatment of filariasis", *Proc. Natl. Acad. Sci.* 2019, **116**, 1414-19.
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Chemical Tools for Investigating Histone Deacetylase (HDAC) Enzymes

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Histone deacetylases (HDACs) are validated targets for treatment of certain cancer types and play numerous regulatory roles in biology, ranging from epigenetics to metabolism. Small molecules are highly important as tool compounds to probe these mechanisms as well as for the development of new medicines. Therefore, detailed mechanistic information and precise characterization of the enzyme substrate preference as well as the chemical probes used to investigate the effects of HDAC enzymes are vital.

Through profiling of both sirtuins and zinc-dependent HDACs, we have developed efficient assay formats for probe characterization and discovered enzymatic activities against novel acyllysine posttranslational modifications (PTMs).

Furthermore, we have interrogated Nature's arsenal of macrocyclic non-ribosomal peptide HDAC inhibitors by chemical synthesis and evaluation of more than 30 natural products and analogs. This furnished surprising trends in binding affinities for the various macrocycles, which were then exploited for design of highly potent class I and IIb HDAC inhibitors. Furthermore, thorough kinetic investigation revealed unexpected inhibition kinetics of important tool compounds as well as the approved drug Istodax (romidepsin). This work provides novel inhibitors with varying potencies, selectivity profiles, and mechanisms of inhibition and, importantly, affords insight regarding known tools compounds that will improve interpretation of their effects in biology and medicine.

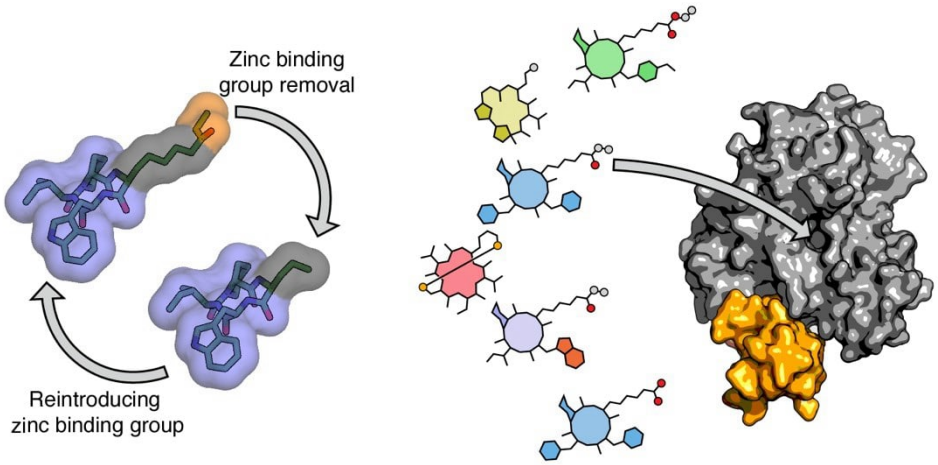

Figure 1. Macrocyclic inhibitors of HDACs.

The use of proline analogues in protein engineering and design

Rubini M

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4-Substituted proline analogues are of particular interest for investigating protein folding kinetics and thermodynamic stability, as substituents at the C^{γ} atom of proline have a strong effect on the two main conformational equilibria of proline residues in polypeptides, namely the *endo/exo* ring puckering of the proline ring and the *cis/trans* equilibrium of prolyl peptide bonds. The installing of electron-withdrawing substituents on the pyrrolydine ring shows to elicit a predictable effect on coiled-coil peptides. However, their impact in the context of the tertiary structure of globular proteins is contradictory.

This presentation will showcase the influence of the fluoroproline analogues (4*R*)- and (4*S*)-fluoroproline (Flp), 4,4-difluoroproline (Dfp) and of 4-thiaproline (Thp) on the thermodynamic stability, folding kinetics and bioactivity of human ubiquitin, Trx1P an *Escherichia coli* thioredoxin (Trx) variant, and barstar.[1-4] Our results show that proline analogues are intriguing tools to modulate protein stability and to elucidate mechanistic questions, although it is difficult to predict their effects, as rules determined for model peptides do not always apply.

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Real-time near infrared fluorescence imaging research tools with the potential for clinical use

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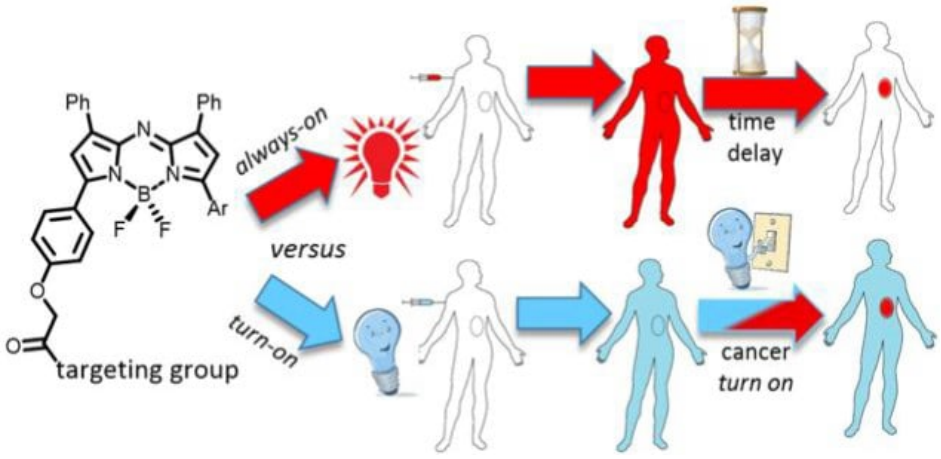
Near infrared (NIR) fluorophores continue to attract research attention due to the ever growing need for their use in material, biological and medical applications. Imaging within the NIR spectral range is advantageous for prolonged live cellular and in vivo imaging while also offering clinical uses such as fluorescence-guided surgery. We have recently developed the BF2-azadipyrromethene (NIR-AZA) class of near infrared fluorophore from which in vitro and in vivo imaging probes can be developed.[1,2,3] They have excellent photophysical characteristics such as tuneable emission maxima between 675 and 800 nm, exceptional photostability and high quantum yields. However, in spite of the advantages offered by longer wavelength NIR emissions a common limitation with fluorescence imaging is the difficulty in discriminating non-specific fluorescence from fluorescence localized at a specific region of interest. This can restrict imaging to individual time points at which non-specific background fluorescence has been minimized. As such, it is of significant advantage when emission is modulated from off to on in response to specific biological events as this permits imaging of such events in real-time without background interference. Several of our most recent approaches that achieve this will be outlined and the principles behind each of the NIR-fluorescence bio-responsive off/on switching mechanism will be explained and illustrated in vitro and in vivo.[4-7] Progress towards clinical translation will also be highlighted.[8]



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New Chemistries for Stimuli-Responsive Targeting Drug Conjugates

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Targeting drug conjugates, emerged as a powerful class of chemotherapeutic agents that are capable of sparing healthy tissues by liberating the cytotoxic payload upon specific antigen recognition. A considerable body of work in this field highlighted that targeting drug conjugates therapeutic efficacy, correlates well with the conjugate homogeneity and activation of the drug at the diseased site. Therefore, the linker technology used to connect both functions contributes decisively to the therapeutic usefulness of these constructs. In this communication will be presented our most recent finding on the design of functional likers for targeting drug conjugates, based on boron complexes (B-complexes)[1] that can be modulated to exhibit fluorescence and to respond to glutathione, pH or reactive oxygen species stimulus.[2-4]

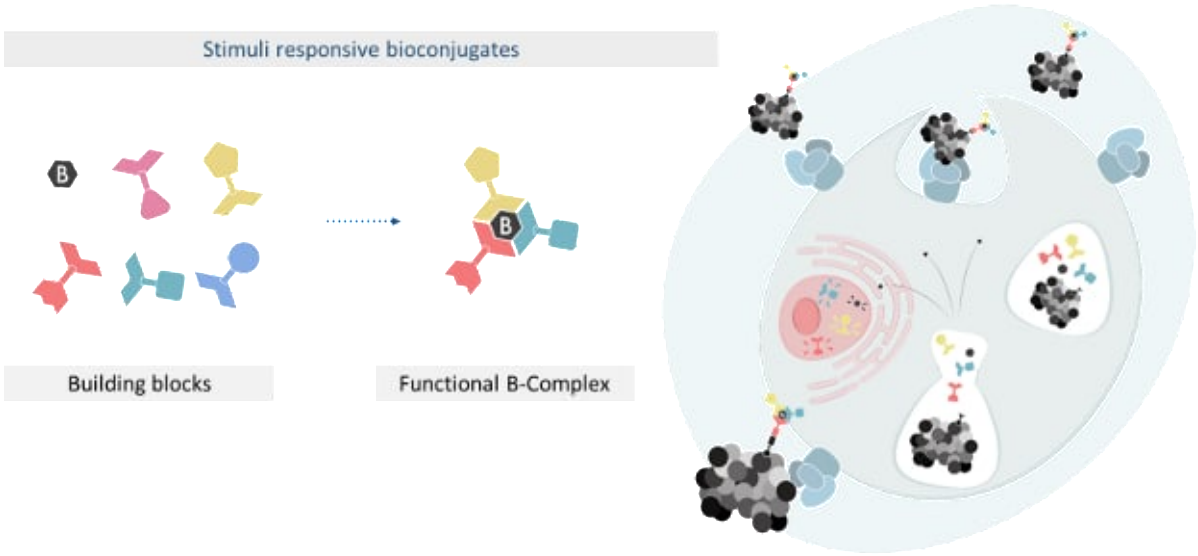

Figure 1: Modular, stimuli-responsive Targeting Drug Conjugates.

Acknowledgements: We thank FCT grants: UIDB/04138/2020; SAICTPAC/0019/2015, PTDC/QUI-QOR/29967/2017); LISBOA-01-0145-FEDER-029967, LISBOA-01-0145-FEDER-32085, PTDC/QUI-OUT/3989/2021

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Copper-containing monooxygenases: from enzymatic systems to bioinspired models

Alda Lisa Concia, Rogelio Gomez Pineiro, Stefani Gamboa Ramirez, Manon Pujol, Rébecca Leblay, Yongxing Wang, Maylis Orio, Olga Iranzo, Christophe Decroos, Marius Réglier, A. Jalila Simaan*

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Copper-containing enzymes have gained attention in the past decades following the discovery of oxygenases with high potential for fuel production. In particular, LPMOs copper-containing enzymes produced by some bacteria and fungi, among a consortium of enzymes that act collectively to degrade recalcitrant polysaccharides such as cellulose or chitin [1,2]. LPMO enzymes were shown to oxidatively cleave polysaccharide chains of the polymeric recalcitrant substrates, in contrast to the well-known hydrolysis reactions carried out by hydrolase enzymes. LPMO active center is constituted of a mononuclear copper ion ligated by two histidines including the *N*-terminal histidine ligated in an unusual bidentate binding mode (Fig 1A & B). LPMO catalyzes the hydroxylation of a strong C-H bond at the glycosidic linkage of polysaccharides leading to glycosidic bond cleavage (Fig 1C). It is not clear whether the natural oxidant employed by LPMO consists of O_2 or H_2O_2. Furthermore, the nature of the reactive copper-oxygen species responsible for the initial activation of the strong C-H bond (>90 kcal/mol) remains to be established.

The preparation of relevant bioinspired models provides important mechanistic tools and could lead to the development of catalysts for strong C-H bond activation. Our group combines studies on enzymatic systems (including LPMO) to the development of bioinspired complexes [3,4]. Our recent results directed towards the understanding of structure-function relationships and strong C-H bonds activation at copper centers will be presented.

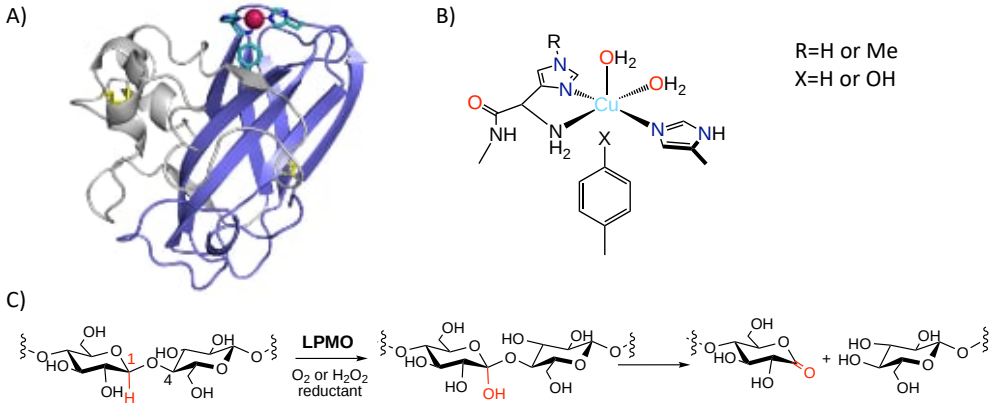

Figure 1. A) structure of LPMO [3] B) schematic representation of LPMO active site. C) C1-oxidation of cellulose catalyzed by LPMO

This work has been supported in part by the French National Research Agency (CUBISM ANR-18-CE92-0040) and by the Provence Region.

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Polyanions to counteract the detrimental interaction between Cu(II)/Zn(II) and the Alzheimer's-related amyloid-β peptide

Lucie de Cremoux, Elena Atrian-Blasco, Xudong Lin, Zeren Xu, Nicolas Giraud, Sébastien Blanchard, Christelle Hureau

Alzheimer's disease (AD) is characterized by the extracellular deposits made of supramolecular assemblies of the amyloid-β (Aβ) peptides, in which up to mM level of metal ions, mainly copper and zinc has been found. Two Aβ-related events are involved in the etiology of AD: (i) the production of reactive oxygen species by Cu(Aβ) species and (ii) the self-assembly of the Aβ peptide leading to aggregates, including amyloids.[1]

The self-assembly of the Aβ is modulated by metal ions, leading to different morphologies of aggregates.[1] Recent evidence shows that natural polyphosphates (PP) [2] and synthetic polyoxometallates (POM) also change the Aβ self-assembly paths,[3] leading to more fibrillar species, while POM has the additional ability to prevent Cu(Aβ) ROS formation.[4]

Here, we will show how PP and POM impact the self-assembly of Aβ, including in presence of Cu(II) and Zn(II), and how the observed modulation effect is linked to the chemical nature (length, size, charge) of the polyanions at play.

The molecular interactions at an atomic level (between the peptides and the polyanions) responsible for such modulatory effects will also be described, based on data obtained from spectroscopic studies including EPR and NMR. The morphologies of the formed aggregates and their interactions with the polyanions will be proposed from imaging microscopy and indirect titration methods.

ERC StG 638712 ('aLZINK') and ANR-21-CE06-0030-03 SUPRAMY are acknowledged for financial support.

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Polyoxovanadates with biological and biomedical activities

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Polyoxometalates (POMs) represent a broad class of anionic inorganic clusters with versatile structural topologies resulting in a variety of chemical and physical properties which can be modulated by molecular design. These features make them attractive materials in a wide range of fields like catalysis, electrochemistry, biological chemistry, including protein crystallography, as well as biomedicine with focus on cancer, bacterial and viral infections [1-4]. Despite the increasing number of studies investigating anticancer effects on POMs, the underlying mechanisms of action in each type of cancer cell still remains elusive [1,4]. Herein, we describe the interaction of several POVs, particularly decavanadate (V_{10}), with several key cellular proteins including phosphatases, NTPDases, TRPM4 channel, tyrosine kinases, myosin, actin, transferrin, albumin and glucosidases, among others [5]. Moreover, POVs' biomedical activities and effects against cancer, bacteria and viruses include: apoptosis, cell cycle arrest, interference with ions transport system, inhibition of mRNA synthesis, cell morphology changes, changes in metabolic pathways, phosphorylase enzyme inhibition and cell signaling, formation of reactive oxygen species, lipid peroxidation, inhibition of viral mRNA polymerase, inhibition of virus binding to the host cell, penetration and interaction with virus protein cages, etc. The protein POV targets and types of interactions are summarized in Fig. 1 [4].

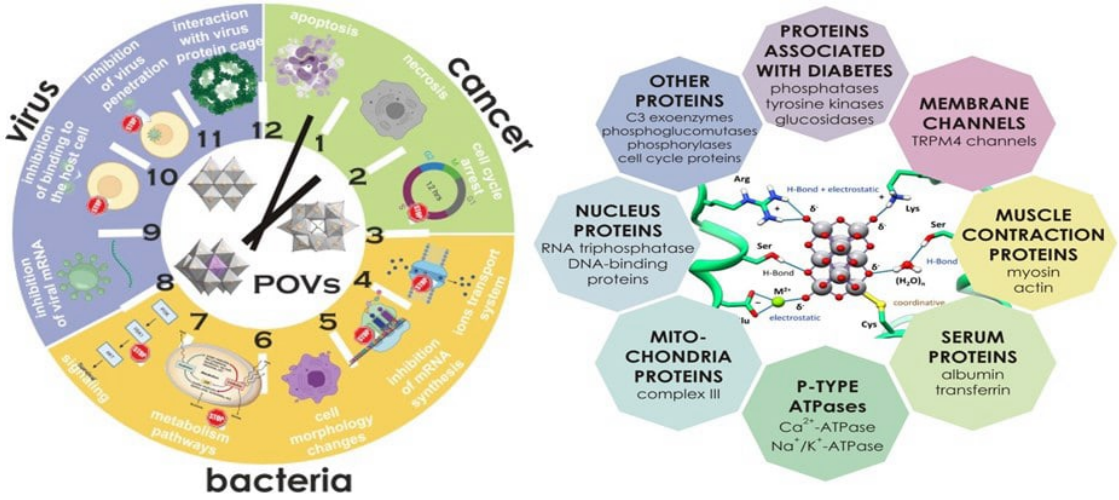

Figure 1. POVs' biomedical activities and effects against cancer, bacteria and viruses (left) [4]; types of POVs interactions with proteins (right) [5].

However, POVs' stability and speciation are of paramount importance to understand not only *in vitro* but particularly the *in vivo* and *ex-vivo* biological effects [6]. We are confident that a number of different hetero-POVs will be biologically active. This communication summarizes the reports on biological effects of POVs and highlights the importance of stability and speciation in the assessment of biological effects. The future is indeed bright for POVs.

This research was funded by Fundação para a Ciência e a Tecnologia (FCT) (UIDB/04326/2020), and Austrian Science Fund (award No. P33089 and P33927).

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Making and breaking bonds: Spectroscopic studies of energy converting enzymes

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The efficient and reversible storage and release of energy in chemical bonds is an essential aspect, and a great challenge in energy research. The activation of small molecules (N_2, O_2, CO_2) can be achieved by homogenous, heterogeneous and biological catalysts. Of the possible metal catalysts, nature is unsurpassed in terms of facilitating small molecule activation with stunning efficiency and selectivity. This has inspired much fundamental research directed towards understanding the enzymatic mechanisms on an atomic level. In this talk, I will discuss recent studies using advanced X-ray spectroscopic approaches, as well as laboratory spectroscopy, to understand the processes of biological methane reduction and dinitrogen reduction on a molecular level.

DNA-assembled functional materials

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DNA has proven to be an excellent choice of molecule for programmable self-assembly. In recent years, DNA self-assembly has surpassed its early stages and today is routinely used for constructing functional two- and three-dimensional nanomachines and materials [1,2].

By defining attachment sites for active components on DNA structures, our group has realised complex and nanometer-precise assemblies of biomolecules, organic fluorophores and inorganic nanoparticles [3]. We employed these devices as autonomous force spectrometers [4] and to create new plasmonic effects. These effects, in turn, enable the selective and sensitive detection of proteins and RNA molecules [5].

The initial thrust catalyzing the rapid development of DNA nanotechnology has been to arrange periodic DNA frameworks to host guest molecules for crystal structure analysis. Despite enormous efforts and fundamental progress, placing guest molecules in designed DNA crystals remains a challenging goal. By adopting design principles of Ned Seeman and Chengde Mao [6], we are now able to crystallise DNA origami structures that grow into three dimensional, micrometer-scale assemblies [7]. Silicification of these crystals leads to designer nanomaterials that withstand drying without structural deformation [8]. We further employ nanoscale surface patterning [9] to achieve precise placement of plasmonic particles on DNA origami in user-defined arrays with controllable optical responses.

Our results demonstrate the assembly power of DNA and our ability to fabricate functional devices and 3D materials that are designed on the molecular level while reaching macroscopic dimensions.

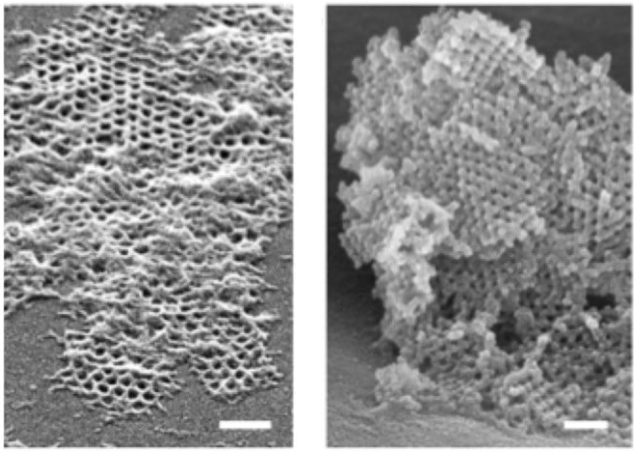

Figure 1: Silica growth on DNA origami crystals. Left: 60° tilted view of bare DNA origami crystals. The crystals flatten upon adsorption to the grids. Right: 60° tilted view of silica coated DNA origami crystals. The 3D structure is preserved. Scale bars are 200 nm.

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Supramolecular Polymers with Life-Like Mechanical Functions

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Artificial molecular motors and switches have the potential to become essential elements for supramolecular chemistry and responsive materials [1]. However, a wide gap in length scales still remains unaccounted for, between the operation of these molecules in solution, where their individual mechanical action is randomly dispersed in the Brownian storm, and on the other hand their action at the macroscopic level, *e.g.* in polymer networks and crystals. Our work aims at bridging this gap, by developing chemo-mechanical transduction strategies that will allow dynamic molecules to perform a broad range of unprecedented tasks at the nanoscale.

In this work we focus on generating strong directional forces at the nanoscale. I will present how we draw inspiration from the operational principles of cellular microtubules, in order to engineer artificial microtubules that disassemble under irradiation with light [2]. The strategy involves synthesizing stiff supramolecular tubes that incorporate molecular photo-switches in their supramolecular design. The molecular photo-switches enable the controlled growth and disassembly of the tubes in water, by using light as the energy input. Because the dynamic exchange between the tubes and the solution is slower than photo-switching, the light-driven disassembly follows a complex mechanism, that is similar to the conformational wave disassembly of cellular microtubules [3]. Atomistic and coarse-grained simulations support a (sub)-molecular understanding of the mechanics by which supramolecular strain builds up in these systems [4]. We demonstrate that fuelled growth [5] and disassembly of stiff tubular systems can exert sufficient forces to pull micro-scale objects in fluid environment thus producing useful work.

Further, we explore strategies to encode combined strain-stiffening and plastic behavior in synthetic hydrogels systems. Such systems can adapt to small small mechanical perturbation by stiffening and switch to a “survival” mode by plastic adaptation when the mechanical perturbation becomes overwhelming. While such behavior is critical in the developmental stages of life designed artificial systems has not been able to display such a level of sophistication so far.

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Tailoring surface chemistry of colloidal nanomaterials for life science applications

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In the last years, the extraordinary advances in the field of nanomaterial science have resulted in a great potential for applications in life science.

A variety of preparative and post-preparative colloidal routes have demonstrated able to obtain a wide choice of nanoparticles (NPs) and nanocrystals (NCs), with different compositions, that can be achieved with a high control on size, shape and surface chemistry, ultimately tailoring their electronic, optical, magnetic, thermal and chemical size dependent properties. A range of functionalization strategies have been developed to suitably engineer the surface of NPs and NCs and tune their specific chemical reactivity towards the surrounding environment. The control of nano-bio interfaces has demonstrate essential to enable nanomaterials conjugation and combination with biologically relevant entities, thus producing advanced materials for diagnostics and therapy. The ability of engineering the surface of specialized nanomaterials, such as emitters, plasmonic and magnetic nanostructures, with tailored procedures, allows to ingeniously combine them with a variety of nanocarriers, such as silica nanostructures [1], lipid-based (e.g. micelles, liposomes, solid lipid nanoparticles) as well as polymeric nanoparticles [2], in unique nanoplatforms, able also to incorporate drugs or other functional agents and target them to the specific disease sites.

Such nanoplatforms present all a great potential in the clinical field, as their photoactivity and/or magnetic properties along the targeting, drug delivery ability, can be decisive for application in diagnosis and treatment of different diseases, including cancer and neurodegenerative disorders.[1-6]
Examples of drug delivery, labelling, diagnostic and theranostics systems, based on Vis-NIR photoactive nanomaterials, plasmonic nanostructures and magnetic NPs will be reported.

Acknowledgments: the work has been supported by Italian PON TITAN-Tumor Immunotherapy by Nanotechnology (ARS01_00906), the University of Bari Horizon Europe Seeds Project BIOMAD and Bilateral CNR-RFBR Project (2021-2023).

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Searching for porous materials for sorption, separation, and catalysis - from non-covalent systems to porous organic polymers

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Porosity is one of the basic textural and structural characteristics of solids. Porous materials are the subject of intensive research due to a number of extremely interesting properties and potential applications, e.g. in the storage and separation of molecules, catalysis or drug encapsulation [1-2]. The main challenge is to design porous materials in such a way that they have specific shape and size of the pores, exhibit permanent porosity, and can play specific functions due to the presence of functional groups.

Due to the nature of interactions between building units, porous materials with a defined structure include Metal-Organic Frameworks (MOF), Covalent Organic Frameworks (COFs), Porous Organic Polymers (POP) and less common non-covalent Porous Materials (NPM), where molecular building units are stabilized only by weak non-covalent interactions.

In the first part of the presentation, examples of porous materials designed by us with the use of various types of interactions between building units will be presented [3-5]. Potential possibilities of using these materials in the sorption of gases and vapors, separation of hydrocarbon molecules as well as innovative drug delivery systems will also be presented.

In the second part our simple strategy of tandem post-synthetic modification of metal nodes in selected mesoporous MOFs based on solvent-assisted ligand incorporation (SALI) protocol will be discussed [6]. Our approach allowed us also to investigate the influence of the co-catalyst moieties inside introduced in close proximity to the inorganic nodes, and perform a more detailed analysis of factors governing the structure−reactivity relationship in a model MOF-based heterogenous catalytic system.

This work was supported by National Science Center, Poland, Grant No. UMO-2014/14/E/ST5/00652 as a part of the project entitled “Development of new strategies for synthesis of inorganic-organic porous materials.”

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Molten salts to address the solid-state chemistry of nano-objects

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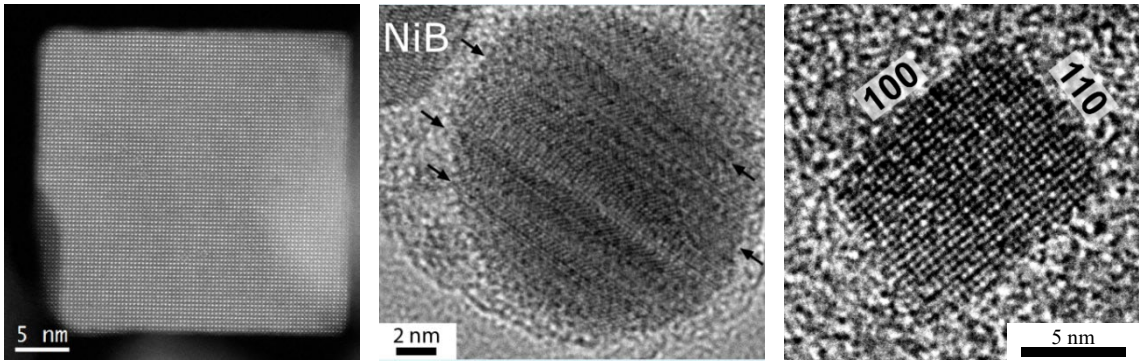
Nanoparticles enable the emergence of properties that can be used to address urgent challenges of energy conversion and storage, medicine, information and communication technologies. They also offer an opportunity to address fundamental questions pertaining to the relationship between crystal structure, surface states, solids reactivity and properties. Most nano-objects currently accessible rely on relatively common solids, like eg. binary oxides, metals and alloys. On the opposite, more complex compositions and crystal structures are mostly known in bulk solids despite their unique properties. For instance, the specific (electro)catalytic properties of metal-metalloid compounds could be enhanced by controlling the nanoparticle size [1,2]. Because these solids are traditionally obtained by conventional high-temperature solid-state reactions, their synthesis as nanoparticles is a strong challenge and is intimately linked to the development of synthesis methods.

In this talk, we will show that by taking inspiration from natural geological events, we can lay out reaction pathways towards nano-objects of original compositions, structures, and then properties. We will especially focus on the use of inorganic molten salts as reaction media [2], some of them being met in Nature. Through some case studies picked out of the families of perovskite oxides [3], mixed anionic solids, metal borides [4], boron carbides [5], and metal silicides|6,7], we will show that these inorganic liquids enable addressing several questions: how to tune the reaction pathways into high temperature liquids towards nano-objects of selected solids? How to trigger deviations to ideal compositions and structures within original nanocrystals? How to adjust surface reactivity and develop efficient water splitting electrocatalysts? How to process molten salts-derived nanoparticles into nanostructured bulk materials to tune mechanical, charge and heat transport properties?



(Left) $La_{0,6}Sr_{0,4}MnO_3$, (middle) NiB, and (right) NaB_5C nanocrystals synthesized in molten salts.

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Hybrid Plasmonic thin-films for SERS-based sensing in solution and in gas phase

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Plasmonic nanoparticles made of Au and/or Ag exhibit unique and tuneable optical properties in the visible-NIR range that have been extendedly exploited in a wide range of sensing and imaging applications. On the other hand, Surface-enhanced Raman scattering (SERS) is a powerful analytical technique that uses plasmonics to obtain detailed chemical information of molecules or molecular assemblies adsorbed or attached to nanostructured metallic surfaces. Therefore, the fabrication of novel hybrid plasmonic platforms based on the synergetic combination of plasmonic nanoparticle (NPs) assemblies with either organic or inorganic thin films such as, Zeolitic imidazolate framework-8 (ZIF-8) or molecularly imprinted polymers (MIPs) would give rise to SERS substrates with highly sensitive and selective capabilities. Both approaches comprises a two-step procedure, first, the layer-by-layer deposition of the plasmonic NPs on glass and their further coating with a uniform inorganic/organic thin film. Herein, we will describe the fabrication of MIP thin film with Au NPs assemblies, noted as Au@MIP, for the SERS-based recognition of polycyclic aromatic hydrocarbons (PAHs) in aqueous media 1]. Additionally, the synthesis of thin films constituted of close-packed core–shell Au@Ag nanorods individually encapsulated within a ZIF-8 framework (Au@Ag@ZIF-8) will be described and their SERS-based gas sensing capabilities will be explored [2].

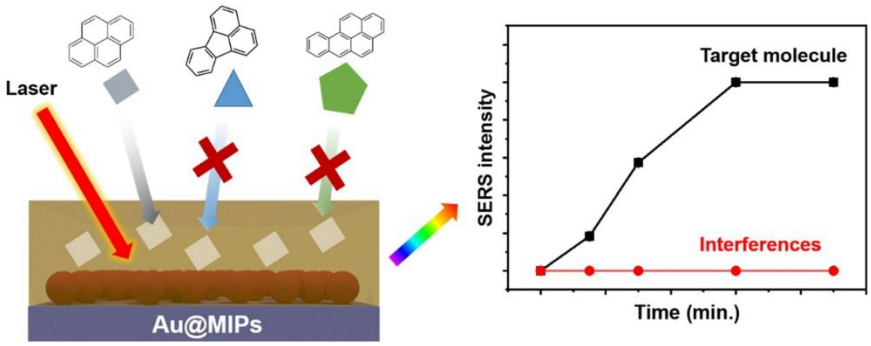

Figure 1. Schematic representation of the Au@MIP sensing platform.

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Computational approaches towards bioinspired dynamic materials

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Nature builds dynamic materials and complex molecular systems possessing characters and unique functional properties that far exceed in terms of performances, efficiency and fidelity the conventional synthetic technological materials. Typically, these are supramolecular systems built via self-assembly of fundamental building blocks (e.g., proteins, lipids, peptides, to name a few) that interact with each other forming assembled structures in continuous dynamic exchange and communication with the external environment. Notable examples are microtubules, tubulin protein assemblies capable of converting chemical energy into mechanical forces and motion. Other examples are leukocyte cells, capable to bind surfaces and to autonomously scan them in search of specific marker groups indicative of, e.g., inflammations or tissue damages.

Learning *a priori* how to design artificial molecular systems with similar programmable bioinspired properties would be a breakthrough in many fields.[1] However, the molecular factors that control such dynamic behaviors are often difficult to catch, and the design of such materials typically still relies on inefficient trial-and-error approaches.

Recent computational efforts combining multiscale molecular models,[2] advanced computer simulation approaches[3] and machine learning[4] show that molecular simulations are a key support to reaching such an ambitious goal. Providing high-resolution insights into such complex systems, molecular models allow to studying the key factors imparting to artificial assemblies bioinspired stimuli-responsive,[5,6] dynamically reactive,[7] chemotactic,[8] and/or living behaviors[9] proper of natural systems. The fundamental knowledge that can be obtained holds great potential towards the rational design of next-generation dynamic materials and programmable molecular systems for many technological applications.

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Tailoring magnetic and topological fingerprints in graphene nanoribbons

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Graphene nanoribbons (GNRs) -narrow stripes of graphene- hold great promise for nanoelectronics, due to their unique combination of highly desirable properties such as atomic thinness, chemical stability and ultra-high electron mobility. Other remarkable properties recently discovered in GNRs are the existence of stable spin-polarized and exotic quantum topological states. These extraordinary findings have been enabled by a novel chemical tool named on-surface synthesis (OSS), emerged in the last decade as a bottom-up strategy to produce atomically precise graphene nanostructures. [1]

In this talk, I will review some recent studies on magnetism and topology of GNRs, performed in close collaboration with our experimental colleagues.[2-3] In particular, using Density Functional Theory (DFT) and model calculations, we have investigated the topological properties of nanoribbons with different edge conformations, such as chiral and armchair GNRs. Our findings show that the topological phase of these systems can be tuned by modifying their width or shape, and that spin-polarized states of topological origin can be induced in GNRs by substitutional doping with boron atoms. In combination with Scanning Tunneling Microscopy (STM) experiments, our results demonstrate that spin and topological states can be engineered in GNRs, turning them into promising elements for spintronic and quantum applications.

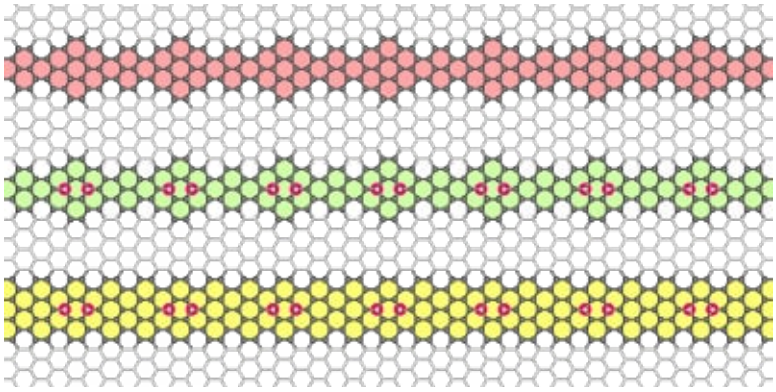

Figure 1: Atomic structure of some of the investigated pristine (top) and boron-doped GNRs (middle and bottom), overimposed on graphene's lattice for visualization purposes.

Thanks to the European Union (EU) through Horizon 2020 (FET-Open project SPRING Grant No. 863098), the Spanish Ministry of Science and Innovation (PID2019-107338RB-C66), the Basque Department of Education (IKUR Strategy and PIBA-2020-1-0014), the Provincial Council of Gipuzkoa (RED Gipuzkoa Next 2021-CIEN-000070-01).

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Spectroscopy and transport in defected 2D materials

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Interest in the optoelectronic properties of 2D materials has increased due to the discovery of the coupling between spin and valley degrees of freedom in transition metal dichalcogenides (TMDs), which can be manipulated experimentally using a circularly polarized laser. After excitation the newly formed carrier populations move towards the other valley until balance is reached. However, this relaxation process is not entirely understood in the literature, where the relative importance of the electron-electron and electron-phonon interactions is still a subject of debate. Using a fully ab-initio framework [1] we study the influence of the e-p interaction on MoSe2 after its excitation by a laser field. We show how phonons allow carrier relaxation and how the Kerr signal and total magnetization are affected at different temperatures, with the latter exhibiting a non-monotonic behaviour as the temperature increases [2].

An important conclusion was that long lived spin states probably reside within defects, which pushed us to consider the spectral signatures of different types of point defects in TMDs (figure). We find two main classes based on the presence of in-gap states, and estimate the experimental resolution needed to provide quantification of the defect concentration [3]. In hexagonal BN the negatively charged boron vacancy (V_B-) has been proposed as a qubit candidate for solid state quantum computing. Its photoluminescence dynamics is central to the preparation and readout of qubits, but is not well understood. Here we combine the approaches used above for electron phonon dynamics with those for defects: we use many body quantum dynamics within the Bethe Salpeter equation, and incorporate the coupling with phonons to analyse the deceptively simple photoluminescence spectrum of V_B-[4].

The localization of excitonic states around defects provides a benchmark for scanning probe characterization and sample quality control, and opens vistas for quantum computing platforms based on 2D materials.

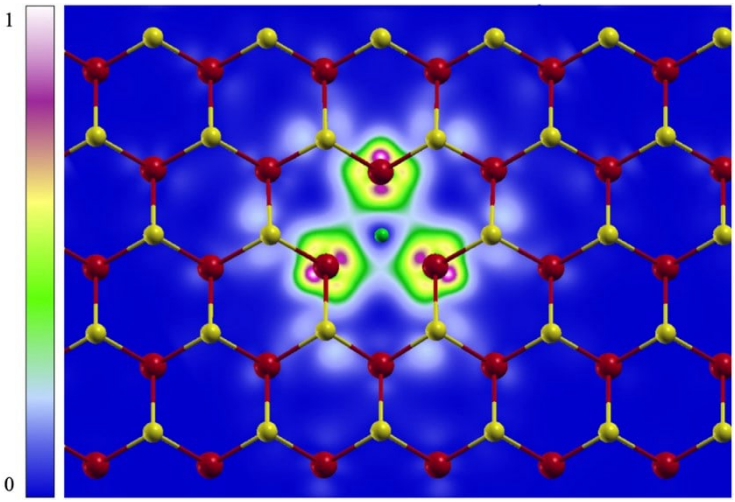

Figure 1: Exciton wave function around a chalcogen vacancy in WS2

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Direct Access to Organic-Inorganic Hybrid Materials through Hydrothermal Synthesis

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In organic-inorganic hybrid materials' synthesis, it is intrinsically challenging to, at the same time, achieve (i) the concomitant synthesis of the components, (ii) nanoscopic interpenetration of the components, and (iii) covalent linking of the components. Here, we discuss the potential of hydrothermal synthesis (HTS) to achieve all three aforementioned goals in one pot.

HTS is very well established for accessing inorganic materials, such as zeolites or various metal oxides. We could recently show, that different fully organic compounds, ranging from small molecules to linear polymers to networks can be generated by HTS.[1-3] Hydrothermal synthesis (HTS) of organic materials is strikingly simple: a dispersion of the starting compounds in water is enclosed in an autoclave, heated to the hydrothermal regime and kept there for the necessary reaction time. In the hydrothermal regime, water is (i) less polar than at room temperature and (ii) acts as both acidic and basic catalyst through its increased ionic product. Thereby, formation reactions of organic compounds become possible.

As both inorganic and organic materials have been shown to be attainable by HTS, combining their formation towards hybrid materials in one-pot seemed the next logical step. At the hand of several examples, we here discuss the technique's challenges and advantages towards inorganic-organic hybrids. The challenges comprise, e.g., finding the right reaction conditions that enable the formation of both components. The advantages, comprises, e.g., the generation of synergistic materials properties through the nanoscopic dispersion that results from the simultaneous formation of the components.

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Exploiting the role of metal atoms in MOFs with main group elements and ments of multiple cations

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Many of the physical and chemical properties exhibited by metal-organic frameworks (MOFs) are strongly dictated by the choice of metal elements that conform their crystal structures. For instance, MOFs built up from main group elements are highly attractive for their use as heterogenous catalysts due to their marked Lewis acid character. Through control and modification of the metal atom coordination environment, as well as the MOF network topologies, we have explored the use of MOFs built up with elements such as indium, gallium, or bismuth, as heterogenous catalysts in several chemical transformations, including multicomponent reactions. Additionally, MOFs that combine multiple metal cations within their structure continue to receive increasing attention because the possibility to combine various metal cations results in new or enhanced properties and behaviors. However, addressing the incorporation of selected combinations of various metal elements is still challenging. We have studied several MOF families composed of combinations of multiple metal elements, and found that the adjustment of the initial metal combinations has a key impact on the distribution of the cations within the MOF secondary building units, which can be exploited to obtain different types of atomic arrangements and sequences.

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Nanocrystal Coupled Dimers and Hybrid Nanostructures

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A growing interest has recently been devoted to the synthesis and organization of nanostructured materials in systems of increasing complexity. In nanoscopic regime, the electronic properties can be tuned by varying the physical size of the nanocrystal, leading to original or collective phenomena, as size-dependent electronic transitions in semiconductor quantum dots (QDs) or plasmonic oscillations in metal nanoparticles, mediated by the organic molecules coordinated at the surface of the nanocrystals and nanoparticles.

QDs synthesized by colloidal chemistry routes represent potential building blocks for inexpensive manufacturing of low cost and large area optoelectronic devices for application in detection, sensing, and lighting. Currently, intensive research has focused on the fabrication of QDs based organized meso and hybrid structures in solid state, which have shown new properties due to the collective interactions, , among nanoparticles or at the interface with molecular dyes. QDs with controlled size and shape, coupled and/or functionalized with suitable organic chromophores demonstrated efficient energy transfer (ET) and charge transfer (CT) processes.

Here, systems of QDs conjugated with organic dyes [1] or tightly coupled with other nanocrystals [2,3] have been investigated to understand the transfer phenomena occurring at organic/inorganic interfaces in both ET and CT processes The obtained results demonstrate as the control of the geometric parameters of the assembly and the size and distance between the organic and inorganic fluorophores can strongly influence the transfer rate and the coupling efficiency among the nano-objects and, then, their electronic properties, with possible relapse in photonic or optoelectronic application.

Acknowledgments
This work has been financially supported by the European H2020 FETproject COPAC (Contract agreement n.766563). The project MIUR PRIN 2015 n. 2015XBZ5YA is also acknowledged.

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Formulation of therapeutic deep eutectic systems targeting current challenges in pharmaceutical sciences

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The concept of green solvents was introduced by John Warner and Paul Anastas, in 1998, when they listed the 12 principles of green chemistry. One of these principles assumes that the use of solvents, should be as an auxiliary substances, in the synthesis and preparation processes, and emphasises that they should be made unnecessary wherever possible, and if used they should be innocuous.[1] The sustainability of a process or a product is, hence, a result of the complex interaction between the product or process implemented and environment, technology and economy factors.[2] In the current scenario of a worldwide quest for sustainable and "greener" alternatives for current applications, in the past two decades the number of reports on NADES/DES applicability in various situations has rapidly grown. The tailor-made versatility of these eutectics, meaning in practical terms a wide range of chemical and physical properties, has resulted in promising studies applied in industry, biotechnology, cosmetics, pharmaceuticals, food, and health.[3]

In pharmaceutical sciences, therapeutic deep eutectic systems (THEDES) could be used as a single mixture, providing higher dissolution rates of the API, enhancement of solubility, permeability and absorption through tissues, or they can be incorporated in suitable polymer to potentiate the efficiency of biomedical devices. The use of DES as therapeutic agents reveals to be very promising to enhance the characteristics of existing drugs and optimize or develop new formulations that could be easily administrated and more effective. In this communication the focus will be on the application and development of deep eutectic solvents in pharmaceutical field and their importance for the improvement of the API's properties, namely the increase of their bioavailability and the development of alternative therapies for high impact diseases such as tuberculosis or cancer.

Keywords
Pharmaceutics; Therapeutic deep eutectic solvents; Green chemistry; Tuberculosis; Colorectal cancer

Acknowledgements
This project has received funding from the European Union's Horizon 2020 (European Research Council) under grant agreement No ERC-2016-CoG 725034 and was supported by the Associate Laboratory for Green Chemistry-LAQV which is financed by national funds from FCT/MCTES (UIDB/50006/2020).

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Nucleoside phosphonate prodrugs as prominent source of hepatitis B virus (HBV) inhibitors

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Small molecule oral treatments currently approved against hepatitis B virus (HBV) comprise nucleoside analogues [lamivudine, entecavir (ETV), and telbivudine] and acyclic nucleoside phosphonate prodrugs [adefovir dipivoxil, tenofovir disoproxil, and tenofovir alafenamide (TAF)]. However, these drugs are not effective for achieving HBV eradication, and chronic HBV infection remains endemic in many areas with an estimated 296 million people infected worldwide (2019, WHO) as well as the leading cause of end-stage liver diseases. Moreover, these figures can be expected to increase over the coming decade, particularly in low-income countries. Current efforts by our group are devoted to identifying novel nucleoside phosphonates that could completely inhibit the HBV polymerase to avoid accumulation of nuclear covalently closed circular DNA (cccDNA) molecules that are responsible for viral persistence and reactivation. To this end, we synthesized three series of nucleoside phosphonate prodrugs featuring either a cyclic (e.g., phosphonomethoxydeoxythreosyl) or acyclic [e.g., 3-fluoro-2-(phosphonomethoxy)propyl, 2-ethynyl-3-hydroxy-2-(phosphonomethoxy)propyl] sugar moiety connected to natural nucleobases, which exhibited potent in vitro anti-HBV activity. Effective synthetic routes were designed that allowed to gain access to multigram quantities of these compounds for further in vivo studies. Selected prodrugs were demonstrated to effectively inhibit the replication of ETV-resistant HBV and significantly reduce HBV cccDNA in cell-based assays. An antiviral efficacy comparable to TAF was observed for these prodrugs in a hydrodynamic injection-based HBV mouse model.

Towards selective delivery of novel metal-based photosensitizers for anticancer photodynamic therapy

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Photodynamic Therapy (PDT) has expanded the range of treatment opportunities for some fungal and bacterial infections and cancer. The first clinically approved photosensitizer (PS) was Photofrin®, which is used to treat various types of cancer (e.g., non-small lung, bladder, oesophageal or brain cancer). As the majority of clinically accepted and investigated PSs are based on the same structural scaffold, these compounds are usually associated with similar drawbacks (e.g., poor water solubility, tedious synthesis and purification, photodegradation and slow clearance from the body causing photosensitivity). To overcome these limitations, existing PSs have been modified and new classes of PS developed. As an emerging class of compounds, Ru(II) polypyridyl complexes have gained much attention due to their attractive chemical and photophysical properties (e.g., high water solubility, high ROS production, chemical stability and photostability).[1, 2] Despite recent research efforts, the majority of investigated Ru(II) polypyridyl complexes lack absorption in the biological spectral window (600-900 nm), limiting their use for the treatment of large or deep-seated tumours. During this talk, we will present our latest results (including *in vivo*!) on the use of novel Ru(II) polypyridyl complexes as long wavelength absorbing PSs for PDT. We will also discuss our recent endeavours to selectively bring our PSs to cancer cells.[3-7]

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Development of novel diagnostics and antibody-drug-conjugates using a combination of click chemistry and enzymatic ligation

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Recombinant antibodies currently attract the majority of pharmaceutical research and development investment and therapeutic success can be seen in various areas of medicine. Progress in diagnostic imaging is driven by the application of antibodies for molecular and functional imaging using various modalities. Nanomedicine plays an increasing role in the development of antibody diagnostics as well as therapy because of the potential for increased payload of both contrast agents and therapeutic molecules.

An ideal example demonstrating the potential of antibody-targeted nanomedicine are single-chain antibodies (scFvs) directed against the integrin αIIbβ3. These scFvs are not only targeting an epitope that is specific for platelets but also to the activated form of the αIIbβ3 receptor thereby providing unprecedented specificity towards activated platelets. This allows the development of diagnostic approaches for the detection of thrombosis or emboli as well as many inflammatory processes in which platelets are involved such as atherosclerotic plaque instability and ischemia reperfusion injury.

We have developed several generally usable approaches to couple various tracers and nanoparticles to these scFvs. These approaches include genetic, biological (e.g. sortase coupling) and chemical (e.g. click chemistry) approaches. The coupled products include various effector molecules, contrast reagents, radiotracers as well as particles such as liposomes, ultrasound microbubbles, iron beads, micelles and layer-by-layer particles. For imaging we used various modalities such as ultrasound, MRI, PET/CT and fluorescence imaging.

In conclusion, antibody targeted nanoparticles hold great promise to provide major advances in various fields of diagnostic imaging as well as therapeutic targeting, including the combination of both in personalised theranostic approaches

Acknowledgements
This work has been supported by the Australian National Health and Medical Research Council, Australian Research Council and National Heart Foundation.

Gated materials for drug delivery and biomedical applications

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Progress in bio-molecular chemistry and nanotechnology has recently resulted in the design of biologically inspired systems with innovative bio-related functions. A key issue in this field is the design of new "smart" systems based on nanoscopic structures and a variety of biomolecules which perform unprecedented functions, boosting areas such as bio-engineering, bio-sensing, bio-nanotechnology and drug delivery into new directions.[1] In delivery applications, the development of stimuli-responsive nanoscopic hybrid gated materials involving (bio)molecules as caps and showing the ability to release entrapped guests upon application of an external stimulus has attracted tremendous attention.[2] These devices contain a support that constitutes a reservoir in which certain compounds can be stored and molecules or molecularly appended objects attached on these containers that act as "gates", allowing the controlled release of entrapped molecules at will. Both components have been carefully selected and arranged to achieve a wide range of control functions. Capped materials have been mainly used in drug delivery but also other biomedical applications. Based on this, selected examples on controlled delivery for different applications will be shown.[3]

Acknowledgements: We thank the Spanish Government (project RTI2018-100910-B-C41) and the Generalitat Valenciana (project PROMETEO 2018/024) for support.

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A Bioorganometallic Journey from Peptide Bioconjugates to Novel Metal-based Antibiotics

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Our group uses the unique spectroscopic and chemical properties of organometallic complexes for research in biomedical applications. The experimental challenge is to identify air- and water stable organometallic compounds with the desired properties, and to devise methods for the mild, biocompatible synthesis of bioconjugates with these metal complexes.

This presentation will highlight various synthetic strategies to obtain bioactive metal-peptide bioconjugates that have been developed in our group, and will present some exemplary biomedical applications of such metal complexes and metal-peptide conjugates. I will show how the versatile reactivity of metal complexes can be matched with peptide chemistry and purification techniques. Potent novel anticancer agents based on a number of different metals such as Fe, Ru, Re, and Au were developed, characterized and tested for their antiproliferative activity against a range of different cancer cells. In-depth studies were carried out to study uptake and intra-cellular localization of the compounds, as well as their potential mode of action. Also, I will present novel organometallic-peptide conjugates with very potent antibacterial activities that even surpass that of a last-resort antibiotic, vancomycin. Importantly, these organometallic-peptide conjugates have a novel mode of action, allowing them to avoid the common mechanisms of bacterial resistance. As a promising outlook towards clinical applications, these conjugates can be optimized to have little toxicity against human cells and low hemolytic potential.

N. M.-N. acknowledges the help and support of the many coworkers and collaboration partners, postdocs, PhDs, and students of all levels who have contributed to the success of the group over the years. Also, funding from German and European Institutions that has enabled our research and the many international collaborations is gratefully acknowledged.

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Siderophores and their potential applications in the development of antimicrobials

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Urgent action is required to combat the ongoing threat of antimicrobial resistance. Trojan horse conjugates, in which antimicrobial agents are linked to nutrient carriers, such as iron-binding siderophores, aim to evade permeability-related resistance mechanisms through active transport of drugs into bacterial cells [1]. Whilst some Trojan horse antimicrobials are highly potent, many exhibit a lower antibacterial activity than their parent antibiotic. In the latter case, it is often difficult to determine the underlying cause of an observed drop in potency, as will be illustrated by means of a number of recent examples of siderophore-antibiotic conjugates with cytoplasmic drug targets. Inhibition studies with the corresponding drug target combined with bacterial uptake studies with the radioactive iron-mimetic $^{67}Ga^{3+}$ can reveal in how far an observed reduction or increase in antibacterial potency is due to a change in cellular uptake of the siderophore-antibiotic conjugate, a change in target inhibition or a combination of both, thus informing the choice of siderophore and the design of the linker between the functional components of a conjugate.

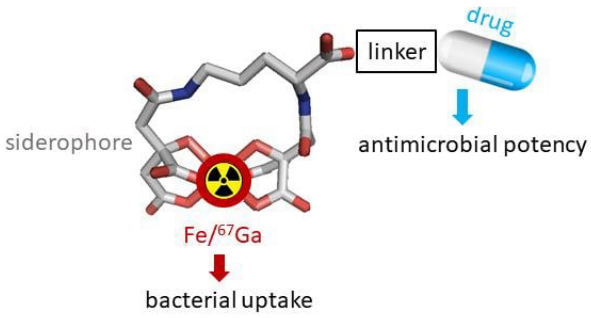

Figure 1: Schematic representation of a siderophore-drug Trojan horse conjugate.

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Supramolecular Medicine: From basic research to gluten-related disorders

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Supramolecular medicine (SupraMed) is defined as the supramolecular formulation of diagnostic and therapeutic agents to diagnose, treat, and prevent diseases. Additionally, in protein aggregation diseases like Alzheimer's disease or even cancer to develop a successful therapy, it is necessary first a profound understanding of the disease at the molecular and supramolecular level [1].

Our SupraMed approach focuses on the design, synthesis, (bio)-physicochemical and cellular evaluation of supramolecular systems based on small molecules and peptides in water. The final aim is to obtain a profound understanding of the relationship between molecular structure, morphology, and function in a biologically relevant environment and translate this fundamental knowledge into biomedical research. My presentation aims to show the power of SupraMed to investigate the early stages of hydrogel formation and to elucidate the role of gliadin oligomers in gluten-related disorders.

First, I will present the use of a short peptide, Ac-Phe-Phe-Cys-NH2 to evaluate the role of cysteine oxidation in amyloid hydrogel formation. We found that the intermolecular S-S formation promoted amyloid-type fibrils, meanwhile the fibrils were dissolved by chemical reduction and transformed into soluble oligomers. This report provided fundamental information on the modulation of amyloid fibrils by external stimuli [2].

Second, gluten-related disorders are the most common food intolerances in Western societies, affecting around 1-5% of the general population. In wheat gluten, gliadin protein is not fully degraded by humans, and an immunodominant peptide of 33 amino acids reaches the intestinal epithelium and lamina propia. It is well-defined that the 33-mer fragment triggers an adaptive immune response in susceptible individuals. However, the early events leading to activation of the innate immune response are not well understood. My research team discovered that 33-mer oligomerizes and forms different size oligomers and superstructures under physiologically relevant conditions. Based on the structural and morphological similarities with amyloid aggregation, we focused on immunological aspects, discovering that the presence of 33-mer large supramolecular structures induces an innate immune response in macrophages mediated by human Toll-like receptor 4 (TLR4) [3]. Moreover, we discovered that the presence of gliadin amyloid-type aggregates leads to the up-regulation of different chemokines in a suitable cellular model [4]. The latest findings on the mechanism of gliadin peptide oligomerization and the oligomers visualization in the cellular context will be presented.

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Macromolecular design in natural-origin hydrogels for tissue engineering applications

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Tissue Engineering has been integrating principles of engineering, chemistry, materials science, biology and health sciences in order to develop regenerative-based therapeutic strategies combining stem cells and biomaterials. From the different sources of biomaterials, natural-based polymers have been proposed to produce matrices able to interact favourably with cells. Due to their hydrophilic nature and richness in chemically active groups, such polymers can be used to produce a variety of structures fabricated using aqueous-based or other environmental-favourable procedures. Examples are shown on the precise chemical modification of polysaccharides, human-derived proteins and the surface of cells and processing of devices into different sizes and shapes with structural and functional characteristics suitable to be used in tissue engineering and regenerative medicine applications. The macromolecular design of the systems may be used to produce special hydrogels with improved mechanical properties and with special functionalities, including the self-feeding of cells through the enzymatic degradation of glucose-based polysaccharides. Distinct strategies involving bioinspired approaches and nano/micro-technologies will be shown to prepare hybrid soft systems containing cells, in the form of microparticles, microgels or liquified capsules, that could give rise to biomedical devices using bottom-up strategies.

Acknowledgements
This work was supported by the European Research Council grant agreement for the project “ATLAS” (ERC-2014-ADG-669858) and by the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020 & UIDP/50011/2020, financed by national funds through the FCT/MEC and when appropriate co-financed by FEDER under the PT2020 Partnership Agreement

Design and Function of Nanostructure Probes for Bacteria Discrimination

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There is an urgent need to develop a rapid and selective method for the detection of bacteria because delayed diagnosis and the overuse of antibiotics have triggered drug resistance in bacteria. In this study, we have developed novel nanostructure probes exhibiting a bacterial discrimination function using the phenylboronic acid as sugar recognition site and dipicorylamine metal complex as phosphate derivatives recognition site. The fluorecent silica nanoparticle (**Dpa-FSiNP**), in which dipicorylamine unit is introduced on the surface of fluorescent silica nanoparticles (**FSiNP**) containing a trisbipyridyl ruthenium complex having a red fluorescence color, exhibited no response for the Gram-positive bacteria such as Staphylococcus aureus (S. aureus). However the copper (II) complex of **Dpa-FSiNP** (**Cu-dpa-FSiNP**) was found to form large aggregates with S. aureus in 10 min. This response was easily confirmed by the naked eye (Fig. 1) [1].

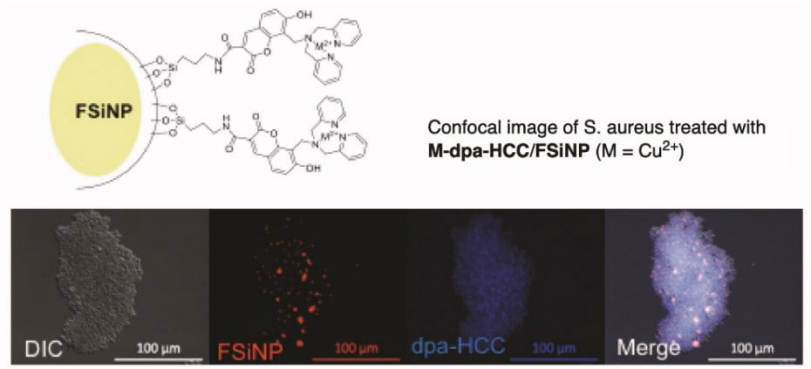
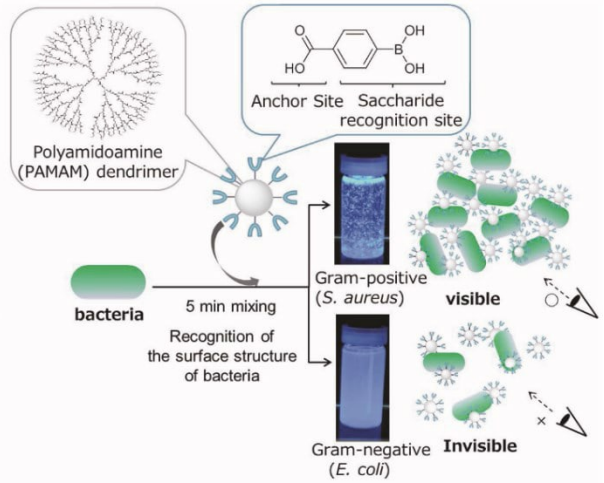


Fig. 1 Bacteria recognition by fluorescent silica nanoparticle modified with metal-dipicolylamine complex

We have also developed boronic acid-modified poly(amidoamine) generation 4 (**B-PAMAM(G4)**) dendrimer as cross-linking molecules that form aggregates with bacteria. Within 5 min of adding **B-PAMAM(G4)** dendrimer solution to a bacterial suspension, large aggregates were observed. Interestingly, the aggregate formation with various bacteria was pH-dependent. In basic pH, both Gram-positive and Gram-negative bacteria formed aggregates, but in neutral pH, only Gram-positive bacteria formed aggregates. We revealed that this bacteria-selective aggregation involved the bacterial surface recognition of the phenylboronic acid moiety of B-**PAMAM(G4)** dendrimer (Fig. 2) [2, 3]. These nanostructure probes are expected to be a powerful tool for the rapid and selective discrimination between Gram-positive and Gram-negative bacteria.



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Engineering Magnetic Nano-platforms to Combine Magnetic Hyperthermia with other Therapeutic Treatments for Tackling Cancer

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Heat is a very ancient tool to cure cancer. Among the different types of hyperthermia, approaches that enable to precisely deposit the heat in a specific body regions and with external and remote actuation, represent advanced heat treatments with less side effects. Among these approaches "magnetic hyperthermia" (MHT) exploits magnetic nanoparticles as heat agents that can be excited under alternating magnetic fields (AMF) of clinical use with no tissue-depth attenuation. In addition, magnetic nanoparticles that show superparamagnetic behavior at body temperature are also ideal carries for drugs or other therapeutic elements such as radioisotopes [1].

This talk aims at providing an overview of our last year's research to combine magnetic hyperthermia with other clinical accepted therapeutic modalities [2]. In particular, I will focus on combination of MHT with chemotherapy, [3] induced cytotoxicity [4] and internal radiotherapy based on Cu-64 radioisotopes [5]. In the first part of the presentation, I will describe our progress on non-hydrolytic methods for the preparation and scale up production of magnetic nanoparticles with benchmark heating performance for MHT. I will also provide an example of magnetic-semiconductor inorganic heterostructure which enables to merge MHT with photo-therapy and internal radiotherapy based on Cu-64. In a second part, I will report about our in vitro/in vivo studies on tumor cell models to determine the magnetic hyperthermia effects, with or without the association of chemotherapeutic drugs. Also, MNP-based platforms with cytotoxicity based on mild hyperthermia, toxic compositions and mechanical stressed based on the ability of magnetic nanoparticles to form chain under the AMF will be discussed. [1].

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Make them blink! - A chemistry approach to advanced fluorescence microscopy

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Advanced fluorescence microscopies including but not limited to super-resolution techniques have seen tremendous progress over the past 15 years. While in the early days the developments were mainly driven by improvements of the optical microscopes and associated procedures for data acquisition, more recent developments with protein tags and click chemistry have opened new opportunities for improving and creating novel fluorescent probes significantly contributing to the advancements in fluorescence microscopy. In this context, we have explored the use of reversible and irreversible chemical reactions to control the emissive and none-emissive states of fluorescent probes. This not only enabled alternative approaches for multiplexing but also resulted in novel probes for single molecule localization microscopy (SMLM) and correlative microscopy approaches in living cells.[1,2] Thorough studies of the involved photo physical process ultimately led to a new class of fluorescent probes that can be used in live-cell experiments without the need of further washing procedures.[3]

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Exploring new reactivity patterns through the organocatalytic activation of small– and medium–sized carbocycles

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In the last years, our group has been especially active in the development of new methodologies for the enantioselective synthesis of heterocyclic entities through organocatalytic cycloaddition reactions, using different organocatalytic activation manifolds.[1] More recently, we have evolved towards the use of the strain release associated to the ring-opening process of cyclopropanes as an expedient thermodynamic driving force that can lead to the identification of novel unconventional reactivity patterns under organocatalytic activation. In addition, ring strain does not only appear within small cycles but also shows up in compounds incorporating medium and large size carbo- and heterocyclic scaffolds in which unnatural bond angles are needed in order to close the cyclic architecture.

In this lecture, the different methodologies developed in our group for the stereoselective synthesis of relatively complex carbo- or heterocyclic compounds starting from strained starting materials will be presented. Our research has been conducted through two different approaches: (a) using ring strain to promote ring-opening processes on cyclopropane-containing substrates, generating a reactive polyfunctional intermediate, which can undergo subsequent chemical transformations, (typically a cycloaddition or rearrangement process)[2] and (b) using ring strain to promote a transannular reaction[3] in a conveniently functionalized large size carbo- or heterocyclic starting material.[4] All these reactions have been applied to the total synthesis of several examples of natural products or scaffolds with relevant biological activities.

Acknowledgments: This research was supported by the Spanish MCIU (FEDER-CTQ2017-83633-P and PID2020-118422GB-I00), the Basque Government (Grupos IT908-16) and the UPV/EHU.

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Enantioselective α-Arylation of Ketones via a Novel Cu(I) Bis(phosphine) Dioxide Catalytic System

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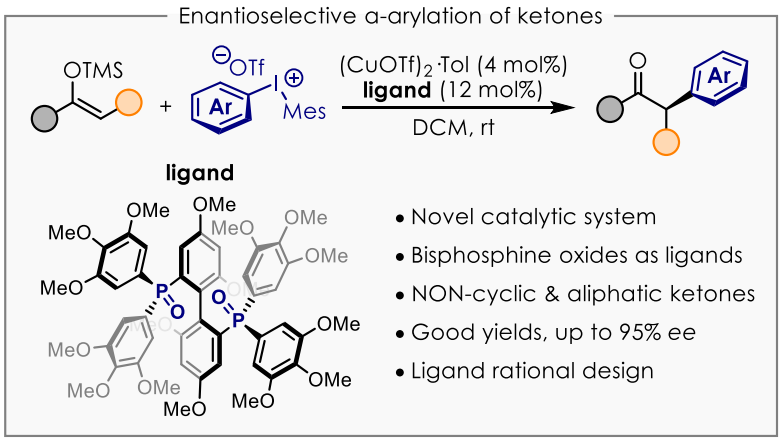
The transition metal catalyzed α-arylation of carbonyl compounds was first reported by Buchwald and Hartwig in 1997. This transformation has been used and studied extensively over the last two decades. Enantioselective variants were also developed that allow for controlling the product stereochemistry.[1] However, these suffer several limitations in the context of formation of tertiary stereocenters.[2] We present here our group's contribution to this research area.[2,3] We developed a novel catalytic system based on copper(I) and chiral bis(phosphine) dioxides as ligands. This allowed the arylation of silyl enol ethers to access enolizable α-arylated ketones in good yields and ee up to 95%. Noncyclic and dialkyl ketones are amenable substrates with this method, which was unprecedented and complementary to other approaches based on palladium catalysis.[4] Optimization of the ligand structure was accomplished via rational design driven by correlation analysis.[5] Preliminary studies concerning the reaction mechanism involving the unusual pairing of chiral bis(phosphine) dioxides with transition metal catalysts is also given.



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New Electrophilic Amination Strategies for N-Heterocycle Synthesis

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Our group develops catalysis platforms that enable the efficient generation of chiral building blocks and heterocyclic scaffolds. Selected recent highlights of our activities in N-heterocyclic chemistry will be presented, focusing specifically on aza-Heck reactions that are triggered by oxidative addition of N-O bonds to Pd(0)-complexes. The seminar will encompass methodological advances,[1] mechanistic aspects and applications in total synthesis.[2]

Representative Publications

[1] X. Ma, I. R. Hazelden, T. Langer, R. H. Munday and J. F. Bower; Enantioselective aza-Heck cyclizations of N-(tosyloxy)carbamates: synthesis of pyrrolidines and piperidines. *J. Am. Chem. Soc.* **2019**, *141*, 3356-3360.

[2] B. T. Jones, J. García-Cárceles, L. Caiger, I. R. Hazelden, R. J. Lewis, T. Langer and J. F. Bower; Complex polyheterocycles and the stereochemical reassignment of pileamartine A via aza-Heck triggered aryl C-H functionalization cascades. *J. Am. Chem. Soc.* **2021**, *143*, 15593-15598.

Developing new bio-based chemicals by direct functionalization of biomass with acetals

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The development of various renewable chemicals sustainable such as plastics or solvents from abundant renewable feedstocks has been limited by the complexity and efficiency of their production, as well as their lack of competitive properties. Here, I will discuss the direct integrated transformation of biomass into a functionalized lignin fraction that can be used as a surfactant, and a xylan derived solvent or polyester precursor at high yields (>80%)) by fractionation in the presence of multifunctional aldehydes. Using simple aldehydes such as formaldehyde can lead to diformylxylose production, which is an interesting polar aprotic solvent candidate that can be used for several commercially relevant reactions. Using glyoxylic acid as the aldehyde leads to a hydrophilic lignin fraction that can be used as a surfactant and a diacid from xylose that can be esterified and separated for use in polymer chemistry. Melt polycondensation of the resulting xylose-derived diester with a range of aliphatic diols led to high-molecular weight amorphous polyesters with combined high glass transition temperatures, tough mechanical properties, and strong gas barriers, which could be processed by injection-molding, thermoforming, and 3D-printing. These polyesters could then be chemically recycled from mixed plastic waste streams or digested under biologically relevant conditions. The production of these useful chemicals by straightforward acid-catalyzed functionalization during biomass fractionation could drastically simplify the production of several biobased chemicals.

Supramolecular Quantasomes for Artificial Photosynthesis

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All of Earth's oxygen is the result of water oxidation performed by photosynthetic organisms using solar light as the only energy source. The O_2 necessary for our aerobic life is produced by the photocatalytic cleavage of the extremely stable H-O-H bonds.(1,2) In the early studies, on Oxygenic Photosynthesis, the "quantasome hypothesis" led to seminal discoveries correlating the structure of natural photosystems with their complementary photo-redox functions.(1,2) According to this vision, Nature has evolved specialized "multi-component pigment-protein "quantasomes", working as one integrated photosynthetic "body" (from the Greek term "soma"), Indeed, and despite the vast bio-diversity footprint, just one protein complex is used by Nature as the H_2O-photolyzer: photosystem II (PSII). Man-made systems are still far from replicating the complexity of PSII, showing the ideal co-localization of Light Harvesting antennas with the functional Reaction Center (LH-RC). Here we report the design of multi-perylenebisimide (PBI) networks shaped to function by interaction with a polyoxometalate water oxidation catalyst (Ru_4POM).(3-5) Our results point to overcome the classical "photo-dyad" model, based on a donor-acceptor binary combination, with integrated artificial "quantasomes" formed both in solution and on photoelectrodes, showing a: (i) red-shifted, light harvesting efficiency (LHE>40%), (ii) favorable exciton accumulation and negligible excimeric loss; (iii) a robust amphiphilic structure; (iv) dynamic aggregation into large 2D-paracrystalline domains.(5) Our results include the X-ray diffraction analysis of a dense, quasi-hexagonal packing of the functional motif, showing a striking analogy with the coexistence of fluid-to-crystalline phases in the native photosynthetic membrane. Photoexcitation of the PBI-quantasome triggers one of the highest driving force for photo-induced electron transfer applied so far.(5) The modularity of the building blocks, the simplicity of the non-covalent chemistry and the biomimetic appeal of this approach, offer a unique opportunity for innovation in Artificial Photosynthesis.(6)

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Making and Breaking Chemical Bonds with Visible Light: Challenges and Opportunities

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Reactions involving phosphorus centered radicals play a pivotal role in the construction of organophosphorus ligands, biologically active and –conjugated scaffolds.[1] Common synthetic approaches for the generation of such radicals imply the use of harsh reaction conditions.

In this lecture, we show that access to a large variety of organophosphorus compounds can be achieved under mild reaction conditions through: *i*) visible light photoredox catalysis or *ii*) visible light irradiation of Electron–Donor-Acceptor complexes (EDA). The scope and limitations of these methods will be discussed with a special focus on their mechanistic aspects.[2]

Furthermore, applications of these approaches for the formation of C–C as well as C–Si bonds will also be covered.[3]

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Metal-based biocatalysts for sustainable production of H_2 and reduction of CO_2

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Most catalysts used for simple but important reactions such as producing H_2 or reducing CO_2 or N_2, rely mainly on expensive and rare precious metals, or energy intensive processes, strongly reducing the sustainability of associated technologies. Intensive research is addressing the development of alternative catalysts based on earth abundant materials, but efficiencies and selectivities are still far from desired. In nature these difficult transformations involving multi-electron and multi-proton reactions, are achieved by enzymes containing metal cofactors, which display outstanding catalytic efficiencies in mild conditions and using abundant metals. Many of these enzymes are oxygen-sensitive and susceptible to degradation, but recent technologies are remarkably extending the lifetime of such biocatalysts. Here I will present the characterisation of two remarkable metalloenzymes, a NiFeSe-hydrogenase[1] and W/Sec-formate dehydrogenase[2], both of which are highly active and show remarkable oxygen stability, as well as some variants with improved properties[3]. These enzymes are excellent model systems and have been exploited for development of biohybrid photo- and electrocatalytic systems[4,5], and are also the basis for whole-cell photocatalysis[6].

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High-resolution imaging of molecules by means of scanning probe microscopy

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It is a bit of an exaggeration to say that scanning probe microscopy represents our eyes and hands in the nanoworld. The invention of scanning microscopy in the 1980s not only enabled the atomic resolution of individual atoms on solid surfaces, but was also an important factor in the advent of the era of nanotechnology.

The development of scanning microscopy in recent years has brought another important milestone: the possibility of chemical resolution of individual molecules on solid surfaces [1]. This technique, combined with recent development of on-surface reactions, which are not available by traditional methods of chemical synthesis in solutions, opens up completely new possibilities for the preparation and characterization of molecular nanostructures [2].

In this lecture, we will introduce the basic principles of the high-resolution scanning probe microscopy, including the chemical resolution of individual molecules. Moreover, we will demonstrate a real-space image of the σ-hole associated with a strong anisotropic atomic charge distribution on halogen atom [3].

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Optical biosensors based on surface plasmons: advances and applications

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Optical biosensors are a promising technology that holds potential for applications in numerous areas, including molecular biology, medical diagnostics, environmental monitoring, food safety, and security. In the last two decades, optical biosensors based on surface plasmons (sometimes referred to as surface plasmon resonance (SPR) or plasmonic biosensors) have received much attention and have become the most advanced optical label-free biosensor technology [1, 2]. While plasmonic biosensors have been widely adopted to investigate biomolecular interactions, their penetration to bioanalytical applications has been somewhat limited so far.

In this paper, we discuss the main challenges in developing plasmonic biosensors for bioanalytical applications and present selected advances in plasmonic biosensor research that aim to address some of these challenges. Specifically, we present new approaches in plasmonic sensor instrumentation for parallelized detection of multiple analytes, discuss transport of target molecules in microfluidic systems of plasmonic biosensors and routes to improving the performance of nanoplasmonic biosensors and report on advances in the development of functional coatings for the detection of low levels of biomolecules in complex biological media. Finally, we present two applications of plasmonic biosensors related to the diagnosis of Myelodysplastic syndromes (MDS), a group of hematological malignancies with a risk of progression into acute myeloid leukemia (AML). First, we present a new extremely sensitive assay for detecting MDS-related microribonucleic acids (miR-125b, miR-16) and demonstrate that in conjunction with a plasmonic biosensor the assay enables the detection of miRNAs in blood plasma with a limit of detection < 350 aM [3]. Second, we use a plasmonic biosensor to quantify interactions between selected MDS-related proteins (ICAM, VCAM, fetuin, LRG, clusterin, and S100A8) immobilized on the surface of the plasmonic imaging sensor and blood plasma of MDS patients and healthy donors and show that this interactomic approach can discriminate among different MDS subgroups as well as between MDS patients and healthy donors [4].

This research was supported by the Czech Science Foundation under contract #20–23787X.

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Quo Vadis, Mid-Infrared Spectroscopy? From Exhaled Breath Analysis to In-Vivo Biodiagnostics

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Vibrational spectroscopies - and especially infrared spectroscopy - apparently play an increasingly important role in modern biodiagnostics. This begs the question - quo vadis, where do we go from here?

With applications ranging from non-invasive exhaled breath analysis to the in-vivo assessment of cartilage damage, mid-infrared (MIR; 3-20 µm) photonics ranges among the most flexible molecular sensing platforms nowadays available. With the emergence of quantum and interband cascade laser technology, the on-chip hybridisation and/or integration of entire MIR sensing devices is on the horizon ultimately leading to IR-lab-on-chip systems. The inherent molecular selectivity of MIR signatures enables studying small molecules (e.g., volatile organic compounds; VOCs) in the gas phase, as well as biomacromolecules (e.g., proteins) in the liquid phase at unprecedented detail in a label-free and non-destructive fashion. Most importantly, the combination with advanced multivariate data evaluation algorithms facilitates analyses in real-world complex mixtures of biomedial and clinical relevance. The discussion of latest MIR photonic technologies we will be complemented by highlight applications underlining the utility of next-generation MIR photonics.

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Dye Doped Silica Nanoparticles as Photoactive Organized Systems for Nanomedicine

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Silica nanoparticles are versatile platforms with many intrinsic features, including a low toxicity. Their proper design and derivatization yield particularly stable bright nano-systems displaying multiple functions [1], which can be used for either optical and photoacoustic imaging [2] and for photoluminescence (PL) and electrochemiluminescence (ECL) sensing [3]. In addition, silica nanoparticles can also be used as platforms for photodynamic and photothermal therapies [2]. For these reasons, silica nanoparticles offer unique opportunities, and further improvement and optimization can substantially expand their possible applications in fields of high impact, such as medical diagnostics and therapy, environmental analysis, and security.

In this context, we have developed a direct micelle assisted strategy based on the use of Pluronic F127 as high molecular weight surfactants. The one-pot synthesis yields PEGylated silica nanoparticles endowed with very high monodispersity, colloidal stability and core-shell structure. These Pluronic Silica NanoParticles (PluS NPs), with a silica core of about 10 nm and an overall hydrodynamic diameter of about 25 nm, can be tailored for optimization of processes such as directional energy transfer, providing systems with extremely valuable functions: high light-harvesting capability, signal-to-noise maximization, multiplex output, and signal amplification. A proper use of the silica precursor can allow to tune important properties of the silica core, such as polarity and permeability to oxygen [4]. *In-vivo* experiment proved the absence of toxic effects on mice even after three months from injection [5]. A library of functionalized Pluronic surfactants allowed for a straightforward and modular method for surface derivatization, a fundamental step since we found that their possible applications can be controlled by nanoparticle functionalization; the control of surface charge (density and localization) allows, for example, for sentinel lymph node targeting [5]. Furthermore, we demonstrated their ability to act as nanoantioxidants [6] and that the drug loading ability can be tuned with a suitable choice of the silica precursor [7]. Finally, we investigated the interaction with fluorogenic hyaluronan, a synthetic nanogel that improves cell internalization of PluS NPs [8].

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Tailoring electrochemical sensor materials for novel sensor platform architectures

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The choice of electrode materials and electrode modifier materials can offer significantly improved control of electrode reactions in terms of electrocatalytic effects, selectivity and sensitivity, which impacts in many fields of electrochemistry. Materials for sensor and biosensor platforms additionally need to obey the requisites of stability, lead to good analytical parameters and be sufficiently reproducible, which is influenced by their nanostructure. The use of carbon nanomaterials as modifiers has become widespread as well as that of metal or metal oxide nanoparticles. This can be combined with electrodeposition of films of electroactive redox polymers prepared from phenazine or triarylmethane dyes, as redox mediators, to give further enhancement of the sensor performance [1,2]. Benefits of modification by carbon nanomaterials and gold nanoparticles and the resulting synergistic effects can be evidenced, by themselves and as enzyme biosensors [3].

The electropolymerisation of phenazines and triarylmethanes on electrodes of carbon or modified with carbon nanomaterials exhibits interesting electrochemistry. The microenvironment produced by the polymers is also suitable for the immobilization of enzymes and other biomolecules. This has been explored in aqueous electrolytes and in deep eutectic solvents (DES) which rely on strong hydrogen bonding interactions to give sufficient conductivity, especially if acid-doped, and are normally of low toxicity [4]. The high viscosity influences the rate of polymer nucleation and of polymer growth, normally leading to improved polymer deposition compared to aqueous electrolytes. Polymerisation in several DES has been investigated, particularly in ethaline (choline chloride: ethylene glycol in a 1:2 ratio). It has been demonstrated that polymerization of phenazine dyes in acid-doped ethaline on nanomaterial modified electrodes increases the polymer surface uniformity and leads to improved sensing capabilities, better electrocatalytic effects and film stability than in aqueous electrolyte. Composites of these nanostructured redox polymer films plus carbon nanotubes, iron oxide (Fe_2O_3), CuO or Prussian blue nanoparticles are successful combinations [5-8]. They will be used to demonstrate the strategy followed for the construction, characterisation and application to key environmental, food and pharmaceutical analytes, of such sensors, enzyme biosensors and enzyme inhibition biosensors.

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Mid-IR Laser-Based Photothermal Spectroscopy: New Opportunities for Sensing and Imaging

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Advances in Instrumental Analytical Chemistry are often linked to technological developments in neighboring disciplines. This is the case with respect to recent advances in Mid-IR quantum cascade lasers (QCLs) which are increasingly used as a new light source in mid-IR spectroscopy. QCLs offer high spectral power densities, fast amplitude and frequency modulation possibilities, polarized and coherent radiation. Based on these properties a range of new sensing schemes, often clearly outperforming established FTIR based analyzers, have been developed recently. This presentation will center on photothermal sensing schemes for trace analysis of gases, liquids as well as label free mid-IR imaging with nanometer spatial resolution. As opposed to established mid-IR absorption spectroscopy based on Beer´s law, mid-IR photothermal spectroscopy is an indirect method where the generated analytical signal scales directly proportional to the laser power. In one way or another it detects temperature induced changes (refractive index changes, sample expansion) in the sample matrix which are caused by absorption of the mid-IR photons by the present analyte.

After introducing the general concept of QCL based photothermal spectroscopy in comparison to absorption spectroscopy, applications will be shown covering different fields. For trace gas sensing interferometric cavity assisted photothermal spectroscopy (ICAPS) will be introduced [1]. This technique uses a Fabry-Perot interferometer to read out temperature induced refractive index changes in gaseous samples and achieves single digit ppb sensitivities for SO_2, CO and similar IR active gases. ICAPS employs CW operated frequency tunable distributed feedback QCLs as an excitation source to target isolated ro-vibrational transitions of the target gas molecule and an NIR probe laser to monitor the induced refractive index changes. With respect to the analysis of liquids trace analysis of water in organic solvents will be shown and introduced as an alternative to Karl Fischer titration. This technique uses a broadly tunable pulsed external cavity QCL for measuring the characteristic bending vibration of condensed water. Again temperature induced refractive index changes are read out, this time using a HeNe based Mach Zehnder Interferometer with one arm containing the liquid sample in a flow cell. [2] Nanometer spatial resolution in mid-IR imaging is achieved by coupling an atomic force microscope to a broadly tunable pulsed EC-QCL source (AFM-IR). Using resonant enhancement and applying multivariate modelling the intracellular distribution of cell components can be revealed. This has been demonstrated by imaging the distribution of major cellulases and xylanases in *Trichoderma reesei*, using the co-location of a fluorescent label (enhanced yellow fluorescence protein, EYFP) with the target enzymes to calibrate the chemometric model. [3] The obtained PLS model successfully shows the distribution of these proteins inside the cell and opens the door for further studies on protein secretion mechanisms using AFM-IR.

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Mass Spectrometry in urban water profiling for environmental and public health assessment

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The year 2020 witnessed a crisis in healthcare systems due to the COVID19 pandemic. SARS-CoV-2 has had an unprecedented impact on humanity globally. It exposed the acute inability to manage the virus due to lack of reliable surveillance systems focussed on rapid identification of SARS-CoV-2 hotspots. Wastewater-Based Epidemiology (WBE) has since enabled SARS-CoV-2 surveillance. Post-COVID applications will include the development of big data driven WBE systems for other biological, chemical and physical threats. Mass spectrometry will play critical role in identification and quantification of biomarkers informing environmental and public health. This talk will introduce the concept of WBE and its rapid advances. It will also explore new avenues in the utilization of urban water fingerprinting with mass spectrometry in the assessment of population health and health risk prediction.



Microcavity Supported Lipid Bilayers: Versatile Microfluidic Models for Biophysical Studies of Membrane Proteins and Lipids

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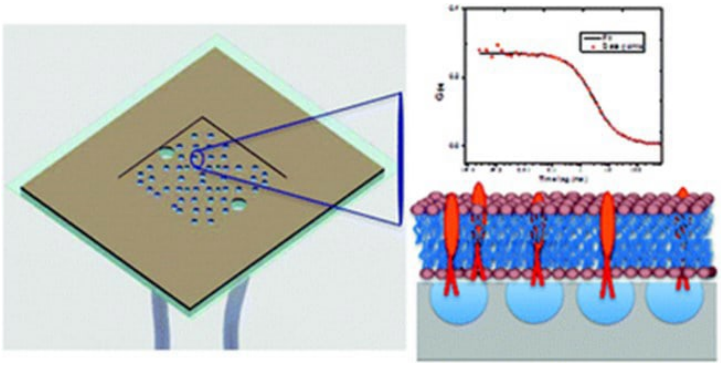
Artificial models of biological membranes can provide valuable insights into the behaviour of the membranes lipids and associated proteins by mimicking key facets of the cell membrane structure decoupled from the challenging complexity of the living cell. Key requisites of an ideal biophysical model of the cell membrane are that the mobility of both the lipid matrix and its components are unhindered by any underlying support and that asymmetric distribution of lipids is controlled across each leaflet. Combined, these characteristics are not trivial to accomplish in a single model. Whereas for example, liposomes accomplish high lateral lipid mobility, their individual leaflet compositions are difficult to control. While conversely leaflet compositional control is easily accomplished in supported lipid bilayers, the mobility of constituent proteins in such platforms can be compromised. Herein, we overview a versatile cell membrane model platform for study of membrane proteins and membrane permeation developed by our group that addresses these requisite characteristics. The platform, coined Memsense, Figure 1, comprises lipid bilayers assembled over surface modified, buffer-filled, arrays of spherical cap microcavities formed in polymer or metal.



The platform is built into a simple flow -through microfluidic platform suitable for fluorescence correlation spectroscopy (fig 1) or as an electrode for interrogation by electrochemistry or by Raman spectroscopy when fabricated in gold.

So it is highly versatile and addressable by multiple analytical modalities.

Examples of the utility of the platform will be discussed across diverse applications; including
(i) As supports for the study of membrane and peripheral proteins
(ii) A simple model of membrane repair using light induced Annexin aggregation
and
(iii) A model for understanding drug delivery and endosomal escape from delivery vehicles.

Acknowledgment
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Nanostructuration, The key for the understanding of ionic fluids properties

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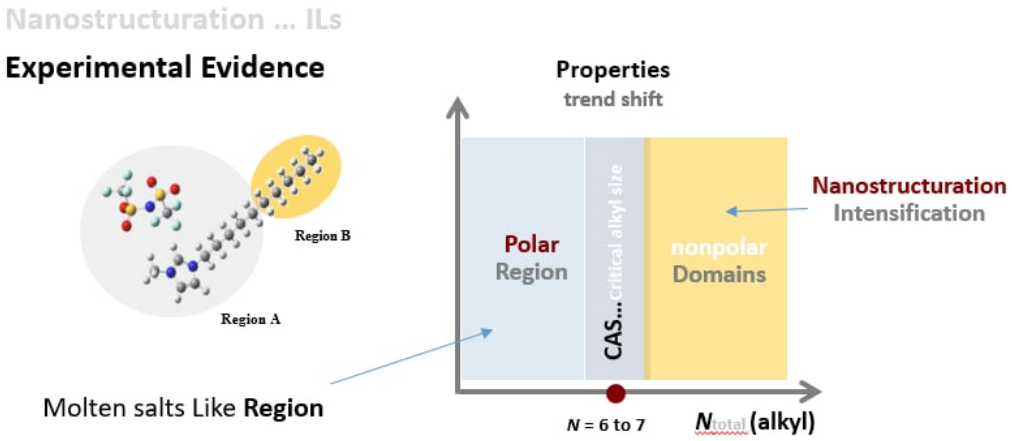
In the last years, it was found that the nanostructuration plays a major rule on the interpretation of physical chemistry properties of ionic liquids families. Ionic liquids form nanoaggregates constituted by anions and cations giving rise to a network of polar regions ruled by coulombic forces and nonpolar ones corresponding to regions of alkyl chains dominated by van der Waals interactions.

The nanostructuration in the ionic fluids affects the trend of properties along the series and is dependent of the alkyl chain size, cation and anion nature. In some recent publication [1-5].We were able to give additional support to the nanostructuration effect on the thermodynamic and transport properties on several ionic liquids families.



A significant differentiation of the trend of the thermodynamic properties before and after CAS (critical alkyl size of n=6) was observed due to the change of the cohesive electrostatic potential that rules the network packing both in solid and liquid phases. Further studies allowed us to unravel the role of IL nanostructuration and acidity on the preferential interactions established between the alcohol and the IL, the speciation and cohesive energy of protic ionic liquids [6] as well as their nucleation and growth of micro droplets of ILs deposited by physical vapor method onto different surfaces.[7]

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Fit for the purpose supercapacitors: A new path to enable electrochemical energy storage

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The energetic transition is raising many challenges and many traditional and emerging sectors are demanding energy storage solutions meeting the application requirements. This is coming in force in different sectors, from portable electronics, mobility and stationary storage to biomedical and smart wear.

Nowadays the market is dominated by the conventional carbon ultracapacitors (low energy-high power densities) and batteries (high energy-modest power densities). Between these two families of systems there is an important gap. To fill this gap it is crucial to design new materials and to combine them appropriately, to fully explore their electrode potential. Such strategy enables the development of hybrid or asymmetric electrochemical energy storage devices with tailored metrics that meet the application requirements. Thus, electrode materials play a pivotal role in defining the metrics of the energy storage device and this research area paves the way to solve many bottlenecks in the electrochemical energy storage field.

This presentation overviews the latest advances in the design, production and testing of electrode materials, including hybrid materials, and their potential applications in a novel generation high power and higher energy devices. The electrodes selected are prepared using non scarce raw materials and target the use of environmentally friendly aqueous electrolytes. A comprehensive overview of the most promising materials and electrolytes will be given and a set of selected examples will highlight how scale up and commercialization can be reached in this important field.

Acknowledgments: The author would like to express her gratitude to all team members working in this topic. The author thanks Fundação para a Ciência e a Tecnologia (FCT, Portugal) for financial support under the projects PTDC/QUI-ELT/28299/2017, UIDB/00100/2021, UIDP/00100/2021 and PTDC/QUI-ELT/2075/2020 and ANI for the financial support under Baterias 2030, LISBOA-01-0247-FEDER-046109, co-funded by Operational Programme for Competitiveness and Internationalisation (COMPETE 2020), under the Portugal 2020 Partnership Agreement, through the European Regional Development Fund (ERDF).

Attochemistry: imaging and controlling electron dynamics in molecules with attosecond light pulses

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In most attosecond experiments performed on molecules with high-harmonic generation sources or ultrashort X-ray free-electron lasers, a single broadband pulse or a train of attosecond pulses suddenly ionize the system and create an electronic wave packet that subsequently evolves under the influence of the nuclear motion until it is interrogated by a second pulse at a given time delay. To access the early electron dynamics induced by the first pulse, the experiments usually record photoelectron and/or fragmentation yields as a function of the temporal delay between the two pulses with attosecond resolution. However, in spite of the successful observation of sub- and few-fs dynamics in the recorded yields [1-4], it is not yet clear how the early electron dynamics leaves its signature in molecular fragments that may be created long after those initial steps (usually after going through a series of non adiabatic processes) or why one should expect a reminiscence of such electron dynamics at all. To answer these questions, one must understand i) the ionization by the first pulse, ii) the coupled electron and nuclear dynamics that follows, iii) the ionization by the second pulse of a molecular cation in a coherent superposition of states, and iv) the coupled electron and nuclear dynamics that follows the previous step and eventually leads to fragmentation of the molecule. Every step is in itself is a theoretical and experimental challenge for molecules containing more than two nuclei. In this talk I will review recent theoretical efforts to account for these four steps and discuss the optimum conditions to visualize electron dynamics in molecules [5].

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The application of multi-dimensional fluorescence spectroscopy, anisotropy, and chemometrics as a process-wide, analytical technology platform for Biopharmaceuticals

Prof. Alan G. Ryder

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Multi-dimensional fluorescence spectroscopies like excitation-emission matrix (EEM) and polarized excitation-emission matrix (pEEM) offer unique possibilities for the quantitative and qualitative analysis of the many different complex biogenic liquids encountered during biopharmaceutical manufacturing. EEM and pEEM spectra of complex solutions are very sensitive to chemical and physical changes and this can be quantified using multivariate analysis (chemometrics). Over the past 15 Years, our group has been exploring the use of EEM and chemometrics to robustly analyse all the various chemically complex liquid samples encountered during manufacturing including raw materials, cell culture media, bioreactor broths, and proteins. Using a variety of chemometric techniques, and an appreciation of chemical complexity, much useful chemical and process information can be extracted for both chemical engineers and biologists. The talk will present a range of case studies [1-5] illustrating the efficacy of these approaches and how by including a polarization dimension we have been able to better characterise proteins and their interactions based on changes in rotational diffusion and/or molecular size which is particularly useful for the manufacture of biopharmaceuticals.

Acknowledgments: This research has been funded by multiple grants from Science Foundation Ireland and the Irish Research Council.

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Biography: Prof. Alan G. Ryder is currently a Personal Professor in the School of Chemistry at the National University of Ireland, Galway (NUIG). He has a B.Sc. and Ph.D. in chemistry from NUIG. After a stint as a postdoctoral researcher in UCC, he rejoined NUIG in 1997 to work on developing quantitative Raman spectroscopy-based methods for measuring illicit narcotics. In 2003, he formed the Nanoscale Biophotonics Laboratory (NBL) which is focussed on the use of photonics and chemometrics technologies for life and physical science applications. In 2006 he joined the School of Chemistry at NUIG where he lectures mainly in spectroscopy and has two core research areas: Analytical Sciences and Photonics, which cover a wide range of applications. In the Analytical Sciences domain, the main research area is the development of rapid, quantitative analytical methods for the analysis of complex materials with particular focus on biopharmaceutical manufacturing. Key methods employed include Raman and Fluorescence spectroscopies and chemometrics. He has collaborated with a range of biopharmaceutical industry partners on developing rapid spectroscopic methods for cell culture media analysis. To date, he has authored in excess of 100 publications, generated 3 patents, secured >11M€ in funding, and graduated 21 PhD students. Web: www.nuigalway.ie/chem/nanoscale

3D Structure of Nanomaterials under Realistic Conditions

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Nanomaterials are important for a wide range of applications because of their unique properties, which are strongly connected to their three-dimensional (3D) structure. Electron tomography has therefore been used in an increasing number of studies. Most of these investigations resulted in 3D reconstructions with a resolution at the nanometer scale, but also atomic resolution was achieved in 3D. However, the increasing complexity of nanomaterials has driven the development of even more advanced 3D characterization techniques, which will be discussed in this contribution.

For example, 3D characterization of structural defects in nanoparticles by transmission electron microscopy is far from straightforward since the presence of diffraction contrast in a tilt series of images violates the projection requirement for tomography. However, being able to visualize defects is of great importance to understand e.g. the initial growth of metallic nanoparticles or the effect of pulsed laser irradiation on the crystal structure. By simultaneous acquisition of tilt series using different annular detectors, we were able to visualize both the morphology and the defect structure of several types of nanostructures (Figure 1) [1,2]. Moreover, also a 3D characterization at the atomic scale could be performed. Such studies are of great importance to link the structure to the specific functionalities of the nanomaterials.

In order to preserve the carefully designed morphologies and functionalities, understanding the stability of nanomaterials during application is of equal importance. It is hereby important to note that most electron tomography investigations have been performed at the conventional conditions of an electron microscope. An emerging challenge is therefore to fully understand the connection between the 3D structure and properties under realistic conditions, including high temperatures as well as in the presence of liquids and gases. Therefore, innovative methodologies are required to track the fast 3D changes of nanomaterials that occur under such conditions.

Recently, we proposed an acquisition approach where a tilt series of 2D HAADF-STEM projection images is acquired within a few minutes. By continuously tilting the holder and simultaneously acquiring projection images while focusing and tracking the particle, we were able to reduce the total acquisition time for a tilt series by a factor of ten [3]. Moreover, a new approach was developed to compute high quality 2D virtual slices through nanoparticles in approximately 60 ms time. This technique drastically improves the efficiency of 3D characterization of nanomaterials by TEM. It enables explorative imaging and provides valuable information to dynamically adjust the acquisition parameters during an electron tomography experiment [4].

In this manner, we were able to study the 3D morphological evolution of anisotropic Au (Figure 2) and AuPd nanoparticles as a function of both heating time and temperature [3,5]. Moreover, we measured the elemental diffusion dynamics of individual anisotropic Au-Ag nanoparticles in 3D [6]. We conclude that for a given composition, the shape of the nanoparticle does not influence the alloying process significantly. Based on our analysis, it is clear that interdiffusion of metals at the nanoscale is more complex than predicted by simple Fickian diffusion and that other factors such as surface diffusion need to be taken into account.

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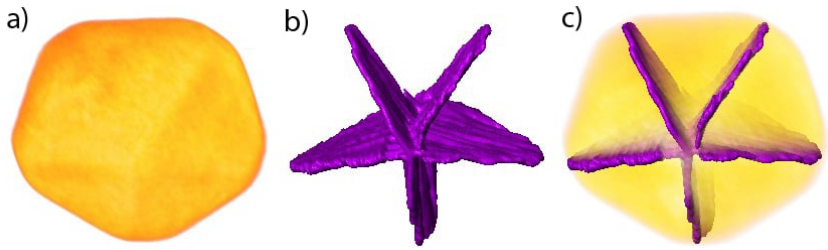

Figure 1: 3D visualization of the HAADF-STEM reconstruction (a) and the twin planes segmented from the LAADF-STEM reconstruction (b) of an Au decahedron. Both volumes are superimposed to evaluate the position of the twin planes in the correct volume (c).

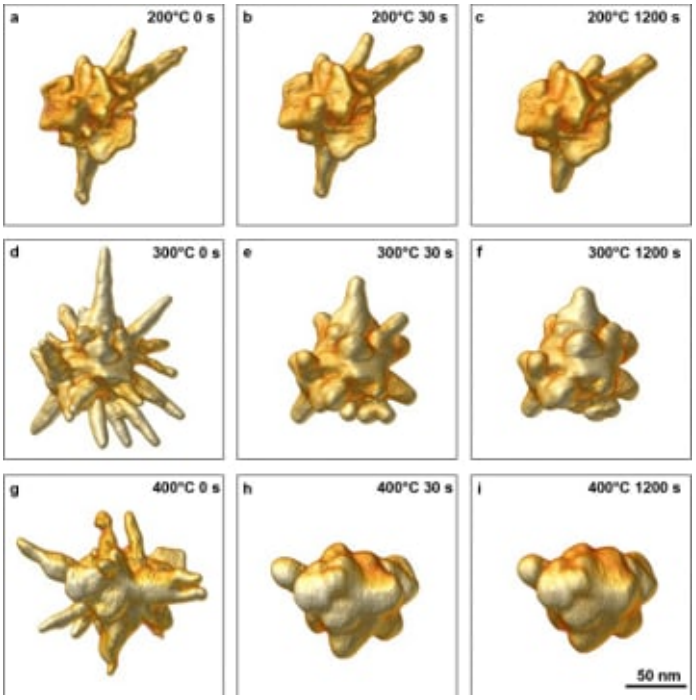

Figure 2: 3D visualizations, using fast tomography, of an Au NS before (a) and after heating for 30 s (b) and 1200 s (c) at 200 °C. 3D visualizations for the same time steps are shown for 300 °C (d-f) and 400 °C (g-i).

Imaging the forces driving cellular behaviour: from material characterisation to 3D cell models

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Tissue engineering has emerged as a promising approach to regenerate biological substitutes for damaged or lost tissues. Due to their huge biocompatibility and soft tissue-like properties, hydrogels have been widely used as vessels for culturing cells and as tissue-engineering scaffolds, to rebuild and repair tissues in vivo. Recent studies have shown that the structure and mechanical properties of the materials at the nano- and micrometer scale play a crucial role in regulating cell behaviour. However, the mechanical characterization of new materials is still performed at the bulk level.

In our group we are developing new approaches to investigate the structure of hydrogels and their influence on cell behaviour using advanced microscopic approaches. As a model system, we use a hydrogel formed from oligo(ethyleneglycol)-functionalized polyisocyanate (PIC) polymers. This biomimetic material presents structural and mechanical properties similar to biological hydrogels whilst being fully synthetic. Using fluorescently labelled PIC polymers, we were able to evaluate the fiber architecture of PIC gels at the micrometer scale and evaluate how the presence of contractible cells induced fiber remodeling.

Rheological tests showed that the PIC matrix can be intensively stiffened by cell-generated forces within 24h after cell encapsulation. Three-dimension traction force microscopy indicated that matrix stiffening is correlated with the cell-induced fiber displacements that occur at the micrometer scale. Similar to what is observed in collagen and fibrin gels, PIC-based hydrogels also support a force propagation over a long distance (>> 100 µm). Interestingly, changes in the mechanical properties of PIC gels affect the degree of fiber remodeling while the distance of the force propagation remains similar.

The results acquired showcase the potential of fluorescence microscopy to investigate structural properties of polymer matrices and how physical cues can regulate the reciprocal cell-matrix interactions. The microscopy-based toolbox here developed can be readily applicable to other (synthetic) supramolecular hydrogels.

CO_2 electroreduction to valuable products with high productivities

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The electrochemical conversion of CO_2 produces valuable chemicals and fuels. It constitutes a promising route to convert carbon emissions to products that can replace those obtained from routes based on fossil sources. From industrial point of view, this replacement claims new technology, catalysts and electrode microstructure, able for offering high productivity with feasible energy balances. So, electrocatalysts that operate at such required high current densities are welcome as they reduce the capital costs, but it becomes a significant challenge for achieving a rational design of the catalyst as well as the functional microstructure configuration of the electrode. Operating at high reaction rates gives rise to many phenomena that render CO_2 electrolysis inherently unstable. Utility of CO_2 in a single pass can be very low to obtain valuable products if the active sites are not accelerating the CO_2 activation to enable efficient CO_2R pathways; the local production of no wanted sub products can affect the porous cathode structure blocking CO_2 transport and reduce reaction efficiency or the inadequate catalyst load on carbon and polytetrafluoroethylene (PTFE)-based gas diffusion electrodes can dramatically reduce the conversion efficiency. In this contribution, all these elements that must be overcome and their functional role will be presented in order to build a useful strategy for the design of an electrochemical cell optimized for the reduction of CO_2 with a high level of CO_2 utilization, a high density of current and a high efficiency in the energy balance will be discussed from the perspective to achieve the replacement of fossil routes.

Ternary Metal Oxide-based Photoanodes for Solar Energy Conversion

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Solar energy conversion into hydrogen is a valuable approach to capture the energy that is freely available from sunlight and to turn it into a clean fuel. To this aim, photoelectrochemical (PEC) water splitting is an established powerful technology requiring the development and optimization of efficient oxide-based semiconductor photoanodes for water oxidation, the kinetic bottleneck of the overall PEC water splitting process. Two ternary metal oxides able to absorb a relatively large portion of the solar spectrum, i.e., $BiVO_4$ and $CuWO_4$, have been recently investigated as photoanode materials.

Bismuth vanadate has emerged as a leading photocatalyst for the oxygen evolution reaction despite its poor electron transfer ability and slow water oxidation kinetics. We found that the PEC performance of $BiVO_4$ can be largely improved either i) by coupling it with WO_3 in a heterojunction, for which transient absorption spectroscopy (TAS) revealed an excitation wavelength-dependent efficiency in photoproduced charge separation [1,2], or ii) by doping it with hexavalent metal ions such as Mo^{6+}. In this case, the largely improved water oxidation activity results from multiple factors, including increased electron conductivity of $BiVO_4$, longer lifetimes of photoproduced holes, evidenced by TAS, and surface effects reducing the interfacial charge transfer resistance [3].

On the other hand, an efficient use of $CuWO_4$ as photoanode material requires to overcome its severe internal charge recombination, due to intra gap states, acting as electron traps, as ascertained by a PEC investigation on this material coupled with ultrafast TAS analysis [4]. A partial Mo^{6+} for W^{6+} substitution results in $CuW_{1-x}Mo_xO_4$ electrodes with a greatly enhanced visible light-induced photoactivity compared to pure $CuWO_4$, with a 1:1 W:Mo molar ratio leading to the optimal compromise between light absorption and photogenerated charge carriers separation [5].

The best performing $CuW_{0.5}Mo_{0.5}O_4$ material was then combined either with $BiVO_4$ in a single heterojunction, or with WO_3 and $BiVO_4$ in a double heterojunction. Both $CuW_{0.5}Mo_{0.5}O_4/BiVO_4$ and $WO_3/CuW_{0.5}Mo_{0.5}O_4/BiVO_4$ coupled systems exhibit a definitely superior performance, over the entire investigated spectral range, compared to the individual components under irradiation from the front-side of a $BiVO_4$ layer thick enough to absorb most of the incident radiation, i.e. under conditions in which detrimental cross-back electron-hole recombination at the heterojunctions is minimized.

This work received partial support from the MIUR PRIN 20173397R7 Multi-e project.

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Playing with Molecular Rings and Strings: New Directions for Nanoscale Machines and Motors

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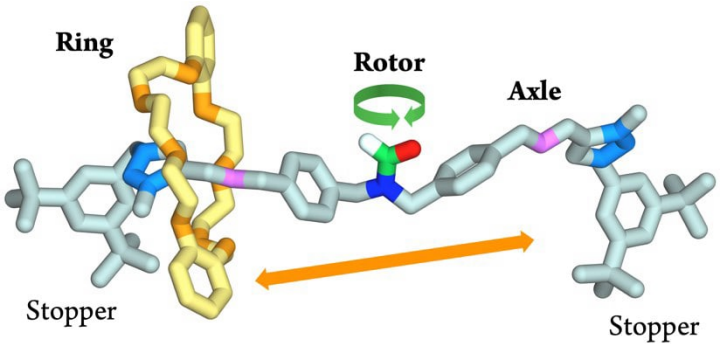
The construction of molecular scale devices and machines have formidably stimulated the creativity of chemists in the past three decades.[1,2] The interest on this kind of systems arises from their ability to perform a (useful) function in response to chemical and/or physical signals (e.g., light). Mechanically interlocked molecules exhibit appealing structural and functional properties for the construction of nanoscale devices and machines; molecular shuttles based on rotaxanes constitute common examples.[2]

We describe investigations undertaken in our laboratories, aimed at exploiting the nanoscale movements in rotaxanes and related species[3] to perform functions such as transmitting information and motion between sites[4] (see Figure) and activating mechanically chiral structures for enantioselective guest recognition.[5]



From a fundamental viewpoint these systems behave as molecular switches under thermodynamic control. In appropriately designed architectures, however, kinetics can play a major role in governing intercomponent movements. By exploiting energy and/or information ratcheting effects, directional and autonomous movement of the molecular components can occur.[1,2] We have combined this strategy with a minimalist chemical design to realize artificial nanoscale pumps powered by light[6] and electricity.[7]

Support from the European Union (H2020 ERC AdG 'Leaps' 692981, FET-OPEN 'Magnify' 801378, ITN 'ArtMoMa' 860434) and the Ministero dell'Università e Ricerca (Grants 20173L7W8K and R16S9XXKX3) is gratefully acknowledged.

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Artificial molecular machines that work on all scales

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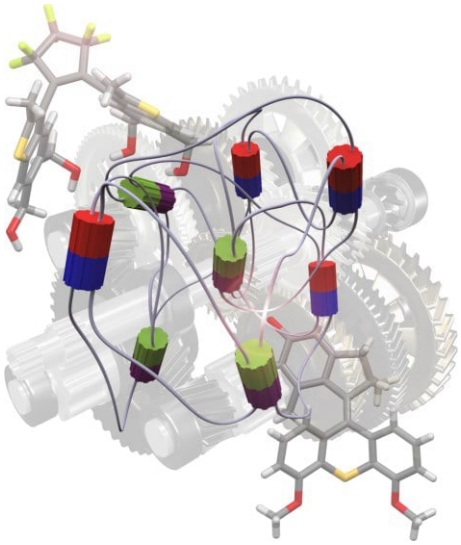
Making molecular machines that can be useful in our macroscopic world is a challenging long-term goal of nanoscience. Inspired by the protein machinery found in biological systems, and based on the theoretical understanding of the physics of motion at nanoscale, organic chemists have developed a number of molecules that can produce work when triggered by various external chemical or physical stimuli.[1] In particular, basic molecular switches that commute between (meta)stable states, and more advanced molecular motors that produce unidirectional cyclic motions out-of-equilibrium when fueled with external energy, have been reported. However, the integration of individual molecular motors in a continuous mechanical process that can have measurable effects at various length scales and up to the macroscale remains an important objective. We will discuss advances developed by our group on artificial molecular machines, which involve their mechanical coupling with polymer systems. We will show how it becomes possible to integrate them and to make use of their mechanical work going from individual molecular devices to macroscopic materials.



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Building nanographenes by combining organic synthesis and surface science

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The emergence of graphene materials has revolutionized the field of materials science. One of the biggest challenges in this field is the development of efficient methodologies for the synthesis of well-defined graphene materials with customized properties. In this respect, organic chemistry in solution has significantly contributed to the preparation of tailor-made graphene molecules. However, the extremely low solubility of these compounds is a major drawback in the further development of this bottom-up approach to graphene materials. Fortunately, the introduction of atomic force microscopy (AFM) and scanning tunnelling microscopy (STM) with functionalized tips has allowed the visualization of graphene molecules adsorbed on surfaces with submolecular resolution. This breakthrough, together with the possibility to induce on-surface chemical reactions, opens exciting possibilities related with graphene materials [1].

In this talk, I will comment on how these advances in AFM/STM, in combination with organic synthesis, allowed us to obtain and characterize structurally appealing graphene nanostructures. In particular, I will discuss the synthesis and characterization of three-fold symmetric nanographenes such as starphenes and cloverphenes [2]. In addition, I will comment on the preparation of fascinating materials such as nanoporous graphene [3] or triangulene-based nanostructures (Figure 1) [4], by combining solution chemistry and on-surface synthesis.

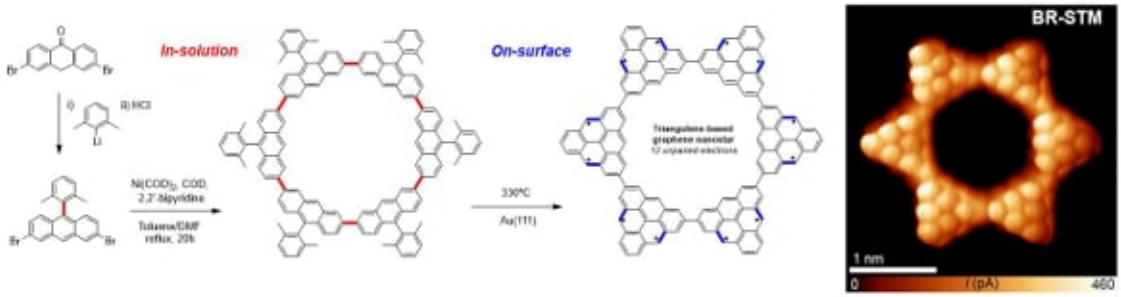

Figure 1. Synthesis of a triangulene-based graphene nanostar by combining in-solution and on-surface chemistry, and STM image of one single triangulene nanostar on Au(111).

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Molecular Solar Thermal Energy Systems

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Since the beginning of civilization, humanity has built houses to sustain comfortable living conditions throughout the seasons. In our modern society, about 50% of the total energy consumption is used for heating and cooling. Growing demands for thermal management in many different sectors, from electronics to housing, inevitably mean increased energy consumption. The primary source of heat is coming from the combustion of fossil, bio or waste-based feedstocks, all contributing to carbon emissions.

In this lecture I will present how we are working on developing materials that capture, store, and release both solar and ambient heat without creating any emissions.

These molecular solar thermal systems (MOST) are based on molecular photoswitches that absorb light and convert it into stored chemical energy, that can be released on demand (Fig.1). The MOST energy system operates through different principles than traditional solar thermal and can be introduced into compact energy capture and release devices. Recently, the first example of integration of the energy storage system in windows, and in electric power generation devices was published[7-8].

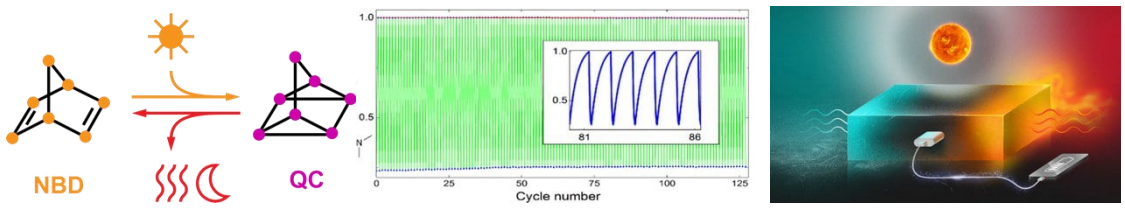

***Figure 1**. (Left)) Molecular structure of on NBD/QC photoswitch system. (Centre) Stability test performed at 60 ℃ through 127 energy storage cycles (right) Illustration of MOST power generation concept.*

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On-surface synthesis of pi-conjugated polymers

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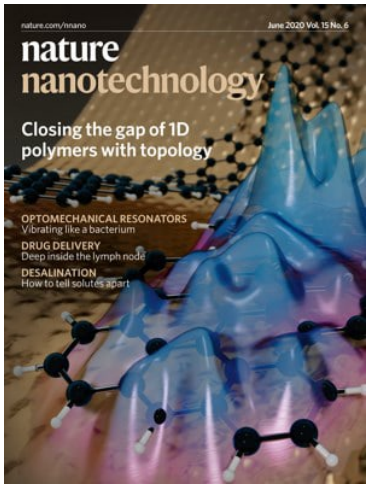
On-surface synthesis has emerged as a powerful strategy to design unprecedented nanomaterials. In this talk, I will revise our recent achievements regarding the synthesis of one-dimensional pi-conjugated polymers, featuring emerging physical properties such as non-trivial topology or pi-based magnetism.[1-6]



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Chemistry Teachers' Personalized Professional Development Framework

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Chemistry is continually being developed through research in academia, research institutions, and industry. However, school chemistry and the curricular contents are hardly affected by the development of chemistry. This gap does not provide an opportunity to expose school students to the beauty and relevance of contemporary chemistry research. Students are unaware of how chemistry contributes to addressing the global challenges; they are not exposed to the nature of modern science and to actual scientists who conduct chemistry research today, and who are more likely to be perceived as models for the students [1].

Changing the school curriculum usually takes a long time, and many informal activities and outreach programs have been developed to communicate contemporary research to school students [2]. However, a deeper approach that does not require curricular changes is to focus on chemistry teachers' professional development (PD) and to update and expand their knowledge by learning and experiencing contemporary chemistry. Indeed, many courses and other PD frameworks for chemistry teachers have been developed and conducted over the years around the world (e.g., [3, 4])

The main concern is whether the teachers actually integrate contemporary contents into their teaching and expose their students to modern chemistry. Many barriers can inhibit this transfer of contents from the teachers' course to be an enacted PCK and become part of their teaching practice in their chemistry class [5]. Parts of the inhibitors consist of the teachers' beliefs and attitudes; but another essential part is the variety of educational contexts: this includes different school settings and different students' characteristics, requiring a personal adaptation of the PD contents for each teacher.

In my presentation, I will reflect on my work during the last 15 years with chemistry teachers and describe the development of a model for teachers' personalized PD on contemporary chemistry research. Although the course focuses on contemporary chemistry, the personalization supports the development of teachers' self-efficacy beliefs [6] and the integration of the teachers' educational context as an integral part of the PD.

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Importance of learning of scientistic language at the university level

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In general, it is known that language is a key for communicating knowledge. Thus, the scientific language of chemistry is essential for communicating in and understanding of chemistry. At the same time, this scientific language is one of the major difficulties in teaching and learning chemistry both in the school context but as well in tertiary education.

Since understanding and using the scientific language of chemistry – the *Chemish* [1] – is a competence to be acquired in chemistry, the chemistry educators at different educational levels are responsible to support students in acquiring and using *Chemish*. As Laszlo [2, p. 1682] describes: "Chemistry teachers are linguistic guides, they are interpreters. They teach their students how to craft well-formed chemical sentences". Starting from here, we must conclude that all of as must be adequately prepared to address their students' difficulties in learning and using *Chemish* and to make scientific content accessible to all our students. This is especially true for (future) chemistry teachers.

To do so, (future) chemistry teachers must be aware and confident not only in our understanding of the concepts but also be aware of *Chemish* and its characteristics. Furthermore, they need to possess knowledge on how teach *Chemish* to our student and how student learn this language to adapt this it in their repertoire and use it properly. Thus, the research on *Pedagogical Scientific Language Knowledge* (PSLK) is missing.

Since research on (pre-service) chemistry teachers' knowledge on teaching and learning *Chemish* is rare, in the presentation, a study on evaluation of the extent of knowledge about teaching and learning *Chemish* pre-service chemistry teachers already possess will be presented and conclusions for further chemistry teacher education and research will be drawn. We evaluate the extent of 41 pre-service chemistry teachers' PSLK. The answers are analyzed using qualitative content analysis. Results show that pre-service chemistry teachers' content knowledge resembles the level of knowledge for higher secondary schools. Likewise, the pre-service chemistry teachers have a lack of incisive pedagogical content knowledge: although recognizing problems within *Chemish*, the pre-service chemistry teachers hardly address those and do not focus on the characteristics of *Chemish* while explaining scientific terms. First needs on changes in tertiary education as well as ideas of secondary chemistry teaching will be given and discussed.

This research was part of the project "ESTA – Educating Science Teachers for All" that is co-funded by the Erasmus+ Programme of the European Union, under the grant number 609719-EPP-1-2019-1-DE-EPPKA2-CBHE-JP. The European Commission's support for the pro-duction of this publication does not constitute an endorsement of the contents, which reflect the views only of the authors, and the Commission cannot be held responsible for any use which may be made of the information contained therein.

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EuChemS Historical Landmarks: chemists, their past and the sharing of chemical heritage

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Science History Institute

In 2017, the European Chemical Society (EuChemS) established the EuChemS Historical Landmarks Award (HLA). This new award is the first and only among EuChemS prizes dedicated to chemistry long past and wishes to identify places of historical significance in the development of the discipline.

This presentation will briefly clarify why and how this award scheme was conceived and will situate this program in the context of other similar initiatives at the national (such as the RSC "Blue Plaques" or the GDCh "Historische Stätte der Chemie") and international (the European Physical Society or the American Chemical Society) level. Among other things, the HLA aims to stress the European dimension of chemistry for at least two audiences: chemists and the general public. To chemists, the HLA aim at reinforcing the sense of belonging of European chemists and reminding them that as far as the history of chemistry goes, people and ideas alike have circulated. And it brings some sense to the general public of how chemistry is part of the general cultural heritage and history of every European citizen.

This presentation will highlight how that rationale has materialised so far, with the 2018, 2019 and 2020 awards, including the challenges and accomplishments, with a look on future.

Didactic physics and chemistry instruments from Portuguese high schools - trash for the bin or a heritage to preserve?

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The creation of publics for science dates back to the Enlightenment period, when demonstration machines/instruments illustrated the new properties of matter (electricity, vacuum, magnetism, …) and traveling amateur demonstrators swarmed and contributed variously to the development of experimental sciences. The consolidation and institutionalization of science and scientific disciplines during the 19th century forged new professional characters, different specialties and concerns with education and the construction of a wide public for science. The creation of secondary (and technical) schools was a milestone, although particular attention was paid then to the generalization of elementary education. Almost simultaneously, "science for all" appears as an epistemological counterweight to the specialization and formalization of the sciences, both trends contributing to the construction of knowledge [1, 2]. The establishment of a national secondary education system in Portugal dates back to 1836, also emphasizing the need for specific spaces for teaching physics, chemistry, and natural sciences, together with materials and equipment for the practice of teachers and students. It faced different obstacles over time, but it was also the object of different acculturation processes, many of an international nature in which instruments were included

The survey of and research on the old didactic instruments still present in some high schools, which we have been conducting, reveal the existence of a most valuable scientific heritage, which needs to be protected_baudafisica.web.ua.pt [3]. Some of the instruments followed more closely the development of specific scientific concepts, or measurement techniques. Simultaneously, the existence of different networks for the circulation of knowledge and the formation of trends becomes evident, from instruments to furniture to suggested readings, stabilizing practices, behaviors, and spaces [4]. We will reflect on meanings that can still be found through a closer look at instruments that testify to the rooting of the physical sciences in the Portuguese high school culture.



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This work is financially supported by National Funds through FCT – Fundação para a Ciência e a Tecnologia, I.P., under the project UIDB/00194/2020 (CIDTFF).

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Initial Steps towards an Evolutionary System leading to the Emergence of Life

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All evolutionary biological processes lead to a change in heritable traits over successive generations. The responsible genetic information encoded in DNA is altered, selected, and inherited by mutation of the base sequence.

While this is well known at the biological level, an evolutionary change at the molecular level of small organic molecules is unknown but represents an important prerequisite for the emergence of life.

Here, I present a class of prebiotic imidazolidine-4-thione organocatalysts able to dynamically change their constitution and potentially capable to form an evolutionary system. These catalysts functionalize their own building blocks and dynamically adapt to their (self-modified) environment by mutation of their own structure.

Depending on the surrounding conditions, they show pronounced and opposing selectivity in their formation. Remarkably, the preferentially formed species can be associated with different catalytic properties, which enable multiple pathways to the formation of nucleotides, oligomers and lipids for the transition from abiotic matter to functional biomolecules.

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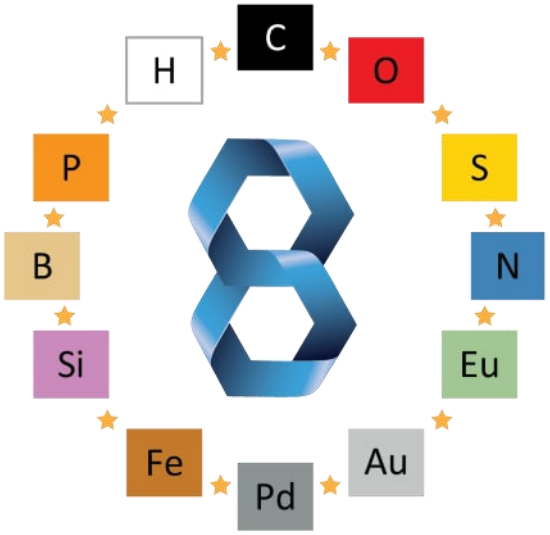

ORAL COMMUNICATIONS (OC)

Divergent functionalization of four-membered heterocycles

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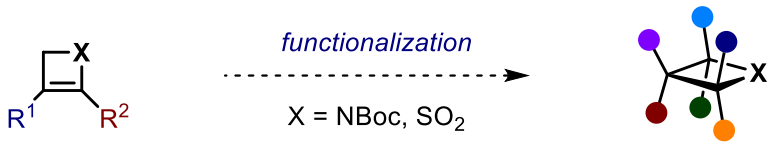
A large number of bioactive structures contain aromatic moieties. Current trends in medicinal chemistry aim at substituting these flat motifs with 3D-architectures to give more perspective to the molecules and tune structure-activity relationships. However, replacing a phenyl by a cyclohexyl gives a certain degree of flexibility to the molecule, which is not always desirable. In this context, an interest in functionalized cubanes and propellanes has been recently witnessed within the community of organic synthetic chemists, as the different substituents are locked into a defined binding angle, due to the rigidity of the systems.

Since 2015, our group has been involved in the synthesis and functionalization of unsaturated four-membered carbo- and heterocycles, using simple strategies based on organometallic chemistry. We have established efficient and diversified methods to access cyclobutenes, azetines and thiete dioxides. With a strained endocyclic double bond, those compounds represent an ideal platform for the formation of elaborated saturated structures such as cyclobutanes, azetidines and thietanes.



- efficient, reliable access
- broad scope

- unprecedented structures
- defined exit vectors

In this communication, we will present different divergent methods for the functionalization of azetidines and thietanes, as these structures could be used as analogs of pyridines, pyrrols or thiophenes, balancing both rigidity and flexibility.

Dioxomolybdenum catalyzed C–N bond-forming reactions in reductive amination reactions with nitrocompounds

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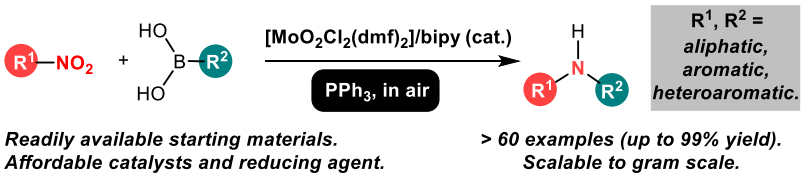
Aromatic amines are almost ubiquitous compounds that are found in pharmaceuticals, biologically active compounds, material science, building blocks in synthesis.[1] The significance of aromatic amines has grown in parallel with the available methods for their synthesis.[1] The development of C–N bond-forming reactions has contributed decisively to the simple and effective production of collections of anilines. These amination methodologies employ amines as the nitrogen source, particularly anilines, which are usually obtained by the reduction of nitroarenes. Thus, developing a general and efficient methodology for synthesizing aromatic amines directly from abundant and readily available nitroarenes is very attractive and remains an active research field. The use of nitro compounds as starting materials improves step-economy, saving time and cost and allowing higher tolerance of functional groups such as unprotected amines. Although nitroaromatics are efficiently engaged as starting materials in C–N bond-forming reductive cyclization to synthesize indoles or carbazoles, intermolecular amination to afford anilines in one single operational step has proved to be more challenging. In recent years, notable advances have been described in the reductive amination of nitroarenes employing arylmagnesium compounds, highly reactive alkyl radicals, or zinc organyls [2]. More recently, boronic acids have emerged as efficient coupling partners.[3,4]

Based on dioxomolybdenum catalyzed reactions,[5] it was hypothesized that a fine-tuning of a Mo oxo-transfer catalyst might provide access to the direct amination of boronic acids with nitro compounds. Achieving a suitable partially-reduced intermediate without over-reduction of the amine from the nitro compound is crucial for the C-N bond coupling with the boronic acid. The use of $MoO_2Cl_2(dmf)_2$ combined with bipyridine ligand and affordable PPh_3 as the reducing agent was detected to give optimal results.[4] This simple method that can be carried out under air was demonstrated wide functional group compatibility (aldehydes, esters, free amines, alkenes, ketones). A general synthesis of aromatic amines was described through practical, scalable air and moisture tolerant procedures. The wide availability of nitro and boronic acids makes this strategy suitable for generating libraries of amines.



Thanks to *MICINN (PID2020-115789GB-C21); and "NextGenerationEU/PRTR" (PDC2021-120825-C21), and Junta de Castilla y León and FEDER (BU049P20) for financial support. R.H.R. and S.S.-P. thank Spanish Government and Junta de Castilla y León and Fondo Social Europeo for contracts respectively.*

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Infrared irradiation-assisted Pd-catalyzed dehydrogenative coupling of fluoroarenes with heteroarenes: a new frontier in double C–H activation

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Organic compounds based on the (hetero)aryl scaffolds have been extensively investigated in recent years. The development of efficient methods for the generation of (hetero)aryl-aryl bonds is the key step to produce these molecules. In this context, the Palladium-catalyzed dehydrogenative coupling of (hetero)arenes can be definitely included among reactions with the lowest economic and environmental impact, since they occur between two different (hetero)arenes without pre-activation of both coupling partners (that is, double C–H activation).[1] Currently, the development of efficient methodologies is still very challenging, due to relevant limitations such as the regioselectivity issues on both (hetero)aryl scaffolds, the formation of undesired homo-coupling products, or the need of high temperatures and long reaction times.

Non-conventional energy sources have recently earned increasing attention as valid alternative to the traditional thermal heating, due to their possibility of minimizing reaction time, improving product yields and also avoiding undesired by-products.[2] In this context, infrared (IR) irradiation is very appealing: it is a highly efficient form of heating emitted from an inexpensive lamp, with high heat transfer rate, good heating homogeneity, low energy consumption and short heating time.[3] Thanks to these properties, the application of IR irradiation in organic synthesis could provide relevant advantages, including reduced energy requirements, shortened reaction times and even access to new mechanistic pathways, in addition to its potential compatibility with solvent-free methodologies. However, its true potential is still unexplored, especially in the Pd-catalyzed chemistry.

Here we report the first IR irradiation-assisted methodology for the Palladium-catalyzed dehydrogenative coupling reactions, performed under solvent-free conditions. The synthetic protocol was successfully applied in the reaction of fluoroarenes with heteroarenes bearing relatively acidic C–H bonds (thiophene, benzo[*b*]thiophene, furan, benzo[*b*]furan, 1*H*-indole), affording the corresponding coupling products in good yields after only 30 minutes (**Figure 1**). The broad substrate scope and high versatility of this fast, cheap and green protocol for heteroaryl–aryl coupling, could open a new frontier in double C–H activation.

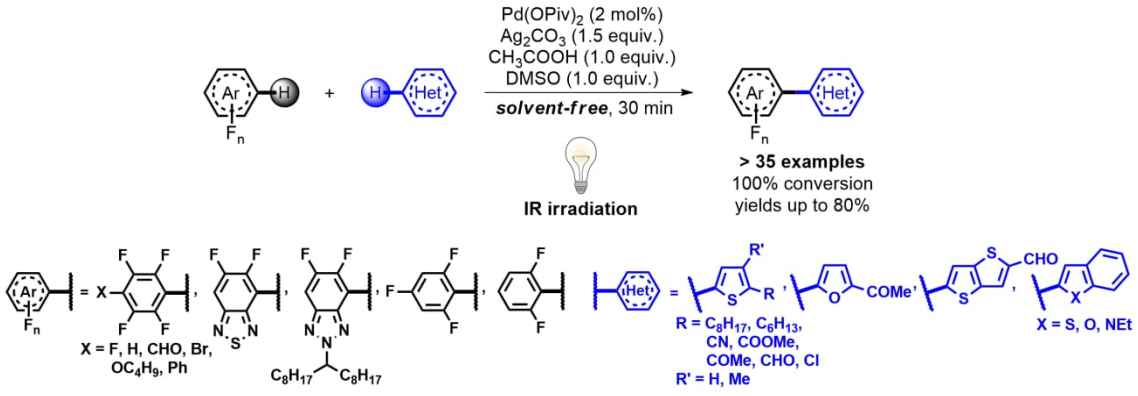

Figure 1. IR irradiation-assisted, solvent-free Palladium-catalyzed dehydrogenative coupling of fluoroarenes with heteroarenes.

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Combining photoflow of pyridinium salts with Pd-catalysis to access new aminocyclopentene

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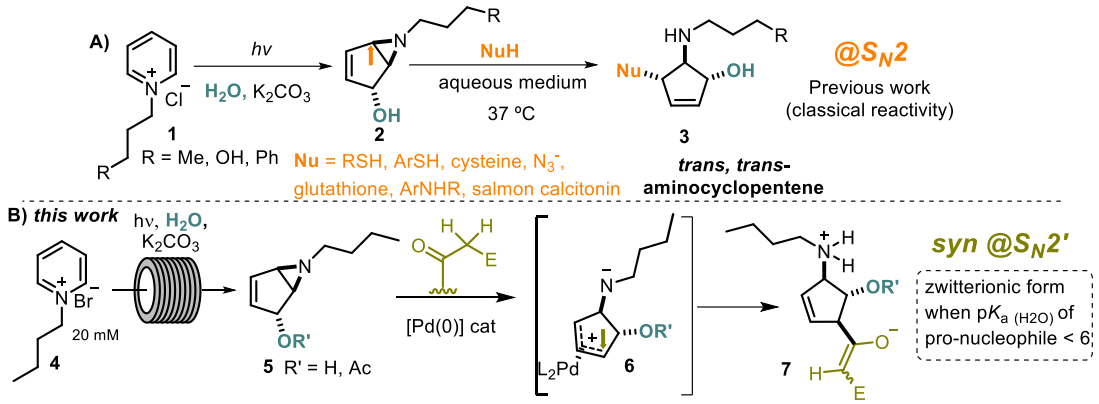
In 1972 Kaplan *et al*, reported a pioneer study in photochemical transformation of *N*-methylpyridinium chlorides to 6-methylazabicyclo[3.1.0]hex-3-en-2-ols (bicyclic aziridine).[1] In 2016, we described the photoreaction of several pyridinium salts **1** into the corresponding bicyclic aziridines **2** under batch conditions with low productivity. S_N2 ring opening reaction of **2** in water with heteroatom-based nucleophiles allowed the synthesis of new *trans, trans*-aminocyclopentenes (**Scheme 1-A**).[2] This powerful photocyclization, stereo and regioselective S_N2 aziridine ring opening sequence, was applied to the total synthesis of several natural and non-natural products, like (+)-mannostatin A and (+)-castanospermine.[3] Here will be presented the application of flow on photoreaction of *N*-butyl pyridinium salt **4** (**Scheme 1-B**) allowing to solve the scalability problem of this rearrangement and consequently producing bicyclic aziridine **5** on a gram scale.[4] Furthermore, palladium-catalyzed ring opening of bicyclic aziridine **5** with active methylenes (**Scheme 1-B**) presented a new selectivity due to η^3-allylpalladium complex formation and nucleophile addition anti to the allylic oxy group **6,** resulting in a new aminocyclopentenes **7**.[5]



Scheme 1: A) Photoreaction of pyridinium salt followed by classical S_N2 aziridine ring opening reaction. B) Photoflow of pyridinium salts and palladium catalyzed aziridine ring opening reaction.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (PhD grant 2020.04589.BD) and project (PTDC/QUI-QOR/32008/2017, UIDB/04138/2020, UIDP/04138/2020 and PESSOA 2018/2019 (Proc. 441.00 França and PHC PESSOA 2018 No 40875QJ)).The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951996.

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New polypyrazolylborates complexes with increased electrophilicity and small catalytic pocket

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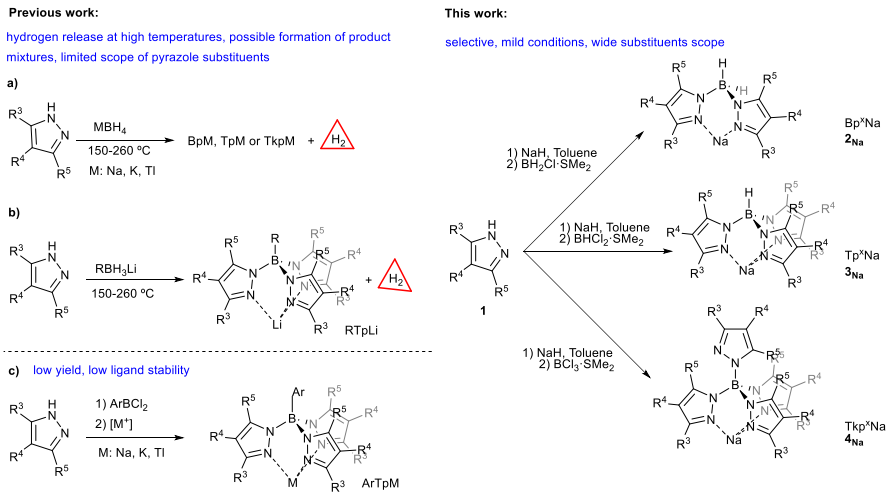
Polypyrazolylborates have found a wide variety of applications in organometallic chemistry, catalysis, or polymeric materials since their discover in the 60´s by S.Trofimenko.[1] Numerous examples of this family of ligands have been prepared, including those presenting two, three or four pyrazole rings attached to the boron center. The conventional preparation of these ligands present two important drawbacks, hazardous release of hydrogen at high temperatures and severe limitations related with the functional groups that can be present on the heterocyclic rings.[2]

For this reason, only trispyrazolylborates presenting either voluminous or electron-withdrawing substituents on the heterocyclic rings have been obtained. In the case of tetrakispyrazolylborates, the examples are scarce and restricted to non-substituted pyrazole or its derivatives containing small donating groups.

We have developed a new methodology that use more reactive boron sources that can be smoothly transformed to the desired ligands through their reaction with the corresponding pyrazolate under mild conditions. Correct election of the boron source allows for the selective obtention of bis-, tris- or tetrakispyrazolylborates under mild conditions in good yields, supporting a wide variety of substituents on the heterocyclic rings, including both, encumbering and electron withdrawing groups.

The development of this new procedure for the preparation of these challenging ligands will provide a significant breakthrough in several catalytic transformations.



The authors acknowledge MICIN for financial support through Grant MICIN/AEI/10.13039/501100011033/PID2019-109706RB-I00 (ERDF A way of making Europe). The authors also thank Generalitat Valenciana for Grant AICO/2020/215. A. O. thanks MINECO for a Ramon y Cajal fellowship (MICIN/AEI/10.13039/501100011033/RYC-2017-22640) (ESF Investing in your future).

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Photocatalytic α-C–H Heteroarylation of Unprotected Primary Alkylamines

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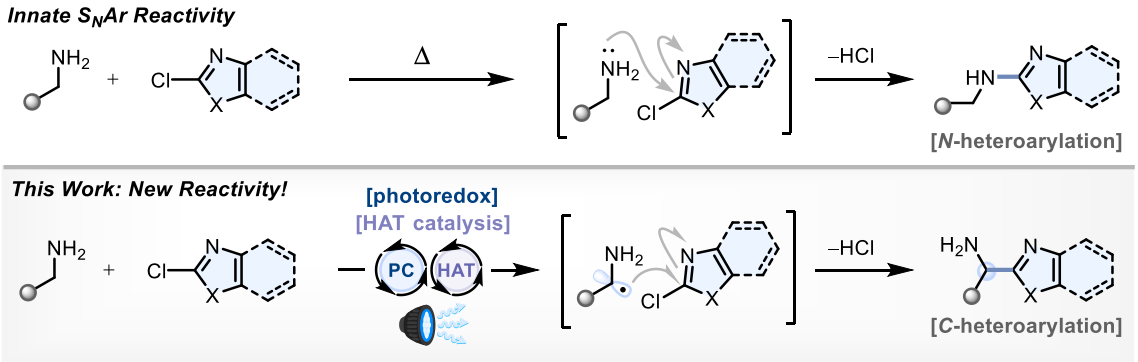
The S_NAr reaction between halogenated heteroaromatics and primary alkylamines is a prototypical C–N bond-forming process and one of the most widely utilised reactions in medicinal chemistry.[1] We questioned whether the innate reactivity of unprotected primary amines to react at nitrogen with S_NAr-active electrophiles could be overturned using catalysis, such that an unprecedented C–C bond-forming transformation could be realised using the same reactants. Following our work on related C–H *alkylation* processes,[2–4] we now describe the first photocatalytic α-C–H heteroarylation of unprotected primary alkylamines, using 2-chloro(benzo)thiazoles as coupling partners.

Using an organic photocatalyst in combination with a hydrogen atom transfer (HAT) catalyst, a wide variety of α-(benzo)thiazolyl primary amines of relevance to drug design can be accessed in a single step, removing the need for multistep reactions or *N*-protection strategies. This mild and highly modular process can readily be executed on multigram-scale in continuous flow, and we have applied it to the concise synthesis of several drug candidates.



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Asymmetric Nucleophilic Fluorination under Hydrogen Bonding Phase-Transfer Catalysis and beyond

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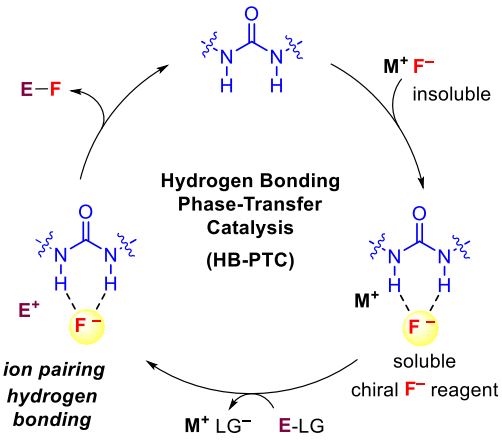
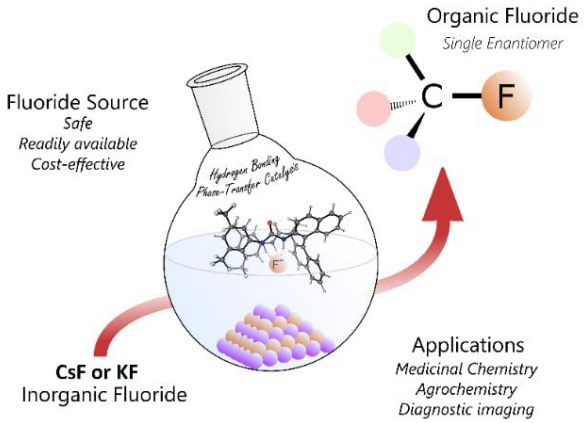
Phase-transfer catalysis (PTC) is a powerful manifold for asymmetric catalysis. Chiral cationic or anionic phase-transfer catalysis strategies have enabled a wide variety of transformations, yet studies employing insoluble inorganic salts as nucleophiles in enantioselective synthesis have remained elusive. A long-standing challenge is the development of methods for asymmetric C-F bond formation from readily available and cost-effective alkali metal fluorides. We herein present how hydrogen bond (HB) donors can provide a solution to this problem by relying on fluoride binding. By taking inspiration from the mode of action of the fluorinase enzyme, we show how HB interactions can be harnessed to control fluoride reactivity and bring solid phase alkali metal fluorides in solution. We describe the development of Hydrogen Bonding Phase-Transfer Catalysis (HB-PTC), a catalytic manifold which allows for the first time the use of alkali metal fluorides as fluorinating reagents in asymmetric catalysis.[1-2] We highlight its synthetic applications in the synthesis of enantiopure *β*-fluorosulfides, [1] *β*- and *γ*-fluoroamines (up to 200g scale) [3-4] and provide mechanistic insight derived from in-depth NMR, X-ray and computational analysis.[5] Finally, looking ahead, we present our latest advances in expanding this catalytic manifold beyond enantioselective fluorinations and the succesfull use of non-fluorinated alkali metal salts in asymmetric catalysis for C-N bond formation.





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Exploring the facile synthesis of bis(3-indolyl)methanes derivatives

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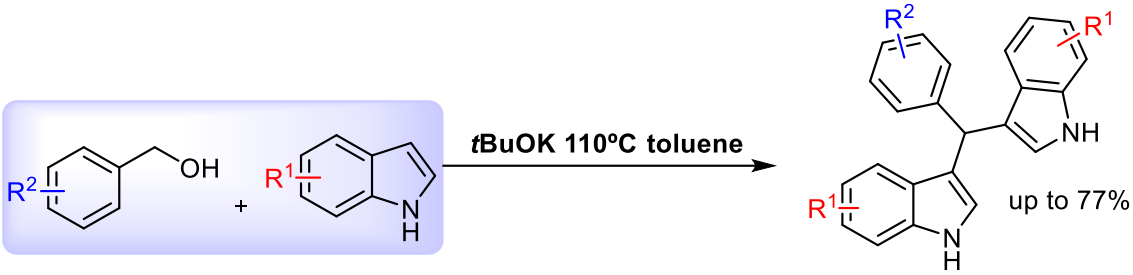
The indole nucleus is an important *N*-heterocyclic core found in natural products, and a key structural component of many value added chemicals including pharmaceuticals.[1] In particular bis(3-indolyl)methanes (BIMs), composed by two indole units, are an important subgroup of indoles.[2] Synthesis of BIMs commonly involves metal-catalysed reactions, still some drawbacks remain regarding the stability of metal catalyst to air and the complexity of the synthetic pathway. Metal-free reactions, in particular *t*BuOK-mediated oxidative coupling, have proven to be of great use in the efficient synthesis of *N*-containing compounds.[3] Thus, the establishment of a simple metal-free method to access BIMs derivatives is herein reported in high yields by exploiting a *t*BuOK catalyzed coupling. Furthermore, mechanistic insight are also given regarding a possible radical pathway.



Thanks to the Fundação para a Ciência e Tecnologia (FCT, PTDC/QUI-QOR/0712/2020). This work was supported by the Associate Laboratory for Green Chemistry- LAQV which is financed by national funds from FCT/ MCTES UIDB/50006/2020, UIDP/50006/2020 (LAQV). The National NMR Facility is supported by FCT, ROTEIRO/0031/2013–PINFRA/22161/2016, co-financed by FEDER through COMPETE 2020, POCI, and PORL and FCT through PIDDAC) and CERMAX (022162). We thank to the FC&T for fellowship PD/BD/142876/2018. LBM also thanks to FCT/MCTES for the CEEC-Individual Program Contract (CEECIND/03810/2017).

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Synthesis of sulfonyl hydrazides mediated by hypervalent iodine reagents

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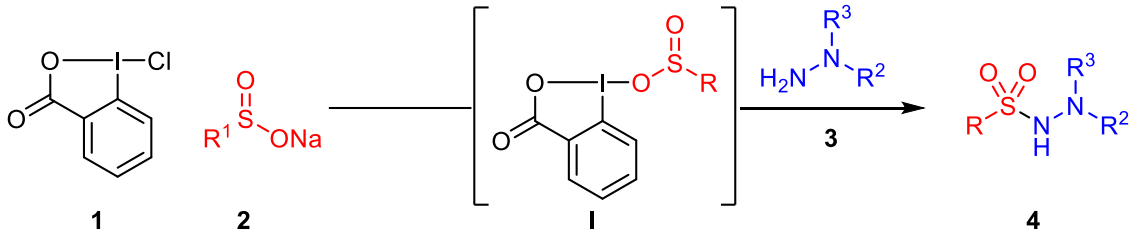
Sulfonyl hydrazides are important synthetic intermediates, useful in total synthesis of many natural compounds. In addition, sulfonyl hydrazides have been described as a synthon for a terminal hydrazine.[1] Due to the hydrazine inherent unique reactivity, traditional methods for the synthesis of sulfonyl hydrazides are limited to the use of sulfonyl chlorides or halogenated aryl compounds. A modern alternative is the use of DABSO as a sulfone surrogate in the presence of metal catalysts.[2]

The umpolung concept, reverse of polarity, offers the possibility to explore electrophilic synthons that are inherently nucleophilic in nature. In this respect, cyclic hypervalent iodine reagents are extremely attractive, and have been reported in many functional group-transfer reactions.

Our group has been applying the umpolung concept on the synthesis of sulfonamides by using cyclic hypervalent iodine reagents, sulfinic acid salts and amines.[3] Furthermore, we have developed a polymer-bound hypervalent iodine reagent that enables the synthesis of sulfonamides in up to 95% yield with recovery and reuse of the reagent.[4] On the follow-up of our previous approach, we now described the synthesis of sulfonyl hydrazides mediated by hypervalent iodine reagents.

The method consists of using sodium sulfinic acids, chlorobenziodoxolone and nucleophilic hydrazines, to form a new S-N bond, similarly to the sulfonylation method reported by us. Herein, we will present the optimization studies, mechanistic studies and reaction scope.



Thanks to the FCT for fellowships PD/BD/142864/2018. This work was supported by the Associate Laboratory for Green Chemistry-LAQV which is financed by national funds from FCT/ MCTES (UID/QUI/50006/2019) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265). The National NMR Facility is supported by FCT (ROTEIRO/0031/2013 – PINFRA/22161/2016, co-financed by FEDER through COMPETE 2020, POCI, and PORL and FCT through PIDDAC). JASC thanks the Fundação para a Ciência e a Tecnologia (FCT) for Scientific Employment Stimulus 2020/02383/CEECIND. DFT calculations were conducted in the computational facility of the Coelho group at FCUL.

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Toward the synthesis of Julandine and Cryptopleurine. One-pot sequential hydroamination to selectively access tri-, tetra-, and penta-substituted pyridines

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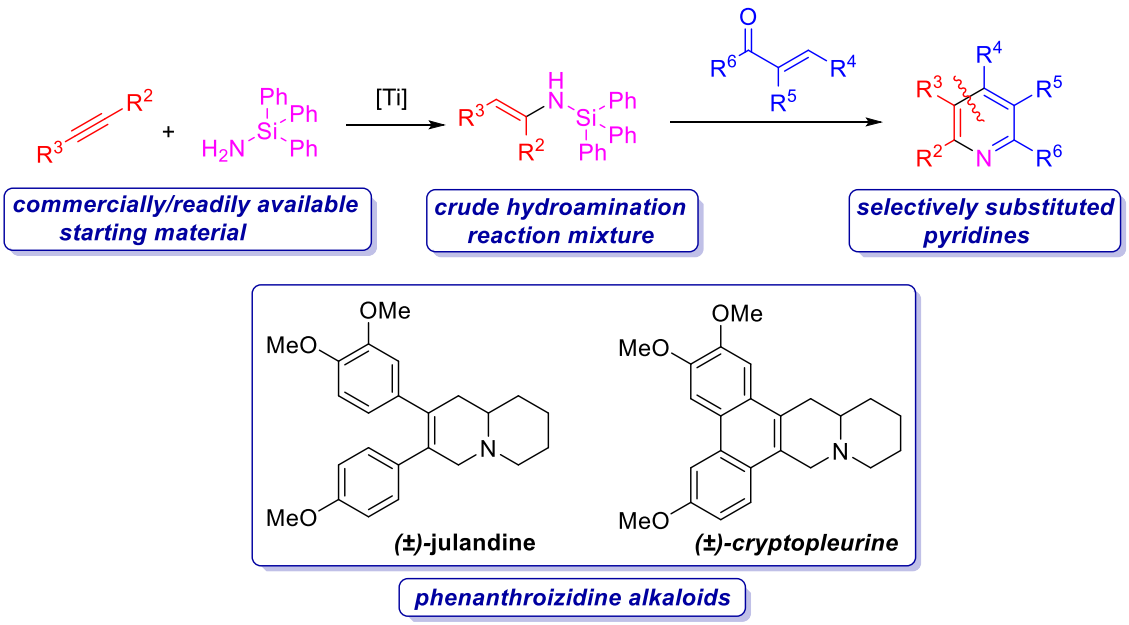
Functionalized pyridines have long been known as biologically active compounds [1]. Owing to their prevalence in natural products, pharmaceuticals, and agrochemicals, new and improved synthetic methods are important in the field of medicinal chemistry and drug design. Recent advances in the synthesis of multi-substituted pyridines include transition-metal-catalyzed intermolecular cyclization to access functionalized pyridine derivatives using pre-functionalized substrates [2]. Only a limited number of methodologies are available to access 2,3,4-, 2,4,5-, 3,4,5-, 2,3,4,5- and 2,3,4,5,6-substituted pyridines [3]. This limitation calls for a facile synthetic route that can be used to access new substitution patterns to allow medicinal chemists ready access to new pyridine derivatives. Herein we report a one-pot protocol for the assembly of selectively substituted and less explored tri-, tetra- and penta-substitution patterns for pyridines. Titanium-catalyzed hydroamination of alkynes with commercially available *N*-triphenylsilylamine selectively generates *N*-silylenamines. One of the advantages of using *N*-silylamine as a substrate is the selective formation of the enamine product, with no tautomerization to the imine form. These, *N*-silylenamines can be used for further reactivity without any requirement for purification. The *in situ* generated *N*-silylenamines upon reaction with an *α,β*-unsaturated carbonyl compounds followed by oxidation furnish 32 examples of selectively substituted tri-, tetra- and penta-substituted pyridines in isolated yields of up to 78%. This modular reaction features a high functional group compatibility providing an expeditious approach for the construction of a diverse range of less investigated pyridine derivatives. The expandability of this approach is under investigation in the total syntheses of Julandine and Cryptopleurine which belong to the class of phenanthroizidine alkaloids.



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Amino acids derived diazoketones – shelf stable reagents for organic synthesis

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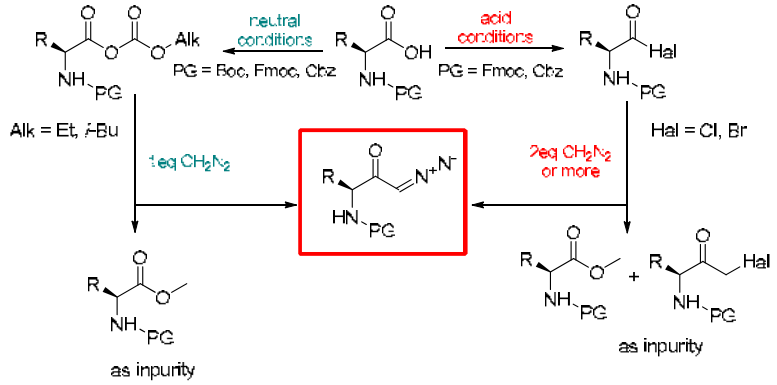
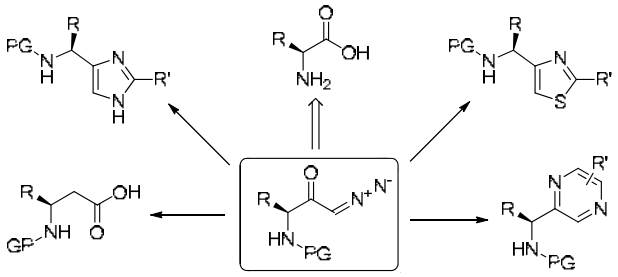
α-Amino acids derived diazoketones (AADDK) are an important class of reagents in organic synthesis. Using natural proteinogenic α-amino acids as starting material leads to easy excess to chiral AADDK. Therefore the reagents could be considered as one of the instruments for chiral pool α-amino acids synthesis. In this research, we have elaborated the semi-industrial methodology for generating a solution of diazomethane in the organic phase via alkaline decomposition of NMU in the flow reactor. All reaction conditions and the reactor's construction were optimized. This made it possible to achieve a productivity of 0.45 mol/h of diazomethane. Using the reactor an efficient and practical flow procedure for Boc-protected aminodiazaketones was developed on the basis of the reaction of activated Boc-protected amino acids with CH_2N_2. The optimized protocol allows making the compounds with productivity ca. 100 g/h. After investigation of the thermal properties, as well as the shelf-life time of diazoketones, it was claimed that the compounds are good “shelf-keeping” reagents for the medicinal chemist.



The utility of diazoketones was demonstrated by multi-gram (up to 150 g from 1 synthetic run) synthesis of Boc-protected amino acid-derived bromoketones – valuable intermediates for the API synthesis. The proposed procedure gives the target compounds a high purity level avoiding additional purification (e.g crystallisation, chromatography, etc.). We are also reporting their utilisation as haloketone's surrogates in different cyclisations to thiazoles, imidazoles, pyrazines, β-aminoacids etc.



The work was funded by the National Research Foundation of Ukraine (project 0120U104008). Authors thanks Enamine Ltd and Prof. A. Tolmachev for the financial and technical support of the work.

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Preparation of aminals (and thioaminals) under mild conditions and their remarkable applications

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Aminals are the condensation product of aldehydes and secondary amines. Structurally similar to acetals, these compounds have been used as intermediates, chiral auxiliaries and protection groups in reactions and in the biology field.[1]

The most common methodology for the formation of aminals involves the condensation of aldehydes with amines in ethanol or toluene under high temperatures using dehydrating agents to remove the water in the reaction, shifting the equilibrium to the product.[2] However, performing the reaction in aqueous media instead of organic solvents is an environmentally competitive process for the preparation of aminals.

This work reports on the formation of aminals, from aromatic aldehydes and furfural derivatives with different secondary amines in water under mild conditions **(Figure 1a)** as well as the formation of several thioaminals with yields up to 97% **(Figure 1b)**.[3] This is followed by the stability studies of different aminals and their use as protection group for aldehydes. Applying this approach together with the advantages of a continuous flow system allowed us to develop a new, simple and rapid methodology for selective removal of genotoxic aldehydes from APIs (Active Pharmaceutical Ingredient). Our method uses the diamine scavenging resin in a continuous flow system, generating the aminal within the microreactor efficiently **(Figure 2)**.[4]

The described aminal compounds were prepared with a more sustainable methodology allowing the use of these interesting molecules as protection group and presenting a noteworthy role on the removal of genotoxic impurities of the APIs.

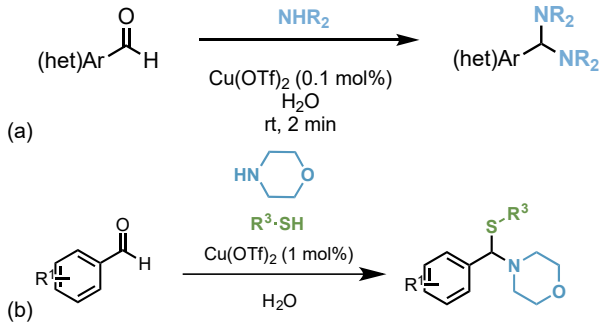

Figure 1. (a) Preparation of aminals from aromatic aldehydes and furfural derivatives with different secondary amines and (b) preparation of thioaminals from aromatic aldehydes with alkyl and aryl thiols, and morpholine in water under mild conditions.

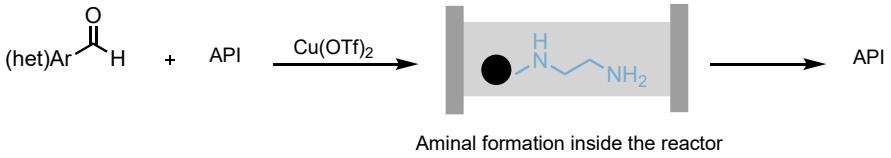

Figure 2. A new strategy for selective removal of genotoxic aldehydes from APIs.

Acknowledgments: We thank the Fundação para a Ciência e Tecnologia (PD/BD/143162/2019, UIDB/04138/2020 and UIDP/04138/2020), COMPETE Programme (SAICTPAC/0019/2015) for financial support. The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951996.

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Upcycling of Abundant Fatty Acids to Form Cyclic Carbonates and their Use as Monomers in NIPU Synthesis

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Fatty acids are an important and valuable bio-derived feedstock due to their wide versatility, whereby they have found many applications, such as, in biodiesel, plastics, and lubricants as additives. In particular, erucic acid, which is mainly found in the seeds of *Brassicaceae* and therefore the resulting oils derived from these (e.g. rapeseed oil and mustard seed oil), is toxic when it overcomes a tolerable daily intake of 7 mg/kg body weight. Only the *canola* oil, with a low erucic acid content <1-2%, is available for human consumption and animal feeding. The non-food uses cultivars, with high erucic acid content 30-50%, are still grown to achieve the demand of the oleochemical industry.[1] Thus, the upcycling of erucic acid, which could be extracted from theses oils, and would be considered as waste, represents a bi-directional opportunity. Firstly, the non-food oils would be safe for consumption, adding value to the industrial process. And secondly, the realization of bio-derived chemical products is a potentially important contribution to the challenge of developing sustainably derived chemicals.

One reported use of fatty acids as bio-based sources is the preparation of cyclic carbonates (CCs).[2] These are commonly obtained from the epoxidation of unsaturation in the aliphatic chains and subsequent reaction with carbon dioxide (CO_2). An important opportunity for the use of di-CCs is their reaction with diamines to form valuable Non-Isocyanate PolyUrethanes (NIPUs), which offers an alternative to traditional polyurethanes which use toxic isocyanates. In this contribution, we will describe the application of our recently developed highly-efficient catalytic system based on Ga for the synthesis of CCs,[3] towards epoxides derived from erucic acid and the conversion of the resulting di-CC monomers into NIPUs through the reaction with diamines. In addition, optimized multigram regio- and stereoselective syntheses of the CCs will be detailed.

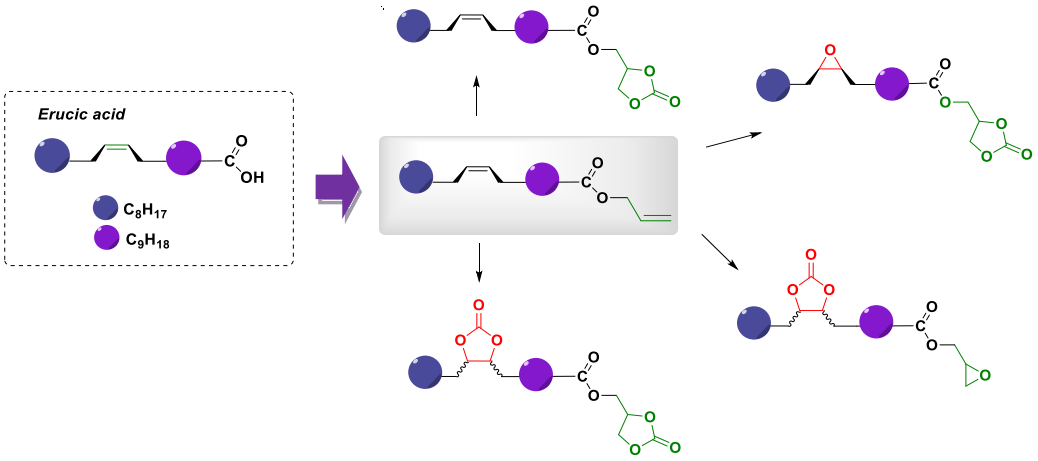

Figure 1. Synthesis of regio- and stereoselective CCs monomers derived from the erucic acid.

C.W. and L.A.M. would like to thank the Comunidad de Madrid (Spain) for funding (Programa de Atracción de Talento 2019: Modalidad 1; Award number 2019-T1/AMB-13037, and CM/JIN/2021-018). We would like to also acknowledge funding from the Spanish Government (RTI2018-094840-BC31 and PID2020-113046RA-I00) and the Universidad de Alcalá (UAH-AE-2017-2).

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Palladium-Catalyzed Direct(Hetero)Arylation in solvent free condition assisted by Infrared Irradiation

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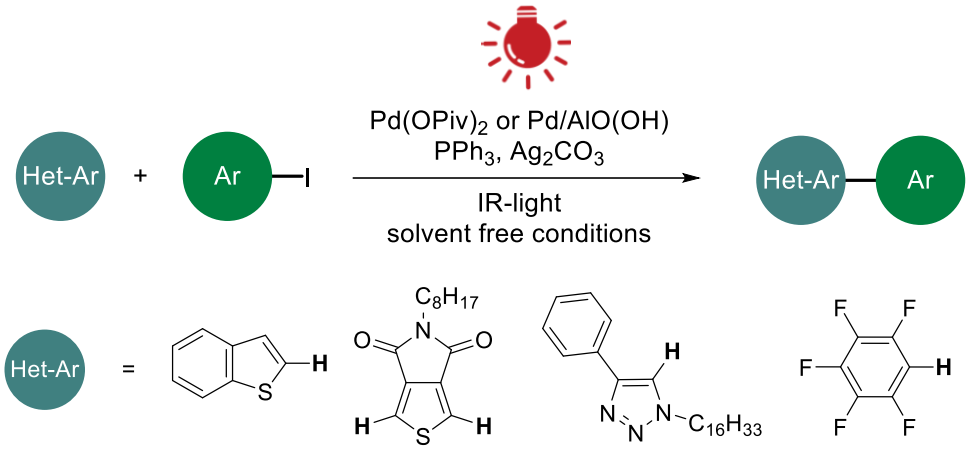
The biaryl structure is a common feature in many compounds of technological and pharmaceutical relevance, it has been studied comprehensively in recent years to find advanced and more cost-effective methods for the formation of aryl-aryl bonds.

The direct C-H bond activation is the most convenient choice for the formation of the (hetero)aryl-aryl motif: it eliminates the need for the preliminary preparation of air- and moisture-sensitive, expensive, and toxic organometallic reagents used in other cross-couplings reactions [1]. The main drawback is represented by the use of harmful solvents (e.g. DMA, DMF). Recently, innovative and more environmentally friendly protocols for direct arylation have been explored: they include the use of more sustainable solvents, such as water, or even the absence of solvent [2].



This study combines the advantages of direct arylation with those of infrared (IR) heating [3], making it possible to achieve high yields in a short time, avoiding the formation of undesired byproducts and making workup easier. In particular, the coupling of different (hetero)aryls with electron-rich and electron-poor aryl iodides has been successfully performed, affording yields as high as 87% in just fifteen minutes reaction.

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Deep-Eutectic Solvents as sustainable media for the Pd-catalyzed direct arylation of thienyl-derivatives with (hetero)aromatic bromides under air

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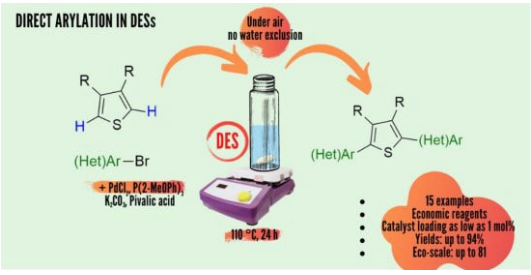
Among all the components of a chemical reaction, the solvent choice is often dictated by the solubility of the reagents and/or the medium polarity, but rarely by safety, health, and environmental (SH&E) criteria. Nevertheless, solvents represent most of the waste at the end of a classic batch reaction for the preparation of fine chemicals, both in terms of flammability and toxicity issues [1]. As an alternative to traditional volatile organic solvents (VOCs), Deep-Eutectic Solvents (DESs) [2] drew the attention of academic and industrial researchers for the possibility of using inexpensive and environmentally benign components, and their unique physicochemical properties like low volatility and high thermal stability.

Applications of DESs as reaction media in organic transformations are many and various [3] but still limited to a few and particular examples in the field of Pd-catalyzed direct arylation (DA), a kind of cross-coupling reaction that does not require the employment of any preformed organometallic reagent, but usually employs toxic and volatile solvents like toluene or *N*,*N*-dimethylacetamide. For these reasons, we developed a general synthetic protocol for the DA reaction of 3,4-ethylenedioxythiophene (EDOT) and other substituted thiophenes with (hetero)aromatic bromides in a mixture of choline chloride/glycerol (1:2), under air and in non-anhydrous conditions, with moderate-to-high yields [4]. This DA protocol was demonstrated to tolerate many functional groups, like aldehydes, ketones, nitriles, esters, carboxylic acids, and nitro-groups. The sustainability of the protocol was established through calculations of green metrics, such as Eco-scale and *E*-factor, and compared with the literature, when possible. Remarkably, such a procedure can be successfully applied for the simple preparation of conjugated organic compounds with potential applications in optoelectronics and photovoltaics.



Thanks to the Ministero dell'Università e della Ricerca (MUR) within the National PRIN program (project "NATUREChem") and Consiglio Nazionale delle Ricerche (CNR) within the Ricerca@CNR program (project "VertiGROW"). Alessio Dessì, as a recipient of the Young Investigator Award 2019, kindly acknowledges CNR-DSCTM funding in granting the attendance.

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On the Green road towards the synthesis of challenging N-heterocycles

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Azaindoles are bioisosteres of the indole nucleus, a privileged structure, which have enticed the interest of the scientific community for their physicochemical and pharmacological properties. Azaindoles are rare in nature and highly interesting in medicinal chemistry and drug discovery programs. This is mainly due to the fact that its solubility, lipophilicity, target binding and ADME-tox properties can be modulated and tuned, constituting an enormous advantage over other heterocyclic compounds.[1] However, synthesis of azaindoles is challenging. The electron-deficient nature of the pyridine ring alters the electronic properties of the conjugated system in such a way that many classic indole synthetic methods are not as efficient or simply do not work. Due to their important value, we have developed methods for the synthesis of azaindoles, relying on palladium-catalyzed cross-coupling reactions and developed different practical approaches compatible with all azaindole isomers.[2,3] Our group has been focused on metal-catalyzed cross-coupling reactions for the straightforward synthesis of azaindoles from commercially available aminopyridines. In particular, we have been exploring Pd-catalysed one-pot methodologies such as the C-N cross-coupling/Heck reaction[4] also with Pd-nanocatalysts;[5] the N-arlyation/Sonogashira/cyclization reaction;[6] and Pd-catalysed C-N cross-coupling/C-H functionalization.[7] Herein we will present our latest achievements on the one-pot reactions, and simple protocols towards not easy to make heterocycles.

Thanks to Fundação para a Ciência e Tecnologia (FC&T) (project PTDC/QUI-QOR/0712/2020). This work was supported by the Associate Laboratory for Green Chemistry- LAQV which is financed by national funds from FCT/ MCTES (UID/QUI/50006/2020) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265). The National NMR Facility is supported by FCT (ROTEIRO/0031/2013 – PINFRA/22161/2016, co-financed by FEDER through COMPETE 2020, POCI, and PORL and FCT through PIDDAC).

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Greener Pharmaceuticals: Short and Modular Enantioselective Organocatalyzed Synthesis of new BET Bromodomain Inhibitors with Anti-inflammatory Action

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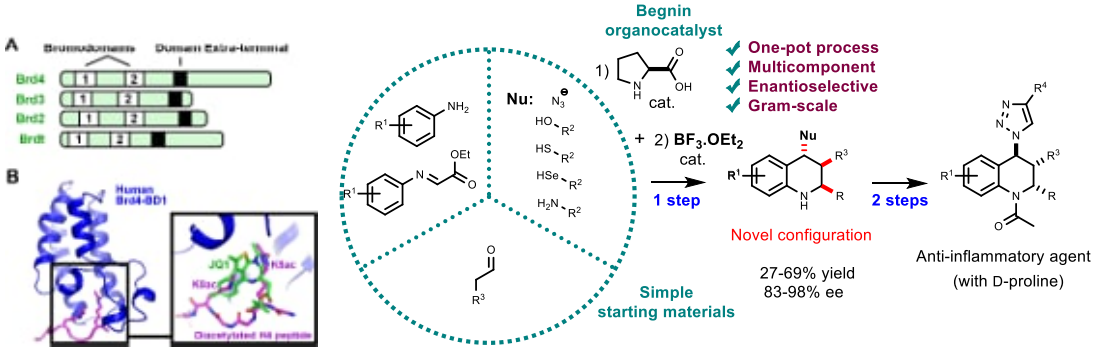
Asymmetric organocatalysis is both an ecological and economical solution for its ability to create molecular complexity from very simple elements.[1] In this context, we are interested in the acetylated tetrahydroquinoline (Ac-THQ) motif which belongs to the bromodomain inhibitors.[2] Recently, the identification of molecules that selectively inhibit BET BD2, but not BD1, has elicited great interest as they impair the activation of pro-inflammatory genes without affecting the expression of housekeeping and maintenance genes, thereby limiting their toxicity and improving the drug safety profile.[3] We developed a new reaction sequence involving the use of proline or silyl prolinol as catalysis combined with the addition of a catalytic amount of Lewis acid to form the 1,2,3,4-tetrahydroquinoline (THQ) structure in one pot process.



This key reaction involves an initial enantioselective Mannich reaction carried out *via* the proline-catalyzed List-Barbas reaction.[4] The addition of a catalytic amount of Lewis acid ($BF_3.OEt_2$) allowed the *in situ* formation of an aza-*ortho*-quinone methide that can be trapped by various nucleophile (Nu) to form the THQ structure. When Nu = N_3, copper-catalyzed Huisgen reaction allows easy extension for diversification by the addition of a new substituent (R^4). In this communication, we will report the synthesis of various analogues, their optimisation and the identification of selective inhibitor of bromodomain BD2 by *in vitro* and cell-based assays. These compounds showed a good anti-inflammatory activity with a favourable efficacy/toxicity profile. RNA-seq analysis provided insight into the genes involved in therapeutic action.

Thanks to the Agence Nationale pour la Recheche (ANR), the labex ARCANE and CBH-EURE-GS, grant number ANR-17-EURE-003; La Ligue Contre le Cancer-Comité régional de l'Isère, grant number LNCC-R20015CC ; Fond AGIR pour les Maladies Chroniques.

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Turning on Blue Light on Carbopalladation: a Practical Access to ɔcycles at Room Temperature

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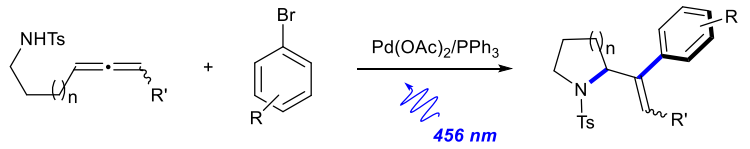
Between the most important tools of modern organic chemistry, transition metal-catalysed reactions have a prominent role. In the last years, the already wide reactivity of metals as catalytic species has been farther broadened thank to the last developments in photocatalysis. In fact, the association of classical organometallic catalytic systems (Ni, Co, Cu, Pd) with light has opened the way to an orthogonal and unconventional reactivity never achieved before [1-3]

Considering the limited number of methodologies available to access substituted saturated *N*-heterocycles with ease and efficiency [4] (*e.g*. cyclization of suitable precursors or modification of readily available pyrrolidines and piperidines), we envisioned a novel synthetic strategy to obtain arylated vinyl pyrrolidines and piperidines starting from *N*-tosylaminoallenes [5]. The combination of the simple catalytic system $Pd(OAc)_2/2PPh_3$ with blue light allowed for an unprecedented visible light enhanced room temperature Heck reaction with wide scope. Electron-donating, electron-withdrawing aryl and heteroaryl bromides were efficiently coupled with allenes in a Pd(0) catalysed cross coupling. A subsequent domino cyclisation triggered by the tosylamino functionality afforded valuable branched vinyl pyrrolidines and piperidines. Mechanistic investigations highlighted the prominent and new role of light in boosting the carbo-palladation step.



- room temperature Heck reaction
- C-N and C-C bond formation

>50 examples

up to 85% yield

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Homodimerization of isocyanides towards the elusive 1,4-diazabutatriene

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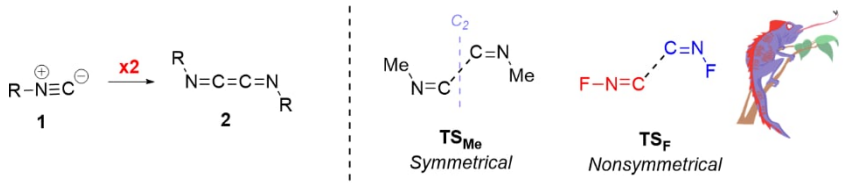
Isocyanides are commonly qualified as chameleonic compounds because of their reactions with both nucleophiles and electrophiles. Although they are known to polymerize easily, the dimerization of isocyanides affording head-to-head dimers, namely 1,4-diazabutatrienes R-N=C=C=N–R, has been scarcely explored. Curiously, these species have been never isolated but eventually proposed as reaction intermediates [1].

We herein present a computational study on the homodimerization of isocyanides **1** towards **2**, in particular on the influence of the substituents onto the evolution of structural and energetics parameters along the reaction coordinate [2,3]. Of special significance is the computed non-least motion character of this kind of reactions and, also, the homodimerization of the F−NC, in which the two units are notoriously distinguishable in all the parameters under scrutiny. Moreover, the 1,4-diazabutatrienes are stabilized by π-donor or σ-acceptor substituents and, in some cases, by the combination of one donor with one acceptor substituents at both N termini [4].



This work was supported by the MINECO (Project CTQ2017- 87231-P) and the Fundación Seneca-CARM (Project 20811/PI/18) and the Ministerio de Ciencia e Innovacion of Spain (PID2020-113686GB-I00 MICIN/AEI/10.13039/501100011033)

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Visible Light Triggered Cascade Processes for the Synthesis of Saturated N-heterocycles

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Nitrogen saturated heterocycles are privileged scaffolds for innovative drug design [1],[2],[3]. Lately, the interest of our research group in photoredox catalysis and in the synthesis of pharmaceutically relevant molecules have merged towards the preparation of such aliphatic heterocycles by means of domino processes triggered by visible light.

Exploiting the photoredox behavior of ruthenium photocatalyst, we reported the synthesis of three different classes of tetrahydropyridazines from γ,δ-unsaturated N-arylsulfonylhydrazones by appropriately tailoring the structure of the reactant [4].

Currently, we are exploring a synthetic strategy towards saturated N-heterocycles where blue light irradiation promotes a haloamination of allene C-C bond. Such functional group, bearing two adjacent double bonds, allows a domino process to occur with an intramolecular cyclization followed by an intermolecular halogenation. Thus, α-(chlorovinyl)-*N*-heterocycles are delivered, providing installation of a versatile lateral functional group (α-chlorovinyl moiety) to allow otherwise still arduous further derivatizations of these nitrogen saturated heterocycles.

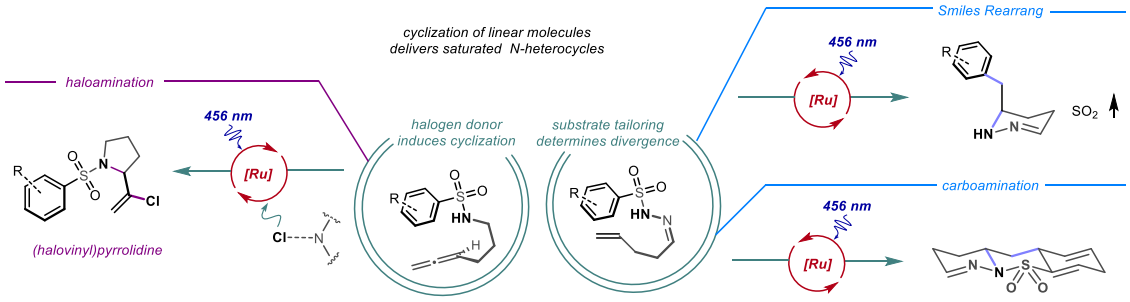

Figure: Summary of the visible light triggered cascade processes for the synthesis of saturated N-heterocycles currently under investigation

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Phosphorus(V)-promoted Py-Py and CF_3-Py ligand couplings and Hal-Py S_NAr from phosphonium salts: emerging metal-free functionalization of nitrogen heterocycles

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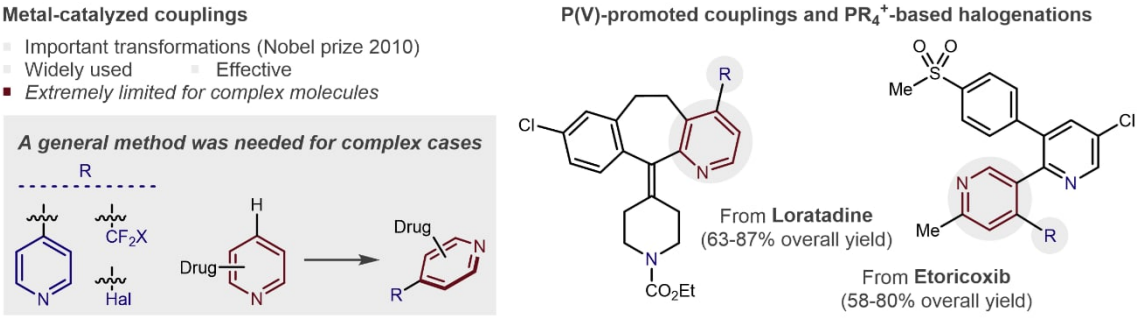
Recently, the McNally laboratory employed pentacoordinated phosphorus (P(V)) intermediates to promote metal-free biaryl couplings of heteroaromatic groups. This type of phosphorus-based reactivity, known as ligand-coupling, was further developed to perform challenging transformations such as the trifluoromethylation and halogenation of heteroaromatic nitrogen compounds (e.g. pyridine). All these synthetic methodologies were successfully applied in late-stage functionalization of complex molecules, opening new ways to construct therapeutic candidates.

In this work, we present the most relevant mechanistic insight of the P(V)-based Py-Py [1] and CF_3-Py [2] ligand couplings obtained with computational chemistry. We also examine the fundamental differences with an analogous Hal-Py S_NAr [3] triggered by phosphonium salts. The results of these theoretical studies, combined with experimental results, deliver a quantitative analysis of the competing reaction pathways and a stereoelectronic model for the excellent levels of selectivity observed in all the reactions. Additionally, the role of ligand apicophilicity and orbital symmetry in controlling reactivity, selectivity and type of chemical transformation will be discussed. The quantum mechanical calculations were carried out with DFT (ωB97X-D) and coupled cluster theory (DLPNO-CCSD(T)) as well as the SMD solvation model.



J.V.A.-R. and R.S.P. acknowledge the RMACC Summit supercomputer, supported by the NSF (ACI-1532235 and ACI1532236) and the Extreme Science and Engineering Discovery Environment (XSEDE) allocations TG-CHE200033 (J.V.A.-R.) and TG-CHE180056 (R.S.P.).

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Origin of the α-Effect in S_N2 Reactions

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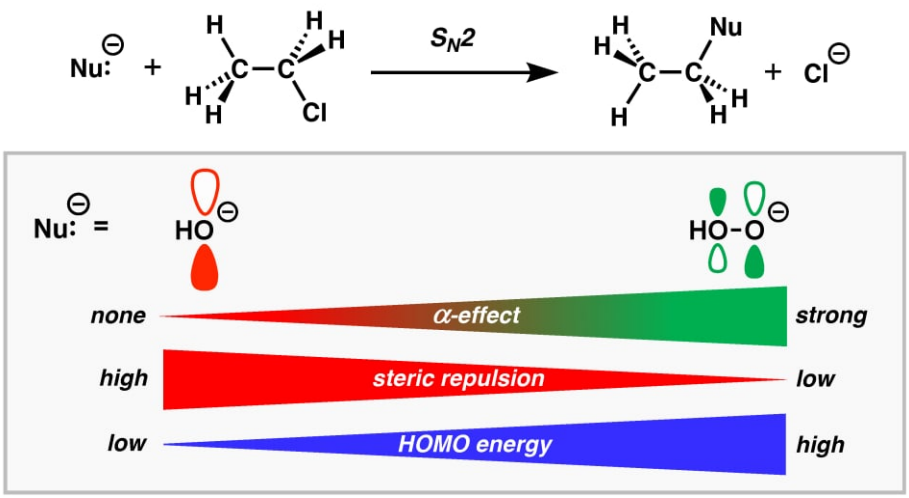
The α-effect is a fundamental phenomenon in organic chemistry that refers to the dramatically enhanced reactivity of nucleophiles featuring a lone pair-bearing heteroatom adjacent to the nucleophilic center, resulting in a deviation from the classical Brønsted-type reactivity–basicity relationship [1]. Despite extensive experimental and computational studies, the exact origin of the α-effect remains elusive and under debate. Our state-of-the-art quantum chemical activation strain analyses [2,3] revealed the intrinsic properties an α-nucleophile needs to exhibit α-effect: i) a small HOMO lobe on the nucleophilic center to reduce the repulsive occupied–occupied orbital overlap and hence steric (Pauli) repulsion with the substrate; and ii) a sufficiently high-energy HOMO to overcome the loss of favorable HOMO–LUMO orbital overlap with the substrate, as a consequence of the first criterion [4]. If one of these two criteria is not fulfilled, one can expect no α-effect or inverse α-effect. This contribution will show how and why these properties ultimately lead to the deviation from the classical Brønsted-type correlation between reactivity and basicity. In all, these principles will allow one to qualitatively predict if a nucleophile possesses α-effect solely based on its intrinsic electronic structure and, therefore, have the potential to enable chemists to better understand and design these fundamental reactions.



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High-pressure reaction profiles and activation volumes of 1,3-cyclohexadiene dimerizations computed by the extreme pressure-polarizable continuum model (XP-PCM)

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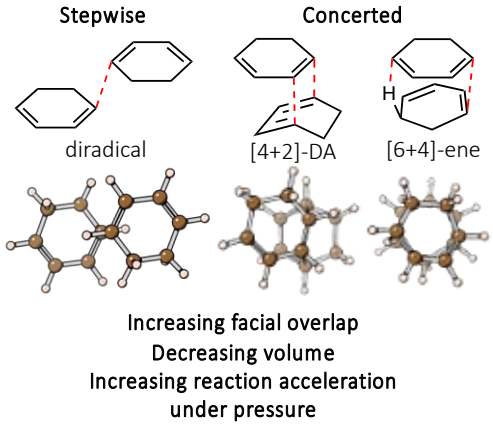
Quantum chemical calculations are reported for the thermal dimerizations of 1,3-cyclohexadiene at 1 atm and high pressures up to the GPa range. Computed activation enthalpies of plausible dimerization pathways at 1 atm agree well with the experiment activation energies [1] and the values from previous calculations [2]. High-pressure reaction profiles, computed by the recently-developed extreme pressure-polarizable continuum model (XP-PCM) [3], show that the reduction of reaction barrier is more profound in concerted reactions than in stepwise reactions, which is rationalized on the basis of the volume profiles of different mechanisms. A clear shift of the transition state towards the reactant under pressure is revealed for the [6+4]-ene reaction by the calculations. The computed activation volumes by XP-PCM agree excellently with the experimental values, confirming the existence of competing mechanisms in the thermal dimerization of 1,3-cyclohexadiene.

This work [4] demonstrates that accurate computation of activation volume is a powerful tool in deciphering competing reaction mechanisms in the current, and likely other reactions. The evolution of the cavity volume of the reactive system upon proceeding from the reactants to products, proves to be a useful diagnostic for analyzing the effect of the pressure on the reaction profiles. The analysis of partition of activation volume into physically meaningful contributions provides a new and extremely useful way to understand the origin of activation volume. The insights from such analysis will be useful in designing new high-pressure reactions.



We thank Roald Hoffmann and Frank Klärner for helpful discussions. R.C. thanks the support of the framework of the COMP-HUB Initiative of the Department of Chemistry, Life Sciences and Environmental Sustainability of the University of Parma, as part of the 'Departments of Excellence' program of the Italian Ministry for Education, University and Research (MIUR, 2018-2022).

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New eco-friendly pathways for the synthesis of insect pheromones by iron-catalyzed cross-coupling: development, industrial applications, and mechanistic aspects

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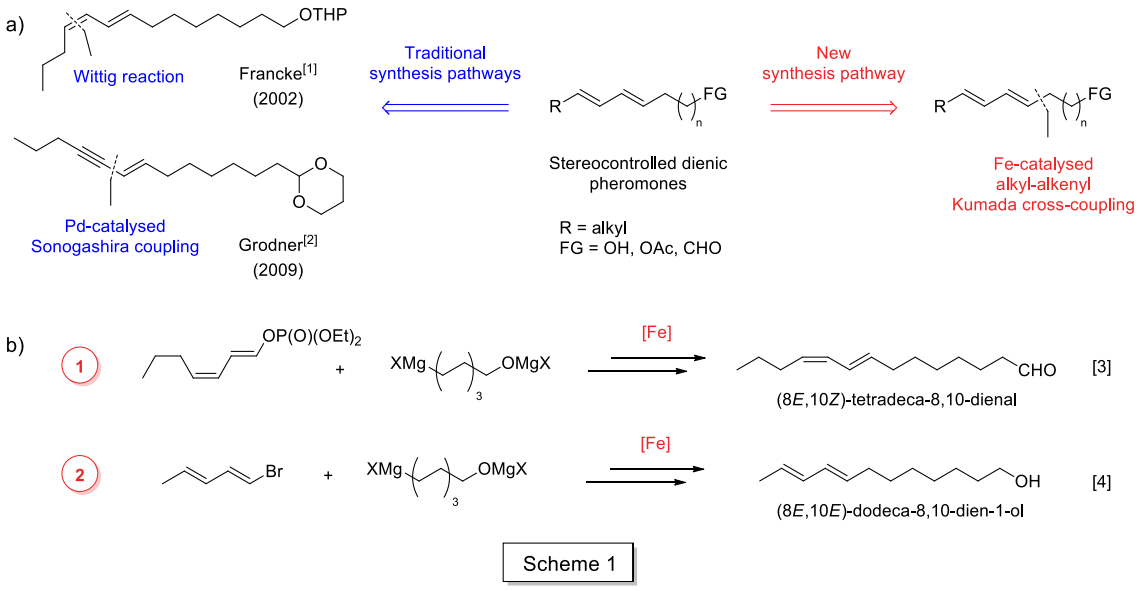
Unlike the use of pesticides, which has led to significant ecological and health issues, biocontrol based on use of pheromones is an eco-friendly solution for the protection of a wide range of crops, vineyards, and plants against pests. In addition, pheromones are fully biodegradable and specific to the sole target species, and they do not display toxicity to human health. However, at this time, few pathways for the synthesis of insect pheromones reported in the literature are applicable on an industrial scale. Indeed, the key step of the synthesis, the introduction of the C=C unsaturations, traditionally involves expensive and waste generating methodologies such as Wittig reaction[1] or Pd-catalyzed cross-coupling[2] (Scheme 1a).

To address this issue, we developed new synthetic routes relying on iron-catalyzed cross-coupling as a key step, capitalizing on the low eco-toxicity and the cheap cost of this metal. In the first example given in scheme 1b, a short six-step convergent high-scale synthesis of the horse-chesnut leaf miner sex pheromone is achieved with an overall yield of 40%.[3] Importantly, neither ligands nor additives are used to perform the key stereoselective iron-catalyzed Kumada cross-coupling. In the second example, we tried to replace the dienyl phosphate by a stereocontrolled bromodiene for atom economy, cost, and practical issues to achieve another sex pheromone synthesis. Again, no ligand or additive is used thanks to the -OMgX moiety which seems to improve the stereoselectivity and the efficiency of iron-catalyzed cross-coupling.[4] Mechanistic investigations are under progress to explain this point.



Scheme 1

The M2i Company is thanked for its financial support (CIFRE Grant Program for P.C.) in the frame of the M2i-CNRS Joint Research Program "PheroChem". NMR facilities from Chimie ParisTech are acknowledged for technical support.

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Reactive Deep Eutectic Solvents (ReDESs): an underexploited option for organic chemistry

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Transition toward sustainable chemistry is boosting the search for solvents endowed with safe, renewable and environmentally friendly profiles which can be suitable alternative to traditional volatile organic solvents. In this context, Deep eutectic solvents (DESs) emerged as one of the most encouraging media for several research areas. DESs are binary mixtures of two distinct species which display freezing temperatures at the eutectic point well below the ideal expected ones. Usually, this deviation from ideality is rationalized considering the strong hydrogen bonding interactions between a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA) that cause in some cases impressive freezing temperature decrement.[1] A very attractive feature of the DESs is the possibility to fine-tune their physico-chemical properties by choosing the appropriate partners, molar ratio and amount of water. This peculiar aspect holds true for a subset of DESs, the so-called Natural DESs (NaDESs), which are mixtures composed solely by natural partners (such as organic acids, plant metabolites, sugars or aminoacids). NaDESs are regarded as the most promising solvent option for the development of sustainable chemistry on account of the ease of preparation and low cost, the modulability of their physicochemical properties, their benign (eco)toxicological profiles.[2]

In the last years, the use of DESs as *green* innocent solvents in organic synthesis has been reported for a wide range of reactions. Particular emphasis has been direct towards the possible dual solvent-catalyst role played by DESs. However, their use as reactive media has been almost completely overlooked. In the present work, the potential of reactive DESs (ReDESs) as innovative media for the synthesis of bio-derived compounds has been investigated. Sustainability aspects have been evaluated by using green metric parameters.

The solvation effect of these complex and structured systems can be very specific like the one observed in ionic liquids [4]. DFT calculations can help to elucidate reaction mechanisms in which solvent components assume an active reactive role.

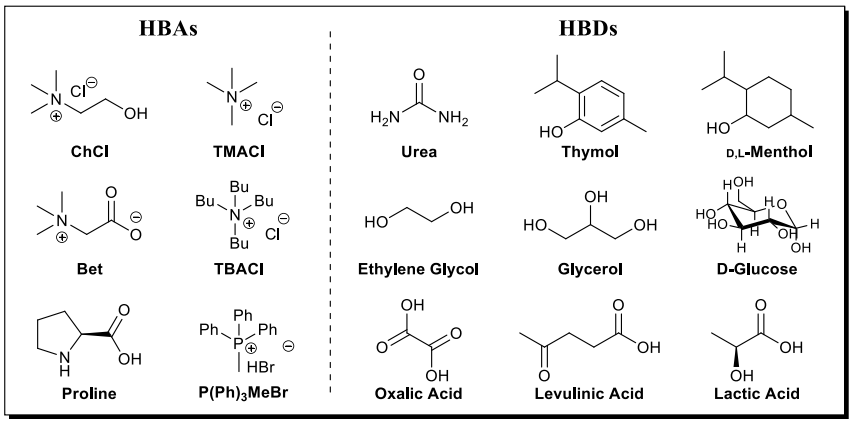

Figure 1. Common hydrogen bond acceptors (HBAs) and hydrogen bond donors (HBDs) DES partners.

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Straight from the bottle! Wine and juice dicarboxylic acids as templates for supramolecular cage self-assembly

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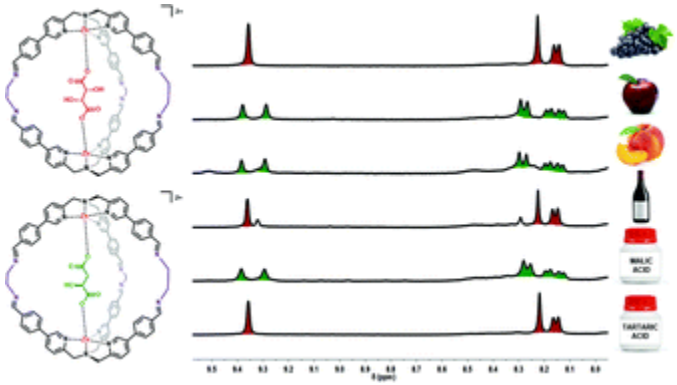
Supramolecular cages are able to self-assemble in the presence of a complex mixture like wine or fruit juices. Taking advantage of templating agents present in these mixtures the systems are able to form and to selectively encapsulate dicarboxylic systems present in the mixtures. This capability has been exploited to develop molecular systems able to report the enantiomeric excess and composition of (a)chiral dicarboxylic acids in fruit juices and wines using ^{1}H-NMR.[1]



Thanks to CARIPARO FOUNDATION and UNIVERSITY OF PADOVA.

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Hydrogen-bonding patterns of amidophosphine sulfides in solution and in the solid-state

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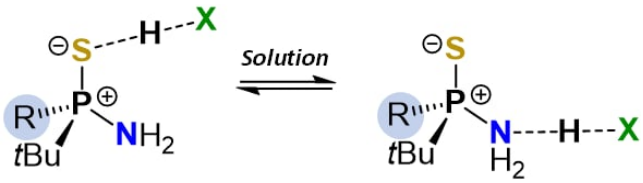
Well-defined structural patterns form the basis for the self-organization of the molecules of life and for mineralization processes in our nature [1,2]. Knowledge about noncovalent interactions in supramolecular assemblies in solution and in the solid-state is therefore a key to understanding the molecular mechanisms of their formation and leads us to the origins of complex matter [3,4,5].

Amidophosphine sulfides can be considered as simplified bifunctional molecular model systems combining both an amido (NH_2) and a phosphorus sulfide (PS) group within the same molecule [6]. Both functional units are in principle capable of forming hydrogen bonds. Our presentation addresses the question of how the two competing acceptor atoms are involved in hydrogen-bonding both in the solid-state and in solution, and under which conditions one of the two bonding modes is favored. An achiral and an enantiomerically pure phosphorus-stereogenic model have been investigated. Insights into supramolecular assembling and hydrogen bond switching are provided on the basis of structural, spectroscopic, and computational studies.



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Synthesis and characterization of new cationic diketopyrrolopyrroles with biological activity

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Diketopyrrolopyrroles (DPP) represent a class of brilliant red and strong fluorescent high-performance dyes and pigments that gained wide attention in recent years due to their outstanding properties. The excellent photostability, high fluorescent quantum yields, and environment and thermal stability make them excellent candidates for technical and biological applications [1]. The photodynamic therapy with DPP dyes is one of the most relevant recent applications for those compounds [2,3]. In this work is demonstrated the synthesis and structural characterization of four diketopyrrolopyrrole derivatives containing one or two pyridinium moieties (**1a**, **1b**, **2a** and **2b**) (Figure 1) [4]. These compounds have been evaluated as photosensitizers in photodynamic therapy, as well as ligands for the stabilization of G-quadruplex DNA structures [5], and the results confirm their usefulness for biological applications.

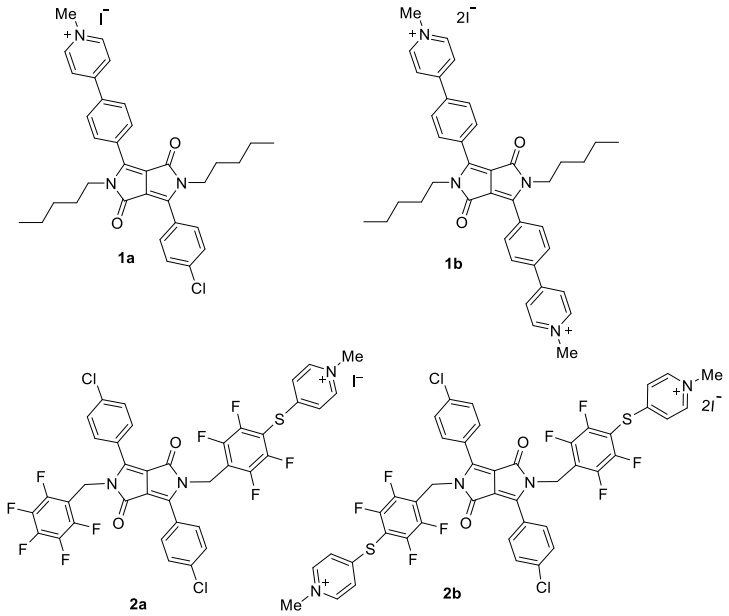

Figure 1. Structures of synthesized cationic diketopyrrolopyrrole derivatives.

Thanks are due to the University of Aveiro and Fundação para a Ciência e a Tecnologia (FCT) for the financial support to project PTDC/QEQ-QOR/6160/2014 and the LAQV-REQUIMTE (UIDB/50006/2020) through national funds and, where applicable, co-financed by FEDER, within the PT2020 Partnership Agreement, and to the Portuguese NMR Network. Vítor A. S. Almodovar thanks FCT for his doctoral grant (SFRH/BD/135598/2018).

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[7]Helical Indenofluorenes: Their Enantioselective Synthesis and Applications

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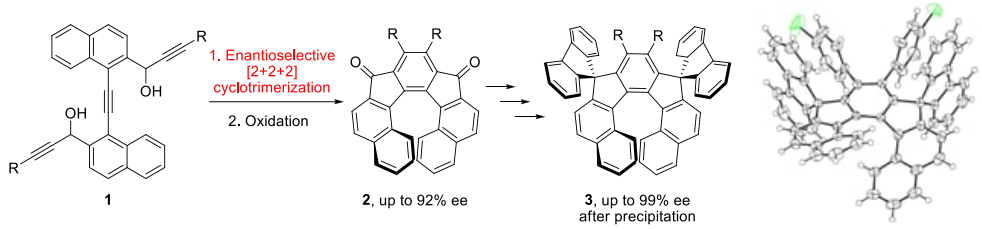
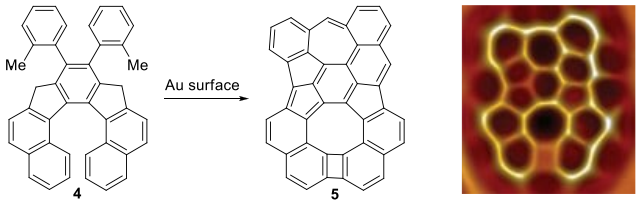
Enantiopure helicenes and other aromatic helical compounds are important classes of molecules that find potential applications in material science based on organic molecules [1]. Recently, we have developed a method for the synthesis of highly fluorescent compounds possessing the fluorene [2-4] and indenofluorene [5] scaffolds by using a catalytic intramolecular [2+2+2] cyclotrimerization.

We have focused on development of a simple synthesis of enantioenriched [7]-helical bispiroindeno[2,1-*c*]fluorenes **3** based on enantioselective [2+2+2] cyclotrimerization of triynols **1** via indenofluorenediols **2** [6]. It proceeded with asymmetric induction as high as 92% *ee* and depended on the nature of R substituents. The subsequent transformations of **2** gave rise to bispiroindenofluorenes **3** in high enantiopurity (up to 99% *ee*). Structure of several products and their configuration was unequivocally determined by X-ray diffraction analysis. All prepared [7]-helical Indenofluorenes **3** exhibited high fluorescence in the region of 410-430 nm (Φ_F up to 0.87) and were CPL active (g_{lum} ~1×10^{-3}). In addition, depostion of a structurally related [7]-helical bispiroindeno[2,1-*c*]fluorene **4** led to its planarization and skeltal rearrangements giving rise to a nonalternant non-benzenoid aromatic compound **5**.[7]



Scheme 1. Synthetic pathway to chiral [7]helical bispiroindenofluorenes **3** and X-ray structure of **3f**.



Scheme 2. Skeletal rearrangement of **4** to **5** on a gold surface.

This work was supported by Czech Science Foundation (reg. No. 18-17823S and 21-39639L).

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Modulating the catalytic performance of prolinamide-based organocatalysts with the mechanical bond

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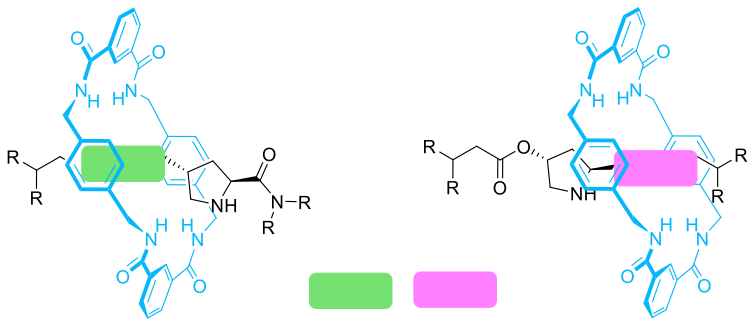
The integration of mechanically interlocked molecules (MIMs)[1] in the catalyst´s tool-box for asymmetric catalysis is attracting significant attention, with different research groups applying mechanized systems as organocatalysts or ligands for metal-catalyzed processes.[2] Herein, we described the synthesis of a series of prolinamide-based rotaxanes and their use as organocatalysts. The structural and conformational features of these entangled scaffolds make them promising players in asymmetric catalysis. We explored the catalytic outcomes of these systems and their non-interlocked threads in various enamine-type transformations, finding interesting behaviors as a consequence of the mechanical bond.[3],[4] As a result, we were able to develop enantio- and chemo-divergent processes catalyzed by these systems.



This research was supported by the Spanish Ministry of Science and Innovation (PID2020-113686GB-I00/AEI/10.13039/501100011033) and the Fundacion Seneca-CARM (Project 20811/PI/18).

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Synthesis, characterization and polymerization of fluorinated dopamine: evaluation of structural features in bioinspired polydopamine

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Dopamine, also known as 2-(3,4-dihydroxyphenyl)ethylamine, is an important biomolecule produced both by animals and plants and synthetized for an enormous number of functions. Like other catecholamines, it has attracted great interest in material sciences. Indeed, its polymerization reaction is a non-enzymatic spontaneous process in aqueous solutions in mild conditions. Since polydopamine (PDA) is composed by different monomer and oligomer moieties, further arranged in supramolecular interactions and highly influenced by the reaction conditions, its deep characterization is still under debate. All the intermediates create a dark brown branched polymer exhibiting a high number of hydrogen donor and acceptor units and aromatic rings held together by covalent and π-π stacking [1]. PDA finds applications in metal chelating and reducing properties, ultrathin coatings and in adhesives [2]. In particular, PDA and related dopamine-rich proteins are responsible for the exceptionally high adhesion of marine creatures, such as mussels (*Mytilus spp.*). We focused on the chemical modification of dopamine through selected chemical reactions involving fluorine atoms addition. Fluorine is a well-known substituent able to dramatically modify the hydrophobic/hydrophilic behavior of a molecule or a surface [3]. The presence of a perfluoroalkyl pendants is mandatory when an increase of water repulsion is desired as, for instance, in the design of new stronger underwater adhesives. Fluorinated dopamines still maintain their unique ability to polymerize in the typical PDA structure. Electrochemistry showed that polymerization preserves the hydroxyl residues, making PDA a new bioderived material for high tech applications in the field of water-resistant hydrophobic materials. This fine chemistry on dopamine could shed light on the true mechanisms of polymerization through the study of chemical environments of fluorine atoms specifically included in the molecule.

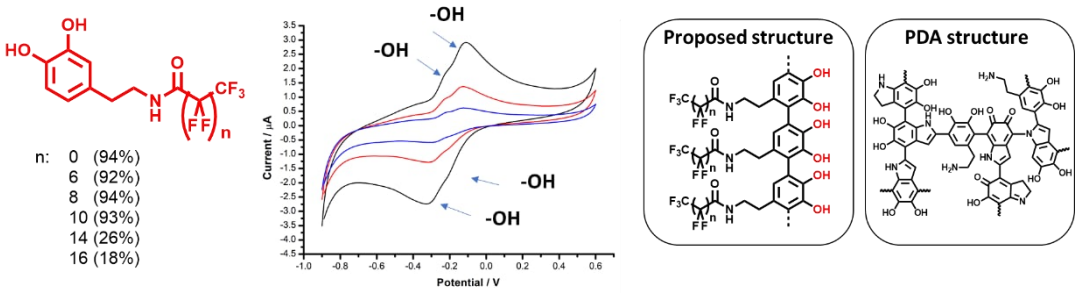

Figure 1. Study on the effect of fluorination on the final PDA structure. On the left, some examples of synthesized products (yields in brackets). In the middle, the Cyclovoltammetry curves of polymerizing fluorinated dopamine, suggesting a polymerization pathway in which -OH are maintained. On the right, the proposed structure of our fluorinated PDA in contrast to the most probable structure of PDA.

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Regioselective bis-functionalization of fullerene C_{70} via supramolecular masks

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Isomer-pure poly-functionalized fullerenes are required to boost the development of fullerene chemistry in any field, specifically in solar cell design [1]. Developing new synthetic strategies capable to restrict the regioisomer formation is a challenge, especially for C_{70}, less abundant than C_{60}, and with 8 distinct bonds at which mono-functionalization may occur, leading to a complicate mixture of multiple adducts when functionalized.

In this work we show the regioslective synthesis of bis-C_{70}–adducts upon Bingel cyclopropanation using supramolecular nanocapsules as masks [2]. In order to deep into the subtle mask-mediated regiofunctionalization, a tetragonal prismatic nanocapsule (C_{70}@(Pd-pp)Cage) and a three shell Matryoshka complex [2] (C_{70}@[10]cycloparaphenylene@(Pd-pTp)Cage) have been explored; additionally a series of malonates differing in bulkiness have been tested.

Strikingly, a single pure regio-isomer (2 o'clock) of the Bingel bis-adduct of C_{70} is obtained by using the dibenzyl bromomalonate and the three shell Matryoshka complex, preventing the poly-functionalization and achieving a 100% regioselectivity. Molecular Dynamics simulation have help in rationalizing the experimental results showing that the high regioselectivity is due to the conformation of the 2 o'clock regio-isomer inside the Matryoshka complex.

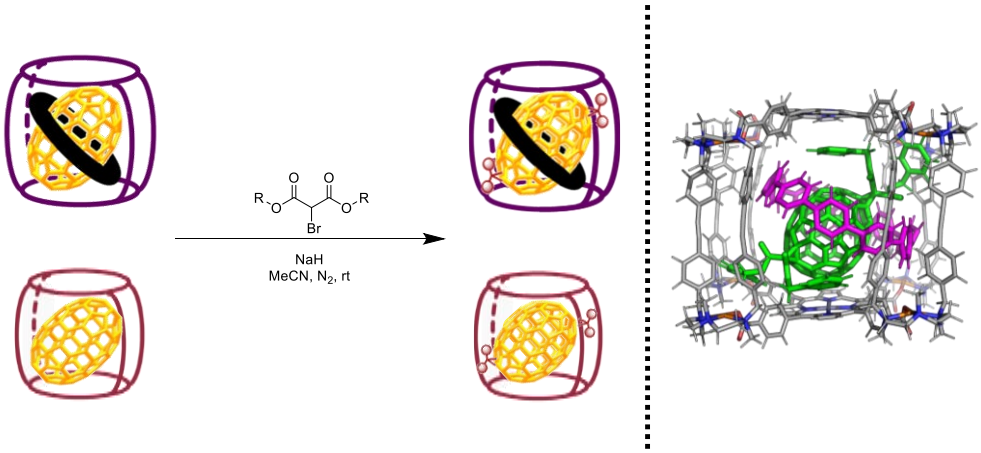

Figure 1. Bingel cyclopropanation of C_{70} using supramolecular nanocapsules and Matryoshkas as masks. MD Simulation of the (2 o'clock) bis-adduct inside the Matryoshka complex.

This work was supported by grants from MINECO-Spain (CTQ2016-77989-P and PID2019-104498GB-I00 to X.R., and a PhD grant to V. I.), Generalitat de Catalunya (2017SGR264). M.v.D. is grateful for financial support from the Deutsche Forschungsgemeinschaft (project number 182849149-SFB953). X.R. is also grateful for ICREA-Academia awards. We thank STR-UdG for technical support.

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Flexible synthesis of functional perylene 3,4,9,10-tetracarboxylic acid derivatives using ester functionalities as solubilizing, protective and functional groups

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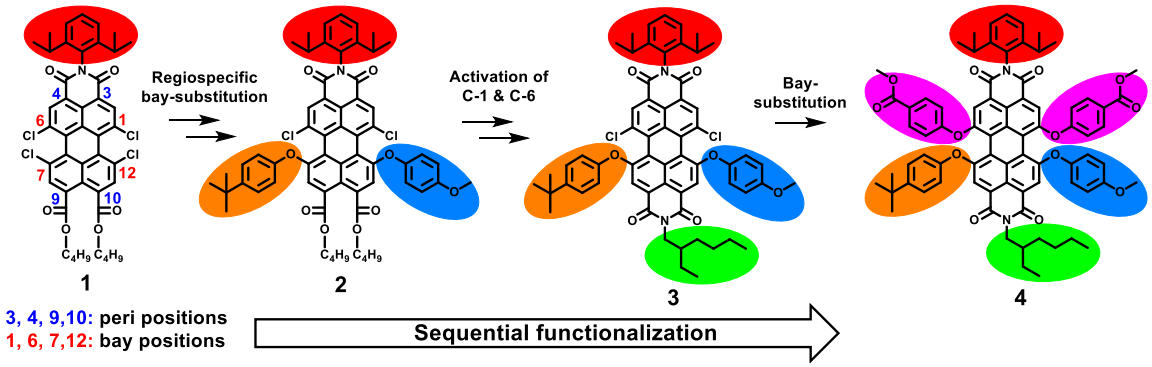
Perylene 3,4,9,10-tetracarboxylic acid derivatives (PTCAs) are a class of organic dyes that have benign optoelectronic properties, possess unprecedented stability and are chemically extremely versatile, with 12 positions on the perylene scaffold that can be functionalized. Due to low solubility and limited synthetic methodology,[1] most compounds that have been synthesized for use as functional materials and molecular devices are highly symmetrical. Additional synthetic methods, for addressing all positions at the perylene scaffold individually, are needed.

Our group has recently developed a novel strategy for the synthesis of functional PTCAs, exploiting esters at the peri positions, as solubilizing *and* protective groups. Esters are formed early in the synthesis to circumvent low solubility, followed by halogenation at bay positions.[2,3] Peri modification, generally converting esters to imides, followed by substitution of the bay halogens yields the final products. Interestingly, partial ester removal from the peri-positions induces pronounced differences in reactivity of the bay halogens, thereby gaining direct control over the substitution pattern at the bay positions.[4]



In this presentation I will demonstrate the potential of our synthetic strategy by presenting the synthesis of PTCA regioisomers with different substituent patterns at the bay positions. Despite small structural changes, these isomeric compounds exhibit markedly different photo physical properties.[5]. Subsequently the synthesis of perylene diimides (PDIs) with 5 independent substituents[6] will be presented and evaluated. The options to add additional substituents to the PTCA scaffold by using more advanced halogenation schemes will be discussed. Finally, the recently discovered room-temperature synthesis of PDIs, using conditions at which all intermediate amic acid intermediates are soluble and highly reactive, will be presented.[7].

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Synhesis, cytotoxicity and SAR analysis of novel dephenylated (–)-goniofufurone analogues

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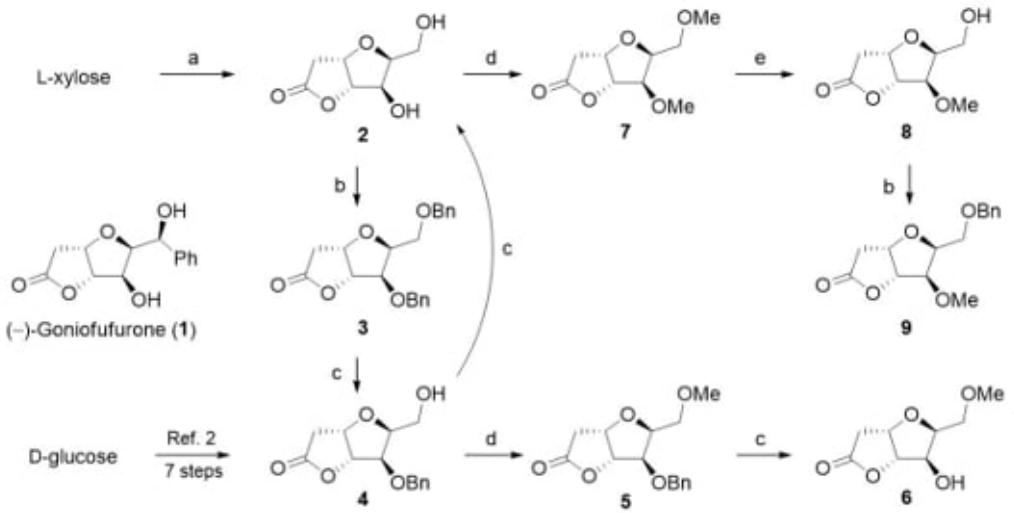
(–)-Goniofufurone (**1**) is opposite enantiomer of natural product (+)-goniofufurone. Both compounds show good cytotoxic activity *in vitro* [1].

Herein we want to report the synthesis of four novel dephenylated (–)-goniofufurone analogues, compounds **3**, **5**, **6** and **9** (*Scheme 1*), as well as the results of their biological activity. Citotoxic activity was examined against 9 malignant and one healthy cell line. Also, structure-activity relationship (SAR) of novel and analogues previously synthesized in our laboratory (**2**, **4**, **7** and **8**) will be discused in details.

The synthesis of novel analogues was firstly achieved from D-glucose [2] and then optimised from L-xylose, which is also commercialy available. This way, seven synthetic steps (from D-glucose) were replaced with only three (from L-xylose). Results were great savings in chemicals and time. It is also important that the yields of compound **4** are slightly improved, from 13% (from D-glucose) to 17% (L-xylose).



Scheme 1. (a) Meldrum's acid, Et_3N, DMF, 71%; (b) BnTCAI, TfOH, CH_2Cl_2/hexane, 43% for **3** and 89% for **9**; (c) H_2, 10% Pd/C, EtOH, 55% for **4**, 62% for **2** and 88% for **6**; (d) CH_3I, Et_2O, Ag_2O, AgOTf, 82% for **5** and 79% for **7**; (e) BF_3·Et_2O, NaI, $ClCH_2CH_2Cl$, 57%.

Acknowledgement: The work was supported by a grant from Ministry of Education, Science and Technological Development (Grant No. 451-03-9/2021-14/200125), and (in part) by research projects from the Serbian Academy of Sciences and Arts (Grants No. 01-2019-F6501-2019-F65 and F-130).

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Unusual enantioselectivity in silver-catalyzed intramolecular [4+2] cycloaddition reaction of amide-1,6-enynes

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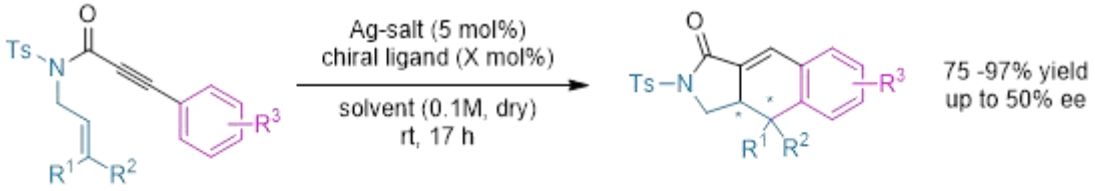
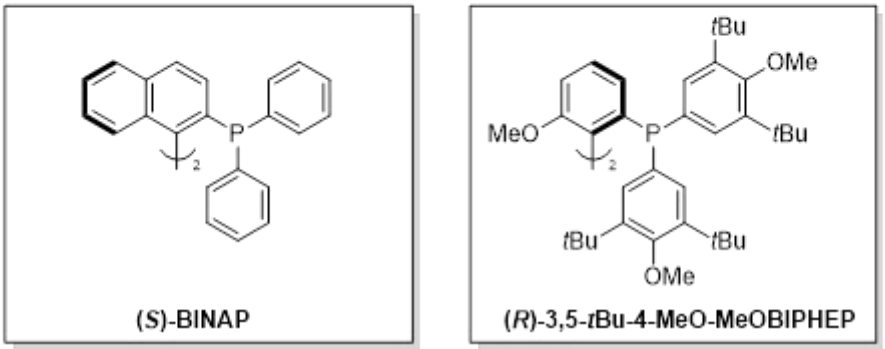
Recently, cyclization of enyne systems has became one of the most active fields of prototypical atom-economical research in synthetic methodologies, while transition-metal catalysis is still a very powerful and straightforward method to prepare carbo- and heterocyclic molecules [1]. Following our interest in cycloisomerization reactions [2] and silver catalysis [3], we got interested in asymmetric silver-catalyzed processes, which are still scarce in the literature [4]. Here, we would like to present the racemic and unprecedented asymmetric intramolecular [4 + 2] cycloaddition in the presence of Ag salts and chiral atropisomeric diphosphine ligands for the construction of 2,3,3a,4-tetrahydro-1*H*-benzo[f]isoindol-1-ones. These skeletons as well as their γ-lactams analogues are particularly ubiquitous motifs in many bioactive and natural compounds [5]. The asymmetric reaction conditions were also investigated and afforded the cyclic amides in good yields and enantiomeric excesses up to 50% [6]. In addition, using the same enantiomer of chiral atropisomeric diphosphine ligands and only by solvent changing, an opposite sense of enantioselectivity was observed. This rare phenomenon was also studied by ^{31}P-NMR [7].





This work was supported by the Centre National de la Recherche Scientifique (CNRS) and the University Côte d'Azur.

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Scope and Applications of 2,3-Oxidative Aryl Rearrangements for the Synthesis of Isoflavone Natural Products

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Hypervalent iodine compounds such as phenyliodonium diacetate (PIDA), phenyliodonium trifluoroacetate (PIFA) and [hydroxy(tosyloxy)iodo]benzene (HTIB) have emerged as highly useful reagents in organic transformations.[1,2]. Among the various transformations, a reaction involving oxidative rearrangements of flavanones resulting in flavones, isoflavones or 2,3-dihydrobenzofurans is of key interest as similar rearrangements with thallium(III) salts have been reported.[3,4] Hypervalent iodine compounds have an advantage of being environmentally friendly over thallium(III) salts.[1,2]

Our interest in such oxidative rearrangements arose from a research project directed at the total synthesis and biological evaluation of isoflavones isolated from East African medicinal plants of the genus *Erythrina*, traditionally used for the treatment of malaria and infectious diseases.[5,6] Secondary metabolites with a prenylated isoflavone core appear to contribute significantly to their antiinfective activity.[5,7] Consequently, three natural antiinfective prenylated isoflavones; 5-deoxy-3'-prenylbiochanin A (**1**), and erysubin F (**2**), isolated from *E. Sacleuxii*[7] and 7-methoxyebenosin (**3**) isolated from *Millettia griffoniana*[8] and their non-natural analogues **4**-**9** (Figure 1) have been synthesized via 2,3-oxidative aryl rearrangements of the respective flavanones using PIFA or HTIB followed by olefin cross metathesis to accomplish the prenyl subatitution.[5,9]

We herein present an investigation into the scope of the oxidative rearrangement reaction[9] as well as the preliminary results on the antibacterial activity of some isoflavones. Impressively, both erusubin F (**2**) and its non-natural flavone isomer **7** show activity against methicillin resistant *Staphylococcus aureus* (MRSA) strains at micromolar concentrations.[5]

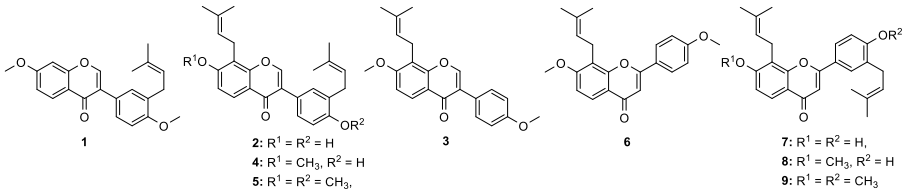

Figure 1: Synthesized natural prenylated isoflavones and non-natural analogues

A PhD scholarship (2018-2022) for GK from the German Academic Exchange Service (DAAD) is gratefully acknowledged. We thank Mr. A. Foß for the synthesis of precursors; Dr. M. Heydenreich and Prof. H. Möller for analytical support (NMR-spectroscopic characterization). We thank Dr. S. Kersting and Dr. M. Von Nickisch-Rosenegk (Fraunhofer IZI-BB) for the antimicrobial assay testing.

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Multistep enantioselective flow synthesis of chiral active pharmaceutical ingredients: A journey towards scalability and sustainability

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A large portion of active pharmaceutical ingredients (APIs) possess one or more stereogenic centers typically with marked differences in biological effects of the individual enantiomers. Current manufacturing strategies of single enantiomer drugs utilize chiral auxiliaries or homochiral building blocks to introduce asymmetry or employ various resolution techniques to separate racemates. Such processes involve numerous and diverse synthetic steps, which necessitate individual reaction control, work-up and purification for each segments involved entailing considerable technical challenges for process development and scale-up. Another serious issue is chemical waste generation. Complex procedures for the synthesis of APIs typically involve E-factors of >100, which means that during the production of a kilogram of a pharmaceutical substance, at least 100 kg of chemical waste is generated [1].

Not only novel chemistries, but also enabling technologies may help advancing chemical processes. Continuous flow reaction technologies have received an upsurge of interest in the context of green and sustainable syntheses while ensuring a more direct transferability from bench to the process-scale [1].

Inspired by the above backgrounds, we developed an academic research project with the aim to potentiate enantioselective API synthesis under multistep continuous flow conditions. In the present contribution, our most recent results will be communicated. Enantioselective flow procedures for the synthesis of GABA-derived APIs (rolipram, baclofen and phenibut) as well as of a chiral paroxetine key intermediate will be disclosed [2–4].

In order to achieve a more direct access to valuable enantio-enriched products directly from inexpensive and readily available achiral components, catalytic asymmetric conjugate additions were exploited using a solid-supported diphenylprolinol as a heterogeneous chiral organocatalyst. By harnessing solvent-free or highly concentrated conditions in packed-bed flow systems, the productivity and the scalability of the asymmetric key reactions were largely improved as compared with earlier organocatalytic strategies [2–4]. As downstream reactions to yield the targeted GABA derivatives, novel oxidation methodologies were developed which took advantage of *in situ* generation and consumption of persulfuric acid or performic acid as effective oxidizing agents [3–5]. To access the selected chiral paroxetine precursor, an effective continuous flow protocol was established for amide and ester reduction using neat borane dimethylsulfide complex [2,6]. Where possible, individual reaction segments were telescoped in order to eliminate intermediate purifications and to reduce waste formation. The multistep flow processes developed offers key advances in terms of productivity, scalability, and sustainability (E-factors <10) compared to earlier batch approaches.

All the co-authors in references [1-6] are greatly acknowldeged for their valuable contribution. We thank the Austrian Science Fund (FWF) for financial support through Projects M 2413-B21 and P 34397-N.

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P-stereogenic ligands in the iridium-catalyzed asymmetric hydrogenation of 2,3-diaryl allyl amines. Preparation of tetrahydroquinoline and tetrahydroisoquinoline scaffolds

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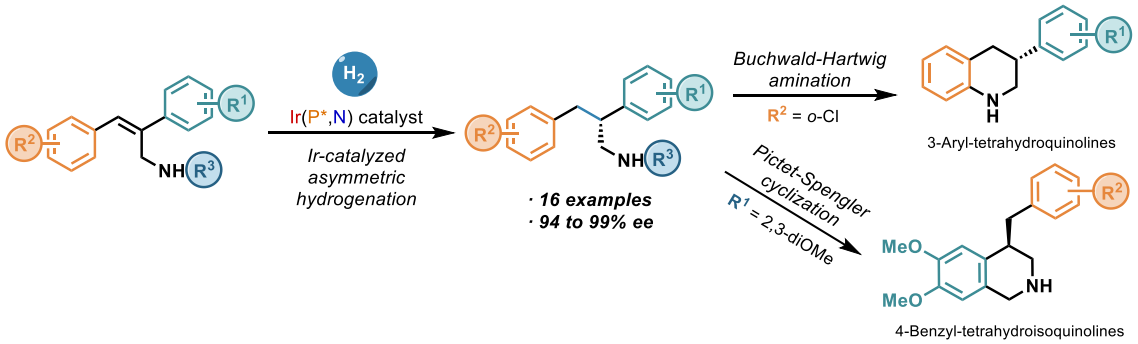
For many decades, chiral compounds containing nitrogen heteroatoms have proved to be fundamental substances for the chemical, pharmaceutical and agrochemical industries [1]. Thus, many research groups have put their efforts in the synthesis of diverse optically active amines [2]. However, the preparation of certain of these interesting scaffolds is still underdeveloped. In the last decade, our group has contributed to this field by designing several catalytic systems that have shown excellent results in the hydrogenation of different allyl amines, enamines and imines [3].

Herein we introduce the preparation of a new family of P-stereogenic phosphinooxazoline iridium catalysts that provides very high enantioselectivities in the asymmetric hydrogenation of 2,3-diaryl allyl amines. The hydrogenation process proved to tolerate different functional groups in the aromatic ring, substitution in both rings, and alternative protecting groups for the amine, with minimal loss on the enantioselectivity. Furthermore, the synthetic utility of the obtained 2,3-diaryl-propylamines was demonstrated by their transformation to 3-aryl-tetrahydroquinolines, yielding such structures with the highest enantioselectivity reported up to date. The utility of the propylamines was further expanded with the preparation of 4-benzyl-tetrahydroisoquinolines.



Scheme 1: Asymmetric hydrogenation of 2,3-diaryl allyl amines and their transformation to tetrahydroquinolines and tetrahydroisoquinolines.

Thanks to FEDER/Ministerio de Ciencia, Innovación y Universidades (MICINN), Agencia Estatal de Investigación (CTQ2017-87840-P and PID2020-115074GB-I00) and IRB Barcelona for financial support. IRB Barcelona is the recipient of institutional funding from MICINN through the Centers of Excellence Severo Ochoa Award and from the CERCA Program of the Generalitat de Catalunya. P. R. thanks AGAUR (Generalitat de Catalunya) for a FI PhD fellowship. A. C. thanks MINECO for a FPU PhD fellowship.

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Pd-Catalyzed Photoactivated Late-Stage C-H Functionalization of Biginelli/Suzuki-Derived Substrates for Generating Medicinally-Relevant Compound Libraries

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Direct C–H activation methodologies for the late-stage functionalization of bioactive small-molecules and other valuable substrates constitute an ongoing challenge for organic chemists, especially when functional group compatibility needs to be considered. We have recently demonstrated that a LED-activated, photoredox-mediated, Pd(II)-catalyzed C–H arylation reaction, employing phenyldiazonium aryl donor and tris(2,2′-bipyridine)ruthenium(II) or (2,2′-bipyridine)bis[3,5-di-fluoro-2-[5-(trifluoromethyl)-2-pyridinyl-kN][phenyl-kC]iridium(III) as photoredox initiator, may successfully generate a series of unprecedented mono- and bis-phenyl derivatives of functionality-rich 2,6-diphenylpyrimidine substrates, under mild conditions [1]. The selected substrates share a medicinally-relevant *N*-heterocyclic scaffold, 4-methyl-2,6-diphenylpyrimidine-5-carboxylate. These were obtained via a (3-component) Biginelli condensation, oxidative dehydrogenation of the obtained 3,4-dihydropyrimidin-2(1*H*)-one to 2-hydroxypyrimidine, *O*-sulfonylation, and Suzuki-Miyaura C–C cross-coupling. Submission of these substrates to our N-atom-directed C–H arylation conditions caused regioselective phenylation at the *ortho* site(s) of the pyrimidine-C2-connected phenyl ring, revealing substituent-dependent electronic and steric effects. A focused compound library of mono- and bis-phenyl derivatives was generated, exhibiting interesting 3D and peripheral substitution diversity among its members, which render them promising for evaluation in drug discovery efforts.

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Capability of cyclometaled iron(III)-complexes for photocatalytic water splitting

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Establishing hydrogen as ecological energy carrier, may receive more importance if abundant water as H_2 source and solar radiation as driving force for the endothermic separation process is used. Water splitting, sub-classified in water oxidation (O_2-formation) and reduction (H_2-formation), demands the implementation of a light-driven photocatalytic system which absorbs within the UV-Vis region. The light harvesting part of this catalytic cycle requires the application of a photosensitizer (PS) able to transmit electrons towards proton reduction.[1]

Application of PS in sunlight induced catalytic systems demands physical and chemical stability alongside a long-lived metal-to-ligand charge transfer state (MLCT) as catalytically active species. In this excited state an electron was raised from metal centered orbitals to ligand centered orbitals and returns to the ground state through electron transfer via the reductive or oxidative quenching pathway.[1] As a capable transition metal iron displays extensive quantities in the earth crust, consequently cost-effectiveness, and is environmentally safe. Unfortunately, weak ligand-field splitting constrains persistence of the MLCT state, instead populating the lower-lying metal-centered states (MC) terminating the needed electron transfer and likewise re-excitation for a significant time span. Therefore, iron has been introduced in ligand motifs with strong σ-donating abilities like *N*-heterocyclic carbenes to destabilise undesirable MC states, inducing the MLCT state as more favorable.[2] As a result, the capability of cyclometalated Fe(III) complexes exhibit significant MLCT lifetimes up to 4.2 ns, as shown in our group.[3]

We herein report the synthesis of a series of Fe(III)-complexes (figure 1) with bidentate phenyl-pyrazole ligands, with a diversity of functional groups in the backbone. In UV-Vis and fluorescence spectra these complexes show absorption and emission processes from 200 to 550 nm. Additionally lenient change of oxidations potentials from Fe(III) to Fe(IV) from -0,35 V to -0,17 V are observed, which may encourage catalytic activity. Additionally, we observe structural changes of the complex when exposed to UV-Vis light. We are investigating the behavior of the PS before and during irradiation, to gain further insights into its implementation potentials in catalytic cycles (figure 1). This includes the effect of the ligand variations on photophysical behavior, as well as insights on the Fe(III/IV) center assisted by DFT calculations.

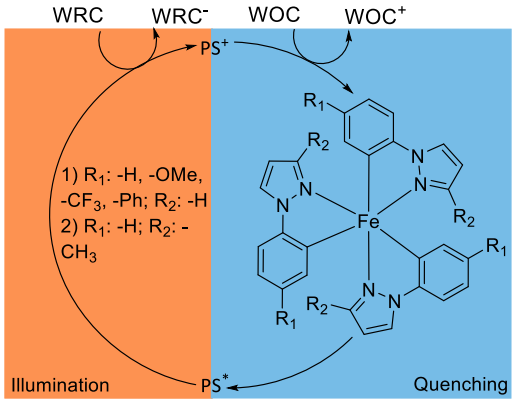

Figure 1: synthesized PS with varying backbone; proposed catalytic pathway for the oxidative quenching, WRC: water reduction catalyst, WOC: water oxidation catalyst

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Importance of two-electron processes in Fe-catalyzed aryl-(hetero)aryl cross-couplings

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Iron-catalyzed cross-coupling reactions have known a revival in the last decades. Thanks to its abundance and low price, this metal led to a significant breakthrough in transition-metal catalysis. However, the mechanistic facets is still a challenging issue, especially due to the short lifetimes [1] of the active species and the large panel of oxidation states formed under catalytically-relevant coupling conditions.

Recently, we have demonstrated that two drastically distinct mechanisms can be involved in aryl-(hetero)aryl Fe-mediated cross-couplings between Grignard reagents and organic halides, depending on the nature of the latter (see **Figure 1**) [2]. (Hetero)aryl electrophiles which easily undergo one-electron reduction can be involved in a Fe^{II} / Fe^{III} coupling sequence featuring an in situ generated organoiron(II) species, akin to their aliphatic analogues [3]. On the other hand, less easily reduced substrates can be activated by transient Fe^0 species formed by reduction of the precatalyst [4-5]. In this case, the coupling mechanism relies on 2-electron elementary steps involving the Fe^0 / Fe^{II} redox couple, and proceeds by an oxidative addition / reductive elimination sequence.

Attesting to the feasibility of this bielectronic mechanism, high-spin organoiron(II) intermediates formed by 2-electron oxidative addition onto (hetero)aryl halides in catalytically relevant conditions were characterized for the first time. Those results are sustained by paramagnetic ^{1}H NMR, kinetics monitoring, as well as by DFT calculations.

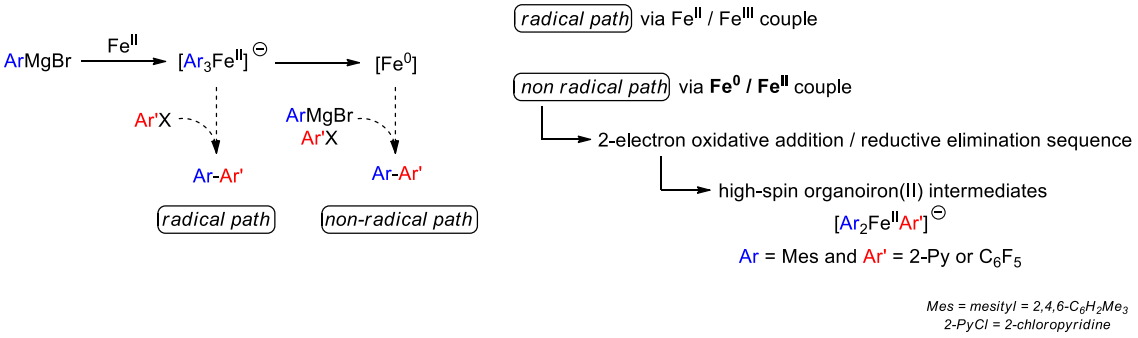

Figure 1: two drastically different routes at work in aryl-(hetero)aryl Fe-mediated cross-couplings

We thank the ANR (Project JCJC SIROCCO), the ERC (Project DoReMI StG, 852640), and the CNRS (Project IrMaCAR) for their financial support. The NMR shared facilities of Chimie ParisTech (Dr. M.-N. Rager) are thanked for technical support.

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Au(III) Complexes: From Structure Analysis to Reactivity Studies

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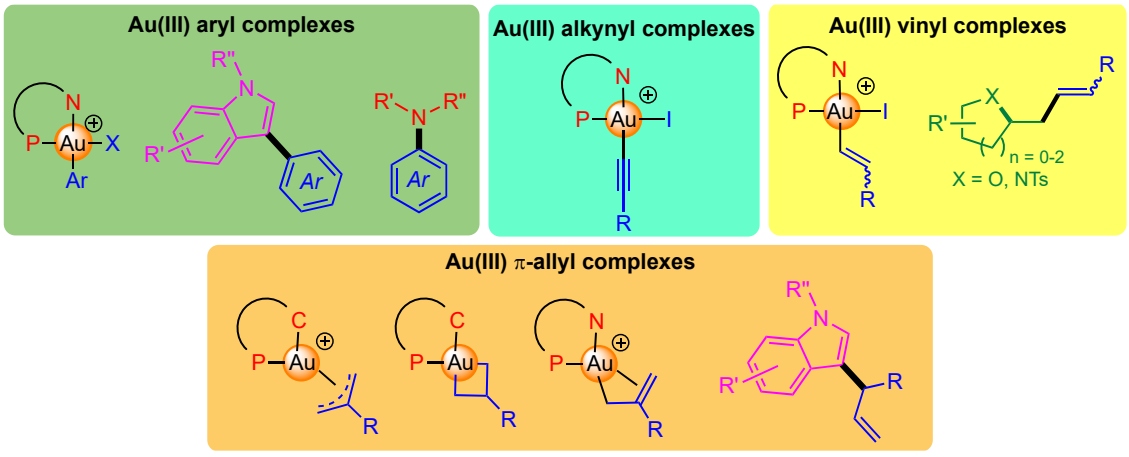
Oxidative addition is well established for late transition metals, but very rare in gold chemistry. Our group has explored the reactivity of gold complexes toward elementary steps of transition metal catalysis, and has shown that judicious ligand design enables C–X oxidative addition reactions to be achieved with gold under mild conditions, opening the way to new reactivities. We have demonstrated that hemilabile (P,N) ligands can provide a suitable balance between reactivity and stability of the key Au(III) species. The derived cationic Au(I) complex readily promotes oxidative addition of a large scope of aryl halides [1], vinyl and alkynyl iodides [2] and allyl acetates [3].

The potential of (P,N) Au(I) complexes in Au(I)/Au(III) catalysis was also demonstrated by the development of gold-catalyzed C–C, C–O and C–N cross-coupling. In particular, we have successfully developed the catalytic arylation of indoles and amines [1], the catalytic allylation of indoles [3] and the heterovinylation of alkenols [2]. Interestingly, the reactions were found to be completely regioselective regarding both coupling partners. An appealing feature of all these gold-catalyzed reactions lies in the mild conditions in which they operate, without any external oxidant or directing group. Furthermore, the transformations tolerate a broad variety of functional groups in the different coupling partners.

The synthesis and study of Au(III) π-allyl complexes was also performed with a (P,C) ligand and a thoroughly study of the properties of the obtained (P,C)Au^{III}(π-allyl) complexes was carried out, from their first authentication as stable species to their use as key intermediates in reactions with nucleophiles [4,5].



Acknowledgments: Spanish grants PID2019-108624RB-I00 and ORFEO-CINQA network CTQ2016-81797-REDC, the Xunta de Galicia (grants 2015-CP082, ED431C 2017/19 and 2021-CP054, ED431C-2021/25). JR thanks the Ministerio de Economía y Competitividad for her Postdoctoral fellowship (IJC2019-040358-I).

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Understanding self-assembly of luminescent Pt(II) complexes: synthesis and properties

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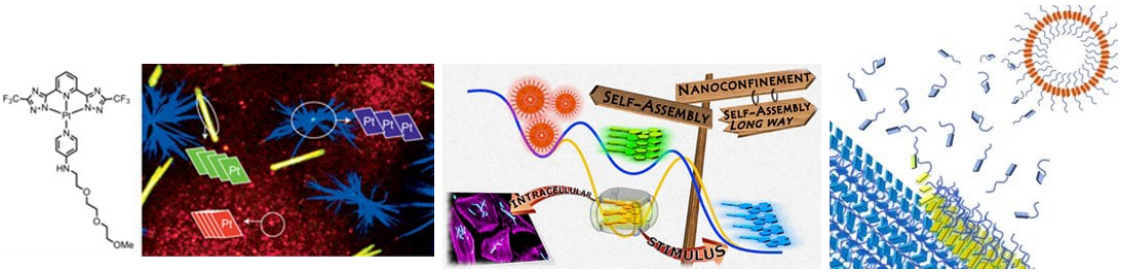
In square planar Pt(II) complexes the presence of the filled dz^2 orbital normal to the molecular plane is, in some cases, responsible for the establishment of weak dispersion intermolecular interactions as consequence of the closed-shell metal-metal electronic overlap, called metallophilic interaction. When such interactions occur, the luminescence can be switched ON and reach photoluminescent quantum yield close to unity, a phenomenon known as aggregation induced emission (AIE). Typically, the closer the metal centers are, the greater the metallophilic interactions and the bathochromic shift of the emission. The distance between the metal centers can be modulated not only by chemical species such as volatile organic compounds (VOCs), but also, by mechanical forces such as friction and pressure, known as mechanochromism and tribochromism.[1] This peculiar feature has found a plethora of applications from sensing to the discovery of the aggregation induced electrochemiluminescence phenomenon.[2] The dynamic change of the photoluminescent properties in terms of emission color, intensity and excited state lifetime makes such class of compounds a prefect probe to study self-assembly process. Herein, we present how we can characterize a complex system with multiple self-assembly pathway[3] (kinetic and thermodynamic). In particular we will show the role of the molecular design[4] in the self-assembly process and how stimuli responsive silica capsule can be used to stabilize metastable states and to trigger the formation of the thermodynamic assembly on demand.[5] Finally, we will show how the media play a pivotal control on the self-assembly process leading even to co-assembled structures.[6]



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Acknowledgement. This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement No949087).

Self-Assembly of Multifunctional Coordination Cages

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Metal-mediated self-assembly of supramolecular architectures has been proven to be an efficient tool for developing new materials with well-defined shapes and geometries. Proper ligand design and choice of metal centers, allow to obtain a large variety of compounds with nanosized pockets able to host specific guest molecules [1]. Besides the structural properties, appropriate choice of the building blocks enables to introduce functional groups in the system, such for instance chromophores or photoswitches [2]. However, most of the reported examples are highly symmetric structures carrying only one functionality. Introducing different ligands, and therefore different functionalities, can easily results in statistical mixtures, lacking of control over stoichiometry and stereochemistry. To overcome this, recent approaches have been developed to introduce multiple ligands in a non-statistical fashion, and to obtain heteroleptic cages [3]. Herein we report a new strategy, based on precise introduction of steric bulk, to form a $Pd_4LA_4LB_4$ tetrahedron (Figure 1a), retaining emission properties from one of the ligands [4]. Next, we exploited a consolidated strategy, namely shape complementarity assembly [5], to yield multifunctional cages where we combine chirality and emission properties, resulting in heteroleptic species showing circular polarized luminescence (CPL, Figure 1b), or electron donor and acceptor groups, achieving light induced charge separation (Figure 1c).

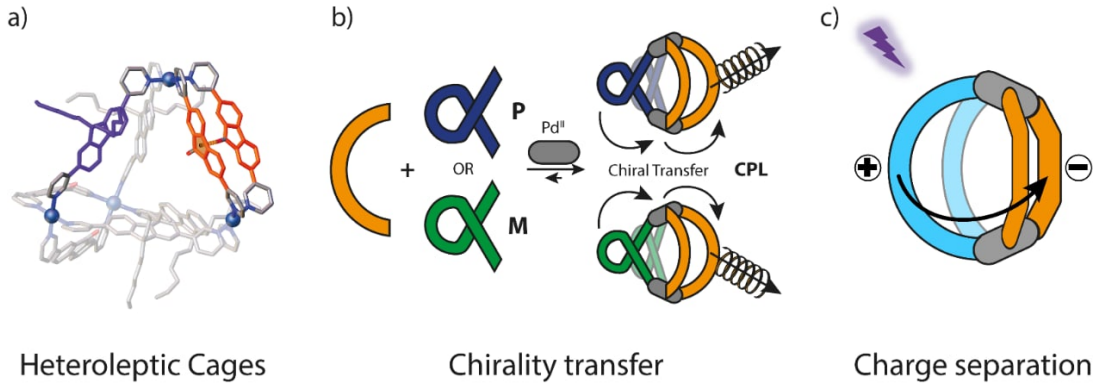

Figure 1. a) Heteroleptic tetrahedron promoted by backbone steric bulk; b) chirality transfer achieving CPL emitting heteroleptic cages; c) light induced charge separation in a Donor-Acceptor heteroleptic cage.

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Spin crossover in Fe(triazole)-Pt nanoparticle self-assembly structured at the sub-5 nm scale

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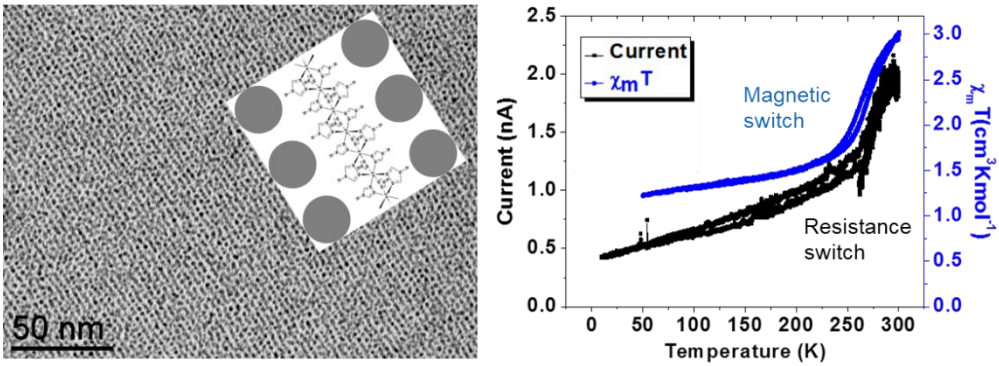
A main goal of molecular electronics is to relate the performance of devices to the structure and electronic state of molecules. Among the variety of possibilities that organic, organometallic and coordination chemistries offer to tune the energy levels of molecular components, spin crossover phenomenon is a perfect candidate for elaboration of molecular switches. The reorganization of the electronic state population of the molecules associated to the spin crossover can indeed lead to a significant change in conductivity. However, molecular spin crossover is very sensitive to the environment and can disappear once the molecules are integrated into devices. Here, we show that the association of ultra-small 1.2 nm platinum nanoparticles with Fe^{II} triazole-based spin crossover coordination polymers leads to self-assemblies, extremely well organized at the sub-5 nm scale. The quasi-perfect alignment of nanoparticles observed by transmission electron microscopy, in addition to specific signature in infrared spectroscopy, demonstrates the coordination of the long-chain molecules with the nanoparticles. Spin crossover is confirmed in such assemblies by X-ray absorption spectroscopic measurements and shows unambiguous characteristics in both magnetic and charge transport measurements. Coordinating polymers are therefore ideal candidates for the elaboration of robust, well-organized, hybrid self-assemblies with metallic nanoparticles, while maintaining sensitive functional properties, such as spin crossover [1].



Left: TEM image and geometrical structure of the self-assembly. Right: Charge transport and magnetic measurements.

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Amino-functionalized Supermagnetic Fe_3O_4 Nanoparticles. Synthesis and interaction with the silver ion

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Magnetic nanoparticles are a class of nanomaterials that can be manipulated using a magnetic field. Materials such as Fe_3O_4 behave like ferromagnetic in an induced magnetic field, but after subtracting this field, they do not exhibit any magnetic assets. This phenomenon is called supermagnetism. Those nanoparticles commonly consist of magnetic elements, for example: iron, nickel, and cobalt and their chemical compounds. The preparation methods are critical in determining the iron oxide nanoparticles size and size distribution, morphology, magnetism, and surface functionality. These particles have shown attractive properties in catalysis, biomedicine, magnetic resonance imaging, data storage and environmental water treatment remediation, and thus have attracted broad research interests [1].

Nanoparticles have shown great potential in the removal of heavy metal ions from water [2] by surface modification with chelating ligands. In this case, the bound ions can easily be removed by an external magnetic field. The ability to transfer ions and molecules between solutions may be particularly useful in the development of new analytical methods with high sensitivity. Magnetic isolation is a promising way to specifically trap analytes from a complex environmental or biochemical sample.

This work describes the synthesis of magnetic Fe_3O_4 nanoparticles using the modified co-precipitation method and their modification with aminosilanes of various chain lengths and the number of amino groups. The obtained structures were characterized using Fourier Transform Infrared Spectroscopy, Dynamic and Electrophoretic Light Scattering, and Scanning Electron Microscopy.

The objective of the work was also to develop a technique of investigation nanoparticles with potentiometric titration methods using a silver-silver electrode. The presented technique was used to determine the ability to coordinate silver and the total adsorption of silver on the surface of nanoparticles [Fig 1.]. The adsorption was described by using the Freundlich and Langmuir isotherms.

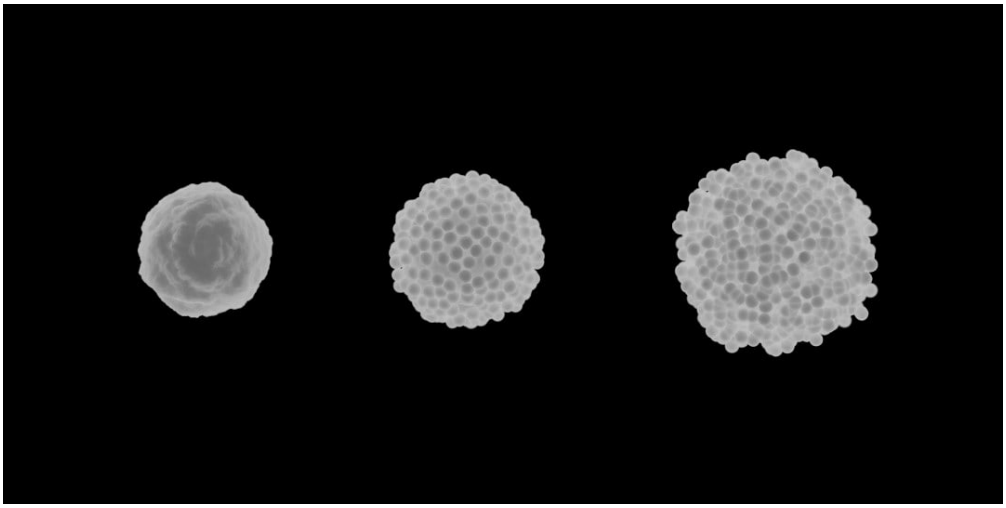

Fig 1. The graphic shows from the left a pure nanoparticle, a nanoparticle coordinating silver ions in a monolayer, a nanoparticle adsorbing silver in a polylayers

This research was financially supported by the University of Gdansk - Project Supporting young Scientists and PhD students (grant No. BMN 539-T050-B039-22)

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Effect of metal complexation on the DOTA radiolysis

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For both diagnostic and therapeutic purposes, radioisotopes are increasingly used in nuclear medicine. To reach the target cells in the biological environment, these elements are attached to a vector via a chelating molecule. In contact with radioisotopes, the chelating molecule is subjected to the effects of radiation, which can lead to its degradation and induce an alteration of its complexing properties. Therefore, it is important to study the impact of radiolysis on the speciation of "radioisotope-chelating molecules" complexes to identify the points of weakness of these molecules, and to guide the syntheses towards new molecules more stable in solution (or leading to less troublesome degradation products).

The ligand DOTA (1,4,7,10– tetraazacyclododecane -1,4,7,10-tetraacetic acid) has been studied for a long time because it is currently used for medical imaging, especially as a chelating molecule for gadolinium. DOTA forms very stable complexes with metals. Zirconium has a positron-emitting radionuclide, ^{89}Zr, which is an isotope of interest for medical PET imaging (Positron Emission Tomography). The complexes formed between the chelating molecules and the radioisotopes must be very stable in order to avoid the release of the metal in the body. Many clinical trials were done to find the best chelating molecule for ^{89}Zr. [1] More recently, a study showed that the DOTA ligand allowed the formation of the most stable zirconium complexes (Figure 1). [2]

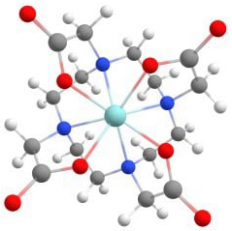

Figure 1. DFT optimized structure of Zr-DOTA complex

Previous work has been done on the degradation of the DOTA ligand under alpha irradiation. The study revealed that the ligand is degraded preferentially by decarboxylation and cleavage of an acetate arm CH_2-COOH. [3]

The aim of this study is to investigate the radiolytic stability of the DOTA ligand and the Zr-DOTA complex in aqueous solution.

In this work, the degradation products obtained by gamma irradiation were identified by Electrospray Ionization Mass Spectrometry (ESI-MS). Quantum chemistry calculations by DFT were also performed to determine binding dissociation energies (BDE) and estimate the relative strength of the bonds in the DOTA ligand free or complexed to a Zr cation.

The degradation of the ligand when complexed with Zr is significantly less important than when it is free in solution, which indicates that the metal protects the ligand from degradation. Moreover, the degradation products are different within the complex. These results have been strengthened using theoretical chemistry calculations.

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Hybrid magnetic nanoparticles coated with Molecularly Imprinted Polymers for hazardous pollutants sequestration from water

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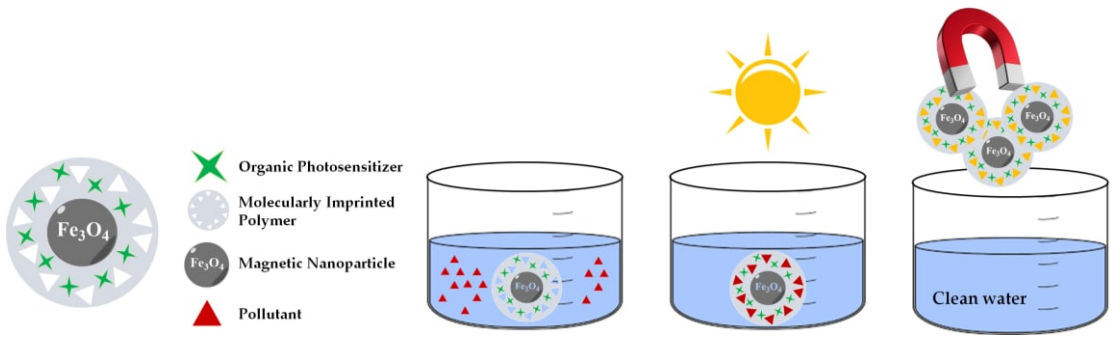
The occurrence and effects of emerging contaminants (i.e. drugs, antibiotics, chemicals, microplastics, etc.) on the environment, especially in water, is a global concern that has attracted many scientists' attention. Industrial, municipal and domestic wastewaters are the primary pathway for the wide diffusion of emerging pollutants in the aquatic environment. Wastewater treatment plants do not provide complete elimination of pollutants, leading to their release into the environment, with dramatic consequences for human and animals health, but also for the economy [1,2]. Among different methods for contaminants removal, adsorption, and photocatalytic degradation have been considered the most innovative, sustainable, and scalable technologies to address the problem of water pollution [3]. The existing adsorption methods, however, lack in efficiency and selectivity. To overcome the current limits of water remediation tools, the use of Molecularly Imprinted Polymers (MIPs) represents a successful approach [3].

Easy and versatile syntheses have been exploited to obtain sustainable organic MIP (acrylate-based and bio-based) able to selectively capture organic contaminants from water. The synthesis/extraction of organic photosensitizers such as porphyrins and bio-derived porphyrinoids (i.e. chlorophyll), their synthetic functionalization, and their inclusion in the polymer network, allowed to perform photocatalytic degradation of the pollutants in harmless, less toxic derivatives [4]. If compared with the more diffused inorganic nanoparticles, the great advantage related to organic photosensitizers, is the use of solar energy as a plentiful unlimited source, thus reducing the costs required for water treatment [5]. The characterization of such materials with cutting-edge techniques, such as MALDI-TOF mass spectrometry, Thermal Analysis, and Scanning Electron Microscopy have been performed. The imprinted polymer network was synthesized as a coating for magnetic nanoparticles, in order to remove the active nanomaterial from the water after the treatment, by simply using a magnet. UV-Vis spectroscopy, GC-MS spectrometry, and High-Pressure Liquid Chromatography were exploited to study the degradation products, assessing the remediation efficiency of the nanosystems.



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New methodologies to characterize ZnO nanoparticles in cosmetic samples

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In recent years, based on their good properties as solar radiation filters and antibacterial agent, the use of zinc nanoparticles (ZnO NPs) in cosmetic industry has been increased. According to the literature, the potential toxicity of these NPs could be size-dependent and also by the amount of solubilized metal from the NPs in solution. This work investigates new reliable and straightforward methodologies that enables the determination of ZnO NPs, discriminating them from ionic zinc in cosmetic samples. Two different strategies of analysis have been applied in this study: solid sampling high-resolution continuum source electrothermal atomic absorption spectrometry (SS-HR-CS-GFAAS), and "single particle" inductively coupled plasma mass spectrometry (sp-ICP-MS). Triton X-100 has been used as a surfactant, for the formation of homogeneous and stable slurries, which allowed the determination of the concentration and sizes of ZnO NPs in baby creams and eyeshadows. To achieve stable suspensions of the samples, two compound central design experiments (CCD) were performed to optimize the concentration of Triton X-100 and sonication time. The concentration of each sample in the slurry was adjusted considering the customer % ZnO content. The results of Zn^{2+} and ZnO NPs contents achieved by the two techniques were compared, and the total Zn content was analyzed by acid digestion of the samples. A size comparison was also carried out with the data obtained with transmission electron microscopy (TEM).

The authors thank "Plan Propio, Universidad de Málaga" for supporting this study and also FEDER funds and Junta de Andalucia (Project UMA18-FEDERJA-060) for financial support of this work.

Tailor-Made Modification of Siloxanes and Investigation of the Reactivity of Cyclic Five-Membered Diaminosilanes

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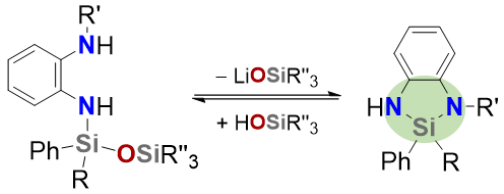
The Si–O–Si bond is ubiquitous both in our nature as an integral part of a plethora of silicate minerals and in materials science in the form of silicone polymers [1,2]. The development of synthetic methods for a controlled construction and selective modification of functional siloxane units has become a major concern in current research [3,4]. However, both construction and cleavage of Si–O–Si units require a high degree of reaction control and selectivity.

Herein, we present a new method allowing for a tailored step-by-step design of functional siloxanes [5]. By the incorporation of unsymmetrically substituted 1,2-diaminobenzene derivatives, which act as molecular scissors, the Si–O–Si linkage in siloxane frameworks can easily be cleaved at a desired position and siloxy groups exchanged for one another (see Figure). Removal of the molecular scissors by hydrolysis leads to siloxanols as valuable building blocks suitable for further functionalization. We will demonstrate our concept using a variety of oligosiloxanes with different substitution patterns. Mechanistic insights into the interesting reactivity of cyclic five-membered diaminosilanes will also be given [6].



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Rational design of porous organic materials based on azo, azoxy and azodioxy linkages for the selective adsorption of CO_2 over N_2

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The rising emissions of CO_2 have a dramatic impact on the environment, such as global warming and sea level rising. Porous organic materials based on nitrogen-nitrogen linkages recently emerged as a suitable alternative for the selective adsorption of CO_2 over N_2. In comparison to amorphous azo-linked covalent organic polymers [1], it was shown that self-addition polymerizations of polynitroso monomers resulted in crystalline materials due to reversible dimerization reaction of nitroso compounds to *cis*- or *trans*-azodioxides, thus allowing a self-correction of errors during polymerization [2].

Recently, we have focused on the synthesis and application of new functional nitrogen-nitrogen linked porous organic materials. Prior to the synthesis, a comprehensive computational approach including calculation of binding energies, visualization of electrostatic potential maps and using GCMC simulations to obtain adsorption isotherms and density plots was performed using model systems constructed between four different connectors (trisubstituted amine, benzene, pyridine and triazine) and three different nitrogen-nitrogen linkages (azo, azoxy and azodioxy). Such approach provides us with complementary data not accessible through experiments and help us to better understand structural characteristics regarding the efficient and selective adsorption of gases. Different type of stackings between 2D layers made of hexagonal pores may directly affect the adsorption properties of the predicted porous frameworks. Preliminary studies indicated that azodioxy linkages can promote adsorption of CO_2 in comparison with other investigated nitrogen-nitrogen linkages having the same arrangement of layers. The results of the computational study were also tested against the experimentally obtained data to verify the potential of the selected nitrogen-nitrogen linked porous organic materials for the selective binding of CO_2 over N_2.

This work has been fully supported by Croatian Science Foundation under the project IP-2020-02-4467.

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Size and Shape Controllable Synthesis of Seedless Gold Nanoparticles for the Development of Immunochromatographic Assay

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Gold nanoparticles (AuNPs) of different shapes and sizes represent significant color changes in a reaction mixture that act as a promising biosensing tool to develop the rapid Lateral Flow Immunochromatographic Assay (LFIA). Herein we report that the growth transformations of AuNPs are a function of physicochemical reaction parameters. Surface Plasmon Resonance of anisotropic nanoparticles is dependent on their morphological features and geometry. In this study, we have synthesized the seedless AuNPs by using various molar ratios of HEPES and $HAuCl_4$. The shape and the geometry of the gold nanostructures were modulated under the influence of pH (5, 7, and 9) of the HEPES, molar concentrations of HEPES to $HAuCl_4$, and temperature ranges (20 °C, 40 °C, and 60 °C). The change in the color of reaction mixtures over time was recorded in terms of the absorbance of the UV-Visible light in the range of 300-800 nm of the light wavelength. The scanning transmission electron microscopic images employed that the gold nanostructures exist in various shapes and corroborate with the UV-Vis spectrum.

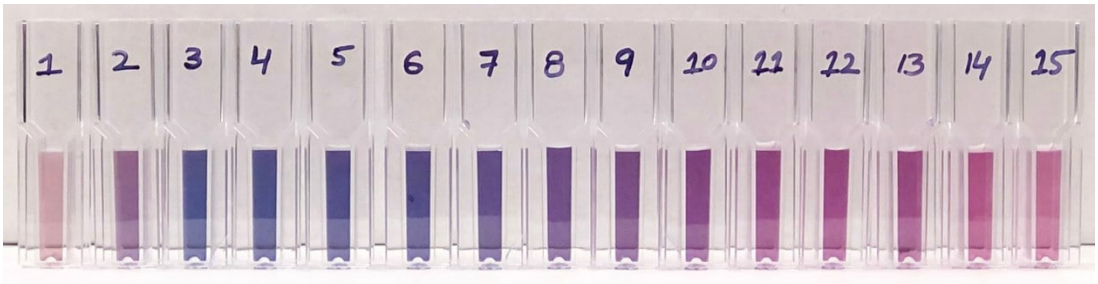

Figure 1: Change in the color of the reaction mixture with the increasing concentration of disodium phosphate.

It was confirmed that the nano-moieties are anisotropic, stable, and exist in the size range of 1 nm to 100 nm. The present study confirms that the change in the color of nanostructures reactions mixtures is a function of the surface plasmon resonance bands under the influence of physicochemical reaction conditions. Physicochemical parameters such as temperature, pH, the molar concentration of the reactants act synergistically to influence the reaction kinetics, molecular mechanics, and enzymatic catalysis that aid to affect the size, shape, and biochemical corona of nanoparticles. The findings of the present study explain the growth kinetics of the AuNPs of various colors that can be observed by unaided eyes and have promising applications for the development of the rapid LFIA for the detection of mycotoxins in food samples.

Keywords: Surface Plasmon Resonance, Gold Nanostructures, Lateral Flow Test, Physicochemical Reaction Factors.

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Detection of hydrogen peroxide vapours with a fluorescent dioxazaborocane: molecular insight into the mechanism

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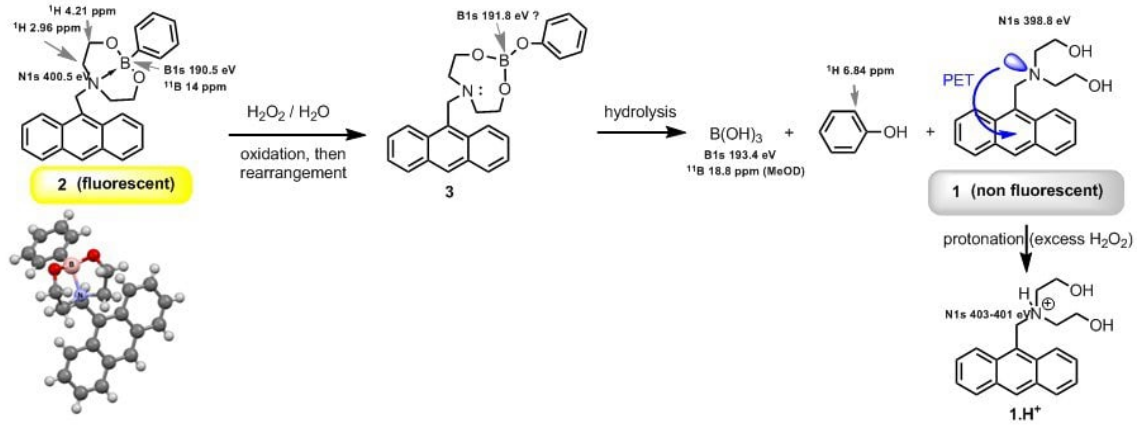
In the context of counter-terrorism, detection of peroxide-based explosives (PBEs) has now evolved as a crucial need. Boron compounds are attractive for hydrogen peroxide (HP) sensing, since they are known to react in solution with HP through an oxidation process. However, direct attempts to address the deboronation reaction have been reported in only very few papers [1]. Dioxazaborocane **2** was thought to be a useful sensing material through a turn-off concept, in which a deboronation reaction would release the N lone electron pair so that the anthracene fluorescence would be quenched. Following synthesis and characterisation of **2**, excellent hydrogen peroxide sensing properties in the solid state were demonstrated, as 64% of the fluorescence of a thin film of **2** was quenched by HP vapours. Our efforts focused on probing the concept at the molecular level, through the determination of the chemical reactions that resulted in the observed sensing properties in the solid state. To do so, solid/gas reactions between **2** and HP vapours were monitored by XPS and NMR analyses.

NMR studies unequivocally showed that, upon exposure to HP vapours, dioxazaborocane **2** has produced diol **1**, boric acid and phenol. These results were in close agreement with XPS data, which showed a substantial chemical reactivity of dioxazaborocane **2** upon exposure to HP. A mixture of diol **1**, its protonated form **1.H$^+$** and boric acid were observed as well of traces of unreacted **2**. These observations strongly support the mechanism depicted below. Thus, upon exposure to vapours of aqueous hydrogen peroxide, fluorescent dioxazaborocane **2** is mainly oxidised to the expected intermediate **3** through a commonly accepted mechanism, followed by hydrolysis to get a mixture of non-fluorescent diol **1**, boric acid and phenol [2]. Part of **1** is protonated with excess HP to **1.H$^+$**. Simple hydrolysis only marginally occurs.



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Tuning Cellular Biological Functions Through the Controlled Release of NO from new MOF structures

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Nitric oxide (NO) is a key signalling molecule involved in numerous biological processes. Its exogeneous administration through molecular NO donors or NO-releasing platforms has been proven to be a potential alternative to conventional therapies [1]. Ordered nanoporous materials, like zeolites, titanosilicates, clay-based materials, and metal-organic frameworks (MOFs), have been recently explored to obtain a controlled local delivery of pure NO, and demonstrated considerable NO storage and release capacity [2]. To date, many suffer from either toxicity and stability issues and/or low performances.

We have recently identified new MOF structures with exceptional properties. A new robust titanium-carboxylate based MOF, MIP-177 [3], is a new benchmark porous NO carrier, due to the combination of key properties required for such application never achieved by other porous materials [4], namely: (1) high NO storage capacity (3 µmol mg^{-1} solid), (2) excellent biocompatibility over several cell lines, including primary keratinocytes (no cytotoxicity at 90 µg/mL for wound healing), (3) high stability under biological conditions (< 9% degradation in 72 hours) and (4) slow release of pure NO in biological medium (≈2 hours). The new NO binding mechanism is based on the formation of chelated nitrite species over the material's structure. These species subsequently decompose upon exposure in biological fluids to slowly release NO (Fig. 1). The first indicators of potential therapeutic action of these MOFs were demonstrated by controlling important biological functions. For example, NO-loaded MIP-177 regulates cells O_2 consumption and stimulates the cell migration, achieving a significant improvement in wound closure of 8.4±1.4% after 24 hours (cells treated with 90 µg/mL of NO-loaded material). Other new MOFs with even slower controlled NO release (over 70 hours) in body fluids will also be presented. The possibility of incorporation of NO loaded MOF in polymer composites that are more easily applied under clinical conditions was also explored, and improved stability and more controlled NO release was achieved. These results provide a step forward to the development of successful NO-delivery materials for potential application in wound healing.

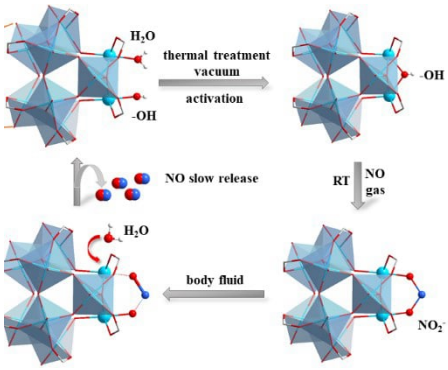

Fig. 1. Illustration of the adsorption and controlled release cycle of NO in the MIP-177 (adapted from [4]).

Acknowledgements: The work was financed by Fundação para a Ciência e a Tecnologia ref. PTDC/MED-QUI/28721/2017.

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The development of new luminescent MOFs for molecular detection.

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Metal-organic frameworks (MOFs) are a fascinating class of hybrid organic-inorganic porous crystalline nanomaterials built from metal-ions and organic bridging ligands [1]. Among the applications of MOFs in different prominent fields [2], the sensing and detecting of specific target components, including toxic and aromatic compounds, volatile organic compounds (VOC), pesticides and explosives, have attracted our attention. In our group, extensive research over the past few years has focused on the design, synthesis, and investigation of a new class of anthracene-based MOFs. Modification of different parameters of these compounds revealed them to very promising candidates for the molecular detection of analytes due to changes in their optical properties through host-guest interactions.

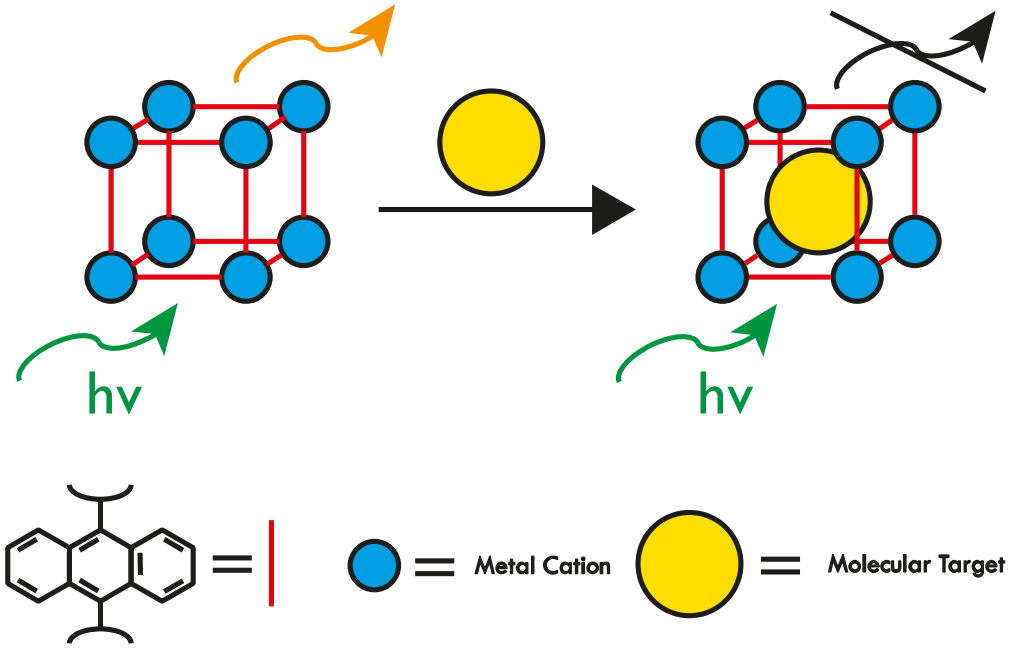

Figure 1: Concept of how MOFs materials based on anthracene building unit can detect the molecular targets by luminescence changes through host-guest interaction.

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Metal-organic framework formation from $[Fe_4S_4]$ clusters and its prospects for gas adsorption

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$[Fe_4S_4]$ or [4Fe-4S] clusters are the active centers of many enzymes. They not only contribute to redox reactions and electron storage, but also catalyze substrate transformation [1]. These $[Fe_4S_4]$ cluster potentials have motivated researchers to adopt them in the synthesis of catalytic and non-catalytic biomimetic systems. For instance, they are used to synthesize redox-active 1D metal-organic frameworks (MOFs) [2]. The redox activity of such clusters can enable electronic adjustment in adsorptive processes. Also, MOF formation can provide high surface area, high porosity, and diverse physiochemical properties. Consequently, careful design of the $[Fe_4S_4]$-based MOFs is expected to offer an efficient option for adsorption-based applications. To assess this prospect, we study the performance of $[Fe_4S_4]^{2+}$ and $[Fe_4S_4]^{0}$ clusters and two simple 1D MOF models with carboxylate and 1,4-benzenedithiolate ligands (shown in Figure 1) in adsorption of several gases including CO_2, CH_4, H_2O, N_2, NO_2, O_2 and SO_2 with important industrial and environmental applications. Our quantum chemical calculations at the optimal computational level of PBE/6-311++g(d,p) show that both the charge state of the $[Fe_4S_4]$ cluster and the MOF ligand (i.e. the chemical microenvironment) affect the performance of the $[Fe_4S_4]$ cluster in gas adsorption. Though the $[Fe_4S_4]^{2+}$ cluster can adsorb all gases, MOF formation using the 1,4-benzenedithiolate ligands reduces its adsorption capacity. In the case of carboxylate ligands, the adsorption capacity reduces less significantly. The cluster and the MOF models can adsorb NO_2 substantially. However, CO_2, N_2 and CH_4 adsorption on the MOFs is nonspontaneous. Because of the cleavage of the $[Fe_4S_4]$ clusters in the presence of oxygen [3], we use the corresponding hydrolysis and oxidation reaction kinetics to evaluate practical applications of the studied MOFs.

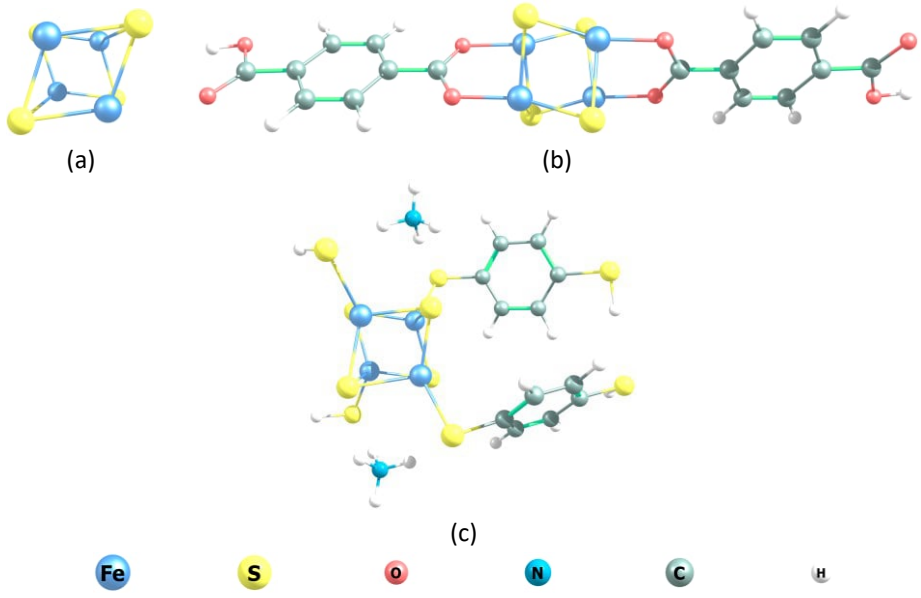

Figure 1. Molecular structures of the studied cluster (a) and the carboxylate (b) and 1,4-benzenedithiolate (c) containing MOF models.

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Engineering porosity in molecular nanocontainers: From molecular sieving to catalysis

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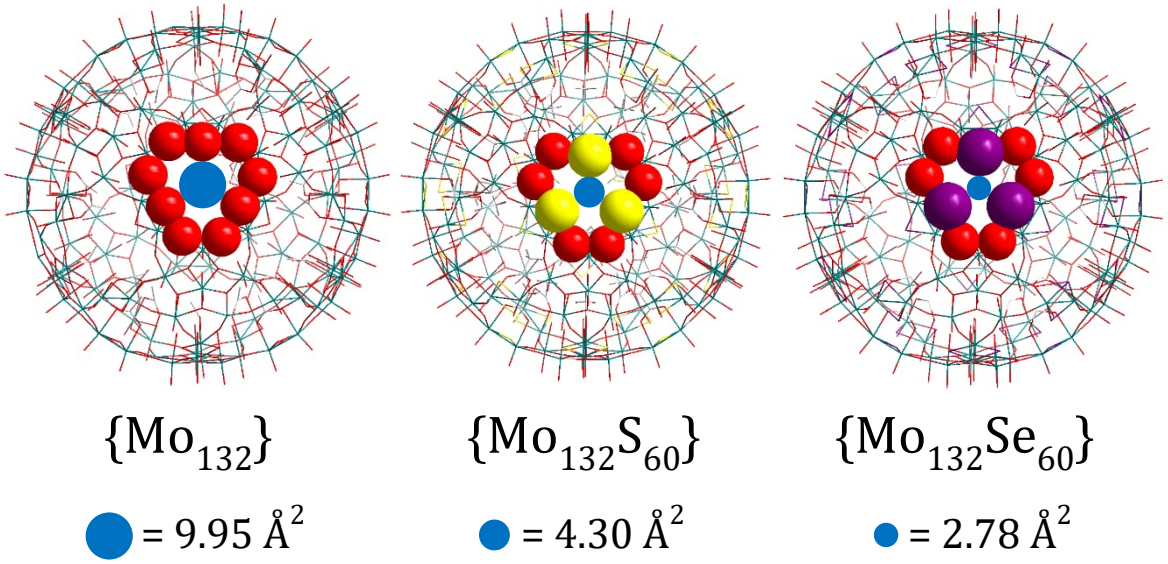
Since it was first reported in 1998 by Müller[1] the 'Keplerate' structure has proved a structurally robust family of high nuclearity inorganic fullerene-type molecules constructed by twelve {M(M_5)} pentagons and thirty dimeric $[Mo_2O_4]^{2+}$ linkers. This forms a giant truncated icosahedron, with large hexagonal $\{O_9\}$ pores bounded on three sides by the linker units.

The introduction of a new selenide building block, $[Mo_2O_2Se_2]^{2+}$ allowed us to engineer $\{Se_3O_6\}$-type pores to the giant $\{Mo_{132}Se_{60}\}$ seleno-Keplerate and design porosities with accessible areas ranging from 9.95 to 2.78 Å, Figure 1. This molecular nanocontainer contains sixty selenide anions bonded directly to molybdenum centers and is the first nanosized polyoxoselenometalate molecular species. The structure was confirmed with single crystal X-ray diffraction.

Interestingly, the exchange of the internal acetate ligands with a variety of organic moieties, can be directly controlled by the porosity of the nanosized framework. When combined with the thio-Keplerate $\{Mo_{132}S_{60}\}^2$ this provides a range of pore radii from 1.78 Å for $\{Mo_{132}\}$ (oxide) Keplerates to 1.17 Å for $\{Mo_{132}S_{60}\}$ (sulphide) Keplerates and 0.94 Å in the new $\{Mo_{132}Se_{60}\}$ (selenide) Keplerates without any additional structural re-arrangements.

A range of carboxylates were successfully exchanged with the internal acetates, using ^{1}H NMR to follow their exchange rate. Rates were compared across oxide, sulphide and selenide-containing Keplerates. Whilst the pore size had a significant effect on the rate of ligand exchange, an anomalous inversion of the relative rates between sulphide and selenide was found to be present for especially large ligands. This interesting observation can be attributed to variations in bond strength giving a lower energy cost to distorting selenide pores compared to the sulphide pores.

The demonstrated control of pore size allows the selective transport of small molecules across Keplerates with implications in molecular separations, catalysis and selective molecular transfer using a range of pore sizes that can be tuned for specific applications.



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Robust MOFs for the Selective VOCs Capture Under Ambient Conditions

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The design of target-engineered MOFs with extremely high selectivity for acidic polar pollutants found at low concentrations (ppm) in the presence of moisture is quite challenging. In a previous work, we proposed new MOFs targeting acetic acid (AA), one of the most acidic VOCs, particularly noxious to movie pictures, paintings, metallic artworks, and many other types of cultural heritage items [1]. Currently we explored two approaches to efficiently capture AA, as well as other noxious vapors under ambient conditions. Environment-friendly routes were followed, where toxic solvents were replaced by green ones. Reproducibility and large-scale synthesis were also addressed.

The first approach consists of developing new generation of perfluoro-functionalized MOFs with optimum performance [2]. The flexible MIL-53(Al) was functionalized with CF_3 groups where it resulted in an exceptional affinity to AA, similar to those of polar MOFs while exhibiting a pronounced hydrophobic character.

The second approach explores the use of MOFs with open metal sites (OMS). A novel chemisorption mechanism of adsorbents of amphiphilic nature was identified to capture acidic VOCs in the presence of water. The ability of acidic VOCs to replace coordinated water molecules on the OMS was investigated [3].

A schematic of each approach is represented in figure 1. Characterization techniques (PXRD, TGA, FTIR, porosimetry, SEM) have been performed to analyze the structure and composition of the new materials. Kinetic and equilibrium AA adsorption experiments were performed to understand the influence of the structure type and group substitution on the equilibrium and dynamic adsorption capacities. AA sorption tests in the presence of moisture demonstrated the ability of MOFs to work under real conditions, to capture AA at ppm level in the presence of moisture. For the second approach, the adsorption selectivity of VOCs over water was demonstrated using programmed temperature desorption spectra. Shaping of the MOFs has been also performed to obtain more application-oriented easy-to-handle products.

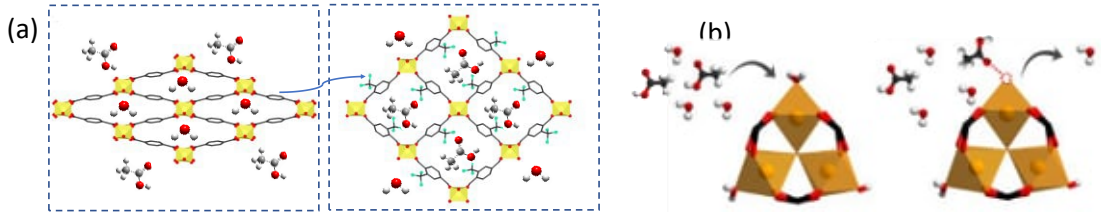

Figure 1: Schematic illustration of acetic acid adsorption by the a) first approach - functionalization b) second approach – OMS.

Acknowledgments: This work has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760801\NEMOSINE.

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Rates of Extracellular Electron Transfer in *Geobacter sulfurreducens* Wild Type and Mutants. Experiments in the Resting and the Growth Phase

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Geobacter sulfurreducens are anaerobic microorganisms that utilize extracellular metal salts as acceptors for electrons generated during their respiration at the inner cell membrane. *G. sulfurreducens* are effective electron sources to synthesize nanoparticles, to purify polluted water as bioremediations, or to produce electrical currents in microbial fuel cells. A vital requirement for their life is the maintenance of ATP homeostasis during mineral respiration under different environmental conditions. ATP homeostasis produces electrons that are transferred via iron/heme cofactors of *c*-cytochromes from the inner cell membrane to extracellular metal ions (Fig. 1). [1]

In this work, oxidation states of iron-hemes in *G. sulfurreducens* were analyzed by UV-VIS spectroscopy during reduction of metal salts to measure Extracellular Electron Transfer (EET). Each microorganism produced about $3.7x10^5$ electrons per second. The influence of a) 6 different metal salts, b) the growth phase, and c) selected deletions of outer membrane *c*-cytochromes on *G. sulfurreducens* electron flux rates have been studied. It turned out that the *c*-cytochromes act as "rate buffers" that adjust the electron outflux rate at the outer membrane to the influx rate at the inner membrane by changing their Fe^{2+}/heme to Fe^{3+}/heme ratios. As a result, the extracellular electron transfer rate of *G. sulfurreducens* in the growing growth phase could increase by a factor of 10 compared to *G. sulfurreducens* in the resting phase, although the extracellular electron acceptor was not changed. On another hand, *G. sulfurreducens* mutant strains slightly decreased the extracellular electron transfer rate.

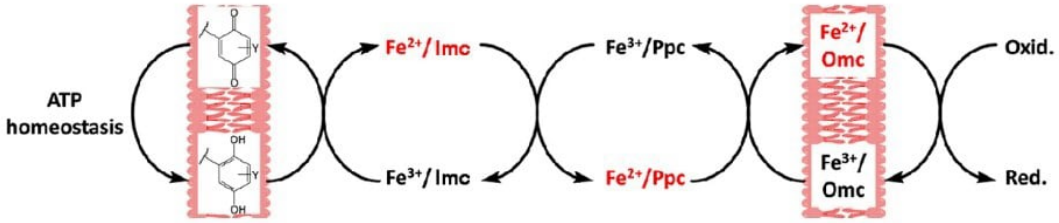

Figure 1. Mineral respiration of *G. sulfurreducens*. The Fe^{3+}/hemes of inner membrane cytochromes (Fe^{3+}/Imc) oxidize menaquinol (MQH_2) to menaquinone (MQ) using enzymatic reactions. This initiates electron transfer between the Fe^{2+}/hemes and the Fe^{3+}/hemes within and between the different cytochromes, and finally reduces oxidants.

The mutant strains of *Geobacter sulfurreducens* were kindly provided by Prof. Derek Lovley, UMASS

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Blue, photo-stable and non-cytotoxic dies, with antimicrobial properties

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Dyes for long-term imaging of live cells need to be non-toxic and photo-stable. Not all molecules have both of these properties simultaneously and therefore, such dies are rare, especially in the blue. New simple pyrene-derived dyes have been synthesized and fully characterized, showing on the one hand an intense emission and an excellent stability due to their flexible conformation, evidenced by the solid-state structures of coordination compounds obtained from these dyes and by ^{1}H-NMR solution studies. Results show that under irradiation, the pyrene-based series of dyes undergoes intersystem crossing (ISC) that leads to a configurational switching occurring at time-scales that are faster than the formation of possible photobleaching products. On the other hand, the dyes display a good cellular uptake without causing toxicity, while antibacterial assays show that they greatly influence the minimum inhibitory and minimum bacteridal concentrations (MIC and MBC) of antimicrobial salts such as Zn, Cd or Hg iodide.

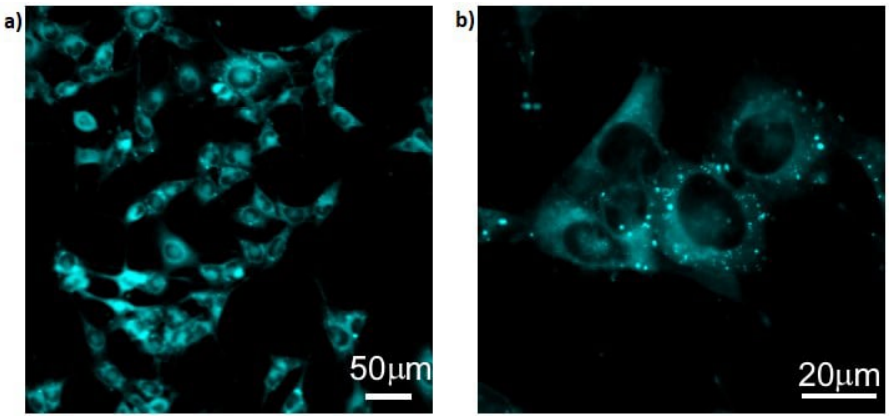

Fig: ***PyPe*** loaded in the OVA-B16 melanoma cell line: a) overview ; b) High magnification fluorescence image of OVA-B16 cells loaded with ***PyPe*** showing cytosolic staining and subcellular partitioning

The authors thank the Swiss National Science Foundation, the NCCR Bioinspired Materials and the University for generous support.

A disulfide-based self-immolative linker as prodrug approach for the release of carboxylic acids in cells

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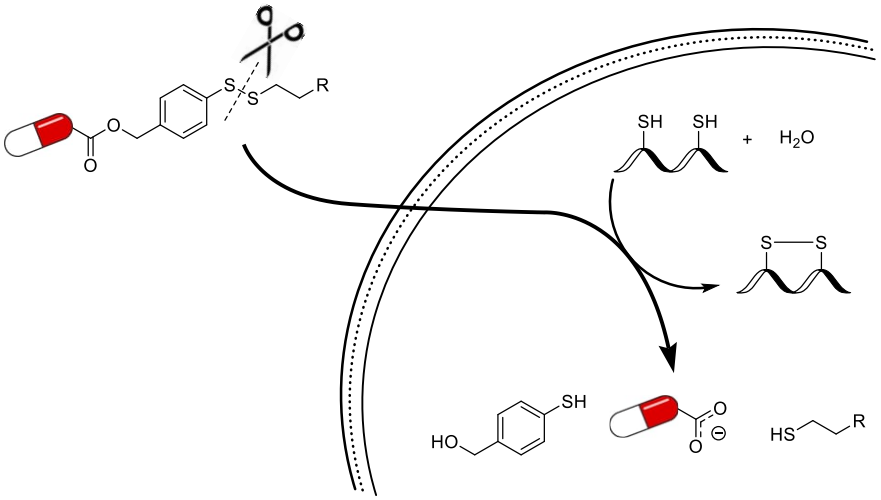
Carboxylic acids are valuable functional groups in active compounds as they can form strong electrostatic interactions and hydrogen bonds. Nevertheless, the presence of a carboxylic acid functionality can pose significant challenges, as passive diffusion through biological membranes is significantly impaired.[1] Traditionally, this can be circumvented by masking the carboxylic acid as carboxylic acid ester. However, the protection of carboxylic acids as their corresponding esters, while simple, raises other issues, such as the slow rate of cleavage and the clearance of the ester.[2] In our work, we are interested in using a self-immolative linker (SIL) as a prodrug approach for the rapid release of carboxylic acids. For this purpose, we have designed a phenyl-alkyl disulfide-based SIL as a function of choice, as its cleavage could allow the deprotection of thiophenol and, through a *p*-thiobenzyl self-immolative linker (SIL),[3] the carboxylic acid group.[4] *p*-Thiobenzyl-based disulfide as SIL has many advantages for a pro-drug approach, such as being a fast-releasing SIL[5] while remaining quite stable in various living media.[6] By modulating the alkyl chain of the disulfide, the selectivity and the kinetics of the disulfide cleavage can be tuned to allow us the use of the most ideal combination.[7] The rapid release is an important feature to counteract the elimination of the active compound before its activation.



Herein we would like to present our investigation on the use of a self-immolative linker based on phenyl alkyl disulfide cleavage as rapid and irreversible carboxylic acid release system. This system represents a stimulus cleavable pro-drug approach, which shows substantial stability in living media with a rapid chemoselective delivery of carboxylic acids under intracellular conditions.

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Inspired by nature´s design: Biomimetic enterobactin analogues for antimicrobial drug conjugates

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In the context of growing resistance of bacteria against established antibiotics, the development of novel antimicrobial drugs and concepts against bacterial pathogens is of vast importance.[1,2] In particular, Gram-negative pathogens provide big challenges in drug development due to the effective permeation barrier of the Gram-negative cell envelope. A smart concept for the development of novel antimicrobials is based on the conjugation of antimicrobial drugs with siderophores, small molecule iron(III)chealtors as carrier molecules showing an active uptake mechanism for translocation over the cell envelope barrier.[1] In this context, analogues of enterobactin, a *tris*-catecholate siderophore, playing an important role during host infection are of high interest.

In our approach,[3] we utilize a γ-modified L-allo threonine derivative as building block for the synthesis of biomimetic enterobactin analogues, showing an attachment point for drug or reporter molecule conjugation in the backbone of the siderophore and simultaneously retain the hydrolyzability of the *tris*-lactone structure, important to enter the cytosol. Based on this approach we synthesized novel siderophore-fluorophore conjugates and evaluated their siderophore-receptor mediated uptake into bacteria via different methods. In addition, first drug conjugates are reported and evaluated for their antibacterial activity.[4,5]

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'*Exit the Cube*': Next-Level Chemical Tools for Ultrafast Bioorthogonal Bond-Cleavage

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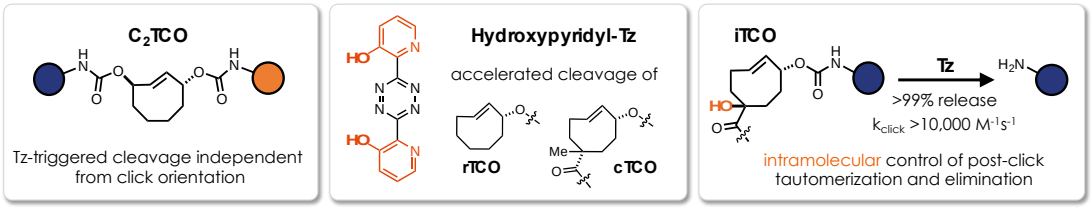
The toolbox of bioorthogonal reactions has expanded substantially in the past decade, providing chemists with highly selective methods to achieve efficient ligation in complex biological environments, even in living systems [1]. In parallel, the concept of bioorthogonal bond-cleavage has further expanded the repertoire of *in vivo* chemical methods, enabling controlled molecular disassembly under physiological conditions [2]. Among these chemistries, the '*click-to-release*' reaction of tetrazines (Tz) and cleavable *trans*-cyclooctenes (TCO) stands out due to favorable reaction kinetics and adaptability [3,4]. This bioorthogonal elimination has enabled strategies for targeted drug delivery [4] and prodrug activation, leading to the first bioorthogonal approach now tested in Phase 1 clinical trials [5], finally marking the beginning of the era of clinical translation of *in vivo* chemistry.

To date, however, the concept of bioorthogonal bond-cleavage has been limited as existing tools have fundamentally lacked the performance characteristics (i.e., click kinetics, cleavage kinetics, cleavage yield) needed to make more advanced strategies plausible. For instance, efficient TCO-release has yet been restricted to Tz with relatively low click reactivity, while highly reactive Tz (e.g., bis(2-pyridyl)tetrazines) achieve only poor release (<10%). Based on our rigorous pursuit of mechanistic understanding [6,7], we have recently developed chemical tools with exceptional performance and unique capabilities. In this talk, I will present our key molecular designs and the challenges we faced on the way to boost bioorthogonal Tz/TCO bond-cleavage reactions.

To outmaneuver the yet uncontrollable orientation of the initial click reaction, we have developed a C_2-symmetric TCO-linker (**C_2TCO**) that can be cleaved nearly instantaneously, enabling the concept of bioorthogonal turn-off [7]. To address the drawback of C_2TCO in turn-on applications (i.e., no regiocontrol of release), **hydroxypyridyl-substituted Tz** have been designed that achieve complete and up to 20-fold accelerated TCO-release under physiological conditions. Finally, a universal *trans*-cyclooctene, **iTCO**, will be presented that can be cleaved independent from the structure of the Tz via an unexpected reaction mechanism based on intramolecularly controlled post-click tautomerization and subsequent elimination. Thereby, highly reactive Tz can be applied as molecular scissors, finally to '***exit the release cube***' [6] and enable bioorthogonal bond-cleavage with unprecedented click kinetics and release efficiency.



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Why not nucleosides in meteorites? An approach based on mechanochemical studies

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The detection of organic molecules in extraterrestrial bodies leads to some proposals focused on the extraterrestrial input of relevant compounds for the emergence of life on our planet [1]. Nevertheless, these extraterrestrial bodies encounter very harsh conditions which can induce chemical transformations in the molecules within them. Besides thermal heating and friction [2], mechanochemistry, which uses mechanical energy as a driving force for chemical transformations, can play an important role in the reactivity of organic molecules in those extraterrestrial materials. For instance, carbonaceous chondrites meteorites are a portion of an asteroid that was able to cross Earth´s atmosphere and land on the Earth´s crust. Despite the wide variety of organic molecules detected in meteorite samples, ribonucleosides were never identified, as opposed to corresponding components, such as ribose and nucleobases [1, 3]. Previously studies indicated that ribose could be degraded by mechanochemistry in the presence of carbonate ions [4]. In this way, the degradation of ribonucleosides to nucleobases could be simulated by mechanochemistry, in presence of carbonate ions and transition metals, explaining in this way, the lack of ribonucleosides in meteorite samples, since carbonate could be formed by oxidation of organic matter and transition metals that are abundant in extraterrestrial bodies. In addition, to reinforce this possibility, the degradation mechanism promoted by carbonate ions and metals can be addressed with computational models, by DFT/TDDFT methodologies, modeling the structures of ribonucleosides, their degradation products, and reactive intermediates. Preliminary results show the degradation of guanosine into guanine by mechanochemistry, intensified by carbonate ions and transition metals, such as nickel. This model compared with a real asteroid sample without mechanochemical activity (Bennu, from OSIRIS-Rex mission or Ryugo, from Hayabusa2 mission) explains our suggestion that ribonucleosides could be detected in asteroids. Furthermore, by relating the shock energy with atmospheric composition, it would be possible to extrapolate to the prebiotic era, whether ribonucleosides could be transported directly to Earth, thus proving that the direct synthesis of ribonucleosides by reaction of ribose and nucleobases is not a favorable step for the prebiological evolution of life, and that life may have started at different points in the Universe, not exclusive to planet Earth.

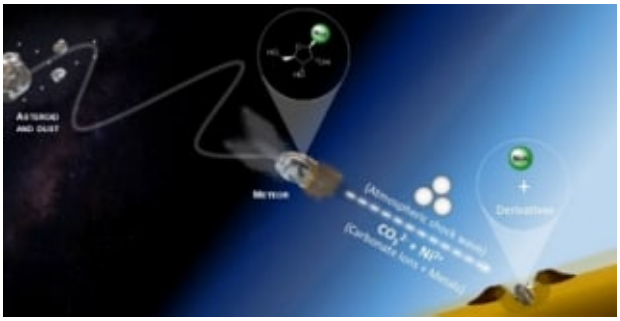

Figure 1 - Degradation model of ribonucleosides in their respective nucleobases and analogs by the action of mechanochemistry, intensified by carbonate ions and metals

This work has been carried out with financial aid of the FCT (Portugal) (Projects number UIDB/00100/2020, UIDP/00100/2020 and IMS -LA/P/0056/2020).

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Dithiocarbazate-Loaded Nanostructured Lipid Carriers: Preparation, physicochemical characterization and environmental safety assessments

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Dithiocarbazate Schiff Bases, such as, 3-methyl-5-phenyl-pyrazoline-1-(S-benzyldithiocarbazate) (DTC) (fig. 1(a)) have received significant attention in the scientific community due to their promising antibacterial and antifungal properties [1,2,3]. However, the exploitation of the biological characteristics of DTC is limited due to its poor water solubility and easy degradation in aqueous solutions and in certain organic solvents. In this context, the nanoencapsulation of DTC can be an excellent strategy to overcome these drawbacks. Nanomaterials based on physiological lipids, such as nanostructured lipid carriers (NLC) have attracted considerable interest as encouraging nanocarriers for the active ingredient (a.i.) delivery, as NLC can improve the solubility of a.i., protect a.i. from premature degradation, as well as can control its release and target to the specific cells or organisms [4]. The main goal of the present work is to design DTC-encapsulated NLC (NLC-DTC) using green synthesis and evaluate their physicochemical properties related to the mean particle size (Z-Ave), polydispersity index (PdI), zeta potential (ZP), morphology (Transmission Electron Microscope (TEM)), structure (Raman Spectroscopy), drug loading capacity (DL) and encapsulation efficiency (EE). Also, this work aims at evaluating the environmental safety of formulations on different aquatic organisms – freshwater algae (*Raphidocelis subcapitata)*, aquatic plants (*Lemna minor)* and marine bacterium (*Aliivibrio fischeri*) at DTC concentration ranging from 8.8 to 150 mgL^{-1} following standard OECD guidelines. The results exhibited a Z-Ave of 150.2 ± 0.4 nm, PdI of 0.24 ± 0.01 and ZP values of -53.2 ± 0.3 mV. The TEM images (fig. 1(b)) revealed spherical morphology and no DTC crystallization was observed on the surface of the NLC after its encapsulation. Therefore, DTC nanoencapsulation did not change the morphology/average size of the nanoparticles. In the Raman spectrum (fig. 1(c)), the peak related to the aromatic ring, the νC=S bond and νC=N of DTC after its encapsulation in NLC appears at 1004 cm^{-1}, 1200 cm^{-1} and at 1613 cm^{-1}, respectively. The percentage of the total amount of DTC loaded into NLC (%DL) was 2.44 ± 0.0001% and %EE was 99.95 ± 0.004%, showing that DTC has great affinity to lipidic matrix of NLC. Environmental safety assays indicated that the growth rates of algae *R. subcapitata* and *L. minor* were not affected by NLC-DTC after 72h and 7 days of exposure, respectively. However, the data showed that NLC-DTC inhibited the bioluminescence of *A. fischeri* (EC_{50}=104.9 mgL^{-1}) when compared to pure DTC (highest effect of 2.6%). Therefore, these findings show that the nanoencapsulation of DTC in NLC can be an excellent approach to maintain its stability in aqueous suspensions and to select the concentrations that are not toxic to the environment to be tested in the further biocide testes against target species, such as pathogenic fungi and bacteria.

T.I. Menezes thanks the NORTE2020 through project Norte-08-5369-FSE-000050 for financial support of a PhD grant. This work was partially supported by the FCT under Research Grant UIDB/00081/2020 – CIQUP

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Towards the emergence of modern cells

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The complexity of modern biochemistry suggests that a systems chemistry approach is required to understand and potentially recapitulate the intricate network of prebiotic reactions that led to the emergence of life.

Early cells probably relied upon interconnected chemistries to link RNA, peptides and membranes.
In this context, I will discuss our recent advancements about:

- what, how and when stable membranes appeared on early Earth;[1]
- whether primitive membranes could be compatible with prebiotic chemistries;[2]
- what biophysical or biochemical mechanisms could enable primitive cell cycles to retain continuity of function.[3]

Addressing all these points can help us to elucidate the prebiotic pathways that led to the emergence of populations of functional primitive cells and, from there, the rise of life as we know it.

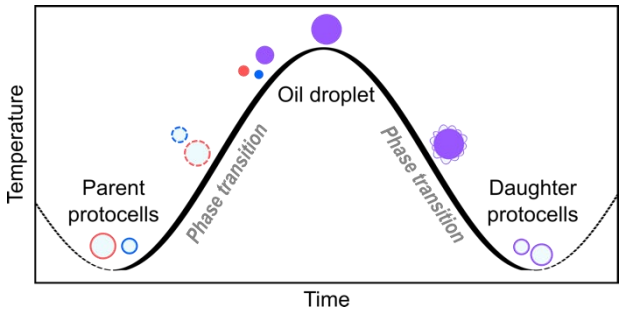

Fig. 1: Scheme representing a possible pathway for the emergence and reshuffling of primitive cells. [3]

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Unconventional bioorthogonal strategies based on transition metal catalysis

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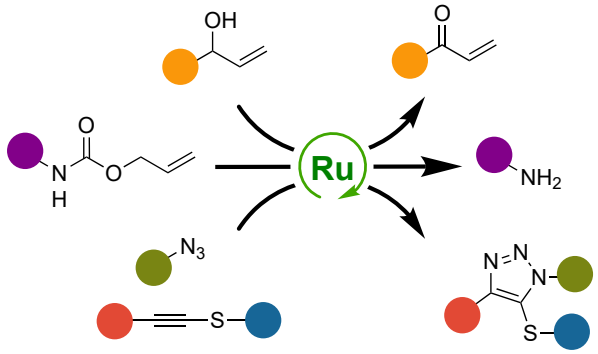
Bioorthogonal chemistry has emerged as a prominent tool in chemical biology to selectively modify and tag biomolecules and cell structures under mild conditions, in extremely crowed biological environments.[1] In this context, transition metal complexes are a new paradigm in the world of chemical biology, not only because of their diversity, non-conventional reactivities or the possibility of fine-tuning, but also due to new options for their activation and control.

Some examples of reactions promoted by organometallic catalysts have been successfully translated to cells or even to in vivo settings. However, this area is still in its infancy, with limitations regarding type of transformations, their scopes, effectiveness under highly diluted conditions, as well as their TON numbers.[2]

Herein, we describe our recent efforts on the development of bioorthogonal transformations based on ruthenium catalysts. Within these transformations, we will highlight the isomerization of allylic alcohols to yield ketones, a redox neutral process that involves ruthenium hydride intermediates.[3] These hydrides are delivered intramolecularly and do not suffer scrambling with the media, and work even inside mammalian cells . Deprotection of allyl carbamates to yield bioactive amines in cells, [4] or cycloadditions between azides and thioalkynes that work under highly diluted conditions (up to 100 μM) with spatio-temporal control will also be summarized.[5] Importantly, we will show that some of these processes can work concurrently to other bioorthogonal methods, such as the copper catalyzed azide-alkyne cycloadditions or even to other natural occurring transformations.



Schematic representation of different transformations based in Ruthenium catalysis

This work has received financial support from Spanish grants (PID2019-108624RB-I00, ORFEO-CINQA network CTQ2016-81797-REDC), the Consellería de Cultura, Educación e Ordenación Universitaria (2015-CP082, ED431C-2021/25 and Centro Singular de Investigación de Galicia accreditation 2019-2022, ED431G 2019/03), the European Union (European Regional Development Fund-ERDF corresponding to the multiannual financial framework 2014-2020), and the European Research Council (Advanced Grant No. 340055). Alejandro Gutiérrez-González thank the Ministerio de Universidades from the Spanish Government for the FPU fellowship (FPU17-00711).

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Polymer – lipid hybrid vesicles made of poly(cholesteryl methacrylate) containing amphiphilic block copolymers

Edit Brodszkij *, **Carina Ade, Isabella Westensee, Jarvi Spanjers, Jan Skov Pedersen, Brigitte Stadler**
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Block-copolymers (BCP) are widely used building blocks in micelle and vesicle self-assembly as they can be tailored to match the required physical-chemical properties by varying the hydrophobic or hydrophilic block. These types of assemblies are common in drug delivery or in cell mimicry as carriers for natural or synthetic active entities.

We prepared a series of BCPs where the cholesterol moiety, in a polymeric form of poly(cholesteryl methacrylate) (PCMA), was utilized as a hydrophobic block. PCMA ensured the insertion of the polymer into the lipid bilayer and several different hydrophilic extension was used, such as poly(dimethylaminoethyl methacrylate)(PDMAEMA),[1,2] poly(ethylene glycol),[3] poly(2-carboxyethyl acrylate) (PCEA),[4,5] and its copolymers with methionine methacryloyloxyethyl[6] to optimize their properties for various applications. PCMA was chosen because cholesterol is a natural compound and plays a vital role in the fluidity of cell membrane. Co-polymers of CMA with butyl methacrylate (BuMA) and 2-hydroxyethyl methacrylate (HEMA) were synthesized and extended with PCEA or with poly(2-methacryloyloxyethyl phosphorylcholine) to evaluate the contribution of the polymers to the physical-chemical properties of the assemblies. The hydrophobic block length was synthesized with low PDI < 1.2 and molecular weights between 4-8 kDa. The hydrophilic extensions were around 20 kDa as determined from 1H NMR. BCPs were successfully assembled into hybrid vesicles (HVs) with various types of lipids, such as DOPC, DOPE and SoyPC, up to 10 mol % BCP content while above that micellar assemblies were found as indicated by TEM images as well as by SAXS measurements. The general polarization probed with Laurdan increased with increasing polymer content whereas, the permeability decreased with increasing BCP content furthermore the addition of HEMA resulted in very high permeability. Confocal laser scanning microscope imaging of giant HVs (> 5 µm) made of Oregon Green labelled polymers and Lissamine Rhodamine labelled lipids showed homogeneous distribution of the components. β-galactosidase was associated with the HVs and the enzymatic reaction was visualized by CLSM to follow the production of the fluorescent dye from a model substrate to evaluate the effect of the membrane composition.

Taken together, the membrane properties of HVs can be tuned by utilizing BCPs with a PCMA containing hydrophobic block and varied hydrophilic extensions. The vesicles offer unique opportunities in self-assembly of soft nanoparticles with promising applications in drug delivery and cell mimicry.

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A quantum of solace for crops - New lead structures against drought stress interacting with ABA receptor proteins via bioisosterism concepts

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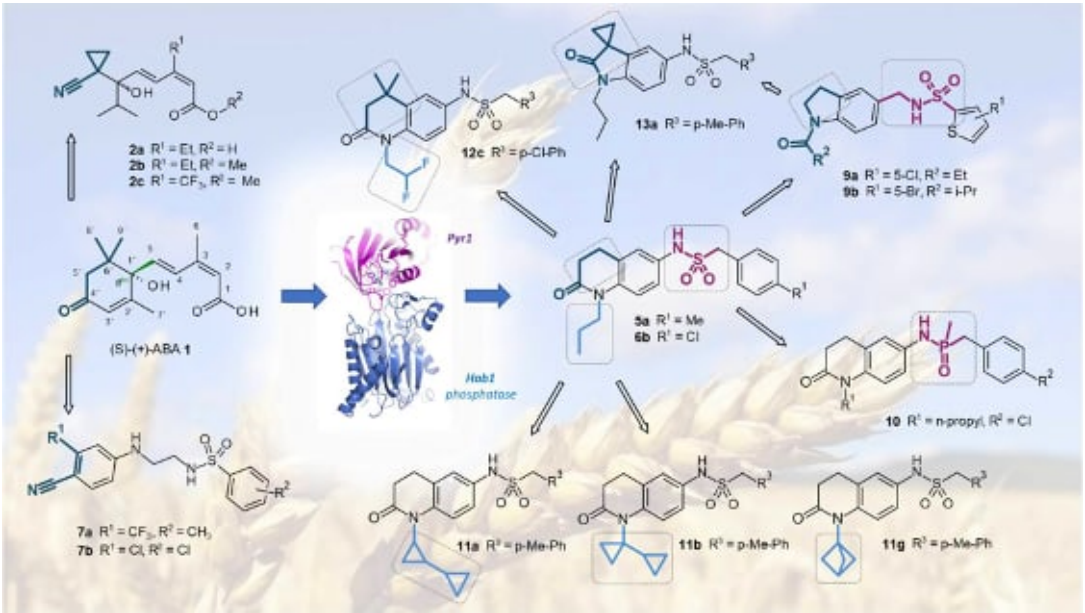
Agricultural crops across the planet are plagued by biotic stresses such as pests, weeds and disease, however yields of broadacre crops in particular can be impacted even further by different abiotic stress types which, critically, are expected to worsen with climate change. Among various abiotic stress types affecting agricultural production, drought stress is regarded as the main source of crop losses around the globe. Naturally occurring plant hormone abscisic acid (ABA) and its receptor proteins play an important role in plant responses towards drought. Within our research efforts to identify new chemical entities against drought stress we have recently identified not only highly potent natural product analogs[1,2], but also unprecedented lead structures interacting with RCAR/(PYR/PYL) receptor proteins in wheat *via* high-throughput screening of our corporate compound library and subsequent dedicated SAR studies[3]. Independently, a transgenic approach has demonstrated that ABA receptor overexpression in wheat improves grain production under drought underlining the potential of new chemical ABA agonists. All our new classes of ABA agonists beared particular structural features that were explored in our SAR studies having an essential impact on both, target affinity *in vitro,* and *in vivo* efficacy[1-5]. Our results demonstrate that cyano cyclopropyl groups, 4-cyanoanilines or certain inverted amides are effective bioisosters of the carbonyl group in ABA's cyclohexenone headgroup and in tetrahydroquinolinyl sulfonamides whilst sulfonamide groups could be replaced by the rare motif of phosphinamidates[4].



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Hypoxia-activated cancer pro-drugs: a new molecular trigger

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In spite of the many powerful drugs against cancer that are available, the inability to find specific drugs comes, among other factors, from the difficulty to distinguish healthy cells from cancer cells. This constitutes a molecular recognition opportunity.

Specially, one of the differences of cancer cells is the low level of oxygen in the tumor microenvironment. This hypoxia state can be used to design new pro-drugs which are activated under the hypoxia-reducing conditions of the cancer cells, [1] avoiding in this way the side effects over the healthy cells.

Here we present a new molecular trigger, which is able to link to cancer drugs through ester, amide, or thioester linkages and is prone to be activated under this hypoxia reducing conditions exploiting the tumor environment. Also, the presence of a dansyl-like motif in the molecular trigger structure will allow us to visualize the internalization of the pro-drug inside the cells and the drug release.

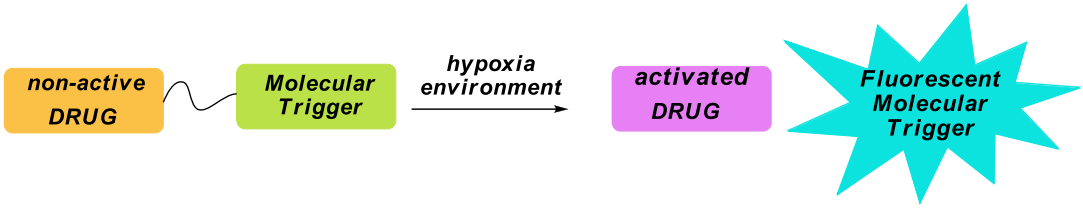

Figure 1. Strategy to target cancer cells under hypoxia conditions.

This work was supported by MICINN (PID2020-118732RA-I00 and PID2019-108994RB-I00), Junta de Castilla y León (European Regional Development Fund-SA069P17), the University of Salamanca (Own Research Programs-KCEP/463AC01 and 18K155/463AC01) and Fundación Memoria de D. Samuel Solórzano Barruso (FS/8-2019). JJGG is gratefully acknowledged to University of Salamanca and Santander Bank for a postdoctoral fellowship. AH is grateful to the Algerian Government for a predoctoral fellowship for "Formation Doctorale résidentielle à l'etranger". ALFA thanks the Spanish Government for a Beatriz Galindo Fellowship (BG20/00233). NUCLEUS platform at University of Salamanca, especially Anna Lithgow (NMR Service), César Raposo and J. F. Boyero Benito (MS Service).

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Exploring immunity and bacterial resistance from the computational side

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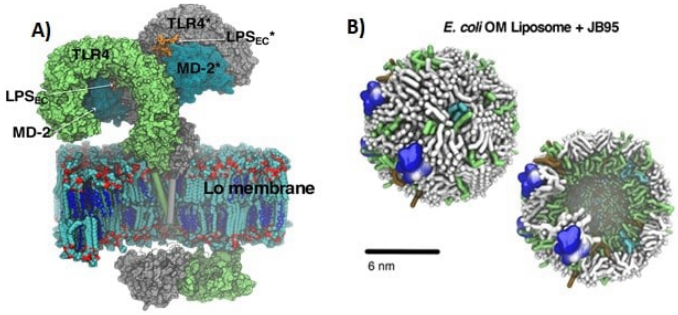
Toll-like receptors (TLRs), classified as pattern recognition receptors, have a primordial role in the activation of the innate immunity. TLRs are transmembrane proteins specialized in the recognition of pathogen-associated molecular patterns, such as lipopolysaccharides (LPS) of Gram-negative bacteria (TLR4), lipoteichoic acids of Gram-positive bacteria, and bacterial lipoproteins (TLR1/TLR2 and TLR2/TLR6). Identification of TLRs has sparked great interest in the therapeutic manipulation of the innate immune system. Deep structural understanding of Toll-like receptors signaling may lead to the discovery of novel small molecules with desirable therapeutic properties.[1,2]

We have addressed the characterization of the molecular recognition processes of agonist and antagonist modulators of TLR2, and TLR4, by computational tools, and have proposed a mechanism for their biological activity.[1] We have modeled, by all-atom MD simulations (Fig. A), the structural assembly of plausible activated full-length TLR4 models, embedded into a realistic plasma membrane, providing an analysis at both atomic/molecular and thermodynamic levels of the TLR4 assembly and biological activity.[2]

On the other hand, studies of pathogenic bacterial membranes by liposome models can contribute to understand infection mechanisms.[3,4] We have captured, by coarse-grained MD simulations, the role of Lipid A on bacterial liposome morphology and physicochemical properties (Fig. B). This study opens a promising starting point to predict the activity of newly designed drugs able to modulate the bacterial membrane properties, accounting for the antibacterial resistance problem.



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Photopharmacology: tools, applications, and structures

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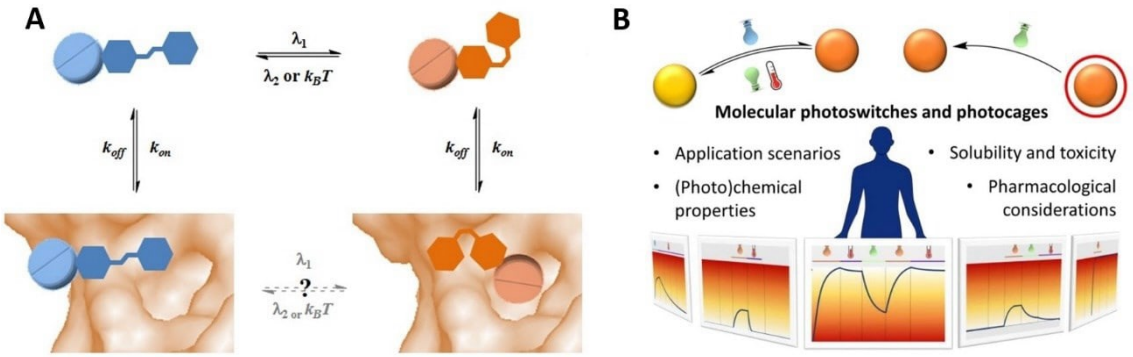
Current pharmacological treatments rely on using bioactive compounds that evoke a response by interacting with molecular targets in the human body. The selectivity of this interaction is crucial and the lack of it leads to the emergence of severe side-effects in the body and toxicity in the environment. This is especially severe in chemotherapy, which employs inherently cytotoxic molecules, and in the antibiotic therapy, where the overuse of bioactive substances has led to the emergence of antimicrobial resistance.

To solve this problem, drugs could be introduced whose activity could be reversibly or irreversibly turned on with light, enabling local activation with high spatiotemporal resolution. The aim of this presentation is to describe the emerging concept of photopharmacology (Figure A),[1] which is currently being developed and applied to precisely control the activity of drugs using UV/visible/NIR light. Light offers unparalleled advantages in regulation of bioactivity. Importantly, light of the same energy is also used as an input/output signal in medical (mostly optical/optoacoustic) imaging. Combination of those two paradigms requires light-responsive tools that empower both therapy and imaging.



The presentation will focus on our efforts towards bridging light and medicine, focusing first on new light-operated tools [2] (molecular photoswitches [3,4,5] and photocages [6], Figure B). Next, I will highlight the synergies between medical imaging and therapy, offered by light, through photoresponsive optical [7] and magnetic resonance [8,9] imaging agents. Finally, using chosen examples of photopharmacological agents,[10-12] I will discuss the structural aspects [13] in photopharmacology.

Acknowledgment: Thanks to the Dutch Scientific Organization (VIDI 723.014.001 and ECHO 711.017.012 grants) for financial support.

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Surface-confined pyrene-based fluorescence sensors for highly sensitive saccharide detection

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Boronic acids have been widely used in conjunction with fluorescent molecules for recognition of saccharides.[1] However, surface-confined fluorescent boronic acid-based sensors with high sensitivity for low saccharide concentrations are currently out of reach.

Herein, we report a fluorescence boronic acid sensor modulated by a PET (photoinduced electron transfer) quenching mechanism, which will be incorporated onto the nanoparticle surfaces to generate a sensitive platform for saccharides. With this aim, a boronic acid-pyrene sensor was synthesized through a straightforward three-step strategy.

Initial functionalization of pyrene with a piperazinyl group provides, both a fluorescence quencher and spacer for the saccharide receptor moiety. A phenylboronic acid is incorporated not only to act as the receptor moiety but as the fluorescence-quenching switch. Finally, the probe is also functionalised with an acetylene group to allow immobilization on the nanoparticle surface via CuAAC.

Synthesized compound displays a fluorescence enhancement after sugar addition due to the suppression of the PET mechanism. Strictly, sugar-binding promotes the interaction between piperazine amino group and boronic acid, interrupting the quenching process of the pyrene probe.

Studies are underway to incorporate the pyrene-fluorescence sensor on silica nano particles and achieve an efficient “off-on” fluorescent switch enabling the sugar detection in the low millimolar range.

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Rosamine dyes: from synthesis to the preparation of functional materials for optical sensing applications

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Fluorescent molecular sensors are key tools in modern biochemical and medical diagnostics. Among the different classes of bright organic molecules, rhodamine and fluorescein dyes stand out as extremely versatile and biocompatible platforms, having photophysical properties that can be fine-tuned through strategic structural modifications, leading to the synthesis of new derivatives that can absorb across all the visible and near-infrared spectrum [1]. With decades of study, these molecules derived from xanthene continue to be excellent scaffolds and their applications range from chemistry and biology to materials science.

Rosamines are rhodamine analogues that lack the carboxylic acid group at the *ortho* position of the phenyl ring, being often considered advantageous over rhodamines as they exhibit very attractive absorption and fluorescence properties and are usually easier to synthesize and to purify [2].

Herein we describe the synthesis of a series of rosamine dyes bearing different aryl and heteroaryl substituents (Figure 1), aiming to achieve molecules with photophysical properties suitable for optical sensing applications and allowing the immobilization into materials, such as SiO_2 and TiO_2 matrices, with improved robustness and sensitivity properties using the xanthene as building block or functional unit [3]. Synthetic sustainable approaches using microwave irradiation and ohmic heating [4] will be present, as well as the most relevant photophysical properties and analyte-responsive behavior of rosamine dyes and materials obtained.

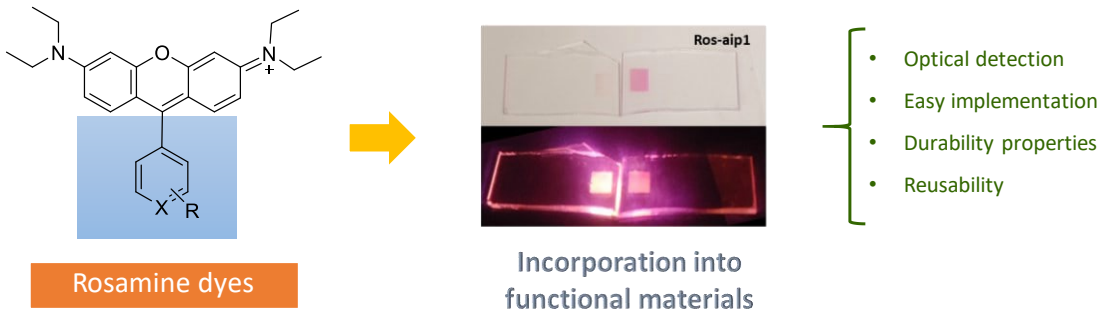

Figure 1. Structure of rosamine dyes and their incorporation into functional materials.

This work received financial support from National Funds (FCT/MCTES, Fundação para a Ciência e Tecnologia and Ministério da Ciência), under the Partnership Agreement PT2020 through projects NORTE-07-0162-FEDER-000048, UIDB /50006/2020, UIDP/50006/2020, and also the projects PTDC/QUI-QIN/28142/2017, PTDC/QUI-QOR/29426/2017 and EXPL/QUI-OUT/1554/2021. A.M.G.S. and A.L. thank FCT for funding through program DL 57/2016 – Norma transitória.

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New biomimetic receptors for biomolecules

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The development of new receptors able to associate organic molecules with high association constant and selectivity is important in many different fields, both in industry and academy, such as chemical sensing, drug delivery or catalysis.

For example, many cancer-targeted therapies rely in the possibility to distinguish any structural or chemical difference in the cancer cells that makes them different from healthy cells. Thus, being able to selectively target a given molecule in a biological media constitutes a challenge with important applications.

In our group, we have been impressed by the way nature employs a structural motif called oxyanion hole to associate carbonyl groups and catalyse chemical reactions inside our bodies with high selectivity and speed and we have tried to mimic this strategy to create biomimetic catalysts and receptors.

Here we present our recent studies on the active center of hydrolases which we have used to create biomimetic catalysts [1] as well as adaptable molecular receptors with an oxyanion-hole motif [2] and biomimetic receptors for sugars such as sialic acid.

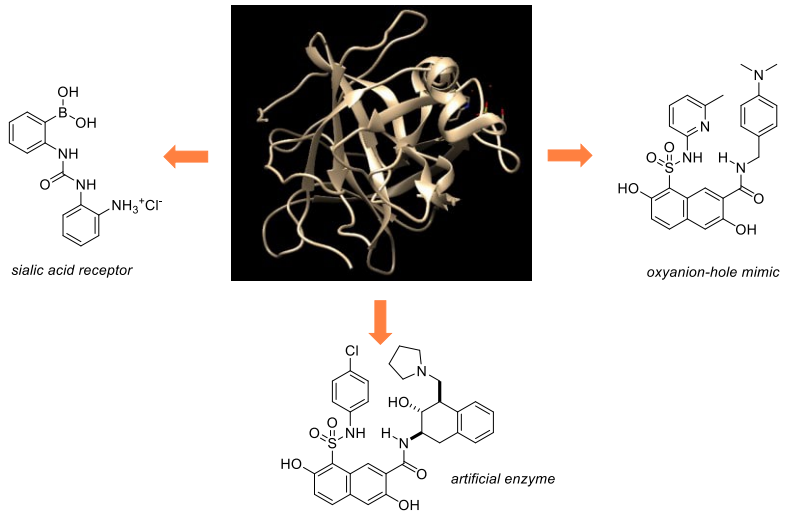

Figure 1. Receptors for biomolecules inspired by enzymes.

This work was supported by MICINN (PID2020-118732RA-I00 and PID2019-108994RB-I00), Junta de Castilla y León (European Regional Development Fund-SA069P17), the University of Salamanca (Own Research Programs-KCEP/463AC01 and 18K155/463AC01) and Fundación Memoria de D. Samuel Solórzano Barruso (FS/8-2019). JJGG is gratefully acknowledged to University of Salamanca and Santander Bank for a postdoctoral fellowship. AH is grateful to the Algerian Government for a predoctoral fellowship for "Formation Doctorale résidentielle à l'etranger". ALFA thanks the Spanish Government for a Beatriz Galindo Fellowship (BG20/00233). NUCLEUS platform at University of Salamanca, especially Anna Lithgow (NMR Service), César Raposo and J.F Boyero Benito (MS Service).

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Improvement of the physicochemical properties of flavylium dyes using cyclodextrins for Photodynamic Therapy

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Photodynamic therapy (PDT) is a type of photochemotherapy that is very efficient in killing cancer cells and has the major advantage of having very low side effects comparing to other therapies. In this methodology, a molecule that is called a photosensitizer (PS) is administrated to the patient, cancer cells absorb this molecule, in a given amount of time, and then these cells are exposed to a radiation. This irradiation leads to the production of reactive oxygen species (ROS) by the PS which results in cell death. The ideal PS must be available in a pure form, be easy to obtain, have a high singlet oxygen quantum yield, have a strong absorption in the red region (600-800nm), and present a low photobleaching to prevent its degradation during therapy. Currently, the approved photosensitizing molecules in dermatology are precursors of protoporphyrin IX, a molecule that absorbs the greatest amount of light at 410 nm so the major problem that researchers are trying to solve is to find compounds that fulfil at once all requirements to be an effective PS for PDT. Anthocyanins are natural pigments that contribute to the red, purple and blue colors found in flowers, fruits, and tubers [1]. Due to such features, their oxidative effects and ability to form quinones and quench singlet oxygen, these pigments can be proposed as promising candidates for PS. Based on the knowledge about anthocyanins and PSs it is possible to develop anthocyanins analogues that properly match the requirements for an efficient PS: for instance, the presence of amino substituents on the 2-phenylbenzopyrylium core originates flavylium dyes with improved maximum wavelength absorption in the visible range from 550–700 nm, which is highly desired for PDT [2]. In addition, cyclodextrins (CDs) are oligosaccharides widely applied in different industrial matrices and the formation of molecular inclusion complexes between these molecules and anthocyanins are known to affect important properties of the pigments, namely water solubility and equilibrium and rate constants [3,4]. Therefore, the aim of this work was to study the influence of molecular inclusion complexes with cyclodextrins on the stabilization and efficiency of flavyliums dyes for use on PDT.

Acknowledgments: This work was supported by the Associated Laboratory for Sustainable Chemistry, Clean Processes and Technologies LAQV through the national funds from UIDB/50006/2020 and UIDP/50006/2020 and by AgriFood XXI I&D&I project (NORTE-01-0145-FEDER-000041) cofi- nanced by European Regional Development Fund (ERDF), through the NORTE 2020 (Programa Operacional Regional do Norte 2014/2020). It was also supported by the project PTDC/QUI- OUT/29013/2017 funded by FCT and FEDER. A.B. (UI/BD/151270/2021) and P.A. (SFRH/BD/143309/2019) gratefully acknowledge their doctoral grants from FCT. J.O. and N.B. would like to thank FCT respectively for contract (IF/00225/2015) and CEECIND/00466/2017. Funding: This work was financially supported by UID/50006/2020.

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A newly discovered Dyp-type peroxidase from a marine actinobacterium immobilization and electrochemical characterization

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Dye-decolorizing peroxidases (DyPs) can oxidize several anthraquinone dyes in the presence of H_2O_2, hence the name dye-decolorizing peroxidase and, besides being known to be present in other organisms, these were recently found in Actinobacteria. Dyps have been recently gained an increased interest as a potential biocatalyst for lignin degradation since it has been shown to have ligninolytic activity[1]. Actinobacteria has been known to be a rich source of enzymes with diverse functions, lignocellulolytic activity among them. For the discovery of new enzymes, data mining has become more relevant due to the growth of available enzyme databases and computational tools[2]. In the current study, a novel Dyp-type peroxidase was found, through the data mining of genome data from the Actinobacteria, presenting a new conserved motif was discovered[3]. The new Dyp was electrochemically characterized allowing to attain the formal reduction potential, its dependence on the temperature and pH, allowing to retrieve data on the electron donor characteristic of ligands, kinetics and thermodynamics associated with the protein centers' redox transition with implications in their catalytic efficiency. The novel Dyp was immobilized on pyrolytic graphite and characterized by cyclic voltammetry. Also, the catalytic activity was assessed.

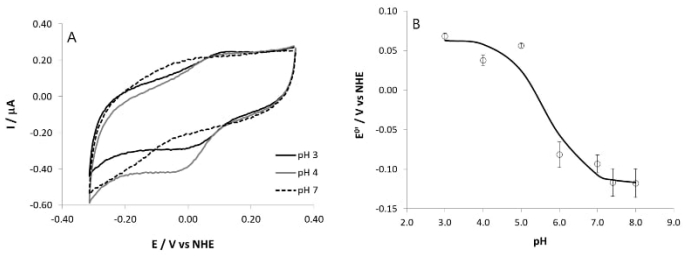

Figure 1. Electrochemical behavior of P1116-C02_Dyp immobilized on PG (adsorption) in anaerobic conditions, A) cyclic voltammograms, at three different pH values showing the protein redox center and B) pH dependence of the formal reduction potential.

Acknowledgments: This work was supported by the project OXYMOD of the Centre forDigital Life Norway (DLN) under Research Council of Norway grant number 269408 as well as SINTEF internal funding. Also, this work was supported by the Associate Laboratory for Green Chemistry – LAQV which is financed by national funds from FCT/MCTES (UIDB/50006/2020), Portugal.

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Functional biohybrid nanomaterials from diatoms microalgae

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Diatoms are a prolific class of single cell algae living in both fresh and marine water ecosystems. The cells are encased in three-dimensional amorphous nanostructured silica shells (frustules).

From the perspective of a synthetic chemist, diatom frustules can be envisaged as a plentiful source of micro/nano structures useful to build up smart functional nanomaterials for photonics, electronics and biomedicine [1].

Contrary to silica industrial production, the biomineralization process naturally occurring in diatoms generates SiO_2 in mild conditions and in the absence of toxic reagents. Frustules exhibit interesting properties such as high surface area, mechanical resistance and nanotexturization. Moreover, frustules' biosilica can be easily chemically modified to add new functions, by surface functionalization and/or by *in vivo* adding specific molecules to the culture medium.

We have demonstrated the production of photonic microstructures by *in vivo* incorporation of tailored light emitting molecules in living *Thalassiosira weissflogii* diatoms [2]. With a similar approach, biosilica has been doped with phosphorescent iridium complexes [3]. We have also reported applications of chemically modified frustules for bone cells growth [4] and demonstrated that *in vivo* incorporation of proper organic dyes favors the enhancement of diatoms' photosynthetic efficiency [5]. More recently, we started to investigate the production of functional structures by coating living diatoms with biomimetic polymers like polydopamine (PDA). The resulting hybrids turn out to be intriguing platforms for additional chemical modifications such as, surface coverage with metal nanoparticles or with several classes of enzymes.

Overall, our studies point out new routes to nanomaterials by combining biotechnological production of microalgae with organic synthetic tools.

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B-DNA Structure and Stability: Insights from Quantum Chemical Analyses

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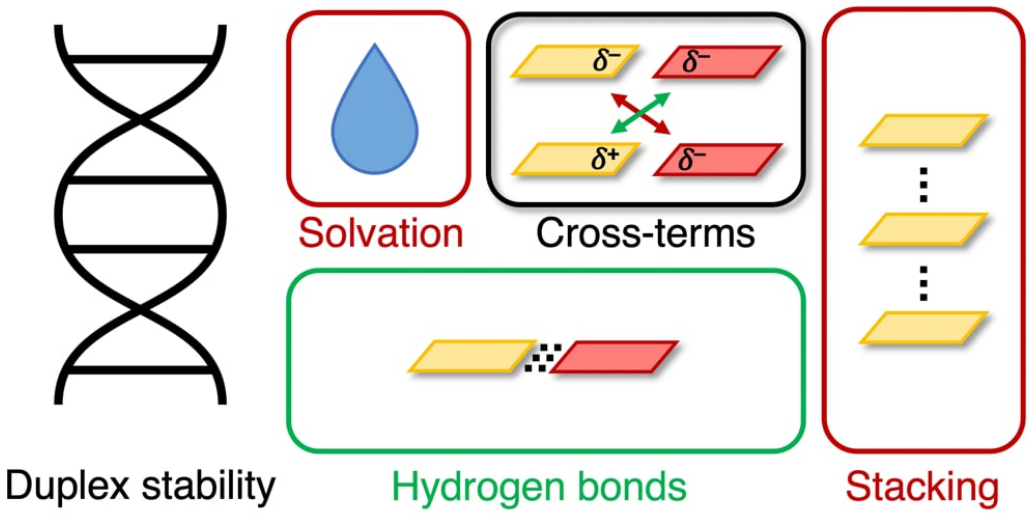
Biomolecules, like DNA, are the product of ages of evolution, involving stability differences that are often small and yet, literally, of vital importance. These circumstances constitute a challenge for elucidating the key physical principles behind the stability differences in DNA duplexes which requires synergy between experimental and theoretical studies.

The stability of duplex DNA does not solely depend on the base pair composition, but also on the order in which the nucleobases occur (i.e., sequence) [1,2]. Using accurate quantum chemical analyses, we pinpoint the origin of these effects and provide guidelines for predicting the stability of DNA duplexes relative to their single-stranded counterparts [3]. Our quantum chemical computations unexpectedly identify the loss of stacking interactions within individual strands as a destabilizing factor in the duplex formation, in addition to the better-known effects of partial desolvation. We show that, and how, the sequence-dependence of the duplex stability originates mainly from the so-called diagonal interactions or cross-terms between nucleobases of two adjacent Watson-Crick pairs. These cross-terms can be stabilizing or destabilizing, depending on the attractive or repulsive nature of the diagonal electrostatic interactions.



The work has been performed under the Project HPC-EUROPA3 (INFRAIA-2016-1-730897) on the Dutch national e-infrastructure with the support of SURF Cooperative. The authors gratefully acknowledge the financial support of the EC Research Innovation Action in the Horizon 2020 program and the Netherlands Organization for Scientific Research (NWO).

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MEDS433 a Novel and Potent human Dihydroorotate Dehydrogenase (hDHODH) Inhibitor, Induces Differentiation and apoptosis of Acute Myeloid Leukemia

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In acute myeloid leukemia (AML), blasts lose their ability to differentiate into mature cells and undergo apoptosis. Accordingly, a proapoptotic and differentiating therapy (arsenic and all trans retinoic acid, ATRA) has dramatically improved survival in acute promyelocytic leukemia; however, such combination therapy is not available for other AML subtypes. While, in 2016, inhibition of dihydroorotate dehydrogenase (DHODH), a key enzyme of the pyrimidine biosynthesis, was found to induce differentiation in several AML models. In fact, brequinar (BRQ) was utilized in vivo studies.[1] We are optimizing hDHODH inhibitors to improve potency and drug-like proprieties. The main objective is to identify the best inhibitor suitable for use in in vivo studies on AML animal model.

In this work we will present a new generation of hDHODH inhibitors able to reach the enzymatic BRQ inhibition potency levels. Our data showed that compound 1, the best of two series, induced apoptosis in multiple AML cell lines, not only because of differentiation, but also directly. Its combination with antileukemic agents further increased the apoptotic rate, but when experiments were performed in the presence of physiological uridine concentrations, results were less impressive. Conversely, the combination of compound 1 with dipyridamole induced metabolic lethality and differentiation in all AML cell lines; this extraordinary synergism was confirmed on AML primary cells with different genetic backgrounds and was unaffected by physiological uridine concentrations, predicting in human activity. [2,3,4] Finally, our preliminary results from in vivo experiments showed that i) compound 1 wasn't toxic on CD-1 mice after 14 days of gavage administration at two different doses 15 and 30 mg/Kg and during acute toxicity experiment was not toxic ad dose of 1 g/Kg; ii) the half-life was limited to 3-4 hours and iii) compound 1 had an optimal in vivo antileukemic activity after 18 days of treatment in THP1-xenograft models obtained from NSG mice. Theoretical design, modelling, synthesis, SAR, X-ray crystallographic data, biological assays, Drug-Like proprieties, pharmacokinetic studies, and in vivo evaluations on AML models will be here presented and discussed.

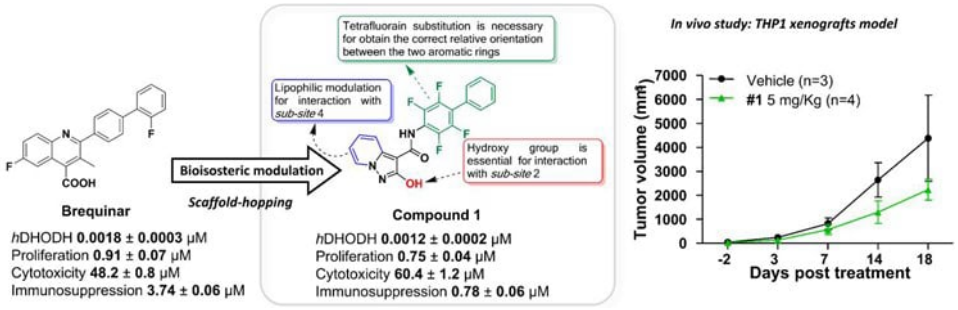

Figure 1. Brequinar and Compound **1** structures. *In vivo* efficacy of compound **1** in THP1-xenograft models obtained from NSG mice

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Cyclic Thiosulfonates for Thiol-Mediated Uptake: Cascade Exchangers, Transporters, Inhibitors

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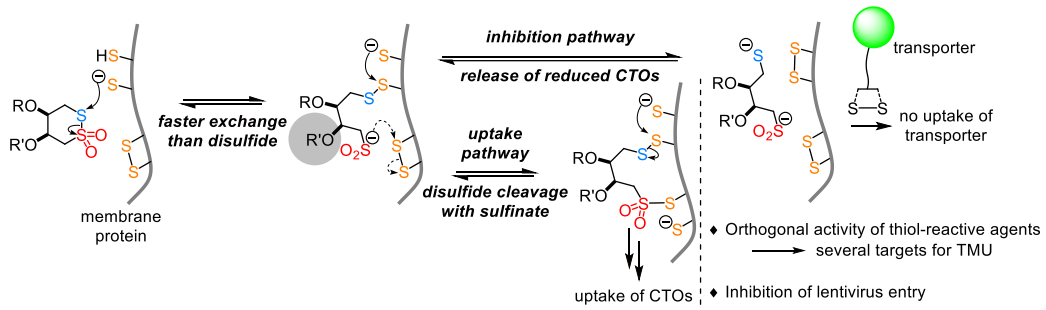
Thiol-mediated uptake (TMU) is one of the pathways of the cellular entry of biomolecules, in which the reversible formation of disulfide bonds between the molecule and a protein on the plasma membrane plays a crucial role. The formation of dynamic covalent disulfide bonds at the cell surface facilitates cellular penetration and ensures internal release by intracellular thiols, such as glutathione. Similar processes are involved in the uptake of HIV [1] and potentially of SARS-CoV-2 [2,3], and thus the development of better transporters and inhibitors of this process is of great importance.

In our exploration of new motifs for efficient transporters and inhibitors, cyclic thiosulfonates (CTOs) have attracted a lot of interest as thiol-reactive agents. However, the use of thiosulfinates and thiosulfonates, oxidized forms of disulfides, has not been much explored so far in the context of cellular uptake, whereas CTOs can serve as anti-HIV agents [4]. Our recent screening showed CTOs have good inhibitory activities against TMU as well as against the entry of lentiviruses expressing the spike proteins of SARS-CoV-2 [5].

In our current research [6], kinetic experiments revealed the excelled reactivity of CTOs with thiols over disulfides and thiosulfinates, and the ability of the sulfinate products to continue the cascade exchange with another disulfide. As expected from their reactivity, CTOs afforded better fluorescent transporters than a standard disulfide transporter. Further enhancement of the activity was achieved with introduction of a hydrophobic group next to the reactive CTO moiety. The uptake of the CTO transporters takes place via TMU, proven by the inhibition with various thiol-reactive agents. An inhibition study with three transporters and more than 50 inhibitor candidates revealed the orthogonality of the inhibition with different TMU-active motifs, which strongly suggests the existence of multi targets for TMU. Good correlation in the inhibition activity against the CTO transporter and against lentivirus entry suggests the potential use of the CTO reporter for the fast screening of antiviral candidates.



Lentiviral experiments were performed by Neurix. pCG1_SCoV-2 plasmid encoding SARS-CoV-2 S-protein was provided by Stefan Pöhlmann (Deutsches Primatenzentrum, Leibniz-Institute for Primate Research, Göttingen).

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New borinic probes for fast detection and imaging of hydrogen peroxide

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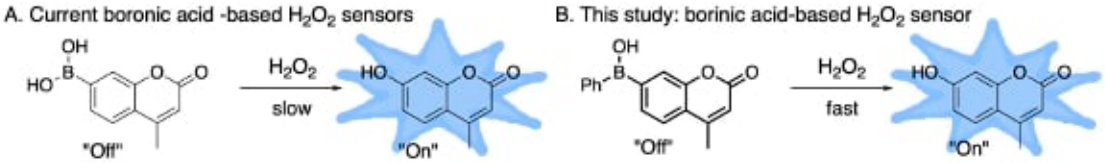
Reactive oxygen species (ROS: hydrogen peroxide, hydroxyl and superoxide radicals) are by-products of aerobic metabolism. Among them, hydrogen peroxide (H_2O_2) plays a crucial role in a wide range of physiological processes in human [1]. However, when our cells are subjected to oxidative stress conditions, its overproduction is directly or indirectly responsible for numerous damages at the molecular level, which can affect cellular mechanisms. This process is associated with aging, as well as cancer and several neuro-degenerative diseases such as Alzheimer's or Parkinson's [2]. The development of selective and sensitive tools allowing H_2O_2 detection in a biological context represents a great challenge for a better understanding of H_2O_2-mediated signaling in physiological and pathological processes

To date, several "off-on" small fluorescent probes triggered by H_2O_2 have been developed for its detection. Among them, probes based on boronate oxidation are amongst the most effective for the detection of H_2O_2 *in cellula* [3]. But these probes also suffer from lack of reactivity, which is not fully satisfactory for biological applications. To address this issue, we envisioned the use of borinic acids which due to electronic effects could be more prone to oxidation compared to their boronic acid counterparts.

Recently, we reported the design, synthesis, and kinetic properties of the first borinic sensor for the fast detection of hydrogen peroxide [4]. Furthermore, a comparative study with its boronic acid counterpart was presented *in vitro* and in a cellular context.



Synthesis - kinetic study - in vitro and cellular study

We are currently further optimizing this strategy for biological applications and will present our latest results in this field.

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Amyloid–ß peptides interaction with curcumin: AFM and voltammetric characterization

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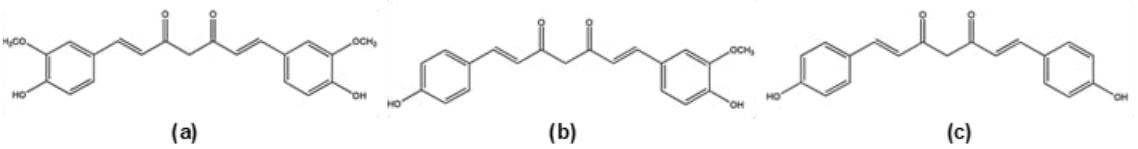
Alzheimer disease (AD) is a progressive age-related neurodegenerative disorder estimated to affect up to 107 million people by 2050, its pathology being associated with the dysfunction of amyloid β (Aβ) peptide mechanisms, among others. In AD brain, the large amyloid precursor protein (APP) is wrongly cleaved first by the β-secretase, and then by the γ-secretase, leading to the formation of soluble monomers $Aβ_{1-40}$ (85-90 %) and $Aβ_{1-42}$ (10-15 %), that further aggregate, forming neurotoxic oligomers and protofibrils, fibrils and plagues.

Curcuminoids are natural phenolic compounds derived from turmeric root (*Curcumae longae rhizoma*), a member of the ginger family (*Zingiberaceae*), that have been used as spices and coloring agents for centuries, been recognized for their antibacterial, antifungal, antiviral anti-allergic, anti-inflammatory and anti-cardiovascular diseases properties. Commercial products of curcumin generally contain curcumin I (curcumin, ~ 77%), curcumin II (demethoxycurcumin, ~ 17%), curcumin III (bisdemethoxycurcumin, ~ 3%).

Several lines of evidence suggest that curcumin has anti-amyloid properties in AD. *In vitro* studies revealed that curcumin and its derivatives inhibit the Aβ peptide aggregation from Aβ monomer into Aβ fibrils, indicating the curcumin protective properties against Aβ toxicity. Curcumin may also promote disaggregation of existing amyloid deposits, prevent aggregation of new amyloid deposits, and even reduce the size of remaining deposits.



Scheme 1 – Chemical structure of (a) curcumin I, (b) curcumin II, and (c) curcumin III.

The structural modifications undergone by the synthetic human Aβ isoform peptides, $Aβ_{1-40}$ and $Aβ_{1-42}$, in the absence/presence of curcumin were investigated by atomic force microscopy (AFM) onto a highly oriented pyrolytic graphite (HOPG) surface and differential pulse (DP) voltammetry at a glassy carbon electrode (GCE). Lower aggregation rates were promoted by incubating the Aβ peptides solutions at room temperature and in free chloride media, within the time windows from 0 h to 168 h (1 week). The human $Aβ_{1-40}$ and $Aβ_{1-42}$ peptides mechanisms of fibrilization in the presence of curcumin were also established.

The $Aβ_{1-40}$ and $Aβ_{1-42}$ oxidation at GCE takes place, in a two-step process, at the electroactive amino acid residues, the first step associated with tyrosine Y^{10} oxidation, and the second corresponding to the three histidine, H^6, H^{13} and H^{14}, and one methionine, M^{35}, oxidation. The Aβ morphological changes during fibrilization, in the absence/presence of curcumin, was detected electrochemically, directly without need of redox labeling, via the time-dependent changes in the Y, H, and M oxidation peaks current.

The inhibition of Aβ aggregation and fibrilization by analytical grade curcumin and by curcumin extracts from commercially available food products was demonstrated, which can lead to new insights regarding the molecular mechanisms underlying the AD pathogenesis and AD treatment.

Dissipative control of DNA-based nanodevices and nanostructures through strand-displacement reaction

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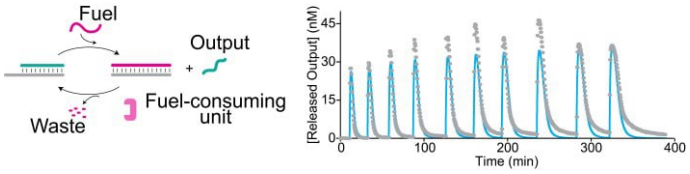
A strong current interest in the field of DNA Nanotechnology is aimed at creating adaptable materials with unprecedented features characteristic of living organism, like temporal activation of their functional properties. Over the past decades, DNA has emerged as a powerful material to engineer non-equilibrium nanomachines and nanostructures with a transient behavior [1]. The toehold-mediated DNA strand displacement is one of the most used reaction in the field of DNA nanotechnology and has been widely employed to control functional DNA nanodevices, like molecular motors, tweezers, nanomachines in a thermodynamically-governed manner. The possibility to achieve a dissipative control on a toehold-strand displacement process will allow to introduce a temporal control on several DNA-based systems, that are generally under thermodynamic conditions.

Here we show two simple general strategies to achieve dissipative control over the toehold-mediated strand displacement reaction, that could enable the operation of several DNA systems in closer analogy to the biological machinery [2]. The approach relies on the rational re-engineering of a classic strand displacement process in such a way that the high-energy invader strand (fuel) is converted into a low-energy waste product through an energy-dissipating chemical reaction mediated by enzymes or chemicals. We also show several possible applications of this strategy: from the transient labelling of DNA nanostructures to their transient reconfiguration [3].



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Phototoxicity of Membrane Permeable Ru(II) Polypyridyl Peptide Conjugates in Cancer and non-Cancer cell lines

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Ruthenium(II) polypyridyl complexes have emerged as promising probes for light-activated therapy, cellular imaging and in-cell sensing. Their photophysical properties, including large Stokes shift, tunable optical and redox behavior and robust photostability make them highly versatile and capable of overcoming many limitations of conventional organic probes. However, a key challenge for metal complex luminophores is their limited membrane permeability and subcellular localisation, which are essential for cellular imaging, intraceullular sensing and also in exploiting their potential as theranostic agents. Bioconjugation to membrane penetrating or signal peptides has proven to be an effective method of enhancing cellular uptake and localisation.

In this contribution a ruthenium complex $[Ru(bqp)(bqpCOOEt)]^{2+}$ (Ru-bqp-ester) was prepared[1] and conjugated to a mitochondrial penetrating sequence (FrFKFrFK) and an octa-arginine sequence (RRRRRRRR) (R8) to develop $[Ru(bqp)(bqpCONH\text{-}ahx\text{-}FrFKFrFK(Ac)\text{-}CONH2]^{5+}$ (Ru-bqp-MPP) and $[Ru(bqp)(bqp)CONH\text{-}ahx\text{-}RRRRRRRR\text{-}CONH2)]^{10+}$ (Ru-bqp-R8). The parent complex was carefully chosen as a probe due to its particularly strong-metal-ligand mixing, which leads to an intense and prolonged and oxygen sensitive triplet emitting state. Both the MPP and R8 sequences were shown to be oxygen sensitive in PBS with de-aerated lifetimes almost twice that of aerated. The peptides have relatively little impact on the photophysics of the conjugates.

Confocal fluorescence imaging of A549 (lung cancer) and CHO (non-cancer) cells demonstrated that both the conjugates enter the cells rapidly within 30 minutes and the mechanism of uptake was explored using temperature dependence and ATP inhibition.

Dark toxicity studies showed CHO cells had poor tolerance to the conjugates at 24-hour incubation, with an IC_{50} of 75µM and 50µM for R8 and MPP respectively, while the A549 cell viability remained high at approx. 90% at 100µM of the parent and 70% at the same concentration of the conjugates. In contrast to the low cytotoxicity of the complexes in A549, phototoxicity studies performed under irradiation with a 470nm LED at a dose of 5J/cm^2 showed the compounds to be highly phototoxic with cell viability of approx. 30% when treated with a concentration as low as 5µM (Figure a).

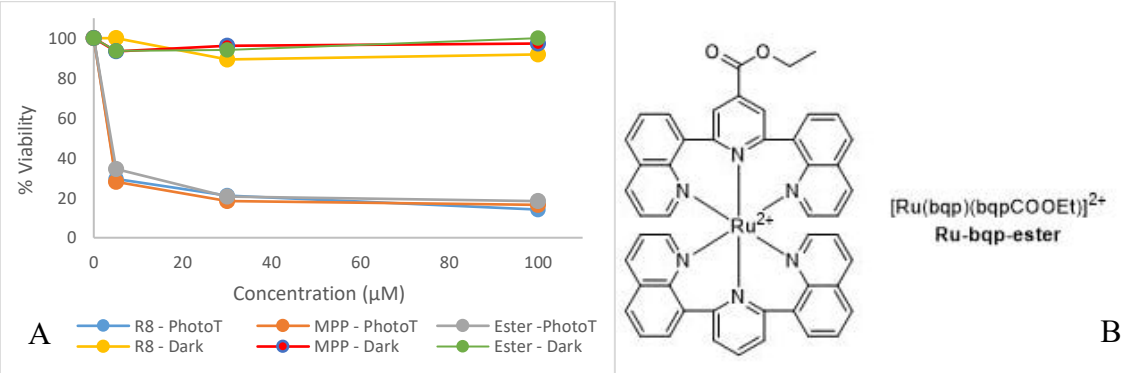

Figure a. Phototoxicity and dark toxicity control of the parent and conjugates at 5, 30 and 100µM in A549 cells
Figure b. Ru-bqp-ester (parent complex)

Acknowledgements: Science Foundation Ireland (SFI) grant number 18/EPSRC-CDT/3585 and 19/FFP/6428 and the Engineering and Physical Sciences Research Council (EPSRC) EP/S023321/1

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Targeting tryptophan in undruggable proteins

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Traditionally, proteins that do not contain a deep hydrophobic pocket have been considered as undruggable targets. Many efforts have been recently made to turn them into druggable molecules even if they lacked obvious association sites. Nevertheless, blocking a flat protein surface to prevent protein-protein interactions is still a challenge.

Molecules showing specific interactions with the amino acid side chains can help to develop useful new drugs as these selective drugs rely on other cooperative association effects. In fact, several receptors selective for single amino acids have already been published [1].

In this work we focus on tryptophan due to its biological relevance exploiting the charge transfer properties of the rich indole fragment to develop new molecular receptors based on electron poor aromatic rings. Combination of this initial binding point with other binding sites could provide the expected cooperative effects [2] which will lead to a reasonable high association constant and selectivity towards a certain protein. Moreover, the design of a Trp-Gly-Trp peptide shows the possibility of targeting this sequence of amino acids in proteins through a molecular receptor with two anchoring points.

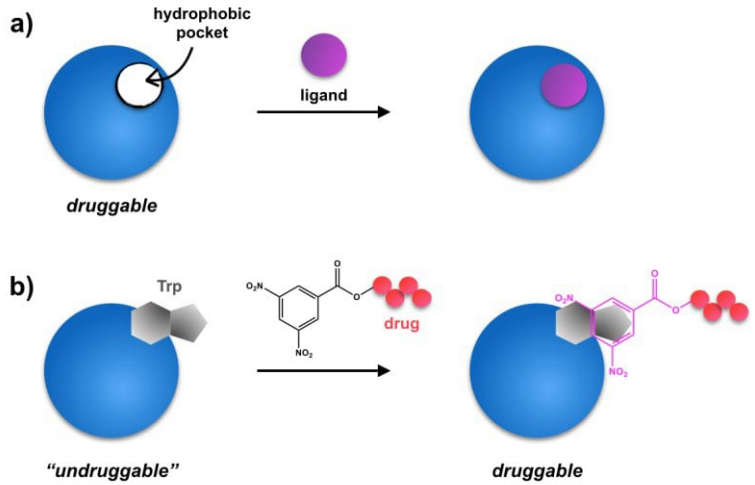

Figure 1. a) Classical approach: "easy" to target. b) New strategy targeting tryptophan amino acids.

This work was supported by MICINN (PID2020-118732RA-I00 and PID2019-108994RB-I00), Junta de Castilla y León (European Regional Development Fund-SA069P17), the University of Salamanca (Own Research Programs-KCEP/463AC01 and 18K155/463AC01) and Fundación Memoria de D. Samuel Solórzano Barruso (FS/8-2019). JJGG is gratefully acknowledged to University of Salamanca and Santander Bank for a postdoctoral fellowship. AH is grateful to the Algerian Government for a predoctoral fellowship for "Formation Doctorale résidentielle à l'etranger". ALFA thanks the Spanish Government for a Beatriz Galindo Fellowship (BG20/00233). NUCLEUS platform at University of Salamanca, especially Anna Lithgow (NMR Service) and César Raposo (MS Service).

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Understanding Oncogenic kRas Cycle through Structure and Multiple Time-scale Dynamics

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The GDP bound state is the inactive form of KRas (Kirsten RAt Sarcoma virus) key element of the EGF signaling pass way. GEF (Guanine nucleotide Exchange Factors) protein catalysis the GDP to GTP exchange and thus kRas becomes active in signal transduction. The KRas GTP hydrolysis is accelerated by GAPs (GTPase Activating Proteins), with GDP in the binding pocket again, 3D-fold changes again and the kRas return to its off-state mode: it stops signal transduction. The central element of this hub is kRas which consists of two structural parts: the effector and the allosteric regions. As a result of our comprehensive NMR-based structure and dynamic analysis, using the Lipari-Szabo model-free and reduced spectral density mapping plus CPMG analysis on the wide type and 3 key oncogenic mutants, G12C, G12D and G12V, we found that both kRas.GTP.Mg2+, kRas.GDP.Mg2+ have a major- and a minor-form. However, the latter on, crucial in understanding the details of GDP to GTP exchange, appears to be an on-pathway intermediate state of the transition. However, to characterize a minor form is indeed a major challenge. We found that the 3D-structure of the Mg2+ -free-state of kRas shows high similarity to the above minor-form. 1) We found that the relative distances of the P-loop, switch-I, and switch-II increase in the Mg2+ -free state, respectively, as they do in the X-ray determined (GDP.Mg2+) free KRas.GEF complex. 2) We observed that in the case of the wt, G12C and G12D mutants, the distance between selected residue pairs of the β2-β3 antiparallel strands increases in the Mg2+ -free-state. β-strands do separate and move away from each other. If we superimpose the wt, G12V and wt(GDP.Mg2+)free kRas.GEF 3D-structures, then will be clear that the bulge described above has functional significance. This bulge will host GEF protein when it forms a complex with kRas to facilitate the release of bound GDP. 3) We found that the strength of the H-bonds formed between HO2'- and HO3' of the furanose ring of GDP and adjacent C=Os (V29 and D30) changes with the Mg2+ ion release. We may ask how relevant all these data are for drug discovery? It would be good to design and then synthesize small molecules that are able to bind the herein described and characterized minor-form of kRas mutants and thus remove them selectively. The selectively elimination of harmful KRas mutants could stop abnormal signaling and thus, have the potential to cure tumor cells.

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Accumulation (and impacts) of rare earths in marine macroalgae: An alternative source of critical raw materials?

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Currently, rare earth elements (REE) are among the most Critical Raw Materials [1], due to their vital importance to the development of strategic technologies (e.g., green energy), and everyday high-tech products (e.g., smartphones), combined with the evident scarcity of sources, where China has a market monopoly (responsible for 98 % of EU's supply) [1]. In addition, the primary source of REE is mining, which is highly polluting and resource-consuming [2].

The recycling of REE from end-of-life products and contaminated waters (known as urban mining) was encouraged as a solution to reduce the dependence on importing these elements and avoid mining impacts. Yet, due to the inefficiency, high cost, and/or hazard of the methods currently available for their extraction from waste(waters), REE recycling rates remain low and far from their potential [3].

Thus, the present study is motivated by the need to find sustainable alternatives for REE recovery. The capability of 6 living marine macroalgae (*Ulva lactuca*, *Ulva intestinalis*, *Osmundea pinnatifida*, *Gracilaria* sp., *Fucus spiralis* and *Fucus vesiculosus*) to capture and concentrate REE (Y, La, Ce, Pr, Nd, Eu, Gd, Tb, Dy) from contaminated water (10 to 500 µg L^{-1}) was assessed and compared [3]. The links between REE uptake and algal metabolism, surface morphology and chemistry were investigated. Green seaweed *U. lactuca* stood out, reaching efficiencies of removal up to 90 % for some REE, and at least 60 % for all elements. Kinetics differed amongst species, although most of the removal occurred in the first 24 h. Lack of mortality demonstrated the high tolerance of macroalgae to these emerging contaminants, although the analysis of biomarkers showed the activation of defence mechanisms. The high bioconcentration factors (c.a. 2500) support that the REE enriched algal biomass (up to 1295 µg g^{-1}) constitutes an effective and environmentally friendly alternative source of REE to conventional extraction from ores.

Bruno Henriques acknowledges FCT for the research contract (CEECIND/03511/2018) under the CEEC Individual 2018, while João Pinto and Jessica Jacinto acknowledge their PhD grant (2020.05323.BD and UI/BD/151290/2021, respectively). Thanks are also due to the financial support to REQUIMTE (UIDB/50006/2020) to FCT/MEC through national funds, and the co-funding by the FEDER, within the PT2020 Partnership Agreement and Compete 2020. This work was supported by the project Nº46998_N9ve-REE, co-funded by Portugal 2020 program (PT2020), PO Centro and European Regional Development Fund.

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Computational Design, Synthesis and Photochemistry of Cy7-PPG, an Efficient NIR-activated Photolabile Protecting Group for Therapeutic Applications

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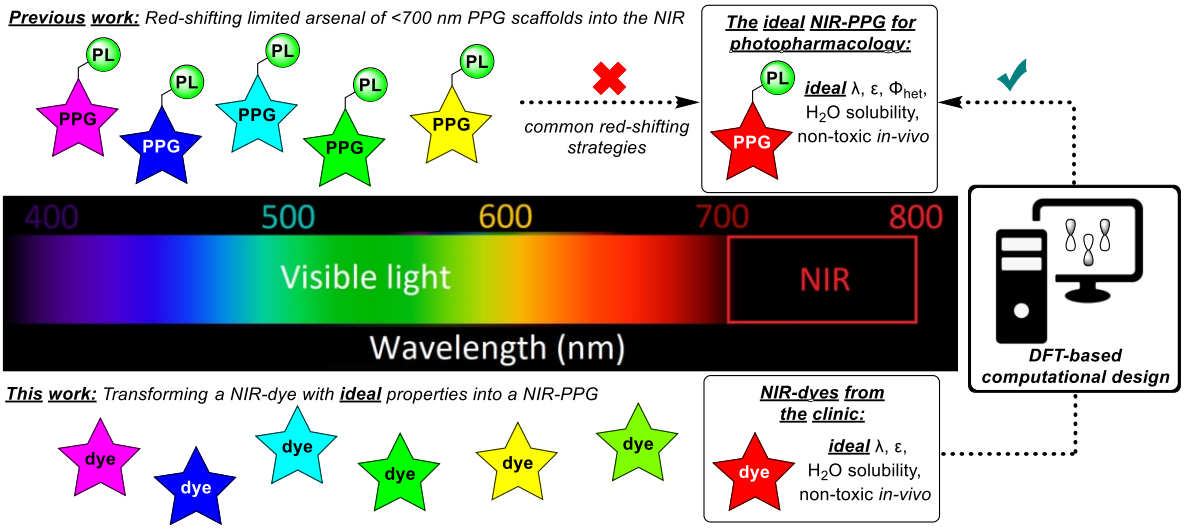

Photolabile Protecting Groups (PPGs) are molecular tools used, for example, in photopharmacology for the activation of drugs with light, enabling spatiotemporal control over their potency. Yet, red-shifting of PPG activation wavelengths into the NIR range, which penetrates the deepest in tissue, has often yielded inefficient or insoluble molecules, hindering the use of PPGs in the clinic. To solve this problem, we report herein a novel concept in PPG design, by transforming clinically-applied NIR-dyes with suitable molecular orbital configurations into new NIR-PPGs using computational approaches. Using this method, we demonstrate how Cy7, a class of NIR dyes possessing ideal properties (NIR-absorption, high molecular absorptivity, excellent aqueous solubility) can be successfully converted into Cy7-PPG. We report a facile synthesis towards Cy7-PPG from accessible precursors and confirm its excellent properties as the most redshifted oxygen-independent NIR-PPG to date (λ_{max}=746 nm).

"Computational Design, Synthesis and Photochemistry of Cy7-PPG, an Efficient NIR-activated Photolabile Protecting Group for Therapeutic Applications" G. Alachouzos,* A. M. Schulte, A. Mondal, W. Szymanski,* B. L. Feringa* *Angew. Chem. Int. Ed.* **2022**, *e202201308 (*highlighted as a *Very important Paper)* (https://doi.org/10.1002/anie.202201308)

Protein-Protein communication mediated by an antibody-responsive DNA nanodevice

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Dynamic interactions between DNA, RNA and proteins play a major role in the functioning of living systems.[1] These communication processes rely on highly complex networks with specific regulative functions.[2] A "two-way" in-vitro DNA-protein and protein-protein communication can be achieved by exploiting the chemical versatility of synthetic DNA-based systems as versatile translator devices.[3] Such interface of two otherwise non-communicating proteins would represent an important step towards the applicability of these systems in more complex clinical settings. Motivated by the above considerations and by the potential power of nucleic acid-based technology, we have developed a class of antibody-responsive DNA-based synthetic devices that can mediate the regulation of a range of target proteins via two related mechanism (Figure 1). In the first, antibody binding to an antigen-conjugated DNA device releases a DNA strand (i.e. translator, green in Figure 1, Mechanism A) that acts as an inhibitor for a downstream target protein. In the second, antibody-induced release of the translator strand disrupts the device's inhibition of a downstream protein, activating it (Figure 1, Mechanism B).[4] By engineering two different antibody-responsive DNA-based devices, we have demonstrated to control and regulate the proteolytic activity of thrombin and the exonuclease activity of Taq DNA Polymerase, respectively. Our strategy is versatile and, in principle, can be easily adapted to modulate artificial protein-DNA and protein-protein communication mediated by DNA-based nanodevices. Recreate communication pathways where DNA, RNA and proteins interact with each other with programmed reaction patterns and create new biotechnology tools can find applications in sensing, drug-delivery, cell imaging and control of logic gates.

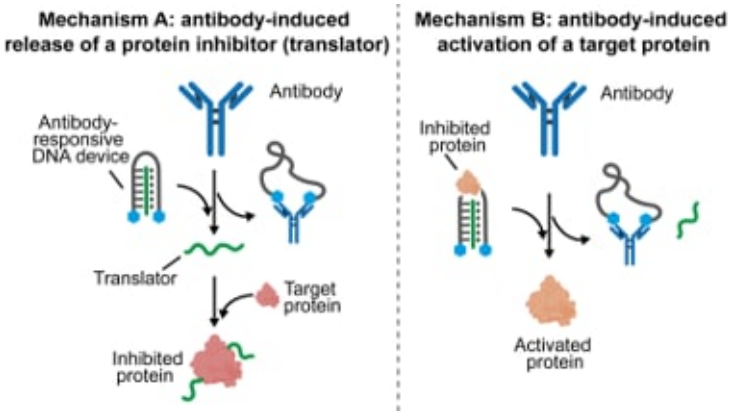

Figure 1. Antibody-protein communication mediated by antibody-responsive DNA devices. Two mechanisms by which a synthetic, antigen-conjugated DNA strand (antibody-responsive device, grey) can mediate communication between an antibody and a target protein. In the first (Mechanism A), the antibody-responsive device releases a translator strand that inhibits a downstream target protein. In the second (Mechanism B), antibody-binding-induced loss of the translator abolishes the inhibitory properties of the device, activating the downstream target protein.

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Regulating the dynamic folding of a DNA-hairpin at the expense of a small, molecular fuel

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Chemical self-assembly holds the key to efficiently build complex structures from relatively simple building blocks in a one-pot process.

When nucleic acids are used as building blocks, almost any arbitrary shape can be realized by choosing the appropriate oligonucleotide sequences. This extreme flexibility of design has brought us closer to create sophisticate structures similar to the ones we are used to finding in nature, in particular in living matter. Unlike life, however, these complex nanostructures are limited in their ability to rearrange and perform work on a system. DNA nanostructures actuated by external stimuli (i.e. molecular switches) have been realized, but examples of truly autonomous and dissipative systems are still rare[1]. In other words, we can potentially build a DNA based molecular machine, but we miss a chemical engine to continuously power it.

To fill this gap, we sought to translate the strategy used for dissipative self-assembly of small molecules into DNA nanotechnology. Over the last years, the lab of Boekhoven devised a chemical reaction cycle driven by a carbodiimide fuel[2]. A dicarboxylic acid precursor is converted to the unstable anhydride (activated state) at expense of the fuel. The activated building blocks lack two negative charges and can interact with each other; upon hydrolysis of the anhydride, the precursor is regenerated and so are the charges, thus leading to repulsion. In this work, we apply such chargeabolishing strategy to control the hybridization of a model DNA hairpin in response to a chemical fuel (EDC). We used click-chemistry to install dicarboxylic acid moieties on the commercially available 5-ethynyl-2'-deoxyuridine and we studied the impact of the modification on the thermal stability of duplex DNA in a hairpin forming sequence. The presence of additional negative charges significantly lowers the stability of the duplex as evidenced by the difference in melting temperature. The modified oligonucleotide is responsive to our chemical fuel and undergo hybridization when the negative charges are abolished via formation of the anhydride. The effect is reversible and when the fuel is consumed the system goes back to the original state.

We expect that on a single molecule level, each DNA hairpin undergoes several cycles of folding and unfolding as long as the fuel is present. In this sense, the system is continuously driven out of equilibrium by the fuel and behaves as true molecular machine.

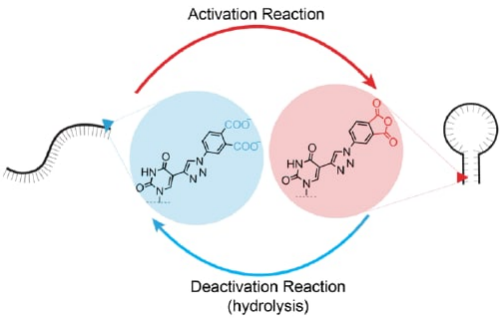

Figure 1. Chemically Fueled DNA-Hairpin system.

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Synthesis of a theranostic platform based on fibrous silica nanoparticles for the enhanced treatment of triple-negative breast cancer promoted by a combination of chemotherapeutic agents

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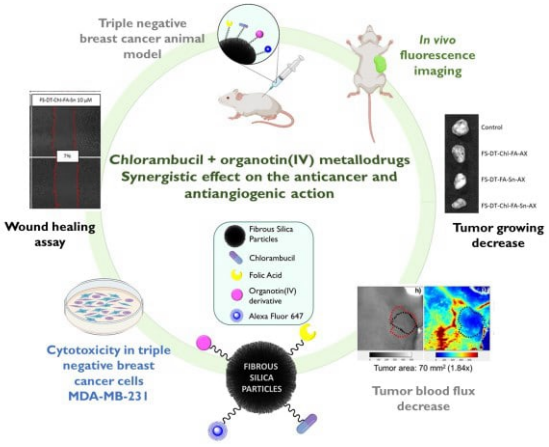
One of the most common causes of death amongst women is breast cancer, specifically, triple-negative breast cancer (TNBC). It is associated with around 20% of newly diagnosed breast cancer cases. It has a very bad prognosis and poor survival rate due to its aggressive nature and very high potential to promote metastasis.

With the intention of developing effective treatments for TNBC, a series of theranostic silica materials based on fibrous silica particles as nanocarriers of two different cytotoxic agents, namely, chlorambucil and an organotin metallodrug have been prepared. These platforms have been additionally decorated with a targeting molecule (folic acid, to selectively target triple negative breast cancer) and a molecular imaging agent (Alexa Fluor 647, to enable their tracking both *in vitro* and *in vivo*). The *in vitro* activity of the multifunctional silica systems showed synergy between the two chemotherapeutic agents in the form of an enhanced cytotoxicity against MDA-MB-231 cells (triple negative breast cancer) as well as a higher cell migration inhibition.

In vivo behaviour was monitored by optical imaging techniques revealing selective tumour accumulation (targeting ability), a marked inhibition of tumour growth paired to a marked antiangiogenic ability confirming the enhanced theranostic activity. Systemic nanotoxicity, by analyzing specific biochemical markers, showed a positive effect in form of reduced cytotoxicity when both chemotherapeutics were administered in combination.

In conclusion, our results confirm the promising potential of these novel silica-based nanoplatforms as advanced drug-delivery systems for the synergistic theranosis of triple negative breast cancer.



Multifunctional platform based on fibrous silica nanoparticles for TNBC cancer theranosis

Interactions of phenolic compounds within oral cavity: deepening the structure-activity to understand astringency mouthfeels

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Phenolic compounds (PC) are linked to astringency sensation [1,2]. Astringency studies typically use simple models, with pure PC and/or proteins, far from what is likely to occur in the oral cavity [3]. Different oral models have been developed in our last works [4,5], comprising different oral epithelia (buccal mucosa (TR146) and tongue (HSC-3)) and other main oral constituents (human saliva and mucosal pellicle). These models, have been used to study the interaction with more or less complex PC extracts as well as with food matrices, such as coffee. The studied extracts were rich in different families of PC, namely flavanols (a green tea extract), anthocyanins (a red wine extract), gallotannins (a tannic acid extract) and flavonols (an onion extract). It was observed a different interaction for the different families of PC and also that the several oral constituents have different implications. For example, for the interaction with flavanols, the PC seem to have a similar binding to both TR146 and HSC-3 cell lines while that is not the case for the interaction with flavonols. When the oral constituents occur altogether, flavanols showed a higher interaction, driven by the salivary proteins. Conversely, anthocyanins showed a lower interaction when the oral constituents occur altogether, having a higher interaction only with oral cells. Moreover, some of these studies aligned the *in vitro* models along with sensory studies. Overall, the results seem to point out a structure-activity relationship, in which the different families of PC and different oral constituents can have a different function in astringency perception as well as being involved at different phases of astringency perception. These differences can be related to the perception of different astringency sub-qualities.

Acknowledgements: The authors thank the Science and Technology Foundation (FCT) for financial support the researcher contracts CEECIND/01598/2018, CEECIND/01265/2018 and the scholarships SFRH/BD/148549/2019, UIDB/50006/2020 and UIDBP/50006/2020. This research is supported by AgriFood XXI I&D&I project (NORTE-01-0145-FEDER-000041 cofinanced by European Regional Development Fund (ERDF), through the NORTE 2020 (Programa Operacional Regional do Norte 2014/2020). This research is supported by cLabel+ Project (POCI-01-0247-FEDER-046080) cofinanced by European Regional Development Fund (ERDF), through the COMPETE 2020 - Incentive System to Research and Technological Development, within the Portugal 2020 Competitiveness and Internationalization Operational Program.

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Bridging the gap between biochar's physicochemical characteristics and plant growth

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Industrialized farming relies heavily on the use of unsustainable synthetic fertilizers to attain their required plant production goals, this usage has several adverse side-effects e.g. eutrophication of water bodies or the increase of atmospheric nitrogen levels [1]. The last decade, the attention of the scientific community has shifted to biobased fertilizers, such as biochars, which can be produced via simple and low-cost methods, while being both energy-negative and carbon neutral. In this regard, Vercruysse et al. [2] synthesized biochars based on extracted common ivy trimmings. Physicochemical characterization of the biochars showed that they had great potential as effective fertilizers, however this was not supported by plant-growth experiments yet.

The aim of this study is to assess whether common ivy-based biochars would have beneficial effects on seedling development. To assess this, lab-scale plant growth experiments on *Arabidopsis thaliana* seedlings were performed and correlations between important biochar properties and plant development were established. Two different biochar pyrolysis temperatures were tested, 400 and 700 °C and the effect of two different valuable compounds extractions, ethanol extraction and steam distillation, on the biochar's effectiveness was investigated. This was done via a lab-scale 96-well plant growth experiment, in which 0.5 and 1% of biochar were added to an adapted ¼ Murashee and Skoog plant growth medium. After 7 and 10 days of plant growth seedlings were harvested. After 7 days of growth, phenotypical analysis was performed and the plant's cell cycle regulation was investigated [3]. Next, plants cultivated for 10 days were also phenotypically analyzed. Furthermore, changes in the plant growth medium due to biochar addition, were evaluated through leaching experiments.

K-leaching from the biochars caused the growth medium's pH and conductivity to increase significantly in the first 7 days of plant growth. This leaching caused the plants to express initial growth stress responses (Pearson = 0.930), proven by changes in their cell cycle regulation. The second part of the investigated cultivation period, 7-10 days, showed total recovery of the seedlings subjected to biochars produced at 400 °C. Moreover, significant increases in plant fresh weight were established at 1% biochar application rate. Besides that, biochars produced at 700 °C did not significantly affect plant development compared to the control group. At high (1%) biochar loading, low-temperature biochars improved plant development significantly better than high-temperature biochars. This was due to the phosphate availability in high temperature biochars decreasing significantly, which would decrease several plant stress remediation mechanisms.

In conclusion, low-temperature (400 °C) biochars significantly outperform high-temperature (700 °C) in terms of plant development. Furthermore, valuable compound extractions are perfectly suitable as a pretreatment process for common ivy trimmings as they do not diminish the biochar's performance as soil amendment.

This work was financially supported by Research Foundation Flanders (FWO SB – 1S92020N)

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Innovation in the Development of Polyphenol C-Glucosides with Disease-Modifying Effects against Alzheimer's Disease

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Alzheimer's Disease (AD) and other dementias are ranked by the World Health Organization as the 7th leading cause of death worldwide [1]. Around 55.2 million people are currently living with dementia and this number is expected to rise to 78 million people by 2030 [1,2]. Despite this disconcerting estimate, only one disease-modifying drug — the monoclonal antibody aducanumab — is currently approved to treat AD.

In the search for new lead molecules suitable for further development, our group has been focusing on the potential of carbohydrate-based molecules against several relevant molecular targets for AD. Based on the well-established role of the binding between the cellular prion protein (PrP^C) and Aβ oligomers (Aβo) for the activation of Fyn kinase and subsequent tau hyperphosphorylation in the brain [3], we herein report the rational design, synthesis, and structural optimization leading up to the discovery of *N*-methylpiperazinyl flavones and their *C*-glucosyl derivatives as protein-protein interaction (PPI) inhibitors against PrP^C-Aβo [4-6]. Furthermore, the identification of small *C*-glucosyl polyphenols as the first sugar-containing inhibitors of Aβo-induced Fyn activation and tau hyperphosphorylation will be explored, including the physicochemical properties that make them good candidates for pharmaceutical development [7].

Importantly, because many planar lipophilic polyphenols are Pan-Assay Interference CompoundS (PAINS), we were also interested in clarifying whether *C*-glucosyl polyphenols lead to unspecific alterations of cell membrane properties. Our results show, for the first time, that well-known membrane disruptors such as resveratrol and genistein lose their ability to reduce membrane dipole potential when linked to a glucosyl moiety through a C-C bond [8], suggesting that our *C*-glucosides should not raise any concerns regarding membrane-related PAINS-type behavior.

The work presented in this communication highlights the promising disease-modifying effects displayed by *C*-glucosyl polyphenols in the context of AD, and explores the role of the sugar moiety not only in tuning bioactivity in a favorable way but also in conferring protection against unwanted aglycone-induced membrane perturbing effects.

Centro de Química Estrutural is a Research Unit funded by Fundação para a Ciência e Tecnologia through projects UIDB/00100/2020 and UIDP/00100/2020. Institute of Molecular Sciences is an Associate Laboratory funded by FCT through project LA/P/0056/2020. A.M. Matos thanks CQE for her PhD Scientific Researcher contract.

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A Nonenzymatic Analog of Pyrimidine Nucleobase Biosynthesis

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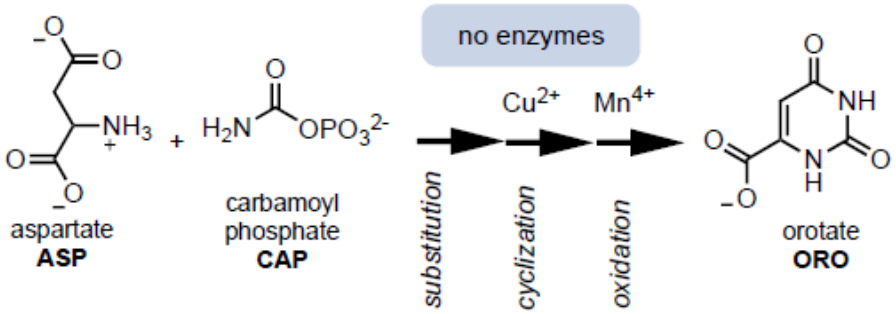
ISIS - Institut de Science et d'Ingénierie Supramoléculaires, CNRS UMR 7008



Abstract: Metabolic theories for the origin of life posit that inorganic catalysts enabled self-organized chemical precursors to the pathways of metabolism, including those that make genetic molecules. Recently, experiments showing nonenzymatic versions of a number of core metabolic pathways have started to support this idea. However, experimental demonstrations of nonenzymatic reaction sequences along the de novo ribonucleotide biosynthesis pathways are limited. Here we show that all three reactions of pyrimidine nucleobase biosynthesis that convert aspartate to orotate proceed at 60 ºC without photochemistry under aqueous conditions in the presence of metals such as Cu2+ and Mn4+. Combining reactions into one-pot variants is also possible. Life may not have invented pyrimidine nucleobase biosynthesis from scratch, but simply refined existing nonenzymatic reaction channels. This work is a first step towards uniting metabolic theories of life's origin with those centered around genetic molecules.

Immobilisation of redox-reversible artificial metalloenzymes

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Substantial advances have recently been made to incorporate synthetic inorganic catalysts in protein scaffolds via several anchoring strategies to produce artificial metalloenzymes (ArMs). These new-to-nature enzymes combine the broadest applicability of metal-based catalysts with the high selectivity of proteins, e.g. enantioselectivity [1]. Mimicking the way bacteria acquire essential iron(III), we developed an iron-siderophore anchor that connects a synthetic catalyst to a periplasmic binding protein (PBP) scaffold, therefore giving rise to an ArM – an artificial transfer hydrogenase (ATHase). Notwithstanding, on chemical reduction to iron(II), the anchor unit disconnects and triggers the disassembly of the artificial enzyme [2]. This feature might be key for the industrial application of ArMs, and has potential to be exploited in the sensing and flow chemistry fields. On the other hand, the application of biocatalysts is known to be costly. To overcome that, the immobilisation of enzymes in solid supports has been thoroughly explored in the last few decades, and this could be the bridge between ArMs and industry. Noteworthy, little work has been done on the immobilisation of ArMs so far.

This study targeted the immobilisation of the redox-switchable ArM on solid matrices, aiming to recycle the protein scaffold and also reversibly bind a chosen catalyst. Immobilised metal affinity chromatography (IMAC) was chosen as a strategy to attach the ATHase on a surface (Figure 1). Sepharose beads coupled with nickel charged nitrilotriacetic acid (Ni-NTA) successfully immobilised the poly-histidine-tagged ArMs. Following, the immobilised ArM-IMAC resin was packed in a column and connected to a flow reactor in which the transfer hydrogenation of a prochiral imine was carried out. 55% yield to *R*/*S* enantiomers was obtained in 144 h, with 26% enantiomeric excess to *R* enantiomers. Despite reduced turnover number compared to the homogeneous ATHase – which is not uncommon even for immobilised natural enzymes due to mass transfer limitations –, this heterogeneous system has nearly preserved its enantiomeric selectivity. Further optimization and recyclability studies are under way. Furthermore, different protein scaffolds are also being tested, as well as alternative catalytic routes.

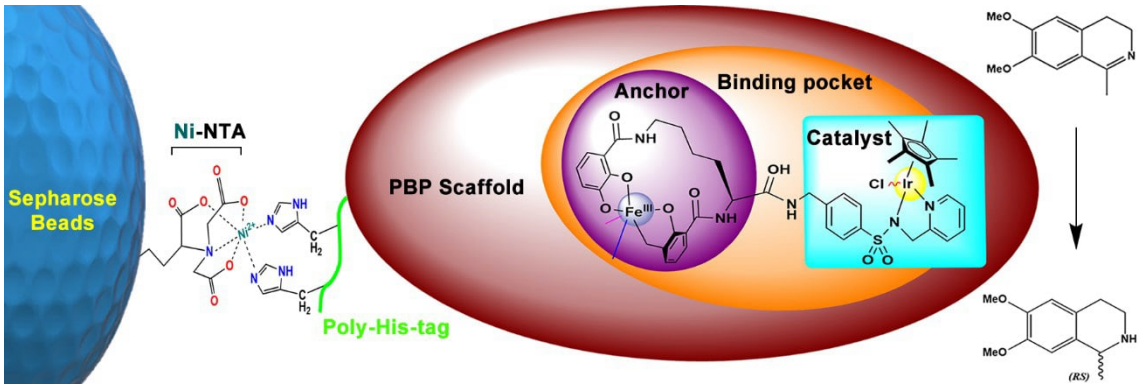

Figure 1. ATHase immobilised on Ni-NTA-sepharose beads applied to prochiral imine reduction.

The authors thank the Engineering and Physical Sciences Research Council (EPSRC) for financial support [EP/T007338/1].

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Bactericidal activity of new NHC carbenes and their Cu(I) and Ag(I) complexes against pathogenic bacteria

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The emergence of pathogenic bacterial strains that are resistant to most available antibiotics is a concern for public health [1]. This is the case of the major human pathogen *Staphylococcus aureus*, namely the methicillin resistant *S. aureus* strains (MRSA) responsible for high rates of morbidity and mortality worldwide in the hospital settings but also in the community. MRSA are, virtually, resistant to all the antimicrobial classes clinically available. Thus, there is a need to develop new antimicrobial compounds, for which metallodrugs have demonstrated promising results in in vitro studies. Silver and copper are known to possess antimicrobial proprieties since antiquity and are excellent candidates as potential germicides due to high abundance, relatively low price when compared to other metals, and low toxicity. Complexes of Ag and Cu using N-heterocyclic (NHC) carbenes, as a mean to stabilize the metal, potentiate in some cases an increase in their bactericidal activity.

Herein we present a new family of Ag(I) and Cu(I) complexes bearing NHC carbenes with an acenaphthene backbone (Figure 1). The activity of both the ligands and complexes will be studied against the Gram-positive bacteria *S. aureus*, namely in four different strains representing different ecological origins, phenotype of resistance to beta-lactam antibiotics and different genetic organizations of the copper resistance determinants. Additionally, this activity was also determined against the Gram-negative pathogen *E. coli* and *Legionella pneumophila* to address the effect of the compounds in different bacterial membrane compositions.

The antimicrobial activity of complexes and ligands was screened by disk diffusion. Those with higher activity were selected and, their minimum inhibitory concentration was estimated. The impact of the ligands and complexes were additionally evaluated regarding its capacity to prevent the formation of biofilms and in its disintegration.

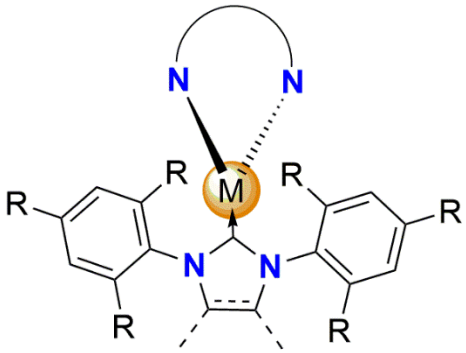

Figure 1 - General structure of the heteroleptic complexes studied.

This work was supported by Fundação para a Ciência e Tecnologia by national funds: PTDC/BIA-BQM/29442/2017 (SRP), and UIDP/04378/2020 and UIDB/04378/2020 (Applied Molecular Biosciences Unit – UCIBIO), and LA/P/0140/2020 to i4HB, UIDB/50006/2020 and UIDP/50006/2020 to LAQV.

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Obtaining a Molecular Movie via in Operando Raman spectroscopy: Catecholate Formation after Phenolate Attack at a Tyrosinase Model

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Oxygen transfer and transport are key processes in bioinorganic chemistry. In this context the structural and electronic properties of the μ-η²-η²-peroxo dicopper(II) dimers and the bis-μ-oxo-dicopper(III) dimers are intensively investigated experimentally as well as computationally for tyrosinase models[1].

Tyrosinase hydroxylates phenols in their *ortho*-position. The guanidine-stabilised Cu_2O_2 represent structural and functional models of the active site of tyrosinase [2-5]. This study deals with the copper coordination chemistry of guanidines, their ability to activate dioxygen and the subsequent oxygen transfer to phenolate substrates (Fig. 1). We investigate the hydroxylation of substrates starting from a bis-μ-oxo-dicopper(III) species followed by the reaction with ortho-phenolate via *in situ* Raman spectroscopy and density functional theory calculations. Within this study we answer the important questions: How does the phenolate attack proceed in detail? The electrophilic attack has been supported experimentally but the theoretical understanding of the oxygen attack is not yet complete. How does the aromatic proton of the attacked ortho-position reach the other oxygen atom? Here radical as well as concerted mechanisms are discussed and our DFT study shall resolve this question for a real-life system. Which bridging mode is correct for the catecholate intermediate? In literarture two possible different bridging modes have been proposed.

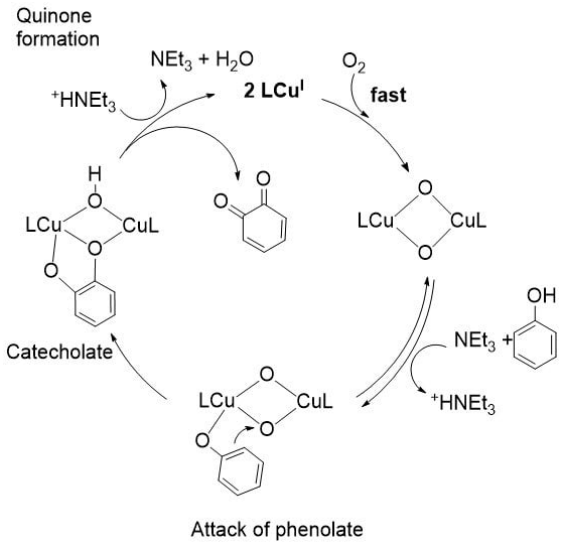

Figure 1: Reaction cycle of the hydroxylation of ortho-phenols

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Controlled nanofabrication of 2D material supported catalysts using electron microscope

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Due to their unique structural and electronic properties, 2D materials are of considerable interest in catalysis. As a typical member of the 2D material family, graphene can be modified owing to perturbations into the perfect hexagonal graphene structure for promotion of its catalytic properties [1]. Nevertheless, graphene could also be used as a 2D support for metal nanoparticles [2, 3]. These supported catalysts demonstrate a significant increase in catalytic activity and selectivity. The increased activity and selectivity are usually lead to electronic properties of the 2D support and the specific interaction between nanoparticles and the support [2]. However, these interactions are difficult to quantify and measure.

For single heterogeneous nanocatalysts, the high selectivity could be elucidated similarly to the well-known enzymes catalytic allostery, which is a change in activity and conformation of the enzyme caused by binding of a molecule at the active site [4]. The active sites on heterogeneous catalysts communicate with each other in a way phenomenologically similar to the catalytic allostery. This communication is ensured by charged messenger species at different ranges. On this basis, the identification of communication (interaction) between active sites on the catalyst with known morphology demonstrate an excellent tool, which can be apply for supported catalysts.

The specific support-nanoparticles interaction and the evaluation of an exclusive effect of 2D support could be investigated by utilization of a model catalytic system with the known size and spatial distribution of nanoparticles. For this purpose, several preparation methods exist: impregnation, deposition precipitation, atomic layer deposition, and colloidal synthesis. Usually, these methods provide a homogeneous distribution of metals on the support, but controlling the particle density, particle size and size distribution of the deposited nanoparticles remains a challenge. Contrary to this, electron beam lithography (EBL) is a highly versatile and powerful technique for controlled fabrication of the nanometer-size characteristic features [5]. These features are extremely useful in correlative spectro-microscopy, i.e., measuring various properties of a catalyst from the same spot on the material. In this study, we use direct EBL incorporated in a dual-beam focused ion beam-scanning electron microscope equipped with a gas injection system, which allow us to create platinum nanoparticles on a 2D support immediately from a platinum organometallic precursor. This approach will be demonstrated on the 2D material family: graphene, black phosphorus and transition-metal dichalcogenide. Thus, the nanofabricated 2D material supported catalyst would enable a rigorous study of the specific interactions between nanoparticles and the support.

Thanks to University of Chemistry and Technology in Prague for the specific research grants No A2_FCHT_2022_112 and A1_FCHT_2022_010.

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Preparation Multifunctional 3D-Gold and Pt nanostructures using the Green and Supramolecular Chemistry principles

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Green chemistry, or sustainable chemistry, focuses on designing products and processes that minimise or eliminate the use and generation of final hazardous substances. Iron is the most abundant element by mass on Earth. Despite being an inexpensive material used in a wide range of applications, its role as a reducing agent for the synthesis of plasmonic nanoparticles has not been explored in detail by now. We have studied the use of iron(II) sulphate as a green reductant in water for the synthesis of gold and platinum nanoparticles (AuNPs-PtNPs) in the absence or presence of different molecules [1-2]. On the other hand, a seed-mediated approach for synthesising branched 3D AuNPs assisted by PAH was explored. The strategy relies on preventing nucleation events while promoting the growth process through tiny Au seeds. The careful control of the experimental conditions allows obtaining branched AuNPs with highly tunable optical properties (ca. 560–1260 nm) excellent for post-functionalised biomedical and optical nanostructures [3].

Supramolecular chemistry is a general definition of any chemical system composed of a discrete number of molecules to form a more complex system using spatial organisation based on weak intermolecular forces, electrostatic charge, hydrogen bonding to strong covalent or metal-metal bonding. Using this approach, Luminescent hollow micro-and nanocrystals have been successfully obtained, taking advantage of the self-assembly behaviour and the aggregation-induced emission enhancement properties of several bispyrazolate Pt(II) metallomesogens decorated with terminal alkyl chains and BF_2 emissive complexes. Oil-in-water droplets have been used to confine all emissive compounds and drive them to be self-assembled via intermolecular Pt-Pt or π-π interactions into spherical micro and nanoaggregates able to be explored in nanomedicine and optical images. [4-6].

The authors acknowledge the financial support by the Associate Laboratory Research Unit for Green Chemistry-Clean Processes and Technologies-LAQV, which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER- 007265), as well as the PROTEOMASS Scientific Society General Funds (Portugal) for funding support, and to the FCT-MEC (Portugal) research grants, SiSi4Bacter (PTDC/QUI-COL/1517/2020) and EXPL/QUI-COL/0263/2021.

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Binary supercrystal assembly controlled by ligand effects

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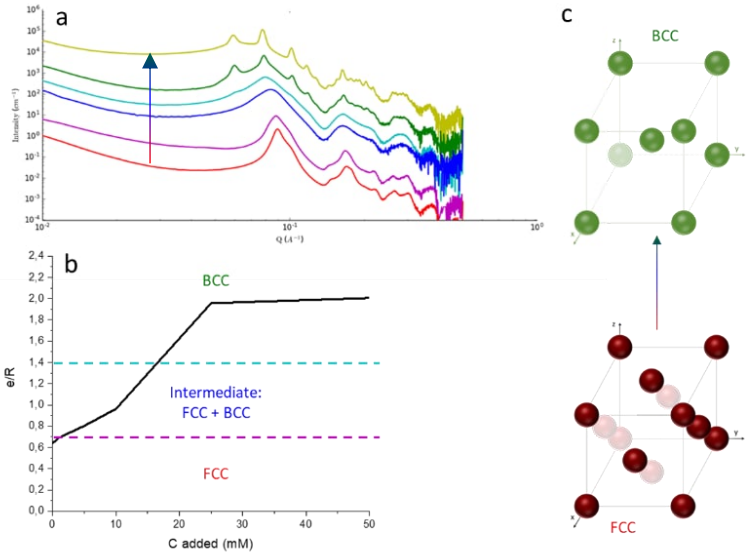
Organization of nano-objects of different nature can lead to superstructures [1] that combine their functional properties [2] (magnetic, semiconducting, luminescent, catalytic, etc.). A broad range of structuration may be envisioned, depending on the processes of self-assembly of the building blocks: periodic superlattices, quasiperiodic arrangements or aperiodic assemblies. In this work, we focused on the formation of periodic assemblies of spherical nanoparticles, and we studied some ligand effects on the formation of superlattices. Work on single component systems, as well as on binary assemblies, has been investigated.

Among the parameters that affect nanoparticle self-assembly, the stabilizing coordination sphere of ligands plays a main role. Several works have been reported revealing the importance of the size ratio between the ligand length and the radius of the nanocrystal core [3]. In a first part, we will explain how the presence of an excess of ligand in the system can also have a strong influence of the assembly. Working with small gold nanoparticles in presence of oleylamine (OAm), we have observed that an increasing excess of ligand leads to a structural change of the superlattice structure from FCC to BCC (Fig. 1). Interestingly, a novel primitive hexagonal structure has been observed for some nanoparticle sizes. In a second part, ligand size effects will be detailed in the frame of binary assembly of gold and ruthenium nanoparticles.



Evolution of gold nanoparticle superlattice structure from FCC to BCC as a function of an excess of oleylamine ligand: a. SAXS diagram, b. phase diagram, c. schematics of the structures.

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Communicating supraparticles: smart additives to foster materials' intelligence

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Small-scaled, flexibly applicable smart additives equip passive matter with an identity (ID) or environmental consciousness. Thus, information about the materials' origin, fate, and encountered history is obtained anywhere upon signal readout, ultimately realizing communication between materials and machines or humans. While an ID functionality opens up applications, such as tracking, tracing, and anti-counterfeiting, with environmental consciousness, (harmful) triggers, like temperature events or exposure to gases, e.g. H_2, are detected across the materials' lifetime. Thereby, smart additives contribute to the realization of innovative, sustainable concepts, like the Internet of Things, Circular Economy, or a safe green hydrogen economy. [1]

A versatile, modular approach to fabricating particle-based smart additives with novel functionalities is the concept of supraparticles. In toolbox-like manufacturing processes, various nanoparticle building blocks with desired properties are assembled into hierarchical supraparticle architectures. Through the cooperative interplay of nanoparticles, namely due to coupling, colocalization, and emergence phenomena, novel functionalities are achieved that are beyond those of the individual constituents. [2]

Here, we report on micrometer-sized communicating supraparticles as smart additives that equip arbitrary objects with a unique identity (Figure 1a), [3-4] or environmental consciousness for temperature events [5] and exposure to H_2 gas, respectively. [6] Ultimately, we demonstrate communicating supraparticles that even unite both functionalities, a unique identity, and a temperature recorder (Figure 1b). [7]

Key to achieving these novel functionalities is the precise selection of nanoparticle and molecular building blocks with suitable optical or magnetic signal characteristics and their defined assembly into supraparticle structures with a specific (multi-)hierarchical architecture. The resulting combined spectral optical or magnetic signature is utilized for communicating the information of the smart additive. While optical signals grant low-tech visual inspection, magnetic signals, which are independent of the materials' optical absorption properties, allow obtaining information from the inside of even dark objects, i.e., the bulk. In summary, the presented communicating supraparticles and their conceptual design give rise to an entirely new family of smart additives to foster materials' intelligence.

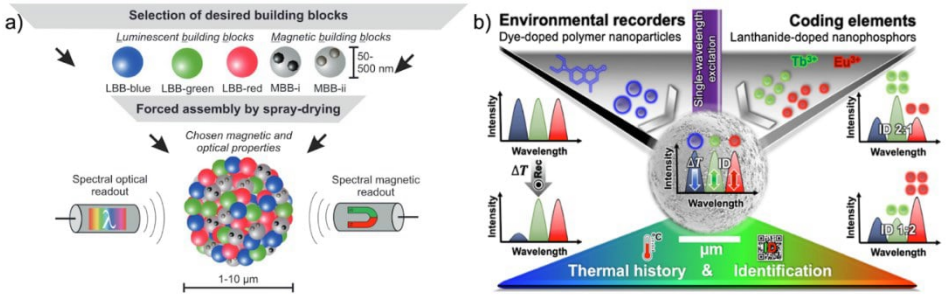

Figure 1. Communicating supraparticles can equip materials with a unique identity (a, [4]) or simultaneously with an identity and a temperature recorder functionality (b, [7]).

This work was financially supported by the BMBF NanoMatFutur Grant 03XP0149 and the PhD scholarship for J.R. from the German Federal Environmental Foundation (DBU).

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Supramolecular porphyrin-based flags in a thermal gradients wind

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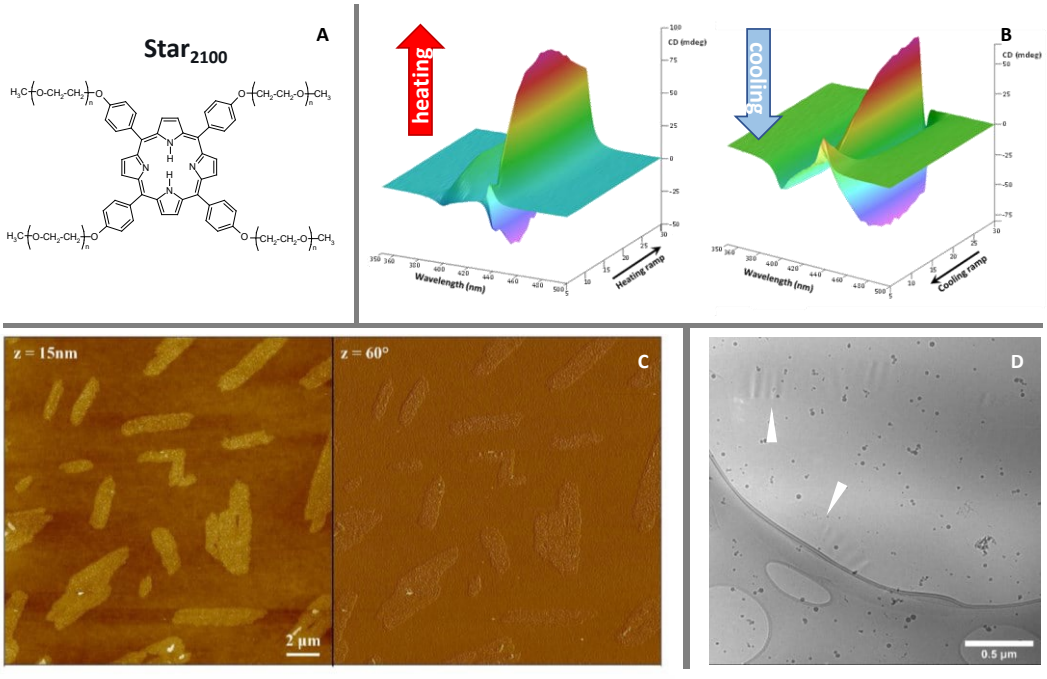
The spontaneous symmetry breaking (SSB) is a controversial natural phenomenon through which Nature chooses one handedness over the opposite, apparently without any reason. It occurs on every size-scale and concerns every scientific field, such as astronomy, nuclear physics, biochemistry and biology. Also in laboratory experiments involving achiral molecules subjected to self-organization or supramolecular aggregation, this phenomenon was observed.
In chemistry, SSB phenomenon is usually investigated by studying charged achiral porphyrin derivatives which aggregate in solution only after chemical or physical triggering; such supramolecular aggregates show enantiomeric excess if subjected to intense external stimuli (e.g. high rpm stirring) and/or in presence of molecular chiral seeds.
In this context, we used a charge free achiral star-polymer derivative to study the Symmetry Breaking event, namely the 5,10,15,20-tetrakis[p-(ω-methoxy-polyethyleneoxy)phenyl]porphyrin (Star2100, Fig. A) [1]. In contrast with the charged ones, the Star2100 aggregates in water spontaneously, and its supramolecular aggregates show high sensitivity to weak asymmetric external stimuli.
In this communication, the interaction of Star2100 supramolecular aggregates with weak asymmetric thermal gradients field in a stagnant water solution is investigated from different points of view.
In particular, the symmetry breaking phenomenon has been thermally-triggered on a stagnant solution of Star2100 through very weak asymmetric thermal gradients [2]. The optical activity of such aggregates was reversed in sign by acting on the direction of the thermal ramp (Fig. B). To avoid any data misinterpretation, the linear dichroism contribution to the CD spectra was evaluated as well.
A model simulation, using a finite element analysis approach, described that weak asymmetric thermal gradient fields in stagnant solutions are capable to generate asymmetric thermophoretic flows.



As a confirmation, it was possible to manage in magnitude or suppress the SSB phenomenon by changing the magnitude of the asymmetric weak thermal gradient generated within the stagnant solution [3].

The role of the size and shape of the aggregates' macro-structure was furtherly taken into account to better understand the supramolecular aggregates' interaction with the thermal gradients of the solution. The cross-correlation of the experimental data obtained from circular dichroism, confocal microscopy, atomic force microscopy (Fig. C), and cryo-transmission electron microscopy (Fig. D), revealed that the Star2100 supramolecular aggregates organize themselves in flag-like structures whose thermally-induced circular dichroism depends on their features.

Finally, thermal gradient-induced enantioselectivity of the supramolecular flag-like aggregates has been linked to their size-dependence mesoscopic arrangement, which could be visualized as waving flags in the wind [4].

These results shed the light on the role of very weak forces (and usually not considered) in an intriguing phenomenon, the Spontaneous Symmetry Breaking, which had an important role in the chiral selection and origin of life.

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Shedding light on biologically relevant colloidal hybrid calciprotein particles: effect of proteins and stabilizing agents

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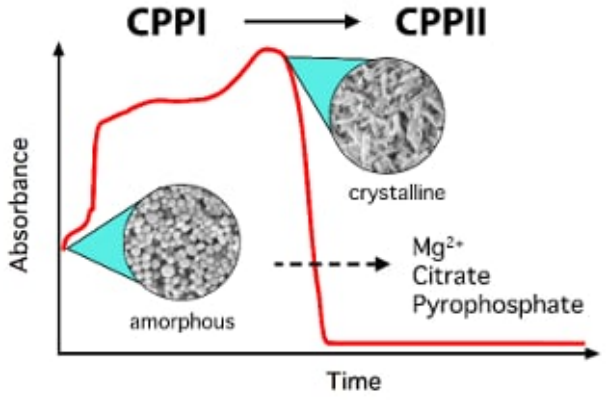
Despite the concentration of calcium and phosphate ions in human blood is supersaturated with respect to hydroxyapatite, the precipitation of calcium phosphate deposits (CaPs) is typically prevented by serum proteins which bind Ca^{2+} and phosphate ions or nascent CaP clusters and inhibit calcification phenomena that would lead to cardiovascular diseases [1]. Among them, the glycoprotein Fetuin-A (Fet-A) interacts with CaP amorphous clusters, producing colloidal protein-mineral hybrid complexes called "calciprotein particles" (CPPs) [2]. In pathological situations, the initially formed amorphous spherical complexes (CPPI) may mature into crystalline particles (CPPII), which eventually lead to ectopic calcifications. In this context, the role of albumin is also of paramount importance, given the abundance of this protein in serum and its ability to complex Ca^{2+} ions [3]. Understanding from a physico-chemical perspective the mechanism of ripening of CPPI to CPPII and the factors affecting the process is thus fundamental to prevent the surge of vascular calcifications by developing strategies to delay the crystallization and precipitation of CaP in serum.

In this contribution we inspect the effect of proteins (Fet-A and Albumin) and different ions (Mg^{2+}, pyrophosphate and citrate) on the formation and crystallization mechanism of CPPs [4]. Synthetic analogs of serum CPPs were initially prepared at different concentrations of Fet-A and their formation and ripening were followed *in situ* by means of turbidimetry and scattering techniques. The morphology of the obtained nanoparticles at different stages of the process was analyzed by means of electron microscopy whereas FT-IR spectroscopy and X-Rays diffraction allowed for the identification of the formed inorganic phases. Experiments were also conducted in the presence of different concentration of albumin within the physiological range and Mg^{2+}, pyrophosphate and citrate. This multi-technique approach allowed us to identify the most effective conditions for preventing the conversion of amorphous CPPI to crystalline CPPII, suggesting novel strategies to inhibit and treat cardiovascular calcifications.



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Hybridization of poly(oxazoline) and PEO-based amphiphilic copolymers into thermo-sensitive mixed micelles of tunable cloud point

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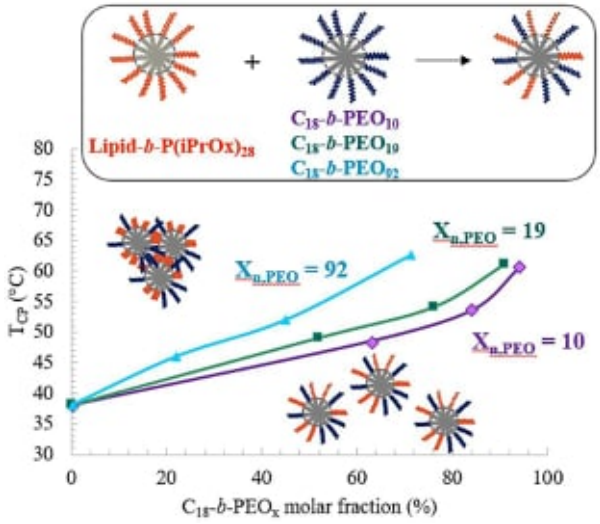
Amphiphilic copolymers as drug delivery systems are of great interest to fully control the release of an active agent through an external stimulus. Multiple stimuli-responsive triblock copolymers are often considered to modulate the systems properties [1]. However, to avoid fastidious syntheses, our team investigates an alternative approach based on the physical blending of copolymers to combine their properties [2,3,4]. Interestingly, when blending two thermo-responsive copolymers of close chemical composition, the cloud point can be modulated depending on the proportions in each copolymer [3,4,5].

The present talk will focus on recent advances in this area, especially the extension of this blending approach to copolymers of different nature and lengths, namely a lipid-*b*-poly(2-isopropyl-2-oxazoline) copolymer, self-assembling into thermosensitive micelles that phase separate above a cloud point temperature of 38 °C, and a commercial C18-b-PEOx (with x ranging from 10 to 92). The thorough characterization by light scattering and turbidimetry of the different blends will be presented. These analyses reveal that hybridization between both copolymers always occurs, independently of the PEO block length. The resulting mixed micelles present T_{CP} values progressively increasing with the C18-*b*-PEOx proportion, from 38 °C to 61 °C [6] demonstrating the relevance of the blending approach to tune the phase separation of micellar systems by formulation rather than by more tedious synthetic efforts



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Two-photon absorption in 0D carbon nanomaterials from nanographenes to graphene quantum dots and carbon nanodots

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Nanographene derivatives are in the spotlight for two-photon induced biomedical applications. Over the last decade, 0D nanocarbons have been reported to operate as tumor markers, sensors in biological environment, NIR emissive labels in bioimaging, and photothermal therapeutic agents under two-photon excitation. For such materials to have a real impact in the many technological applications anticipated, the two-photon absorption (TPA) must be optimized together with other application-depend secondary properties, such as fluorescence emission, energy or electron transfer and heat or reactive oxygen species generation. However, the limited number of studies that focus on the TPA process and the large dispersion of TPA cross-section values found in the literature preclude an unambiguous definition of the design guidelines to produce a material with high TPA cross-section in a reproducible and scalable way.

In this presentation we focus on the TPA properties of 0D carbon nanomaterials produced by three different approaches: bottom-up carbon nanodots (CND), top-down graphene quantum dots (GQD) and step-by-step controlled organic synthesis of distorted nanographenes (NG) (Figure 1). Based on our recent work, we discuss the relatively low emission yields of oxidized 0D nanocarbons produced by top-down or bottom-up methods, we show that the TPA cross-section of the carbon core might not be as high as initially anticipated and that the distortion of the sp^2 network can improve the nonlinear optical properties[1-3].

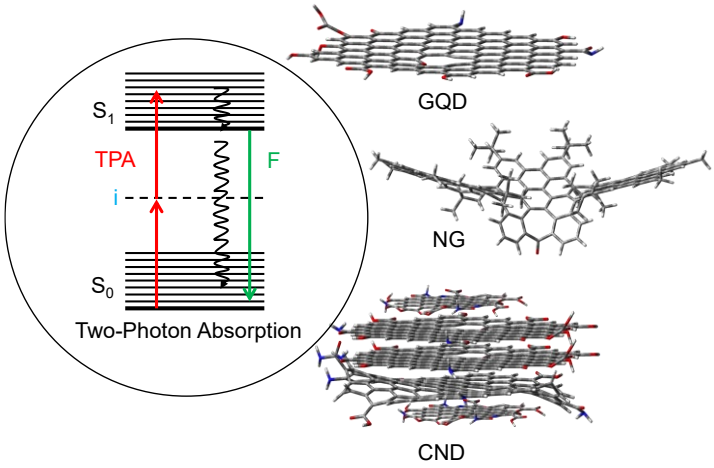

Figure 1. Illustration of the two-photon absorption process together with the 0D nanocarbons studied.

Thanks are due to the Fundação para a Ciência e a Tecnologia (UIDB/00100/2020, LA/P/0056/2020, UIDB/50006/2020, LISBOA-01-0145-FEDER-029319, PTDC/NAN-MAT/29317/2017, REF.IST-ID/95/2018, 2020.01763.CEECIND) co-financed by the FEDER-POCI-COMPETE 2020, within the PT2020 partnership, the European Research Council (ERC-2015-STG-677023) and the MCIN/AEI/10.13039/501100011033 FEDER "A way of making Europe" (PGC2018-101181-B-I00).

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Synthesis and assembly properties of selected T_8 and DDSQ silsesquioxanes ligands

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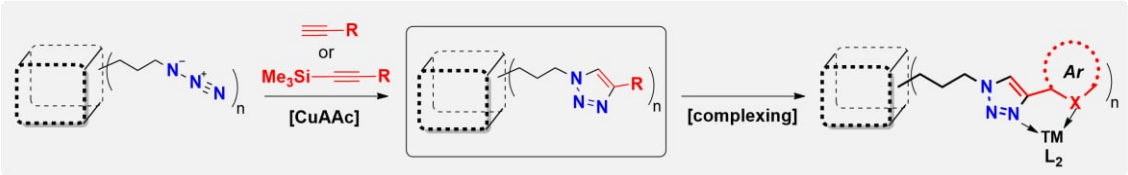
Polyhedral Oligomeric Silsesquioxanes (SQs) have become very attractive and important class of Si-O-Si frameworks within the family of organosilicon systems. They may be obtained *via* a hydrolytic condensation reaction from alkoxysilanes and further modified in catalytic reactions.[1] Due to their organic-inorganic, i.e. hybrid nature, they found applications in many branches of chemistry from materials to medicine.[1] Additionally, their complexing properties, especially when possessing organic moieties with heteroatoms to play a ligand role, have been also confirmed.[2,3,4]

Based on our group's experience, both in the synthesis of various SQs derivatives and also in organometallic chemistry, we have elaborated a synthetic pathway to obtain functionalized silsesquioxanes with groups containing *N*-donating atoms within their structures that may act as potential ligands for metal ions ligation.

In this communication, selected examples of functionalized cubic and double-decker types of SQs that were synthesized in a sequence of reactions, involving i.a. copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC), were tested as scaffolds, i.e. ligands for chosen TMs to assemble respective ions: Pd, Pt and Rh.[5,6]



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α-Synuclein-derived Adhesive Peptide Directing Core-Satellites Assembly of Polydopamine Particle-Gold Nanoparticles for Plasmonic Photothermal Effect

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Molecular soft ligands such as polymers, DNAs, and proteins have attracted substantial attentions to construct diverse architectures of nanocomposites in order to find a range of therapeutic applications[1]. In particular, a human brain protein of α-synuclein (αS) has been demonstrated to be used as a binder to link gold nanoparticles (AuNPs) to form 1-D nanochains[2] and 2-D free standing monolayers of AuNPs[3] by taking advantage of the unique adhesive property of αS[4].

αS is an intrinsically disordered protein known to be related to Parkinson's disease, but it has been recently reported to mediate formation of neuronal protein complexes in physiological condition[5] due to its high degree of structural plasticity and chaperone activity. The sequence of αS has been systemically studied to find a core domain responsible for molecular reason of the adhesion, and thus identified C-terminal sequence of αS, a 17-residue peptide ($_{125}$YEMPSEEGYQDYEPEA$_{140}$) that preserves the versatile binding nature of αS[6]. The αS-derived peptide (αSP) exerted a surface coating onto chemically diverse substrates with AuNPs in the form of a close-packed single layer.

Here, we propose a strategy to fabricate homogeneous core-satellites of polydopamine particle (PDP)-AuNPs nanocomposite mediated by αSP (Figure 1). PDPs have been shown to selectively recognize cancer cells and ablate them by an iron-dependent antineoplastic activity[7]. Our core-satellites of PDP-AuNP nanocomposites would be applied to cancer treatment based on their plasmonic photothermal conversion of AuNPs in addition to antiproliferative ability of iron-loaded PDPs[8]. Moreover, the rich chemistry of αSP encapsulating AuNP surface could provide additional functionalization for precise target at cancer cell. It could be suggested as a multifunctional nano-structures performing photothermal effect as well as selective drug release for cancer therapy.

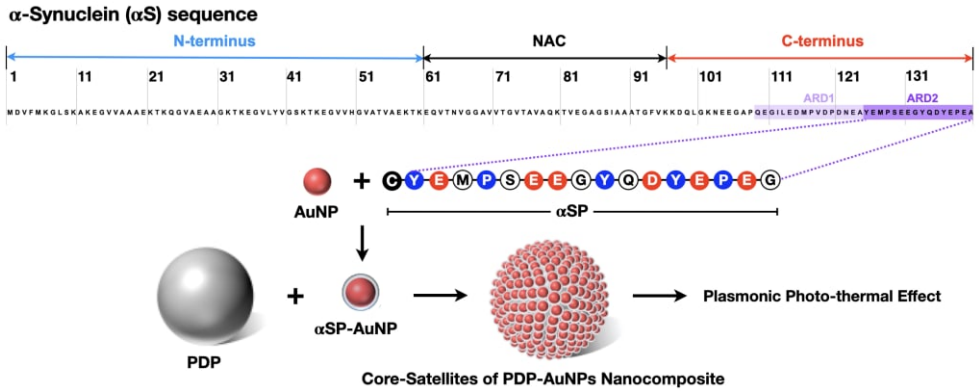

Figure 1. Schematic representation for core-satellites assembly of PDP-AuNPs by using αS-derived adhesive peptide

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Compartmentalized algal-based nanocarriers as vectors for antioxidants: structural and functional characterization

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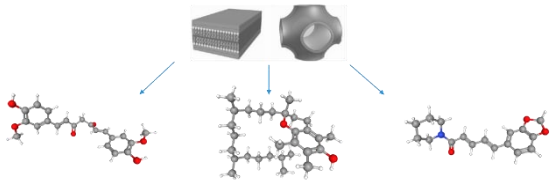
The delivery of poorly water-soluble natural drugs is a longtime challenge that has led to the development of several solubilizing and encapsulating carrier systems, to administrate hydrophobic molecules for biomedical, pharmaceutical, food and cosmetics applications. Among the most popular soft matter nanocarriers, lipid-based vectors are particularly favored thanks to the advantageous properties of lipids as versatile and biocompatible building blocks. Indeed, lipids are the class of bio-macromolecules with the richest polymorphism and spontaneous self-assembly character, that result in a broad variety of hierarchical structures. Several aggregates with different interfacial curvatures and symmetries are obtained, mainly dependent on the lipid class and packing parameter, and can be differentiated in lamellar and nonlamellar mesophases. Lamellar aggregates are characterized by the presence of one or multiple bilayers whit vesicular morphology at larger scale (~μm). Nonlamellar mesophases e.g. bicontinuous cubic phases are lyotropic liquid crystalline systems that possess higher inner ordering [1]. When these systems are in excess water conditions, dispersed nanosystems are obtained and termed liposomes and cubosomes, respectively. The versatility and biodegradability of these nanosystems makes them particularly suitable as carriers for orally administered drugs. Moreover, lipids to be used for formulation development can be obtained from a variety of natural sources and biomasses, to develop nanovectors for bioactive molecules with high carrier-cargo and carrier-target compatibility.

In this work, lipid nanovectors were designed and prepared as biocompatible and biodegradable drug carriers for a commercially valuable antioxidant drug i. e. curcumin, whose therapeutic application is typically hindered by its poor water solubility, that was chosen as the designated natural antioxidant of interest for this investigation [2]. Two other antioxidants i. e. α-tocopherol and piperine were used as adjuvants for curcumin since they are known to act synergistically as bio-enhancers. These three antioxidants were then encapsulated in the formulated lipid nanocarriers to improve their biodistribution and bioavailability. Natural-derived building blocks were obtained by lipid extraction from two biomasses of the marine microalga *Nannochloropsis* sp., containing mostly either phospholipids or triglycerides. Two dispersed nanovector series with different supramolecular structure were thus obtained i. e. liposomes and cubosomes, respectively. The high surface-to-volume ratio and loading efficiency granted successful encapsulation of the guest molecules. These nanoformulations were extensively characterized both from the physico-chemical and functional viewpoint. The structure and morphology was studied by combination of Dynamic Light Scattering, Small Angle X-Ray Scattering and Cryogenic Transmission Electron Microscopy. The guest-carrier and guest-guest interactions, stability and cargo entrapment were investigated by spectroscopic (UV–Vis, Nuclear Magnetic Resonance) and calorimetric (Isothermal Titration Calorimetry) techniques. Finally, the functionality was studied with both chemical and biological approaches, in an integrated structure-function perspective.



Thanks to the ID02 beamline staff of the ESRF (Grenoble, France) for beamtime and scientific support, to Dr Miroslav Slouf and the Polymer Morphology group of the Czech Academy of Sciences (Prague) for Cryo-TEM measurements.

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Water depollution of toxic organic compounds using magnetic graphene composite adsorbents

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As the world population continues to grow and industrialization increases, there is both an increase in the demand for clean water and an increase in water pollution [1]. Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous environmental pollutants present in air and water, with associated health risks [2], so monitoring the presence and removing them from water bodies is essential. However, the extraction and quantification of organic pollutants often remain a challenge.

There are different standard practices for water depollution and among these, adsorption has gained a lot of attention in the past years, especially with the development of nanotechnologies. In particular, graphene-based nanomaterials are known to be highly efficient adsorbents of organic pollutants, due to π-π stacking interactions between the aromatic rings of graphene and the organic pollutant molecules. On the other hand, magnetic nanomaterials, such as iron oxide nanostructures, are also of interest for adsorption applications because they allow an easy magnetic separation of the materials, decreasing the risk of contamination of the treated water with residual adsorbent. The creation of composite materials that couple the high efficiency of graphene with the easy magnetic separation of magnetic nanomaterials is highly attractive to develop effective strategies for water decontamination.

In that context, we have designed magnetic graphene-based composite materials for removal of toxic organic pollutants, in particular PAHs. For the synthesis, few-layers graphene (FLG) coated with tannic acid (TA) was introduced in the reaction media of iron oxide nanostructures. The synthesis of graphene/iron oxide composites was optimized, and the composites (Figure 1(a)) were then used in the adsorption of PAHs. To study their adsorption potential, benzo[a]pyrene (BaP) was chosen as pollutant, due to its high carcinogenicity and low drinking water limit established by the EU (10 ng/L) [3]. Different adsorption times and BaP initial concentrations, and the presence of ethanol as a co-solvent were tested. After the adsorption and magnetic separation of the adsorbent, the depolluted water samples were analyzed to quantify the pollutant still present in solution. For this quantification, it was important to use analytical methods capable of detecting and quantifying very low concentrations of pollutants. Thus, an analytical protocol by Ultra High Performance Liquid Chromatography coupled with Fluorescence detection (UHPLC-FLD) was established. The method developed by UHPLC-FLD had a limit of detection (LOD) of 4.1 ng/L and a limit of quantification (LOQ) of 13.7 ng/L, allowing the detection of very low amounts of BaP.

The results showed very fast and high adsorption of BaP in water (>99%), using very low amount of adsorbent material and confirming the high efficiency of the synthesized composites to remove BaP from water (Figure 1(b)). The adsorbed amount increased with the liquid BaP concentration in the range 0-5 mg/L according to the Langmuir theory (Figure 1(c)). Other pollutants were also tested to evaluate the potential of the magnetic graphene adsorbents in general depollution practices.

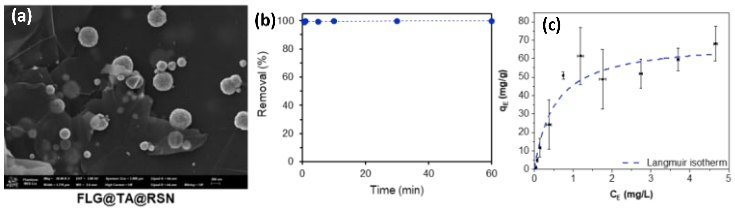

Figure 1. (a) SEM image of FLG@TA@RSN composites; (b) removal efficiency obtained in kinetics experiments; (c) adsorption isotherm studies.

This research project was co-funded by Institut Carnot MICA through the CAPTALL project and, Region Grand Est and ANR through the FIGHTVIRUS project (Resilience Grand Est project).

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Molecule-driven control of magnetic anisotropy in superparamagnetic iron oxide nanoparticles

Leonardo Curti [a, *], Yoann Prado [a], Delphine Talbot [b], Vincent Dupuis [b], Edwige Otero [c], Philippe Ohresser [c], Marie-Anne Arrio [d], Philippe Sainctavit [c, d], Christophe Cartier dit Moulin [a], Jérôme Fresnais [b], Laurent Lisnard [a] and Benoit Fleury [a]

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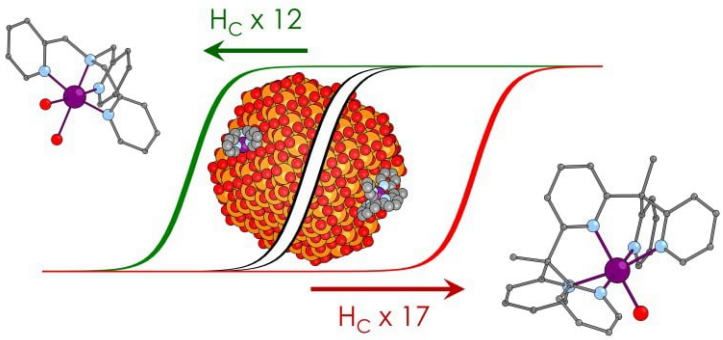
Superparamagnetic iron oxides nanoparticles (SPIONs) have been thoroughly investigated and their properties lead to a plethora of multidomain applications. [1] A fine tuning of the magnetic anisotropy, which shapes their properties, appears then essential. To this end, the surface of the nanoparticles represents an attractive playground for coordination chemists considering its strong contribution to the systems magnetic anisotropy. [2] Prado *et al*. [3] demonstrated that the grafting of magnetic complexes on SPION gives a massive improvement of the magnetic properties. Here we demonstrate how the nature of the grafted coordination complexes acts on colloidal stability and influences the magnitude of the magnetic anisotropy, yielding thus a multi-level molecular tuning of the properties. These two aspects were explored in solution by mean of dynamic light scattering and SQUID magnetometry. Furthermore, the essence of the magneto-chemistry at the interface between the molecules and the nanoparticles was probed by X-ray absorption spectroscopy.



Schematic representation of SPIONs coordinated by anisotropic Co(II) complexes and of the different impact on the magnetic anisotropy of the final hybrid nanoparticles in terms of coercive field.

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Pioglitazone nanoparticles: synthesis optimization and FLIM characterization

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Nanoparticles (NPs) with engineerable physical and chemical properties can potentially transport a drug in an "intelligent" way, i.e. only or mostly in the diseased tissue of interest. This helps in increasing the safeguard of healthy tissues and in protecting the drug from possible systemic degradation, making it possible to reduce the dosage and the side effects [1].

In our laboratories, we work on synthetic strategies and optimization of such "nanobullets", and in studying their interaction with cells or with other models that partially reproduce the environment existing in living organisms. I will discuss our efforts for achieving the most reliable synthetic pathway for the synthesis of pioglitazone (PGZ) loaded poly(lactic-co-glycolic acid) (PLGA) polymeric nanoparticles, in particular by nanoprecipitation and single emulsion-solvent evaporation methodologies. Indeed, recent findings proved the benefits of PGZ in treating or controlling the progression of atherosclerosis and diabetes [2,3], but this is a poorly soluble drug and therefore its availability will improve if included within NPs [4]. We examined the influence of several variables (e.g. component concentrations, phases ratio, injection flux rate) on the synthesis of the PGZ-loaded PLGA NPs, and compared the results in terms of nanoparticle size, polydispersity index (PDI), zeta potential (ζp), drug loading (DL %), entrapment efficiency (EE %), stability, and cost, analyzing also the drug release from the best obtained formulation.

On the other side, I will review our efforts for characterizing (i) free PGZ and his polymorphs, (ii) PGZ-loaded polymeric nanoparticles and (iii) PGZ-NPs uptake within insulinoma (INS-1) cell model via 2-photon microscopy and phasor approach to fluorescence lifetime imaging (phasor-FLIM) [5], pointing to potentially novel processes for theranostics and anti-diabetics outcomes.

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Influence of dispersion protocols on multicomponent nanomaterials properties and toxicity in the context of safe by design approach

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Over the last decade, significant efforts by different authors [e.g. 1-3] and by international organizations [e.g. 4-6] have been devoted to understand if a generally applicable dispersion protocol for different kind of engineered nanomaterials (ENMs) could be provided prior to toxicological testing. However, the high degree of variability in the main physicochemical properties of ENMs, including size, morphology, surface area, chemical composition and surface chemistry, have represented a barrier to this harmonization, even more if the complexity of multi-component nanomaterials (MCNMs) is considered. Therefore, within the Horizon2020 SUNSHINE project, the colloidal characterization of both single- (i.e. SiO_2, ZnO, SiC and TiO_2) and SiO_2-ZnO and SiC@TiO_2 MCNMs, intended to be used in cement and ceramic nanocomposite coatings respectively, was investigated to highlight how the different dispersion protocols and cell culture conditions can affect the MCNMs properties and toxicity results. In detail, hydrodynamic diameter, surface charge, sedimentation velocity, and protein corona composition of MCNMs were investigated after performing either the Nanogenotox [4] or the dispersion protocol proposed by Deloid et al. [7] in relevant cell-culture medium, either with or without the addition of serum. Cell viability and release of inflammation markers were tested using both epithelial and macrophages cell lines. The set of information from both the colloidal characterization and from the *in vitro* toxicity assays performed were exploited to understand if and which are the main parameters of the dispersion- and exposure protocols which could influence the MCNMs properties and their *in vitro* toxicity. Preliminary results indicate that the use of serum in the cell culture medium decreases the toxicity of SiO_2-ZnO MCNM, which is probably related to the formation of a protective protein corona at the particle surface. This could have relevant implication on the MCNM risk evaluation. Especially in relation to the Green Deal ambitions to develop materials that are safe-by-design (SbD), materials should be tested in a realistic manner without changing characteristics. Extensive sonication could damage a material surface treatment, thereby interfering with the SbD intervention. A generally applicable dispersion protocol is not suitable for all ENM and MCNM. We propose to tailor sonication to the specific MCNM, supported by thorough colloidal characterization. This approach should result in better understanding of what drives MCNM toxicity, enabling SbD solutions.

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Functionalization of synthetic saponite: addition of anion exchange property

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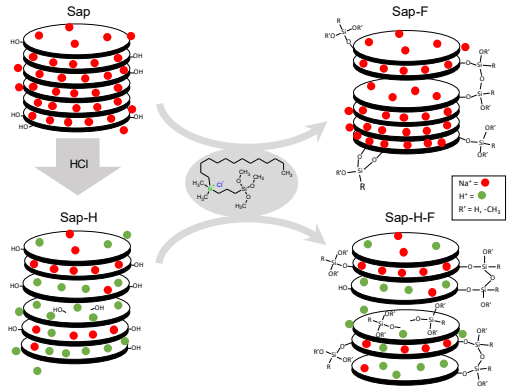
Approximately 80% of wastewater is returned in ecosystem without any treatment mainly in low-income areas in developing countries [1]. In wastewater treatment, ion exchange is one of processes applied to remove unwanted ionic species from wastewater. A cheap and local material capable to adsorb wide range of species (anionic, cationic, neutral) could be a material of choice in such cases. Clay minerals are cheap and abundant; however, they possess only cation exchange capacity. The functionalization is then needed to increase the range of possible species to be adsorbed, i.e. neutral and negative species.

This study explores the functionalization of clay minerals by silylation. The formation of covalent bond through hydrolysis and condensation reactions between the surface of the solid particles and alkoxysilane compound during the silylation, stabilizes the organic component and prevents its leaching during application. The particularity of clay minerals is the presence of several type of surfaces with different properties, such as basal, interlayer and edge surfaces. In order to gain understanding in the interaction of alkoxysilane with clay mineral surfaces, a synthetic clay mineral saponite was prepared [2].

The grafting of the alkoxysilane was observed regardless the starting material was pristine or acid pre-treated saponite. The more significant layer-to-layer distance increase observed after the functionalization of acid pretreated saponite indicated some interlayer intercalation/grafting of the alkoxysilane. Electrochemical characterization (cyclic voltammetry and electrochemical impedance spectroscopy) showed that the modified clay mineral exhibited anionic exchange property due to the presence of grafted cationic alkoxysilane. This anionic exchange capacity was confirmed when successfully applied for the adsorption of the anionic dye Congo Red. In all cases, the acid pre-treatment tended to improve the anion exchange property of the organoclay [3].



Schematic representation of change of saponite layer-to-layer stacking upon acid treatment and functionalization.

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Cage–···Cage– interaction: Boron cluster-based noncovalent bond and its applications in solid-state materials

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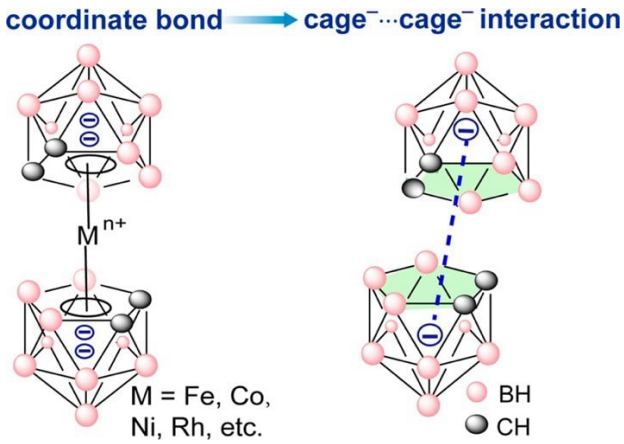
Carboranes are boron–carbon clusters with important applications in fields of materials, catalysis, pharmaceuticals, etc [1-4]. However, the non-covalent interactions that could determine the solid-state structures and properties of such boron clusters have been rarely investigated. Herein, inspired by the coordinate bond in metallacarborane or ferrocene, the boron cluster-based non-covalent interaction (denoted as cage$^-$···cage$^-$ interaction) between two nido-carborane clusters was successfully realized by using a pyridinium-based molecular barrier. The X-ray diffraction studies uncover that the cage$^-$···cage$^-$ interaction has a contacting distance of 5.4–7.0 Å from centroid to centroid in the systems reported here. Theoretical calculations validate the formation of the non-covalent interaction and disclose its repulsive bonding nature that is overcome thanks to the positively charged pyridinium-based framework. Interestingly, such bulk crystalline materials containing the cage$^-$···cage$^-$ interaction show relevant properties such as full-color absorption in the visible light range and important photothermal effect, which are absent for the control compound without carboranes. This study may offer fundamental insights into the boron cluster-based non-covalent interactions and open a new research avenue to rationally design boron cluster-based materials [5].



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Toward Chemotactic Supramolecular Nanoparticles: From Autonomous Surface Motion Following Specific Chemical Gradients to Multivalency-Controlled Disassembly

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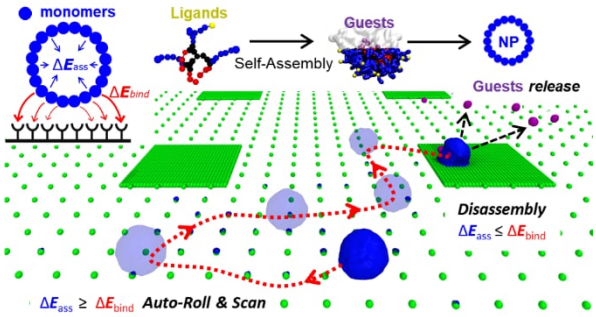
Nature designs chemotactic supramolecular structures that can selectively bind specific groups present on surfaces, autonomously scan them moving along density gradients, and react once a critical concentration is encountered [1]. Such properties, key in many biological functions, offer inspirations for designing artificial systems capable of similar bioinspired autonomous behaviors. Molecular models and computer simulations are fundamental to understand the molecular factors controlling the selective noncovalent interactions and their complex role at the interface [2]. However, finer-level molecular models are needed in the perspective of designing supramolecular assemblies (e.g., self-assembled NPs) which can selectively bind surfaces, autonomously scan them moving along chemical surface gradients, and trigger controlled dynamic responses (e.g., NP binding, rolling, disassembly, and release of encapsulated guests).

In this study, we exploit soft molecular units that self-assemble in an aqueous solution generating nanoparticles (NPs) with specific surface chemical groups, enabling multivalent interactions with complementarily functionalized surfaces. Specifically, we investigate the (autonomous or driven) motion of self-assembled NPs on a receptor-grafted surface at submolecular resolution. First, we validate via classical Molecular Dynamics simulations the adhesion of self-assembled NPs composed of facially amphiphilic oligomers on surfaces characterized by different distribution of interacting receptors. Subsequently, with enhanced sampling techniques, we explore the dynamics of the NPs on a receptor patterned surface. In particular, we observe how the tuning of multivalent interactions between the NP and the surface allows to control the NP binding, its diffusion along chemical surface gradients, and ultimately, the NP reactivity at specific surface group densities. Finally, in silico experiments provide physical–chemical insights on key molecular building block features which determine the dynamic behavior and fate of the NPs on the surface: from adhesion, to diffusion, and disassembly. In fact, the use of such oligomers also permits modification of the hydrophobic groups [3], making the assembly more/less stable.

In conclusion, we have highlithed the key role played by the competition between the self-assembly stability of the NP and the strength of its interaction with a receptor decorated surface. This work identifies some chemical routes to achieve controlled bioinspired chemotaxis in artificial self-assembled systems, therby offering a privileged point of view into the chemotactic properties of supramolecular assemblies.



G.M.P. acknowledge the support received by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (Grant Agreement no. 818776 - DYNAPOL) and by the Swiss National Science Foundation (SNSF Grant 200021_175735). The authors acknowledge the U.S. Army Research Office (Grants W911NF-18-1-0355 and W911NF-15-1-0568) for supporting this work. The authors also acknowledge the computational resources provided by the Swiss National Supercomputing Center (CSCS) and by CINECA.

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Membrane Phase Drives the Assembly of Gold Nanoparticles on Biomimetic Lipid Bilayers

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Over the past several years, the number of reports on the design and application of engineered nanoparticles (NPs) in nanomedicine has grown exponentially; however, to date, the clinical translation of NPs is still limited mainly due to a lack of fundamental knowledge on their fate in living organisms, which is intimately related to the nature of the interactions with biomolecules and biological barriers, such as cell membranes.[1] In this context, the development of synthetic lipid membranes, such as liposomes, represents a valuable strategy to systematically investigate how the physico-chemical parameters of NPs affect their interactions with lipid bilayers in simplified and controlled conditions and to predict the relevant aspects that govern the biological fate of NPs.[2]

Recently, many efforts have been devoted to investigating the interaction of nanoparticles (NPs) with lipid biomimetic interfaces, both from a fundamental perspective, aimed at understanding relevant phenomena occurring at the nano-bio interface, and from an applicative standpoint for the design of novel lipid-nanoparticle hybrid materials. In this area, recent reports have revealed that citrate-capped gold nanoparticles (AuNPs) spontaneously associate with synthetic phospholipid liposomes, and, in some cases, self-assemble on the lipid bilayer, forming promising hybrid composites for several nanomedical applications.[3,4] However, the mechanistic and kinetic aspects that rule this peculiar aggregative phenomenon are not yet completely understood. In this study, we address the kinetics of interaction of citrate-capped AuNP with lipid vesicles of different rigidities (gel phase rigid membranes on one side, liquid crystalline phase-soft membranes on the other). The formation of AuNPs-lipid vesicle hybrids was monitored over different time and length scales, combining experiments and simulations. The very first AuNPs-membrane contact was addressed through Molecular Dynamic simulations, while the structure, morphology, and physicochemical features of the final colloidal objects, were studied through UV-Visible spectroscopy, Small Angle X-Ray Scattering, Dynamic Light Scattering, and Cryogenic Electron Microscopy. Our results highlight that the physical state of the membrane triggers a series of events at the colloidal length scale, which regulate the final morphology of the AuNPs-lipid vesicles adducts. For lipid vesicles with soft membranes, the hybrids appear as single vesicles decorated by AuNPs, where the AuNPs are in direct contact with each other (Fig. 1), while more rigid membranes lead to the hybrid flocculation, with AuNPs acting as bridges between vesicles (Fig.2). Overall, these results contribute to a mechanistic understanding of AuNPs adhesion/self-assembly onto biomimetic membranes, relevant for phenomena occurring at the nano-bio interfaces. The deep comprehension of the main physicochemical parameters which rule the spontaneous association of citrated NPs on zwitterionic membranes paves the way to engineer and finely control lipid-NPs hybrids through simple self-assembly.

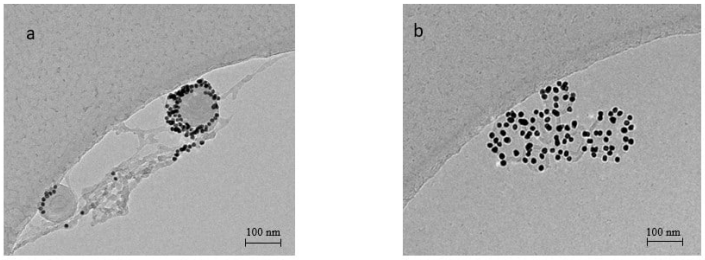

Fig. 1. Cryo-Tem images of a) soft liposome-AuNPs composites and b) rigid liposomes-AuNPs composites.

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Unsupervised machine learning of intrinsic structural dynamics in simple-to-complex micelles

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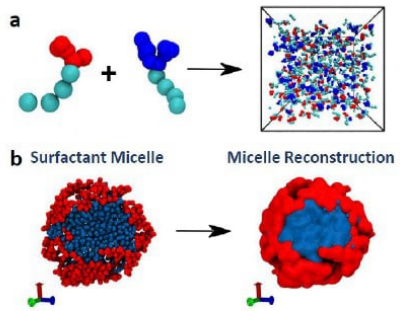
Understanding the intrinsic dynamics and internal structure of soft self-assemblies has always received a wide appeal both in science and technology. A detailed comprehension of Lipid Liquid Nanoparticles (LLNs), for instance, is crucial in developing stable drug delivery vehicles [1]. Conformationally distinct states of assembled surfactants show remarkable potential in amplifying catalytic reactions which causes configurational changes and disassembly [2]. In supramolecular polymer, a finer control of defect dynamics, and a more reliable identification of monomer exchange pathways are key to study bioinspired properties such as the ability to respond, adapt, and reconfigure after external stimuli [3,4]. However, although relevant progresses have been carried out from the experimental point of view, many challenges still exist to detect and capture the dynamics properties of soft self-assemblies, especially at the nanoscale. Advanced modelling approaches, on the other hand, have brought a step forward in this research area.

Here, we couple molecular modelling with an unsupervised machine-learning (ML) technique to systematically identify and reconstruct the internal dynamics of bi-component surfactant micelles. Specifically, our data-driven analysis relies on the smooth overlap of atomic potential (SOAP) framework in combination with the probabilistic analysis of molecular motifs (PAMM). First, with a minimalistic model of surfactant micelles, we unveil the essential role of both geometrical and non-covalent interactions for a successful identification of specific surfactant types within micelles. Then, inspired by the experimental works on transiently formed catalytic nanostructures [1], we translate and validate the approach on a more realistic case study modelled with a finer chemical resolution. Specifically, we analyse bi-component micelles made of n-stearoyl L-histidine and p-nitrophenyl ester of n-stearoyl L-phenylalanine. The results show that our modelling framework based on unsupervised ML technique allows to reconstruct a micelle configuration according to its internal distribution of surfactants. In addition, our modelling platform provides some reliable evidence on the intrinsic dynamics of building-blocks, including their mobility and transfer probability across localized micelle patches. Beyond the theoretical insights, the modelling framework here presented demonstrates practical benefits toward perfecting the design of a variety of assemblies and supramolecular systems.



G.M.P. acknowledges the support received by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (Grant Agreement no. 818776 - DYNAPOL) and by the Swiss National Science Foundation (SNSF Grant 200021_175735). The authors also acknowledge the computational resources provided by the Swiss National Supercomputing Center (CSCS) and by CINECA.

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Theoretical Description of the Oxygen Evolution Reaction: Quo Vadis?

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Electrochemical transformations, particularly those involving hydrogen, oxygen, and water, are discussed as fossil-free pathways to produce fuels and chemicals of global importance, thereby reducing harmful carbon dioxide emissions **[1]**. For the corresponding electrocatalytic reactions, active, stable, and selective electrocatalysts need to be developed that preferably do not contain scarce noble metals to enable large-scale operation of these processes. To identify promising electrode materials, commonly, material-screening techniques in a heuristic fashion are applied that enable categorizing electrodes into active and inactive materials **[2]**. Most of these studies rely on the initial idea of Nørskov, Rossmeisl, and coworkers in that only the binding energies (thermodynamics) of potential reaction intermediates (RIs) within the electrocatalytic cycle are assessed whereas the kinetics (transition states) or the applied overpotential are neglected in the analysis **[3]**.

The thermodynamic theory of Nørskov, Rossmeisl, and coworkers consists of four main paradigms: i) electrocatalytic activity is approximated by the thermodynamic overpotential, η_{TD}, which corresponds to the largest free-energy change at the equilibrium potential of the respective electrocatalytic process; ii) multiple electron-proton processes such as the oxygen evolution (OER) reaction are thermodynamically restrained by scaling relations; iii) breaking scaling relation is a universal remedy to enhance electrocatalytic activity; iv) the optimum OER catalyst reveals a thermoneutral thermodynamic free-energy landscape (corresponding to a symmetric shape) at equilibrium conditions **[4]**.

Recent studies, however, challenge several of the above paradigms in that it was shown that i) approximation of electrocatalytic activity by a single free-energy change, such as encountered with η_{TD}, is insufficient **[5]**; ii) breaking scaling relation may cause deteriorated electrocatalytic activity **[6]**; iii) the optimum thermodynamic free-energy landscape may reveal an asymmetric rather than a symmetric shape under reaction conditions **[7]**. These advanced insights could only be derived by making use of an activity descriptor that goes beyond the common thermodynamic reasoning at the equilibrium potential of an electrocatalytic process: the concept of $G_{max}(\eta)$ allows factoring overpotential and kinetic effects into the analysis of activity trends at the same computational costs as the descriptor η_{TD} but relies on a more sophisticated evaluation scheme of the free-energy changes of the OER mechanism **[8]**.

While in the last decade breaking scaling relation was put forth as the design criterion for the development of highly active OER catalysts, it becomes evident now that new thought approaches beyond this notion are urgently needed. In my lecture, I am going to ponder about future theoretical investigations of the elementary steps of the OER mechanism, ranging from a correct description of the lattice oxygen evolution reaction, surface reconstructions due to the interaction with the aqueous electrolyte, or the combination of dynamic and static electronic structure approaches to spur materials development of OER catalysts **[9]**.

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Biobased and UV- sensitive nanoparticles

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Getting hollow nano-objects has been extensively studied during the past years. One strategy to obtain hollow objects with controlled dimensions is to use a sacrificial template easy to synthesize, add a shell around, and finally get rid of the sacrificial core[1] . The treatments for core withdrawal are diverse, from acidic hydrolysis to calcination[2] [3] [4]. In the case of sensitive materials, like polysaccharides such as cellulose or starch derivates, aggressive treatments would damage both the core and the shell, preventing the obtention of hollow nanostructures. A possible solution could be the use of a physical treatment, like UV-irradiation. If one can produce a UV-sensitive core that would be solubilised under UV-irradiation, the preservation of some biobased shells would no longer be an issue (as cellulose or starch can be stable under UV, in "soft conditions" like for few hours without too intense irradiations[5] [6]), and hollow biobased-objects might be obtained.

The solution studied in this project consists in producing UV-sensitive cores, by integrating a UV sensitive molecule during the synthesis of inorganic nanoparticles. These UV-sensitive molecules ensure the integrity of the inorganic network, possibly by covalent bonds, otherwise their breaking under UV would not help the solubilisation of the inorganic core. Once these cores are synthesized, and their UV-sensitivity confirmed (by evaluating the change in suspension turbidity), a bio-based shell is built using a layer-by-layer process. The addition of bio-based polymers layers can be confirmed by different technics, such as zeta potential[7] [8] or AFM (Atomic Force Microscopy). The last step consists in irradiating the hybrid core-shell nanoparticles with UV and evaluating the core withdrawal, using for example TEM (Transmission Electronic Microscopy) imaging.

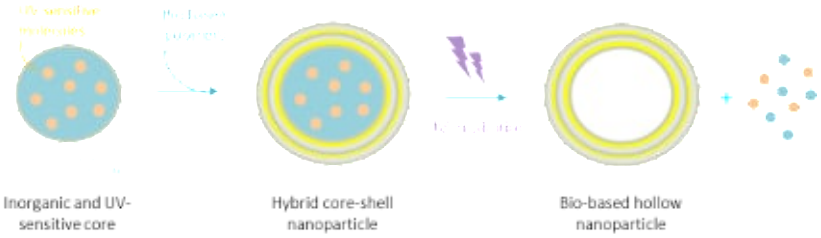

Figure 1 : Biobased hollow nanoparticles production

LGP2 is part of the LabEx Tec 21 (Investissements d'Avenir - grant agreement n°ANR-11-LABX-0030) and of PolyNat Carnot Institute (Investissements d'Avenir - grant agreement n° ANR-16-CARN-0025-01). The funding of this project is provided by LVMH Recherche. The authors also thank Jean-Luc Puteaux and Christine Lancelon-Pin (CERMAV, Grenoble) for the TEM and SEM images.

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Hybrid inorganic organic luminescent supraparticle taggants with switchable dual level ID

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Tracking and tracing of objects are of paramount importance for realizing a Circular Economy and can be achieved by utilizing micron scaled luminescent identification (ID) taggants as smart additives. While established ID systems are passively displaying an ID feature, for monitoring a products´ elapsed life cycle, conscious taggants with stimuli triggered switchable ID signals, e.g. to record a recycling step, are desired. Herein, micron-scaled hybrid inorganic-organic taggants with a temperature-triggered switchable luminescent ID are reported.[1] Their spectral optical coding relies on relative intensity ratios of spectrally distinguishable emission bands, provided by different luminescent coding elements combined in one taggant.[2,3] To produce these smart additives, nano-sized building blocks were assembled into hierarchically structured, micron-sized units termed supraparticles (SPs).[4] As a tool to assemble SPs, spray-drying has proven to be advantageous due to its scalability, flexibility, and ability to freely combine all kinds of nanomaterials, even with repulsive properties. Spray-drying is thus a versatile tool to entangle organic and inorganic nanoparticles and thus to create hybrid functional materials.[1,5]

By assembling different types of organic (dye-containing polystyrene nanoparticles) and inorganic (lanthanide doped CaF_2 nanoparticles) luminescent nanoparticles via a two-step spray-drying process, hybrid core(inorganic)-shell(organic) SPs possessing multiple switchable spectral ID levels were developed. Initially, the temperature inert inorganic luminescent ID level, located in the core, is concealed by a mutable organic ID level, emitted by the shell. Upon specific heat treatment, the ID is switched by irreversible degradation of the first, organic ID level, revealing the second, inorganic ID level. Both ID levels are read out ratiometrically using the same excitation wavelength for detection.

The versatility of a hierarchically structured SP design was exploited to realize flexibly adjustable multi-level ID taggants with stimuli triggered switchable ID signatures. Besides the chosen SP architecture, well-balanced mass-ratios of the utilized nano-sized building blocks are key to controlling coupling effects within the SP, thus, obtaining the switchable ID functionality. Based on the SPs´ toolbox-like manufacturing, the ID signals are readily adjustable to yield the demanded code variety on both ID levels.

This approach might open up the perspective of monitoring the product history even after the end of the product life and could therefore be interesting to identify recycled raw materials and refurbished or reused product components. If plastics are recycled, the elevated temperatures during processing should cause a degradation of the organic ID signatures either gradually or completely, thus initiating an ID switch. It is conceivable that this approach not only enables to easily distinguish between virgin polymer and recyclate but also indicates how many times a material has already been recycled, which is valuable information in terms of quality assurance for manufacturing processes in a well-functioning circular economy.

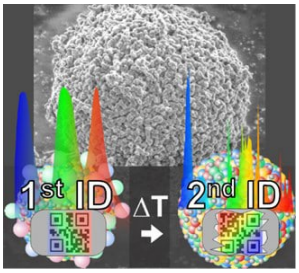

Figure 1 (Sub)micron-sized hybrid inorganic-organic supraparticles that exhibit temperature-triggered switchable luminescent IDs are smart taggants, that enable materials identification. Moreover, their thermally induced ID switch could indicate a materials' history within a Circular Economy by recording thermal processing steps like recycling.

The BMBF NanoMatFutur Grant 03XP0149 financially supported this work.

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Are Silsesquioxanes Susceptible to be Part of Hybrid Ligands?

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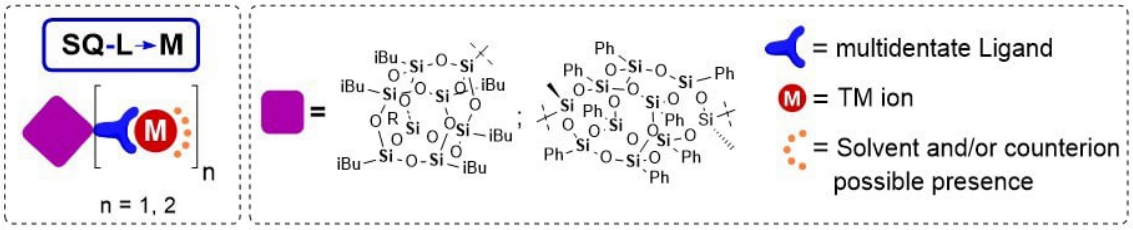
Oligomeric silsesquioxanes (SQs) are specific representatives among organosilicon systems of diverse architectures. Their uniqueness results from the presence of inorganic siloxane Si-O-Si core and tuneable functional organic coronae which classify them as hybrid systems. Additionally, those functionalities drive their plausible appliance in many directions of chemistry, materials and medicine [1].

Owing to the appealing features of SQs, some attempts to use them as scaffolds for organic moieties possessing the possibility to ligate metal ions, resulting in the formation of coordination compounds have also been explored. There have been several reports on the application of mono- and octafunctionalized silsesquioxanes with a specific functional group, playing a role of ligand, mainly bi- or tridentate, e.g. diketones, carboxylic acids but also monodentate, e.g. phosphines derivatives, used for coordination of selected TM. Obtained systems form diverse architectures from molecular to macromolecular 3D coordination polymers exhibiting attractive physicochemical features [2].

In this communication, recent results on the formation of silsesquioxanes differing in their structure type with anchored functionality(ies) possessing heteroatoms and susceptible to ligate selected TM ions will be presented (**SQ-L->M**). The organic moieties of ligand features contain bi- and tridentate molecules, i.a. substituted triazole ring(s) and ethynylterpyridine derivatives and with respective TM ions, e.g. Fe(II), Pt(II), Rh(I) or Eu(III), may form 0D discrete molecules (mono- and binuclear complexes) or 1D coordination polymers [3-5]. The results obtained for double-decker SQs are of our special attention. Some of their interesting physicochemical properties will be also presented. These systems could be smartly so-called *Metal-Inorganic-Organic-Materials* (MIOMS).



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Smart hybrid silica nanocarriers with finely tuned structure for control release

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Mesoporous silica nanoparticles (MSNs) have been used in theranostic applications as nanocarriers in cutting-edge applications due to their excellent biocompatibility, high surface areas, large pore volumes, high loading capacity, uniform and tunable pore sizes, and versatile surface functionalization [1]. This synthetic versatility allow i) the incorporation of fluorescent dyes into the silica structure yielding hybrid nanomaterials with excellent optical properties for imaging [2]; ii) the modification of the external surface with biomolecules for active targeting [3]; and iii) coating of the external surface with stimuli-responsive polymers for delivery control [4]. One important challenge remaining in their preparation is the ability to tune their diameter in the range of a few tens of nanometers, with narrow size dispersity, preferably using a simple and sustainable process.

In this communication we will start by presenting a fully controllable low-temperature and purely aqueous sol-gel method to prepare MSNs with user-defined diameters from 15 nm to 80 nm and narrow size dispersity [5-6]. The method also allows modification of the pore structure and offers the possibility of incorporating a luminescent species in the silica network for optical traceability. Control was achieved by tuning the colloidal stability of the assembly of cylindrical micelles that template the MSN synthesis. Using CTAB cylindrical micelles as template and NaOH as catalyst, precise diameter control was achieved either by changing the pH (that controls micelle surface charge) or by adding ionic compounds at constant pH (to tune the ionic strength and charge screening). The specific interactions of salts counterions with surfactant head groups affect their self-assembly properties through intra- and intermolecular forces, and we have rationalized these results based on the Hofmeister series.

We will show how MSNs modified at the external surface with a polymer shell featuring conformational changes induced by pH [7] or temperature [8], can act as precise gate keepers to control cargo release from the MSNs pore system. The nanoparticles feature either a polymer brush or a gel-like responsive shell, produced by grafting from RAFT polymerization that offers low size dispersity and well-defined end-groups. Additionally, the internal surface was modified to interact preferentially with the cargo to improve decrease leakage in the “off” release state. These new methodologies open a new path for the use of hybrid polymer-shell MSNs in theranostics.

This work was partially supported by FCT-Portugal and COMPETE/FEDER, projects UIDB/00100/2020, UIDP/00100/2020 and PTDC/CTM-CTM/32444/2017.

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Polyoxometalate hybrid materials: effects on the photoluminescent properties of lanthanopolyoxometalates

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Polyoxometalates (POMs) are remarkable for their molecular and structural diversity and their significance in diverse fields, such as catalysis, analytical chemistry and materials science. A main class of POM clusters include Mo(VI) or W(VI) and oxygen in their composition but a large variety of elements can be further incorporated. This variability in chemical composition and associated structural diversity confer to this type of compounds an important role for the design of hybrid materials with new electronic, magnetic, optical and topological properties.

In order to obtain new properties in the final material due to the POM as functional unit, the hybrid materials are mostly prepared by integration of POM units in different matrices. Several examples on the preparation of POM-containing functional hybrid materials will be presented. Nanostructured materials were obtained by assembling POMs in Langmuir–Blodgett films or in layer-by-layer assemblies, or by incorporating these large anions in double layer hydroxides or in biopolymer matrices [1]. Also, several POM based materials were prepared by using nanosilicas or graphene as substrates [2,3]. The encapsulation of POM species inside amorphous silica shells has been particularly explored, namely due to the ease of surface functionalization of the ensuing POM/SiO_2 core/shell nanoparticles that allows their use in the fabrication of biosensors, cell labelling and drug delivery systems. Optically active materials were obtained when lanthanide containing POMs were used, or new heterogenous catalysts prepared by incorporating transition metal ions in POMs.

The photoluminescence processes occurring in lanthanopolyoxometalates (LnPOMs) and its assembly into new nanostructured materials were thoroughly investigated. Very often the prepared materials have a hybrid nature due to the presence of a second component coupled with the LnPOMs. Here, preparative strategies and the photoluminescent behaviour of the following types of LnPOM hybrids will be specifically addressed: i) LnPOMs incorporated in solid matrices, thus increasing the stability and handling of the original compounds [2,3]; ii) organic-inorganic hybrid materials in which LnPOMs are used as inorganic components linked to organic moieties (Figure 1); iii) nanocomposites having LnPOMs dispersed in biopolymer matrices [1].

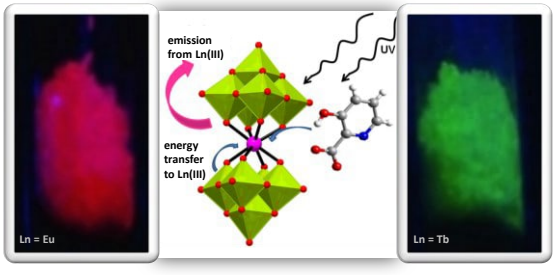

Figure 1 - Lanthanopolyoxometalates as building blocks for photoluminescent organic inorganic hybrid materials.

Acknowledgements: This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC).

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Surface lattice plasmon resonances by direct surface growth of gold nanoparticles in ordered arrays

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Over the last decades, soft-lithography and self-assembly combinations have been developed to incorporate plasmonic building blocks into functional devices. In particular, ordered plasmonic arrays result in photonic structures capable of sustaining surface lattice resonances exploiting the hybridization of localized plasmons with Bragg diffracted modes, achieving long lifetimes and large area delocalization.

In this work, we explored two different approaches for the fabrication of colloidal-based plasmonic arrays for the development of innovative synthetic paradigms for the preparation of solid-state platforms based on catalytic, optical, and magnetic properties of plasmonic nanoaprticles. In the first approach, we used templated self-assembly for the preparation of plamsmonic arrays of silver nanoparticles directly on top of a Rhodamine B gain media. This architecture exibits high Q-factor lattice resonances (> 50) that enable a low treshold (0.3 mJ/cm^2) lasing behavior (**Figure 1, left**). By modifying the lattice parameter of the arrays we demonstrated the possiblity of achieving off-normal lasing emission.

In our second approach, we developed a site-directed *in situ* growth approach based on a reductant chemical ink and a sacrificial hydroxypropyl cellulose stencil capable of producing nanscaled ordered plasmonic arrays over hundreds of microns squared in a single step and within minutes (**Figure 1, right**). This direct *in situ* nanoparticle growth takes advantage of the versatility and high-quality plasmonics of bottom-up synthesis and avoids time consuming ligand-exchange, concentration, and assembly steps that limits scalability and reproducibility of standard colloidal self-assemblies. The technical capabilities of this *in situ* growth method were demonstrated through modulation of particle size and shape directly on the surface *via* wet-chemical synthesis. Moreover, ordered square arrays were successfully synthetized, and their lattice plasmon resonances were measured and fully characterized for different geometries.

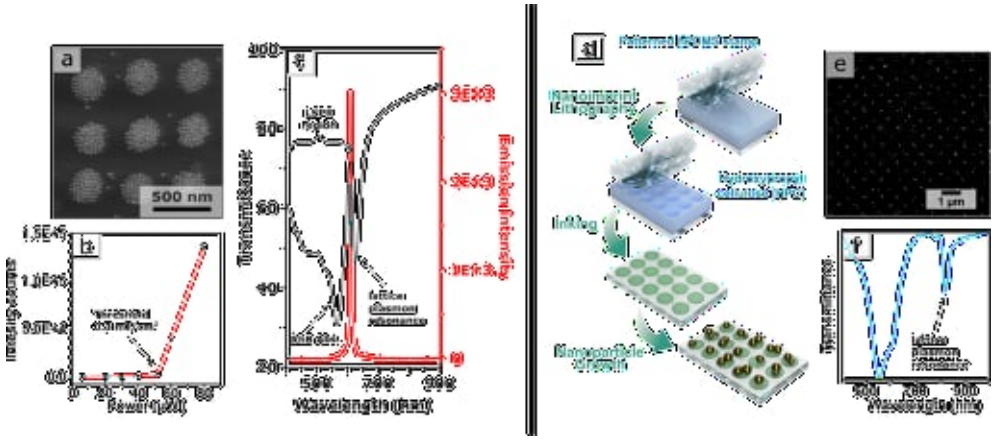

FIGURE 1. Left: (**a**) SEM of a silver nanoparticle square array with a pitch of 400 nm. (**b**) Threshold behavior of the emission intensity as a function of the power density. (**c**) Overlaps between the lasing emission and the trnasmittance at normal incidence. **Right:** (**d**) Schematic of hydroxypropylcellulose stencil fabrication, inking, and gold nanoparticle growth. (**e**) SEM of the *in situ* grown nanoparticle array. (**f**) Transmittance at normal incidence of a gold nanoparticle square array with a pitch of 600 nm.

Acknowledgments
This project had received funding from the Spanish Severo Ochoa Centre of Excellence program FUNFUTURE (CEX2019-000917-S), and from "La Caixa" Foundation Junior Leader-Incoming Fellowship ID 100010434, fellowship code LCF/BQ/PI20/11760028.

Designer Pd nanoparticles for reductive amination using hydrogen: Now one of the best methodology for Reductive Amination?

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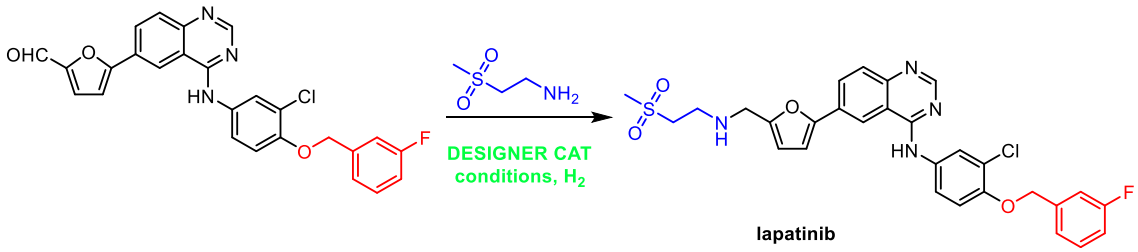
Reductive amination is one of the most important transformations in organic chemistry and is used throughout academia and industry for C-N bond construction.[1]

The most common reducing agents involve hydrides, which leads to significant waste issues and problems at scale-up. Hydrogen (H_2) is seen as a very green alternative. However, a number of challenges remain which halter the widespread use of hydrogen. These include issues associated with using hydrogen at elevated temperatures, pressures and with flammable organic solvents.

Palladium nanoparticles, acting at the interface of homo- and heterogeneous catalysis,[2] possess unique properties, and when judiciously coupled with appropriate stabilizing agents, can effect very precise chemistry.[3,4] Here, in a collaboration with Eli Lilly, we describe how use of a designer Pd nanoparticle catalyst, allows all of the above-mentioned obstacles, to be overcome.[5]



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Halloysite nanotubes as nanocontainers in binder materials

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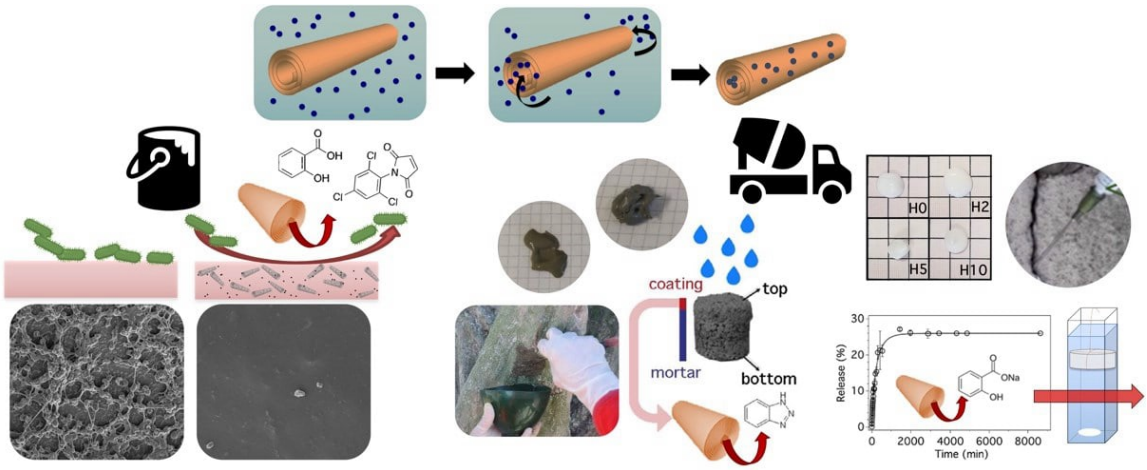
Halloysite nanotubes (HNTs) are eco-friendly aluminosilicate clays ideal for reinforcing purposes, abundant in many locations around the world, cheap, non-toxic, and with a hollow tubular structure which can be loaded with active molecules to obtain a sustained release [1,2]. Nowadays, HNTs are used in many applications, both as nanocarriers and to increase the physico-chemical performances of various materials. The development of binder formulations enriched with inorganic admixtures for the achievement of additional benefits is an innovative approach to develop new materials, and to face the conservation of degraded structures. To this purpose, in some recent works we developed some new composites containing HNTs loaded with active molecules and incorporated in different binders. We showed that these nanotubes can be successfully used in various applications, spanning from the preparation of polymeric coatings endowed with antifouling properties [3], to the formulation of various cementitious materials, specifically tailored for the repair of common damages affecting cement-based monuments. To this purpose, some formulations were prepared using Portland cement and HNTs loaded with benzotriazole for the slow delivery of corrosion inhibitors [4,5], while other quick repair materials were prepared using magnesium phosphate cements, enriched with HNTs to improve their handling and mechanical properties, and to provide slow delivery of antifouling molecules [6]. All these composites were thoroughly characterized with a multi-technique approach and, following the promising results achieved, some formulations were also used by expert restores at the War Memorial of Torricella Peligna (Italy).



Thanks to H2020 InnovaConcrete Project (grant Agreement number 760858), CSGI Consortium, and MIUR-Italy ("Progetto Dipartimenti di Eccellenza 2018-2022" allocated to Department of Chemistry "UgoSchiff").

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Colloidal methods for the fabrication of advanced electrodes for supercapacitors

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Supercapacitor electrodes with high active mass loading of 35-45 mg cm^{-2} were fabricated using colloidal methods based on the use of advanced dispersants and binders. Advanced dispersants, such as celestine blue, gallocyanine, rhamnolipids and murexide were utilized for co-dispersion of inorganic charge storage materials and carbon nanotubes, which were used as conductive additives. MXene-carbon nanotube and Fe_3O_4-carbon nanotube electrodes were developed for operation in a negative potential range. MnO_2-carbon nanotube and Mn_3O_4 -carbon nanotube electrodes were developed for operation in a positive potential range. The dispersants facilitated co-dispersion of MXene, Fe_3O_4, MnO_2, and Mn_3O_4 with carbon nanotubes. The chelating properties of the dispersants facilitated their strong adsorption on the particle surface. Catecholate type celestine blue and gallocyanine dispersants exhibited redox active properties and acted as charge transfer mediators, which enhanced charge storage properties of the electrode materials. Rhamnolipids and murexide were also used as capping agents for the synthesis of Mn_3O_4 nanoparticles of controlled shape and size. The use of capping agents and dispersants allowed for the fabrication of advanced electrodes for operation in Na_2SO_4 electrolyte. The highest capacitance of 6.2 F cm^{-2} was obtained using Fe_3O_4 -carbon nanotube nanocomposites, which were used as negative electrodes. The capacitance of 7.5 F cm^{-2} was obtained for Mn_3O_4 -carbon nanotube nanocomposites, which were used as positive electrodes. Moreover, the use of murexide or rhamnolipids as capping agents for Mn_3O_4 synthesis and co-dispersants for Mn_3O_4 and carbon nanotubes eliminated the need in a time-consuming activation procedure for electrochemical activation of electrodes with high active mass. Good electrochemical performance was achieved using co-polymer binders, which facilitated the fabrication of electrodes with reduced binder content, enhanced capacitance and reduced electrical resistance. The Mn_3O_4 -carbon nanotube electrodes outperformed MnO_2-carbon nanotube electrodes. The advances in colloidal processing of Mn_3O_4-carbon nanotube nanocomposites make such nanocomposites very promising for practical applications. The analysis of testing results provided an insight into the influence of chemical structure and properties of the dispersants on electrode microstructure and performance. Asymmetric devices were fabricated for operation in a voltage window of 1.6 V. The devices prepared using new colloidal strategies showed high capacitance and advanced power-energy characteristics at a low electrical resistance, which were achieved at commercially important high active mass loadings.

Development of hydrophobic paper-based substrates by inkjet printing for SERS detection of pesticides

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Surface-enhanced Raman scattering (SERS) is a versatile analytical technique widely used to detect trace contaminants in water and food.[1] SERS technique offers several advantages such as simple sample preparation, fast detection, high sensitivity and the possibility of on-site analysis, provided that portable Raman instruments are available. Developing materials that can act as highly sensitive substrates in SERS is crucial in this type of surface analysis. In particular, hydrophobic SERS substrates are attracting significant attention because in certain conditions allow the analyte molecules to concentrate in a smaller area of the sensor, thereby increasing its sensitivity.[2]

This communication describes a new strategy to prepare hydrophobic paper-based substrates for SERS analysis (Fig. 1).[3] The substrates have been manufactured by inkjet printing formulations containing Ag colloids and polystyrene (PS) beads emulsions. SERS performance of the substrates was optimized by varying the relative amounts of polymer/metal colloidal nanoparticles on the ink formulation and the number of printing layers, using crystal violet as a molecular probe, which is well known for its strong SERS activity. The selected substrates also proved to be efficient SERS platforms for detecting trace levels of pesticides in water and fruit juices. Using the new hybrid SERS substrates, thiram was detected in spiked mineral water and apple juice at a level of 24 ppb. Therefore, the results of our research demonstrate that the hydrophobic paper-based SERS substrates allow the detection of thiram at concentrations lower than the MRL established by the European Union (Commission Regulation (EU) 2016/1).

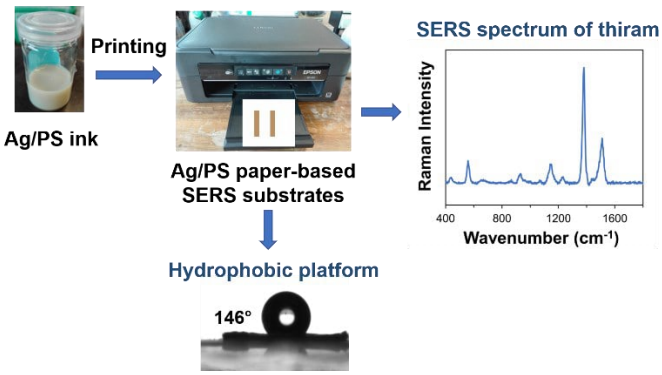

Fig.1. Preparation of hydrophobic paper-based substrates for SERS detection of pesticides

Acknowledgements
This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020 & UIDP/50011/2020, financed by national funds through the Portuguese Foundation for Science and Technology/MCTES. Natércia C.T. Martins and Sara Fateixa are funded by National funds (OE), through FCT- Fundação para a Ciência e Tecnologia, I.P., in the scope of the framework contract foreseen in the numbers 4, 5 and 6 of the article 23, of the Decree-Law 57/2016, of August 29, changed by the law 57/2017, of July 19.

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Peptide-based low-molecular-weight gels as versatile and functional materials

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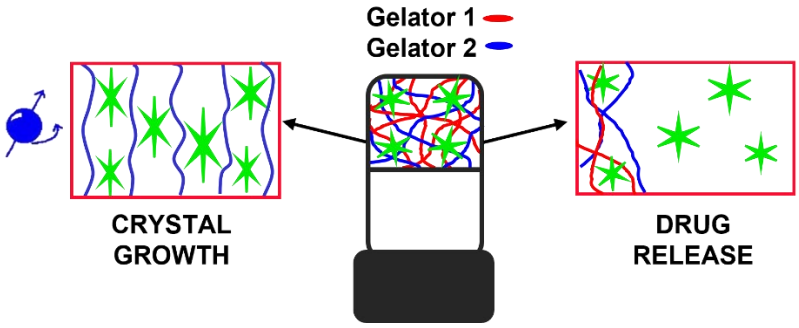
Low-Molecular-Weight Gelators (LMWGs) are compounds able to self-assemble into supramolecular architectures thanks to non-covalent interactions [1]. Peptides are ideal candidates for the preparation of such materials because they are usually biocompatible and can be effectively synthesised and functionalised. The gelation process requires the addition of a trigger (pH change, ultrasound sonication, salt addition), that induces the self-assembly of the gelator molecules into fibres, which over time entangle together forming a network and entrapping the solvent.

The versatility of LMWGs can be foreseen by the wide range of fields in which they are studied and used, including water remediation, [2,3] biomineralization [4] and cell culture [5,6]. The final properties of the materials can be tuned with the gelator structure, its concentration, the solvent and the trigger used. It is also possible to further functionalise the gels with the introduction of fillers or by mixing two or more gelators together in a multicomponent system, tuning the properties for a specific application.

Two works on multicomponent self-assembled gels will be here presented. In the first work, we mixed a LMWG able to crystallise over time and a LMWG which forms worm-like micelles at high pH that can be aligned using a magnetic field and preserve the alignment once the gel is formed. We were able to induce a preferential growth of the crystals in the direction of the aligned gel medium [7]. This system can be exploited to control the kinetic of formation and the shape of crystals formed *in situ*.

In a second work, a tripeptide not able to form gels alone was used to induce the gelation of a second gelator in phosphate buffer solution, acting as both co-gelator and trigger. The ratio between the two peptides influenced the final pH of the gels, in a range useful for both biomedical and cosmetic applications (7.4 - 6.5). These peptide-based self-assembled gels are now studied for the release of drugs and bioactive ingredients, as they represent promising scaffolds for both topical and injectable formulations.



Schematic representation of the multicomponent gels reported. On the left: crystallization in a gel medium aligned with magnetic field; on the right: drug release.

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Magnesium phosphate-based bone cements: physico-chemical study and colloidal approaches to tailor their properties towards orthopedic applications

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Magnesium phosphate-based cements (MPCs) have recently attracted great attention as materials for bone repair, because they possess some characteristics (faster setting, higher early strength, good biocompatibility and superior degradation behavior) that represent a valuable improvement with respect to Calcium Phosphate cements. In addition, *in vitro* studies suggest that Mg^{2+} ions stimulate osteoblast differentiation and inhibit osteoclast formation. [1] This contribution focuses on the most recent results obtained from our group in the investigation of the physico-chemical characteristics of MPCs and in the optimization of some of their features. A thorough investigation on the effect of the preparation conditions on the composition and on the main physico-chemical and mechanical properties will be first presented [2]. Then, this contribution will show that MPCs can be successfully formulated to release active molecules directly on the site of application: in particular, the results of the preparation and characterization of MPCs containing citrate will be presented. The choice of citrate relies on the evidence that it is an ion naturally present in bone, whose supplementation in the proximity of newly forming bone tissue has shown beneficial effects. The release of citrate upon incubation in aqueous media was studied, and we demonstrated that this molecule could be successfully released from the cements, while contributing to the alkalinization of the surroundings. The cytotoxicity of the materials toward human fibroblasts was also tested, revealing the importance of a fine modulation of released citrate to guarantee the biocompatibility of the material. [3] As a last example, this contribution will present an innovative strategy to prepare macroporous MPC cements. In fact, despite the great number of appealing features of MPCs, the lack of macroporosity, fundamental for cells permeation and bone ingrowth, is one of the main limitations hampering their full exploitation. To handle this issue, we used gelatin microparticles (prepared by a water-in-oil emulsion method) as templating agents for the creation of macroporosities. The simple incubation at physiological temperature of the MPCs-gelatin composites allows for gelatin dissolution and endows the inorganic matrix with hundreds-micron sized porosities. This dissolution step can also be used to release active molecules on site (in this case alendronate, a well-recognized drug for the treatment of osteoporosis). The kinetic study of the release phenomena has been studied in detail. [4] The final aim of this talk is to show that a Physico-Chemical and, in particular, a Colloidal Science approach enables to fully exploit the versatility and the potential of these materials, whose properties can be tailored according to specific requirements in the field of bone repair.

Thanks to prof. Nicola Baldini's group (BST Biomedical Science and Technologies Lab, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy) for the cytotoxicity tests and for the invaluable discussion. Thanks to Dr. Samuele Ciattini and Dr. Laura Chelazzi (CRIST, University of Florence) for the technical support in X-Ray micro computed tomography experiments. Thanks to Fondazione CR Firenze, CSGI consortium, Ministero dell'Università e della Ricerca MUR for funding.

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pH responsive pHEMA/PAA hydrogel for the capture of Copper Ions and Corrosion Removal: implication in Cultural Heritage Fields

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In case of metallic objects, cleaning requires a deep knowledge of the alteration processes, especially in case of outdoor monuments, buried or underwater artefacts. The alteration products of Cu-based alloys cause the formation of overlapping structures, characterized by the presence of cuprite (a Cu(I) oxide) at the interface with the metal, and by an external layer of Cu(II) salts. Cuprite represents a protective layer against further corrosion; on the other hand, the presence of Cu(II) salts is usually considered as a symptom of the so called "bronze disease", a particularly dangerous phenomenon induced by the presence of copper oxychlorides (atacamite and paratacamite) [1]. For this reason, an adequate cleaning procedure should aim at the complete removal of the corrosion products while preserving the protective cuprite layer. We propose the formulation and application of novel poly(2-hydroxyethyl methacrylate) (pHEMA) networks semi-interpenetrated (SIPN) with poly(acrylic acid) (PAA) to achieve enhanced capture of copper ions and removal of corrosion products. The pHEMA/PAA SIPNs were designed to improve previous pHEMA/poly(vinylpyrrolidone) (PVP) networks [2], taking advantage of the chelating ability of pH-responsive carboxylic groups in PAA. Increasing the pH ionizes carboxyls, increases the porosity in pHEMA/PAA, and leads to the co-presence of enol and enolate forms of vinylpyrrolidone (VP) [3], changing the macroporosity and decreasing the mesh size in pHEMA/PVP. The ion–matrix interaction is stronger in pHEMA/PAA, where the process occurs through an initial diffusion-limited step followed by diffusion in smaller pores or adsorption by less available sites. In pHEMA/PVP, the uptake is probably controlled by adsorption as expected, considering the porogen role of PVP in the network. Upon application of the SIPNs loaded with tetraethylenpentamine (TEPA) onto corroded bronze, copper oxychlorides dissolve and migrate inside the gels, where Cu(II) ions form ternary complexes with TEPA [4] and carboxylates in PAA or carbonyls in PVP. The removal of oxychlorides is more effective and faster for pHEMA/PAA than its /PVP counterpart. The selective action of the gels preserved the cuprite layers that are needed to passivate bronze against corrosion, and the pH-responsive behavior of pHEMA/PAA allows full control of the uptake and release of the Cu(II)–TEPA complex, making these systems appealing in several fields even beyond Cultural Heritage conservation (e.g., drug delivery, wastewater treatment, agricultural industry, and food chemistry).

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3D printing of magnesium-based cements: towards the preparation of bioceramics

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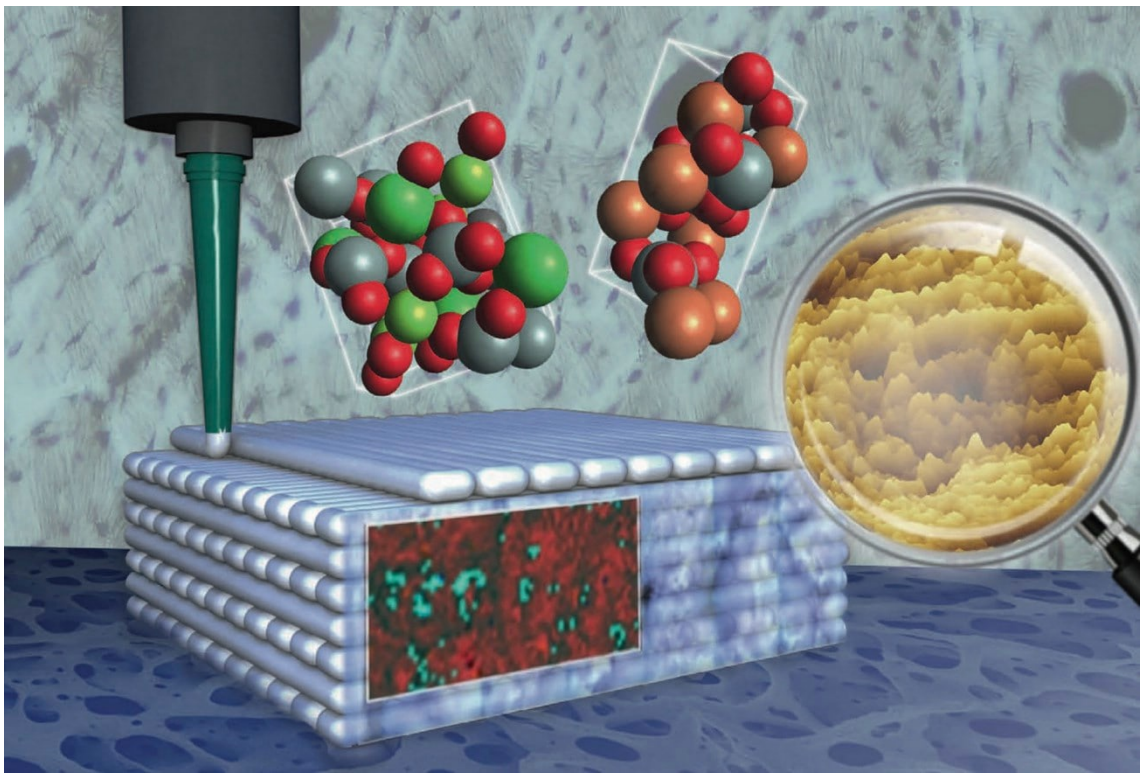
The recent progresses in additive manufacturing (AM) techniques and their exploitation in tissue engineering have imposed the need to develop new processable materials and, at the same time, to implement the properties of the materials already in use, especially in terms of the mechanical properties of the final products.[1,2]

Among all the materials used so far to replace and repair damaged bone tissues, magnesium silicate bioceramics are one of the most promising, thanks to their biocompatibility, osteoinductive properties and good mechanical stability.

In this work, magnesium silicate cement pastes were prepared by hydration of MgO mixed with different SiO_2 batches at different Mg/Si molar ratios. Pastes were either moulded or 3D printed to obtain set cements that were then calcined at 1000 ˚C to produce biologically relevant ceramic materials. Both cements and ceramics were characterized by means of X-ray diffraction, while two selected formulations were thoroughly characterized by means of injectability tests, Raman confocal microscopy, scanning electron microscopy, atomic force microscopy, gas porosimetry, X-ray microtomography and compressive tests. The results show that bioceramic scaffolds, namely forsterite and clinoenstatite, can be effectively obtained by 3D printing MgO/SiO_2 cement pastes, paving the way towards important advances in the field of bone tissue engineering.[3]



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Influence of Amino Acids on the Antibacterial Activity of Copper Oxide Nanoparticles

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Owing to the well-known antifungal and antibacterial properties of copper compounds, Cu-based NPs are currently used as additives in wood preservatives, in antifouling paints and in agricultural pesticides, causing concern about their possible release in the environment [1,2]. However, little is known about the processes to which these materials may be subjected when they come into contact with the different biotic and abiotic components [3]. These interactions between NPs and the surrounding media may affect their environmental fate, as well as their antimicrobial activity. Specifically, ligands present in biological and environmental media may greatly influence particle solubility, aggregation status and surface properties, by attaching to the particle surface, through ligand-assisted ion release and/or through the formation of complexes with copper ions. Aim of this study was to investigate the interactions between CuO NPs and a series of natural amino acids (Arg, Asp, Glu, Cys, Val, Leu, Phe, Tyr), chosen as model molecules to evaluate the effect of ligands on the physico-chemical properties and the antimicrobial activity of these type of nanoparticles. To this purpose, multiple analytical techniques were used to carry out an extensive physico-chemical and colloidal characterization of both pristine and amino acid-treated CuO NPs. These included FTIR, DSC-TGA, ICP-MS, light scattering techniques (DLS, ELS and CSA) and SEM. Moreover, the antimicrobial activity was tested using the Gram-positive bacterium *Staphylococcus epidermidis*. A thorough evaluation of the obtained data allowed to point out the major role played by the nature of the aminoacidic side chain [4]. Examples of physico-chemical characterization and antimicrobial activity of CuO NPs treated with L-Cys are reported in Figure 1.

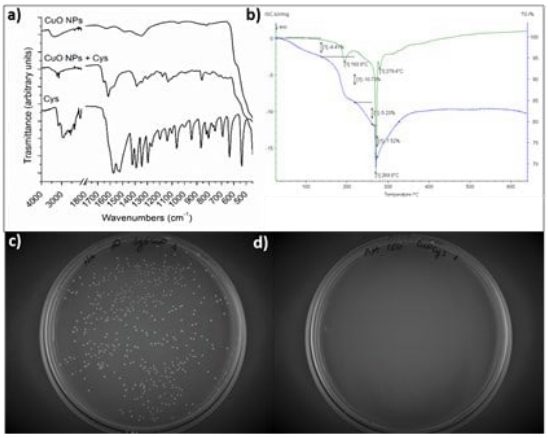

Figure 1: a) FTIR spectra of pristine CuO NPs, CuO NPs treated with L-Cys and pure L-Cys. b) TGA-DSC analysis of CuO NPs treated with L-Cys. c) and d) Optical microscope pictures of Gram-positive bacterium *Staphylococcus epidermidis* in Nutrient Agar plates with CuO NPs-Cys at concentrations of 10 and 160 μg/mL respectively.

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Visible-light driven $BiVO_4$ photocatalysts for the degradation of contaminants of emerging concern

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Heterogeneous semiconductor photocatalysis has attracted great interest among available Advanced Oxidation Processes (AOP) applied to wastewater decontamination [1]. These methods have been regarded as particularly effective alternatives for eliminating certain organic pollutants, potentially harmful for living organisms even if present in small amounts.

Among the photocatalysts explored in this context, TiO_2 stands as the most prominent material, forming the basis of several photocatalytic technologies, already implemented in certain practical contexts [2]. However, the optical band gap of pure TiO_2 is in the UV region, and visible photons are not harvested in the photocatalytic process. Although this limitation has been tackled by several strategies that use TiO_2 materials, there is a clear interest to develop other semiconductors whose band gap is located in the visible spectral region. In particular, bismuth vanadate ($BiVO_4$) has been investigated as a photocatalyst of interest due to the ability to harvest photons efficiently in the visible spectral region [3]. In addition, powdered $BiVO_4$ shows high photochemical stability, good dispersibility and resistance to corrosion in oxidative conditions. On the other hand, carbon-based materials have also attracted great importance due to their unique properties. The implementation of chemical routes aiming to combine these two types of materials opens new routes for the development of innovative clean water technologies [4,5].

In this context, we have investigated the *in-situ* growth of monoclinic $BiVO_4$ nanoparticles on carbon spheres obtained by the hydrothermal carbonization of *κ*-carrageenan, a biopolymer extracted from red seaweeds. The carbon supported photocatalysts were prepared by varying a range of experimental conditions, allowing to select materials showing exceptional chemical stability and well-defined particle morphology for specific synthesis conditions. The ensuing carbon supported photocatalysts were then investigated in the degradation of tetracycline (TC) dissolved in water, for distinct operational conditions, such as the presence of H_2O_2 and their reuse in further catalytic cycles. Noteworthy, the materials described in this communication have shown better photocatalytic activity, as compared to the powders of pure monoclinic BiVO4, for similar conditions. The potential application of these hybrid photocatalysts in the degradation of contaminants of emerging concern will be discussed, taking into consideration the results obtained so far for water samples spiked with TC.

A.C. Estrada acknowledges the research position funded by national funds (OE), through FCT-Fundação para a Ciência e a Tecnologia, I.P., in the scope of the framework contract foreseen in the numbers 4, 5 and 6 of the article 23, of the Decree-Law 57/2016, of August 29, changed by Law 57/2017, of July 19. J. L. Lopes thanks FCT for doctoral grant SFRH/BD/126241/2016. This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC).

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Targeting respiratory syncytial virus replication by antiviral molecules

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Respiratory syncytial virus (RSV), responsible for bronchiolitis and pneumonia, represents an important cause of hospitalization and mortality of young children. However, there is no vaccine and no efficient treatment against this virus. Therefore, new specific and cost-effective anti-RSV therapeutics would cover a real medical need. Several viral cycle steps are potential targets for the development of antiviral drugs. Most RSV antiviral molecules in preclinical or clinical studies target the entry of the virus into the host cell, by blocking the fusion step between virus and cell membranes via two surface proteins, RSV F and G. An alternative strategy chosen in this work, is to target the viral RNA polymerase complex responsible for the synthesis of viral mRNA during transcription and genomic RNA during replication. This complex is virus specific, and there are no counterparts in non-infected cells. For this purpose, we suggest inhibiting the interaction between two RSV proteins by small molecules, *i.e.* the interaction between the nucleoprotein (N) and the phosphoprotein (P) [1]. We have previously shown that the interaction between RNA-bound N, as found in the RSV nucleocapsid, and P is required for RSV transcription and replication [2]. We also obtained structural data at high resolution for this interaction and identified a compound able to inhibit it [3]. In order to identify new anti-RSV candidates, we develop three complementary strategies in parallel: pharmacomodulation of the first hit, a peptidomimetic approach and *de novo* exploration on the target. To evaluate the capacity of small compounds or peptides to inhibit the N-P interaction, we designed and optimized a fluorescence polarization (FP) assay, using a fluorescent peptide that mimics the C-terminus of the P protein and binds to N. By testing different conditions, in particular different fluorescent P peptides, we also got closer insight into the formation of the fuzzy N-P complex, highlighting the binding properties of the intrinsically disordered P protein [4,5]. High Throughput Screening of Fr-PPIChem compounds library [6] was performed. Identified hits are being optimized and validated in cellular assays using a recombinant virus [1].

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Synthesis and *SAR* study of novel cytotoxic butanolide

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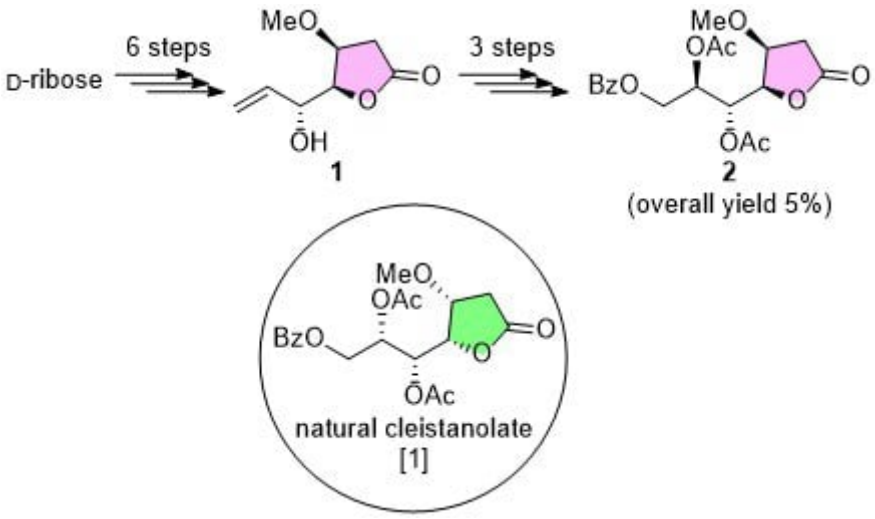
Natural cleistanolate is isolated from methanol extract of *Cleistochlamys Kirkii* (Annonacae) in 2017 [1]. This plant is located in eastern and southern Africa where it is traditionally used as medicine for tuberculosis, rheumatism and healing wounds [1–3].

Herein, we report the synthesis of novel cytotoxic butanolide **2** which is stereoisomer of natural product. Unsaturated lactone **1** was used as a key intermediate in this synthesis (Scheme 1). Additionally, antitumour activity of compound **2** is evaluated and its cytotoxicity will be compared with its' analogues which has been already synthesized in our laboratory.



Scheme 1. Cytotoxic butanolide **2** and natural cleistanolate [1].

Thanks to financial support of the Ministry of Education, Science and Technological Development of the Republic of Serbia (Grant No. 451-03-68/2022-14/200125) and (in part) research projects from the Serbian Academy of Sciences and Arts (Grant No. 01-2019-F6501-2019-F65 and F-130).

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Design and synthesis of novel ligands for the flavin mononucleotide riboswitch

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To prevent the looming antimicrobial resistance crisis, we need to discovery new antibiotics with new mechanisms of action. The WHO published a few years ago a list of bacteria for which antibiotics are in high demand and urged that research and drug discovery efforts are directed toward these bacteria [1].

Riboswitches, which are mostly found in bacteria are considered as one promising class of targets for future antibiotics with a novel mechanism of action [2,3]. Riboswitches are *cis*-acting gene regulatory elements which are located to the 5' untranslated region of mRNAs. They consist of an aptamer domain that binds to small ligands (typically an important metabolite) and an expression platform that controls the expression of the downstream gene(s) which are involved in the synthesis or uptake of the metabolite.

The flavin mononucleotide (FMN) riboswitch is found in 41 human pathogens and is the 3rd most widespread riboswitch known [3], however, only a limited number of FMN riboswitch ligand classes are known. These are ribocil A-C (discovered by Merck), synthetic FMN analogues and the natural product roseoflavin [4]. Based on results from virtual screening combined with information on the binding modes of FMN and ribocil, we have designed 5 different compound series and developed synthetic routes to these. These efforts have resulted in the identification of several compound series that show binding affinities toward the FMN riboswitch in the low micromolar range. The design and synthesis of these compound series will be reported herein.

This work was supported by the Research Council of Norway (FRIMEDBIO and BIOTEK2021 programs and the JPI-EC-AMR initiative) and by the University of Bergen.

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Photoactivated cell-killing amino-based flavylium compounds

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Six amino-based flavylium dyes (5OH4'NMe_2, 5,7$OH_2$4'NMe_2, 5,7OH_2st4'NMe_2, 7$NEt_2$4'NMe_2, 7NEt_2st4'NMe_2 and 7$NEt_2$4'NH_2) were synthesized through acidic aldolic condensation reaction between 2,4,6-trihydroxybenzaldehyde or 4-diethylaminosalysaldehyde with different acetophenones (4-amino– or 4-dimethylamino–acetophenone or *p*-(dimethylamino)-phenyl-but-3-en-2-one). Compounds presenting a 2-styryl linkage have a higher maximum absorption wavelength, probably resulting from their extended electronic delocalization. On the other hand, the presence of stronger electron donating groups such as dimethyl- or diethyl-amino leads to a bathochromic shift in the maximum absorption wavelength of dyes when compared to the ones presenting hydroxyl groups or a primary amine [1].

This work also reports the study of their potential as photosensitizers towards topical PDT. 7$NEt_2$4'NMe_2, 7NEt_2st4'NMe_2 and 7$NEt_2$4'NH_2 showed significant fluorescence quantum yields (from 3.40 to 20.20%) and production of singlet oxygen ($^1O_2$). IC50 values regarding the growth inhibition of keratinocytes were between 0.9 and 1.5 µM, after 10 min of photoactivation with a white light. This cellular damage in keratinocyte cells upon white light activation was accompanied with the production of reactive oxygen species (ROS). It was also found that the compounds can induce damage by either type I (ROS production) or type II (singlet oxygen) PDT mechanism, although a higher cell survival was observed in the presence of $^1O_2$ quenchers. Overall, a structure-activity relationship could be established, ranking the most important functional groups for the photoactivation efficiency as follows: C7-diethylamino > C4'-dimethylamino > C2-styryl [2].

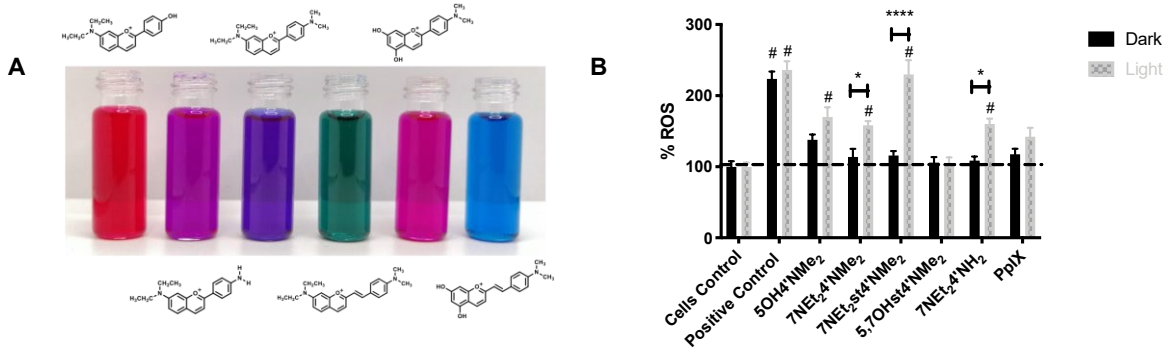

Figure 1 – A) Synthesized amino-based flavylium dyes and respective color in methanol [1]. B) Production of Reactive Oxygen Species (ROS) by the different compounds at 25 µM upon white light irradiation (6.6 J cm-2) or in dark maintenance. As Cells control, cells were not treated with any compound but the addition of DCF-DA was performed. As positive control the cells were treated with H_2O_2 (100 µM) 30 min prior to the addition of DCF-DA to induce a high production of ROS [2].

Acknowledgements: P.A. and A.R.P. gratefully acknowledge their doctoral grants from FCT (SFRH/BD/143309/2019 and SFRH/BD/146549/2019, respectively). The authors thank AgriFood XXI I&D&I project (NORTE-01-0145-FEDER-000041) cofinanced by European Regional Development Fund (ERDF), through the NORTE 2020 (Programa Operacional Regional do Norte 2014/2020).

Funding: This work was financial supported by the Associated Laboratory for Sustainable Chemistry, Clean Processes and Technologies LAQV through the national funds from UIDB/50006/2020 and UIDBP/50006/2020.

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Development of New Toll-Like Receptor 4-directed adjuvants and Clarification of their Mechanism of Action

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Vaccines are one of the most cost-efficient approaches to tackle infectious diseases. They aim to provide a specific protection to a certain pathogen by inducing a long-lasting immune response.[1] Nowadays, subunit vaccines are a very attractive approach but, despite having clear advantages in respect to the conventional vaccines, subunit vaccines are less immunogenic since they are developed using an antigen or a combination of antigens and do not contain the entire pathogen. [2] Therefore, they can be formulated with an adjuvant to increase their ability to provide an adequate immune response in order to enhance the immune response of the antigen as well as its durability.[3] TLRs can recognize pathogen-associated molecular patterns (PAMPs) in different cellular compartments and trigger key immune cellular events.[4] TLR4 is one of the most important receptors of this family since it binds to the bacterial lipopolysaccharide (LPS) and is able to rapidly initiate innate immune responses.[5]. LPS binding triggers the formation of the complex TLR4-MD2 which then interacts with adaptor proteins MyD88 and TRIF, activating two different intracellular pathways.[6] Both pathways result in the generation of pro-inflammatory cytokines and T and B-cell antigen specific responses.[3] The approval and commercialization of 3-*O*-desacyl-4'-monophophoryl lipid A (MPLA), which is a detoxified portion of LPS, extracted from *Salmonella minnesota*, shows that TLR4 targeting adjuvants are a promising strategy in vaccine development .

This project aims to design and synthesise new glycolipid-based TLR4 agonists that can be used as vaccine adjuvants and clarify their mechanism of action using different cell-biology techniques. In our group, new TLR4 agonists have been synthesised based on the structure of lipid X, a monosaccharide precursor of the LPS's Lipid A. [7] Lipid A is a glycolipid portion of LPS that corresponds to the minimal portion required to activate TLR4 signalling. A small library of triacylated and mono or di-phosphate monosaccharide FP derivatives was obtained by means of a six-step synthesis. Furthermore, C6 functionalization of the sugar moiety was achieved yielding new promising derivatives. Their biological characterization was done on a human macrophage cell line (THP-1 X-Blue) and on human blood-derived macrophages using ELISA and western blot techniques to measure cytokine production, namely TNF-α, IL-6 and IL-1β and protein expression. Confocal imaging techniques followed by high content analysis were also used to follow the activation of intracellular inflammatory pathways using fluorescence labelling and digital phase contrast. Preliminary data shows that C6 functionalization of FP derivatives results in an increased TLR4 activation.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 860325.

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Structural investigation of human cystine/glutamate antiporter Sx_c^- using homology modeling with multiple templates and molecular dynamics simulations

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The cystine/glutamate antiporter system x_c^- (Sx_c^-) is a main plasma membrane transpoter that mediates the cellular uptake of extracellular cystine in exchange for exporting glutamate [1]. Its rate of of cystine uptake in turn regulates the biosynthesis of intracellular glutathione (GSH), a tripeptide thiol crucial in drug resistance and protection of cells against oxidative stress [2]. Overexpression of Sx_c^- has been found in liver cancer, breast cancer and cell lung cancer [3–5]. Moreover, it is linked with multiple functions of the central nervous system and is very important for the glutamate balance in many brain region [6–8]. Accordingly, this transporter is considered a relevant drug target for the treatment of cancel as well as neurological diseases like Alzheimer's, Parkinson's, Huntington's... In the present work, we present four main conformations of system x_c^- using multiple-template homology modeling and molecular dynamic simulations. Comparison with a recently published, relatively high-resolution Cryo-EM inward open structure of Sxc-, revealed an excellent agreement in overall distribution and position of helices and loops, except for the positions of the C-terminal helix and the intracellular half of the 6th transmembrane helix. This confirms the validity of our model of the inward-open state and reveals a remarkably high accuracy of our homology modelling protocol for this particular protein. Intriguingly, the same protocol yielded additional conformations which appear to correspond to other stages in the transport mecanism. In addition, our inward-open model contains a well-formed lateral N-terminal helix preceding TM1, which is not resolved in the experimental structure and may fulfill a "gating" role in the transport mechanism. Therefore, our structures including this domian were subjected to MD simulations, out of which a consensus conformation was used as a target for virtual screening. While the resulting compounds proved modestly potent, the structures and methodology in the present work are a promising starting point for future drug design efforts against this interesting target.

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Spirooxadiazoline oxindole: a new antiplasmodial chemotype with dual-stage activity.

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The current arsenal of drugs comprises different types of molecules, including peptides/proteins, nucleic acids, and small molecules. This latter class covers a limited portion of the chemical space [1], and there is still an urgent need to disclose unexplored chemotypes to address novel diseases, as well as to overcome drug resistance to available drugs. In this context, the spirooxindole scaffold is the basic core of bioactive products of natural and synthetic origin, with two derivatives in clinical trials: APG-115 in Phase I for advanced solid tumors, and cipargamin in Phase II for malaria. In the future of medicinal chemistry, the spirooxindole core will continue to be an important scaffold for the development of novel drugs for several diseases [2]. In particular, malaria is a prevalent parasitic infectious disease with high mortality, especially among young children. Due to drug resistance responsible for the failure of the current treatments, new chemotypes with different mechanisms of action and activity against multiple stages of the parasite life cycle are urgently needed for the prevention and eradication of malaria worldwide [3].

In this communication, we report a new chemotype that combines two privileged scaffolds in medicinal chemistry (the oxadiazoline and the indolin-2-one) acting as dual-stage antimalarial [4]. Specifically, we report the synthesis of a novel library of spirooxadiazoline oxindoles, which was obtained by 1,3-dipolar cycloaddition of isatin derivatives with nitrile imines (formed *in situ* from hydrazonyl chlorides). Activity screening against the blood-stage of the chloroquine-resistant *P. falciparum* W2 strain, and against the liver-stage of the rodent parasite *P. berghei* led to the identification of seven new spirooxadiazoline oxindoles with dual-stage antiplasmodial activity, not cytotoxic in mammalian cells. To shed light on the mechanism of action of these compounds, we have performed a ligand-based molecular modeling study to compare the chemical and shape features of our bioactive compounds with known antimalarials. From this study, cipargamin has emerged and our most active spirooxadiazoline oxindole derivative was evaluated as *Pf*ATP4 inhibitor (target of cipargamin). Despite some evidence for inhibition of *Pf*ATP4 at high concentrations, the inhibition of this protein does not seem to be the primary mechanism of action of our bioactive compounds. The identified promising spirooxadiazoline oxindole represents a promising starting scaffold to search for novel antimalarials, combining excellent activity against both stages of the parasite's life cycle with low cytotoxicity.

This work was supported by FCT through iMed.ULisboa (UID/DTP/04138/2019), project PTDC/QUI-QOR/1304/2020, Ph.D. fellowship SFRH/BD/137544/2018 (E. Lopes), LISBOA-01-0145-FEDER-402-022125 (with Portugal 2020), OpenEye Free Academic Licensing Programme and Australian Red Cross Lifeblood.

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Synthesis Of Antineoplastic Pro-Drugs Activated Under Hypoxia Conditions

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Cancer is a generic term used to describe a group of at least a hundred diseases that occur when malignant forms of abnormal cells grow and develop in one or more body organs. It is a disease which has disturbed researchers and oncologists for decades.

Novel strategies of chemotherapy have been developed to fight against it. However, the main problem with antineoplastic drugs is their lack of selectivity. Since the drugs designed are usually toxic both to tumor and healthy cells, this effect can damage cancerous tissues but also cancels the regeneration of the healthy tissues by producing side effects in the body like vomiting, dizziness, hair loss or lack of nail growth. Consequently, it is important to develop new drugs as new strategy to target cancer cells selectively.

In the present project, it is proposed to exploit the fact that tumor cells present very small concentration of oxygen, less than 1%. This fact is due to the rapid growth of tumor cells that cannot be followed by the effective growth of capillaries, so that cancer cells do not receive enough oxygen to maintain the original phosphorylative oxidation, and they use a metabolism based on glycolysis. This change affects the environment in which the tumor cell develops, since now the generation of lactic acid decreases the pH of the medium, new carbonic anhydrases appear, and a reducing medium is generally generated in which the amount of glutathione is generally high. Hypoxia-activated prodrugs (HAPs), also referred to as bioreductive drugs, are compounds that can be selectively reduced under hypoxic conditions to form cytotoxic agents that precisely target hypoxic tumor cells. These changes in cellular metabolism can be exploited to find drugs that act selectively on tumor [1], drugs that only show their high toxicity in reducing environments, in which glutathione produces the structural changes necessary to activate the drug.

The proposal of this project is to attach drugs whose antineoplastic activity is well recognized to protecting groups such as disulfide bonds [2] and nitro groups which under hypoxic conditions allow the drug to be released and show its lethal activity against the cancer cell, while keeping the normal cell in good condition.

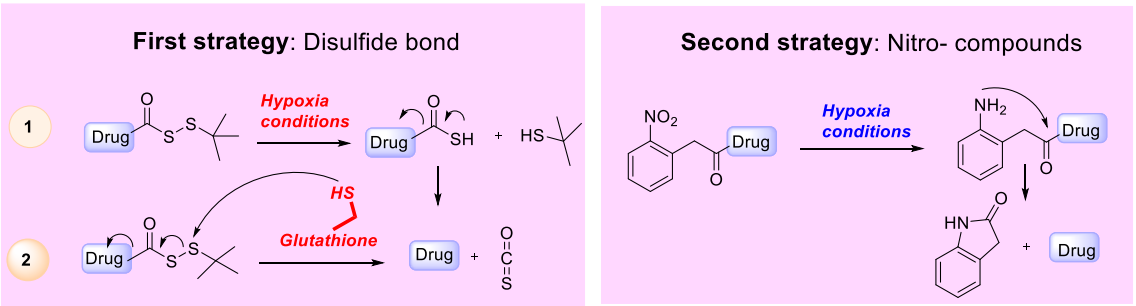

Figure 1. Strategies to target cancer cells.

This work was supported by MICINN (PID2020-118732RA-I00 and PID2019-108994RB-I00), Junta de Castilla y León (European Regional Development Fund-SA069P17), the University of Salamanca (Own Research Programs-KCEP/463AC01 and 18K155/463AC01) and Fundación Memoria de D. Samuel Solórzano Barruso (FS/8-2019). JJGG is gratefully acknowledged to University of Salamanca and Santander Bank for a postdoctoral fellowship. AH is grateful to the Algerian Government for a predoctoral fellowship for "Formation Doctorale résidentielle à l'etranger".. ALFA thanks the Spanish Government for a Beatriz Galindo Fellowship (BG20/00233). NUCLEUS platform at University of Salamanca, especially Anna Lithgow (NMR Service) and César Raposo and J. F. Boyero Benito (MS Service).

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Synthesis of bio-based polyester from microbial lipidic residue for biomedical application

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In the last decade, selectively tuned bio-based polyesters have been increasingly used for their clinical potential in several biomedical applications, such as skin tissue engineering, bone, and wound healing, and drug delivery, among other applications [1], [2].

This work describes the synthesis and characterization of a polyester, using the microbial oil residue collected from distillation after β-farnesene (FDR) industrial production by genetically modified yeast, *Saccharomyces cerevisiae* [3].

For that purpose, a flexible polyester was prepared by melt-polycondensation of FDR polyol with azelaic acid, together with a chain extender, cross-linker, and mechanical enhancer [4].

The synthesized polyester exhibited good mechanical (elongation up to 110 %) and thermal performance at high temperatures (Tm = 167.8 ºC). *In vitro* biodegradation revealed a mass loss of about 87 % after storage in PBS solution for 11 weeks under accelerated conditions (40 ºC, 75 % RH). The water contact angle (70 %) showed a hydrophilic character, and the biocompatibility with skin cells was demonstrated (HaCat- Presto Blue). 3D and 2D scaffolds were produced by salt-leaching, and a controlled release study at 30ºC was performed with Rhodamine B base and curcumin, showing an average adsorption capacity of 1.6 mg Rhodamine B/g of 3D scaffold while 2D scaffolds adsorbed about 0.64 mg curcumin/g. The release showed a diffusion-controlled mechanism with about 29.3 % of rhodamine B base released after 48 h and 50.4 % of curcumin, after 7 h.

In the light of a circular economy, the valorization of a waste stream in the synthesis of a bio-based polymer offers a sustainable and eco-friendly alternative [5] for the potential use in the controlled release of active principles for wound dressing applications.

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Photocross-linked gelatin methacryloyl microparticles prepared by double emulsion method for drug delivery

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Gelatin, a protein-based biopolymer, has been extensively studied for many applications in the biomedical field, such as drug delivery vehicles, also in the form of porous microparticles [1], or scaffolds for adhesion and proliferation of anchorage-dependent cells [2], due to its excellent biocompatibility, and versatility. Despite the great advantages, gelatin's use is hindered due to its reversible sol-gel transition, which leads to a strong increase of gelatin solubility in water at physiological temperature. Therefore, gelatin systems often require a chemical cross-linking treatment to enhance their stability against dissolution and, consequently, to extend gelatin's applicability. Considering that conventional cross-likers, such as glutaraldehyde, have raised some concerns in terms of cytotoxicity, the introduction of acryloyl moieties has been proposed as a more biocompatible alternative. Gelatin methacryloyl (GelMA) is a photopolymerizable gelatin derivative that has been proven to be suitable for tissue engineering [3] and drug delivery [4] applications. Although GelMA microparticles obtained with a single emulsion approach have been already proposed in the literature [5,6], to our knowledge this is the first study where the double emulsion method is combined with photocross-linking treatment.

We prepared porous microparticles (GMA-MP) starting from gelatin methacryloyl using an oil-in-water-in-oil emulsion (O/W/O) and then cross-linked with a photopolymerization treatment. GelMA with different degrees of substitution (DS) was synthesized using a novel approach, proposed by Shirahama *et al.* [7], which allowed to obtain high DS (90 % and more) using relatively low amount of methacrylic anhydride. All the GelMA formulations have successfully led to the formation of porous microparticles. The effects of the DS and cross-linking on the structural properties, including size and surface porosity, of GMA-MP were assessed by optical and electron microscopy. The swelling properties and stability against dissolution of GMA-MP were evaluated, while X-rays scattering was used to shed light on the influence of the cross-linking on the gelatin network structure at the nanoscale. As expected, an inverse correlation between GMA-MP swelling abilities and cross-linking degree was observed, with a difference of about two times in terms of absorbed water between the lowest and highest DS. The cross-linking extends microparticles' stability in water at 37 °C from a few minutes up to several days. The resulting GMA-MP were tested for their drug release properties using methylene blue as a model drug, at two different temperatures (*i.e.*, 20 °C and 37 °C). To obtain information about the transport mechanism, the data were fitted according to the Weibull model. The analysis of the experimental results demonstrates that gelatin methacryloyl microparticles, obtained by double emulsion approach, can be cross-linked with a photo-treatment. The direct control of the cross-linking density enables tailoring the swelling and release properties of the gelatin microparticles.

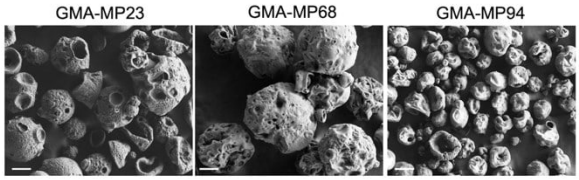

Figure. FE-SEM micrographs of photocross-linked gelatin methacryloyl porous microparticles prepared by double emulsion method. The scale bar is 100 µm.

Thanks to CSGI and MIUR-Italy ("Progetto Dipartimenti di Eccellenza 2018−2022" allocated to Department of Chemistry "Ugo Schiff") for the financial support. This work benefited from the use of the SasView application, originally developed under NSF Award DMR-0520547.

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Tailor-Made, Self-Healing Hydrogels For Biomedical Applications

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3D cell cultivation plays an invaluable role in a broad variety of applications in the medical field, especially in cell culture and tissue engineering. In recent years, research interest had been focused on modulating hydrogels as a cell cultivation platform.[1] Hydrogels are 3-dimensional, water-swollen networks of crosslinked polymers with mechanical properties that are similar to natural tissues.[2]

In order to control stem cell differentiation and enable cell migration, the elasticity compliance between cells and their hydrogel matrix is an important factor.[3–6] However, it remains a challenge to stabilize cells mechanically while enabling their mobility as they evolve.[7]

A promising solution for this problem are reversibly crosslinked hydrogels in which polymer chains are connected by physical interactions. In this study, biocompatible and reversible crosslinks are designed on the basis of host-guest interactions between the host molecule β-cyclodextrin (β-CD) and the guest molecule adamantane. By mixing adamantane-modified and β-CD-modified polymers in an aqueous medium, fast gel formation takes place. The permanent association and dissociation process of the two complexing molecules renders the hydrogel self-healing and therefore provides a flexible environment for cells (Figure 1).
Composition and dispersity of the polymers was controlled by NMR and SEC, respectively. Varying the crosslinker concentration had a strong influence on the mechanical properties of the generated materials. In particular, rheological characterization by amplitude and frequency sweeps showed enhanced stiffness and elasticity of the hydrogels with increasing crosslinking density. Thus, by changing the amount of adamantane and β-CD in the polymer, the elastic modulus can be fine-tuned to study how cells respond to defined mechanical inputs. Moreover, step-strain measurements demonstrated the self-healing properties of the hydrogels.
Cell viability assays in presence of the host and guest polymers using COS7 cells confirmed the very good biocompatibility of the system components. Hence, these tailor-made, self-healing, elastic hydrogels present a very promising approach for basic cell biological investigations and applications in tissue engineering.

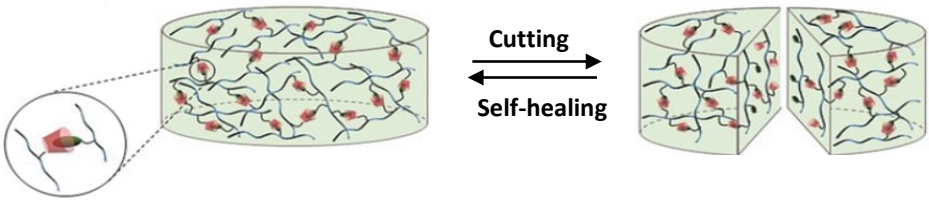

Figure 1: Cutting and self-healing of a host-guest hydrogel.[8]

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Nature-based 3D bioprinted films for controlled in-situ synthesis of bactericides

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Nature-based approaches make up one of the key areas of current scientific development as society shifts towards sustainability. Certain natural remedies can be used to halt the emerging threat of multi-drug resistant bacteria. In our research, we try to replicate the natural antibacterial mechanism of garlic (*Allium sativum*) based on allicin – an unstable volatile thiosulfinate. This compound is produced by the rapid transformation of a sulfoxide alliin catalyzed by the enzyme alliinase. In nature, this reaction occurs upon mechanical damage to garlic cell membranes during the bacterial attack. The active substance is formed but, thanks to its volatility and low stability, the development of bacterial resistance is hindered significantly.[1] However, this advantageous behavior also prevents the direct use of allicin in medicinal products.

Here, it is addressed via systems containing separately both alliin and immobilized alliinase. [2] The enzyme is immobilized and stabilized in biopolymers. [3] Hydrophilic alliin is encapsulated inside a water/wax emulsion with the wax melting at 37 °C. Thus, the reaction is then triggered environmentally by contact with the human body (temperature and presence of moisture).

Porous thin films were chosen as the final formulation for this system. It combines layers of immobilized alliinase in hydrogels and water/wax emulsion containing alliin. For film production, we used 3D bioprinting – a process widely used in tissue engineering for its relatively high resolution and compatibility with enzymes or living cells. It is based on the extrusion printing of hydrogels (´bioinks´) with good printability and the ability to maintain the desired shape post-printing. [4] In this case, the shape maintenance is realized through the bioink's transition from viscous liquid to a hydrogel/solid-state upon cooling. For this technique, two types of bioinks were developed: *i)* alginate-gelatine hydrogel for the immobilization of alliinase (hydrogel transition upon cooling of gelatine), *ii)* water-wax emulsion bioink containing alliin (solidification upon cooling of the wax). Moreover, we characterized the properties of bioinks (rheology) and thin films of varying porosity and composition (tensile strength, water absorption). Finally, we evaluated the antibacterial properties of our products using a modified disc diffusion method.

This work was supported from the OP RDE registration no.:CZ.02.2.69/0.0/0.0/19_073/0016928", funded by the ESF.

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Bioinspired Tunable Laminarin Biomaterials for Biomedical Applications

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Based on nature, bioadhesive systems often show useful qualities that have inspired many studies to clarify their adhesive mechanisms and mimic their functionality to improve the performance of actual available synthetic adhesive systems. For example, the adhesive pads on geckos suggest methods for creating strong and reversible dry adhesion, leading to mimicry of gecko adhesive functionalities.[1] Also, the marine environment encompasses an enormous number of invertebrate organisms glued to wet surfaces due to particularly adhesives.[2] These adhesives are secreted by marine sessile organisms, such as mussels, barnacles, and marine tubular worms, and adhere effectively and strongly to almost any underwater surface.[2] Combining these active biomolecules present in the proteins secreted by the organisms, such as catechols, and take the advantage of the use of marine polysaccharides due their desirable biological and physicochemical properties, including i) biocompatibility, ii) biodegradability, and iii) versatility in modification, is possible to develop ground-breaking biomaterials for biomedical applications.[3]

The development of a personalized biomaterial that comprises all the key features all-in-one, such as a) improved vascularization, b) bioactivity towards tissue regeneration, c) easy appliance and d) avoid host-rejection, remain a major research topic nowadays. Here we will focus on the development of simple and selective chemical methodologies to be applied in Laminarin (LAM), [4-5] a natural origin polysaccharide from brown algae, modifying its chemical backbone structure, for further conjugation with different small molecules, such as active -functional or -catechol groups (Figure 1). Herein, novel derivatives were prepared and used to produce several LAM-based biomaterials with potential for Tissue Regeneration purposes. Diverse chemical modification steps, such insertion of -functional, -allyl, -alkyl, -azide, -methacrylated and -catechol groups, are reported. Characterization techniques of the derivatives (^{1}H NMR, FTIR, UV-Vis and SEM) and the final properties of the develop biomaterials (microparticles, hydrogels and cryogels) will be shown and discussed.

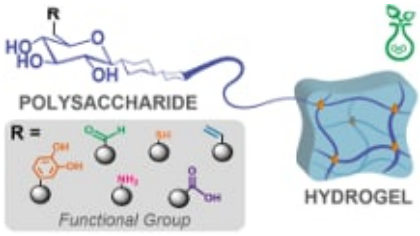

Figure 1 – Chemical modifications of LAM polysaccharide

This work was developed within the scope of the project CICECO – Aveiro Institute of Materials, (UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020) and project COP2P (PTDC/QUI-QOR /30771/2017, POCI-01-0145-FEDER-030771), financed by national funds through the FCT/MEC (PIDDAC) and when appropriate co-financed by FEDER under the PT2020 Partnership Agreement. J.M.M.R (CEECIND/01363/2018) and E.J.C. (SFRH/BD/144880/2019) also thanks FCT for the individual contract and PhD grant, respectively.

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Carbon xerogels as a purification platform for L-asparaginase purification

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L-asparaginase (ASNase, EC 3.5.1.1) is an enzymatic biopharmaceutical used as chemotherapeutic agent for acute lymphoblastic leukaemia (ALL) treatment [1]. Since patients with ALL cannot synthesize L-asparagine due to the absence of asparagine synthetase, the starvation of serum asparagine by ASNase leads to selective death of tumour cells. Current techniques for therapeutic enzyme purification are focused on the use of chromatography, which is highly costly and time-consuming [2]. Compared to conventional approaches, the use of nanomaterials in medical applications presents massive advantages due to their peculiar properties and biocompatibility. Carbon xerogels (CXs) are known for their unique properties such as high surface area, customizable porosity and high adsorption capacities [3].

This work aims the development of an efficient and fast strategy for cost-effective ASNase purification. For that, pristine and functionalized CXs were studied as a purification platform for ASNase from a cell extract of *Bacillus subtilis*. Different operating conditions were studied during cell extract adsorption onto CXs, such as cell extract concentration (1-15 mg mL^{-1}), materials functionalization and mass (12, 18 and 24 mg), and net adsorption volume (1.5, 2 and 15 mL tubes). SDS-PAGE analysis was carried out to complement the results.

The most promising results were obtained during the adsorption of 3 mg mL^{-1} of cell extract onto pristine CXs in 15 mL tubes, attaining a 1.63-fold increase in the ASNase specific activity in the supernatant through adsorption of unwanted proteins onto the nanostructured carbon materials while keeping ASNase free in solution. SDS-PAGE analysis confirmed that these conditions seem to be the ideal relationship between cell extract concentration/material type and mass/net adsorption volume. The adsorption of cell extract onto functionalized CXs proved to be unfavourable, as the purity of the enzyme decreased in most cases.

The results obtained in this work revealed a promising and straightforward alternative to traditional ASNase purification processes through carbon xerogels nanomaterials. This method allows the removal of most impurities from a cell extract of *B. subtillis* containing ASNase, increasing the purity of the enzyme and decreasing the number of steps in the enzyme purification process.

This work was financially supported by: LA/P/0045/2020 (ALiCE) and UIDB/50020/2020 - UIDP/50020/2020 (LSRE-LCM) funded by national funds through FCT/MCTES (PIDDAC), and POCI-01-0145-FEDER-031268 funded by FEDER, through COMPETE2020-Programa Operacional Competitividade e Internacionalização (POCI), and by national funds (OE), through FCT/MCTES. This work was also developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC). Ana P. M. Tavares acknowledges FCT for the research contract CEEC CEECIND/2020/01867.

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Dextrans, pullulan and lentinan, new scaffold materials for use as hydrogels in tissue engineering

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Gel-like biomaterials play a key role as backbone materials in regenerative medicine.[1,2] Hydrogels based on biomacromolecules are developing increasing importance as scaffold materials due to their natural origin and biocompatible properties, especially in the field of tissue engineering.[3,4] In recent years, we have synthetically expanded the structural space of polysaccharides for the formation of hydrogels and their use in tissue engineering, both in terms of the choice of natural polysaccharides as well as the use of chemical processes for hydrogel formation.[5,6]

Despite the fact that selected polysaccharides such as hyaluronic acid are well established, little is known, how these polysaccharides can be chemically altered to create hydrogels under controlled conditions. In this work we present a small library of chemically modified polysaccharides (such as dextran, pullulan and lentinan) which are used for a divergent approach to achieve biomedical relevant hydrogels. In this case the crosslinking is based on thio ether formation between thiol modified donor and vinylsulfone or maleimide modified acceptor components. After succesful synthesis of the linker systems and coupling at the polysaccharides, hydrogel formation takes place under physiological conditions. We extended the study by coupling small molecules like adhesion factors for increasing biocompatibility and dye for further studies. The different hydrogels were studied to their rheological properties, water up take, their permeability, biodegrability and their cytotoxicity. With this results in hand we generated potential material for biomedical applications.

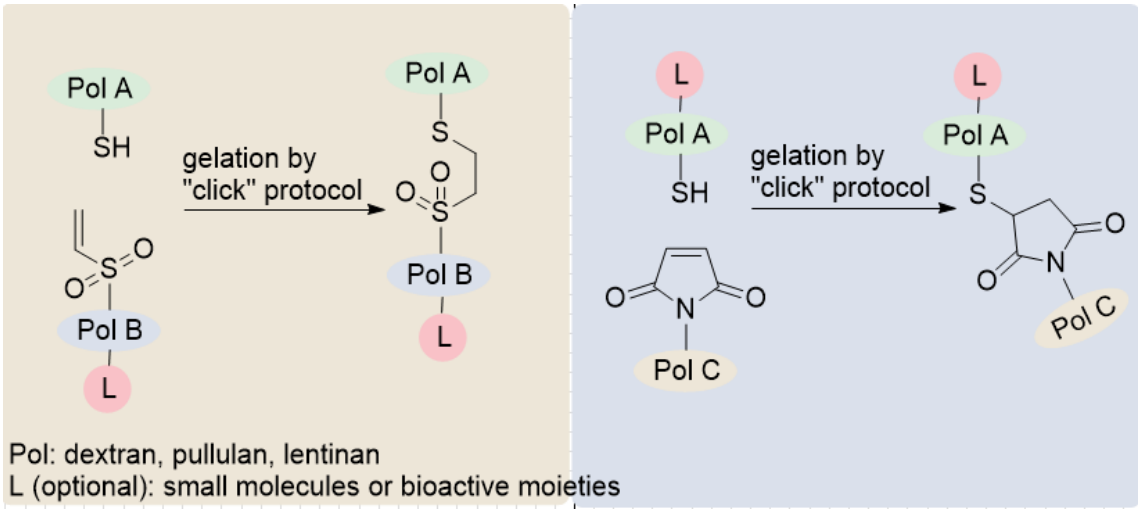

Figure 1

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Natural royleanones as building blocks for a Drug Delivery Platform based on Self-assembled Nanoparticles

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Natural products isolated from plants have been a successful source of potential drug leads with unique structural diversity. As an example, 6,7-Dehydroroyleanone (DHR, Figure 1) is a caspase-inducer cytotoxic abietane diterpene, frequently found on *Plectranthus* spp [1]. Cytotoxic effectiveness is, however, often insufficient to ensure the successful development of a new medicine. Properties such as chemical stability, crystal polymorphism, or aqueous solubility also play a critical role, since they can strongly affect bioavailability, shelf life and other key pharmaceutical properties [2].

In the present work, three molecules derived from natural products were employed as lead molecules for the synthesis of self-assembled nanoparticles. The royleanones were conjugated with squalene, oleic acid, and/or 1-bromododecane self-assembly inducers, and conjugates were successfully synthesized and characterized. To overcome the chemical stability, crystal polymorphism, or aqueous solubility problem, a pharmaceutical formulation consisting of water-dispersible nanoparticles was successfully prepared through the synthesis of a DHR-squalene conjugate. Scanning electron microscopy (SEM) showed that the nanoparticles had spherical morphology. Dynamic light scattering (DLS) analysis, further revealed that the aqueous dispersion had a narrow size distribution and a significant stability over time in terms of particle size, polydispersity, and zeta potential [3]. Bioactivity was assessed suggesting these nano assemblies can act as prodrugs for the release of cytotoxic lead molecules.

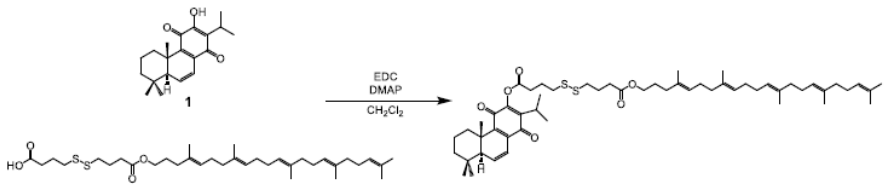

Figure 1. Conjugation of DHR (1) with squalene-type chain using a labile linker.

This work was supported by Fundação para a Ciência e a Tecnologia (FCT), Portugal, under the references UIDB/04567/2020, UIDP/04567/2020, UIDB/00100/2020, UIDP/00100/2020, and PTDC/QUI-OUT/28401/2017 (LISBOA-01-0145-FEDER-028401).

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ZnO nanoparticles as effective antivirals against SARS-CoV-2

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Since 2019, the new coronavirus disease (COVID-19), related to the severe acute respiratory syndrome coronavirus (SARS-CoV-2) started spreading around the world. First cases were reported in China, but suddenly the contagion extended to Europe and America, giving rise to the pandemic we are still facing [1]. Since then, many tactics for the prevention and management of COVID-19 have been studied and employed.

Besides pharmacological treatments and vaccines, prevention of viral diffusion can help the fight against SARS-CoV-2. As to this aspect, one of the characteristics desired in a (nano-)antiviral treatment is the insurance of cleaning and sterilization of common touch surfaces, especially in all those contexts where contagion could run fast: hospitals and clinical laboratories, schools, transport and public places in general [2]. These (nano)antivirals could be crucial for the treatment of nosocomial wastes and infected sludges [3].

Here we report on the efficacy of electrosynthesized metal oxide nanoparticles (NPs) against SARS-CoV-2. NPs have been produced by a scalable and ecofriendly method [4], based on the so-called electrochemical sol-gel approach [5]. The use of different stabilizers (both cationic and anionic ones) allows us producing variously shaped nanomaterials, ranging from small nanometer-sized spheres to micron-long rod-like structures. The results of microscopy (TEM), diffraction (SAED and XRD), and spectroscopy (UV-Vis, ATR-IR, XPS) analyses will be discussed, offering a clear view of the materials structure, composition and surface reactivity.

The NP antiviral activity has been tested in vitro against SARS-CoV-2; specifically SARS-CoV-2 nucleocapsid (N) protein antigen was quantified before and after the exposure to the antiviral material, showing a significant (e.g., up to 90%) decrease of the viral loading. The same (nano-)antivirals were also used for the preparation of polymer composites, embedding ZnONPs in polyethylene oxide (PEO). In this case, antiviral activity was correlated with the ionic release of antiviral Zn^{2+} ions in the contact medium [6].

Financial support from Fondo Sociale Europeo "Research for Innovation (REFIN)"; project n° 435A866B is acknowledged by M.C.S..

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A leukocyte transmigration inhibitor: a novel drug candidate for the treatment of auto-immune diseases

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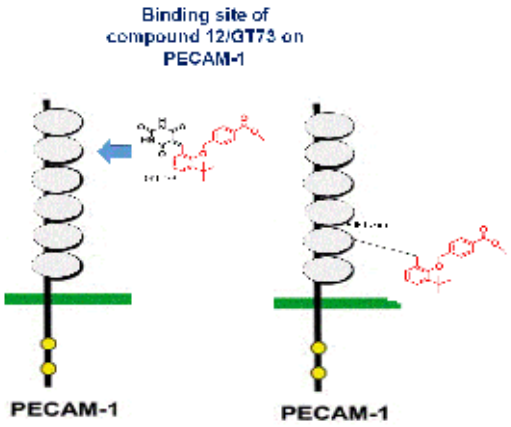
Leukocyte transmigration is one of the most important events in physiological immune response. However, over-activation of the immune system leads to damage of healthy tissues. Thus, effective leukocyte transmigration inhibitors are considered as promising potential therapeutic agents against auto-immune, inflammatory diseases and a disorders where the inflammatory element is very significant. We have developed a novel leukocyte transmigration blocker, compound **12 (GT-73)**, which blocked human leukocyte transmigration (95%-100% rate) without damaging white blood or endothelial cells. The compound also displayed a highly significant therapeutic effect in fat liver, arthritis, IBD, acute respiratory distress syndrome, lupus and multiple sclerosis mouse models in pharmacological doses. A detailed acute toxicity profile of compound **12** was also studied and no toxic effects, even in high administered doses, were observed [1-3].

The compound is a prodrug that is be able to form imine based covalent reversible bond with lysine residues of PECAM-1 (Platelet endothelial cell adhesion molecule-1) on the surface of endothelial cells and leukocytes [2]. Also, broad structure-activity relationship study were conducted [1,2]

Compound **12** now is under advanced stages of drug development.



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Extracellular vesicle-coated organosilica nanoparticles as targeted delivery nanocarriers

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Mesoporous organosilica and porous silicon nanoparticles have been highly investigated and showed several advantages, including high biocompatibility, degradability, large surface area for drug loading, stability and low costs.[1] On the other side, extracellular vesicles (EVs) are emerging as key elements for communication between cells that preferentially transfer biomolecules amongst target cells.[2] These vesicles present a diameter in the nanoscale and exhibit a strong fingerprint properties associated to the differential composition of their membranes (mainly phospholipids and proteins), maintaining the same homing tropism of the secreting cell lines such as their preferential accumulation in cancer and metastatic areas.[3,4]

In this study, we present the synthesis and characterization of porous organosilica nanoparticles loaded with cytotoxic drugs. These nanoparticles are characterized by exhibiting a cage-type morphology and the silica network contain disulfide groups allowing their breakability by reduction of the S-S bonds to thiols, by the cellular glutathione present in every cell line and in very large amount in cancer tissues. Then, in order to create a more biomimetic system, the porous organosilica nanoparticles have been covered with lipidic membranes and cholesterols and their viscosity was evaluated using polarization emission techniques. Evidences of the formation of the lipidic shell came from fluorescence microscopy, FTIR, zeta potential and electron microscopy analysis.

Targeting properties and selectivity towards specific tissue has been addressed using fragments coming from the membrane of EVs. EVs from healthy (NIH-3T3) and tumoral (B16-BL6) cells have been isolated and characterized. Their ability to target certain tissues is due to the presence of specific proteins on their membranes. The preliminary experiments of such artificial EVs and the advantages of our approach *vs* natural EVs (such as monodispersity, different loading, and scale up of the materials illustrated) are presented in this work. In addition, the advantage of such core-shell structured *vs* the more conventional lipid carriers is in the targeting functionalities intrinsic in the extracellular vesicle membrane and in the much higher stability of the core that will allow a better protection of the drug, prevent the leakage and can be tailor made in shape and size.

We gratefully acknowledge financial support from the EU H2020 MIMI-KEY Project (ID 964386). María Sancho-Albero thanks to the the AIRC -Foundation for cancer research for a two-years fellowship Gemma Hartmann (ID 26907).

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Understanding and controlling the toxicity and stability of MIL-100(Fe) toward effective drug-gene dual delivery carrier for anticancer therapy

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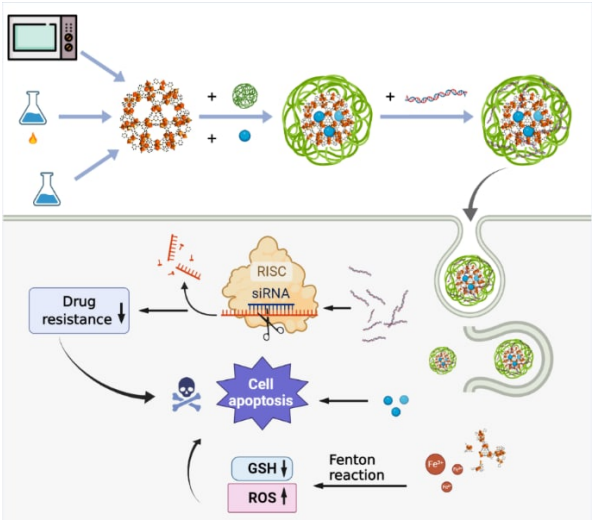
Metal Organic Frameworks (MOFs) are crystalline hybrid micro or meso-porous solids [1]. Since their discovery end of the 80's [2], MOFs have emerged as one of the most attractive classes of porous solids, largely due to their unprecedented structural and chemical diversity. These features, combined with good biocompatibility and biodegradability, by a careful choice of metal and organic linkers, are suitable for biomedical applications [3]. But there are still several issues that hinder their practical use in biomedicine such as a lack of control of the toxicity and/or chemical or colloidal stability of the nanoMOFs once in contact with body fluids.

In this talk, I will first show how to better control these properties under physiological conditions. Herein, three sets of MIL-100(Fe) nanoparticles of similar size (~ 100 nm) fabricated by different routes (room temperature, heating under ambient pressure and microwave-assisted hydrothermal) were synthesized [4-6]. Their physio-chemical characterizations, degradation and toxicity were carefully studied to understand the relation between toxicity and the physico-chemical features of the MOF. It turned out that these particles, although of the same structure type, exhibit strong differences in stability which leads to differences in cell toxicity effect on human normal cells and macrophage cells.

Second, the nanoMOF was functionalized with linear or branched polyethylenimine (PEI) with distinguished molecular weights to improve the chemical and colloidal stability in physiological conditions as a potential effective drug-gene dual delivery carrier for anticancer therapy. Both PEI-MIL-100's showed improved chemical stability, while linear PEI coated MIL-100 showed a significant increased colloidal stability in comparison with the bare MOF. As a proof of concept, the single-stranded DNA, as functional gene example of siRNA, was successfully encapsulated with linear PEI coated MIL-100 as shown by UV-vis analysis and gel electrophoresis. This paves the way for the use of PEI modified MIL-100 as an efficient drug-gene dual delivery carrier for breast cancer therapy.



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Nanovectors for proteins release and barrier crossing

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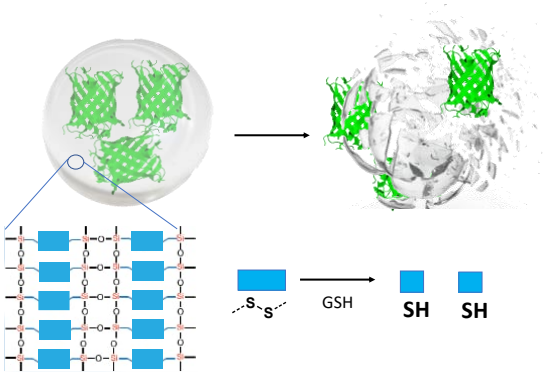
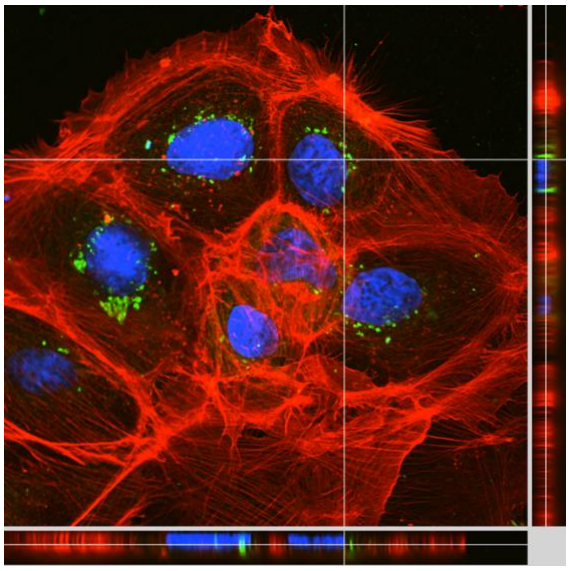
Nanoparticles have recently emerged has possible vectors for the protection, transport, and release of biomolecules, as recently demonstrated in their use for COVID vaccine. The long nanovectors circulation time and eventually their ability to accumulate in a disease site can improve efficacy, stability, and safety of therapy. Amongst the biggest challenges for the use of nanoparticles for drug delivery are their complete elimination and their capability of crossing barriers [1] within the human body.

Many materials have been tested for biocompatibility and degradability *in vivo*. Silica has emerged as a possible component for the creation of capsules and porous systems able to entrap a large number of active components and even deliver them on demand [2].

In this study we report a carrier based on organosilica nanocapsules, able to entrap both small and large molecules to be used for diseases treatment. We demonstrated that Green Fluorescent Protein (GFP) can be successfully encapsulated into nanocapsules and can be internalized by different cell lines showing their localization on the nuclear membrane. Due to the presence of the disulfide groups in the sílica framework, constituting the shell of the capsules, a reducing agent, such as Glutathione (GSH), can destroy the capsules [3]. The disulfide bridges are infact reduced into thiols allowing the breakability of nanocapsules and their release of GFP. Different sizes of nanocontainers have been investigated in order to assure biological barrier penetration and integrity of cell membranes. We demostrated that these breakable nanocarriers for the delivery of proteins can cross the natural EpiIntestinal barrier (provided by MatTek), and the unchanged values of Trans Epithelial Electrical Resistance (TEER) indicate that the capsules are well tolerated and safe.





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Supramolecular design of hybrid biopolymer/peptide soft multicomponent biomaterials for regenerative medicine

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Nature provides us with an unprecedented toolbox of stunning supramolecular systems that regulate the biological processes. Among them, the native extracellular matrix (ECM) is a compelling example of a structural and functionally complex biological supramolecular landscape that orchestrates cell functions and is formed by the non-covalent molecular self-assembly and reciprocal recognition of mainly proteins and glycosaminoglycans. Inspired by the ECM structural composition, dynamics and functional features, scientists have long been devoted to the development of ECM-mimetic soft supramolecular multicomponent biomaterials aimed at pursuing advanced regenerative medicine therapies [1-3].

In this work, emphasis will be given to the supramolecular design of soft ECM-like multicomponent biopolymeric materials through the synergistic use of biocompatible natural and synthetic polymers and bioactive self-assembling peptides, as well as bottom-up molecular self-assembly and Layer-by-Layer (LbL) assembly technology to instruct cell behavior. The secondary structure and morphology of the individual and co-assembled materials were studied by circular dichroism, attenuated total reflectance Fourier transform infrared spectroscopy, and scanning electron microscopy (SEM). The fabrication of supramolecular multilayered thin films was monitored by quartz crystal microbalance with dissipation monitoring and further translated into robust native and cross-linked free-standing membranes displaying distinct nanotopography and biochemical cues. Their physicochemical, mechanical and morphological properties were assessed by water contact angle, universal mechanical testing machine, atomic force microscopy and SEM. The *in vitro* biological performance of the developed multitactical supramolecular matrices, exhibiting distinct mechanical, topographical and biochemical cues was assessed at different time points using primary neuronal cortical cells, with the nanopatterned and cross-linked membranes imparted with bioactive signaling molecules revealing an enhanced cell behavior. The potential of such hybrid biopolymer/peptide soft supramolecular biomaterials to stimulate cell-signaling pathways that are critical in regenerative medicine, including in neural tissue regeneration will be discussed.

Acknowledgements: This work was funded by the Center Region Operational Program (Programa Operacional Regional do Centro – Centro 2020), in the component FEDER, and by national funds (OE) through FCT/MCTES, in the scope of the project "SUPRASORT" (PTDC/QUI-OUT/30658/2017, CENTRO-01-0145-FEDER-030658), as well as by the project "BAITS" (FCT). J. Borges, S.G. Patrício, M. Lopes, C.F.V. Sousa and M. Torrado gratefully acknowledge FCT for the Assistant Researcher contracts (2020.00758.CEECIND – J.B.; 2020.00366.CEECIND – S.G.P.) under the Scientific Employment Stimulus – Individual Call, and the PhD grants (2020.05210.BD – M.L.; 2020.04408.BD – C.F.V.S.; SFRH/BD/146754/2019 – M.T.). This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC).

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Theragnostic agents for breast cancer treatment: design of Iron Oxide Nanoparticles for multimodal therapies strategies

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One of the aims of nanomedicine is to develop multimodal nanoparticles (NPs) to enhance the treatment and diagnosis of cancer. Breast cancer is the most diagnosed cancer and the leading cause of cancer death in female population. Because of the resistance of cancer to typical chemotherapy and for the secondary effects these therapies present on patients, there is a strong need to develop precise medicine. The combination of therapies to target individual cancer-specific vulnerabilities is a way to increase the efficacy of anticancer treatment. Therefore, besides precision diagnosis, challenges for personalized nanomedicine are to develop multifunctional theragnostic nanoplatforms to be able to target specifically tumoral cells, to test quickly different treatments and to follow-up the effect(s) of the treatments by imaging.

The selective accumulation of NPs in diseased organs to enable precise diagnosis and targeted therapy is a relevant issue. Most of developed NPs accumulate, after intravenous injection, in eliminatory organs and usually low amounts achieve the tumor site. For a precise treatment, active targeting with affinity ligands to achieve tumor specificity is crucial. Among NPs developed for nanomedicine, superparamagnetic iron oxide nanoparticles (IONPs) are promising as they may be designed to display multimodal therapy. Indeed, besides being excellent T2 contrast agents for MRI, IONPs are promising as therapeutic agents by magnetic hyperthermia when suitably designed.

We developed dendronized IONPs (DNPs) coated with an original dendron molecule. Studies *in vivo* have demonstrated that they have antifouling properties, for example, they do not present a strong accumulation in the reticuloendothelial system. They present a favorable biodistribution and bioelimination profiles, and due to these characteristics, they are interesting nanoplatforms for the investigation of precise treatments. Through the dendron molecule we conjugated different TL (specific peptides) whose have affinity for certain molecules overexpressed in two types of breast cancer: MCF-7 and MDA-MB-231 cell lines (Figure 1). We saw a rise in the internalization amount of DNPs with TL compared with the same DNPs without TL. In this sense, the magnetic hyperthermia showed to be more efficient when working with the targeted DNPs. The biosdistribution and the specific internalization of DNPs bearing TL have been also checked *in vivo* by MRI. To provide also insight into morphological and functional behaviors, we conjugated also chelating agents (CA) for performing PET/SPECT imaging. With this approach, a radioisotope was successfully loaded and the different DNPs were studied *in vivo* by these imaging techniques. These results demonstrated that DNPs bearing TL are promising theranostic nanoplatforms.

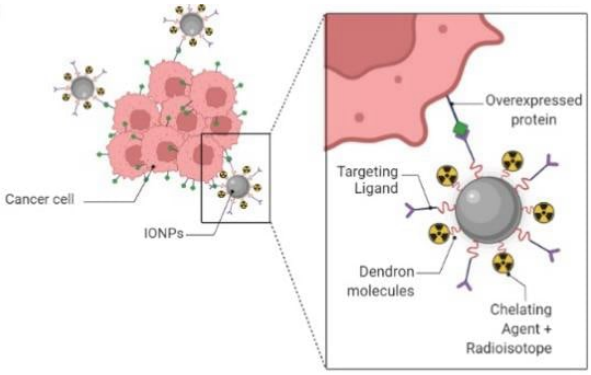

Figure 1 Overexpressed proteins on cancer cell membranes (green square). IONPs with dendron on the surface (red chains) functionalized with TL (purple) and CA (yellow).

Cyclodextrin Supramolecular Complexes Based on Specific Bonding Groups for the Selective Detection of Human Metabolites

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Metabolites like fructose, glucose and adenosine-triphosphate (ATP) are targets of top importance in many fields, from medicine to food industry. The enzyme-based biosensors are the most developed for the sensing of metabolites because of their high selectivity, but they present important limits, e.g. the interference by uric and ascorbic acid, two molecules greatly present in human fluids that oxidize at the same potential as the oxidases. As alternative to the oxidases-biosensors, in this work we developed a novel electrochemical assay based on specific bondings with the target. Different kinds of cyclodextrins (CDs) are employed for the formation of supramolecular complexes with a ferrocene probe (Fc) chemically modified by a phenylboronic acid group (PBA) for the detection of fructose, glucose and ATP.

We synthesized a novel electroactive Fc probe, introducing a phenylboronic acid group (**4-Fc-PB**) and we combined it with three kinds of CDs: natural-β-CDs for the detection of fructose, β-CDs chemically modified by a phenylboronic acid group (3-PB-β-CDs) for the detection of glucose, and β-CDs modified by a dipicolylamine group (dpa-*p*-HB-β-CDs) for the detection of ATP (Fig.1). Inclusion studies and the calculation of the binding constant of the Fc probe into cyclodextrin cavity have been performed through Nuclear Magnetic Resonance (NMR) studies. Electrochemical measurements were performed through differential pulse voltammetry (DPV) technique.

Fructose was detected in a linear range up to 3 mM with sensitivity of 4.39 ± 0.19 $\mu A \cdot mM^{-1} \cdot cm^{-2}$ and Limit of Detection (LOD) of 0.34 ± 0.02 mM; glucose was sensed in a linear range up to 5 mM with sensitivity equal to 6.81 ± 0.36 $\mu A \cdot mM^{-1} \cdot cm^{-2}$ and LOD amounting to 0.32 ± 0.02 mM; ATP was detected in a linear range up to 1 mM with 28.87 ± 2.49 $\mu A \cdot mM^{-1} \cdot cm^{-2}$ of sensitivity and 0.24 ± 0.02 mM of LOD. The news of the work consists in the role of cyclodextrins. Here, the aim is not the inclusion of the latter, and the driving force of the mechanism is not based on the binding constant of the latter anymore[1]: it is substituted by the presence of specific bonding groups present in both CDs and in the electroactive probe **4-Fc-PB.** They guarantee the desired selectivity, since they act as lariats that grasp the desired target molecule. This allows the electrochemical sensing of analytes even they are hydrophilic and/or larger than CD cavity, e.g. metabolites[2-3]. Moreover, this method can be applied to a huge range of target molecules, just by changing one or both the specific bonding groups of CDs and/or 4-Fc-PB probe.

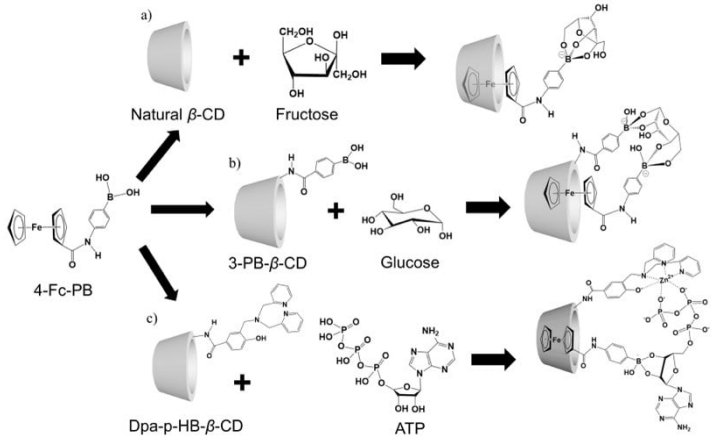

Fig. 1 **4-Fc-PB** electroactive probe combined with three different cyclodextrins for the sensing of fructose, glucose and ATP.

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Nanomagnetic logic gates for cellular hyperthermia

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Information about crossing a given temperature threshold is vital in many areas of daily life: devices, food and organisms are designed to function and preserve their properties within well-defined temperature limits. In other cases, those limits are deliberately exceeded, as in the case of hyperthermia, a widely used clinical procedure that promotes the heating of tissues and tumors, leading to necrosis [1]. One of the difficulties of the practical use of hyperthermia is temperature assessment, namely getting information about the crossing of a defined temperature threshold in a point.

We recently developed Fe_3Se_4 magnetic nanoparticles that work as logic gates giving a "yes or no" answer to the question "did temperature exceed a critical threshold?". These logic gates are hard magnetic nanoparticles with a magnetic phase transition tuned at a defined temperature threshold (42° C), which allows them to record a binary response: 1, if the temperature of the system exceeded 42° C during a heating event, or 0, otherwise.

Using a layered design, without direct contact between nanoparticles and cells, we applied a layer of these nanoparticles under a layer of cells submitted to hyperthermia assays using different heat doses, to identify which doses result in surpassing the 42° C threshold [2]. It was observed that for low thermal doses, the threshold of 42° C was not crossed, and most cells appeared to be viable, whilst in the case of high thermal doses, the results show the opposite. This shows the potential of these materials to behave as logic gates having temperature and magnetic field as inputs and as the output a "yes or no" answer to the question "did temperature exceed 42° C?". This proof of concept was a pioneer assay using hard nanomagnets in a biological application, opening the pathway to other note-worthy applications.

More recently, polymeric PLGA-PVA microcapsules were used to incorporate Fe_3Se_4 nanoparticles, which can lead to a higher cellular internalization and biocompatibility. This can work as a step towards 3D cellular hyperthermia, where Fe3Se4 nanoparticles will be inserted into cells to give information about the temperature threshold crossing *in situ*.

This work was developed within the scope of the projects CoolPoint, P2020-PTDC-CTM-NAN-4511-2014, and CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC). The work in Zaragoza has been supported by the research grants Aragon government group E10-17D. Access to advanced electron microscopy facilities received funding from the European Union Seventh Framework Program under Grant Agreement 312483 - ESTEEM2 (Integrated Infrastructure Initiative). This work was supported by a STSM Grant from COST Action MP1306 and from COST Action TD1402. RAP, VMG, and NJOS acknowledge FCT for the SFRH/BD/143320/2019, SFRH/BPD/119983/2016, IF/01533/2015 grants.

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Synthesis of sulfamethoxazole derivates for coupling to hydrogel microparticles in biosensing applications

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The accumulation of antibiotics in the environment is a major concern within the medical sector, as it leads to the evolution of multiresistant pathogens. The first class of widely distributed, synthetic antibiotics are the sulfonamides, with sulfamethoxazole (SMX) as a famous representative of this class. An important task of today's research is to determine the widespread distribution of substances, like SMX, to reliably assess their impact on the environment and human health. This raises the need for a novel, fast and easy to perform analytical method. In this regard, we aim at adapting a biosensor technology to fill this gap with a straightforward, but sensitive and selective detection of SMX in environmental and food samples.

The so-called soft colloidal probe (SCP) assay addresses this task as it was proven to detect analytes like glyphosate and estrogen-derivatives, as well as other targets in water samples. The SCP assay was able to detect those analytes with high selectivity and sensitivity, even in the range of tap water regulatory limits [1,2]. For the implementation in the SCP platform technology, poly(ethylene glycol) (PEG) hydrogel microparticles have to be functionalized with the target molecules. On doing so, the inhibition of their functional binding of relevant binding partners, like enzymes, needs to be circumvented.

Therefore, a modified SMX derivate has been prepared in a four-step synthesis. The SMX derivate was equipped with a linker for coupling to the PEG SCPs. The modified SMX has been synthesized de novo using a functionalized isoxazole amine and a sulfonyl chloride as commercially available starting materials. The isoxazole ring was used as an anchor point for the coupling of the thiol linker, because of its spatial distance from the sulfonamide moiety which is crucial for enzyme binding. All intermediates, as well as the product, were isolated by simple purification methods in up to very good yields. The modified SMX was coupled to the PEG-SCP, utilizing a high yielding and mild thiol-ene "click" reaction in aqueous solution.

The SMX coupled SCPs are now applied in a SCP assay to investigate the sensitivity and selectivity for the detection of sulfonamide antibiotics in aqueous samples.

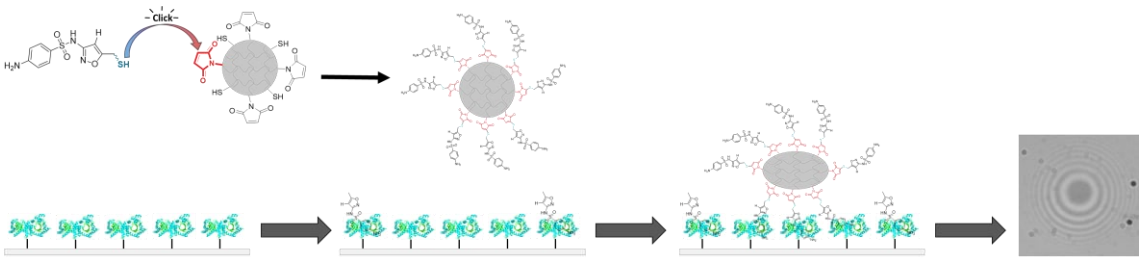

Figure: *Sulfonamide biosensing approach using SCP assay. Left to right: Functional coupling of PEG-SCPs with synthesized SMX-derivatives, application in SCP assay with the competitive binding of functionalized SCPs and target analytes and biochip surface and subsequent optical microscopy read-out.*

The authors acknowledge the support by a grant for the research and transfer center b-ACT^{matter} from BMWK within the STARK program (grant 46SKD023X).

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Selective isomerization of α-pinene oxide to campholenic aldehyde by ionic liquid-supported indenyl-molybdenum(II)-bipyridine complexes

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Campholenic aldehyde (CPA) is an important intermediate in the synthesis of sandalwood fragrances, e.g. Sandalores and Javanols (Givaudan), Bacdanols (IFF), Brahmanols (Dragoso) and Polysantols (Firmenich). CPA may be produced via the acid-catalyzed isomerization of α-pinene oxide (PinOx) in the presence of Lewis acids. The use of ionic liquid (IL)-standing catalysts (ILSC) for CPA synthesis has shown some promise in a limited number of published studies. Combining organometallic Lewis acids such as $[IndCpMo(MeCN)_2](BF_4)_2$ with ILs has thus led to systems that can give quantitative CPA yield within a few minutes of reaction under mild conditions (35 °C). Besides catalytic activity and selectivity, the catalyst recovery/reuse is an important aspect for practical application. In previous work, we found that the ILSC system $[IndCpMo(MeCN)_2](BF_4)_2$/[choline bis(trifluoromethylsulfonyl)imide] led to increasing CPA yield in consecutive batch runs [1].

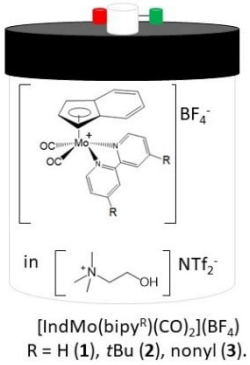

Figure 1 – Schematic representation of ionic liquid-supported indenyl-molybdenum(II)-bipyridine complexes.

In the present work indenyl-molybdenum(II)-bipyridine complexes $[IndMo(bipy^R)(CO)_2](BF_4)$ ($bipy^R$ = 2,2'-bipyridine (R = H) or 4,4'-disubstituted-2,2'-bipyridine) have been combined with various ionic liquid solvents to develop an efficient process for the selective conversion of PinOx to CPA under mild (35 °C) conditions. Excellent CPA yields (95 %) were repeatedly obtained within 1 minute reaction time for the easily recyclable catalytic system comprising [IndMo(4,4'-dinonyl-2,2'-bipyridine)$(CO)_2$](BF_4) and choline bis(trifluoromethylsulfonyl)imide [2].

Acknowledgments: We acknowledge funding provided within the project CICECO - Aveiro Institute of Materials, UIDB/50011/2020 & UIDP/50011/2020 & LA/P/0006/2020, and the CENTRO 2020 Regional Operational Programme (project references CENTRO-01-0145-FEDER-028031 and PTDC/QUIQOR/28031/2017), financed by national funds through the FCT/MEC and when appropriate co-financed by the EU through the ERDF under the Portugal 2020 Partnership Agreement.

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Sustainable Gold Catalysis in Water
Using Cyclodextrin- or PQS-tagged NHC-Gold(I) Complexes

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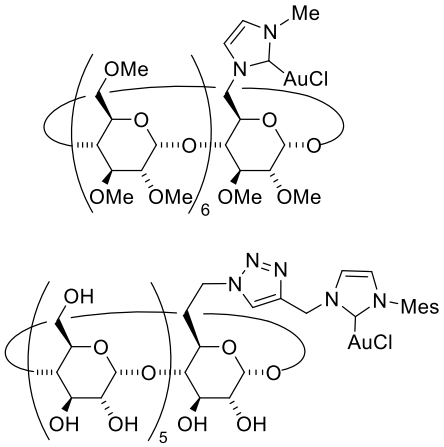
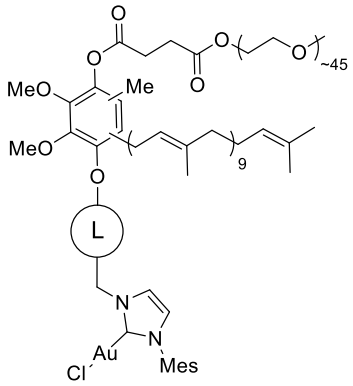
Organic solvents continue to be the reaction media of choice for transformations of organic substrates, notwithstanding the fact that they are the major source of waste produced by chemists in industry and academia.[1] An attractive alternative is the use of water as reaction medium for catalytic transformations. This can be achieved by using micelles as nanoreactor for unpolar substrates and catalysts,[2] or by designing water-soluble catalysts.[3] Thus, we have synthesized a library of cyclodextrin-tagged NHC-gold(I) complexes by nucleophilic substitution, as well as, by copper-(CuAAC)- or ruthenium-(RuAAC)-catalyzed azide alkyne cycloaddition as the key step.[4] These CD-tagged gold complexes show excellent catalytic activity and recyclability in cyclization reactions of functionalized allenes and alkynes in bulk water. Moreover, we have attached the NHC-gold(I) moiety to the designer surfactant PQS and obtained water-soluble catalysts which show extremely low gold leaching during recycling experiments in bulk water.[5]

Cyclodextrin-tagged NHC-Gold Catalysts:



PQS-tagged NHC-Gold Catalysts:



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Direct synthesis of 3-aryl substituted isocoumarins through Palladium mediated C(sp^2)-H Activation in Ionic Liquids

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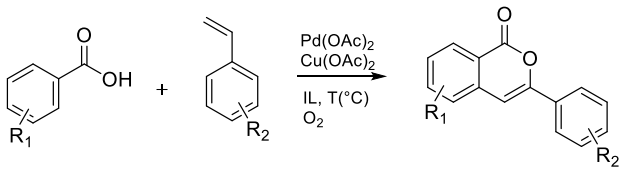
Isocoumarins and 3,4-dihydroxicoumarins are an important class of molecules that play a crucial role in pharmacology and medicine, with biological properties ranging from anti-HIV activity [1], diuretic and antihypertensive activity [2], or treatment of problems related to the lymphatic system [3]. Due to their importance, several synthetic methods have been described until now, which can be mainly divided in two different categories: metal-free or metal-catalyzed reactions. Among them, other subdivisions can be made, depending on the nature of the substrate. In fact, several protocols start from 2-alkynylbenzoic (or benzoate) acids, obtaining the target molecule *via* an intramolecular metal free cyclization [4] or catalysed by silver, copper, or palladium compounds [5]; other procedures refer to the coupling of 2-halo-/triflate benzoic acids (or other haloderivatives) with enolates or alkynes [6], while recent papers perform the synthesis of isocoumarins *via* C-H functionalization of benzoic acids without decarboxylation [7].

Few years ago, some of the authors succeeded in the synthesis of cyclopropanes by using a combination of palladium and copper salts as catalyst in tetrabutylammonium acetate (TBAA) as the solvent. The unusual cyclopropanation process was achieved *via* a twofold C-H activation when methyl ketones and styrenes were coupled in the ionic liquid. In this case, we supposed that the cycle was initiated by Pd^{II} which led to the C-H activation at the α position of the carbonyl group [8]. Comparably, since the *ortho*-CH aromatic activation driven by the presence of a carboxylic group is also a known process, we speculated that, under similar conditions, the coupling between different styrenes and various benzoic acids can lead to the formation of isocoumarin, mediated by the presence of Pd^{II} salts in ionic liquids. Due to the value of the products and following our studies on the use of ionic liquids as alternative solvents in catalysis, we describe here a straightforward strategy to selectively obtain 3-substituted isocoumarins by an ease Pd-catalyzed annulation of various olefins with benzoic acids.



This work was carried out with partial financial support from Università degli Studi di Bari Aldo Moro and with support of the project "PON Ricerca e Innovazione 2014–2020. Progetto: 20 Energie per l'Ambiente TARANTO–Cod. ARS01_00637".

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Sterically demanding, flexible phosphoric acids for constructing multi-purpose asymmetric organocatalysts

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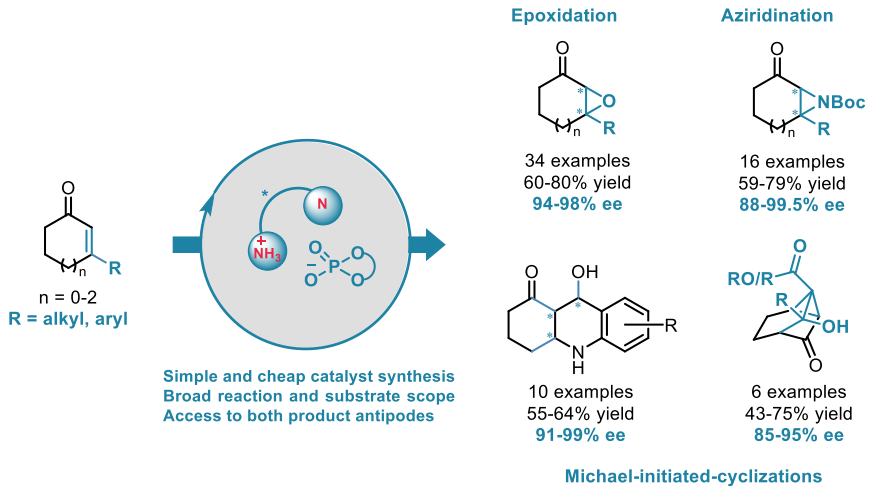
In light of the growing awareness for safe and sustainable strategies, asymmetric organocatalysis is of special interest. As metal-free catalytic reactions, these transformations feature great air– and moisture tolerance, providing a convenient and robust access to enantioenriched products. Pioneered by B. List, the field of BINOL-derived chiral phosphoric acids (CPAs) emerged to be an indispensable organocatalytic tool, providing elegant examples for the β-functionalization of enals and enones using enantiomerically pure, chiral phosphoric acids *via* Asymmetric Counteranion Directed Catalysis (ACDC) [1,2] Despite the remarkable advances on this field, lot of the existing methods suffer either from multi-step and tedious catalyst synthesis and/or from the difficult catalyst tunability for obtaining both product enantiomers.

As a conceptual spin-off of ACDC, we designed novel chiral frameworks composing of natural-derived chiral diamines and sterically demanding, yet flexible phosphoric acids. Such catalysts could be prepared through a straightforward parallel synthetic strategy, enabling a rather simple parameter tailoring. The optimization of the catalyst components led to the identification of a particularly powerful organocatalyst, which could be successfully applied in asymmetric epoxidations, aziridinations, as well as in two different Michael-addition-initiated cyclizations. Excellent stereocontrol was observed for all four different reactions; moreover, a simple change of the amine's configuration provided an easy access to both product antipodes in all cases.

Based on extensive NMR studies we found, that our phosphoric acids are eventually too flexible to form stable diastereomers in chiral environment under ambient conditions, and therefore they might behave as single stereoisomeric catalysts. This could be an important aspect for avoiding the generation of matched-mismatched scenarios as a key point for achieving similarly high enantioselectivities when aiming for the opposite product antipodes.



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Development of Powerful Ga-based Catalysts for Cyclic Carbonate Synthesis and Application in the Synthesis of Value-added Bio-derived Compounds

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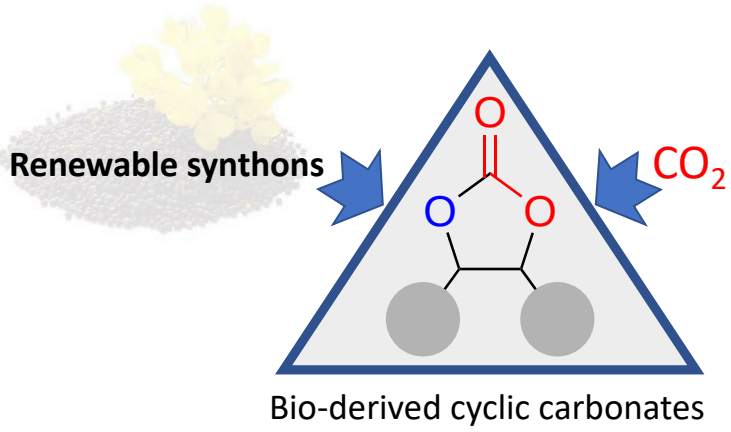
The use of carbon dioxide (CO_2) as a C1 chemical feedstock is attracting a significant amount of interest, mainly as a result of it being a cheap, renewable and non-toxic compound. Whilst many methods for its utilization have been developed [1], one of the most appealing is the atom-economic coupling of epoxides and CO_2 to form cyclic carbonates, which are themselves finding an increasing number of applications. A vast number of Lewis acid-based catalysts have been developed for this conversion, with some of the most active examples based on aluminium [2]. However, and rather surprisingly, despite the important successes with aluminium, few catalysts have been reported based on other group 13 elements. This has resulted in a large void in the research landscape given the well-established and exploited Lewis acid properties of these other elements (boron, gallium and indium). This contribution will present some of our most recent results on the search for group 13 catalysts beyond aluminium [3], and also demonstrate the application potential of our highly active gallium catalyst beyond traditional substrate scoping. In particular, these latter results will showcase the use of these catalysts in the context of the incorporation of cyclic carbonates into bio-based compounds, which themselves have potential application as monomers for sustainable polymer synthesis.



C.W. and L.A.M. would like to thank the Comunidad de Madrid (Spain) for funding (Programa de Atracción de Talento 2019: Modalidad 1; Award number 2019-T1/AMB-13037, and CM/JIN/2021-018). We would like to also acknowledge funding from the Spanish Government (RTI2018-094840-BC31 and PID2020-113046RA-I00), the Universidad de Alcalá (UAH-AE-2017-2) and the Royal Society of Chemistry for a Research Fund Grant for CW, enabling the purchase of the pressure reactors required for catalytic studies (ID RF17-1110).

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How Lewis Acids Catalyze Diels-Alder Reactions

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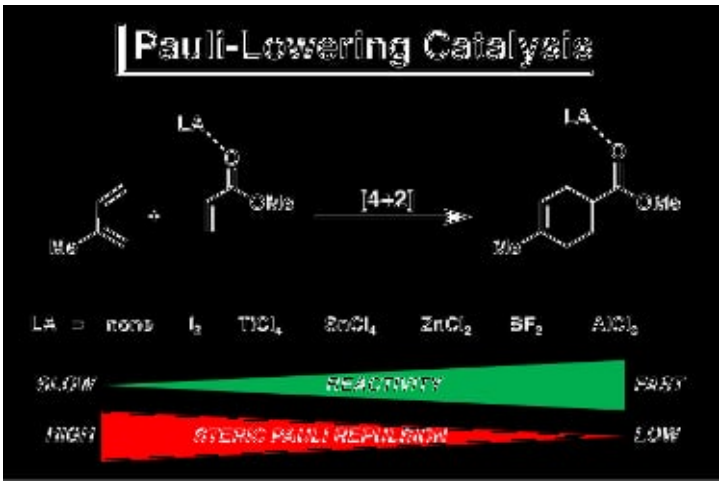
Lewis acids (LA) are efficient catalysts of various organic reactions. Numerous studies have claimed that the origin of LA catalysis stems from the strong donor–acceptor interaction between the LA and one of the reactants, which, in turn, results in a significant stabilization of the LUMO of that reactant and, therefore, a smaller HOMO–LUMO energy gap [1,2]. This contribution will show that the wide-accepted rationale behind the rate enhancement of LA-catalyzed organic reactions is incorrect. By studying the textbook LA-catalyzed Diels-Alder reaction between isoprene and methyl acrylate using state-of-the-art computational techniques [3,4], we uncovered that LA catalysis is driven by a hitherto unexpected electronic mechanism [5]. We found that LAs do not catalyze Diels-Alder reactions via a reduction of the prior mentioned HOMO–LUMO energy gap, but, instead, by diminishing the steric Pauli repulsion between the filled orbitals of the diene and dienophile. This novel concept of *Pauli-lowering catalysis* is not solely restricted to Diels-Alder reactions, but is, in fact, a more general phenomenon in chemistry with examples ranging from LA-catalyzed ene reactions [6] to Michael addition reactions [7] to ring-opening reactions [8].



This work was supported by the Netherlands Organization for Scientific Research (NWO), Dutch Astrochemistry Network (DAN), and the Spanish MINECO (CTQ2016-78205-P and CTQ2016-81797-REDC).

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Can simple amines mimic organotin?: Aminoalkyl radicals as halogen-atom transfer (XAT) agents for redox chemistry

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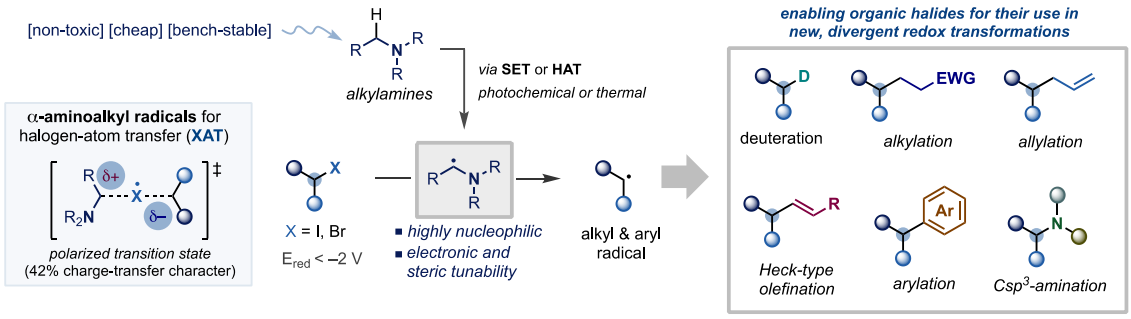
The emergence of (photo)redox catalysis has enabled the development of new methodologies that generate highly reactive radicals under mild conditions [1]. Notwithstanding, the general and reliable generation of carbon radicals from inactivated alkyl and aryl halides remains an unsolved problem in redox chemistry, in view of their often inaccessible SET reduction potentials (E_{red} < –2 V vs SCE) [2]. In fact, nowadays synthetic chemists still rely on the same systems based on halogen-atom transfer (XAT) developed more than 40 years ago to engage organic halides in radical transformations, sometimes underutilized due to the acute toxicity (e.g. tributyltin hydride) or hazards (e.g. explosive initiators) associated to the reagents employed.

We have recently demonstrated how simple amines (*e.g.* triethylamine), some of the cheapest and most common reagents present in any synthetic lab, can be used as surrogates of tributyltin hydride for the homolytic activation of carbon-halogen bonds [3-4]. Aminoalkyl radicals, easily generated under thermal or photochemical conditions from amines, can be engaged in kinetically-favored polarized XAT processes providing effective access to alkyl and aryl radicals. The utility of this strategy has been showcased in a wide range of redox transformations allowing the construction, with high chemoselectivity, of sp^3–sp^3, sp^3–sp^2 and sp^2–sp^2 carbon–carbon and Csp^3–N bonds under mild conditions. Moreover, it opens a new gateway for the modular use of alkyl and aryl halides in (photo)redox and radical chemistry beyond dehalogenation, further expanding the use of widespread organic halides in redox settings.



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Substrate-dependent Mechanistic Differences in Ni-catalyzed Carbonylations to Carboxylic Acids

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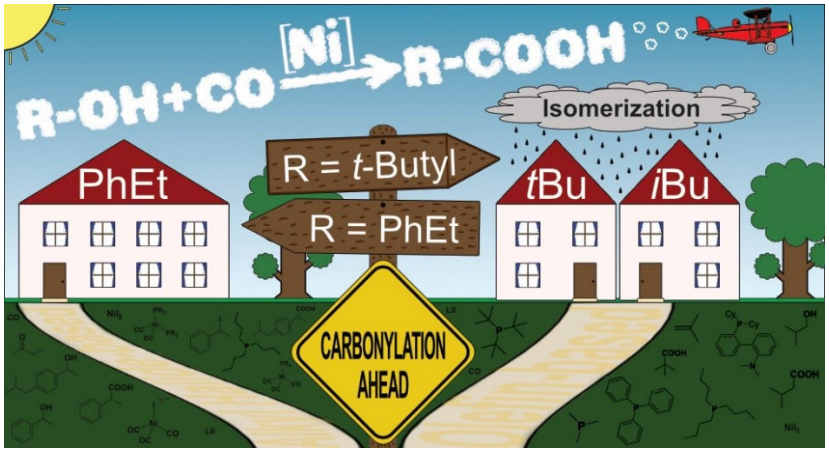
The carbonylation of alcohols represents a straightforward and atom-efficient methodology for the preparation of carboxylic acids. To perform these reactions under precious metal-free and low-pressure conditions, with regioselectivity control, is highly desirable with current state-of-the-art processes either relying on harsh reaction conditions (*e.g.*, propionic acid) or on the employment of precious metals (*e.g.*, ibuprofen). Additionally, the latter process requires large amounts of HCl necessitating the use of expensive reactors to withstand corrosion. After the recent establishment and detailed mechanistic investigation of a Ni-based regioselective protocol employing non-corrosive and low-pressure conditions,[1] the scope of this experimental protocol was extended from carbonylating benzylic alcohols to tertiary aliphatic alcohols, yielding Koch-type carboxylic acids. Reactivity was observed at elevated reaction temperatures of 200 °C, however, the selectivity and unexpected results from key mechanistic experiments quickly led to the conclusion that the same catalytic system performs the carbonylation of alcohols via different pathways that are determined by the nature of the alcohol. As in the original study, a combination of experiments and quantum-chemical calculations was used to evaluate the underlying mechanistic processes. Furthermore, these methods were used to probe the role of iodide-containing salt additives, that had led to a significant performance increase for benzylic alcohols, and to screen ligands that could further improve reactivity of the system.[2]



Acknowledgments:
Catalysis Research Laboratory (CaRLa) is co-financed by Heidelberg University and BASF SE.

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Synthesis of Densely Functionalized Isochromans through a Cascade Reaction Mediated by HFIP

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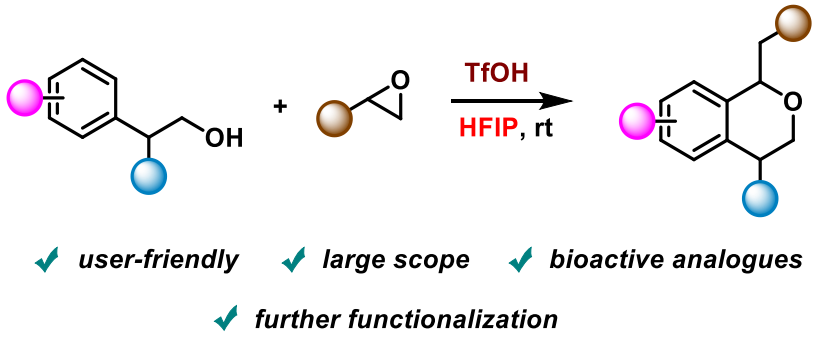
There is currently strong demand from the fine chemicals industry to develop synthetic methods that avoid expensive transition metal catalysts and that use readily available starting materials, for reasons of availability, cost and toxicity. In that respect, employing simple alcohols, alkenes and epoxides directly as electrophiles for C–C or C–heteroatom bond forming reactions is truly appealing, but it can remain challenging, notably when the substrates are highly deactivated or prone to sequester the catalyst. Recently, we have demonstrated that inexpensive Brønsted acid catalysts in combination with the solvent hexafluoroisopropanol (HFIP) could be harnessed to activate epoxides and alcohols in arylation and reduction processes [1,2]. In this way, we were able to outperform common Lewis and Brønsted acids in terms of activity and efficiency in several reactions, helped by the coordination of HFIP to the catalyst and the formation of H-bond clusters. Moreover, due to its strong H-bond donor ability, HFIP has the capacity to facilitate the release of the catalyst trapped by unwanted coordination to the substrate (or the product), allowing the catalytic process to turn over [3]. In particular, the combination catalyst/HFIP can be a powerful tool to promote arylation reactions. These reactions proved to be general and compatible with a wider range of substrates than the traditional catalytic systems.

Recently, we have extended this type of reactivity to alcohol nucleophiles, notably phenyl ethanols, to devise a complex cascade reaction that provides isochroman frameworks. Our methodology enables the otherwise challenging synthesis of this biologically relevant moiety for which the direct synthesis was only scarcely reported thus far.



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New CO_2 fixation Routes to Access Cyclic Carbamates and Carbonates Under Ambient Conditions

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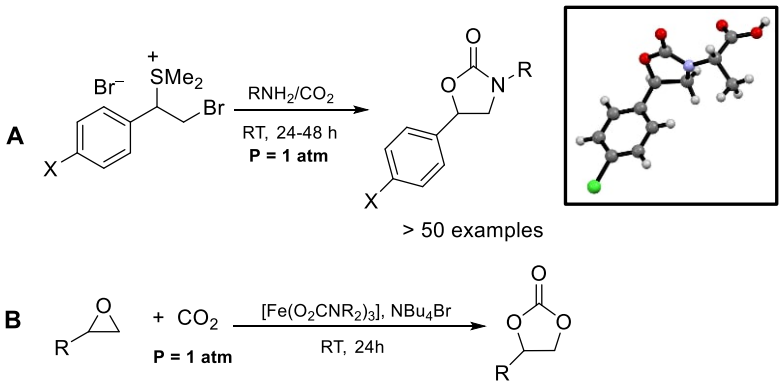
One of the most intriguing challenges of contemporary chemistry research is using carbon dioxide as a convenient C_1 synthon to obtain fine chemicals [1]. 2-Oxazolidinones and cyclic carbonates constitute two classes of heterocyclic molecules finding application as monomers for polymerization, pharmaceuticals and chiral auxiliaries. Synthetic routes affording these valuable compounds from CO_2 have been intensively investigated and usually require a catalyst/co-catalyst system and possibly harsh conditions [1,2].

Here we report a catalyst-free, gram-scale synthesis of several 5-aryl-2-oxazolidinones via CO_2 fixation at room temperature and ambient CO_2 pressure (Scheme 1A) [3]. This strategy also provides access to a novel family of 2-oxazolidinone compounds conjugated with natural α-aminoacids [4].

Carbamato complexes, i.e. $[M(O_2CNR_2)_n]$, have been studied as catalytic precursors for the epoxide-carbon dioxide coupling reaction affording cyclic carbonates. In particular, the inexpensive and easily-available iron(III) *N,N*-diethylcarbamate, $[Fe(O_2CNEt_2)_3]$, works efficiently, in combination with NBu_4Br, to produce cyclic carbonates (Scheme 1B) with excellent yields and selectivity under ambient and solventless conditions. The implicated reaction mechanism will be discussed, relying upon a dynamic CO_2 exchange between the carbamato ligand and the gas phase, thus providing a low energy route for CO_2 conversion [5].



Scheme 1. A. Catalyst-free synthesis of 5-aryl-2oxazolidinones (X = H, CH_3, Cl, F, OCH_3, NO_2, CO_2Me) (inset: X-ray structure of alanine-oxazolidinone conjugate); **B** Formation of cyclic carbonate from CO_2/epoxide coupling reaction using iron(III) carbamates as catalysts.

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DEAROMATIZATIVE *SYN*-DIHYDROXYLATION OF ARENES

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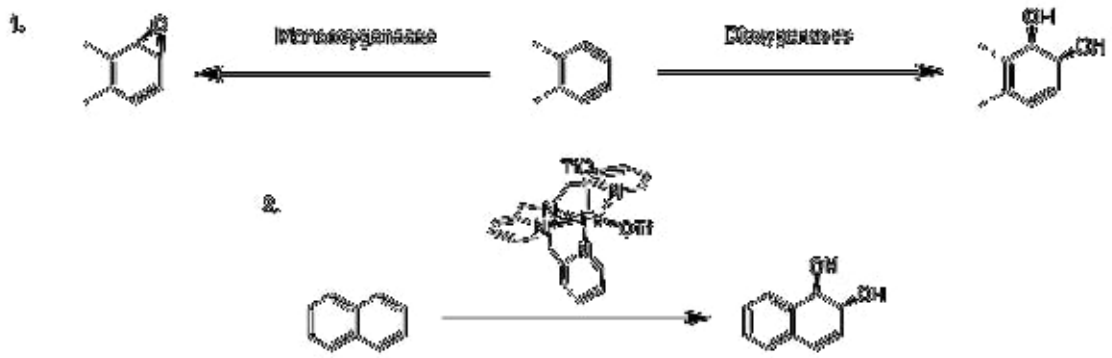
The abundance of arenes in nature makes them very interesting substrates in organic synthesis. Through their dearomatizative oxidative reactions, they can be easily converted into very elaborated molecules, containing multiple stereogenic centers with potential biological interest.

In nature, heme and non-heme iron oxygenases can oxidize arenes disrupting their aromaticity while using mild conditions. On one hand, monooxygenases can produce the epoxides of arenes, and on the other hand, Rieske Dioxygenases can perform the syn-dihydroxylation of alkenes and arenes.[1] The most studied enzyme within this family is naphthalene-1,2-dioxigenase (NDO) which can realize enantioselectively the syn-dihydroxylation of naphthalene.

Even though enzymes can perform those reactions with good yields and excellent enantioselectivities, due to the complexity of those reactions very little is currently known about their realization using artificial systems.

In literature we can find an example that imitate the behavior of those dioxygenases. It consists in an iron catalyst that can perform the same reaction of the NDO enzyme, unfortunately, the yield obtained for the product is very low and cannot be used for synthesis. [2]



Taking this into account, in this work we want to use transition metal-based catalysts to perform oxidative dearomatizative reactions using naphthalene as a model substrate and hydrogen peroxide as oxidant. We want to break the aromaticity while generating different stereogenic centers through the oxidation. Our main objectives are to achieve yields that can be used for synthesis, and to combine the transition metals with chiral ligands to induce enantioselectivities on our reactions, since till now those enantioselective reactions remain exclusive for enzymes.

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How Lewis Acids Catalyze Ene Reactions

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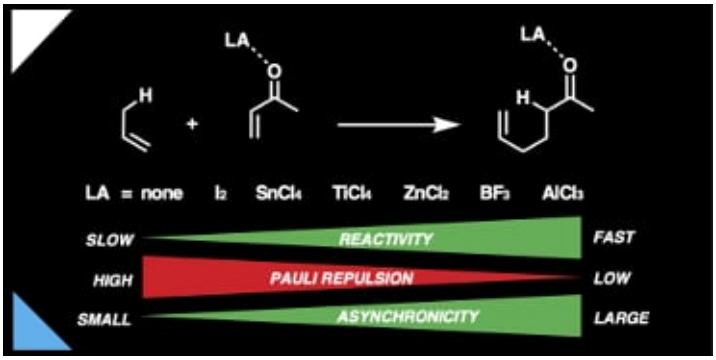
The ene reaction represents a convenient methodology to forge new C–C bonds. Over the course of the ene reaction, a new C–C bond is formed between an alkene with an allylic hydrogen (ene) and a compound that has an electron-deficient multiple bond (enophile), by migration of the double bond and in conjunction with a [1,5]-hydrogen shift. Lewis acids catalyze ene reactions, but only little is known about the physical factors that govern the enhanced reactivity of LA-catalyzed ene reactions. The traditional explanation is based on the frontier molecular orbital (FMO) interaction between the HOMO of the ene and the LUMO of the enophile, in which a LA lowers the LUMO of the enophile thereby reducing the $HOMO_{ene}$– $LUMO_{enophile}$ energy gap and thus leading to an enhancement of the orbital interactions [1].

This research studies quantum chemically the catalytic effect of various Lewis acids (LAs) on the ene reaction between propene (ene) and but-3-en-2-one (enophile) by using density functional theory and with coupled-cluster theory [2].

The catalytic ability of the LA increases when going from I_2 < $SnCl_4$ < $ZnCl_2$ < $TiCl_4$ < BF_3 < $AlCl_3$ by lowering the reaction barrier up to 12 kcal mol^{-1} compared to the uncatalyzed reaction. Our detailed activation strain and Kohn-Sham molecular orbital analyses reveal that coordination of a LA catalyst to the enophile decreases the reaction barrier of the ene reaction by inducing an asymmetry in the π-electronic system, which increases the asynchronicity and hence relieves the otherwise highly destabilizing activation strain and Pauli repulsion between the closed-shell filled π-orbitals of the ene and enophile.

In contrast to the traditional explanation, our work demonstrates that the orbital interactions are actually less stabilizing for the LA-catalyzed reactions compared to the uncatalyzed reaction. This is due to a significant weakening of the inverse electron demand π-$LUMO_{ene}$–π-$HOMO_{enophile}$ interaction, which overcomes an only slight strengthening in normal electron demand $HOMO_{ene}$– $LUMO_{enophile}$ interaction for the LA-catalyzed ene reactions. This work consolidates the generality of the *Pauli-lowering catalysis concept*, which applies to many other organic reactions [3].



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New generation of improved catalysts for the construction of chiral C-C and C-X bonds. Enhancing Pd-catalyzed asymmetric allylic substitution reactions

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Pd-catalyzed asymmetric allylic substitution is a powerful and sustainable method for preparing chiral compounds.[1] However, most catalysts are still only tested in benchmark substrates, eluding challenging ones that would yield to more appealing compounds. Our group has taken advantage of the adaptability of biaryl phosphite-based ligands to overcome the substrate specificity and low nucleophile scope in the this process.[1-3] Here we present our recent findings in this field with the design of two new catalyst libraries. They present the advantages of being synthesized in a few steps from unexpensive starting materials plus being solid, stable to air and therefore, easy to handle. Improving the approaches reported to date, these new catalysts present a broad substrate and nucleophile scope.[4,5] Excellent enantioselectivities have been achieved for a broad range of linear (including challenging unsymmetrical di- and monosubstituted) and cyclic substrates with different electronic and steric properties, using many C-, N- and O-nucleophiles (70 compounds in total).[4,5] Furthermore, the combination of computational (DFT) and NMR spectroscopy studies of the key Pd-complexes provide an explanation on the origin of the enantioselectivity. Finally, the application of these catalysts for the preparation chiral (poly)carbo- and heterocyclic compounds, with multiple stereocenters, will be demonstrated by the use of straightforward sequences of allylic substitution and either ring-closing metathesis or Pauson-Khand reactions.[4,5]

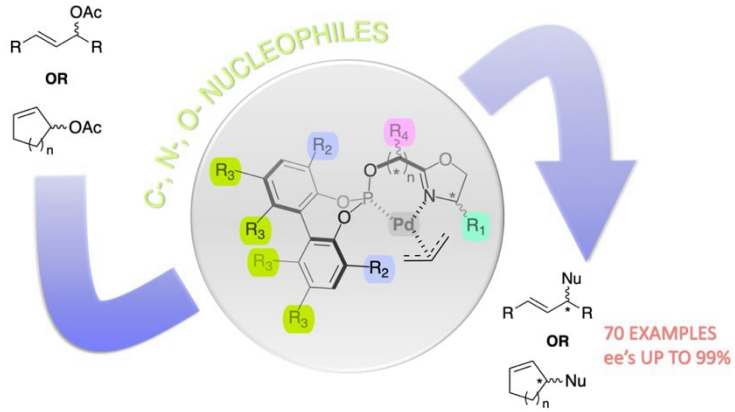

Fig 1. Formation of C-C and C-X chiral bonds with biaryl phosphite-containing Pd catalysts.

Thanks to Societat Catalana de Química (SCQ) for kindly sponsoring the registration fees for the 8th EuChemS Chemistry congress.

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Strategies for an increased selectivity in the catalytic synthesis of highly fluorinated biaryls

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The transition-metal catalyzed aryl-aryl cross-coupling reactions are well solved for conventional aryls but have much higher difficulty when polyfluorinated aryls (Ar^F) are involved. These present higher barriers to coupling and become particularly difficult for highly fluorinated aryls possessing F_{ortho} atoms [1]. Consistently, the C_6F_5-C_6F_5 coupling is the most difficult case. This reluctance to coupling can lead to undesired processes such as substrate decomposition or competitive transmetalations [2].

Herein, we describe two new strategies to circumvent these limitations. Firstly, a nickel- or palladium-catalyzed Negishi cross-coupling, employing a Phosphine-Electron Witdrawing Olefin ligand (PEWO) that enhances the rate of the reductive elimination step (Figure 1, left) [3]. Secondly, a bimetallic Pd-Cu system, where the *in situ* generation of the copper nucleophile reduces the undesired transmetalations (Figure 1, right) [4]. Mechanistic studies for both systems are also discussed. These two complementary methodologies increase the ways to synthetize unsymmetrical highly fluorinated biaryls, with higher yields and increased selectivity compared to previous results.

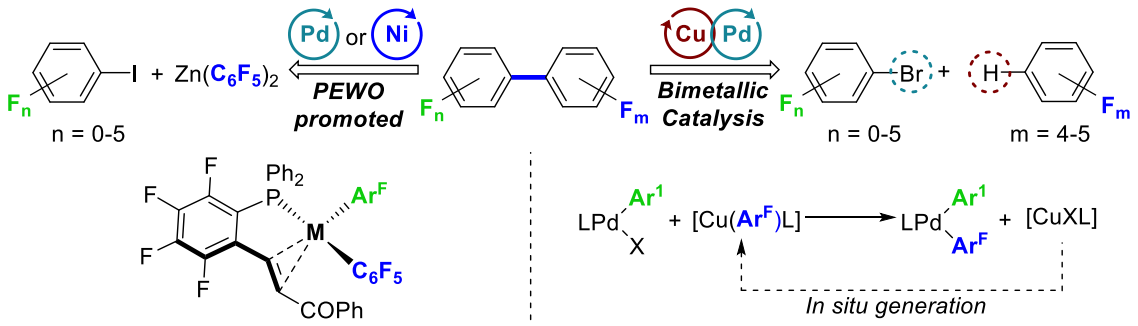

Figure 1. Catalytic approaches to the selective synthesis of highly fluorinated biaryls.

Thanks to the Spanish Ministerio de Ciencia e Innovación (MCINN) for financial support (Project PID2020-118547GB-I00). Jaime Ponce de León thanks the Spanish MCINN for a FPI scholarship (BES-2017-080726).

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Use of Iridium-Catalyzed Transfer Vinylation as an Efficient Synthetic Route towards Bio-Based (bis)-Vinyl Ethers

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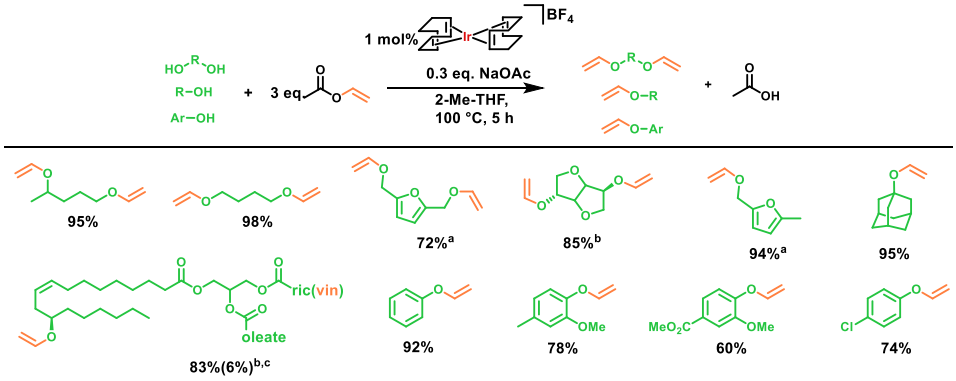
Vinyl ethers (VE) have a great potential for the preparation of sustainable adhesives, coatings, and other novel materials, being obtained from alcohols and polyols which are widely abundant in bio-based feedstocks [1-2]. Even though, their use in adhesive formulation is limited because of the small number of commercially available VE and their higher cost compared to other reactive systems [3]. Stoichiometric routes towards VEs typically possess problems of operating potentially explosive mixtures, functional group tolerances or require extremely high energy input [4-6]. Several catalytic transfer vinylation approaches have been proposed to address the forementioned issues. Mercury, gold, palladium and iridium have been so far reported [7-10]. In particular, Ishii et al developed an efficient protocol that uses vinyl acetate as vinylating agent, which is cheap and available [10]. In this work, we apply the commercially available complex bis(1,5-cyclooctadiene)iridium(I) tetrafluoroborate in the presence of a base for the synthesis of a variety of vinyl and bis-vinyl ethers [11]. Interestingly, the green solvent 2-methyl-THF shows the best performances in terms of yields and selectivities. The formation of (thermodynamically stable) cyclic acetals is the main side reaction that must be addressed, particularly when diols where the 2 alcohol moieties have different reactivities. Using 1,4-pentanediol as model substrate, we investigated different iridium complexes in the presence of a base. Sub-stoichiometric amount of sodium acetate resulted in remarkably high yields of divinyl ether. Selectivity was shown to be largely influenced by the polarity and basicity of the solution. After a screening of different solvents, 2-methyl-THF was found to form the desired bis-vinylether in yield as high as 95%. The protocol was successfully applied on gram-scale, and a number of different mono- and diols were converted in good to high yields (for selected examples, see the scheme). The difference in reactivity between primary and secondary alcohols was emphasized by *in situ* FT-IR experiments. Additionally, the proposed reaction mechanism was supported by computational calculations that showed the C-O formation between the alcoholate and the C-C double bond from vinyl acetate as the rate-determining step.



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Cobalt Complexes supported by Phosphinoquinoline Ligands for the Catalyzed Hydrosilylation of Carbonyl Compounds

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Current issues led us to develop more sustainable synthetic pathways. In the 90's, Barry Trost introduced the concept of atom economy which defines the fact that all reagents involved in a reaction should be incorporated in the final product.[1] Moreover, transition metal catalysis can play a role in eco-friendlier synthesis allowing to decrease the energy barrier of the reaction to perform the reaction under smoother conditions. Additionally, the use of catalytic reagents instead of stoichiometric amount minimizes the generation of wastes which responds to actual ecological issues.[2] Our strategy is to combine both of these concepts to device straightforward synthetic processes using every atom involved in the transformation with a very low catalytic loading and high efficiency reaching a completely clean reaction with no waste. An attractive reaction is the hydrofunctionalization which uses a direct addition of H-X to multiple bonds to form C-Y bonds (Y=N, P, O, S…).[3] In particular, the hydrosilylation of carbonyls allows the simultaneous formation of C-H and O-Si bonds.[4] However, one drawback is the frequent use of one or more reagents in excess, such as the silane, which does not clearly respect the atom economy concept. Furthermore, catalysis using non-noble transition metals has become more and more attractive, in particular cobalt catalysis due to its earth abundance,[5] its cheaper price and lower toxicity compared to noble metals.[6] For several years, our group reported various synthesis of cobalt complexes and several cobalt-catalyzed transformations in particular cross-couplings.[7]

Therefore, in this communication we present the simple and straightforward synthesis of unprecedented cobalt complexes bearing easily accessible bidentate phosphinoquinoline ligands and their complete characterization. Moreover, these complexes demonstrated an efficient catalytic activity toward the hydrosilylation of various substituted carbonyl compounds using a low catalyst loading (1 mol%), with strict stoichiometry of the two coupling partners and under mild conditions making an atom-economical and waste-free synthetic methodology for silyl ether synthesis.[8]

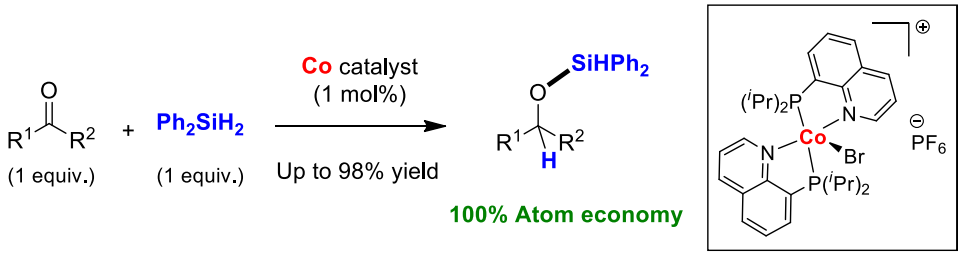

Figure 1: Hydrosilylation of carbonyl compounds catalyzed by well-defined cobalt complex.

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Direct Mechanocatalysis – The Milling Ball is the Catalyst

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Direct Mechanocatalysis is a novel concept of catalysis neither utilizing light, thermal heating nor an electric potential as in conventional catalysis, but simply mechanical energy.[1,2] In a mechanochemical approach, mechanical energy is provided by the collision of milling balls inside a ball mill. The catalyst is neither dissolved (as in homogenous catalysis), nor a powder or bed of shaped bodies (as in heterogeneous catalysis), but the milling ball itself. We showcase how even in the absence of any solvent, solid reactants can be brought into reactions mechanocatalytically - only using milling balls that refresh their catalytically active surface constantly during their continuous collisions. The solid-state concept of direct mechanocatalysis is fundamentally different from conventional solution-based procedures and involves reactants that can hardly be brought into reaction via conventional approaches because of low solubility or limited stability in solution. Moreover, it is highly sustainable as it makes the use of any solvent obsolete and allows for an exceptionally facile catalyst separation after synthesis; simply taking the milling ball out of the vessel. We demonstrate this concept for a variety of reactions that are commonly in the hand of homogeneous catalysis such as Suzuki-, Sonogashira-, or Glaser-coupling and show its versatility for small organic molecule- and polymer-syntheses.[3] Moreover, we elucidate the reaction mechanisms by in situ characterization techniques and shed light on the location of the catalytically-active species.



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Remote Amino Acid Recognition Enables Effective Hydrogen Peroxide at a Manganese Oxidation Catalyst

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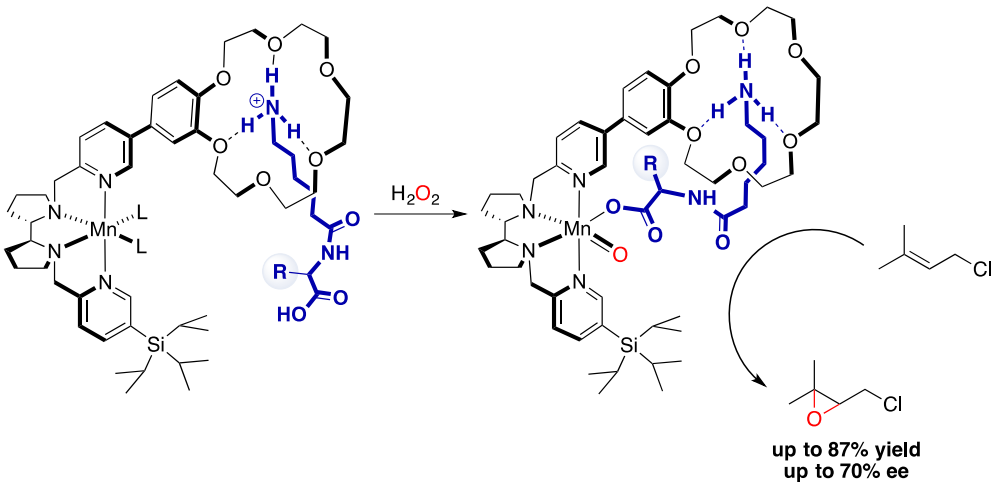
Oxygenation of organic substrates by iron metalloenzymes occurs with high levels of selectivity, mainly because of the exquisite control of both the primary and the secondary sphere of the iron center [1]. Due to its efficiency, chemists have tried to mimic these systems with artificial catalysts, with a very defined first coordination sphere [2]. One of the most studied families are Fe and Mn complexes with tetradentate *bis*-amine-*bis*-pyridine ligands. These coordination compounds can efficiently activate the H_2O_2 to form a high valent metal-oxo species able to oxidize a large range of substrates. However, a proton source is required for peroxide activation; and while a single acidic function is needed in enzymes, a high excess of carboxylic acid is required by artificial catalysts, especially with manganese complexes (up to 17500 equivalents with respect to the catalyst), resulting in a highly acidic solution and the production of high amounts of carboxylic acid waste [2].

Herein, we present an effective, enzyme-like hydrogen peroxide activation at a Mn catalyst with amounts of acid that are almost stoichiometric to the metal [3]. Our approach relies on supramolecular recognition of an α,ω-amino acid to a crown ether receptor present in the ligand. Such interaction occurs in the second coordination sphere of the manganese, and locates the carboxylic acid in an optimal position to access the first coordination sphere and get involved in the catalytic cycle, enabling effective H_2O_2 activation for asymmetric epoxidation reactions.



NMR analysis of the binding and catalytic oxidation experiments demonstrates that remote binding of the amino acid to the ligand is crucial for effective epoxidation. This work can serve as a proof-of-concept for the use of supramolecular chemistry to modify the second coordination sphere of bioinspired complexes and to design enzyme-like artificial catalysts.

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Four faces of one compound: Transformations of isoindolinone-derived N(acyl) ketimines

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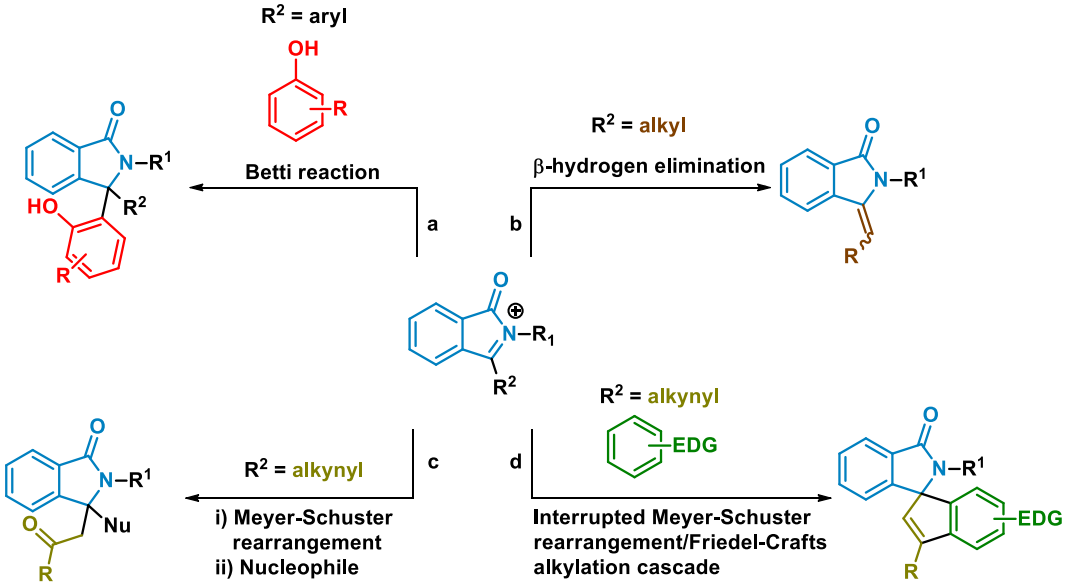
Demand for new bioactive compounds and materials has propelled discoveries of synthetic approaches that incorporate chemical building blocks that can be easily and strategically modified in a minimal number of operational steps. In this respect, from a synthetic point of view, attractiveness of *N*(acyl) ketimines lies in ease of their preparation from cheap and readily available chemicals. In addition, ability to transform these highly reactive species under mild conditions renders them an attractive substrates in organocatalytic and transition metal-mediated/catalyzed reactions [1]. By taking advantage of these properties, herein, we present an acid-catalyzed functionalizations of *N*(acyl) ketimines prepared by dehydration of parent 3-hydroxyisoindolinones. Formal Betti reaction with phenol derivatives afforded sterically congested α-triphenylmethylamines (route a) [2]. In case when C-3 substituent (R^2 group) is an alkyl group, β-hydrogen elimination leads to 3-methyleneisoindolin-1-ones, where stereochemistry around the C=C double bond is affected by the size of the *N*-substituent (route b) [3]. Cascade Meyer-Schuster rearrangement/aza-Friedel-Crafts alkylation afforded highly functionalized isoindolinone derivatives (route c). On the other hand, interrupted Meyer-Schuster rearrangement in the presence of external electron-rich aromatic nucleophile leads to structurally divergent spiroisoindolinones (route d) [4]. Detailed mechanistic investigations and applications of developed methods will be presented as well.



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Tailoring Furfural Reactivity On Au/Ceo_2 Catalysts: Base-Free Oxidative Esterification Enhanced By Protecting Agent And Microwave Irradiation

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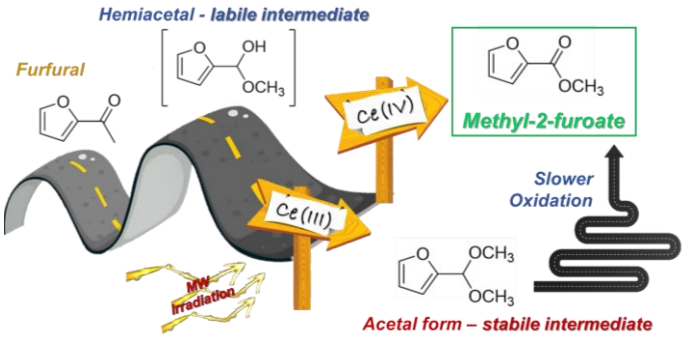
The raising attention for sustainable approaches in synthetic processes led to point great attention towards biomass-derived chemicals. Among these class of molecules, furfural (2-FA) belongs to a limited number of compounds completely obtained from renewable resources. [1] 2-FA results as an attractive intermediate for chemicals production, as a sustainable platform molecule. [2] In particular, the 2-FA oxidative esterification to Me-2-F is one of the main pathways leading to upgrade lignocellulosic biomass residues, exploiting catalysis approaches ranging from transition-metal to organo-homogeneous systems. [3] In the green and ecofriendly approach, however, heterogeneous catalysts appear as the most advisable solution to achieve cost reduction and low environmental impact. In detail, Au nanoparticles are recognized as extremely active under mild conditions, adopting molecular oxygen as benign oxidant, even without the use of a base,[4] helping to design a sustainable reaction protocol.

In this work [5], an Au-based catalyst supported on ceria (AuCePVA) was investigated, synthetized using polyvinyl alcohol (PVA) as protective agent. Complete conversion of 2-FA to Me-2-F was achieved, obtaining full selectivity in oxidative esterification, under conventional heating and in base-free conditions. The role of PVA during the reaction was studied exploiting Au/CeO_2 as benchmark catalyst, demonstrating that polymer chains acted not merely as metal stabilizer, but also showed an active function. Finally, according to process intensification, the application of microwave-assisted (MW-assisted) 2-FA oxidative esterification was explored. Unexpectedly, AuCePVA submitted to MW led to a preferential oxidation of the hemiacetal into the ester rather than the re-oxidation of the acetal into the ester. The detection after catalyst irradiation of new Ce^{3+} acid centers on the support, helped to explain the reaction trend. Hence, two reaction pathways have been proposed (Scheme 1): Path 1 involved the direct 2-FA conversion to Me-2-F with the hemiacetal species as labile intermediate. In this case, the activated C=O bond of the aldehyde underwent a nucleophilic attack by methanol and further deprotonation to form the hemiacetal. Alternatively, the reaction proceeded following Path 2 and 2-FA can form the acetal right after the hemiacetal intermediate and furtherly converted to Me-2-F.



Scheme 1: Proposed reaction pathways, MW-assisted 2-FA esterification to Me-2-F

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Zeolites Made out of Other Zeolites

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Zeolites are not only extremely useful, which is why they are so widely used in the chemical industry, but also fascinating, as they display intricate structures and truly unique properties [1-3]. During the last years, our research group has developed hierarchical zeolites with new architectures through the use of other zeolites either as starting materials, as seeds, or as a source of zeolitic building units. [4,5] During my presentation, I will describe new phenomena we observed by using this strategy, such as the spontaneous self-pillaring of zeolites through the use of seeds. [4] We were able to capture the moment when this new structure emerges from the gel (Figure 1a) and to follow the self-pillaring process (Figure 1b). On the other hand, we have developed a new family of hierarchical catalysts prepared by zeolite interconversion. [5] By stopping this process at different times, we obtained Interzeolite Transformation Intermediates (ITI), which have a large surface area, high percentages of external acid sites, and contain in their structure building units from various zeolites, which markedly improves their catalytic performance.

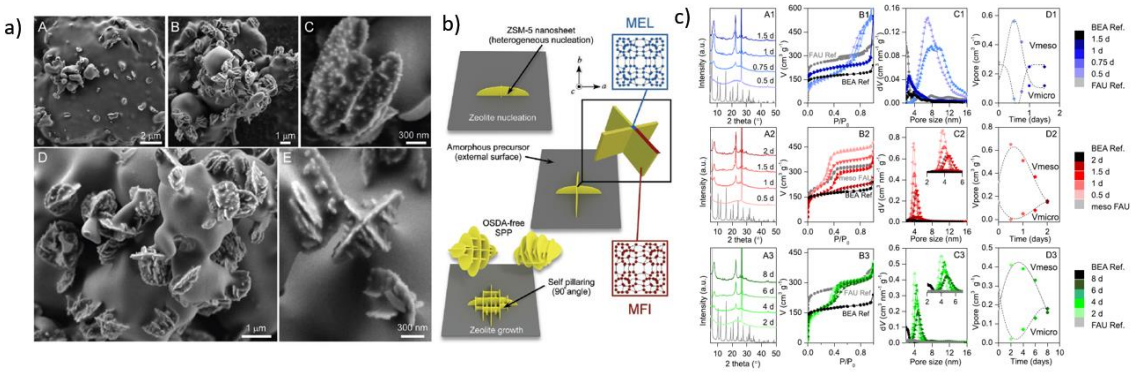

Figure 1. a) Self-pillared zeolites emerge from the gel, as captured by TEM, b) scheme of the mechanism of formation of Self-pillared zeolites with seeds, and c) evolution of the structural and textural properties of Interzeolite Transformation Intermediates

During my presentation, I will describe the evolution of the structural, textural and chemical properties of these materials that we have followed through a wide variety of spectroscopic techniques (Figure 1c). Finally, the hierarchical materials that we have prepared using zeolites, present exceptional catalytic performance for the transformation of voluminous molecules. Specifically, self-pillared zeolites showed a two-fold increase in selectivity in the Friedel–Crafts alkylation reaction of mesitylene with benzyl alcohol. Similarly, we observed a significant increase in their lifetime and exceptionally enhanced turnovers for these catalysts, as much as fourfold, relative to conventional zeolite, in the methanol-to-hydrocarbon reaction. On the other hand, the Interzeolite Transformation Intermediates show superior catalytic performance over conventional zeolites for the Friedel−Crafts alkylation of indole with benzhydrol, the Claisen−Schmidt condensation of benzaldehyde and hydroxyacetophenone, and the cracking of polystyrene. These results show the enormous versatility of zeolites and the opportunities that remain to be explored for the preparation of more accessible, selective and useful catalysts.

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Spatially-resolved insights into activity and structure of mixed metal oxide catalysts during selective propylene and isobutene oxidation

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Catalysis is a key technology in modern society, being involved in an estimated 90% of industrial chemical processes. Historically, catalyst development often involved trial and error approaches, while knowledge-based catalyst design is now coming into focus. This includes optimization of metal oxide-based catalysts used in selective oxidation reactions to functionalize hydrocarbon feedstocks [1]. Commonly, catalysis research focuses on revealing structure-activity relationships by performing reactor in- and outlet measurements, with the reactor itself often treated as a "black box" [2,3]. However, a detailed understanding of the catalyst workings requires knowledge of local gas phase concentration, temperature and structural evolution along the reactor. Such spatially-resolved insights can provide further conclusions on the reaction kinetics and mechanism [4]. For this purpose, we investigated selective oxidation of light olefins over Bi-Mo-Co-Fe-oxide catalysts in two ways: i) integral synchrotron-radiation based *operando* experiments ii) spatially-resolved experiments with a Compact Profile Reactor (CPR, REACNOSTICS GmbH). Bi-Mo-Co-Fe-O catalysts were prepared with one-step flame spray pyrolysis (FSP) and tested for several days on stream to obtain integral catalytic performance data. In contrast to single or binary metal oxides, such 4-component systems show superior catalytic performance in light olefin oxidation and provide a suitable picture of complex metal oxide phase mixtures, thus representing more closely the industrially-applied catalysts [2,3]. However, this complex phase ensemble requires *operando* synchrotron experiments (XAS, XRD) to unravel structural changes during catalytic reaction (cf. Fig. 1). Based on variation in Co and Fe content, we observed a pronounced influence of the different crystalline and amorphous phases on catalyst performance, including selectivity during propylene and isobutene oxidation towards acrolein and methacrolein, respectively. Using the combined approach in one reactor, we performed spatially-resolved characterization (XAS, XRD, Raman spectroscopy) with (simultaneous) spatially-resolved activity data and temperature profiles (cf. Fig. 2). Finally, the combination of integral and spatially-resolved insights into Bi-Mo-Co-Fe-oxides differing in activity/selectivity, as well as the comparison of their behavior in propylene and isobutene oxidation allowed us to gain new insights into the role and interplay of individual metal oxide phases present in such complex 4-component systems.

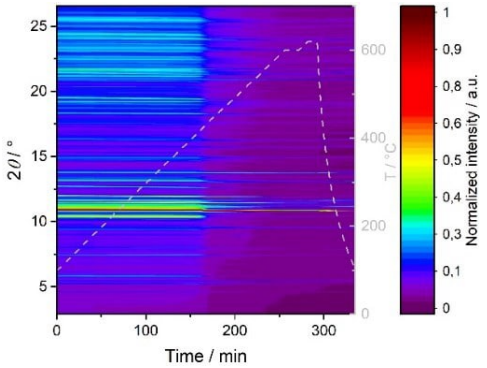

Figure 1: Structural evolution of $Bi_1Mo_{12}Fe_3Co_8O_x$ derived from XRD during selective isobutene oxidation ($He/O_2/C_4H_8/H_2O$= 70/14/8/8 vol%, 100-600 °C, 2 K/min).

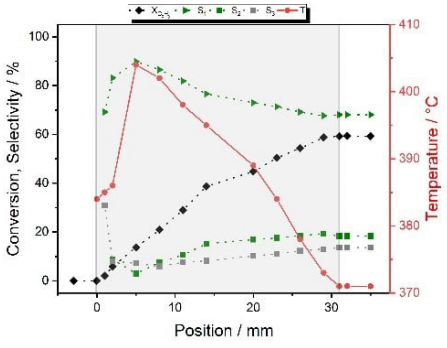

Figure 2: Conversion, selectivity and temperature profiles along the packed catalyst bed during selective olefin oxidation.

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Upgrading the Heavy Pyrolytic Oil from End-of-Life Tyres to High-Quality Carbon Black Feedstock via Hydrodesulphurization and Aromatization

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Globally, an estimated one billion tyres reach the end of their useful lives every year [1]. End-of-Life Tyres (ELT) are used today into a variety of recycling, public works and civil engineering applications, or are used as a fuel substitute in cement kilns, boilers and power plants. However, current ELT treatment processes are not circular and do not result in many raw materials that can be reused in the tyre industry. Furthermore, as there are not enough solutions to valorize materials from ELT in the EU, more than half of ELT are exported to far-off destinations. The recycling of materials in semi-closed loops is more circular and sustainable than burning materials for energy, especially when end-of-life products can be reconverted into equally high-added value new products.

The EU-funded Horizon2020 BlackCycle project aims at creating, developing, and optimizing a full value chain from ELT to Secondary Raw Materials (SRMs) which can be used for the production of new tyres, with no waste of resources in any part of the chain and a specific attention for the environmental impact. This value chain consists of the ELT collection, pyrolysis and refining of the crude pyrolytic oil into added value fractions, and conversion of these fractions to SRMs for the manufacture of new tyres. In particular, the heavy fraction of the pyrolytic oil will be used as feedstock for the production of carbon black, a major tyre component (~20%) that is used as filler. However, upgrading of the pyrolytic oil is necessary to reduce its sulphur content and increase its aromatics content and C/H ratio, in order for it to become a suitable feed for the production of carbon black. The aim of this study is the hydrodesulphurisation (HDS) and the aromatisation of the heavy oil fraction of an ELT pyrolytic oil. The HDS of the heavy oil fraction was performed in a high-pressure fixed bed unit, with different commercial NiMo- and CoMo-based catalysts, at different reaction temperatures (325-375 °C), liquid hour space velocities (0.6-2 h^{-1}) and at a pressure of 60 bar. Overall, a maximum sulphur reduction of 84% was achieved with a commercial NiMo catalyst. The aromatization process of the heavy oil fraction was studied over zeolites with different properties (silica-to-alumina ratio, surface area, acidity, etc.), such as USY, HZSM-5, HZSM-5 diluted and HY, under different experimental conditions. The results (C/H ratio versus liquid yields) of the zeolite screening in a micro-activity test unit at 400 °C and catalyst-to-oil ratio 1, 2, 3) are presented in Figure 1. The screening revealed that among the zeolites, HZSM-5 increased the C/H ratio up to 0.85 (from 0.76 for the heavy oil fraction). Further investigation of the aromatization process will take place with the investigation of the effect of metal(s) impregnation (such as Zn and Ga) and varying metal(s) loading over the zeolites.

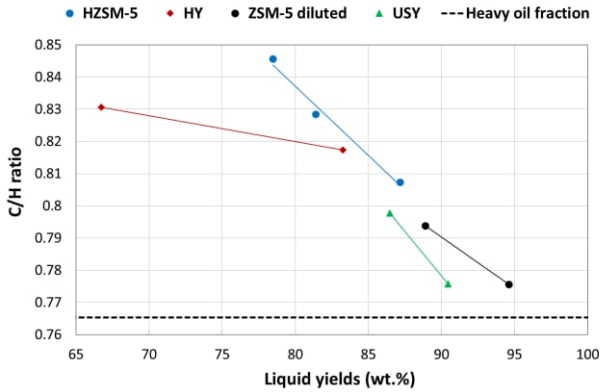

Figure 1. C/H ratio as a function of the upgraded liquid yield for the aromatisation tests using different zeolites as catalysts *(reaction conditions: T = 400 °C, P = atmospheric, cat/oil ratio = 1, 2, 3).*

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Methanolysis of Non-activated Esters Catalysed by Novel Artificial Enzymes

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Hydrolase enzymes, like chymotrypsin, are able to catalyze hydrolytic reactions by using a nucleophilic hydroxyl or thiol group, a basic nitrogen and an oxyanion hole which stabilizes the tetrahedral intermediate in a two-step mechanism [1]. Mimicking enzymes is still a challenge in Organic Chemistry, due to the difficult synthesis of the whole enzyme, but imitating the active centre is a good starting point to prepare hydrolytic enzyme mimics [2].

In our research group artificial enzymes which mimic the active centre of natural hydrolases have been developed [3]. The first generation of catalysts has a pyrrolidine (basic nitrogen), a hydroxyl group and a dicarboxylic acid pyridine moiety as oxyanion hole unit. Here we present second and third generation of improved structures [4] with narrow and adjustable oxyanion-hole moieties as oxyanion-hole units, as well as a second hydrogen-bond network in order to increase the substrate association and tetrahedral intermediate stabilization. These catalysts have been tested in the methanolysis of acyl-enzyme-mimic intermediates, achieving meritorious half-life times up to $2.8 \cdot 10^8$ which are similar to enzymatic reaction rates (10^{10}). They have also shown catalytic activity in the transesterification of ethyl acetate with methanol at room temperature. To the best of our knowledge, it is the first time that a synthetic enzyme which mimics the active center of natural hydrolases is able to perform this reaction.

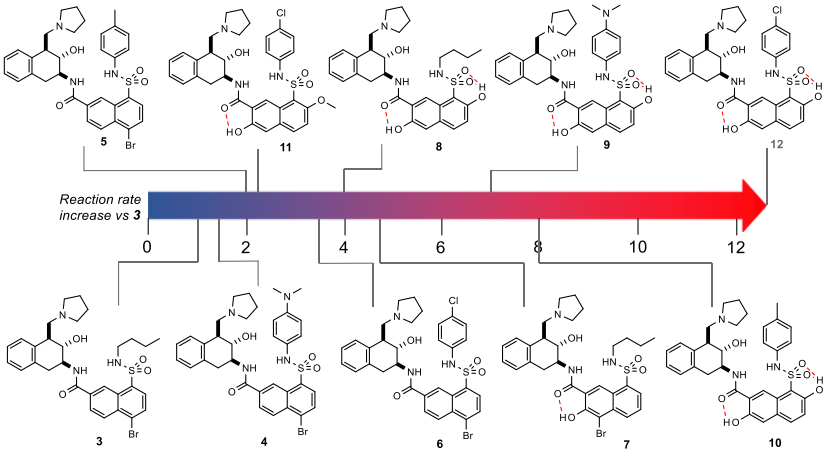

Figure 1. Biomimetic catalysts used in transesterification reactions.

This work was supported by MICINN (PID2020-118732RA-I00 and PID2019-108994RB-I00), Junta de Castilla y León (European Regional Development Fund-SA069P17), the University of Salamanca (Own Research Programs-KCEP/463AC01 and 18K155/463AC01) and Fundación Memoria de D. Samuel Solórzano Barruso (FS/8-2019). JJGG is gratefully acknowledged to University of Salamanca and Santander Bank for a postdoctoral fellowship. AH is grateful to the Algerian Government for a predoctoral fellowship for "Formation Doctorale résidentielle à l'etranger". ALFA thanks the Spanish Government for a Beatriz Galindo Fellowship (BG20/00233). NUCLEUS platform at University of Salamanca, especially Anna Lithgow (NMR Service) and César Raposo (MS Service).

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Rethinking the Active Site Concept in Computational Heterogeneous Catalysis

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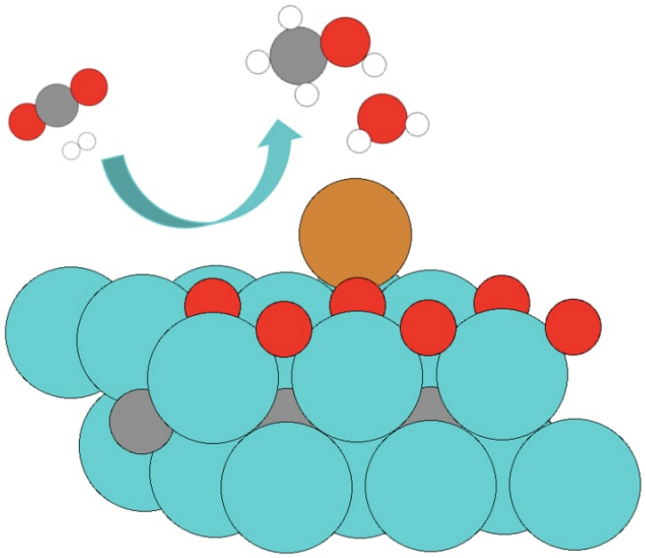
Theoretical calculations are essential to understanding heterogeneous catalysts at the atomic level. Nevertheless, these materials are highly complex to model because several physicochemical processes occur under reaction conditions. Present computational methods do not fully capture their complexity, hampering the theory-based design of better materials.

This talk will show our work to understand heterogeneous catalysts via a computational approach. CO_2/CO and hydrocarbon conversion reactions catalyzed by metal particles on oxide/carbide supports [1,2,3,4]. The selected systems will showcase the static and the dynamic approach t simulating these materials, discussing strategies to bridge the gap between theory and experiment. Overall, it will allow us to revisit the concept of the active site showcasing techniques to understand the dynamics of heterogeneous catalysts better.



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Unleashing the Potential of Zeolites for the Transformation of Bulky Molecules

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The development of intracrystalline mesoporosity within zeolites has been a long-standing goal in catalysis as it significantly contributes to alleviating the diffusion limitations of these microporous materials.[1] In the last years, our group has described the surfactant-templating in zeolites, which allows for the introduction of tailored mesoporosity within a given zeolite, while broadly preserving its key properties such as strong acidity, crystallinity, and hydrothermal stability, Figure 1A.[2] Moreover, we have recently reported unprecedented insights on the formation of intracrystalline mesoporosity in zeolites by surfactant-templating obtained by combining *in situ* synchrotron X-ray diffraction, Liquid Cell Transmission Electron Microscopy (Liq-TEM) and Atomic Force Microscopy, and Raman Microscopy.[3]

In this communication, we present the application of these novel materials in the transformation of a number of bulky molecules. First, our hierarchical zeolites were successfully tested in petrochemical related processes,[4] showing enhanced activity and selectivity for the first cracking products (Figure 1B). Second, we tested them in fine chemistry related processes where surfactant-templated zeolites shows activity in the production of steroidal analogs and indole scaffolds, which are very interesting intermediates for pharmacological applications (Figure 1C).[5] Finally, we will present new data on the use of the hierarchical zeolites as basic catalysts and as nanoparticles supports.[6] In all the examples studied, surfactant-templated USY zeolites are both more active and selective than conventional zeolites (CBV720) for the transformation of bulky molecules, due to their improved accessibility.

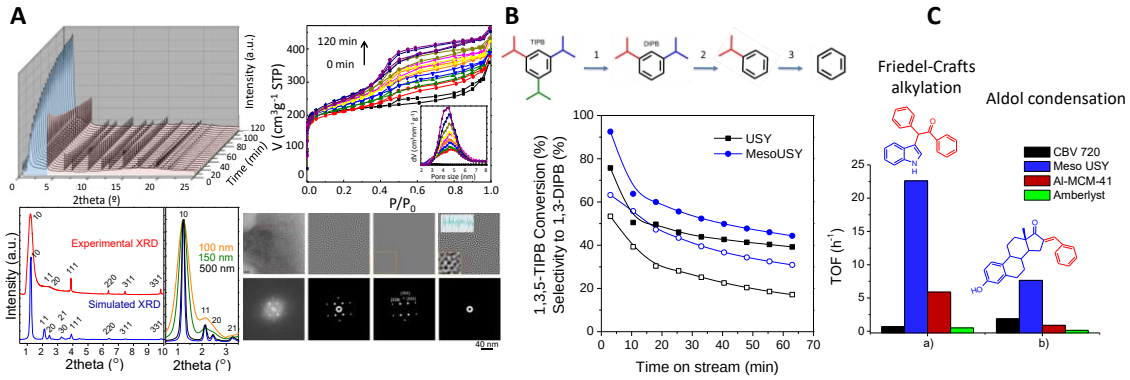

Figure 1. A) Textural, structural and morphology characterization of the surfactant-templating process in FAU zeolite. B) Catalytic performance of surfactant-templated FAU for the catalytic cracking of 1,3,5-TIPB and C) Catalytic activity of surfactant-templated FAU in Friedel-Crafts alkylation and aldol condensation reactions using bulky reagents.

Thanks are due to the European Commission for funding through the H2020-MSCA-RISE-2019 program (Ref. ZEOBIOCHEM – 872102) and Spanish MICINN (Ref. RTI2018-099504-B-C21). M.J. Mendoza thanks the GVA for a PhD fellowship (GRISOLIAP/2020/165). N.L. also acknowledges the UA (ref. UATALENTO17-05).

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N-Hydroxyphthalimide role in Aerobic Oxidations: Homogeneous versus Heterogeneous Catalysis

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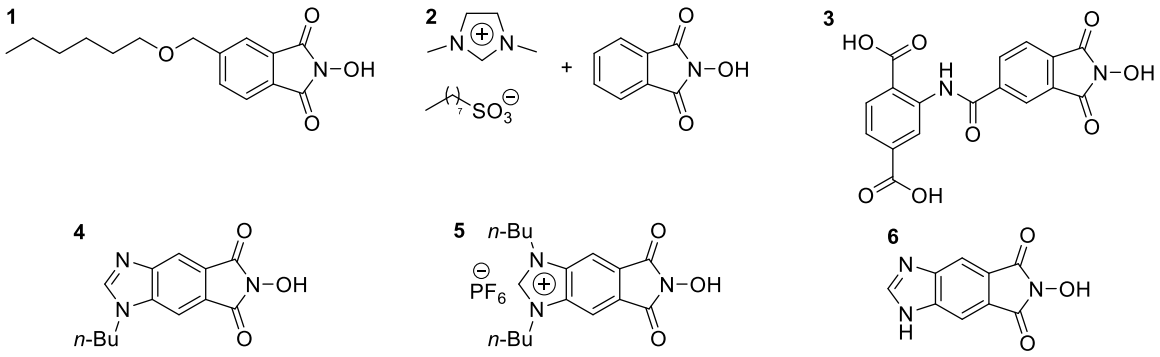
N-hydroxyphthalimide (NHPI) has emerged as a "green" alternative to the use of transition metal complexes to promote the selective aerobic oxidation of hydrocarbons via hydrogen atom transfer.[1] Nevertheless, three main interconnected problems still prevent its final implementation for large-scale processes. They are: i) its poor solubility in apolar media at room temperature; ii) its autodecomposition at high temperatures and iii) the difficult catalyst recovery process.[2] As a consequence, NHPI-promoted liquid phase aerobic oxidations have always been performed in the presence of polar co-solvents, thereby introducing further economical and ecological drawbacks.[3]

To overcome these limitations, we have investigated the development of solvent-free processes, and both homogeneous and heterogeneous conditions have been considered.

As far as homogeneous systems are concerned, on the one hand, we designed a novel lipophilic NHPI derivative (**1**) showing high solubility in aromatic hydrocarbons with unprecedented catalytic efficiency.[4] On the other hand, we developed a novel NHPI/ionic liquid combined system (**2**) operating under effective homogeneous solvent-free conditions.[5]

As to heterogeneous systems, we synthesized an NHPI-tagged ligand (**3**) suitable for the construction of metal-organic frameworks (MOFs), an innovative class of crystalline, intrinsically porous, non-inert supporting materials.

Finally, we designed a novel multipurpose NHPI derivative with tunable reactivity to be used both under homogeneous and heterogeneous conditions. Its derivatization to lipophilic (**4**), ionic liquid-like (**5**), and zeolitic-imidazolate framework (ZIF) ligand (**6**) analogs is reported.(**6**)



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Selective hydrogenation and hydrodeoxygenation of aromatic ketones using bimetallic FexPt100-x nanoparticles immobilized on supported ionic liquid phases

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Achieving specific selectivity in catalytic hydrogenation of aromatic unsaturated substrates is a principal point in biomass valorization, pharmaceutical and chemical industries. While homogeneous catalysts provide good selectivity they typically suffer from low recyclability. At the same time, heterogeneous bimetallic catalysts have the potential to afford high activity and recyclability with a possibility to control selectivity in hydrogenation by adjusting ratios of metals in the catalyst (e.g. FeRu, CoRu, CoRh catalysts) [1, 2]. In the present study, we aim at preparing bimetallic iron (Fe) platinum (Pt) nanoparticles (Fe_xPt_{100-x} NPs) combining the excellent hydrogen activation capability of platinum (Pt) with the oxophilicity of iron (Fe) in order to achieve the effective and selective hydrogenation and hydrodeoxygenation of C=O bonds. An imidazolium-based supported ionic liquid phase (SILP) will serve as support material for these NPs, as it was shown to be a suitable matrix for the preparation and stabilization of various bimetallic NPs [2].

Fe_xPt_{100-x}@SILP were synthesized by decomposition of organometallic precursors of Fe ([bis(trimethylsilyl)amide]diiron (II)) and Pt (tris(dibenzylideneacetone)diplatinum (0)) in H_2 atmosphere in presence of the SILP (fig. 1a). This organometallic approach allowed precise control of the composition of bimetallic NPs (Fe_{100}, $Fe_{75}Pt_{25}$, $Fe_{50}Pt_{50}$, $Fe_{25}Pt_{75}$, Pt_{100}) which is an essential point to gain control over the catalyst selectivity. Fe_xPt_{100-x}@SILP catalysts were characterized by transmission electron microscopy (TEM) and scanning electron microscopy with energy dispersive X-ray analysis (SEM-EDX). TEM showed well-dispersed NPs with a mean size around 1.6 - 2.3 nm depending on the metals ratio. SEM elemental mapping evidenced an even distribution of metals on a support. SEM-EDX analysis gave ratios of metals in accordance with theoretically calculated values. Small size and good dispersion prove that SILP is a perfect stabilizing agent for Fe_xPt_{100-x} NPs.

The reactivity of Fe_xPt_{100-x}@SILP catalysts was probed using the hydrogenation/hydrodeoxygenation of aromatic ketones as model a reaction. The activity and selectivity of Fe_xPt_{100-x}@SILP catalysts for the conversion of acetophenone (**APh**) as model substrate were found highly dependent on the Fe:Pt ratio (fig. 1b). In particular, while Pt@SILP led to the full hydrogenation of acetophenone to give the saturated alcohol (**3**) in quantitative yield, the incorporation of small amounts of Fe in $Fe_{25}Pt_{75}$@SILP resulted in a sharp activity and selectivity switch, with the complete hydrodeoxygenation of the ketone and conservation of the aromatic ring (89% of **2**). While the shut-down of aromatic ring hydrogenation in bimetallic NPs has been previously observed and attributed to the interruption of the necessary arrangement of noble metal atoms at the NPs surface, [2] this is the first time that an effect on deoxygenation activity is reported. Further increase of the Fe content in $Fe_{50}Pt_{50}$@SILP revealed the aromatic alcohol **1** as main intermediate. Above Fe_{75}, no activity was observed.

These results show that careful control of the Fe:Pt ratio in Fe_xPt_{100-x}@SILP materials allows the preparation of multifunctional catalytic systems with improved selectivity towards challenging products without deteriorating the catalyst activity.

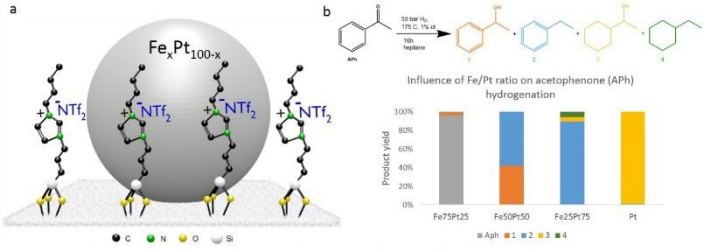

Figure 1 a: schematic representation of Fe_xPt_{100-x}@SILP catalysts; b: results of catalytic hydrogenation of acetophenone using Fe_xPt_{100-x}@SILP catalysts.

The authors are grateful to the Agence Nationale de la Recherche and to the NanoX project for the financial support.

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Hydrodechlorination of chlorobenzene derivatives catalyzed by Pd/GO in water. A new route to cyclohexanone

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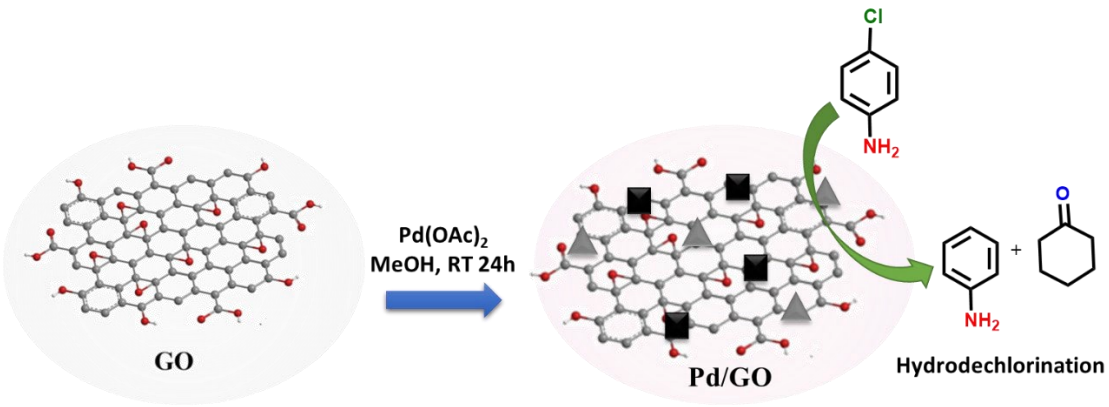
The dehalogenation of aryl halides based on the reduction of carbon-halogen bond, is one of the fundamental reactions in organic synthesis. It is also important for the environment as a method of disposal of health hazardous chlorinated compounds present in water, such as polychlorinated biphenyls (PCBs) [1].

In this work, the material, comprising palladium nanoparticles anchored on graphene oxide, Pd/GO, was synthesized. It is worth noting that highly dispersed nanoparticles with very well defined geometrical shapes were formed under mild conditions, without additional reducing agents. The material was fully characterized by a set of experimental techniques, including XPRD, RAMAN, XPS and TEM imaging.

Ultimately, graphene oxide in catalysis has aroused great interest, due to its unique properties **[2]**. Its two-dimensional structure with a large specific surface area can serve as the ideal support for metallic nanoparticles with high dispersion. In addition, a big advantage of GO is excellent mechanical resistance, which allows to obtain highly stable and durable catalysts **[3].**

The Pd/GO catalysts was used for dehalogenation of different aryl chlorides in water. Two hydrogenation methods were applied, based on the reaction with H_2 under 10 bar pressure, and transfer hydrogenation with 2-propanol/NaOH as the hydrogen source. Interestingly, both methods provided different results when chloroanilines were used as substrates. Under hydride transfer conditions, aniline was obtained as the only product while under H_2 pressure cyclohexanone and N-phenylcyclohexylamine were also formed. Cyclohexanone is an important of high technological importance because it is used in a production of caprolactame and adipic acid for manufacture nylon 6 and nylon 66 [4]. Therefore, its formation as the dehalogenation product presents a very attractive option. In such process an environmentally hazardous compound would be directly transformed to the highly desired raw material. Further studies shown that under applied conditions cyclohexanone can be also obtained during dehalogenation of dichlorophenols. The possible reaction mechanism was proposed.



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Is doping an efficient strategy to activate the basal plane of 2H-MoS_2 for the hydrogen evolution reaction?

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MoS_2 is a promising low-cost catalyst for the hydrogen evolution reaction (HER) [1]. In order to enhance the HER activity of the inert basal plane, we perform an extensive density functional theory screening (DFT) of substitutional doping (Figure1). Substituted basal planes may have many more active sites per MoS_2 formula unit compared to the active sites located on the edges. We assess the electrocatalytic activity by explicitly considering the electrochemical potential via grand canonical DFT in combination with the linearized Poisson-Boltzmann equation [2]. We screen 17 abundant elements for Mo doping and 5 elements for S substitution. For the first time in such a screening study, we investigate not only the adsorption of H, but also of OH and H_2O to explore the solvent effect, since the reaction takes place in an aqueous medium [3]. Two other phenomena that could hinder H_2 production at these sites are investigated, namely H_2S release and the (local) segregation/dispersion tendency of the dopants on the basal surface. Compared to the pristine MoS_2 nanosheets, our results show that most of the dopants significantly enhance electrocatalytic activity. Considering all the evaluated factors, we identify the most promising systems: Dimers of Ti, Zr, and Hf, and the substitution of S by P are predicted to lead to stable active sites at the basal level with overpotentials of about 0.2 V.

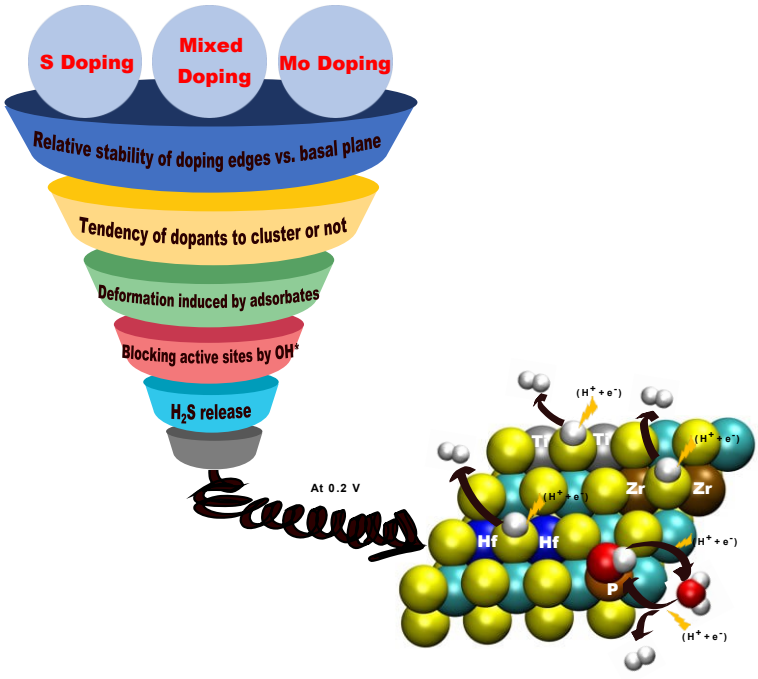

Figure1: Computational identification of the most promising elements for substitutional doping for enabling HER on the basal plane of MoS_2.

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3D spatially-resolved catalyst characterization by X-ray tomography

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Understanding catalyst structure is important for a knowledge-based design of new materials with improved properties, e.g. higher activity and stability. Ideally, materials applied in heterogeneous catalysis should be studied in both a spatially- and time-resolved manner in order to establish structure-function relationships. Synchrotron based X-ray techniques offer a toolbox of methods for this purpose [1]. However, the relevant length scales in heterogeneous catalysis span nm to cm (Figure 1), which is a significant challenge requiring a multiscale characterization approach with different imaging techniques.

This contribution outlines recent catalysis applications in the rapidly developing field of X-ray microscopy. First, we present the combination of different X-ray tomography techniques, i.e., micro X-ray computed tomography and X-ray holotomography, together with electron tomography as a set of methods allowing for full porosity characterization of an industrial Ni/Al_2O_3 catalyst applied in the CO_2 methanation process. It is shown that conventional porosity analysis techniques (N_2 sorption and Hg porosimetry) fail to reveal the true pore structure, which can feasibly be accessed only with combined imaging methods [2].

Second, we highlight the potential of hard X-ray nanotomography, i.e., X-ray ptychography, to unravel the structural evolution of catalysts during synthesis [3] and deactivation by coke formation [4]. This X-ray nanotomography method can produce quantitative 3D representations of the sample electron density with <100 nm resolution, on catalyst particles of several tens of µm in size. The electron density contrast can be used to unravel the location of formed coke species, which are often related to catalyst deactivation [4]. Furthermore, X-ray ptychography can reveal changes in macropore structure during calcination as part of catalysts synthesis. Here, in addition to the high resolution of the method, the quantitative electron density contrast enables to retrieve sub-resolution information about the catalyst mesoporosity and its changes [3]. In summary, we show the huge potential of X-ray tomography to understand the structure of catalysts in 3D as a prerequisite for future knowledge-based catalyst design.

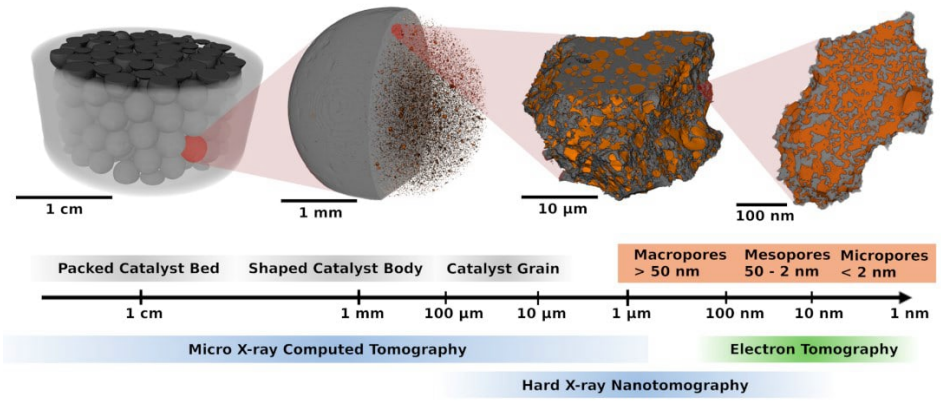

Figure 1 Illustrated multiscale challenges in the characterization of solid catalysts applied in heterogeneous catalysis with selected relevant length scales and features, together with imaging techniques capable of probing these features.

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Highly active magnesium-based catalyst for low-energy PET depolymerization

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Polyethylene terephthalate (PET) is the most widely used condensation polymer in the world. Hence, its disposal has become one the most serious environmental problems facing modern society. Among several recycling methods, chemical recycling, which allows to depolymerize plastic complex chains into their raw monomers has gained in attention [1-2]. In particular, methanolysis appears as the most promising technology for industrial application, however, it normally takes place at super critical conditions, it means, high temperature and pressures (>200 °C, >40 bar). For performing low-energy PET depolymerization, the presence of catalyst is key. Nevertheless, a scarce number of heterogeneous catalyst can be found in literature. Therefore, in this contribution, we propose the preparation of an aluminum-based catalyst in the presence of pectin for the depolymerization of PET waste. Materials characterization (SEM, XRD, TGA, FTIR, BET), a kinetic study and catalyst reusability experiments were performed.

All experiments were developed in a batch pressure reactor using commercial drinking bottles and dried methanol. From several synthesized materials, Figure 1a shows the most adequate catalyst (MgP-6) for the transesterification reaction [3]. The presence of pectin and calcination at 600 °C (MgP-6) showed to be the best parameters for the formation of well-structured nanospheres (≈224 nm), which were found to be fundamental for the catalytic activity. From experiments, PET was depolymerized into its constituent monomers, such as dimethyl terephthalate (DMT) and ethylene glycol (EG). According to the kinetic study, at 180 °C the kinetic constant showed to be four times higher than in pure-thermal reactions (see DMT formation at Fig. 1b). This effect, was even higher (≈40 times) at lower temperatures. Thus, the propose catalyst could develop a complete reaction at temperatures, as low as, 140 °C. Remarkably, as shown in Fig. 1c, MgP-6 revealed to be stable even after 5 consecutive runs without product separation. It shows, catalyst is not deactivated by reaction products. All in all, we consider that the synthesized catalyst is an important step forward for the industrial application of methanolysis of PET waste at lower cost and safer conditions.

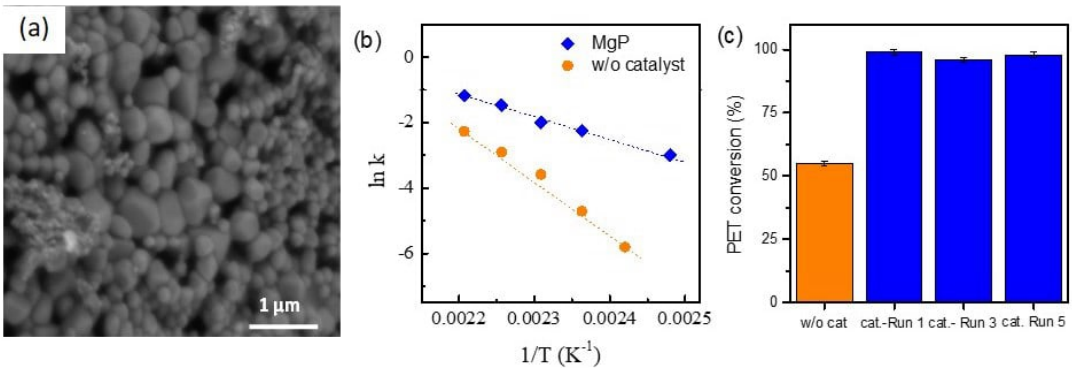

Figure 1. (a) SEM image of MgP-6 synthesized catalyst. (b) Arrhenius plot for reactions developed with and without catalyst. (c) Catalyst stability after five consecutive runs. Reaction conditions: methanol as solvent, N_2 purged system, cut PET waste as raw material.

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Few atoms metal clusters with high catalytic and cytotoxic activity characterized by X-Ray Absorption Spectroscopy

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Here, we show three examples of how XAS techniques are very useful to provide an exhaustive information about the oxidation state and coordination environment of MCs and SACs:

- Pd SACs spontaneously formed after dissolving in neat benzyl alcohols. The gram-scale preparation and stabilization of Pd SACs within the functional channels of a novel methyl-cysteine-based metal–organic framework (MOF) was accomplished, to give a robust and crystalline solid catalyst (Figure 1).[1]

- Ligand-free, few-atom Pd Cs in solution that catalyse the α-selective intramolecular Mizoroki–Heck coupling of iodoaryl cinnamates. The α-selective intermolecular coupling is also achieved with Pd Cs encapsulated within fine-tuned and sterically restricted zeolite cavities.[2]

- Fluorinated pyridine-Pd^{2+} coordinate cages synthesized within the channels of a metal-organic framework (MOF), and used as catalysts during the aerobic oxidation of aliphatic alcohols to carboxylic acids without any additive, a rare example of stable per-fluorinated cationic metal complex.[3]

- Pt Cs prepared in water by just adding a biocompatible extremely mild external reductant. The PtCs show 400 times higher antitumoral activity than cisplatin and thousand times higher activity than Pt NPs for various cancer cell lines.[4]

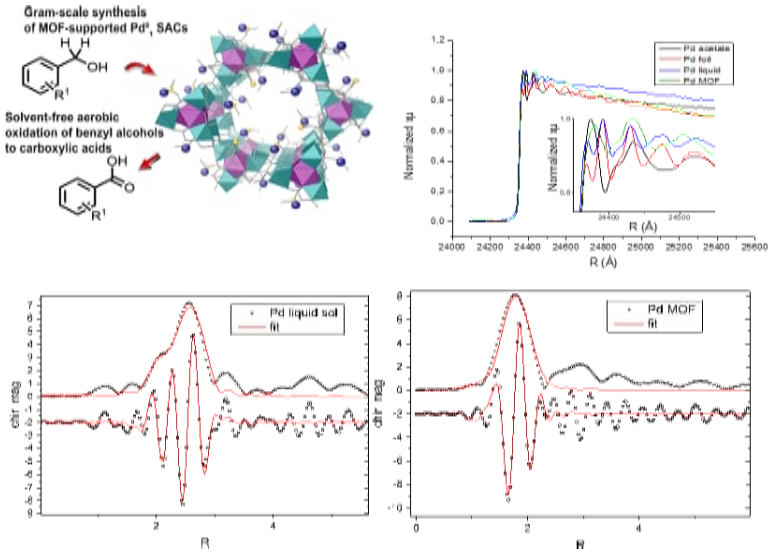

Figure 1. Top left: schematic representation for the oxidation of benzyl alcohol catalyzed by Pd SACs in MOFs. Right. NEXAFS spectra of the Pd SACs in solution and in MOF. Bottom: fitting representation for Pd SACs in solution (left) and in the MOF (right).

Thanks to MINECO (Spain, Projects CTQ 2017–86735–P, PID 2019-104778GBI00, PID 2017-86735-P, PID2020-115100GBI00) and Severo Ochoa program SEV–2016–0683). J. O.-M. thanks to the MICINN for the concession of the Juan de la Cierva Incorporacion contract (IJC2018-036514-I). We acknowledge ALBA Synchrotron for allocating beamtime and CLÆSS beamline staff for their technical support during our experiment.

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Innovative activation strategies of molybdenum sulfide-based catalysts for sustainable chemical transformations in fine chemistry

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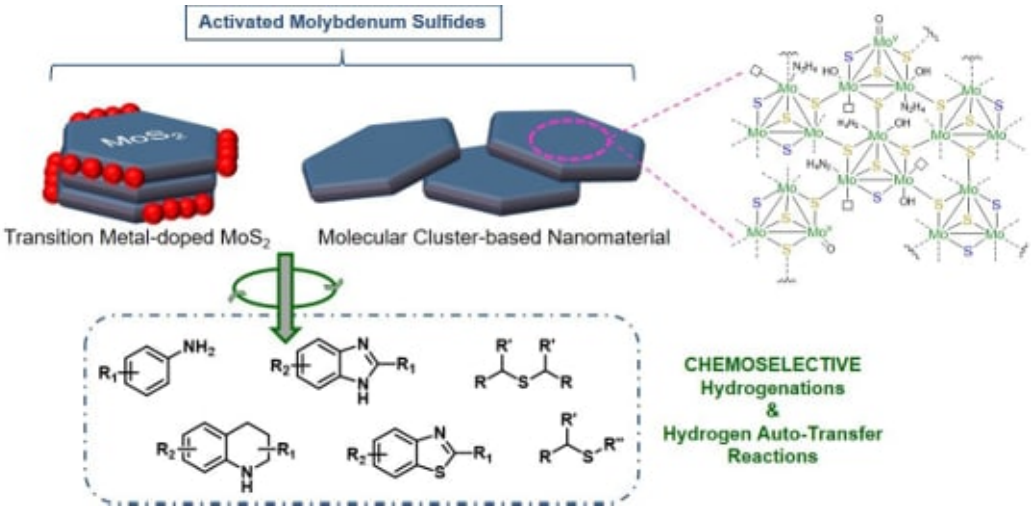
The development of more efficient and cost-effective catalysts is of vital importance to deal with global challenges related to sustainability. Indeed, the desirable future evolution of chemical, pharmaceutical and agrochemical industries towards more selective, energy-efficient and environmentally friendly processes, which reduce the use of hazardous reagents and promote a better utilization of raw materials, largely depends on purposely design catalysts for innovative organic synthesis.

Molybdenum disulfide (MoS_2)-based catalysts have been widely used in fossil fuel refining, and in recent times, they have been applied for sustainable chemical transformations in fine chemistry [1-3]. Within the lamellar structure of MoS_2, theoretical and experimental studies have confirmed that active sites are mainly located at the edges whereas the basal planes are largely inert. Unfortunately, the small perimeter-to-basal area ratio in this type of catalysts implies a limited catalytic activity.

In this communication, innovative activation strategies to obtain highly efficient catalysts will be presented, and especial emphasis will be focused on the use of molecular clusters as precursors to engineer a molybdenum sulfide material displaying structural defects (*i.e.* active sites) on both the naturally occurring edge positions and along the typically inactive basal planes [4]. The catalytic applications of these catalysts for industrially-demanding chemoselective hydrogenations and hydrogen auto-transfer reactions, including those involving new domino or tandem synthetic processes, will also be showcased. Through the use of advanced characterization techniques, the different composition of the prepared nanostructured catalysts and how they undergo a continuing evolution during catalysis will be disentangled. Hence, active phases responsible for the outstanding activity, chemo- and regioselectivity of these catalysts will be accurately determined.



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Spent Lithium-Ion Batteries: from Waste to an Efficient Heterogeneous Catalyst for the Reductive Upgrading of Biomass-Derived Furfural

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The global warming and the climate change can be mitigated by an effective and aware use of recyclables in the light of the circular economy model. In the last years, we have witnessed a lot of research efforts from both academia and industry players in the recycling of electronic wastes (e-wastes) also considering that, at global scale, they already exceed more than 54 Mt in 2019 with an average of 7.3 kg per capita [1]. The management, the disposal and the recycling of e-waste are foremost crucial since, if not correctly conducted, can generate serious problems for the environment and the human health [2]. Spent Li-ion batteries (LIBs) are widely present in most of electronic devices including mobile phones, personal computers, electric vehicles and already represent an important secondary resource for the recovery of important metals such as lithium, cobalt and nickel [3].

The mixture of anodic and cathodic materials arising from the mechanical shredding of spent Li-ion batteries (LIBs), also known as "Black Mass" (BM), can be easily converted into an efficient heterogeneous Co-Ni catalyst for the selective hydrogenation of biobased furfural and other biomass-derived aldehydes and ketones. Yet, the approach is general and can be applied to a variety of substrates under widely different conditions.

The production of the new catalyst involves simple calcination of the e-waste material followed by reduction with H_2 at 500 °C. The so-obtained BM catalyst was then tested in the conversion of furfural (FUR) into furfuryl alcohol (FAL), a precious building block widely used in the chemical and pharmaceutical industry, both in the presence as well as in the absence of added hydrogen. Complete conversion of furfural into furfuryl alcohol is achieved after 90 min at 120°C under 10 bar H_2 in 2-propanol. High furfural conversion can also be obtained under transfer hydrogenation conditions by using 2-propanol as solvent/H-donor. The study opens the route to the use and recycle of spent LIBs as valued raw material of precious catalytic materials suitable for use in fine chemicals production. In the present contribution, the way for a new reuse of spent LIBs as a stable and efficient heterogeneous Co-Ni based catalyst for the selective reductive upgrading of biomass derived molecules is presented [4].

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Unprecedented chemoselective behaviour of MAX phase in functionalized nitroarene hydrogenation

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Selective catalytic hydrogenation of only one functional group when several functionalities are present in a molecule is challenging because the thermodynamic driving forces are quite comparable. One way to address this problem is to use a solid catalyst able to differentiate and preferentially interact with one functional group, while avoiding the hydrogenation of the others [1].

Herein, we present the catalytic features of MAX phase powders in catalytic chemoselective hydrogenation of a nitro group from functionalized nitroarene, such as 4-nitrostyrene (4-NS) (Figure 1) and 3-nitrostyrene (3-NS). The functionalized aniline derivatives resulting from hydrogenation of the mentioned compounds are key intermediates for a large palette of chemical products with important industrial applications [2]. MAX phases are ternary carbides or nitrides that combine properties of both metals and ceramics [3], and although they possess the required properties for catalytic processes, they are scarcely used as catalysts. To the best of our knowledge, no hydrogenation reactions have been reported so far where a MAX phase was used as either a catalyst or support.

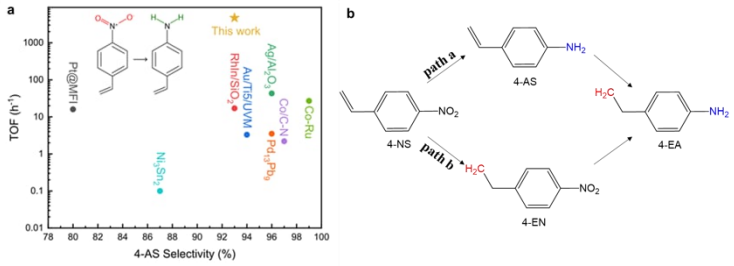

Figure 1: a) TOF results compared with some of the highest reported in the literature for catalysts with 100% conversion and > 80% selectivities of 4-NS to 4-AS. b) Reaction pathways for hydrogenation of 4-NS to 4-AS (4-aminostyrene), 4-ethylnitrobenzene (4-EN) and 4-ethylaniline (4-EA).

This study demonstrates that MAX phase powders of Ti_3SiC_2, Ti_2AlC or Ti_3AlC_2 can chemoselectively hydrogenate 4-NS to 4-AS, with 100 % selectivity; the conversion, however, remains low (~4%). Different Pd loadings were supported on MAX phase with the purpose of preserving its preferential selectivity and boost the conversion. The obtained results underline the critical importance of Pd content/dispersion onto a selective support and that exceeding an optimal Pd value results in masking the selective effect of MAX phase, leaving in place only a non-selective Pd effect.[4] Moreover, Pd dispersion influences the adsorption and activation ways of H_2, that constitutes another crucial step in chemoselective hydrogenation reactions. The sample containing ultra-low Pd loading, e.g. 130 ppm Pd, very well dispersed, provided a conversion of 100% of 4-NS with a selectivity of 93% of 4-NS; higher Pd loadings result in a loss of selectivity. By optimizing the Pd loading, we were also able to increase the turnover frequency 100-fold relative to previous literature results (Figure 1). This is possible due to a very high metal dispersion probably as single atoms that heterolytically activate the H_2 in H^+/H^- pairs, which are more prone to hydrogenate the polar groups (such as nitro) rather the non-polar ones [1].

The newly discovery of this highly efficient and chemoselective system, MAX phase based one, has broad implications for the design of a new generation cost-effective, earth-abundant, non-toxic, metal catalysts.

This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS/CCCDI – UEFISCDI, project number PN-III-P4-ID-ERC-2021-007, within PNCDI III.

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Sub–nanometric metal species in solution and supported in MOFs for organic synthesis

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Ligand–free single metal atoms and clusters can be easily prepared in solution and catalyze relatively complex organic reactions with extremely high turnovers, >1 million in many cases, with just parts per million (ppm) of metal. This catalytic approach is very convenient for industrial purposes, where the amount of expensive metal catalysts must be minimized. Besides, if desired, the sub–nanometric metal species can be prepared in nanostructured solid materials, which allows easy recovery, reuse and implementation in continuous processes. Nanostructured solids have been traditionally used in fields somewhat away of organic synthesis, such as petrochemistry and water treatment, since spatial restrictions have been viewed as an unsurmountable issue when dealing with relatively big molecules, however, we will show here that this view can be incorrect in many cases, and that MOFs can be used as suitable supports for complex organic reactions.[1]

Key industrial reactions such as the chain–walking of terminal alkenes,[2] the NH_4CN formation, CO_2 methanation, olefin hydrogenation,[3] the low-temperature water–gas shift reaction,[4] and the oxidation of alcohols[5] will be shown. Other reactions of interest in organic synthesis such the Büchner reaction,[6,7] and carbon–carbon cross–coupling reactions,[8] will be also described.

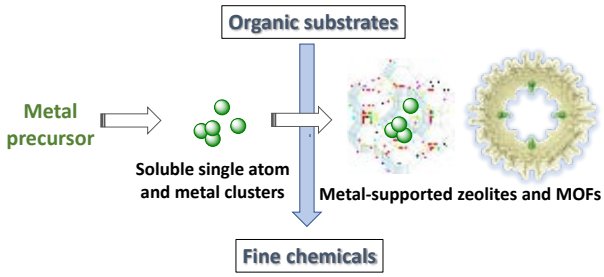

Figure 1. Ligand–free sub–nanometric metal species in solution and supported in MOFs as catalysts for organic reactions.

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Multifunctional catalysts for targeting different biobased products from furfural

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The troubling anthropogenic gas emissions associated with fossil fuel use have led to increasing use of renewable sources, such as vegetable biomass rich in cellulose and hemicelluloses. The acid-catalyzed hydrolysis/dehydration of hemicelluloses gives furfural (Fur) which is a valuable platform chemical for producing several important bio-based products (BioPs). This work presents selective conversion routes leading to furanic ethers (FEs), levulinate esters (LEs), levulinic acid (LA), angelica lactones (AnLs) and γ-valerolactone (GVL) (Figure 1). These routes generally involve multiple acid and reduction reaction steps, and thus their integration is highly attractive from environmental and economical perspectives. Hence, multifunctional catalysts were developed to integrate several steps in a single synthesis operation.
Nanocrystalline Zr-Beta-n and mesoporous Zr-TUD-1 in the presence of a secondary alcohol led essentially to FEs, LEs, LA and AnL in a total yield of 61-76 %, of which 55-58 % was FEs, at 120 °C/(5-7 h) [1]. Hierarchical Zr-Beta-h prepared via top-down strategies favored FEs formation (89 % yield at 150 °C/5 h) [2]. Substituting Zr for Hf triggered the complex reaction routes leading to GVL (65 % yield for nanocrystalline Hf-deAlBeta-n and 73 % for a hierarchical microcrystalline Hf-WdeSAlBeta-m, at 180 °C/48 h) [3]. The BioPs spectrum changed using mesoporous PdNi-TUD-1 and formic acid as H-donor, which led to 2-methylfuran (2MF), 4-oxopentanal and its acetals in a total yield of 90 % (of which 83 % was 2MF), at 170 °C [4]. Characterization of the catalysts, mechanistic and kinetic modelling studies, helped to gauge the roles of the different metal species. While Hf, Zr and Pd were essential for the reduction steps, Al and Ni triggered the acid reactions. All the materials were active and stable for the integrated conversion of Fur to BioPs.

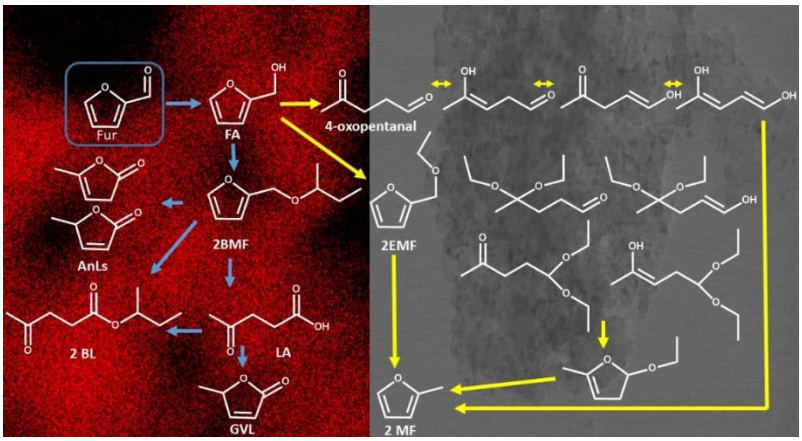

Figure 1- Furfural (Fur) conversion to bioproducts in the presence of catalysts possessing Zr, Hf and Al sites using 2-butanol as H-donor (left side), or Pd and Ni sites using formic acid as H-donor (right side).

Acknowledgement: The Associated Lab. CICECO-Aveiro Institute of Materials, UIDB/50011/2020 & UIDP/50011/2020 was financed by national funds through the FCT/MEC (PIDDAC). The positions of M.M.A and A.F. were funded by national funds (OE), through FCT, I.P., in the scope of the framework contract foreseen in numbers 4, 5 and 6 of article 23 of Decree-Law 57/2016, 29 August, changed by Law 57/2017, 19 July. The position of A.F.S. was funded by Project POCI-01-0145-FEDER-030075 (COMPETE 2020 Operational Thematic Program for Competitiveness and Internationalization) co-financed by national funds through FCT/MCTES and the EU through the ERDF, under the Portugal 2020 Partnership Agreement.

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Heterogeneous Pd-catalyzed efficient synthesis of imidazolones via dehydrogenative condensation between ureas and 1,2-diols

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Catalytic hydrogen transfer reactions, such as hydrogen borrowing or acceptorless dehydrogenation, have become powerful tools in organic chemistry, as they are clean processes that allow the formation of C – N and C – C bonds in a non-classical way that avoids the use of toxic reagents [1]. In fact, the great development of catalysts in this field has led to their application towards the synthesis of heterocycles [2]. Although heterogeneous catalysis community has made important contributions to the transfer hydrogenation field, the number of examples in which a solid nanocatalyst is able to mediate the formation of a heterocycle through a dehydrogenative cyclisation process still remains scarce.

In this work, we have performed a careful design of a heterogeneous nanostructurated material for the efficient synthesis of imidazolones from ureas and 1,2-diols, through an acceptorless dehydrogenation/ condensation pathway (Figure 1, a). Imidazolones and their analogues are relevant scaffolds present in pharmaceutical compounds and natural alkaloids. Here, we studied metal particle size, oxidation state and metal oxide support nature influence in the catalyst efficiency, determining that palladium nanoparticles over γ-Al_2O_3 constitute an optimum reusable catalyst, in comparison with other metal nanoparticles and metal oxide supports. Furthermore, we have also designed a bimetallic [Pd-Zn/Al_2O_3] material able to catalyze the dehydrogenative condensation with unactivated diols such as ethyleneglycol. Employing these materials, more than 25 molecules have been obtained with up to 90% yields and high TON and TOF values, showing the general applicability and efficiency of the procedure. Mechanistic studies reveal the importance of metal-support cooperation in both dehydrogenation and condensation steps and determined that γ-Al_2O_3 acid sites play a crucial role in this green and atom-economical N-heterocycle synthesis starting from very accessible reagents (Figure 1, b).

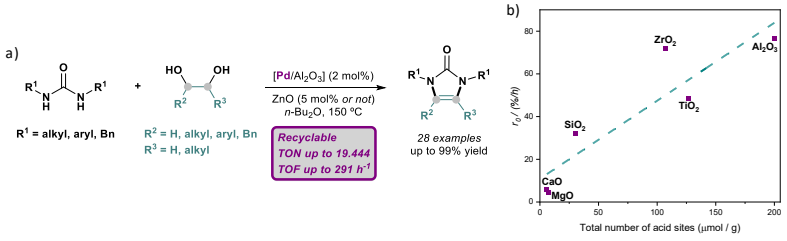

Figure 1. a) [Pd/Al_2O_3]-catalyzed dehydrogenative cyclization between ureas and 1,2-diols to afford imidazolones; b) Initial rate values for diol dehydrogenation *vs* total number of acid sites of Pd materials.

The authors want to thank SEJI program (grants SEJI/2019/006 and SEJI/2020/013) funded by Generalitat Valenciana and RETOS I+D+iprogram from MICINN (PID2019-109656RA-I0 / AEI / 10.13039/501100011033). R. A. thanks to the project that gave rise to these results that received the support of a fellowship from "La Caixa"Foundation (ID 100010434). The fellowship code is LCF/BQ/PI18/11630023. J. R. C.-A. and R. A. thank to MICINN from Spanish Government for two Ramón y Cajal contracts (ref. RYC-2017-22717 and RYC2020-029493-I).

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Unprecedented CO_2 fixation into polycarbonates catalysed by C-scorpionate complexes

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Conversion of CO_2 into fuels and added-value commodities has recently received great attention, from both academia and industry, once it is considered as a sustainable solution to reduce global warming, fossil fuel depletion, energy storage problems and the dependence from traditional pollutant plastics. Therefore, it is not surprising that the catalytic copolymerization reaction between epoxides and carbon dioxide has been heavily studied, aiming at to achieve a sustainable alternative to produce biodegradable plastics [1]. However, even some reported results appear to be quite promising, the design of new and simpler catalysts is needed in order to make this process sustainable at an industrial scale.

Herein, we report the successful use of C-scorpionate palladium(II) catalysts, e.g., $[PdCl_2\{\kappa^3\text{-}HC(pz)_3\}]$ (pz = pyrazol-1-yl), for the solvent free copolymerization of carbon dioxide and cyclohexene oxide into cyclohexene carbonate polymers and/or cyclic carbonates (Figure 1). Conversions over 88 % of cyclohexene oxide were obtained, leading selectively to poly(cyclohexene carbonate) after 24 hours at 150 °C under 40 bar of carbon dioxide.

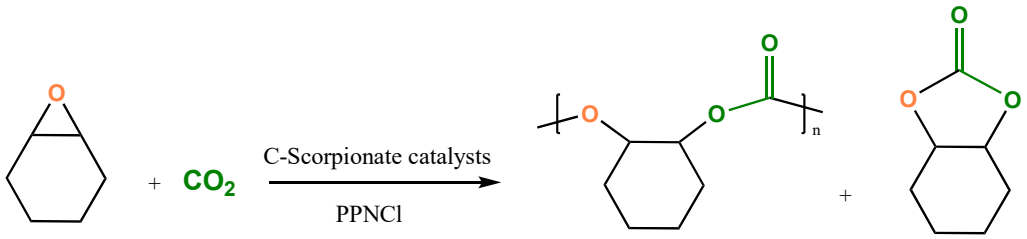

Figure 1 - Copolymerization of CO_2 with cyclohexene oxide catalysed by a C-scorpionate catalyst.

This unprecedented catalytic system reveals an efficient activity of C-scorpionate palladium(II) catalysts for the solvent free ring-opening copolymerization of cyclohexene oxide and carbon dioxide. This is an unexpected outcome as this type of reaction is more focused on different metals, such as zinc, chromium, or cobalt, and tetradentate salens, porphyrins and their derivatives are the most common ligands employed for this purpose. Therefore, it will open up the scope of efficient catalysts to be used in the sustainable manufacture of poly(cyclohexene carbonate).

Several catalytic parameters affecting the catalytic performance and green metrics are presented and discussed.

This research was funded by the Fundação para a Ciência e Tecnologia (FCT), projects UIDB/00100/2020 and UIDP/00100/2020 of Centro de Química Estrutural and IMS - LA/P/0056/2020 and the PhD fellowship (SFRH/BD/146426/2019).

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Enzymatic CO_2 reduction to formate: towards a biocatalyst for the use of the abundant atmospheric CO_2

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The relentless rise of atmospheric CO_2 is causing large and unpredictable impacts on Earth climate. To stop the spiral of destruction, we must actively reduce the CO_2 emissions and develop new and more efficient ways to capture it and give it a new, valuable, life. We should be exploiting this huge carbon feedstock to produce de novo fuels and other added-value compounds. In this scenario, the conversion of CO_2 into formic acid offers key advantages for carbon recycling. Formic acid is a stable, non-toxic compound, liquid at room temperature and pressure, that can be used as a safe "storage and deliverable form" of dihydrogen, the ideal "clean" fuel envisaged by many. For this reason, formate dehydrogenase (FDH) enzymes (eq. 1) are at the centre of intense research, due to the "green" advantages the CO_2 bioconversion can offer, namely substrate and product selectivity and specificity, in reactions run at ambient temperature and pressure and neutral pH [1,2].

$$CO_2 + 2e^- + H^+ \longrightarrow HCOO^- \qquad (1)$$

Recently, we identified a highly active CO_2 reducing FDH, from the *Desulfovibrio desulfuricans* bacterium, that is able to efficiently convert CO_2 into formate at an amazing first-order rate of $3x10^6 M^{-1}s^{-1}$ (K_m^{CO2} of 16μM) [3], thus being one of the most efficient CO_2 bioreducers so far described in the literature. In this communication, the ability of this molybdenum-containing FDH [4] to reduce carbon dioxide will be discussed, as well as, its reaction mechanism [3,5]: formate oxidation and CO_2 reduction proceed through hydride transfer, through a mechanism where the sulfido group of the oxidised and reduced molybdenum centre (Mo^{6+}=S and Mo^{4+}-SH, respectively) are acting as the direct hydride acceptor and donor, respectively.

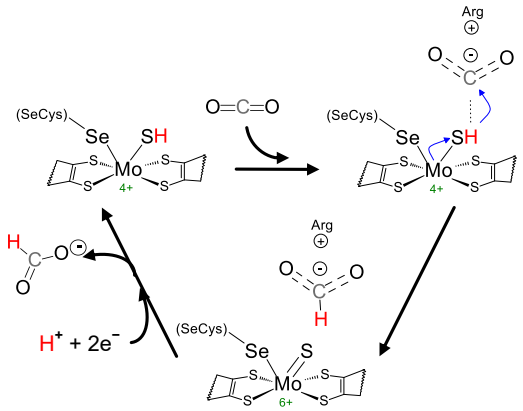

Figure 1. Proposed FDH reaction mechanism.

Acknowledgements: This work was supported by the PTDC/BTA-BTA/0935/2020 project and also by the Associate Laboratory for Green Chemistry - LAQV (UIDB/50006/2020 and UIDP/50006/2020), which are financed by national funds from Fundacão para a Ciência e a Tecnologia, MCTES (FCT/MCTES). LBM thanks to Fundacão para a Ciência e a Tecnologia, MCTES (FCT/MCTES), for the CEEC-Individual Program Contract (CEECIND/03810/2017).

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Bioinspired Polymetallic Sulfido Clusters for Nitrate Reduction

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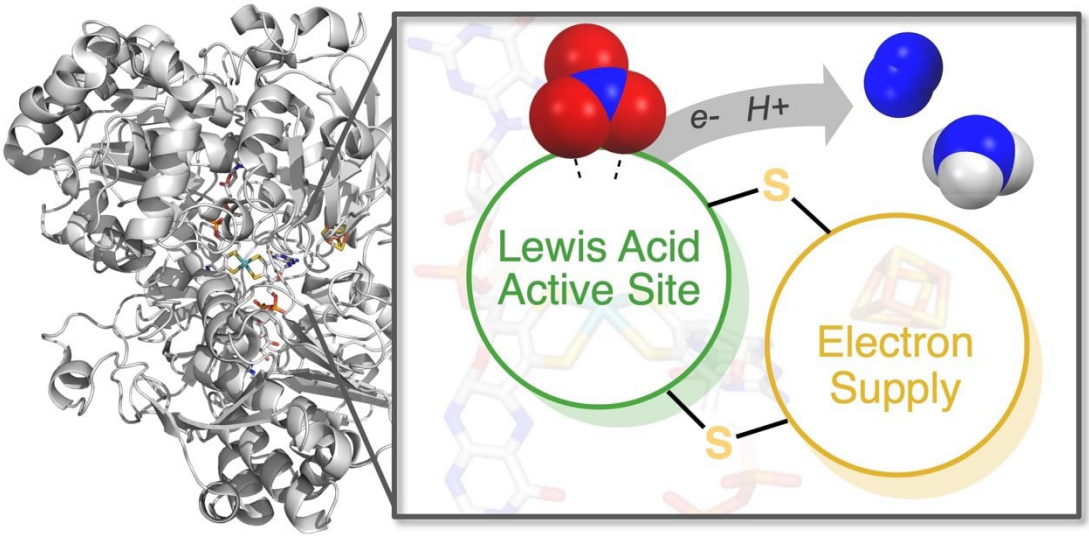
Nitrate pollution of soils and water bodies caused by intensive agriculture has become a pervasive global problem. While the input of fertilizers increased by 800 % during the last 50 years, eutrophication of lakes, ponds and coastal water bodies is now a serious biodiversity threat and a primary water quality issue.[1]

The development of new processes to remove nitrate from polluted water is crucial to address this environmental crisis, and a unique source of inspiration for the design of artificial catalysts can be found in enzymes. Dissimilatory nitrate reductase catalyzes the two-electron reduction of nitrate to nitrite and consists of a molybdopterin active site and a chain of $[Fe_4S_4]$ clusters.[2] The efficiency of the enzymes lies in the powerful combination of a binding site and an electron supply chain in close vicinity. Combining electron relays with potent Lewis acidic site hence has the potential to generate bio-inspired catalysts capable of pre-activating the substrate while providing the electrons necessary for reduction. Trivalent lanthanide ions are hard Lewis acids and are therefore candidates of choice for the reduction of substrates such as NO_3^-. Contrary to other Lewis acids such as early transition metals, they are stable towards hydrolysis and therefore suitable for applications in water. Due to their large coordination sphere, they can accommodate multiple ligands to store electrons. Additionally, tetrathiometallates can act as convenient electron storage and relay sites by accepting electron density in low-lying, empty *d* orbitals.[3] Consequently, we developed an original synthetic route towards the formation of polymetallic sulfido clusters combining lanthanide ions and biorelevant tetrathiomolybdate and tetrathiotungstate.[4] These assemblies can readily bind nitrate and can further be electrodeposited onto Gas Diffusion Electrodes (GDE) to provide a homogenous deposit $Ln_xM_yS_z$@GDL (M = Mo, W). Electrocatalytic nitrate reduction of these materials will be here presented.



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Hybrid L-Tyrosine-titania rutile nanorods and anatase nanoparticles with improved optical properties for photocatalytic applications

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TiO_2 (A), titania in its anatase phase, has been widely used as photocatalysts due to their remarkable properties under UV-light, as its low-cost production, high chemical stability, and low toxicity. However, it is well known that it presents limited photoactivity under visible light. To improve its performance, we have developed a methodology based on the incorporation of organic moieties [1] or metallic complexes [2] during the synthesis of titania has been proved as a method to drastically enhanced their photocatalytic efficiency under sunlight irradiation. In light of these results, this approach has been extended to other morphologies and incorporation of other organic compounds, in particular amino acids.

Amino acids can be effectively incorporated into titania by coordinating their amine and carboxylic groups to the titanium atom of the titania precursor. In fact, the growth of TiO_2 in presence of amino acids may promote a certain polymorph [3]. This work reports the preparation of hybrid L-Tyrosine_TiO_2 rutile nanorods (Figure 1A) and anatase nanoparticles (Figure 1A) as amino acid-modified semiconductors, through the reaction of the titania precursor with L-tyrosine before the hydrolysis and condensation of the titanium (IV) butoxide (TBOT) The control of their morphology and structure has been achieved by tuning the pH of the synthetic mixtures: i) pH=0 for rutile nanorods, and ii) pH=2.2 for anatase nanoparticles [4]. The L-tyrosine incorporation does not cause structural changes as compared to the control (L-Tyrosine-free) titanias.

Also, the incorporation of L-Tyrosine into titania enables the absorption of light in the visible range due to both the decrease in their band gap, as compared to the reference materials (Figure 1B), and the presence of additional absorption edges at wavelengths higher than 400 nm. Consequently, the photocatalytic activity of both L-Tyr_TiO_2 hybrids is enhanced, as compared to that of L-Tyr-free titanias and the commercial P25 (Figure 1C), which confirms their potential application in water remediation.

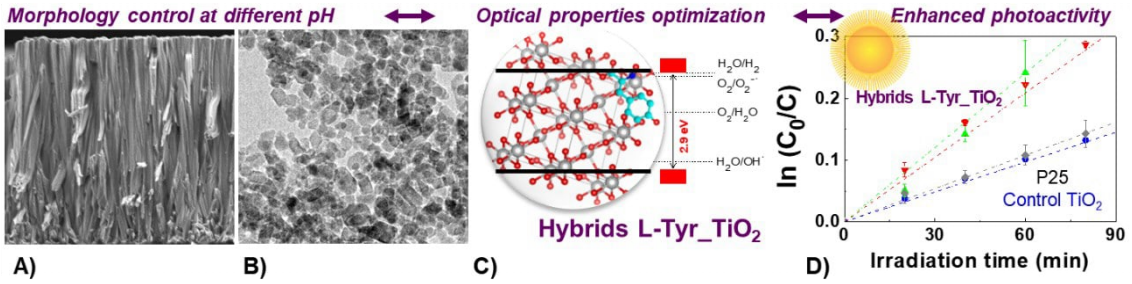

Figure 1. A) Cross-sectional FESEM image of the hybrid L-Tyr_TiO_2 rutile nanoroads. B) TEM image of the hybrid L-Tyr_TiO_2 anatase nanoparticles. C) Density of states (DOS) scheme of the hybrid L-Tyr_TiO_2 rutile nanorods calculated from the direct optical band gap and XPS in the valence band region. D) Rh6G photodegradation reaction using the hybrids L-Tyr-TiO_2 rutile nanorods (red triangles) and anatase nanoparticles (green squares), as compared with the reference materials, i.e. L-Tyr-free titanias and the commercial P25.

Acknowledgements. This work was supported by Generalitat Valenciana (AICO/2021/132), Spanish MICINN and AEI/FEDER (CTQ2015-74494-JIN and RTI2018-099504-B-C21/A-C22), the University of Alicante (UATALENTO16-03 and 17-05), and the synchrotron ALBA (ref. ID 2018022752).

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Photocatalytic deaminative benzylation and alkylation of tetrahydroisoquinolines with *N*-alkylpyrydinium salts

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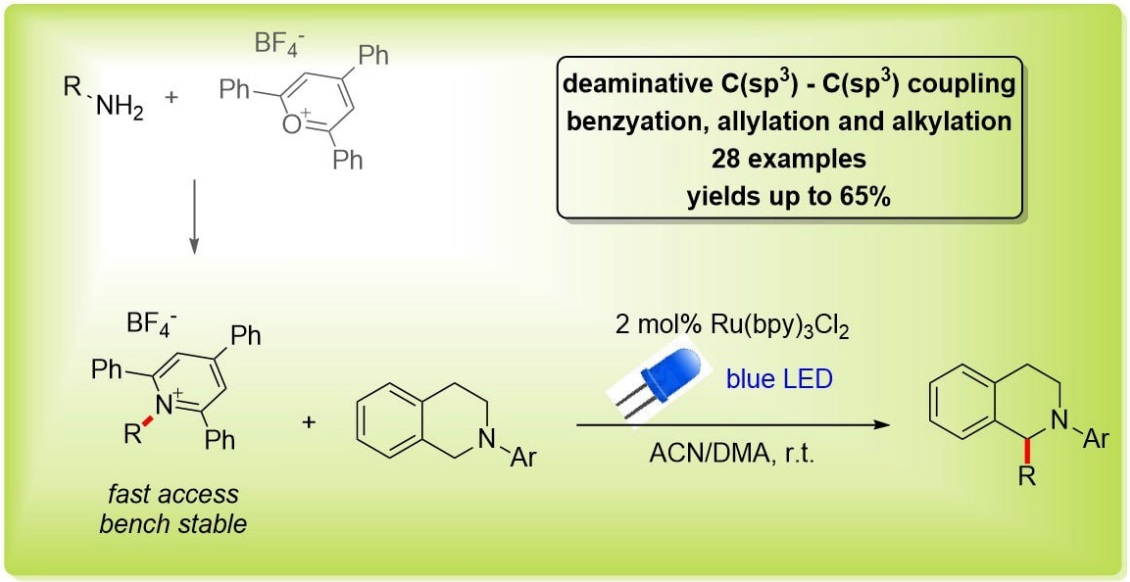
A ruthenium-catalyzed photoredox coupling of substituted N-aryltetrahydroisoquinolines (THIQs) and different pyridinium salts was successfully developed to give fast access to 1-benzyl-THIQs.[1] The THIQ moiety is of special interest due to its presence in several different natural products.[2] Hence, also photoredox catalysis methods were investigating on this scaffold previously, to introduce various moieties.[3],[4] In this contribution, we disclose a C(sp^3)–H alkylation, which proceeds under mild conditions and the applied pyridinium salts for radical generation are bench-stable over long periods of time. Besides substituted benzyl groups, secondary alkyl and allyl groups were also successfully introduced via the same method. Additionally, the typically applied N-phenyl group in the THIQ substrate could be replaced by the cleavable p-methoxyphenyl (PMP) group and successful N-deprotection was demonstrated. Hence, this method can be used for the synthesis of THIQ-containing natural products and bioactive substances, which are typically lacking an N-phenyl group.



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C.S. acknowledges the European Union for a Marie Curie European Fellowship (FlowAct, Grant No.794072)

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PHOTORACEMIZATION-BASED VIEDMA RIPENING OF A BINOL DERIVATIVE

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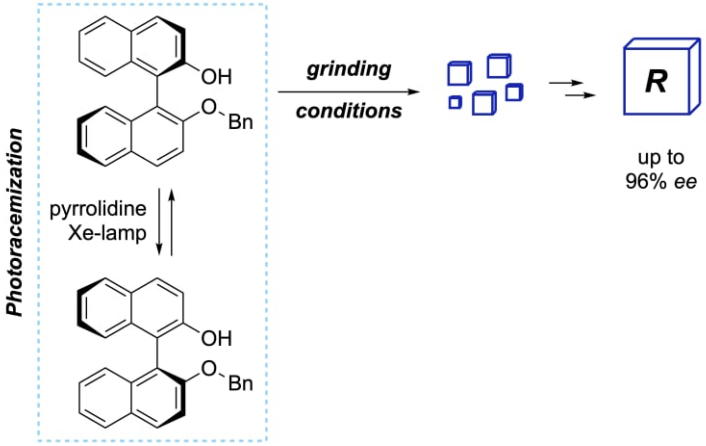
Viedma ripening is a deracemization process discovered in 2005 that has been used lately to deracemize a range of chiral molecules. [1] The method has two major requirements: the compound needs to crystallize as a conglomerate and it needs to be racemizable under the crystallization conditions. [2] Although conglomerate formation can be induced in different ways, the number of racemization methods is still rather limited. Aiming at extending the scope of Viedma ripening, we applied UV-light-induced racemization in a Viedma ripening process and report the successful deracemization of a BINOL derivative crystallizing as a conglomerate. [3]

A BINOL monoalkylated derivative, an axially chiral compound, was selected as target compound for the first application of photoracemization in Viedma ripening, as it undergoes racemization under UV-light irradiation in presence of an organic base, following an excited state proton transfer (ESPT) mechanism. Different organic bases have been tested and corresponding reaction kinetics evaluated in order to find the best conditions in terms of reaction rate. Upon application of optimized reaction parameters during grinding of a supersaturated solution, deracemization up to 96% ee was achieved. This offers a new tool towards the development of Viedma ripening processes, by using a cheap and “green” catalytic source like UV light to racemize suitable chiral compounds.



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Organocatalysis using Ru(II) complexes with pyridine-derived ligands: Implications of photo- and metal-mediated mechanisms

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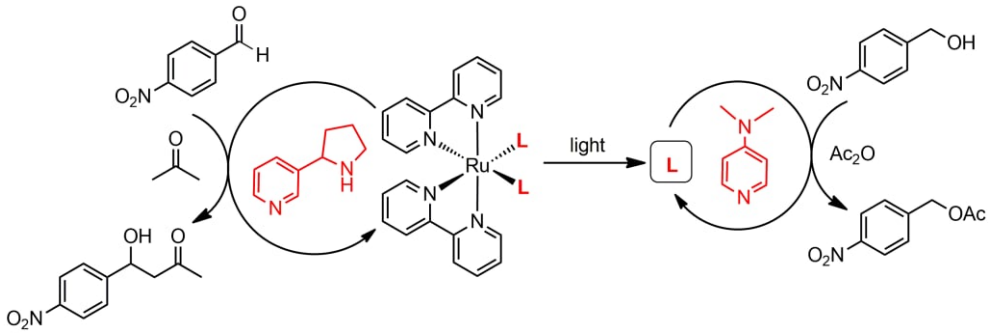
In the last 20 years organocatalysis has developed towards a highly efficient method to enable organic synthetic transformations, especially of low-molecular weight compounds [1]. From the early years of its success the field has been concerned about aspects related to green chemistry and sustainability. For example, there is an ongoing interest in substituting organic solvents by aqueous media [2] or in combining organocatalysis with light-mediated mechanisms [3].



As part of our research program we became interested in light-activatable Ru(II)-pyridine complexes, i.e., $[Ru(bpy)_2L_2]^{2+}$ with L = pyridine derivatives. Our rationale was based on using a ligand L with organocatalytic activity and which upon photorelease from the corresponding Ru(II) complex would involve in an organic transformation. As a first example, we used 4-diaminopyridine (DMAP), known as supernucleophilic catalyst for acetylation reactions. While the $[Ru(bpy)_2(DMAP)_2]^{2+}$ complex was inactive in the acetylation of benzylalcohols, light-irradiation at wavelengths >450 nm triggered the desired product formation [4]. This provides an example for visible-light gated organocatalysis. When switching to nornicotine (Nor), an established organocatalyst for aldol reactions in buffered aqueous media [5], we found that the aldol reaction between acetone and activated benzaldehydes was already catalyzed in the dark [6]. The $[Ru(bpy)_2(Nor)_2]^{2+}$ complex was even more active than nornicotine alone. This was reasoned with the electron-withdrawing effect cause by the metal-coordination, lowering the basicity of the pyrrolidine N in nornicotine, being crucial for the enamine-activation mechanism.

In this contribution we will present the detailed physical organic chemistry of the different mechanisms, including the photochemistry of the Ru(II) complexes and the kinetic analysis.

The financial support by the Spanish Ministry of Science, Innovation, and Universities (grant CTQ2017-89832-P for U.P.) and the University of Huelva (grant UHU-9-542-2019 for J.F.A.) is gratefully acknowledged. We thank Dr. F. Boscá (ITQ/Technical University of Valencia, Spain) for carrying out laser-flash photolysis studies.

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Design of Hybrid Structure for Bioorthogonal Drug Photoactivation and Photocatalysis

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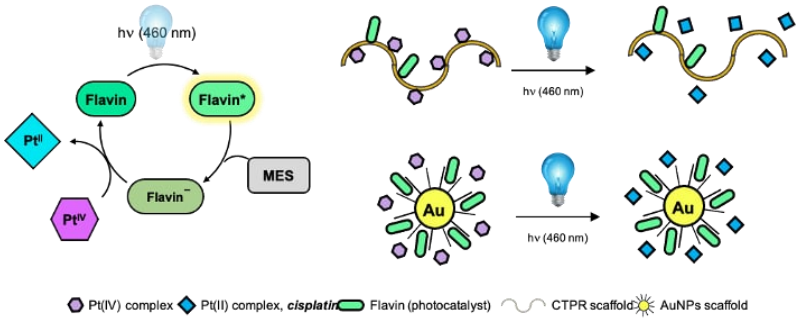
Advances in biorthogonal catalysis are creating new opportunities to perform chemoselective transformations in complex biological environments with applications in biomedicine and bioimaging. Recently, riboflavin photocatalysis has been used to activate Pt(IV) anticancer prodrugs *in vitro* under light irradiation.[1] In this work, we propose to expand this strategy by co-immobilization of both photocatalysts and prodrugs, on engineered repeat proteins as templates[2], and on gold nanoparticles as nanozyme scaffold.[3] These systems are envisioned to have more efficient drug activation and will facilitate controlled cell internalization.

Specifically, we use tetratricopeptide repeat protein as engineered repeat protein with 4-6-8 repeats (CTPR4-CTPR6-CTPR8) and 1.9-nm gold nanoparticles decorated with thiol ligands bearing a TACN (1,4,7-triazacyclononane) headgroup. In this contribution, I will discuss the conjugation between CTPR4, CTPR6, CTPR8, N3-functionalized riboflavin and Pt(IV) complex by exploiting cysteine (Cys) and lysine (Lys) residues of the protein scaffold, the N3 functional group on the riboflavin and NHS ester-reactive group of the Pt(IV) complex, respectively. Currently, we have achieved a distribution in the number of functionalized riboflavins and platinum complexes linked to the three modular proteins. Light-irradiation studies at 460 nm indicated that riboflavin comjugated to CTPR4, CTPR6 and CTPR8 has increased photostability, compared to free riboflavin, likely due to the ability of the protein scaffold to protect the modified riboflavin from the photodegradation of its ribityl chain. Catalysis studies performed show that riboflavin preserves its photocatalytic activity upon conjugation to the protein. In addition, preliminary cell viability experiments were performed in PANC-1 cancer cell line showing that in dark, Pt(IV) prodrugs linked to the three protein scaffold are not toxic in their inactive form.

On the other hand, using the nano-based system, it was observed that the nanozyme affording a catalytic system capable of activating the Pt(IV) prodrug substrate with an almost identical behavior in terms of catalytic activity of the system without AuNPs, reaching 80% conversion already within 7 min and a plateau at 90% conversion after 30 min of light irradiation with turnover frequency (TOF) of 7.4 min^{-1}.



Photocatalytic activation scheme of the cisplatin prodrug *cis,cis,trans*- $[Pt(NH_3)_2(Cl_2)(O_2CCH_2CH_2COOH)_2]$ and schematic representation of the two systems developed in this work.

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Reductive reactions photocatalyzed by super organic electron donors

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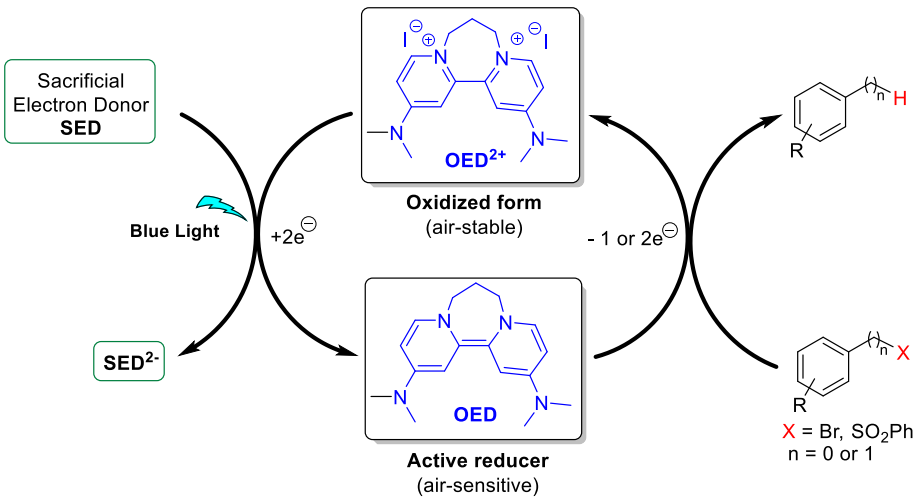
Photocatalyzed reductive methodologies have emerged as a powerful strategy for the generation of original radical species under mild conditions.[1] Among the different photocatalysts explored, organic dyes have been used as an attractive alternative to transition metal complexes.[2] However, most of them present modest reduction potentials limiting their reactivity to the generation of radical intermediates from strong electron-deficient acceptors.

In the quest for innovative and selective reduction methodologies, super organic electron donors (OEDs) represent ideal eco-compatible and powerful reducing agents for the generation of radical or anionic species by single or double electrons transfers.[3,4] Nevertheless, OEDs were used in a stoichiometric amount. Therefore, we developed an OED-photocatalyzed reduction methodology where the active reducer **OED** is regenerated by electron transfers to its oxidized form **OED^{2+}** using a sacrificial electron donor. This new photoredox catalytic system was applied to the reduction of functionals groups with low reduction potentials (sulfone, aryl halide and triflate) into radical or anionic intermediates. This photocatalytic system represents an unprecedented way to catalytically generate carbanions, including aryl anions.



OED-photocatalyzed reduction reactions

The french Ministère de l'Enseignement Supérieur et de la Recherche is gratefully acknowledged for the JCJC ANR grant "iPOD" (17-CE07-000101). Aix Marseille Université (AMU) and the Centre National de la Recherche Scientifique (CNRS) are also acknowledged for financial support.

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Expanding the Reactivity of Allenamides towards Sustainability

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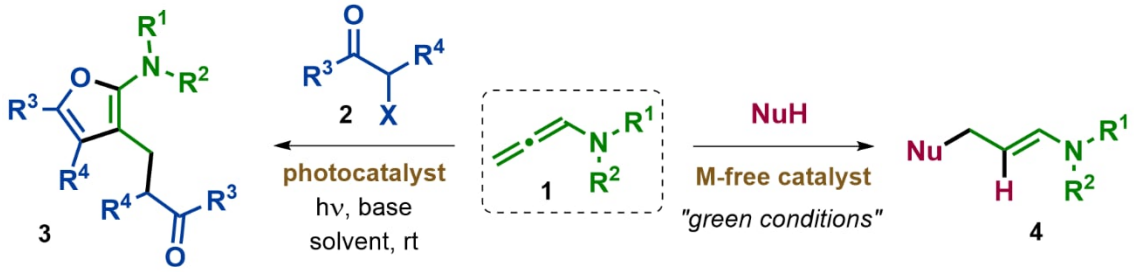
The use of *N*-substituted allenes in organic synthesis has recently experienced a strong growth because of their peculiar reactivity and their utility and versatility in introducing nitrogen functionalities in structurally different scaffolds [1]. However, the reactivity of allenamides has not been evaluated under several conditions, likely enabling the formation of useful functionalized products. As part of our ongoing studies on the construction of heterocyclic compounds [2], we report here our recent results on the visible light-promoted photocatalytic radical synthesis of variably substituted 2-aminofurans (**3**) starting from allenamides (**1**) [3]. The mild reaction conditions and the redox-neutral nature of the transformation make it particularly selective and sustainable, avoiding the use of both sacrificial reactants and stoichiometric strong oxidants, sometimes expensive, potentially environmentally unfriendly and/or source of side-reactions. Given the crucial role of sustainability in the design of a synthetic approach, we are now focusing our attention on the development of a green, efficient and selective protocol for the hydrofunctionalization (**4**) of allenamides.



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Towards Highly Chemoselective Catalytic Photooxidations

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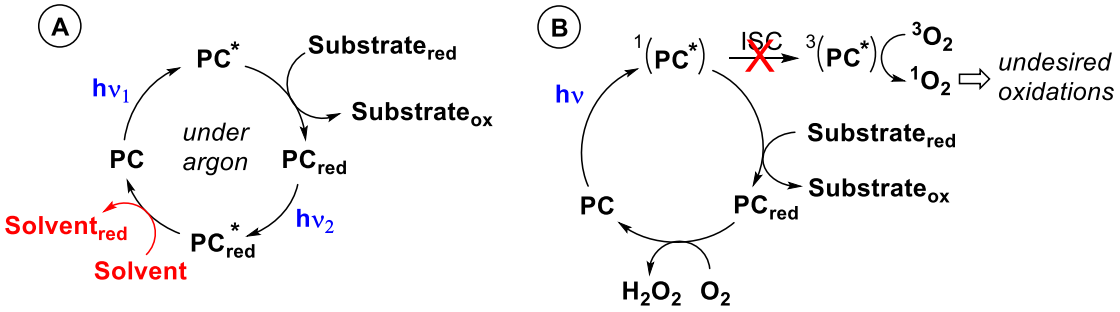
Highly chemoselective procedures are at the forefront of modern organic chemistry [1]. For oxidations, effective chemoselective systems based on stoichiometric agents, such as hypervalent iodine compounds, or catalytic systems using transition metal complexes, nitroxyl radicals or neutral organic molecules have been described. However, most current oxidants lack selectivity and result in undesired oxidation of an adjacent functional group or over-oxidation. Photoredox catalysis has been established as a green alternative tool for redox transformations [2]. However, also in this field, the number of oxidation systems that can tolerate sensitive functional groups is limited [3,4]. Generally, photocatalyst regeneration can cause chemoselectivity problems in photooxidations. Oxygen is a favourable stoichiometric oxidizing agent, both from economic and environmental perspectives. However, when using oxygen, various reactive oxygen species (ROS), such as triplet oxygen or superoxide, are formed, which gives rise to undesired side reactions. Several sacrificial oxidants other than oxygen have been tested in photooxidations but these compounds also produce a range of undesired by-products.

Herein, we describe a novel approach to chemoselective dehydrogenation reactions using a suitable solvent as a sole electron acceptor for catalyst regeneration, in combination with anaerobic conditions (Scheme A). This system does not require any additional agent and avoids the presence of ROS. In general, the approach described herein might be applicable for catalysts with two photoactive redox states: one behaving as a strong oxidant and the other as a strong reductant. Such versatile behaviour is typical of flavins (vitamin B2 derivatives), as demonstrated recently by our group [5-7]. The other approach for chemoselective photooxidations is based on flavin derivatives reacting exclusively from a singlet excited state because of a very low intersystem crossing quantum yield (ISC) of < 0.05 and long-lived singlet excited state (Scheme B). Systems based on these approaches avoid singlet oxygen formation, thus supporting a purely electron transfer pathway. Rational design of flavin photocatalysts and the substrate scope of chemoselective photocatalytic systems will be discussed.



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Visible-Light Mediated Hydrosilylation of Carbonyls Using Mn(I) N-Heterocyclic Carbene Complexes

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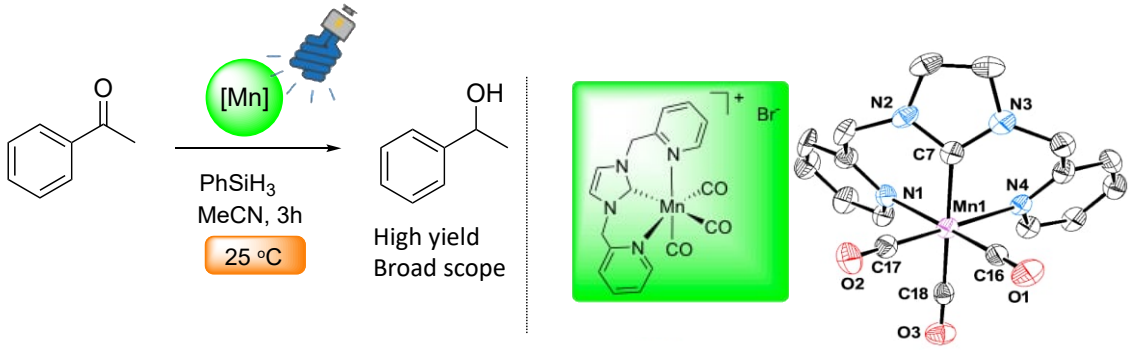
In recent years, visible light-induced reactions have emerged as a powerful tool in organic synthesis. Compared to the conventional cooperative dual catalysis, which combines a photocatalyst (PC) and a transition metal catalyst working in synergy, the employment of simple transition metals as PCs represents a very attractive approach of promoting chemical reactions. This new class of unconventional PCs operate through a single catalytic cycle, using visible light and avoiding the need of expensive photosensitizers. In this case, the transition metal PC plays a double role, harvesting light and catalysing the chemical transformation [1]. In continuation with our work devoted to sustainable catalytic methods for the functionalization of organic molecules [2-4], we describe here the synthesis and characterisation of a rare example of N-heterocyclic carbene-based pincer-type Mn(I) complex (**1**, Scheme 1) and its application as a photocatalyst. Interestingly, complex **1** displayed excellent catalytic activity working as a photocatalyst for the hydrosilylation of ketones with phenyl silane (Scheme 1). The catalytic system operates at room temperature, under visible-light irradiation (blue LED) enabling the conversion of a wide variety of functionalised ketones to the corresponding alcohols in excellent yields in 3 h. A comparison of the catalytic efficiency of **1** with Mn complexes bearing mesoionic- and NHC-based ligands will be presented. Complex **1** has been fully characterised by spectroscopic and analytical methods, including the crystal X-ray diffraction studies. Experimental essays performed for the elucidation of the reaction mechanism will be discussed. The potential of complex **1** as photocatalyst for other organic transformations will be shown.



Scheme 1. Mn-based catalytic system for the reduction of ketones under visible-light

We thank the Fundação para a Ciência e a Tecnologia for financial support of PhD grant SFRH/BD/07285/2020 (H.M.) and projects PTDC/QUI-QIN/0359/2021, MOSTMICRO-ITQB UIDB/04612/2020, UIPD/04612/2020, CERMAX Project No.022162, UIDB-UIDP/50006/2020 and UIDB-UIDP/04378/2020. We also thank C. Almeida for elemental analysis at ITQB NOVA.

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An efficient metal-organic framework-derived nickel catalyst for the light-driven methanation of CO_2

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The possibility to produce solar fuels or chemicals from carbon dioxide (CO_2) represents a promising approach not only to alleviate CO_2 emissions but also to store renewable energy in the form of chemical bonds. In order to overcome the inherent limitations of traditional photochemical processes (*i.e.* low efficiency and poor utilization of solar radiation), photo-thermal catalysis offers the advantage of exploiting both the thermal and non-thermal contributions of sunlight.[1] Given the well-known photo-thermal properties of metallic nanoparticles (NPs) and carbon-based materials, in this work we envisaged the synthesis of Ni NPs dispersed on carbon via the controlled pyrolysis of a metal-organic framework (MOF) precursor.[2] Therefore, Ni-MOF-74 was synthesized according to the reported method.[3] Once synthesized, Ni-MOF-74 was pyrolyzed in a tubular oven under a continuous flow of N_2 for 6 hours at temperatures of 500, 600 and 700 ºC. The photo-thermal catalytic activity of Ni@C-*X* materials (where *X* stands for the pyrolysis temperature) was tested using a quartz photoreactor and a 300 W Xe lamp as UV-visible-IR light source. Among all samples, Ni@C-600 displayed the highest temperature and the most significant pressure decrease after 10 min of reaction, thus leading to very high CO_2 conversions together with CH_4 production rates of 488 mmol g^{-1} h^{-1} (Figure 1a). Once the pyrolysis temperature was optimized, we studied the relationship between reaction rate and light intensity and a distinct exponential correlation between both was observed, therefore suggesting that this system is mainly operated by an effective light-to-heat conversion. We also performed an additional catalytic test using a flow-type reactor and under these conditions the catalytic activity for Ni@C-600 exhibited a notable CO_2 conversion ranging from 42 to 57 % after more than 12 consecutive hours of reaction without evident deactivation (Figure 1b).

In conclusion, we have demonstrated the effectiveness of MOF-mediated approach for the synthesis of metal nanoparticles embedded on carbon matrix as photo-thermal catalysts. Our catalyst shows high performance for the photo-thermal CO_2 methanation reaction under UV-visible-IR irradiation owing to its ability to convert light into heat. Mechanistic studies suggest a reaction pathway dominated by thermal effects.[4]

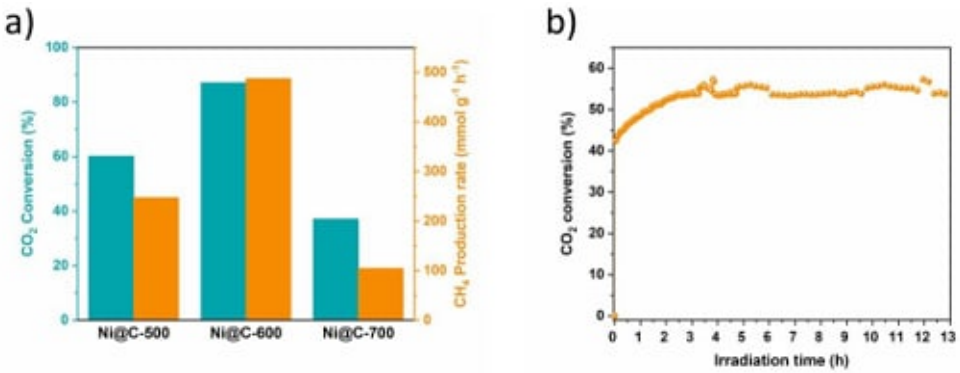

Figure 1. a) CO_2 conversion (turquoise bars) and CH_4 production (orange bars) of Ni@C-*X* materials. b) Photothermal CO_2 conversion of Ni@C-600 under continuous flow configuration.

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Selective Catalytic Conversion of Acetylene to Ethylene Powered by Water and Visible Light

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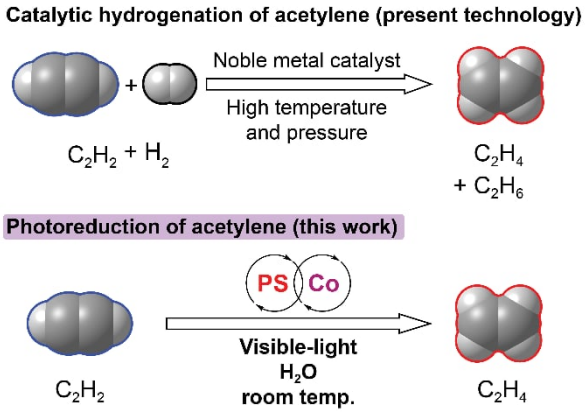

Ethylene is used by manufacturers to make tens of millions of metric tons of polyethylene annually.[1] The production of polymer-grade ethylene requires the purification of ethylene starting material from acetylene contaminant.[2] Accomplishing this task by state-of-the-art thermal hydrogenation requires high temperature, external feed of H_2 gas, and noble metal catalysts, and is not only expensive and energy-intensive but also prone to overhydrogenate to ethane. To help tackle the problem, we have developed a photocatalytic system to reduce acetylene to ethylene with ≥99% selectivity for ethylene under both non-competitive (no ethylene co-feed) and competitive (ethylene co-feed) conditions, and near 100% conversion under the latter industrially relevant condition.[3] Our system uses a molecular catalyst based on earth-abundant cobalt operating under ambient conditions and sensitized by either $[Ru(bpy)_3]^{2+}$ or an inexpensive organic semiconductor (mesoporous graphitic carbon nitride) under visible light. These features and the use of water as a proton source offer substantial advantages over current hydrogenation technologies with respect to selectivity and sustainability.

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Organic dyes in metallaphotoredox catalysis: strategies and perspectives for C-C bond formation enabled by visible light

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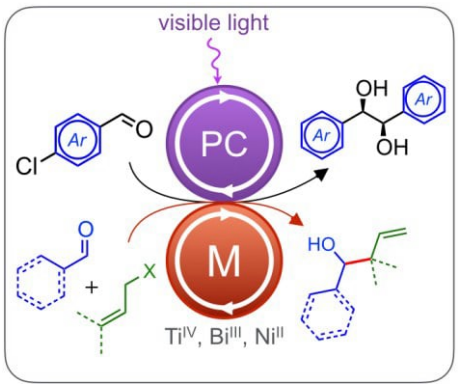

Photoredox catalysis has recently obtained increasing attention as a sustainable means for organic chemists, enabling the formation of suitable radical species through electron- or energy transfer [1]. Specifically, the merger of photoredox and metal-assisted catalytic cycles has rapidly gained popularity as an efficient and environmentally friendly strategy to open the way to new reaction pathways, especially those able to generate highly reactive nucleophilic species [2].

Recently, our attention has been focused on different classes of organic dyes, showing peculiar photophysical properties that can be exploited to trigger photoredox cycles in specific conditions. Firstly, isophthalonitrile derivatives – an easily prepared class of organic dyes – have been studied in detail due to their long-lasting excited state, originating from a thermal-activated delayed fluorescence (TADF) deactivation. Secondly, cationic diaza[4]helicenes have been taken into account due to the combination of their low energy-lying absorption spectrum and tailored redox potentials at the excited state.

The analysis of photo-induced electon transfer kinetics in the presence of such chromophores and suitable metal complexes guided us in the design of C-C bond formation reactions, namely *i*) allylation [3,4], *ii*) propargylation [5] and *iii*) the pinacol coupling of aldehydes [6], which require benign Ti^{IV} or Bi^{III} species in catalytic concentration to operate. These reactions occur upon visible-light excitation in the presence of cheap and widely available sacrificial agents, without the use of toxic and expensive metal species. Moreover, the stereocontrolled versions of the same reactions [6,7], in the presence of either chiral Ni^{II} complexes or Ti(salen) metal catalysts, has been developed to obtain excellent enantioselectivities.

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Straightforward modelling of reactivity induced by electric fields

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In the oriented external electric-field-driven catalysis, the reaction rates and the selectivity of chemical reactions can be tuned at will.[1] The activation barriers of chemical reactions within external electric fields of several strengths and directions can be computationally modelled. Notwithstanding, the calculation of all of the required field-dependent transition states and reactants is computationally demanding, especially for large systems.

In this communication, we present a method based on the Taylor expansion of the field-dependent energy of the reactants and transition states in terms of their field-free dipole moments and electrical (hyper)polarizabilities.[2] This approach, called field-dependent energy barrier (FDB_β), allows systematic one-dimensional (1D), two-dimensional (2D) (Figure 1), and three-dimensional (3D) representations of the activation energy barriers for any strength and direction of the external electric field in a straightforward manner. The calculation of the field-dependent FDB_β energy barriers has a computational cost several orders of magnitude lower than the explicit electric field optimizations, and the errors of the FDB_β barriers are within the range of only 1–2 kcal·mol^{-1}. The achieved accuracy is sufficient for FDB_β to be used as a fast-screening tool to study and predict potential electric-field induced catalysis, regioselectivity, and stereoselectivity. As illustrative examples, four cycloadditions (1,3-dipolar and Diels–Alder) will be presented.

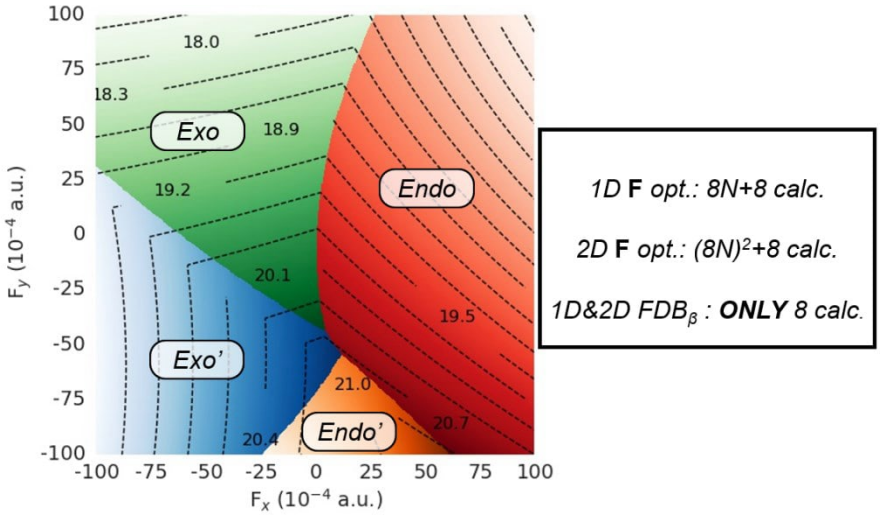

Figure 1. 2D representation of the FDBβ barriers for the catalysis and selectivity of the (3 + 2) dipolar reaction between phenyl diazomethane and methoxyethene.

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Engineering Continuous-Flow Photochemical Microreactors Integrating Single-Atom Catalysts for Clean Water Applications

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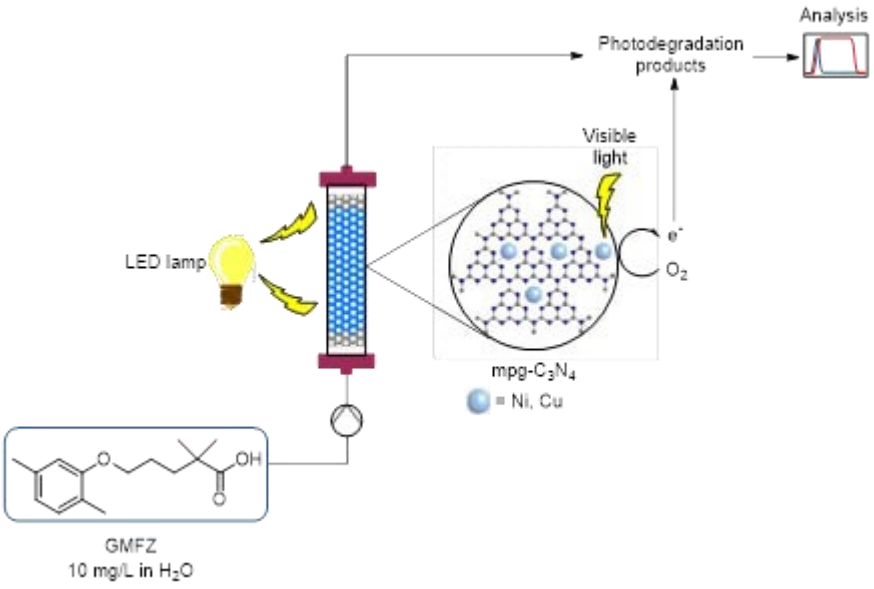
Water pollution caused by pharmaceuticals and personal care products (PCPPs) is an important worldwide problem among the UN Millennium Development Goals, due to persistence and accumulation phenomena caused by their lipophilicity [1]. Among PCPPs, Gemfibrozil has been commonly reported as a persistent contaminant all over the world [2]. Substantial efforts have been devoted to studying the removal of this drug from water, predominantly *via* AOP and/or photodegradation, all with limited results [3]. In this work, we integrate for the first time flow photochemistry and single-atom catalysis to engineer a new-generation of continuous-flow catalytic microreactors for the degradation of water pollutants, taking advantage from the particular features of these technologies, such as improved mass transfer and irradiation uniformity, and unique selectivity towards pollutants degradation. To date, no photodegradation of pharmaceuticals has been reported using a combined continuous-flow microreactor integrating single-atom catalysts; this work looks towards the improved efficiency of the removal process, compared to classical approaches and aims as well at understanding the degradation microkinetic mechanisms. Preliminary experiments, conducted to evaluate the effects of irradiation time and initial pH solution, have demonstrated no relevant degradation of GMFZ in the absence of photocatalysts, independently from the initial pH (from 1 to 14) and the irradiation time (from 1 to 4 h). Based on these evidences, we have assembled a platform of intensified continuous-flow microreactors with variable internal geometry, for optimal light irradiation, comparing under differential reaction conditions the activity and selectivity of a series of heterogeneous catalysts (i.e., the photoactive mpg-C_3N_4, the photoactive single atom-catalysts with transition metals Ag@mpg-C_3N_4, Cu@ mpg-C_3N_4. From this investigation, we have rationalized the different performance of the materials under flow photochemical conditions, identifying single-atom catalysts as the most outstanding and selective heterogeneous catalysts for GMFZ degradation.



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Uncovering of spirulina marker peptides for allergen detection in processed foodstuffs by bottom-up approaches

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The identification of reliable marker peptides for allergen detection represents a key step in the development of a mass spectrometry (MS)-based approach because selectivity, robustness, and sensitivity of detection affect the performance of the overall protocol. Very recently [1], we explored the allergenicity of spirulina and chlorella proteins following the WHO/FAO guidelines [2]. A known allergen of spirulina was identified, C-phycocyanin beta subunit along with five putative allergens, namely two thioredoxins, a superoxide dismutase, a glyceraldehyde-3-phosphate dehydrogenase, and a triosephosphate isomerase related to other established food allergens of pistachio, shrimp, maize, and others. Spirulina is a novel food nowadays widespread in western diet being not only included as food supplements in tablets, capsules, powder, or sticks but also in processed food products such as bread, biscuits, pasta, fruit juices, and crackers [3,4]. For this reason, a study concerning the stability of spirulina allergenic proteins aimed to suggesting putative marker peptides useful for allergens discovery and/or quantification is mandatory. Here, spirulina (Arthrospira platensis) proteins were extracted, digested with trypsin, and analysed by liquid chromatography coupled with high-resolution tandem MS by electrospray ionization (LC-ESI-FTMS/MS) to find highly conserved peptides that can be used as markers of microalga occurrence in foodstuffs. Putative markers were firstly chosen after *in silico* digestion of allergenic proteins, according to the FAO and WHO criteria [2]. Different conditions of protein extraction were tested, and the tryptic peptide pools were processed via commercial software for sequence identification. Each peptide was chosen after assuring its presence in both processed and unprocessed foods, such as capsules, incurred and spiked spirulina cookies, bread, and juice. Their abundance for sensitivity, sequence size, and uniqueness for spirulina proteins was also evaluated. Three marker peptides belonging to C-phycocyanin beta subunit (P72508) were designated; two of them were chosen as qualifier peptides, ETYLALGTPGSSVAVGVGK and YVTYAVFAGDASVLEDR, while ITSNASTIVSNAAR was designed as the quantifier. These marker peptides were successfully employed to validate the developed method in terms of linearity, recovery, reproducibility, matrix effects, processing effects, LOD, and LOQ. With the aim to determine spirulina in commercial foodstuffs like pasta, cracker, and bread, the possible inclusion of these reliable peptides in a standardized selected reaction monitoring method on a linear ion trap MS instrument was also demonstrated.

This work was supported by projects: (i) PONa3_00395/1 "BIOSCIENZE & SALUTE (B&H)" and (ii) Progetto di Ricerca di Interesse Nazionale—PRIN 2017YER72K—"Development of novel DNA-based analytical platforms for the rapid, point-of-use quantification of multiple hidden allergens in food samples", financed by the Italian Ministero per l'Istruzione, l'Università e la Ricerca (MIUR).

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Combined use of forensic science in sexual assault: a case report

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DNA analysis has been widely used in the forensic field in order to contribute to identifying the perpetrator of a crime. Forensic investigation in sexual assaults usually focuses on locating and identifying biological fluids, followed by DNA analysis [1]. The identification of certain compounds present in condoms can be useful to reconstruct the occurred event, especially in cases of sexual assaults where the DNA analysis did not show the presence of a male profile and where RNA analysis did not show the presence of sperm markers [2].

Herein we describe the case of a woman reporting to be victim of sexual assault, who was not able to provide accurate information concerning the dynamics of the event, except for the use of a condom during the assault.

We started from a Short Tandem Repeat (STR) analysis on vaginal and rectal swabs which showed only the presence of vaginal and skin markers. In this situation, the identification of condom compounds residues on vaginal swabs became important as it contributes to the weight of evidence related to the available circumstantial data and to other collected evidence [3]. We therefore developed a protocol based on IR an NMR spectroscopy to successfully analyze and correlate the organic residue of the condoms' lubricant to the condom's brand.



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Developing a Robust Elemental Screening Method for Cell Culture Media used in Biopharmaceutical Manufacturing based on Microwave Plasma Atomic Emission Spectroscopy

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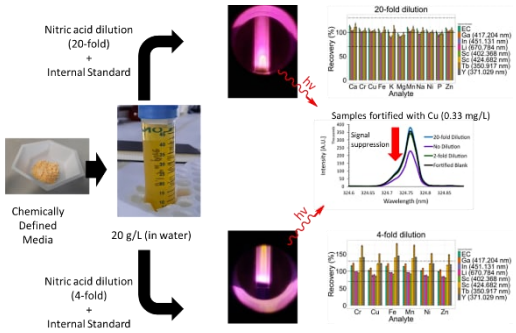
Biopharmaceutical manufacturing is rapidly growing with diverse therapeutic and diagnostics applications [1]. Biopharmaceuticals require complex cell culture media used to suspend and feed cells, which are specially designed to maximise process performance. In recent years, there has been an industry-wide shift to using chemically defined media (CDM) to reduce process variability. However, CDM variability is an ongoing concern indicating that currently employed methods of characterization and control of CDM are unsuitable [2].

Media variability can result from improper manufacture, storage induced compositional changes, or contamination [2] and can be either molecular and elemental (or both) in nature. Elemental variability can have dramatic effects on process performance, particularly with specific transition metals [2]. The impact of alkali/earth element variability is less well reported, presumably due to their typically high concentrations [3]. However, these salts are important for numerous biological functions. Inorganic salts can also be a source of trace impurities (e.g. toxic heavy metals) which might be introduced through contamination during manufacturing [2]. Thus, it is important to screen for CDM elemental variability.

Microwave plasma atomic emission spectroscopy (MP-AES) is an inexpensive elemental analysis method [4]. MP-AES is not widely used in biopharmaceutical manufacturing as it is not as established as inductively coupled plasma (ICP) based methods [4]. Here, we discuss the development of cost-effective methods for elemental screening of CDM using MP-AES. The major goal was to achieve high reproducibility for analysis of a model CDM using simple sample preparation and analysis procedures. Minimizing the effects of easily ionized elements which were shown to impact analyte emission properties [5] was also a key consideration.

Sample concentration (1-20 g/L), instrumental settings and calibration method (external calibration, standard additions method, internal standardization (IS) and intrinsic plasma molecular species (MS)) were evaluated by spike recovery experiments. MS slightly improved recovery but suffered from interference related to storage effects. Cr was applied as an IS which corrected the observed interference, likely originating from freeze/thaw cycles. Nitric acid dilution (2% w/w) and 1g/L CDM concentration gave acceptable reproducibility (<3% RSD), accuracy (recovery between 98% and 108%) and precision (<2% RSD) for determination of Na, K, Ca, Mg, P, Fe, Zn, Cu, Mn, Cr and Ni. The analysis time was ~7 minutes per sample. Control over dilution factor can improve sensitivity for low-level elements. Internal standardization can improve performance although optimal configuration may require dilution factor specific optimization.

Further developments of MP-AES instrumentation such as changing the detector to enable simultaneous measurement of multiple elements would improve technique attractiveness. Implementation of MP-AES can reduce high costs associated with use of ICP-based methods when applied for routine elemental screening of CDM.



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Anthropogenic markers quantified by rapid immunochemical methods – what can their occurrence in wastewater, surface water, and drinking water tell us?

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In urban waters, a multitude of organic micropollutants, often termed emerging pollutants, has been found over the last decades. Analytical methods suitable for trace analysis are needed that are desirably also fast, inexpensive and, if possible, robust and portable. Immunoanalytical, i.e., antibody-based, methods which are available in a broad range of formats, can be profitably used here to screen for the distribution and to monitor the trends of concentration levels of contaminants of emerging concern in the environment. Some of these formats are single-analyte but high-throughput methods. To use them wisely, indicator substances, sometimes called anthropogenic markers, should be selected and used in screening approaches, i.e., as indicators for contamination and the pre-selection of samples at which to have a closer look by multiplex methods like LC-MS/MS. Other methods are suitable to be performed on portable instrumentation in the field (on-site) or in facilities such as wastewater treatment plants for on-line monitoring of the treatment and elimination process. Furthermore, array technologies have been established that allow for parallel (multiplex) analysis of several analytes of interest.

The microtiter-plate based ELISA (Enzyme-linked Immunosorbent Assay) is the method of choice for the analysis of a large number of samples [1]. ELISAs are available to monitor for anthropogenic markers such as the antiepileptic carbamazepine, the analgesic diclofenac, the antihistaminic cetirizine, the steroid hormone estrone, the antimicrobial sulfamethoxazole, psychoactive caffeine and cocaine, the priority pollutant bisphenol A, and the bile acid isolithocholic acid. For on-site screening and monitoring, simpler formats, like mix-and-read assays, e.g., the Fluorescence Polarization Immunoassay (FPIA) [2] or Lateral-flow Immunoassays (LFIA) [3] are more suitable tools, the latter based on dipsticks or little cassettes, with which users have become very familiar during the COVID-19 pandemic via rapid antigen tests. The suitability of multi-analyte formats such as immunomicroarrays depends on the choice of a signal-producing system that provides small uncertainties and good reproducibility of the measurements. Bead-based ("suspension") arrays, read out in flow cytometers, are a powerful platform for multiplex assays [4]. Electrochemical formats, run on portable devices, provide additional advantages as no light source is required. They are most promising for stand-alone analysers and biosensors [5].

The speed, low cost and on-site capabilities of these methods allow to gather a lot more data on anthropogenic compounds which enables to quantify inputs, differences in degradation power of elimination processes, dilution phenomena and a more precise image of individual water cycles which is demonstrated by several examples.

Thanks to all PhD students and researcher colleagues who contributed to the development of the respective immunochemical assays to gather this data.

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Development of Sorption-based Microextraction Techniques for Monitoring VOCs Released from the Four Main Portuguese Tree Species - Influence on wildfire propagation

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Nowadays, climate change persists to increase the incidence of heat waves and periods of drought, which contributes to the development of intense forest fires. The major consequences of extreme wildfires in lives, nature and infrastructures increases the significance of understanding the different sources of sudden changes in the fire's behaviour. Studies have suggested that volatile organic compounds (VOCs) emitted from trees can accumulate under vegetation and at certain atmospheric conditions might be more reactive, accelerating the fire growth [1]. In the last decades, modern sample preparation techniques such as solid-phase microextraction (SPME) have shown effectiveness for trace analysis of VOCs through headspace (HS) sampling mode. More recently, bar adsorptive microextraction (BAμE), a novel static-based microextraction technique, was proposed for trace analysis of target compounds of different polarities, showing great performance in several applications due to the high selectivity of the different sorbent coatings used (*e.g.* polymers and activated carbons) [2].

The present work aimed the development, optimization, validation, and application of both HS-SPME and HS-BAμE methodologies followed by gas chromatography coupled to mass spectrometry (GC-MS) analysis for monitoring VOCs emitted by the leaves of *E. globulus* Labill., *P. pinaster* Aiton, *Q. robur* L. and *Q. suber* L. trees from Sintra region (Portugal). For five case study VOCs (α-pinene, β-pinene, myrcene, limonene and 1,8-cineole), both analytical approaches achieved, under optimized experimental conditions, detection limits ranging from 1 to 25 ng, while showing remarkable linearity ($r^2 \geq 0.9966$) between 0.02 and 0.70 μg (HS-SPME/GC-MS) and from 0.10 to 0.50 μg (HS-BAμE/GC-MS). The application of the HS-SPME/GC-MS for *in-vitro* analysis of VOCs released by the *E. globulus* Labill. and *P. pinaster* Aiton leaves allowed to determine five and four of those monoterpenoids (9.2 ± 1.4 - 7,828.0 ± 40.0 μg g^{-1}), respectively. It was also noticed that the maximum concentrations emitted at 30 °C of these VOCs by both tree crowns (0.01 - 1.26 g m^{-3}) were under their lower flammability limits (38.2 g $m^{-3} \leq$ LFL $\leq$ 38.8 g m^{-3}). As higher temperatures lead to higher VOCs emissions, a preliminary study comprising the variation of the 1,8-cineole concentration emitted by the tree crowns of *E. globulus* Labill., suggest that its LFL can be easily exceeded at 138 °C and, consequently, might act as fuel for the fire's propagation. Also, the volatile charges emitted by the leaves of these two tree species are much higher compared to the other two and, therefore, may contribute more significantly to the accumulation of VOCs in the forest environment. Furthermore, through *on-site* application of the HS-BAμE-μLD/GC-MS methodology, it was possible to detect four VOCs in the air surrounding *E. globulus* Labill. and *P. pinaster* Aiton tree species (ranging from 0.102 ± 0.002 to 0.311 ± 0.008 μg), showing to be a promising alternative for monitoring VOCs in forest environments, given its great simplicity, easy manipulation, and cost-effectiveness.

Financed by Fundação para a Ciência e a Tecnologia (FCT), I.P./MCTES through national funds (PIDDAC) - PCIF/GFC/0078/2018 (MSc grant, O.C. Gonçalves), UIDB/00100/2020, UIDP/00100/2020 and LA/P/0056/2020. The authors thank the entity Parques de Sintra - Montes da Lua, S.A, for the availability of using the Parque de Sintra e Monserrate as sampling sites.

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Online Detection of Metal Containing Nanoparticles in Aerosol via a Single Particle ICP-MS based Technique

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Nanoparticles (NPs) are everywhere being of natural or of anthropogenic origin. It is relevant to be able to identify, quantify and analyze these nano-objects, in terms of size, shape, and composition, in the environment such as in the atmospheric, aquatic, terrestrial, and biological systems [1]. Their behavior and fate are strongly influenced by the matrix. Thus, their study in real environmental systems is a high demanding task [2], and sophisticated techniques are needed. Recently a novel methodology called single-particle inductively coupled plasma mass spectrometry (spICP-MS) has been the hotspot for NPs characterization and quantification because of its ability to determine particle size, particle number concentration, and elemental composition simultaneously at environmentally relevant concentration levels [3]. Nowadays, spICP-MS has been widely used for NP analysis in environmental samples (waters and soils) and even biological tissues. However, a method to characterize and quantify online NPs directly from aerosol by spICP-MS has not been developed yet. Major complications are due to the requirement of the argon atmosphere, a stable flow rate, and a limited number concentration range [4]. In addition, in the atmosphere, NPs can undergo condensation processes, forming new and larger secondary particles and complicating their characterization [5].

The traditional way for aerosol metal measurement is based on the steps of offline collection, acid digestion, and ICP measurements [6]. This methodology can precisely evaluate the total mass concentration of the aerosol metal but the information of particle size and number concentration is missing. In our present work, a setup for online NP characterization is presented consisting of a rotating disk diluter (RDD) coupled to an ICP-MS working in single particle mode. RDD was used as a dilution system, where the dilution ratio may be adjusted during the measurement. The spICP-MS provided the elemental nanoparticle size present in the aerosol generated by an aerosol generator (AG). Moreover, the developed analytical method can characterize NPs contained in mixtures of different-sized particles and the presence of ionic species. The application of AG-RDD-spICP-MS in spiked road dust and PM10 samples demonstrated the capabilities of this setup for monitoring, detecting, and determining NPs in the aerosol.

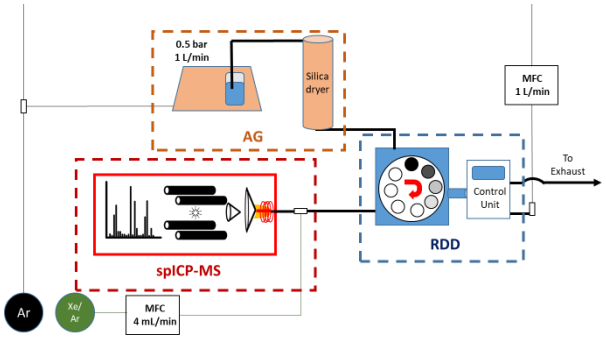

Figure 1. Schematic representation of the proposed coupling method (AG-RDD-spICP-MS) for online dilution and measurement of aerosol metal.

The authors thank the research funding provided by SNSF (ref. 184817).

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A new approach for water-soluble organic carbon extraction from atmospheric particulate matter under optimised analytical conditions

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Water-soluble organic carbon (WSOC) in air particles is a complex mixture of compounds with great effects on climate and human health [1,2]. Although a major fraction of aerosol WSOC still often remains unknown, an increasing amount of literature has been published in the last few years dedicated to the unravelling of WSOC structure and components. Nevertheless, the restricted amount of APM samples, usually collected, presents some serious challenges, which makes untangling the structure of WSOC an exceedingly complex task.

The extraction of water-soluble organic carbon from atmospheric aerosols is, usually, a straightforward process, typically relying on a water-based extraction of filters assisted by ultrasound or mechanical agitation [2]. A full extraction of the WSOC is assured by using a large volume of water which are further concentrated by solid-phase extraction (SPE) or lyophilization. However, some molecular information is usually lost when using these conventional. This methodological issue is solved in this work with the development of a Teflon® based device to extract aerosol WSOC from quartz fibre filter samples, using low volumes of ultrapure water.

Furthermore, a uniform experimental design was employed to establish the optimum extraction conditions using the well-known standard reference urban air particulate matter (NIST®SRM®1648a) as a proxy for atmospheric particles [3]. The experimental conditions in terms of time of extraction and volume of ultrapure water were investigated to allow an 80% recovery of the WSOC present in a sample. The gamma of NIST®SRM®1648a mass varied from 0.2 to 3.6 mg, the range of time of extraction was from 2 to 36 minutes, and the volume range was 2.0 to 17.3 mL. The regression analysis of results showed that, for samples with less than 2.6 mg, a10 minutes extraction using a volume of 8.0 mL was adequate to achieve an 80% extraction of WSOC. Nonetheless, for higher sample masses, the extraction conditions required to achieve this yield largely increased.

The authors acknowledge financial support to CESAM by FCT/MCTES (UIDP/50017/2020+UIDB/50017/2020+LA/P/0094/2020), through national funds. Regina M.B.O. Duarte also acknowledges the financial support from FCT/MCTES through an Exploratory Research Project (IF/00798/2015/CP1302/CT0015) and an Investigator FCT Contract (IF/00798/2015). FCT/MEC and the European Social Fund are also acknowledged for a PhD grant (PD/BD/142931/2018). This work was also supported by project AMBIEnCE (PTDC/CTA-AMB/28582/2017) funded by FEDER, through COMPETE2020-Programa Operacional Competitividade e Internacionalização (POCI), and by national funds (OE) through FCT/MCTES. Surface Ocean-Lower Atmosphere Study (SOLAS) is also acknowledged for endorsing the AMBIEnCE project.

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Multivariate Statistical Model Based on IR and Raman Spectroscopic Data of Blood Serum for Auxiliary Diagnosis of Mental Disorders

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Mental disorders, such as schizophrenia and bipolar diseases, and neurodevelopmental disorders, like autism spectrum disorder (ASD) and attention deficit and hyperactivity disorder (ADHD), have an increasing impact on society in the last few decades and affect approximately 2% of the world population, while 10% of the world's children population have been diagnosed with ADHD. Due to the heterogeneity of their symptoms, accurate diagnosis of these disorders has been a challenge for the clinicians. In the case of schizophrenia and bipolar diseases, due to their similar symptomatology, their differential diagnosis ends up with a 70% error and may remain misdiagnosed for at least a decade since its first symptoms. ADHD also shares common symptoms and frequent comorbidities with other mental and neurodevelopmental disorders (e.g., autism spectrum disorder, bipolar disorder) which makes the accurate and timely diagnosis a difficult task. ASD is another neurodevelopmental disorder in which the early age identification has a fundamental importance for the treatment to be effective.

Current diagnosis of these disorders follows the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition; DSM-5) diagnosis criteria and is based on the clinical evaluation of the symptoms. The absence of auxiliary methods that can complement the clinical evaluation increases the probability of false identification of the disorders. Development of fast and cheap complementary molecular based analytical methods to help clinicians at the diagnosis stage thus has great importance for more accurate diagnosis. Spectroscopic methods, in particular Raman and IR spectroscopies, are promising tools for identification of biomarkers, through the analysis of body fluids. Body fluids are easily accessible, and their use for medical diagnostics is a common practice. The analysis of body fluids using vibrational spectroscopy has progressively gained the respect of clinicians as a complementary diagnostic tool, with advantages over other techniques, such as being a sensitive and reliable approach, but also cheap, fast and easily adaptable to the clinical environment. These approaches have already proven its success for the diagnosis of infectious diseases and cancer, as well as for Alzheimer's and Parkinson's diseases.

In this study, vibrational spectroscopy (either Raman or IR), is used as analytical tool, together with chemometric methods, for the diagnosis of schizophrenia, bipolar disorder, ASD and ADHD through the analysis of blood serum spectroscopic characteristics.

Chemometrics is used to perform the scrutiny of the spectroscopic data obtained by IR or Raman spectroscopies, to find reliable statistical models to discriminate and classify the patients according to their diseases. The global accuracy of the model is 99.4% for schizophrenia and bipolar disorder and 100% for ADHD and ASD.

In this talk, the statistical models developed and tested for the cases of ASD, ADHD, schizophrenia and bipolar diseases (including subgroups: bipolar depressive episode, manic episode and otimic) will be presented.

Acknowledgements: This investigation has been funded by the Scientific and Technological Research Council of Turkey-TUBITAK 1001 Project (Project No.: 116Z294) and TUBITAK 1002 Project (Project No.: 121Z110).

Plasmonic-based imaging sensor for ultrasensitive molecular diagnostics

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Diagnostic biomarkers (i.e. circulating tumor DNAs, cell-free DNA, microRNAs, and proteins) are often in extremely low concentration in body fluids, exhibiting many challenges for their detection [1]. To extend the applicability of the Surface Plasmon Resonance Imaging (SPRI) sensor in detecting biomarkers at ultralow levels in a clinical setting, we combine the advantages offered by Peptide Nucleic Acid (PNA) probes [2] in improving the selectivity when targeting complementary DNA or RNA sequences, with the enhancement of the SPR signal obtained by using functionalized gold nanoparticles [3], minimizing at the same time non-specific adsorptions from biofluids by adopting appropriate antifouling surface [4].

By implementing a sandwich assay, it was possible to reveal ~1 attomolar KRAS mutated DNA circulating in 40 μL of plasma from cancer patients, greatly simplifying the liquid biopsy workflow [5]. Firstly, by using genomic DNA from tissues, we showed that our assay easily differentiates the most frequent RAS colon-rectal cancer (CRC) mutations from the wild-type. For the eleven tested RAS point mutations, the method exhibited 100% sensitivity and 82% specificity. The feasibility of the assay was then investigated by running spike-in experiments with KRAS DNA sequences in plasma from healthy donors. Finally, the plasmonic assay was efficiently applied to detect KRAS mutations in circulating DNAs from the plasma of CRC patients.

More recently, a similar approach is envisaged to be applied for non-invasive prenatal fetal sex determination based on the detection of a Y-chromosome specific sequence (single-gene SRY) in cell-free fetal DNA from maternal plasma, even at the earliest gestational age [6].

Possibilities offered in the detection of proteins as cancer biomarkers will be also discussed. In this direction, a new anti-fouling PEG-pentrimer carboxybetaine-based surface has demonstrated its applicability in plasma for the SPRI biosensing of human Arginase 1 [7].

It is expected that the proposed ultrasensitive SPRI platforms with multiplexing capabilities and high selectivity, will provide a new tool for a straightforward, early, and non-invasive diagnosis in the context of health applications.

We acknowledge support from the European Union's Horizon 2020 research and innovation programme under grant agreement No 633937, project ULTRAPLACAD and from Università degli Studi di Catania, STARTING GRANT 2020, project PATmiREC.

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Quantitative monitoring of test gas atmospheres in real time and verification of a new dosing system for test gas generation by SIFT-MS

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In the field of occupational health and safety, the measurement of hazardous substances is one of the cornerstones in the prevention of occupational diseases. For quality assurance purposes, the Institute for Occupational Safety and Health (IFA) provides proficiency testing schemes for various hazardous substances at its dynamic test gas facility. The provided test gases must meet high requirements regarding correctness, homogeneity, precision and stability. To ensure the quality of the test gas, two systems for online analysis were integrated into the process of test gas generation. In addition to the more conventional online gas chromatography (GC), Selected Ion Flow Tube Mass Spectrometry (SIFT-MS) is used to measure the quantitative test gas compositions in real time. Methods were developed for different substance classes and concentration ranges. Both techniques have already been successfully used during proficiency tests. The results show that SIFT-MS also provides satisfactory results in comparison with more established methods.

In addition to improved quality assurance using SIFT-MS, it also offers the possibility to detect short-term changes in the test gas composition. This made it possible to verify a new designed dosing system for test gas generation of substances with high vapor pressure by SIFT-MS. The special challenge here is that the entire dosage has to be carried out in a cooled environment to avoid outgassing of the substances in the tubing. By combining three individual components, a novel system for generating test gases was developed. The system is modularly composed of a microfluidic pressure-based pump system, a high precision cooling unit and a modified gas chromatographic evaporation system. A schematic drawing of the system is shown in Figure 1. It is suitable to produce aldehyde test gases with the required quality in the dynamic test gas facility of the IFA. The suitability of the system was successfully demonstrated by parallel investigations using SIFT-MS and classical offline-HPLC analysis.

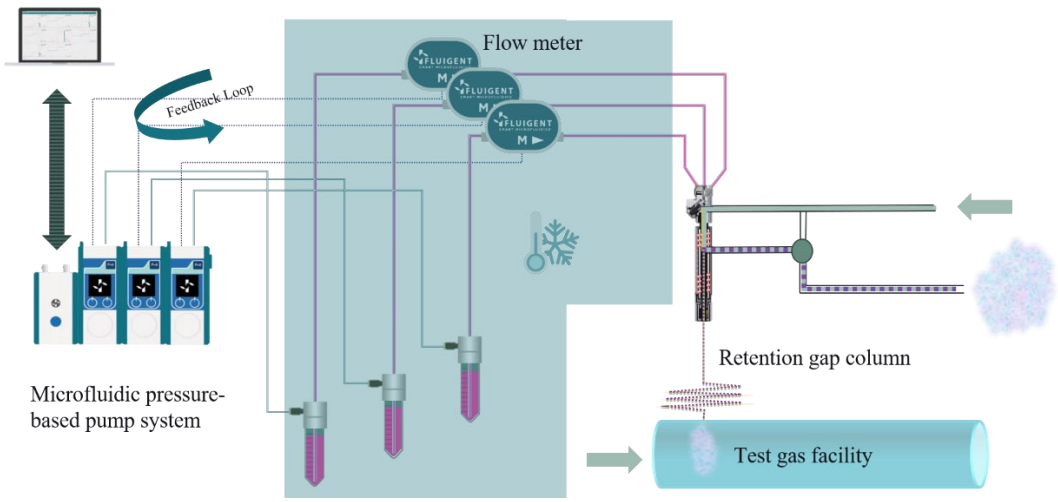

Figure 1: Concept of a new dosage system for generating test gases from liquid substances with high vapor pressures [1]

Thanks to the German Social Accident Insurance for funding this research work within the scholarship for doctoral students.
Thanks to Prof. Dr. Peter Wiesen (University of Wuppertal, Germany) & Prof. Dr. Dietmar Breuer (IFA) for supervising this research project.

[1] Graphic by the author with parts from the commercial product catalog of Fluigent, FLUIGENT Deutschland GmbH, 2017.

Combined ion mobility-mass spectrometry/quantum chemistry approach for direct identification of enantiomers in a natural mixture

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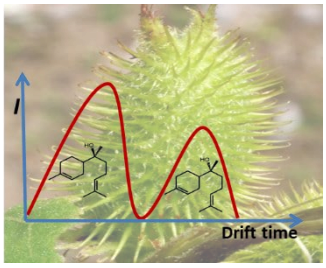
Essential oils (EOs) represent a very interesting class of natural products mixtures [1]. Yet, one of the major drawbacks of EO industrial exploitation resides in the overall high variation in their chemical profile depending on e.g., the extraction methods, plant organ used, age and vegetative stage of the plant, its harvesting time, and soil composition [2]. Moreover, an accurate identification of each EO components constitutes another crucial issue. In particular, the detection and characterization of isomers represents a milestone in EO analysis, enantiomers and diastereoisomers posing the highest challenge in this respect. In fact, such stereoisomers frequently differ in terms of biological activity and pharmacokinetic profiles, and the use of their mixtures may lead to undesirable adverse effects, particularly when associated with the inactive/less active isomer.

In this context, enantiomer-specific identification of chiral molecules in natural extracts is a challenging task, as many routine analytical techniques fail to provide selectivity in multi-component mixtures and/or lack sensitivity for dilute samples. We are presenting here an alternative approach, based on the combination of ion mobility-mass spectrometry (IM-MS) and quantum chemistry (QM), for the direct enantiomer differentiation in crude essential oils. To the purpose, the identification α-bisabolol enantiomers contained in the raw essential oil extracted from the Corsican *X. italicum* fruits is reported as a proof-of-concept. Accordingly, IM-MS experiments performed in Ag^+-doped methanol revealed the presence of both (+)- and (-)-α-bisabolol in the EO, while molecular simulations provided the structures of the two α-bisabolol enantiomer silver (I) adducts [3].



IMS-MS separation of (+) and (-) α-bisabolol enantiomers extracted from *X. Italicum* essential oil

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Formation of an Electroactive Coating Resulting From the Oxidation of Diclofenac on Screen Printed Carbon Electrodes

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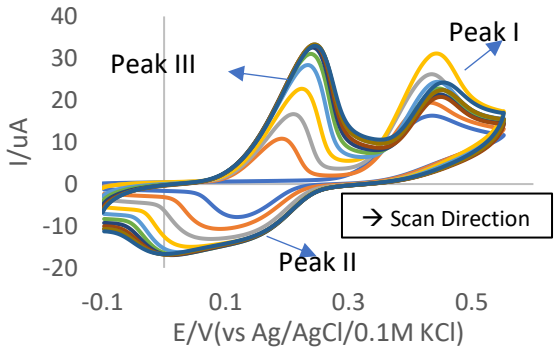
Diclofenac (DCF, 2-[2-(2,6-dichloroanilino)phenyl] acetic (or ethanoic) acid is a fenamic non-steroidal antinflammatory drug which is also a compound of emerging concern in wastewaters, potentially adversely affecting aquatic ecosytems [1]. Cyclic voltammetry and square wave voltammtery, in conjunction with Screen Printed Carbon Electrodes (SPCE) offer an attractive sensor technology for its detection [2]. Cyclic voltammograms of DCF in 0.1 M K_2HPO_4 obtained over a potential range from -0.1 V up to 0.5 V on mesoporous SPCEs (mSPCE) displayed a number of peaks (I, II and III), an example being presented in the figure below. Initially only a single oxidation peak (I) was apparent at ca. 0.4 V(vs Ag/AgCl). Upon scan reversal however, a reduction peak (II) appeared. Successive scans then gave rise to another oxidation peak (III), which showed higher peak currents as the scan number increased reaching a limit after 7 scans.



Consecutive cyclic voltammetric scans (10 mV/s) of 1mM DCF in 0.1M K_2HPO_4 on mesoporous SPCE indicating formation of an additional quasi-reversible peak (II) which increases and broadens during subsequent scans..

In the case of peak I however, following scan 4 the peak current decreased, possibly due to the occurrence of an adsorption-controlled process on the mSPCE surface. This was supported by linear peak current vs scan rate plots for peaks II and III for scan rates ranging from 2 mV/s to 120 mV/s. The reduction peak II also broadened with successive scans suggesting formation of a growing surface film (possibly a conducting oligomer) which was then oxidised in a quasi-reversible manner to yield peak III, as the peak potential varied slightly with scan number. Tafel slopes (b_a) of 53 mV/decade were obtained from initial scans conducted at 10 mV/s, indicative of a two electron, two proton exchange process, in agreement with the dimerisation mechanism proposed by Lucas *et al* on boron doped diamond electrodes [3]. An apparent transfer coefficient of 1 was also found possibly due to the occurrence of a multi-step mechanism [4]. Furthermore the film's surface concentration was estimated to be about 12 nmol/cm^2 when formed at a sweep rate of 10 mV/s and about 4.5 nmol/cm^2 at 100 mV/s. It was not possible however to produce an oligomeric layer on non-carbon Pt and ITO electrodes, although such films have been formed and used to mediate the detection of DCF on graphitic electrodes [5].

The precise nature of these films which has only a limited number of dimers or oligomers, will be explored using Raman and FTIR spectroscopies to clarify which functional groups are present. The layers can be grown to specific thicknesses by continuous cycling, which will then be confirmed by EIS measurements. In addition cationic and anionic redox probes will be used to investigate the coating's properties, including its porosity, as well as to study its mediation capabilities. The layer has been found to repel anionic probes (eg ascorbate) with no mediation observed. Unlike some conducting polymer mediating layers, which are strongly adherent, the layer can easily be removed from the electrode surface.

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New insights into the mechanism of coreactant electrogenerated chemiluminescence facilitating enhanced bioanalytical performance

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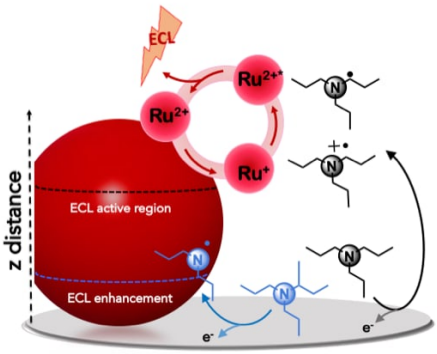
Electrochemiluminescence (ECL) is a leading technique in bioanalysis.[1] Since the excited species are produced with an electrochemical stimulus rather than with a light excitation source, ECL displays improved signal-to-noise ratio compared to photoluminescence, with minimized effects due to light scattering and luminescence background. The most challenging breakthrough in the development of analytical electrochemiluminescence (ECL) applications was reported from Bard and co workers that presented for the first time the generation of ECL with a coreactant.[1] This finding opened the application of ECL to large literature and transformed ECL from an academic curiosity to a real application and industrial success. In this context, the only real used materials for the ECL analytical and commercial application are tripropylamine (TPrA) as sacrificial "oxidative-reductant" coreactant and Ruthenium(II)-tris(2,2'-bipyridine) ($[Ru(bpy)_3]^{2+}$) as emitting species. In this case the mechanism for the ECL generation was proposed by Bard and still nowadays the only one accepted.[2],[3]

Here we show an additional, and very efficient, mechanism pathway for the generation of ECL by using TPrA as coreactant.[4] Thanks to the combination between ECL and microscopy we experimentally prove the alternative mechanism with the standard $[Ru(bpy)_3]^{2+}$/TPrA system.[3],[5] These mechanistic findings allow us to propose alternative amines as coreactant enhancing the ECL signal of more than one order of magnitude.

The reported results, besides contributing to a better understanding of the mechanisms operating in the chemiluminescence generation, also pave the way for the development of very highly efficient ECL coreactants for ultrasensitive bioanalysis.



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Synchrotron radiation for investigating electrochemical energy storage systems

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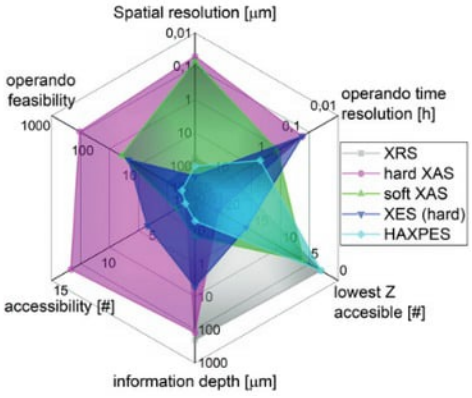
Synchrotron-based techniques have been key tools in the discovery, understanding, and development of battery materials. This talk strives to give an overview of the most prominent synchrotron x-ray spectroscopic techniques employed for addressing key scientific questions in the battery research field, such as elucidating underlying redox mechanism, structure-property relationships and degradation phenomena.

The physical background and general assets of synchrotron based spectroscopic approach will be presented before pointing out the relevance of specific techniques such as x-ray absorption spectroscopy(XAS) or x-ray Raman scattering spectroscopy for the battery research community on the example of selected case studies. This will give the audience insights on the kind of information that can be obtained following this approach but also reveal its limitations and current challenges. The most prominent spectroscopic techniques will be be compared in terms of time, energy and spatial resolution along with their feasibility. This comparison underlines that no single technique can satisfy all requirements[1]. In this manner the author seeks to provide guidance to the interested research community on which technique is the most suitable to address their specific scientific case and which pitfalls to avoid.



Last but not least, a brief outlook will be given on the future trends such as development of next generation synchrotrons, big-data analysis and the coupling of experimental and theoretical approaches.

This work was supported by the public grant ANR-10-LABX-76-01 (Labex STOREX) overseen by the French National Research Agency (ANR) as part of the ''Investissements dAvenir'' program. The authors would furthermore like to acknowledge the Ministerio de Ciencia, Innovación y Universidades of Spain for funding through grant PID2019-106519RB-I00.

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Chemical strategies to merge conversion, storage and integration of energy for a sustainable society

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Efficiency, stability, sustainability and integration of energy devices are milestone targets towards world electrification and renewable sources-dependent society. Chemistry covers a leading role in this scenario.

In this talk, new strategies for materials design, use of biosourced components, unconventional device architectures and structure-propriety-performance correlation will be shown for the design of different energy devices for the storage and conversion of energy.

In particular, the lecture will cover these intriguing aspects in the current energy scenario:

- Solar fuels from emerging conversion technologies;
- The design of stable cell components for post-Li batteries;
- The transition towards aqueous photovoltaics;
- The use new materials for allowing the design of integrated conversion/storage systems for cities and industries.

The importance of considering sustainability, stability and industrial scalability as main targets in the research work will be stressed, along with a real consideration of efficiency results presented in the literature.



This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No. 948769, project title: SuN_2rise).

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Combining FTIR spectroscopy and pressure-decay techniques to analyze sorption isotherms and sorption kinetics of pure gases and their mixtures in polymers

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During the last 40 years, chemometrics and, specifically, gas chromatography (GC) have been playing a crucial role in the investigation of mass transport properties of polymeric membranes in contact with a gas mixture of low MM species [1]. The gas phase composition at sorption equilibrium is measured *ex situ* and the solubility of each species in the polymer is retrieved from a mole balance over the gas phase.

In this work, a new technique is developed to characterize *in situ* the solubility and sorption kinetics of pure and mixed gases in polymers [2,3]. FTIR Spectroscopy in the transmission mode and Barometry are coupled together to perform a calibration of the IR signals of the low MM species in the gas and the polymer phases. The case of pure and mixed carbon dioxide and methane in polydimethylsiloxane (PDMS) is investigated at ambient temperature up to 9 bar. The calibration and sorption experiments are conducted with a short length gas cell. Pure gas samples are prepared at precise pressure and temperature so that the IR absorbance peaks are calibrated with literature gas density data [4]. These signals are used to monitor the concentration depletion of the pure gas species during sorption in PDMS: the penetrant concentration within the polymer is then evaluated from a mole balance over the gas phase. This approach is validated with simultaneous and independent barometric measurements. When the PDMS film is placed within the optical path of the IR beam, the spectrum of the penetrant in the polymer is also retrieved and the absorptivity of the CO_2 peak at 4954 cm^{-1} is calibrated. Both the gas and the polymer phases are analyzed spectroscopically to measure the penetrant solubility in the case of gas mixtures. Preliminary results on the CO_2 solubility in PDMS are obtained with the two IR methods using binary gas mixtures of 0.48 and 0.25 CO_2 mole fraction. The CO_2 sorption isotherm is successfully compared with literature data on the same polymer – penetrants system [1].

Quantification of polymer swelling and identification of host-guest interactions may be accomplished when the sample is traversed by the IR beam so that a complete thermodynamic picture of the sorption process is retrieved. Being the technique applied *in situ*, sorption kinetics are easily measured. Also, thermodynamic models are not needed to identify the composition of the gas mixture.

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Disproportionation in gas-phase di-manganese oxide cluster revealed by X-ray absorption spectroscopy

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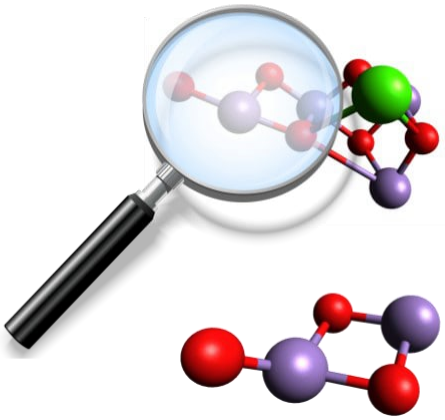
Photosystem II, with its active center a $CaMn_4O_5$ cluster (OEC), is essential for photosynthesis and therefore O_2 production in nature [1]. The understanding of the electronic structure and properties of this complex plays an important role in designing artificial water-oxidizing complexes. During oxygen formation the OEC undergoes five distinct states called S_0-S_4 forming the Kok cycle. Despite detailed knowledge of S0 through S_3 there is still a lack of information on S_4 due to challenges of preparing OEC in this state [2]. However, two major competing models for S_4 have been proposed in the literature which involve distinctively different oxidation states namely Mn(IV) (and an oxygen radical) and Mn(V), respectively.

We performed X-ray absorption spectroscopy (XAS) in ion yield mode at the manganese L-edge and oxygen K-edge on a series of cryogenically cooled, mass-selected manganese oxide ions at 20 K.

Here, we report on gas-phase $Mn_2O_3^+$- a subunit of the OEC – which is a high-valent species with two µ-oxo bridges and a terminal oxo ligand, which forms a subunit of the OEC. Using XAS we find an unusual charge disproportionation in $Mn_2O_3^+$, where one manganese atom is in a high oxidation state. The oxidation states were directly identify based on the absorption spectrum of manganese $L_{2,3}$ edge.



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Identification of reactive metal-oxygen species *via* X-ray absorption spectroscopy

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In transition metal oxides, the way the oxygen atoms are bonded to the metal center is found to play a significant role in their reactivity, in view of different types of oxygen ligands and unusual oxidation states. [1,2] The application of this knowledge can go from industrial catalytic processes to understanding the atmospheric chemistry. [2-4] In this context, finding compounds that present transition metals with unusual oxidation states and/or reactive oxygen species (superoxido, peroxido and oxygen centered radical) is of great scientific, technological and societal interests.

Here, we use X-ray absorption spectroscopy (XAS) at the oxygen K and metal $L_{2,3}$ and $M_{2,3}$ edges of $[MO_n]^+$ systems (M = transition metal, n = integer) to identify the spectroscopic signatures of oxygen ligands and assign the oxidation state of the metal. The $[MO_n]^+$ species in the gas phase are produced by argon sputtering of a metal target in the presence of oxygen. The cationic species are mass selected and accumulated in an ion trap. X-ray absorption spectra are then recorded in partial ion yield mode. [5] Our ion trap instrument is installed at the undulator beamline UE52-PGM at the Berlin synchrotron radiation facility BESSY II.

Fig. *1* schematically shows the analyses of generic cationic metal-oxygen species that can be identified in our set-up. Reactive species, such as the superoxido, the ozonido, the oxygen centered radical and species containing high-valent transition metals, are analyzed in stable conditions in the ground state inside the cryogenic ion trap. This method is here demonstrated to be an important tool to identify oxygen ligands, offering direct access to element specific electronic structures.

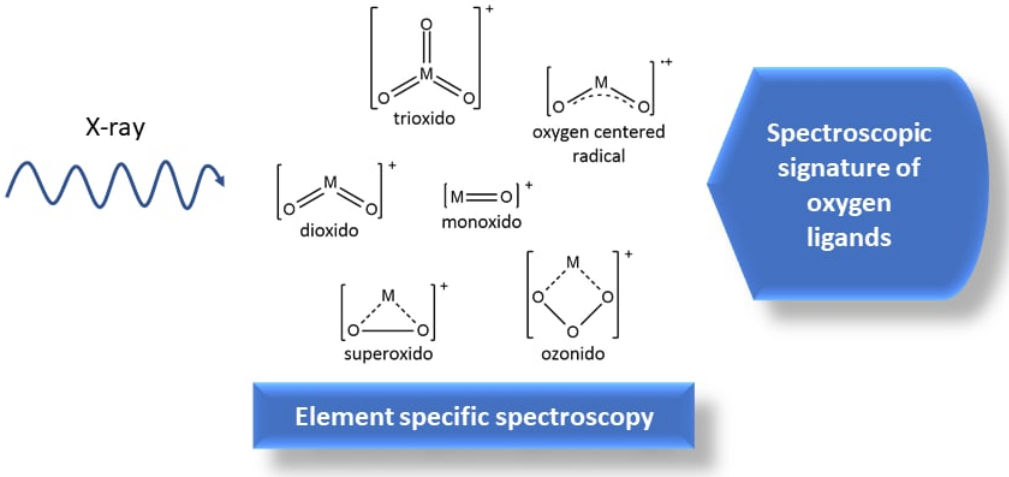

Fig. 1. Schematics of the identification of different cationic metal-oxygen species *via* X-ray absorption spectroscopy. Element specific analysis of the electronic structures gives the spectroscopic signature of different oxygen ligands. M = transition metal.

Beamtime for this project was granted at the Ion Trap endstation of BESSY II beamline UE52-PGM, operated by Helmholtz-Zentrum Berlin. This project has received funding from the German Federal Ministry of Education and Research through Grant No. BMBF-05K16VF1. JTL, MF, and OA acknowledge support by DFG RTG 2717.

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An innovative analytical method based on Stable Isotope Ratios of Carbon, Sulfur and Oxygen to identify sources of pollutants in black crust samples

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The degradation of cultural heritage caused by exposure to atmospheric pollutants is a growing concern. As shown by several studies concerning the degradation of stone materials, the chemical interaction of stone surfaces of historical buildings with such atmospheric pollutants (i.e. SO_2) can originate dark-coloured deposits called black crusts (BCs). BCs are referred to the areas where atmospheric deposition accumulates together with the products of the chemical transformation of materials, and their formation is one of the most dangerous phenomena that occurs in architectural heritage [1].

Knowing the nature and sources of degradation products is important to prevent damaging of cultural heritage. Stable isotope ratio is a valuable tool to assess the origin of a sample and is employed in several fields of environmental science [2]. In the field of cultural heritage conservation, the sulphur and oxygen isotope ratio have been used for the identification of the source of sulphur in BCs on stone surfaces of monuments and buildings [3]. Generally, the most important source of sulphur is SO_2 emissions from fossil fuels combustion by road vehicles and factories, although other sources such as biological ones and construction materials cannot be overlooked. It is important to note that different pollutants are incorporated in BCs during their formation and accumulated over time. Carbon stable isotope ratio can be used to evaluate the sources of carbonaceous pollutants on BCs samples.

The present study is focused on the isotopic characterization of black crusts collected from the Monumental Cemetery of Milan (Northern Italy). The cultural interest in this Monumental Cemetery (built in 1864) has increased during recent years since the site is of great cultural interest and has become part of the tourist itineraries in Milan, as it has happened for other important cemeteries in other European capitals. Numerous architectural and sculpture works of art are present, some of which were created by important artists telling in this way the story (about 200 years) of the city and of the relevant historical figures who lived and worked in Milan.

Stable isotope ratios of carbon ($\delta^{13}C$), sulfur ($\delta^{34}S$) and oxygen ($\delta^{18}O$) of different BCs samples are measured by isotope ratio mass spectrometry (IRMS) and the recorded values are correlated to some parameters such as the organic matter and polycyclic aromatic hydrocarbons contents on BCs. The proposed method, based on stable isotope ratio measurements, can be useful for the identification of sources of hazardous pollutants accumulated on BCs samples.

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Nanoscale Chemical Characterization and Imaging of a Recycled Post-Consumer Waste Polyolefin Blend using AFM-IR

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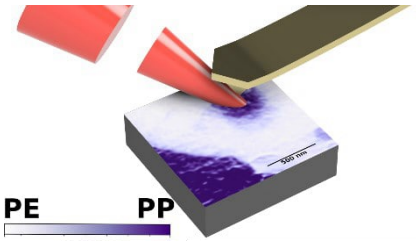
The recycling of polyolefins is a key aspect to reduce the amount of improperly disposed plastic waste. Polyolefins, such as polypropylene (PP) and polyethylene (PE), are the most produced polymer group in Europe [1], it is thus of great interest ensure efficient recycling. The need to sort plastic waste to avoid the effect that the presence of other polymers has on the mechanical properties of a blend increases the cost of the process. Therefore, blends deriving from heterogeneous waste streams that retain desireable properties could have a cost-advantage. To better understand these blends, we must also understand their nanoscale structure and chemical composition. Currently, nanoscale characterization of polymers is carried out using techniques that do not have chemical sensitivity – without prior staining or relying on previous good knowledge of its chemical composition. Examples of such techniques include SEM, TEM and AFM. These approaches often rely on a the predictable chemistry ensured by the tight process control existant in the production of virgin polymers. Thus, they may prove insufficient for the analysis of complex recyclates.

AFM-IR (also known as PTIR), is a rather recent scanning probe-based nanoscale IR technique that combines the resolution of an AFM with the chemical information provided by IR spectroscopy. In addition to reaching lateral resolutions of ≈ 10 nm in tapping mode [2], AFM-IR benefits from the long established spectra-structure correlations established for bulk IR spectroscopy [3]. In this work, we demonstrate how tapping mode AFM-IR can be applied to the analysis of a PE/PP/rubber blend derived entirely from post-consumer waste collected at the municipal level. In addition to the presence of sub-micron particles of other polymers (polyamide and polyurethane), we also imaged small (≈500 nm diameter) PP droplets that are present inside the PE phase. Furthermore, the presence of an interface between the PE and PP was detected with the help of a gaussian mixture model and identified as EPR rubber. The presence of the interface is observable in both the IR maps and full AFM-IR spectra obtained in the same area, and is further confirmed by reference TEM measurements. We believe this work demonstrates the applicability and usefulness of AFM-IR to the analysis of complex polymers at the nanoscale.



The authors acknowledge financial support through the COMET Centre CHASE, funded within the COMET – Competence Centers for Excellent Technologies programme by the BMK, the BMDW and the Federal Provinces of Upper Austria and Vienna. The COMET programme is managed by the Austrian Research Promotion Agency (FFG).

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Nature and Strength of Lewis Acid–Base Pairs

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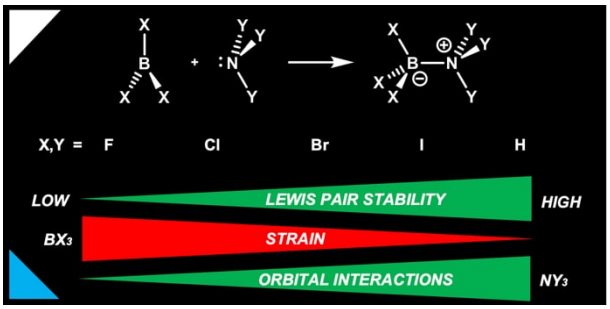
The acidity and basicity concepts of Lewis pervade different areas of chemistry.[1] Lewis acid–base pairs are usually divided into two classes: (i) short bonded, donor–acceptor (DA) complexes, and (ii) long bonded, van der Waals (vdW) complexes.[2] In this work,[3] we demonstrate the more complex interplay of energy components that dictates the bonding mechanism and the stability of the forming Lewis pair, whose importance depends on the molecular system. We highlight the counteracting effects of the strain energy (that is, the energy penalty to deform the Lewis acid and the Lewis base to the geometry they adopted in the final adduct) and the interaction energy (which, among others, accounts for orbital interactions).

We have quantum chemically investigated the bonding mechanism in the archetypical $X_3B{-}NY_3$ Lewis pairs using relativistic dispersion-corrected density functional theory at ZORA-BLYP-D3(BJ)/TZ2P. We evaluate the substituent effect on the Lewis acid and Lewis base by separately varying X, Y from H to F, Cl, Br, and I. The activation strain model (ASM) with the matching, canonical energy decomposition analysis (EDA)[4] are applied to obtain insights into the nature and strength of the Lewis acid–base pairs. For the $H_3B{-}NY_3$ adducts, we show that the bonding trend is driven by the commonly accepted mechanism of donor−acceptor [HOMO(base)−LUMO(acid)] interaction. On the other hand, the bonding mechanism in the $X_3B{-}NH_3$ adducts is determined by the energy required to deform the BX_3 to the pyramidal geometry it adopts in the adduct. Thus, Lewis acids that can more easily pyramidalize form stronger bonds with Lewis bases. The decrease in the strain energy of pyramidalization going from BF_3 to BI_3 is directly caused by the weakening of the B−X bond strength, which stems primarily from the bonding in the plane of the molecule (σ-like) and not in the π system, at variance with the currently accepted rationale.



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Light-switchable buffers

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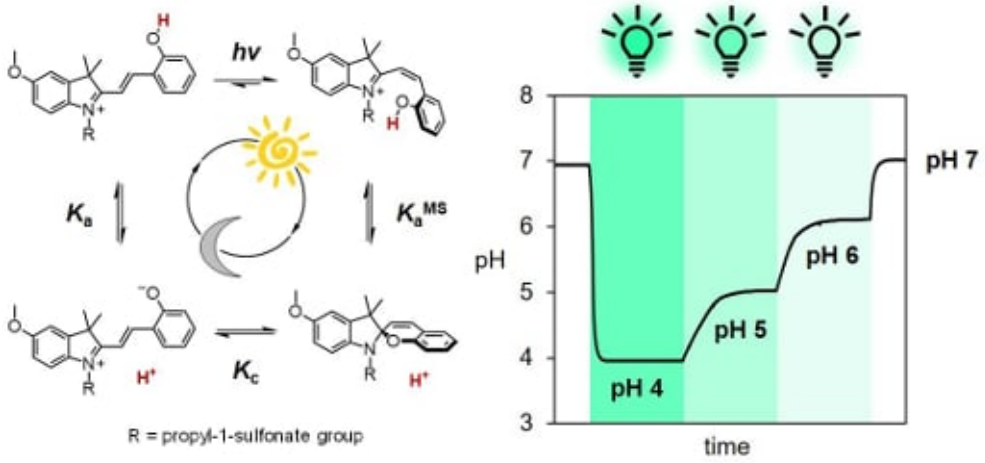
Since the introduction of the pH scale and the word "Puffer" (in German) into the chemical lexicon by Søren P. L. Sørensen [1] in 1909, buffer solutions constitute an essential tool in the study of aqueous (bio)chemical systems. By definition, buffers can resist pH changes when their actual pH equals the pK_a of the acid-base pair they are composed of – i.e., their buffer capacity is maximized. Here, I will discuss the possibility of making buffer solutions whose pH can be set at different constant values according to a light-triggered acid-base pair's pK_a shift.

Protonated merocyanines (MCHs) are spiropyran compounds featuring negative photochromism [2]. They are commonly referred to as "metastable-state photoacids" [3] – i.e., chemical species whose proton photo-dissociation is persistent enough to be coupled efficiently and reversibly with proton transfer reactions in solutions. Recently, we rationalized the thermodynamics and kinetics of MCHs through cross-validation of ^{1}H NMR, UV-Vis, and pH measurements [4]. We demonstrated that, under dark conditions, MCHs are organic weak acids displaying a ground state acidity constant close to neutrality (pK_a = 6–7), whereas, under steady light irradiation, they become more acidic by ca. 4 pK units (pK_a* = 2–3). Here, we screened a library of differently substituted MCHs and found that *para*-substitution of the indolium side with a methoxy group affords a compound suitable for making hydrolytically stable aqueous buffers whose pH can be tuned between 7 and 4 using 500 nm light [5].



Four-state model describing the operation of MCHs in water (left), and pH tuning by modulation of the light source power (right).

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Transition State Theory at the service of Green Chemistry.

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Green Chemistry, defined by IUPAC [1] as "the invention, design and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances", lays its foundations in 12 Principles. 'Design' is thus one of the key concepts in Green Chemistry for which the design of environmentally benign substances and processes plays a key role. Here, we will show how we can use state-of-the-art computational chemistry tools to improve and solidify the 'benign-by-design' concept introduced at the onset of Green Chemistry.

First we will show how our multiconformer transition state theory (MC-TST) protocol [2,3], along with its new improvements based on constrained transition state randomization, can be used to predict accurate rate constants for OH-initiated bimolecular tropospheric degradation reactions of volatile organic compounds, enabling the theoretical design of hydrofluorocarbon replacements with the lowest possible tropospheric lifetimes and therefore offering solutions to the compliance of the Kigali Amendment to the Montreal Protocol.

Second, we will take a deep look into the quantum mechanical tunneling (QMT) phenomenon. Specifically, we will analyze some cases [4-6] of hydrogen-atom and heavy-atom spin-forbidden QMT studied at the Laboratory for Molecular Cryospectroscopy and Biospectroscopy of CQC and demonstrate that non-adiabatic TST [7] can consistently predict reasonably accurate QMT rate constants for these elusive and not fully understood reactions. Such a tool will be invaluable for the prediction and creation of reactions where the application of tunneling control in chemical synthesis can lead to the creation of a larger molecular universe and to new green synthetic route designs, as the generation of species that are not accessible by conventional means will become possible.

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Multiscale Simulations of a Phase Sensitive Probe of Lipid Membrane Structure

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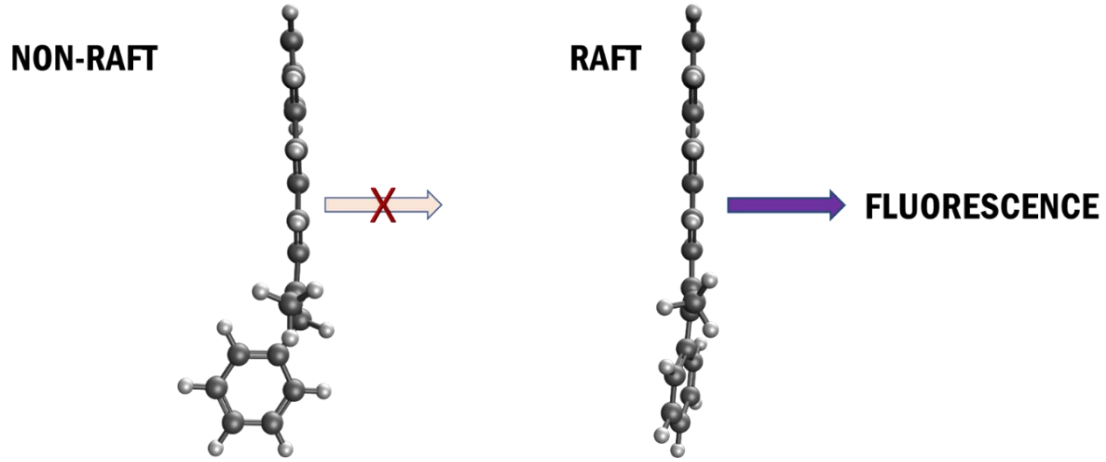
In membranes with low concentrations of cholesterol, the membrane is said to be in a liquid disordered (i.e. fluid) phase, while at high concentrations, the membrane enters a liquid ordered phase. It is in this phase that membrane rafts can form. Detection of the phase change via a fluorescent probe requires phase sensitivity of the probe. We have developed a multiscale computational chemistry approach to simulate several derivatives of the widely used diphenylhexatriene (DPH) lipid membrane probe. Using SF-TDDFT, automatic force-field generation and hybrid QM/MM simulations, we have identified the 2-methyl derivative of DPH as a potential probe of membrane fluidity, which exhibits restricted access to a conical intersection in the liquid-ordered phase but is freely accessible in less ordered molecular environments.



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Intermolecular covalent interactions

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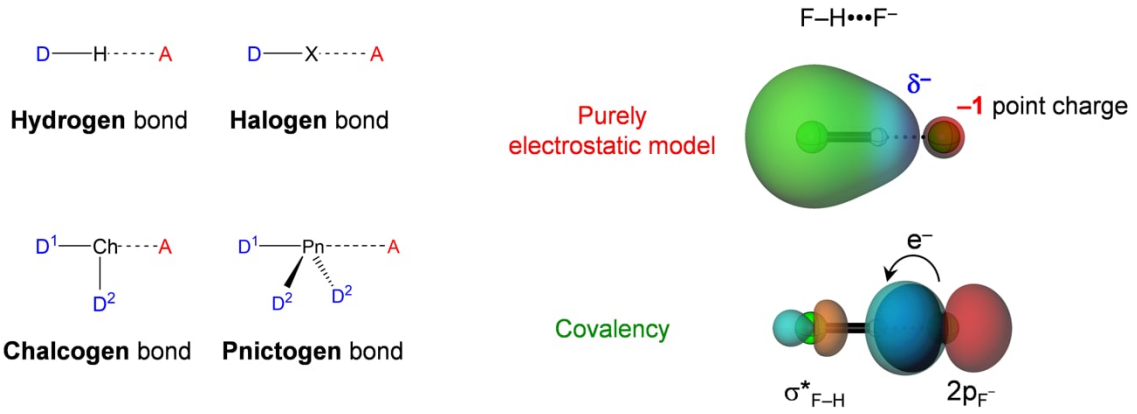
Pnictogen (PnB), chalcogen (ChB), halogen (XB), and hydrogen (HB) bonds are intermolecular interactions formed by the coordination of a Lewis base (A) and a Lewis acid (D_3Pn, D_2Ch, DX, DH; see figure below).[1,2,3] These intermolecular interactions have been the subject of countless investigations due to the key role they play in various areas of chemistry, molecular biology, supramolecular materials, and drug design.[4,5] This work provides a unified framework to understand the physical bonding mechanism behind PnB, ChB, XB, and HB, using quantitative Kohn-Sham molecular orbital (KS-MO) theory.

To this end, we have quantum-chemically analyzed the nature and directionality of PnB, ChB, XB, and HB in $D_mZ\bullet\bullet\bullet A^-$ archetypal model systems (Z = Pn, Ch, X, H; Pn = N, P, As, Sb; Ch = O, S, Se, Te; X = F, Cl, Br, I; D, A = F, Cl, Br) using relativistic density functional theory at ZORA-M06/QZ4P.[6] State-of-the-art activation strain and canonical energy decomposition analyses[7] herein reveal that these intermolecular interactions have a significant covalent component and are certainly not dominantly electrostatic in nature, as is incorrectly suggested by the σ-hole model[8] whose weaknesses are consistently exposed. The σ-hole model is only conceptually correct when the bond acceptor (A) behaves as a point charge. Therefore, the commonly accepted designation "Non-Covalent Interactions (NCI)" for the pertinent intermolecular interactions does not properly cover their nature and it is replaced with the more appropriate designation "Intermolecular Covalent Interactions (ICI)".



We thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), and the Netherlands Organization for Scientific Research (NWO) for the financial support. This work was carried out on the Dutch national e-infrastructure with the support of SURF Cooperative.

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Phase Behavior Profile of a Generical Three-Compound Mixture: A Chemoinformatic Approach

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The present environmental, social and economic context is evolving into a dramatic situation. This framework comprises a challenge to chemists in order to design sustainable processes. The knowledge of phase behavior profile is fundamental on that matter. The virtual infinite number of combinations between chemicals, its proportions, T and P, highlight the importance of predictive methods. The use of chemoinformatic approaches on codification and model build-up constitute valuable tools on phase behavior profile's knowledge. [1] This work aims at responding a question: What is the composition profile of a three-compound mixture in Liquid-Liquid equilibrium at a certain global composition, T and P?

The codification approach is based on MOLMAP technology. [1,2] This method consists on the pattern of activation of the atoms, of a certain chemical system, in a trained *Kohonen* network. The position of each atom in the network (MOLMAP) depends on its atomic property's profile. The model build-up involves the use of Random Forest (RF) algorithm. It establishes a relationship between a chemical system's configuration and the property of interest, input and output, respectively. RF learns with examples (datapoints). A generical datapoint corresponds to a given chemical, from a certain mixture, at particular TP conditions. The datapoint is encoded by the: 1- MOLMAP of mixture (each compound weighted by its global molar fraction); 2- MOLMAP of the chemical weighted by its global molar fraction; 3- T and P. Two complementary RF models were built for a chemical molar fraction in IL-poor and IL-rich phase, Figure.

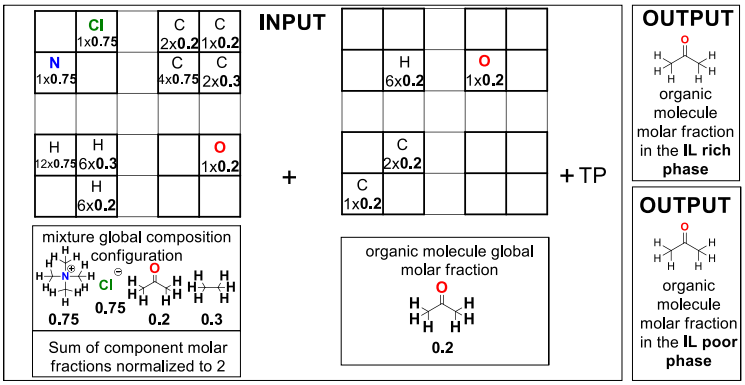

Figure: Chemoinformatic approach.

Mathematica program was used to obtain global composition points within a tie-line linking the IL-poor and IL-rich phases. The training set, for model build-up, comprises 69510 datapoints. Both model's predictive ability, evaluated with an independent test set, is excellent with R^2 and MAE of 0.95 and 0.042 for IL-poor phase and 0.94 and 0.048 for IL-rich phase. This work comprises a valuable contribution for an *a priori* screening of compatible conditions (IL, global composition range and TP) for extractions, extractive distillations and distillations, in order to promote isolation of industrial relevant chemicals. Optimized reactions, based on product separation from reaction media, comprises a distinct end-up for this work.

We thank FCT/MCTES Project: PTDC/EQU-EQU/30060/2017. This work was supported by the Associate Laboratory for Green Chemistry - LAQV which is financed by National Funds from FCT/MCTES (UIDB/50006/2020 and UIDP/50006/2020).

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Community-built analytical systems: from calibration lines to non-targeted methods by using NMR spectroscopy

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Nuclear Magnetic Resonance (NMR) spectroscopy is gaining ever-growing importance in analytical chemistry. In the last decade, quantitative analysis and non-targeted applications are successfully adding to its traditional use in structure elucidation.

The great application potential of NMR spectroscopy is essentially due to the direct proportionality between the signal intensity (I) and the moles (n) of the nuclei generating the signal through a proportionality constant (k), according to $I = k \cdot n$. Since k is a spectrometer constant and applies to all the signals in the spectrum, the ratio between a signal generated by the molecule under investigation and the signal of a reference molecule depends exclusively on the corresponding mole ratio. In theory, no dependence on the spectrometer features is expected when signal ratios are used in quantitative and non-targeted applications. In other words, when a given sample is analyzed by different spectrometers, the same output is obtained in terms of signal ratios. This characteristic of the NMR, which has been demonstrated through interlaboratory comparisons involving 36 to 66 NMR spectrometers [1, 2], paves the way for the development of community-built analytical systems capable of identifying and quantifying a number of molecules.

In this presentation, it will be shown how the development of a suitable database containing many comparable NMR spectra produced by different spectrometers can be used for identification and quantification applications. In particular, the case study of a data-driven grape juice identification system will be presented along with the advantages and the limitations of using non-targeted NMR analyses performed at different magnetic fields. Moreover, quantification of metabolites in grape juices by using a community-built calibration system will be also shown [3]. Finally, the feasibility of NMR spectroscopy to generate statistically equivalent NMR signal ratios from a number of different spectrometers will be demonstrated also for other complex mixtures such as aqueous extracts of wheat and flour [4]. Univariate statistics along with multivariate analysis will be used to establish unbiased criteria for assessing the statistical equivalence of the NMR signals. The factors affecting the signal equivalence will be shown, and possible solutions to reduce the extent of human errors will be proposed.

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Improving Light-Driven Molecular Pumps: Dissecting Thermodynamic and Kinetic Entaglement in a Photoswitchable Molecular Axle

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The development of molecular pumps able to operate autonomously far from equilibrium constitutes one of the major challenges of modern nanotechnology.[1] In principle, these nanoscale devices can be powered by a variety of energy sources, including electrochemical, chemical, and light energy.[2] Light-driven artificial molecular pumps based on (pseudo)rotaxane architectures have recently been realized in our laboratory.[3,4] The operation of our nanoscale pump is dependent on the light-induced modulation of the self-assembly between a crown ether macrocycle and a linear component consisting of a photoswitchable azobenzene unit and a dibenzylammonium unit, which is a recognition site for the rings. To optimize our system, it proved necessary to better understand the nature of the entanglement between the photoswitching of the azobenzene moiety and its thermodynamic and kinetic effects on the self-assembly of the ring and the axle. To achieve this, we developed a symmetric molecular axle in which the two key components of the pump module, i.e., the ammonium recognition site and the azobenzene unit, are separated by a short chain. The novel thread was characterized by means of ^{1}H NMR and UV/Vis spectroscopy. The formation of a supramolecular complex between the axle and DB24C8 crown ether was investigated in the dark and upon irradiation by means of mono and bi dimensional dynamic NMR spectroscopy. Our preliminary results highlight that the small structural variation introduced has nonetheless a large effect on the characteristics of the system. The results obtained suggest that the modulation of the kinetic and thermodynamic parameters induced by the photoisomerization of the azobenzene moiety in this type of systems is mediated not only by steric effects, as previously hypothesized, but also by inductive ones.

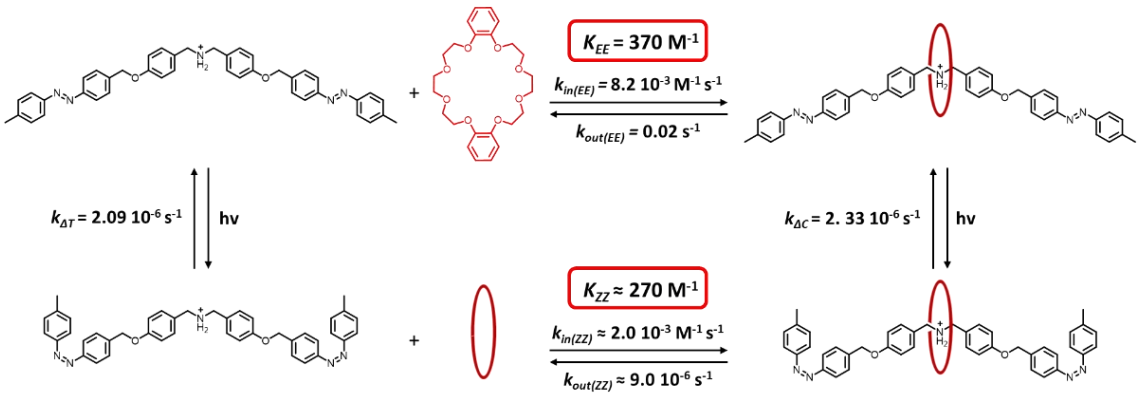

Figure 1: Structures of the components and operating cycle of the supramolecular complex.

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In situ illumination NMR: photoisomerization of naphtopyran derivatives

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Photochromic dyes have been widely used in several commercial applications like photo responsive lenses. For a molecule to become a successful candidate for such application it is required to have a rapid and effective isomerization upon absorption of UV radiation under sunlight exposure and an equally fast return to the initial state. Napthopyran derivatives are successful because of their fast and effective relaxation to the initial state, meaning short lifetimes down to less than 10 seconds at room temperature [1]. *In situ* illumination NMR has been explored to study photo-promoted reactions and offers the possibility to follow molecular transformations that cannot be observed otherwise [2]. This study applies *in situ* illumination NMR to elucidate the photo-promoted isomerization of some naphtopyran derivatives such as Midnight Grey™ (Figure 1). With our setup, a total conversion from the initial Midnight Grey™ into only two isomers was achieved at 233K upon irradiation using a 365nm LED. The photo mechanism and identification of the corresponding isomers was supported by DFT and td-DFT calculations. This study paves the way toward a better understanding of photochromic dyes, their isomerization, and degradation, which should ultimately lead to a better design strategy.

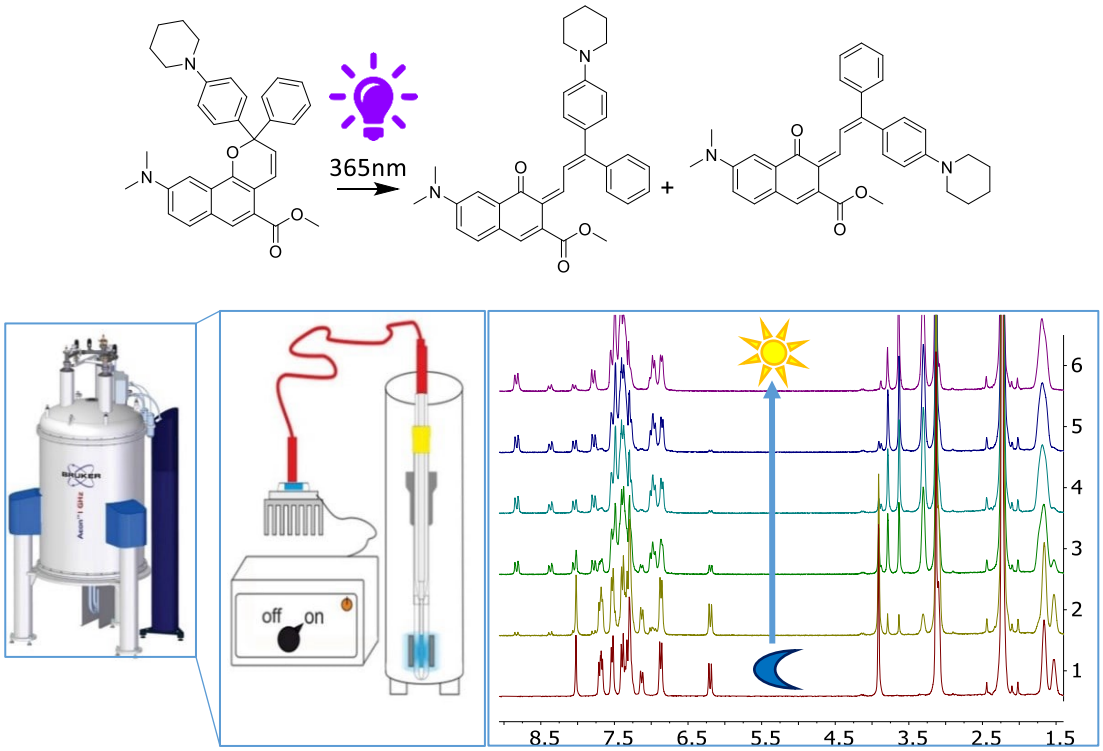

Figure 1: Midnight Grey™ photoisomerization: *in situ* illumination NMR setup and ^{1}H-NMR spectra of total isomerization under UV 365nm irradiation at 233 K for a 200-minute period.

Acknowledgements: Fundação para a Ciência e a Tecnologia. Grant Numbers: LAQV-REQUIMTE (UIDB/50006/2020), CICECO-Aveiro Institute of Materials (UIDB/50011/2020 & UIDP/50011/2020), Portuguese NMR Network, LFBF PhD grant SFRH/BD/150663/2020.

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IR-induced and tunneling reactions in cryogenic matrices: The (incomplete) story of a successful endeavor

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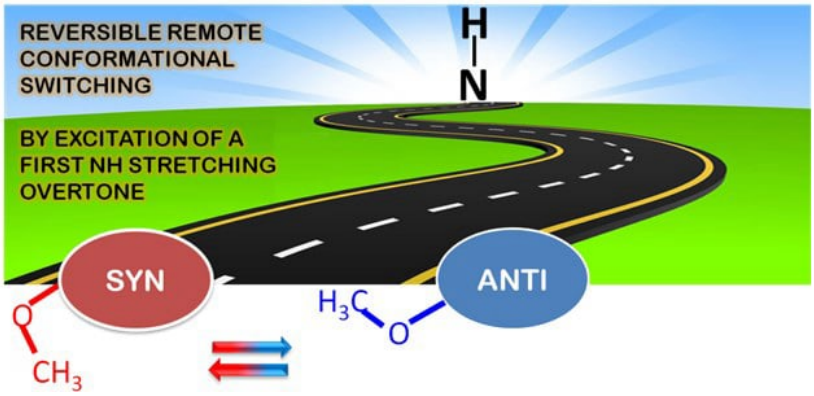
In this lecture, we will survey the major progresses in the field of IR-induced chemistry, and its entanglement with tunneling-driven chemistry. The narrative will follow a historical perspective, highlighting the interweaving of the two types of processes. The story of this still ongoing fascinating scientific endeavor will be presented following closely our own involvement in the field for more than 30 years. It considers a large set of examples, from very selective IR-induced conformational isomerizations to bond-breaking/bond-forming reactions and successful observations of rare heavy-atom tunneling. The lecture aims to introduce vibrationally induced chemistry as a powerful tool to manipulate molecular structures in a highly selective way, and demonstrate how to use and control quantum mechanical tunneling as a tool to explore the reactivity of organic molecules in an unprecedented way.



The concept of remotely located reaction-triggering vibrational antenna: *a chemical group of the molecule placed far apart of the fragment undergoing the structural transformation induced by vibrational excitation of the antenna.*

Acknowledgements:
All members of the LMCB as well as my colleagues from abroad that contributed to the described studies are thanked. This work is being supported by Projects PTDC/QUI-QFI/1880/2020 and POCI-01-0145-FEDER-028973, funded by National Funds *via* the Portuguese Foundation for Science and Technology (FCT). The Coimbra Chemistry Centre is supported by FCT through projects UIDB/QUI/0313/2020 and UIDP/QUI/0313/2020, co-funded by COMPETE. Support from LaserLab Coimbra is also acknowledged.

Multistate of chemical reactions of 4´-dimethyl-7-diethylaminoflavylium. Thermodynamics, kinetics and Photochemistry modulated by water: ethanol, SDS and CTAB micelles

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Aminoflavylium compounds are an interesting family of compounds exhibiting physical chemical properties suitable for different applications beyond those of anthocyanins in food and health [1,2].

In general, all species of the aminoflavylium multistate of species are stable in all pH range, including basic medium, exhibit a rich color pallet, making them appropriate to design sensors or new photochromic systems, for example. However, most aminoflavylium compounds have a severe drawback, because are scarcely soluble in water. In this sense, different micellar systems have been studied to improve the solubility of these pigments.

The photochromic properties of the *mono* and *bis* aminoflavylium base systems, have been extensively studied in organic solvents, polymers and water: ethanol (1:1), by Matshushima and co-workers [3,4]. In particular the photochromic systems based in *bis*-aminoflavylium have a blue output upon irradiation of the yellow *trans*-chalcone [5].

In this work the thermodynamics and kinetics of the compound 4'-dimethyl-7-diethylaminoflavylium was studied in water:ethanol (1:1) in the presence of SDS and CTAB micelles. The blue flavylium cation is in equilibrium with the pink protonated flavylium cation defined by $pK_{AH2+/AH+}$ and the yellow *trans*-chalcone, defined by $pK_{AH+/Ct}$. The difference between these two p*K*s gives the pH domain of the flavylium cation, ΔpK=1.95 in CTAB, ΔpK=5.6 in water:ethanol (1:1) and ΔpK=8.5 in SDS micelles. On the other hand, the pH domain of the *trans*-chalcone is limited by $pK_{AH+/Ct}$ and $pK_{Ct/Ct-}$. It is lower in SDS micelles ΔpK=2.7, increases in ethanol:water (1:1) ΔpK=5.1 and is maximum in CTAB micelles, ΔpK=6.8. All these effects can be explained by the electric charge of the micelles surface.

As conclusion, taking into account the benefits of this pigment in these three different systems (water: ethanol, SDS and CTAB micelles), it can be suggested as pH sensors and photochromic systems used in ophthalmics, textile application.

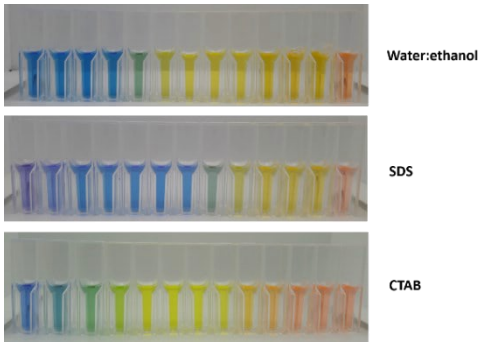

Figure 1. Image of 4´-dimethyl-7´-diethylaminoflavylium in water:ethanol, SDS and CTAB micelles at pH range between 1 and 13.

We thank to FCT from a doctoral grant from (SFRH/BD/143309/2019) and the Associated Laboratory for Sustainable Chemistry, Clean Processes and Technologies LAQV-REQUIMTE through the national funds from UIDB/50006/2020 and UIDP/50006/2020. The authors also thank AgriFood XXI I&D&I project (NORTE-01-0145-FEDER-000041) cofinanced by European Regional Development Fund (ERDF), through the NORTE 2020 (Programa Operacional Regional do Norte 2014/2020).

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Impact of positive charge and ring-size on interactions of calixarenes with DNA, RNA and nucleotides

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Calixarenes were traditionally studied as supramolecular receptors for various low molecular mass cationic or anionic species, but only marginally investigated for their biological effects or applications [1]. However, systematic study revealed that cationic calixarenes can be applied as innovative DNA-transfection agents [2]. We have developed three generations of calix[6]arene-based (funnel), as well as two generations of resorcinarene-based (bowl) supramolecular systems featuring two, three or four methylimidazole-containing coordination arms grafted at the large rim, suitable to bind to variety of nucleid acid sequences [3,4].

In this work we focused on calixarenes with short, triazole-attached positively charged substituents (**2** and **4**) and their neutral analogues (**1** and **3**, Fig. 1.). Their ability to recognize specific sequences of various DNA chains was studied by thermal denaturation experiments, fluorimetric titrations, circular dichroism experiments and molecular dynamics simulations. Comparison of neutral and cationic calix[6]arene and calix[4]arene derivatives revealed that only cationic analogues non-covalently bind to ds-DNA and ds-RNA, by insertion into DNA minor groove or RNA major groove. Also, cationic analogues revealed strong and highly selective charge-dependent stabilization of AT-DNA against thermal denaturation, both neutral and cationic calixarenes bind nucleoside monophosphates with similar efficiency, by forming tweezer-like supramolecular complexes, with nucleobases inserted between aromatic pendant arms grafted to calixarene rims. Such nucleotide-calixarene complexes were monitored by emission change of calixarene as a function of nucleobase insertion, at variance to DNA/RNA complexes in which calixarene is inserted into polynucleotide groove, which do not change calixarene emission – stressing importance of the ligand insertion within calix-basket for the fluorimetric sensing.

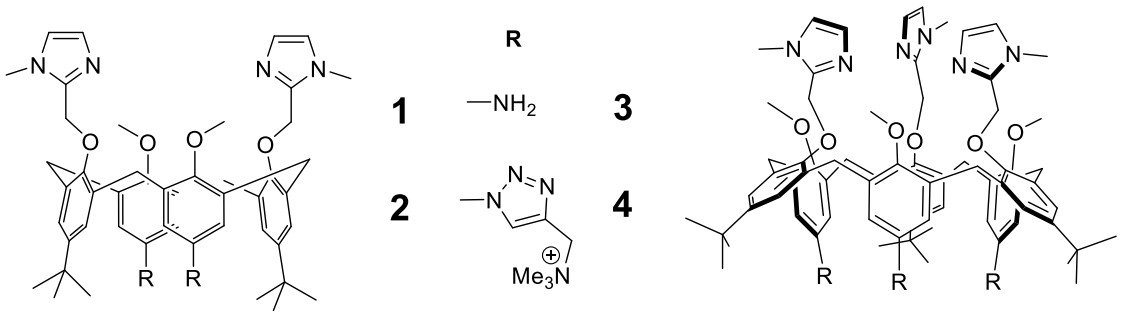

Figure 1. Molecular structures of studied cationic calixarenes **2** (as a chloride salt), **4** (as a nitrate salt) and their non-charged analogues **1** and **3**.

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Highly sensitive fluorescence methods for the selective detection of Cd (II) and Hg (II) in environmental samples

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In recent years, poisonous heavy metal ions have gained much attention because of severe health-related issues to human and biotic life. Indeed, these pollutants are generally not biodegradable and can accumulate in the environment. This results in contaminated waters and food, with serious deleterious effects both on human health and on the environment [1]. Among these heavy metals, cadmium and mercury have attracted the most attention due to toxicity issues. Methods based on fluorescent sensors have gained considerable attention in the past years, due to the simplicity of the operations combined with the high selectivity and sensitivity of the designed sensors.

In this work, fluorescent sensors for Cd (II) and Hg (II) based on rhodamine were synthesized and tested for application to real water samples, which requires low detection limits and high selectivity in competition experiments with other metal ions. Incorporation of a Rhodamine-6G fluorophore and optimization of the buffer system (detection with acetic acid buffer at pH 5.25 for Hg (II) and borate buffer at pH=9.2 for Cd (II)) significantly improved sensitivity up to more than 100 times compared to previously described sensors based on the same ionophore group. Detection limits for Cd (II) and Hg (II) were 0.12 $\mu g.L^{-1}$ (1.1 nM), and 0.27 $\mu g.L^{-1}$ (1.3 nM), respectively. Optimization of the buffer used for detection of Hg(II) also displayed significant effects on selectivity, circumventing the problem of copper interference which generally limits application of mercury sensor on real samples [2]. For the cadmium sensor, copper and zinc interferences couldn't be avoided at environmental concentration levels, as was observed with all other cadmium sensors described in the literature. For this reason, we have developed a new method for the selective extraction and preconcentration of Cd(II), based on a polystyrene resin grafted with a tri-N-acetamide cyclen group (DOTAM macrocycle). The modified resin was characterized by FT-IR, ATG and elementary analysis. Several factors influencing the preconcentration efficiency of Cd(II) and its subsequent determination, such as the pH of the sample, the eluent composition, flow rates and interferences of other cations have been investigated. Cd(II) could be selectively retained by the resin in the pH range of 2-4, and selectively eluted with HNO_3 1M. This protocol is the first example of a solid support capable of a selective extraction of Cd(II) in the presence of real environmental concentrations of Cu(II) and Zn(II). The methods have then been applied for the determination of trace amounts of Hg(II) and Cd(II) in real water samples.

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New heteroleptic copper(I) complexes: towards more sustainable photosensitizers

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Copper(I) complexes have emerged as non-noble metal alternatives to Ru(II), Os(II) or Ir(III) and used for a wide range of different applications like photoredox catalysis [1], optoeletronics [2] and photovoltaics [3].

We aim to synthetize and investigate new heteroleptic copper complexes, based on bulky diphosphines and novel diimine chelating ligands, which could act as photosensitizers. With the target of solar energy exploitation, one of the most important requirements for a photosensitizer is the ability to absorb visible light. Thus, we designed different ligands in order to shift the absorbance of Cu(I) complexes in the visible light region. We started with the synthesis of copper complexes based on a pyridine-unit, which show the ability to absorb violet light up to 400 nm (λ_{max}=350 nm) [4] (**1**, Figure 1). The presence of a methyl in α to the nitrogen atom of the pyridyl ring, restricted the pseudo-Jahn Teller distortion in the excited state, allowing an adequate photoluminescence quantum yield and long-living lifetime. Then, increasing the level of π-conjugation, by substituting the pyridine with a quinoline, we obtained Cu(I) complexes showing a red shift in the absorbance spectra up to 450 nm (λ_{max}=395 nm) (**2**, Figure 1) [5]. These complexes were the first photosensitizers based on copper to be associated with a Ni(cyclam)Cl_2 catalyst in a noble-metal free CO_2-photoreduction system.

With one more nitrogen atom to the diimino-ligand, the quinoxaline-based copper complexes show a further red-shift compared to the quinoline ones, absorbing light up to 500 nm (λ_{max}=425 nm) (**3**, Figure 1) [6]. These copper complexes were tested as catalysts for atom transfer radical addition (ATRA) reactions leading to good results. Finally, the synthesis of benzoquinoxaline-based ligands and their Cu(I) complexes is presented (**4**, Figure 1). Their absorbance is further bathochromic shifted and is up to 550 nm (λ_{max}=460 nm). We will discuss their photophysical and electrochemical properties, corroborated also by preliminary theoretical calculations.

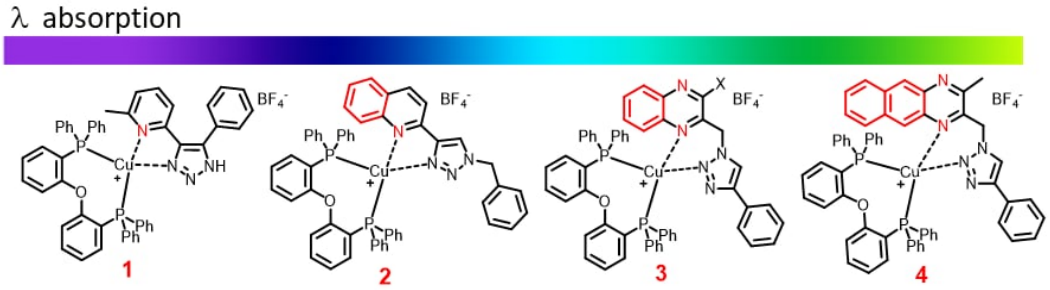

Figure 1. Chemical structures of the new copper complexes mentioned in the text. The upper coloured line shows the redshift of their absorption spectra.

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Origin-Independent Energy-Based decomposition of the first and second hyperpolarizabilities

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The decomposition of (non)linear optical properties (NLOPs, e.g., polarizability, hyperpolarizabilities...) is not straightforward because it runs into the issue of origin-dependence: all obtained atomic contributions will depend on your choice of origin. This means the obtained values will change if the arbitrary origin of coordinates is moved, and also the contribution of a given functional group is modulated based on its distance from the origin, rather than just its nature and environment.

These NLOPs are derivatives of the energy. In our work [1], we decompose the energy into atomic contributions (to then obtain the atomic NLOP contributions), and we show that, without any assumptions or approximations, one can consider *only* the origin-independent energy terms, and the obtained value, which is fully origin-independent, will be related to the total property by a specific exact factor that depends exclusively on the property, as can easily be shown through a simple mathematical demonstration. This makes it possible to perform a decomposition completely avoiding the terms that introduce origin-dependence (i.e., the dipole moment operator).

Since our analyses are done in the real-space, we can also plot the true densities of these properties, in a way that's origin-independent and integrates to the molecular property when integrated over the entire space.

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Intriguing Zn (II) emitters in the *"biological window"* with large Pseudo-Stokes shift for bioimaging

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Over last few years, increasing attention has been paid to develop suitable probes for different cellular organelle-specific targeting live cell-imaging agents. Among the different class of imaging compounds investigated nowadays, luminescent metal complexes which are emissive in the so-called *"biological window"* (700-1000nm), is one of the most studied [1].

In the search of highly emissive compounds in the far-red / NIR region, we focus on Zn (II) bis(dipyrrinato) complexes [2], and novel heteroleptic complexes were successfully prepared as fluorophores for cell imaging (Figure 1). [3]

More precisely, the new molecular architectures contain one plain dipyrrin (Lp) and one π-extended dipyrrin (Lπ), whose photophysical properties are cumulative in the absorption spectra, with two absorption bands identifying the *($^1\pi$-π)* transition localized on each dipyrrinato ligand, presenting very high absorption coefficient *(Ɛ* up to *9000 $M^{-1}cm^{-1}$* for Lp and Ɛ up to *38900 $M^{-1}cm^{-1}$* for Lπ).

Due to an energy transfer mechanism present in the fluorophores, as evaluated in similar structures in the literature [4], the emission spectra of the complexes present a single emission profile with maxima ranging from 635 to 640 nm with shoulders and tail up to 820 nm.

With our tailor-made design, we achieved far-red emissive complexes with a photoluminescence quantum yield up to 45 % in dimethyl sulfoxide and 70 % in toluene. We will present here the results obtained, which prove the versatility of these complexes, as efficient emitters in both live-cell imaging and in fixed-cell experiments.

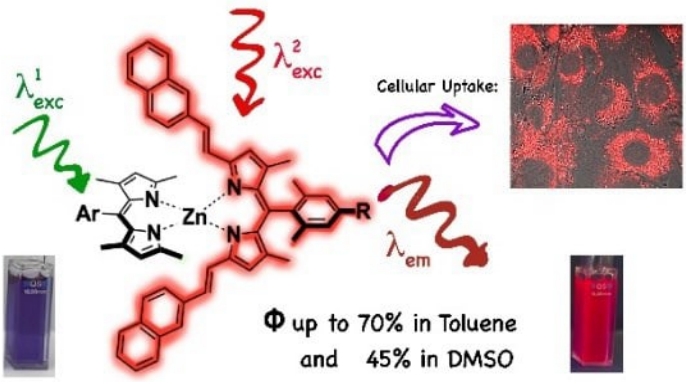

Figure 1: Representative heteroleptic bis (dipyrrinato) Zn (II) complexes used for cell-imaging.

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High-resolution two-color imaging of peptidoglycan and teichoic acids in *S.pneumoniae* by dSTORM

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The Gram-positive bacterial cell wall is composed of two main biopolymers, peptidoglycan (PG) and teichoic acids (TAs). Their highly dynamic biosynthesis involves spatiotemporally controlled processes that shape the morphology, elongation and division (septation) of the bacterium. In contrast to rod-shaped bacteria where elongation and septation are clearly dissociated in time and space, in ovoid-shaped bacteria like *Streptococcus pneumoniae*, these events are synchronous and located at midcell in an annular region of nanometric dimensions. A combined approach of metabolic labeling using copper-free click chemistry and high-resolution dSTORM (direct stochastic optical reconstruction microscopy) has recently revealed the specific PG synthesis sites for cell septation and elongation, and their relative dynamics along the cell cycle.[1] Whether TAs are assembled at septation and/or elongation sites, the degree of coordination with PG synthesis, and the molecular mechanisms ensuring such regulation remain unknown. This study has long been limited by the lack of tools to label TAs but we have recently developed probes that are metabolically and selectively incorporated into new TAs.[2,3] We now need to label and observe PG and TAs in two colors in a same cell to detect fine variations in the localization and architecture of their synthesis site(s), and in the amount of newly inserted material, to eventually unravel the mechanisms allowing their coordinated synthesis. Preliminary co-labeling experiments combining copper-catalyzed and copper-free click reactions have shown poor fluorescent signal-to-noise ratio, precluding so far two-color dSTORM studies. Our data clearly show that the use of copper is the limiting factor, pointing to the need for new pairs of probes and fluorescent dyes whose conjugation does not require catalysis. In this communication, we would like to report the development of chemical approaches using coppe-free click chemistry for two-color labeling of PG and TAs and their study by high resolution dSTORM.

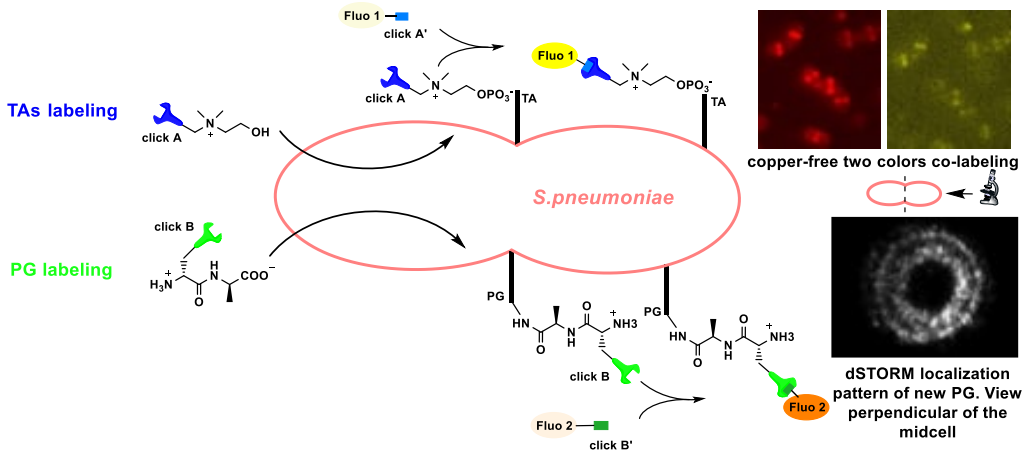

Figure: Two steps labeling of TAs and PG by dSTORM using copper-free click chemistry

Thanks to the Agence Nationale pour la Recheche (ANR), grants number ANR-19-CE07-0035, ANR-16-CE11-0016 and ANR-19-CE15-0011-04, and the labex ARCANE and CBH-EURE-GS, grant number ANR-17-EURE-003

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Hyperspectral Imaging of Drug Penetration Processes in Human Skin

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Recent results on hyperspectral imaging of drug penetration using tunable soft X-rays and infrared radiation are reported. This approach employs label-free spectromicroscopy far below the diffraction limit of optical microscopy revealing details of local drug concentration and drug penetration mechanisms.

The experimental approach relies on the acquisition of full spectroscopic information as a function of location in fixed human skin samples and advanced data evaluation approaches using singular value decomposition [1] and principal component analyses. This provides a sensitive and quantitative method to determine the local drug concentration, reaching into the range of femtogram per μm^3 at a spatial resolution well below 50 nm. Two complementary experimental approaches have been used: (i) scanning transmission soft X-ray microscopy (STXM) using the UVSOR III synchrotron (Okazaki, Japan) as well as (ii) photothermal expansion microscopy (AFM-IR). The anti-inflammatory drug rapamycin was studied, which barely penetrates intact human skin due to its high molecular weight. Human skin samples *ex vivo* were exposed to different drug formulations including redox-sensitive core-multishell nanocarriers [2] as well as two initial skin preparations simulating inflammations. These reveal characteristic differences in drug penetration that are of importance for developing novel approaches of topical dermatotherapy.

Specifically, it is shown that the high molecular weight drug rapamycin (M = 914.172 g/mol) barely penetrates the top horny layer of untreated, i.e., intact skin (stratum corneum). Primary skin treatment with the serine protease trypsin allows us to simulate barrier disruptions that are typical for inflammatory skin diseases. Then, the drug can penetrate the viable skin layers (viable epidermis). Redox-sensitive nanocarriers are shown to release the drug depending on the oxidation state of the skin samples, which is influenced by initial skin treatment. Moreover, complementary work on rapamycin ointment provides evidence for enhanced drug penetration due to occlusion as a function of treatment time.

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Sustainable Ionic and Porous Systems for CO_2 Conversion to Fuels

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Nowadays, the development of efficient and sustainable approaches for carbon dioxide conversion into fuels and other valuable products is highly relevant [1]. Chemical reduction of CO_2 can produce liquid and gas alternative fuels or precursors for fuel production such as higher chain alkanes, methanol, formic acid, methane, among others. Our group is working in the development of sustainable strategies for valorization of CO_2. Our recent achievements include the efficient CO2 hydrogenation to methane using ruthenium nanoparticles (Ru-NPs) prepared in situ in ionic liquid media. [2,3]. Also, task-specific ionic systems are efficient media for catalytic conversion of epoxides to cyclic carbonates [4] as well as the electroreduction of CO_2 to CO [5]. Herein, two promising approaches for conversion of CO_2 into fuels and valuable products will be presented:

i) ***METAL NANOPARTICLES & IONIC SYSTEMS:*** Heterogeneous catalysis using ruthenium and cobalt nanoparticles prepared in situ from fluorinated ionic liquid media for hydrogenation of CO2 to methane or methanol.

ii) ***COVALENT ORGANIC FRAMEWORKS (COFs)*** as a novel class of crystalline porous materials. These porous materials are formed with organic building blocks via strong covalent bonds and display fascinating properties such as low density, large surface area, great thermal stability, tuneable pore size making the material, which makes them promising materials in catalytic applications. It has been reported that metal modified COFs with metal exhibit great catalytic activity towards cross-coupling reactions.[6] In this context, we have been using COFs alone or in the presence of metals and ILs for hydrogenation of CO2 to hydrocarbons.

In all reported approaches, it is possible to discuss the catalytic mechanism associated to each system as well as to explore the continuous process for production of fuels from CO2.

Acknowledgements: The authors thanks to Fundação para Ciência e Tecnologia for financial support in the projects PEst-C/LA0006/2013, RECI/BBBBQB/0230/2012 as well as "SunStorage- Harvesting and storage of solar energy", with reference POCI-01-0145-FEDER-016387 and FCT-CAPES (2019-2021) The NMR spectrometers are part of the National NMR Network (PTNMR) and are partially supported by Infrastructure Project N◦ 022161 (co-financed by FEDER through COMPETE 2020, POCI and PORL and FCT through PIDDAC).

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Functional Photoactive Materials with Tuneable Crystalline Structure and Morphology for Photocatalytic and Solar cell applications

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The quest for materials able to efficiently harvest solar light has become one of the biggest challenges of our time. We have recently developed an unexplored strategy to improve the sunlight-driven efficiency of titania (TiO2). Our approach is based on the insitu incorporation of organic and coordination complexes into the titania structure during their synthesis. These complexing ligands are able to coordinate to the Ti(IV) atom of titanium alkoxides to form polymetallic titanium-alkoxide complexes, which are subsequently used as organotitania precursors, and thus further hydrolized and crystallized at 80ºC [1-2].

In this communication, we present several examples of this alternative way for the integration of the charge-transfer dyes in the semiconductor titania matrix. Different molecules have been used as charge-transfer dyes such us organic compounds [1a,2] or metal complexes [1b], some of them being able to decrease the band gap of the anatase structure up to 2.7 eV. These hybrid organotitanias present highly active and remarkably stable photocatalytic properties, even after multiple cycles under UV or visible light, exceeding, in both cases, the activity and stability of conventional dyesensitized titanias prepared by grafting. Very recently, we have extended this approach to the sol-gel synthesis of biphasic rutile/brookite hybrid organotitanias with a tuneable control of the crystalline phase and outstanding photocatalytic activity under visible light (Figure 1a). Moreover, unprecedented insights on the development of novel photoelectrodes for titania-based low temperature DSSCs (lt-DSSC) will be also presented. We have achieved the highest efficiency reported so far for titania-based lt- DSSC (8.75%) by integrating our hybrid titania containing the cationic Ru(II) complex (N3 dye) into the photoelectrode of a conventional titania-based lt-DSSC, Figure 1b [3]. We are currently working on the improvement of the conductive properties of our electrodes through its functionalization with conductive polymers.

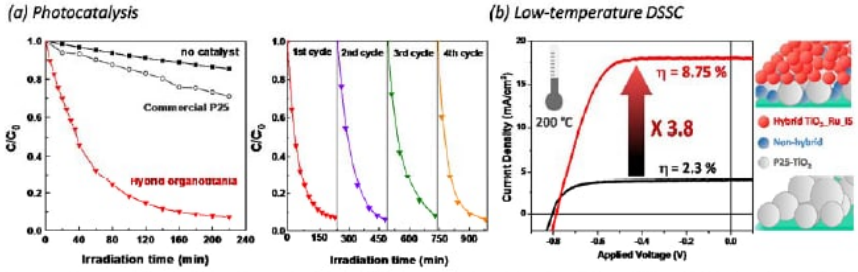

Figure 1. Examples of application of two synthesized hybrid organotitanias. (a) Photocatalytic activity of a biphasic rutile/brookite organotitania as compared with the commercial P25 in the degradation reaction of an aqueous solution of the dye rhodamine 6G ($5*10^{-5}$ M) under visible irradiation (left) and the corresponding recycle tests. (b) Performance of a lt-DSSC prepared by integrating our hybrid Ru(II) complex-titania (red) into the photoelectrode of a conventional titania-based lt-DSSC (black).

Acknowledgements. This work was supported by the Generalitat Valenciana (AICO/2021/132), the Ministerio de Ciencia e Innovación of Spain (MICINN) and Agencia Estatal de Investigación (AEI)/European Regional Development Fund (FEDER) (projects CTQ2015-74494-JIN and RTI2018-099504-B-C21/A-C22). N.L. and E.S. also thank the Universidad de Alicante (Spain) through the "Programa de Retención de Talento" (ref. UATALENTO16-03 and 17-05, respectively). E.S. thanks the synchrotron ALBA for beamtime availability (ID 2018022752) and F. Fauth for helpful suggestions with the flow reactor design and assistance during the powder diffraction experiments. The authors also thank J. J. Carpena Montesinos, from the UA, for assistance with the flow reactor design and construction, and Dr. H. DeColatti from CONICET (Argentine) for his help during the powder diffraction experiments.

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Catalysis in confined spaces: monitoring catalytic activity by modulating the catalytic environment

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Appropriate engineering of a molecular cavity's structural features can lead to the desirable modification of the catalytic environment, and influence accordingly the catalytic performance of a host guest system. In this work, we aim to control and better understand the properties of the dimeric anionic species $Mo_2O_2S_8^{2-}$ which has been shown to be an effective molecular catalyst for the electrochemical production of hydrogen [1]. Engineering of MOF structures that incorporate organic linkers with appropriate functional groups, local geometry and electronic effects, will allow the modulation of the interactions between catalytic species and substrates, correlate the structure-function properties and rationalize the observed changes in catalytic activity [2]. This work predominantly focuses on the structural modification of MOF and molecular cages using a range of di-heterocyclic aromatic carboxylates, where the choice of heteroatom dictates the varying electronic/electrostatic properties within the cavity without compromising the structural features or the stability of the molecular nano-container. This approach is analogous to enzymic structure induced functions, where the active site is supported by secondary structure (proteinic layer) that is crucial for the optimum alignment of the substrate, and in our case may also help the catalytic properties.

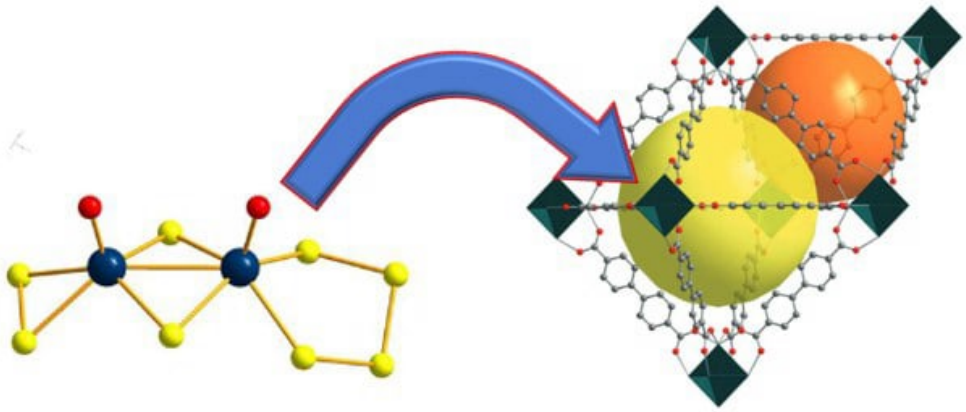

Figure 1 Molybdenum dimer catalyst can be encapsulated within the pores of UiO-type MOF with variable organic linker molecules [1,3]

Stimuli-responsive polymers to induce locomotion in nanomotors

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Nano- and micromotors are a fascinating concept that refers to particles that are able to self-propel to outperform Brownian motion by converting different kinds of energy into kinetic energy. Examples include (enzyme) catalytic reactions or energy conversion harvested from physical stimuli.[1] Further, nanomotors that exhibit locomotion in response of changes in the environment (e.g., pH, temperature, fuel molecule gradients, etc.) are an interesting type of mobile entities.

We have focused our efforts on polymer-based motors. One the one hand, we employed surface polymerization to induce locomotion including swarming in nanoparticles.[2] Alternatively, we used pH-responsive linkers to detach polymer chains from nanomotors. The motors exhibited ballistic motion and directionality in an acid environment due to the loss of the polymer brushes from their surface (Figure 1a). The displacement and velocities were dependent on the properties of the polymer brushes. Further, motors with self-immolative polymers conjugated to their surfaces exhibited enhanced random motion with velocities up to 1.5 μm s^{-1} when the polymer was triggered to disassemble into its monomers (Figure 1b).

Taken together, these efforts demonstrated that polymers are versatile building blocks for the assembly of nanomotors.

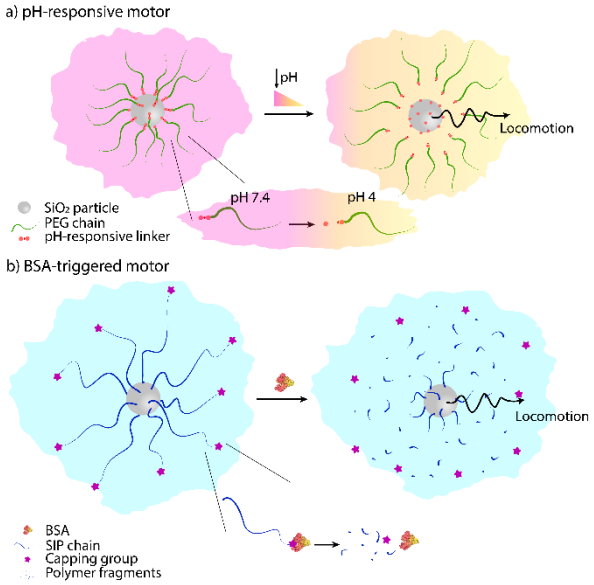

Figure 1. Stimuli-responsive nanomotors. a) pH-sensitive motors respond to a drop of pH in the environment, resulting in the PEG disassembly and consequent ballistic motion. b) BSA-responsive motors show enhanced locomotion due to the fragmentation of the SIP. PEG: polyethylene glycol, BSA: bovine serum albumin, SIP: self-immolative polymer.

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Towards an Autonomous Photochemically Driven Rotary Motor Based on a Catenane

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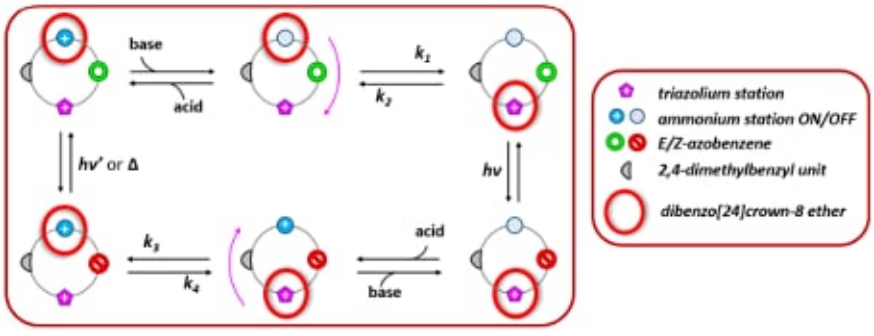
By combining photophysical and photochemical reactivity with appropriately designed molecular and supramolecular systems, it is possible to realize nanoscale devices and machines that can execute sophisticated tasks in response to light stimulation.

In this regard, our group developed pseudorotaxane-based supramolecular pumps able to promote the relative unidirectional transit of non-symmetric molecular axles through macrocycles using only light as external stimulus [1]. More recently, the efficiency of such systems was highly improved through the fine tuning of the interactions between the axle and the ring components [2,3]. Research efforts are now oriented to the translation of the reactivity obtained for this minimalistic supramolecular architecture to more complicated mechanically interlocked molecules.

Here, we report the characterization of a [2]catenane designed to operate as an autonomous photochemically driven motor guided by isomerization and proton-transfer processes.

The interlocked rings are a dibenzo[24]crown-8 ether and a macrocycle comprising a photoswitchable azobenzene unit, primary and secondary recognition sites for the ring (an ammonium and triazolium stations, respectively), and a substituted benzyl moiety acting as a kinetic barrier. Other mechanically interlocked molecules and model compounds have been studied to rationalize the behaviour of the nanodevice.

Our results suggest that, with this minimalist molecular design, it could be possible not only to control the relative unidirectional rotation of the rings, with a simultaneous light-induced thermodynamic and kinetic regulation on the system (energy ratcheting), but also to obtain an autonomous rotary motor, exploiting the photobasic behaviour of the molecule.



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The road to intrinsically dynamic materials: disulfide chemistry as a solution

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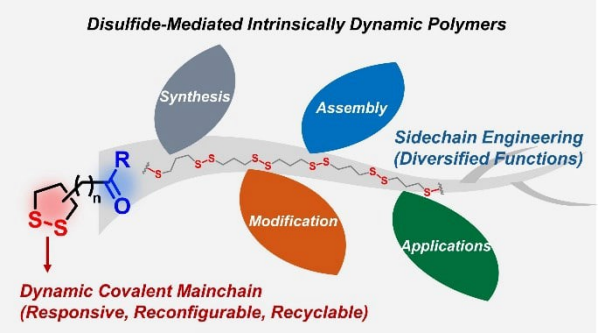
Understanding dynamic chemistry systems in Nature inspires chemists to design biomimetic synthetic materials. Disulfide bonds, the bonds that tie peptides, feature their dynamic covalent nature, that is reversible covalent bonds. Here we propose that making polymers with disulfide bonds can be a solution towards intrinsically dynamic materials. Unlike traditional plastics and noncovalent (supramolecular) polymers, poly(disulfides) can simultaneously exhibit chemical recycling ability and excellent mechanical performances. We will focus on the poly(disulfides) derived from thioctic acid, a natural small molecule, to show the promising applications of these intrinsically dynamic materials in self-healing elastomers, adhesives, and actuators [1-5]. Then I will move to our recent discovery that hydrogen bonds are essential in the control of disulfide chirality and enable stereodivergent chirality transfer. We find that the formation of S−S---H−N hydrogen bonds in solution can drive conformational adaption to allow intramolecular chirality transfer, while the formation of C=O---H−N hydrogen bonds results in supramolecular chirality transfer to form antiparallel helically self-assembled solid-state architectures [6].



This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie actions grant agreement grant 101025041.

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Macrocycle Receptors Incorporating Heptagon-containing Hexa-*Peri*-haxebenzororonene Analogues

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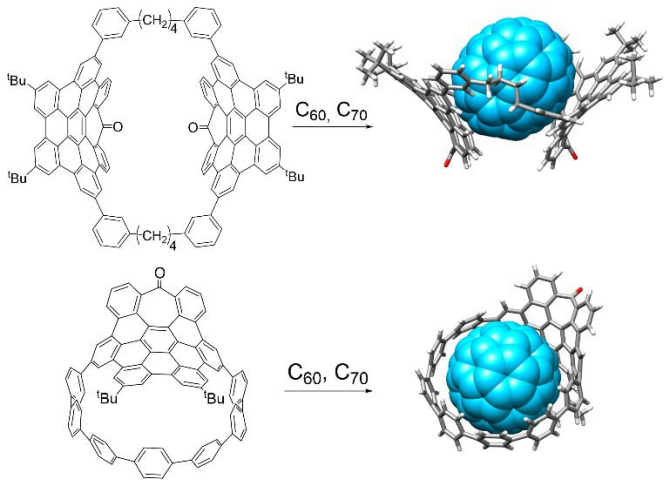
There are many reported examples of organic macrocycles and metallacycles of different sizes and shapes that incorporate polycyclic aromatic hydrocarbons (PAHs) in their structures. However, most of these examples are restricted to PAHs with a small number of fused rings and examples of macrocycles that exhibit extended aromatic systems such as the hexa-*peri*-hexabenzocoronene (HBC) unit are much scarcer [1].

In addition, a growing interest has emerged in the development of extended PAHs incorporating seven-membered rings, resulting in nonplanar structures with a negative saddle curvature [2]. These compounds present high solubility, which enhances their processability and characterization, as well as interesting (chiro)optical or nonlinear optical properties, often when combined with other structural defects. Nevertheless, their inclusion in macrocyclic structures and the study of the resulting supramolecular host-guest interactions with curved π guests, which could be enhanced by the curvature induced by the presence of the seven-membered ring on the aromatic core, has remained practically unexplored.

Following our interest on developing the supramolecular chemistry of heptagon-containing HBC analogues (hept-HBC) [3], here we present the design, synthesis and characterization of novel macrocycles, based on a [10]cycloparaphenylene ([10]CPP) scaffold or a cyclophane[4] structure, incorporating a hept-HBC unit and the study of its supramolecular behavior to form host-guest complexes with fullerenes (C_{60} and C_{70}).



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Graphene field effect transistors for neurotransmitter monitoring

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In the recent years, field effect transistors (FETs) emerged as promising electronic platform to perform biosensing. These devices show several interesting features as amplification capability, low sensitivity to environmental interferences and ease miniaturization that make them suitable to develop innovative bio-electronic devices for in vivo monitoring [1]. Due to its high carrier mobility, the application of graphene as FETs channel material has been widely investigated [2]. Compared to commonly used semiconductor, graphene adds some crucial properties for device fabrication as transparency, biocompatibility, and flexibility. Furthermore, the presence of graphene provides different methodologies to immobilize a specific receptor onto the device surface allowing recognition of the target analytes with high sensitivity and selectivity. This point is one of the main challenges in building such platforms, as the immobilization strategy must preserve the electronic properties of the device while anchoring the receptor at a controlled distance from the surface. In fact, the sensitivity of the device is strongly dependent on the distance between the receptor and the device [3].

The aim of our project is to create a highly sensitive and selective device for neurotransmitter monitoring combining the graphene FETs technology with an aptameric recognition system, previously employed in neurotransmitter sensing [3]. To achieve the controlled modification of the graphene surface, we designed a hindered maleimide aryl diazonium salt and studied different reduction methodologies as thermal, electrochemical, and reducing agents mediated reduction. The grafting of a maleimide moiety enables the fast bioconjugation of a serotonin selective aptamer by further thiol-ene chemistry. Our functionalization strategy can be applied to solution gated field effect microtransistor arrays modification to be used as innovative serotonin sensor.

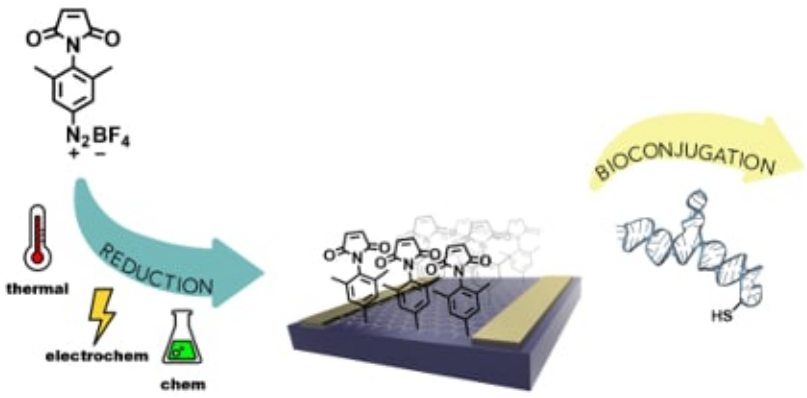

Figure 1. Schematic representation of graphene FET functionalization strategy.

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Molecular bowls as electron donors in photoinduced electron transfer reactions

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In recent decades, remarkable progress has been made in the field of organic synthesis, and, as a result, researchers have been able to synthesize compounds with complicated structures that could not be synthesized in the past, such as curved p-conjugated molecules.[1,2] In this work, we report the results of computational modeling and advanced analysis of the photoinduced processes in a series of C_{60} fullerene complexes with experimentally synthesized molecular bowls. Our results demonstrate that introducing nitrogen into pentagonal rings of the bowl-shaped ▲-conjugated molecules and extending the ▲-conjugation can modulate their electron-transfer properties.

Analysis of the ground and excited-state electronic properties of the complexes revealed that the propensity of a particular complex to photoinduced electron transfer (PET) is mainly determined by the electronic properties of the bowl. In most promising complexes, PET occurs in nano- to picosecond timescale. The effect of geometry relaxation on charge recombination reaction was found to be very important for such complexes.

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Synthesis of Carbon Dots with Green Photostable Emission in Open Reactor: Study of Fluorescence Origin and Mechanisms

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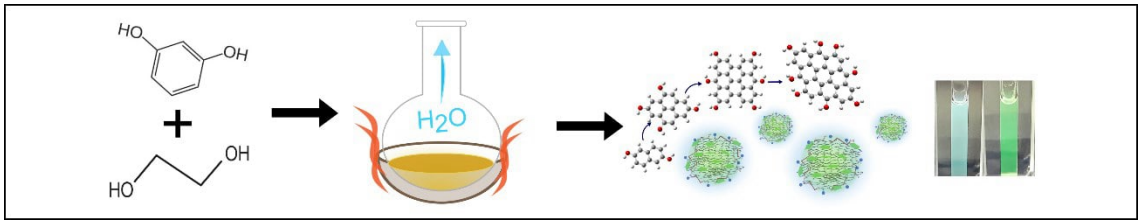
Fluorescent carbon nanoparticles, named Carbon Dots (CDs) have attracted extensive attention in recent years since they combine eco-friendly carbon structure with intense and efficient visible light emission. In the recent period, many studies have aimed at developing new synthetic routes for CDs with enhanced photoluminescence (PL) properties [1]. More specifically, CDs can be easily synthesized employing *bottom-up* approaches. Such routes generally involve thermal carbonization of opportunely selected organic molecules (e.g. citric acid, urea, carbohydrates, small aromatic molecules, …) and are performed mainly by solvothermal or microwave approaches [2].

In this work, CDs are synthesized trough thermally treating resorcinol (1,3-hydroxybenzene) in ethylene glycol at high temperature (180°C) at atmospheric pressure in an open reactor vessel [3]. The use of such synthetic strategy has two main advantages, as it allows (i) to increase the carbonization by promoting water evaporation and (ii) to monitor the evolution of CDs formation and their optical properties during the synthesis.

A spectroscopic monitoring the reaction and a characterization of fluorescence properties of purified CDs isolated at the end of the synthesis, revealed the presence two CDs fluorescence bands. One in the green, originated by highly fluorescent polycyclic aromatic hydrocarbons (PAHs) arising from resorcinol polycondensations and the other in the blue, ascribed to radiative recombination at CDs surface energy states. The rate of resorcinol carbonization could be largely increased by introducing acid or basic catalysts in the reaction solution, namely NaOH and H_2SO_4. Moreover, we carefully characterized the photobleaching resistance of the CDs under exposure to prolonged UV irradiation, proving that green fluorescence is highly photostable if compared to blue CDs surface state emission. Finally, we demonstrate an interesting quenching/enhancing effect of the CDs emission in the presence of acidic or basic compounds in the surrounding environment of CDs, which suggests a profitable use of such CDs in on/off sensors or stimulus-responding devices.



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What Maketh a Pore? The Formation of Porosity in the Solid-State

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In the recent past, mechanochemical reactions inside ball mills have climbed their way back into general chemistry and material synthesis alike. As a green method, the future of this field is promising since the use of toxic solvents can be avoided while generally high selectivities and yields are maintained.[1] For the field of porous materials, by now a plethora of mechanochemical synthesis pathways have been reported. While amorphous materials like porous polymers [2] seem to be the logic results of these reactions, even crystalline materials like Metal-Organic-Frameworks [3] are obtainable in the destructive environment of a ball mill.

This amongst many other observations let us to wonder how the formation of a pore is happening in these solid-state approaches. Common knowledge dictates the need for a porogene in order for permanent porosity to be formed. This is well understood in solution-based systems where the solvent, surfactant or template are used in this capacity. But what happens in the absence of one, two or all of those three components? How can the formation of persistent porosity be explained in those cases? Is the structure of the starting material governing this process or are reaction by-products responsible? And can the formation of porosity be tailored by adjusting the mechanochemical reaction parameters? [4] [5]

In the presentation, I am going to elaborate on these and many other questions and discuss similarities and differences of the solid-state and solution protocols for the synthesis of porous polymers (Figure 1).

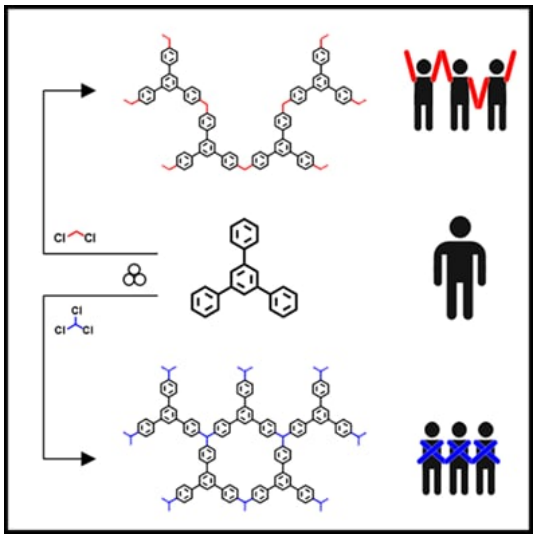

Figure 1: Influence of the milling additive on the crosslinking of porous polymers in the solid state.

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Modern electrochemical sensors in drug and food analysis

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Nowadays, electrochemical (EC) methods have attracted more attention due to cheap instrumentation, fast response and simple operation. Despite the impressive efforts and advances in the field of EC sensors, the application prospects to perform fast and reliable analysis in real systems have not been completely fulfilled and there are still many open challenges to be faced. An open key point is represented by the search and development of advanced materials suitable for EC sensors able to furnish reliable and reproducible signals with high sensitivity and low detection limits. Various conventional materials such as graphite, glassy carbon and carbon paste have been employed as EC sensors in last decades, however, with some drawbacks such as low resistance to fouling and tedious electrode cleaning. Hence, electrochemists are pushed to explore the novel and perspective material platforms as fool-proof EC sensors. Particularly, boron-doped diamond (BDD) has received growing interest thank to its superior EC properties in comparison with conventional materials such as large potential window, low background current and exceptional resistance to fouling [1-3]. These properties make BDD the ideal platform to be applied as an advanced and environmental-friendly EC sensor, even without any surface modification.

Herein, the fundamental objective of this contribution is to introduce EC sensors based on BDD electrodes within extraordinary analytical protocols capable of simple, fast and proper organic electroanalysis. Therefore, a variety of analytical methodologies and protocols, based on the usage of BDD platforms and developed by our working group, will be demonstrated with emphasis on analytical performance of the sensors and methods validation [1-8]. The results of this study could provide invaluable services to clinicians in diagnosis of certain diseases and to analysts in food control analysis as well as to nanotechnologists and material engineers in the design of EC sensors. Finally, the research outputs could stimulate scientific investigation in various disciplines from Material Chemistry and Analytical Chemistry to Medicinal Chemistry and Food Control.

This work has been supported by the Scientific Grant Agency of the Slovak Republic (grant No. 1/0159/20), the bilateral Slovak – Serbian project within the Slovak Research and Development Agency (SK-SRB-21-0019) and the Operational Program Integrated Infrastructure for the project: "Strategic research in the field of SMART monitoring, treatment and preventive protection against coronavirus (SARS-CoV-2)," (Project No. 313011ASS8).

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Tripodal Chromophores for Luminescence Studies on Gold: Towards Organic Optoelectronic Devices

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Surface mounted molecular devices have received significant attention in the scientific community because of their unique ability to construct functional materials. However, electronic decoupling of molecular chromophores from metallic substrates to preserve their optical properties with the objective to develop light responsive system for new optoelectronic devices remains largely unexplored.

Our approach to achieve both an efficient decoupling of molecular chromophore and the spatial arrangement of functional molecules on gold surfaces is based on rigid multipodal scaffolds [1]. Series of functional molecular tripods based on tetraphenylmethane foot-structures have been prepared in order to analyze their arrangement and to investigate the mechanical and/or chemical manipulation of the protruding chromophore (Figure 1). Our particular focus is set on tripodal chromophores based on naphthalene diimides (NDIs) with the intention to tune their optical properties by NDI-core substitution at the positions 2,6 and maintain their electronic decoupling to suppress quenching of molecule's excited states by electrons from the metallic substrate [2]. Furthermore, extended tripodal scaffolds have been developed to guarantee the upright arrangement of these tailor-made multipodal chromophores on gold, resulting in periodic lateral patterns of protruding functional groups in large-area monolayers. In total, three types of NDI-chromophores were prepared and studied on two different molecular platforms. The orientation of molecules on gold has been studied after spray deposition by means of a low temperature UHV-STM technique with electroluminescence setup. Extensive low temperature STML studies of NDI molecules on the small tripodal platform deposited on Au(111) revealed that at most a minority of the tripodal chromophores are standing upright and show luminescence, while the majority are lying flat on the gold substrate [2]. Moreover, we show that fully quenched NDI molecules on a Au(111) surface can be manipulated with the STM tip to decouple the relevant frontier orbitals from the metallic substrate and thus switch a single molecule to a light emitting state [3]. While NDI-chromophores on the extended platform are standing exclusively upright on Au(111) and thus this tripodal anchoring group provides sufficient electronic decoupling of the light emitting chromophores, and in turn, record high quantum yield of 10^{-3} photons/electron is observed. These molecules also allow us to probe intriguing phenomena like hot electroluminescence. Therefore, such extended multipodal chromophores might act as small light sources of single and correlated photons for quantum optical devices.

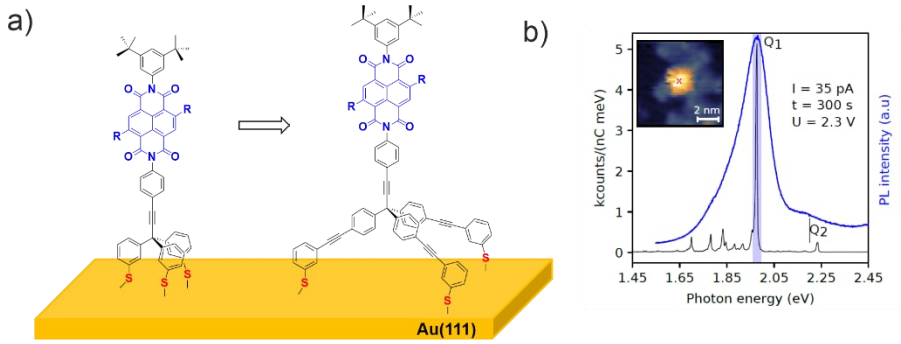

Figure 1. a) Absorption geometry of the small (left) and extended (right) tripodal platforms with the NDI chromophore on Au(111), b) STML spectrum (in black) recorded on an isolated extended chromophore along with the PL spectrum of the bulk molecule in solution (in blue). Inset shows the topography of the molecule on Au(111).

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Cubane and Bicyclo(1.1.1)pentane – Rigid Hydrocarbon Linkers for Flexible Uses

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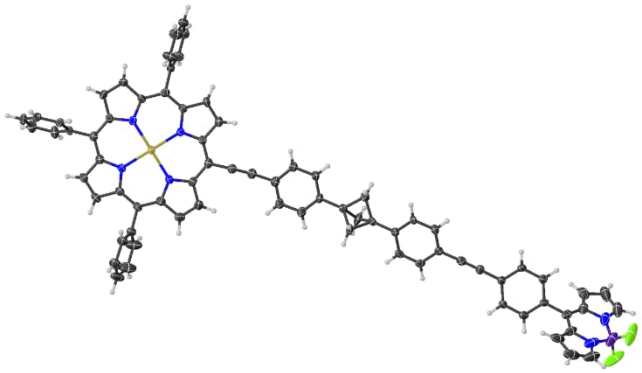
Small rigid hydrocarbon molecules such as cubane or bicyclo(1.1.1)pentane (BCP) are used as bioisosteres in medicinal and materials chemistry and offer potential as rigid (linear) and isolating linker units in electron transfer compounds, as molecular tectons in supramolecular chemistry and as molecular scaffolds with defined geometry [1]. Despite being known for a long time, generally applicable synthetic methods for their functionalization and use are only slowly emerging [1,2].

Our recent work in this area entailed first developing methods for the substitution of cubane with heteroatoms [3] and was followed by adopting redox-active esters for the synthesis of 1,4-disubstituted aryl and heteroaryl derivatives, including porphyrins [4]. Additionally, bisalkynylcubanes could be used in Sonogashira-type couplings with bromoporphyrins for the construction of complex porphyrin arrays in excellent yields. In connection with their use as bioisosteres crystal engineering studies and analyses of solid-state interactions in cubane and BCP derivatives were performed and illustrate their ability to participate in unique bonding patterns [5].



Current studies target complex amide linked porphyrin donor-acceptor dyads with cubane and/or BCP linkers [6] and the development of functionalization methods for propellane and BCP [7]. The latter aims to deliver simple but general BCP derivatives for use in synthetic, supramolecular and materials chemistry, and as molecular tectons for on-surface studies.

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Multi-Potent Precursor Approach for the In-Situ Generation of Conjugated Polymers with Complementary Electronic Properties

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Conjugated polymers, characterized by an extended π-conjugation along their backbone and a semiconductor behavior, have contributed dramatically to the rise of organic electronics, allowing the preparation of flexible and curved devices, cheap organic-based components, and wearable elements. Despite the immense capabilities of synthetic chemistry, however, there are still many materials that are elusive or not easily implemented because of their low processability. In some cases, the use of a polymeric precursor – designed to offer an improved solubility, processability, reactivity, or protection from environmental damage – provided a way to prepare and implement a material which was otherwise unprocessable or synthetically elusive, and which is obtained during the last step through a clean and high yielding transformation.

While a precursor is usually designed to yield a unique compound, here we propose a novel approach in which a single precursor, based on substituted 9,10-dihydro-anthracene compounds, can be used to generate two different molecular structures characterized by complementary electronic properties (i.e. high-HOMO 9,10-diethynyl-anthracene units and low-LUMO anthraquinone units). Such transformations are achieved by different chemical treatments, which can also be applied orthogonally, thus generating different phases on a single substrate.

We characterized the systems proposed and show several examples of how this methodology can be applied to the preparation of conjugated polymers and small molecules of interest in the field of organic electronics, redox polymers, electrochromic displays, and metal-ion organic batteries.

M.C. gratefully acknowledges support from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement MP3 – no. 885881.

Multivariate tool identifying [Cu(N^N)(P^P)]+ design and device architecture enables first-class blue and white light-emitting electrochemical cells

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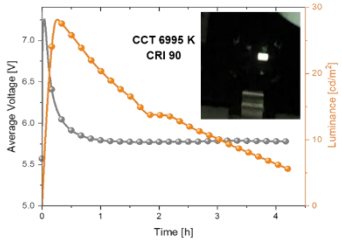
Since the first report of copper (I) complexes based light-emitting electrochemical cells (LECs) in 2005,[1] the milestones of stable blue and white LECs of this family have not been realized. Despite efforts, all the attempts to rationalize the design of high-energy emitting heteroleptic tetrahedral copper complexes ([Cu(N^N)(P^P)]$^+$) for blue devices have been unsuccessful.[2] This is related to the failure of first-order relationships (direct correlation) between the X-ray structure and electronic parameters of [Cu(N^N)(P^P)]$^+$ and their final photo-/electro-luminescent figures of merit in thin-films/devices. Unforeseen structural/electronic changes of the complexes in thin-films prepared *via* solution-based deposition techniques as well as the lack of considering second-order interplay between structural/electronic features have hindered this rationalization.

To bridge the fundamental blue [Cu(N^N)(P^P)]$^+$ design for LECs, this work capitalizes the use of a multivariate analysis using a dataset based on all the prior-art [Cu(N^N)(P^P)]$^+$-based thin-film lighting (>90 papers), reaching an impressive statistical correlation between 15 structural/electronic features of [Cu(N^N)(P^P)]$^+$ and 4 different outputs. On one hand, this method drives the designing rules for [Cu(N^N)(P^P)]$^+$ complexes applied to thin-film lighting, highlighting the complexity of the interactions between the analyzed factors and the desired outputs. On the other hand, it allowed us to fine-tune the N^N ligand identifying the best design of blue-emitting [Cu(N^N)(P^P)]$^+$ for LECs (N^N: 2-(4-(tert-butyl)phenyl)-6-(3,5-dimethyl-1H-pyrazol-1-yl)pyridine and P^P: 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene). The Cu(I) complex was synthetized and tested in device achieving highly satisfying match between predicted/experimental values: thin-film emission at 488 nm/ 470 nm with PLQY of 47%/ 42% as well as efficiencies of 3.6 cd/A@180 cd/m^2 and 3.8 cd/A@170 cd/m^2, respectively. What is more, the first stable [Cu(N^N)(P^P)]$^+$ blue-LEC represents a record performance compared to the state-of-the-art tri-coordinate Cu(I) complexes with 0.17 cd/A@20 cd/m^2.[2] Success and versatility of our multivariate model were confirmed with the synthesis of the analogous complex with 2-(4-(tert-butyl)phenyl)-6-(3,5-dimethyl-1H-pyrazol-1-yl)pyrazine as N^N, showing again a close prediction/experiment match: λ_{max}= 590 nm/ 575 nm; PLQY of 25%/ 20%; efficiency= 0.55 cd/A/ 0.60 cd/A @30 cd/m^2.

Finally, a similar multivariate approach was also applied to develop the best white multicomponent host:guest LEC, significantly reducing the number of trial-error towards the first all-[Cu(N^N)(P^P)]$^+$ white-LEC, which was still elusive. The achieved device performance (CRI>90; 0.6 cd/A@30 cd/m^2) outperform previous [Cu(N^N)(P^P)]$^+$:small molecule based white-LECs (CRI>90; <0.05 cd/A@<12 cd/m^2)[3] as well as similar host:guest LECs with conjugated polymers, quantum dots, small molecules, and Ir(III) complexes (CRI>90; averages <0.3 cd/A@<70 cd/m^2).[3]

Overall, this work sets in a new way to rationalize the design of emitters and active layers in thin-film lighting. We strongly believe that this multivariate analysis model as first step towards advanced machine learning methods will be paramount for the fine design of emitters and charge transport materials that are prone to structural and electronic changes upon thin-film fabrication. As first example, our model has circumvented a 16 years old challenge, achieving first-class [Cu(N^N)(P^P)]$^+$-based blue/white LECs.



Luminance and average voltage for optimized white LECs. The inset shows the champion device *in operando.*

R.D.C. acknowledges Prof. Berenguer for access to his facilities. R.D.C. acknowledges the European Union's innovation FET-OPEN under grant agreement ARTIBLED No. 863170 and the ERC-Co InOutBioLight No. 816856.

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Redox-active organic building blocks for the chemical design of electroactive porous frameworks

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Besides their inherent porosity, Metal-Organic Frameworks (MOFs) and Covalent Organic Frameworks (COFs) may also incorporate tuneable physical (electrical, optical and magnetic) properties which strongly depend on the selected building blocks, becoming very attractive for their implementation as integral components in electronic devices.[1] In recent years, electroactive organic molecules have emerged as promising building blocks for the design and construction of crystalline porous frameworks such as MOFs or COFs for different applications in electronics (Figure 1).[2]

In the first part of the presentation, I will show the electrical conductivity enhancement of an iodine-doped perylene-based MOF by using two-probe single-crystal devices. This conductivity enhancement is ascribed to the partial oxidation of the perylene ligands, as witnessed by spectroscopic studies and supported by theoretical calculations. The charge transport is described by means of a through-space hopping mechanism along the herringbone perylene packing, with highest conductivities of the order of 10^{-5} S·cm^{-1}.[3] In addition, I will also present a new synthetic route to prepare a new family of isostructural perylene-based MOFs with different transition metals (TM = Co, Ni, Zn) exhibiting tuneable optical properties depending on the nature of the metal.

In the second part of the talk, I will present a new family of tetrathiafulvalene (TTF)-based COFs using different extended conjugated linkages to study the influence of the spacer between the TTF moieties on the electrical conductivity. Combining the intrinsic porosity of COFs and electrical conductivity may give rise to multiple applications such as (opto)electronics or energy storage.[4]

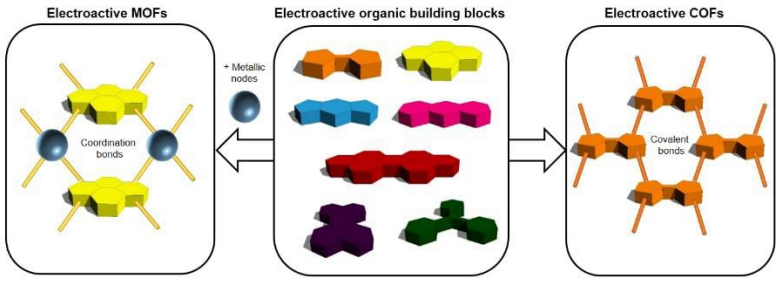

Figure 1. Schematic representation of the construction of metal–organic frameworks (MOFs) and covalent organic frameworks (COFs) based on electroactive organic building blocks.

Acknowledgements:
This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, Grants UIDB/50011/2020 and UIDP/50011/2020, financed by national funds through the FCT/MEC and when appropriate co-financed by FEDER under the PT2020 Partnership Agreement. We thank FCT for funding the project PTDC/QUI-ELT/2593/2021.

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3D printed PLA scaffolds as versatile Platform for Multipurpose Applications in Chemistry, Biology, and Physics

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Poly lactic acid (PLA) is a common thermoplastic polymer for 3D printing via fused deposition modeling (FDM). From a chemical point of view, PLA is a rather unreactive material. Although 3D printing offers the benefit to create a broad variety of shapes, the surface itself does not offer any detached functional groups, only the ester can be cleaved.

We describe different methods of surface activation and modification for a wide spectrum of applications in chemistry, biology, and physics. Our focus is on the activation and modification to obtain a more reactive surface. A first approach was simple treatment with sodium hydroxide, which leads to chemical and physical alteration of the surface. Similar to this, ethylene diamine was used to also add functional groups on the surface. Both reagents react with the PLA itself and alter the polymer surface by exposing hydroxy, carboxy and amine groups. [1]

Different organosilanes were condensed onto the surface to form a self-assembled monolayer (SAM) or a multilayered structure. Due to the limitations in reaction conditions caused by the PLA, an optimized reaction protocol has been developed. Solvents and additives must be chosen so that the PLA is not affected in ways of dissolution or degradation. One of the benefits of organosilanes is the broad availability of different functional groups. Besides hydroxy and amine groups, also thiol groups and unsaturated carbons with double or triple bonds are available. [2]

The success of the modifications was proven and analyzed by different methods. ATR-FTIR-spectroscopy was used to identify the presence of new functionals groups on the surface. Scanning electron microscopy (SEM) and atomic force microscopy (AFM) were used to see differences in surface topology and roughness. Energy dispersive X-ray analysis (EDXS) and X-ray photoelectron spectroscopy (XPS) were used to investigate elemental composition of the samples.

Selected modified PLA scaffolds were treated with spherical gold nanoparticles to work as sensor for other molecules. Surface enhanced Raman scattering (SERS) was used to prove the presence of both, the gold nanoparticles and the test molecules. This gives a detailed outlook for one possible application of modified PLA scaffolds.

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Cavitand-based hierarchical porous organic polymers for gas adsorption/separation and water treatment

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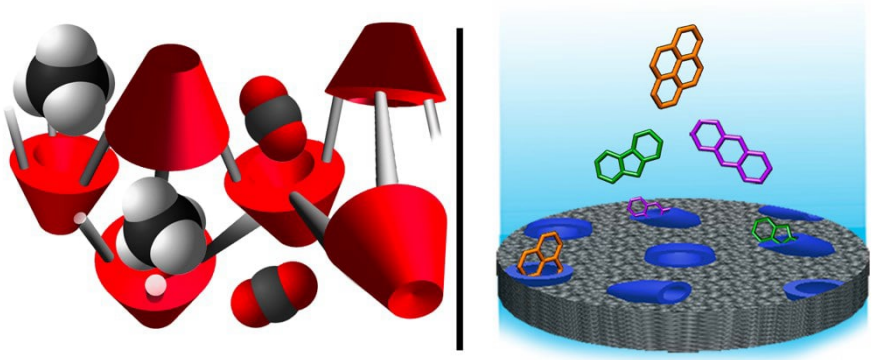
Calixarenes and cavitands play a significant role in supramolecular chemistry and materials science due to their cavities capable of selectively recognize and capture specific guest molecules through host–guest interactions.[1] To be used in real-world devices, these molecular receptors have not only to be devised according to their guest targets, but they also need to be structured in architectures or embedded in polymer matrices capable to retain the designed functionalities. Their organization in hierarchically porous structures is an effective strategy to preserve the access to their preorganized cavities in the solid state retaining the molecular recognition properties of these macrocycles.[2] This approach has been effectively applied to the preparation of a new class of covalent calix[4]arene-based frameworks (CXFs) showing outstanding adsorption properties towards CO_2 and CH_4, while selectively excluding nitrogen.[3] The control of calix[4]arenes conformation, together with their post-synthetic dealkylation to achieve polar phenolic groups, played a crucial role in the formation of small and interacting sites. Quinoxaline-based cavitands, instead, possess a deep hydrophobic cavity capable to engulf aromatic molecules with high efficiency at the solid–water interface. A reusable membrane for the removal of polycyclic aromatic hydrocarbons (PAHs) from contaminated water has been produced by embedding these molecular receptors in an electrospun polyacrylonitrile (PAN) matrix.[4] The high surface area-to-volume ratio and the membrane porosity, combined with the presence of a 8.3 Å deep cavity, afforded the efficient removal of sixteen priority PAHs.



Molecular recognition with covalent calix[4]arene-based frameworks (CXFs, left) and quinoxaline cavitand-based electrospun PAN membranes (right).

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Cyclopentadithiophenevinylene oligomers: a new versatile conjugated material

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Conjugated polymers and oligomers have attracted great research interest in recent years owing to their application in a variety of electronic devices as photovoltaic cells, light-emitting diodes (LED), field-effect transistors (FET) or chemical sensors. Significant experimental and computational efforts have been devoted to studying the electronic properties these materials. However, such studies are quite complicated, as polymers do not have well-defined structures, many of them are insoluble and polydisperse, and computational techniques are significantly less developed for infinite polymers than for well-defined molecules.

Linear π-conjugated oligomers as molecular wires in molecular electronics or nanoscopic systems have attracted considerable attention. Thiophene-based oligomers and their functional derivatives have been extensively studied allowing us the development of materials with specific electronic properties, which arise from both the backbone and the functional groups [1-7]. Nevertheless, the synthesis of highly extended π-conjugated oligomers is of crucial importance to achieve new materials with enhanced opto-electronic properties for device applications and as models for polymers. In this way, 4,4-dihexyl-4H-cyclopenta[2,1-*b*:3,4-*b'*]dithiophene (CPDT) exhibits excellent π-electron donor ability, ease preparation and functionalization, large solubility by incorporation of alkyl chains at the 4-position and complete planarization of the 12 electrons fused π-dithiophene [8-10].

In this work we have designed, synthesized and characterized a new family of oligomers based on CPDT unit alternating with double bonds to create a new oligomeric series from the dimer to the hexamer [11]. The rich redox chemistry observed for these new materials lead to π-conjugated compounds with a variety of structures and properties. CPDTV dimer capped by two rhodamine units was also used as donor material in ternary organic solar cells (OSCs), reaching a PCE of 13.26% [12].

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Universal Crosslinkers for On-Demand Upgrading of Polymer Properties

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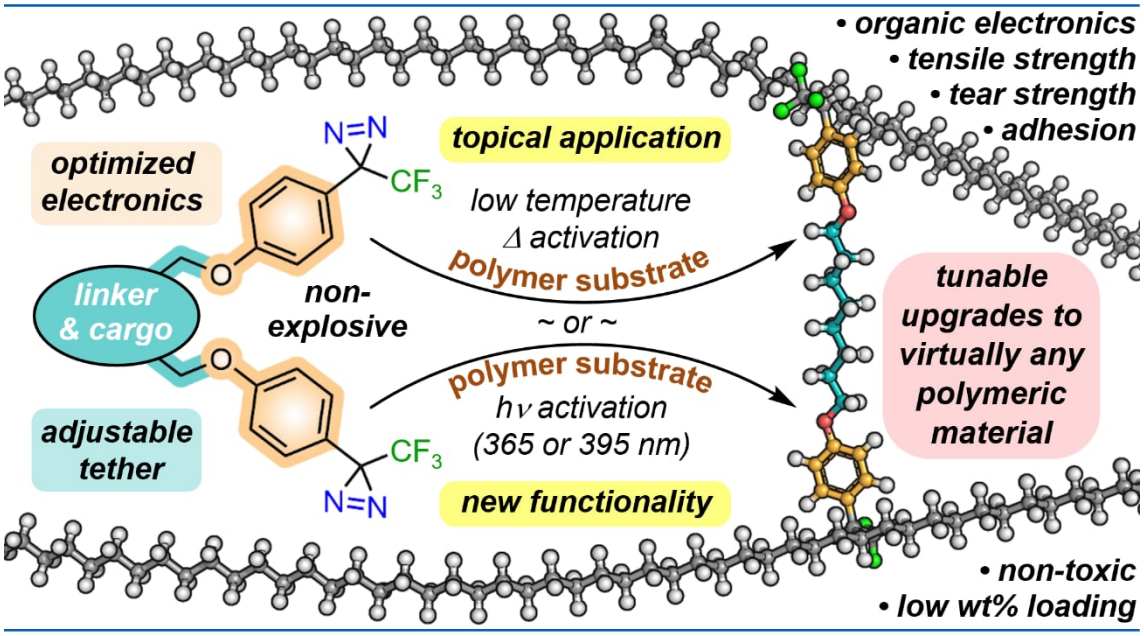
Addition of new bonds (crosslinks) between polymer chains increases mechanical strength and allows for the tuning of important mechanical properties like glass transition temperature, melting enthalpy, tensile strength, etc. Traditionally, however, specific crosslinking technologies needed to be used for each type of polymer substrate (e.g. vulcanization for rubber, or hydrosilylation for silicone) and there remained many commercially important polymers that could not be crosslinked using existing methods.

This presentation will describe our group's development of a new class of diazirine-based crosslinkers [1], which can be used on virtually any aliphatic polymer that contains C–H, O–H or N–H bonds. Fundamental structure-function studies conducted on the core diazirine functional group [2] has recently led to an improved suite of reagents that are even more effective at polymer crosslinking [3], such that low loadings can effect dramatic improvements in mechanical properties of commercially important, low-functionality polymers such as woven ultra-high molecular weight polyethylene (UHMWPE). Bis- and tetrakis-diazirine reagents can also be exploited for adhesion and functionalization of low-surface energy plastics [4,5], while polymeric analogues can be used as primers for the construction of novel composite materials [6].



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Improving the electrical conductivity and structural properties of poly(3,4-ethylenedioxythiophene):polystyrenesulfonate (PEDOT:PSS) for thin film and flexible electronics

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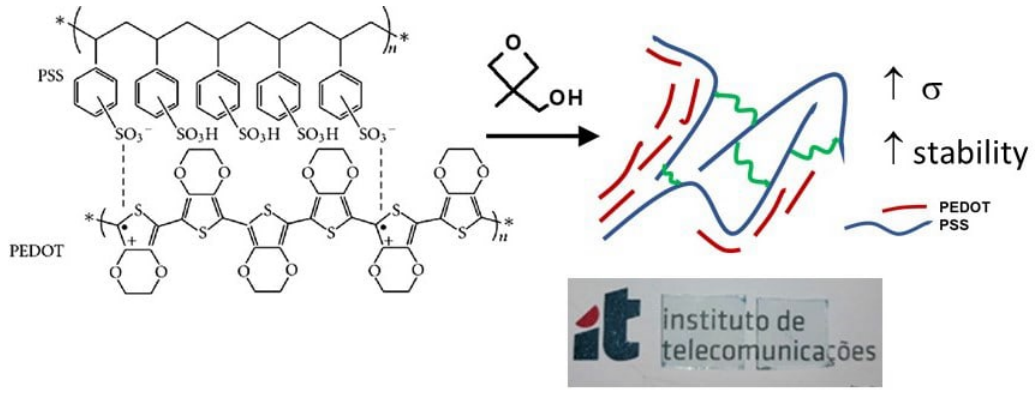
Poly(3,4-ethylenedioxythiophene):polystyrenesulfonate (PEDOT:PSS) is one of the most important intrinsically conducting polymers, owing to its water dispersibility which allows its use as an easily processed aqueous conducting «ink», high thermal stability, electrochemical activity, high transparency in the visible range, and excellent biocompatibility. Nevertheless, although PEDOT:PSS´ applicability is superior among conducting polymers, its electrical conductivity is low and long-term stability against aqueous media must be improved for some applications, such as thin film transparent electrodes or electrically active components for the bioelectronics field.

In this communication, we show that oxetane reagents containing alcohol groups, as additives in PEDOT:PSS aqueous dispersions, can remarkably improve the conductivity (in more than 3 orders of magnitude) and structural stability of PEDOT:PSS thin films against aqueous medium, while maintaining their transparency in the visible [1]. As a result, the developed polymer layers are suitable for applications as the transparent electrode in thin film optoelectronic devices, such as organic photovoltaic devices. It was found that the oxetane reagents produce graft copolymers, composed of polyether blocks anchoring PSS chains, and such structural changes are at the origin of the enhanced conductivity and improved films 'stability. In addition, the modified PEDOT:PSS dispersions, besides enabling preparing thin films by the spin-coating method, are also suitable for high-resolution ink-jet printing, allowing to produce micron-wide conducting wires. Moreover, free-standing and mechanically flexible films could be obtained from the new PEDOT:PSS formulations, this opening the pathway for applications on flexible electronic devices, as medical sensors and others.



Thanks to funding from the projects at Instituto de Telecomunicações (UIDB/ 50008/2020) and SATRAP project (PTDC/CTM-REF/28108/2017–POCI-01-0145-FEDER-028108) funded by FEDER-POCI and Fundaçao para a Ciência e Tecnologia – Portugal S. M. Jorge also acknowledges FCT/Portugal for a PhD Grant (PD/BD/150593/2020).

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A mechanical robust and thermal resistant polyvinyl resin crosslinked by quadruple hydrogen bonding with self-healing and shape memory properties

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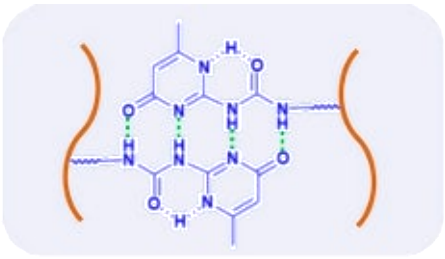
Self-healing materials are a class of intelligent materials that have the ability to repair damages caused by mechanical wear and tear over time. Polymer-based self-healing materials have been actively developed thanks to their diversity functional groups. Since 1997 [1], when Meijer *et al*. first developed the self-complementary 2-ureido-4-pyrimidone (UPy), a booming development occurred in the supramolecular chemistry due to its unique properties, such as high association constant, ease of synthesis, and readily available derivatives for functionalizing polymers [2]. Indeed, the reversible quadruple hydrogen bonding linkages is responsible for the self-healing properties and thermodynamically controlled architectures [3]. Besides, many H-bond cross-linked polymers with tunable mechanical properties have been designed by chemically attaching UPy units to main chains [4], side chains [5] or end chains [6], resulting in its commercial development in supramolecular materials (SupraB™). The UPy unit is a practically effective and versatile design motif that has already been extensively incorporated into almost all type of polymer backbones [7]. While representing significant advances, the existing polymer technologies present profound challenges for commercialization owing to raw material cost and process complexity. Thus, alternative approaches that are intrinsically cost-effective and capable of large-scale industrial production are needed. In this line, commercially available polymeric materials, due to their mature production process and readily available equipment, exhibit strong advantages for large scale applications.

Herein, we report the cross-linking of a commercially available polyvinyl resin (PVR) by the non-covalent self-complementary UPy dimers. This physically cross-linked PVR exhibit self-healing and shape memory properties, accompanied by enhanced thermal and mechanical resistance. This approach not only provides a practical strategy to obtain multi-responsive shape memory polymer with self-healing feature, but it also offers the idea to tune the polymer thermal and mechanical properties.



- Quadruple hydrogen bonding ☑
- Self-healing ☑
- Shape memory ☑
- Stiffness ↗
- Thermal stability ↗

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The teacher's professional knowledge and the interdisciplinarity in a context of technology integration

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The articulation between disciplines has proved to be challenging, particularly in what concerns the process of developing and applying tasks that promote this type of approach.

Mathematics and Chemistry are disciplines closely related, however, their articulation does not seem to be easy to achieve. The knowledge held by the teacher about interdisciplinarity is still scarce, motivated by multiple issues, which relate to the poor initial and in-service training in this area, the lack of time for teacher's use of interdisciplinary tasks in the classroom, as well as organizational issues that prevent its practice [1].

An isolated approach to each discipline does not seem to offer opportunities to promote the teacher's interdisciplinary knowledge, suggesting the need for an integrative approach, capable of including the knowledge of each disciplinary area in an integrative way, as well as knowledge about the use of technology in the articulation process.

Teacher training and professional knowledge to articulate the disciplines of Mathematics and Chemistry using technology thus emerges as the focus of our investigation. Therefore, this study aims to analyze and identify aspects that characterize the professional knowledge held by the teacher, in the context of interdisciplinary articulation with technology.

A qualitative methodology of interpretative nature is assumed, which seeks understanding between the teacher's choices and their professional knowledge based on the model "Application and Pedagogical Content Knowledge" (APCK), where Mathematics assumes prominence among the Sciences, due to its universal language common to the others and therefore integrative per se [2]. The participants in this study are two school teachers with experience as in-service trainers.

The main conclusions suggest that the tasks applied in an interdisciplinary approach imply different dynamics in the classroom; they potentiate the emergence of some students' difficulties, with some unusual characteristics, suggesting different mobilizations of the teacher's professional knowledge.

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Green chemistry in higher education: An upstream approach to addressing sustainable development goals

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The field of chemistry, providing the molecular building blocks of materials and products used throughout society, has a critical and foundational role in addressing the Sustainable Development Goals outlined by the United Nations [1]. Green chemistry provides chemists with principles and a framework to design chemical products and processes that reduce or eliminate hazards and impacts [2]. Chemists, with green chemistry skills, have made significant positive impacts on society through the design of sustainable chemistry technologies [3]. For example, the use of biobased solvents can result in a 97% reduction in greenhouse gas emissions in an industrial setting [4], while break-through green chemistry technologies can reduce the inherent Global Warming Potential of a chemical products [5], enabling chemists to take the urgent action needed to address climate change (U.N. SDG #13). Unfortunately, our current global education systems do not properly prepare most scientists to select and design sustainable chemicals, processes, materials and products. Green chemistry education addresses sustainability at the earliest stages of the value chain, maximizing impacts. Undergraduate and graduate level training is an essential stage in the training of scientists and professionals that are prepared with the skills to address hazards and mitigate impacts at the design stage of a product lifecycle [6].

This presentation will provide an overview of the tremendous opportunities that green chemistry provides for college and university faculty to better prepare students with 21st century skills to address sustainability through chemistry. Beyond Benign, a non-profit organization dedicated to green chemistry education, programs will be highlighted, including the Green Chemistry Commitment, a consortium program for university chemistry departments to adopt green chemistry in their teaching practices. Academic models for adopting green chemistry in education and research will be included. The new Green Chemistry Teaching and Learning Community (GCTLC) will also be discussed, an open-source, on-line platform set to launch in 2023 for the global green chemistry community to share resources, collaborate and network to improve their teaching and practice of green chemistry.

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Time capsules of innovation: The historical spaces of chemistry in Portugal

Marta C. Lourenço, University of Lisbon
National Museum of Natural History and Science

Researchers are increasingly interested in the heritage of their disciplines. Historical spaces of science, collections and archives bring cohesion to a given field, provide a sense of continuity and belonging, and raisescuriosity and awareness about science among general audiences. Heritage can also tell more subtle stories. Using the case of the three Portuguese historical laboratories, recently restored – Coimbra, 18th century, Lisbon 19th century and Porto early 20th century – I will briefly examine the dynamics between innovation and scientific heritage. I will argue that these splendid and majestic spaces, more than about chemistry, tell us stories about inevitability and adaptation in science. I will also argue for the systematic survey and integral preservation of similar spaces everywhere.

BIONOTE:
Marta C. Lourenço is a researcher and present director of the National Museum of Natural History and Science of the University of Lisbon (MUHNAC). She has background training in Physics (University of Lisbon), a MA in Museology (Nova, Lisbon) and a PhD in Museology and History of Technology (CNAM, Paris). She is the national coordinator of PRISC (Portuguese Research Infrastructure of Scientific Collections). She teaches material culture of science in the Masters of History and Philosophy of Science (Faculty of Sciences, University of Lisbon) and is a research member of CIUHCT, the Interuniversity Research Centre for the History of Science and Technology (University of Lisbon). Since 2016, she is the President of the International Committee for University Museums and Collections (UMAC) of the International Council of Museums.

Unveiling the iron-polyphenol complexes behind medieval iron gall inks through a muti-analytical methodology

Natércia Teixeira[a*], André Neto e Silva[a], Luís Cunha-Silva[a], Paula Nabais[b], Maria Rangel[c], Fernando Pina[b], Victor de Freitas[a], Maria João Melo[b]

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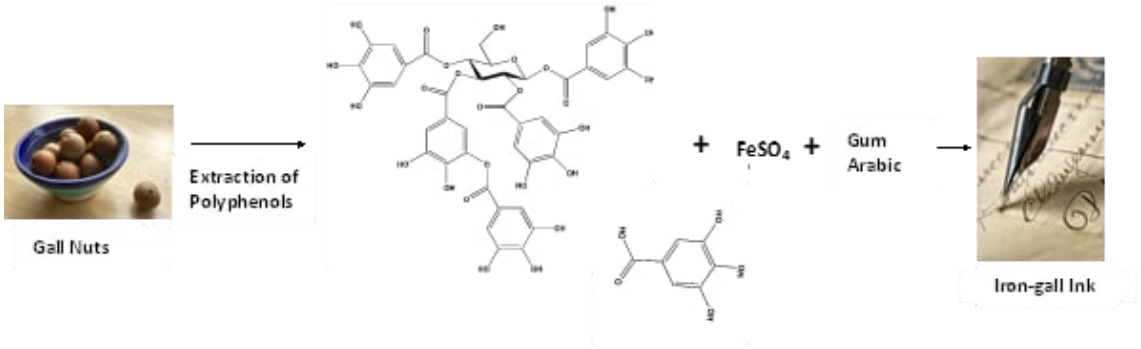
Until the beginning of the 20th century, a significant part of our cultural heritage was recorded [1]. Unfortunately, many historical documents are at risk of total loss due to degradation of the writing support caused by the corrosion of these inks [2].

Medieval iron gall ink recipes typically contain three basic ingredients: a phenolic extract (Quercus infectoria galls), FeSO4, and gum arabic [3, 4]. Our knowledge on the molecular structures of the chemical compounds present in these inks is very limited and this gap prevents us to devise informed strategies for preserving the world written heritage.

The goal of this work is to characterize iron-polyphenol complexes present in iron gall inks. This will be accomplished through studies on isolated tannins from galls by preparative HPLC-DAD. The iron-complexes will be prepared using distilled water and sodium acetate-acetic acid buffers and analyzed through UV-Vis spectroscopy [5].

MALDI-MS and ESI-MS will be used to study the nature of iron complexes in aqueous solution. Structural characterization will be further complemented with SEM, FTIR, Raman microscopy and X-ray analysis.



Acknowledgements: We thank the financial support: project UIDB/50006/2020, funded by FCT/MCTES through national funds and by the AgriFood XXI I&D&I project (NORTE-01-0145-FEDER-000041 co-financed by European Regional Development Fund (ERDF), through the NORTE 2020. NT, LCS and PN thanks FCT for CEECIND/00025/2018/CP1545/CT0009, CEECIND/00793/2018 and CEECIND/01344/2021.

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The chemical space and some ethical consequences of its uneven growth

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Max Planck Institute for Mathematics in the Sciences, Leipzig, Germany

An important aim of chemistry is the discovery of new substances and of methods to procure them. History shows that such a discovery occurs at an exponential rate and that for more than two centuries the driving force for substance discovery has been chemical synthesis. This synthetic activity is strongly tilted towards organic chemistry. If chemistry is about new substances and methods to afford them, to what extent does the historical organic chemistry bias affect the aims of chemistry? If chemists are responsible for chemical synthesis to chemical community, is part of that responsibility to ensure high diversity of substances and of preparative methods? Or is it to achieve deep knowledge on some particular substances and their methods to produce them? I will discuss these and related questions based on recent results on the expansion of the chemical space, as made of substances and reactions reported by chemists over history.

Teaching Responsible Chemistry: A Challenge-Based Learning Framework for the Implementation of RRI Courses in Chemistry Education

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Responsible Research & Innovation (RRI) is a concept of professional attitude and agency in the context of innovation with significant expected societal and environmental impact. In the past decade, it has been framed, theoretically informed, and practically implemented by various disciplines such as the sociology of technology, STS, technology assessment, philosophy and ethics of technology, technoanthropology, and economics,[1] as well as by political organs in the field of science, technology, and innovation governance.[2] By today, the concept is certainly mature enough to be applied in concrete research and innovation practice. Yet, this realisation of RRI's goals faces several methodological and structural difficulties, among them the insufficient implementation of RRI education in STEM majors at higher education institutions, and a lack of normative literacy and discourse skills among researchers, technology developers, and innovators.[3] As a result, design decisions in innovation processes are dominated by scientific-technical and economic thinking (risk assessments, life-cycle assessments, functionality, utility, safety, profitability, economic feasibility, market competitiveness) whereas normative considerations (ELSI, social and environmental integrity, cultural norms, etc.) are underrepresented or not formalised in the innovation procedures.

The proposed course concept aims at filling a gap in the translation of RRI principles into tertiary chemistry education practice. Employing a challenge-based learning (CBL) approach, it draws on a practical framework of RRI as guideline (or orientation) for professional conduct in the context of chemistry (academic research and corporate R&D). This focus is chosen because of the obvious enormous impact of chemical progress on the social and environmental life world, and because of the creative, emerging, and enabling character of most of chemical science and innovation. The highly practical course—with 'lectures' reduced to a minimum—is thematically structured around a fictitious innovation project as it may happen in real-world contexts, potentially in cooperation with local chemical companies and industry. Students form teams, define roles and shared values, identify a challenge of their interest, and are guided through developing and validating a solution. RRI tools such as ethical design thinking, safety-by-design, ethical vision assessment, or normative risk assessment, are brought into the teamwork step-by-step, allowing students to dive deeper into the matters of their interest and needs. The CBL fashion is expected to lead to a high engagement with the course content, a clear realisation of the practical significance and applicability of the acquired skills, and a change in attitude towards normative dimensions of chemical science and innovation activities. The designated course objectives are the formation of normative literacy[3], the shaping of professional integrity and good scientific practice, the strengthening of discourse performance skills, and the ability of interdisciplinary collaboration in multi-stakeholder settings.

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Women in chemistry – in Scientific Careers (SciCar) Horizon Project

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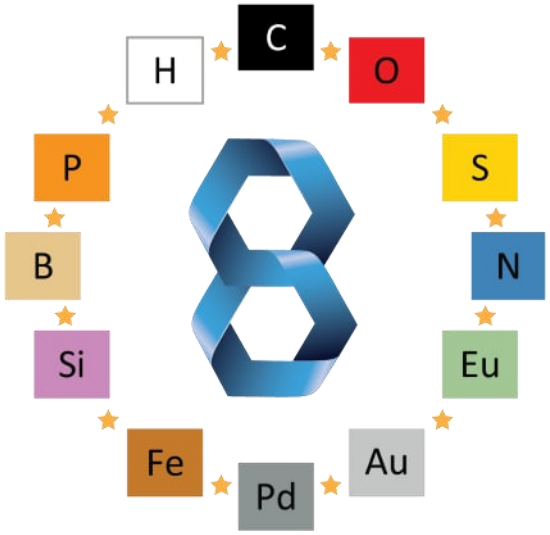
Women continue to represent a small proportion of faculty members in science and technology programs, especially in more prestigious research institutions (Mamlok-Naaman, 2021). They still need to cope with discrimination, with an unconscious bias, as well as with the demands of their families. According to UNESCO institution of Statistics, fewer than 30% researchers all over the world are women. The analysis of "A Global Approach to the Gender Gap in Mathematical, Computing, and Natural Sciences, How to measure it? How to reduce it?" survey, contributed to the understanding of this phenomenon and to the identification of the various factors causing it. The recommendations address a variety of groups: instructors and parents of girls in primary, secondary, and higher education; educational organizations; Scientific Unions and other worldwide organizations. This presentation will deal with the situation of women scientists in the world, as discussed in Scientific Careers (SciCar) Horizon Project.

Mamlok-Naaman, R. (2021). Socio-cultural developments of women in Science. *Pure and Applied Chemistry.* https://doi.org/10.1515/pac-2021-0104



POSTER

COMMUNICATIONS (PC)

Preparation of optically active isoindolinones with quaternary stereogenic center bearing three aryl groups in organocatalytic fashion

Arben Beriša [a,*], Danijel Glavač [a], Chao Zheng [b], Shu-Li You [b], Matija Gredičak [a]

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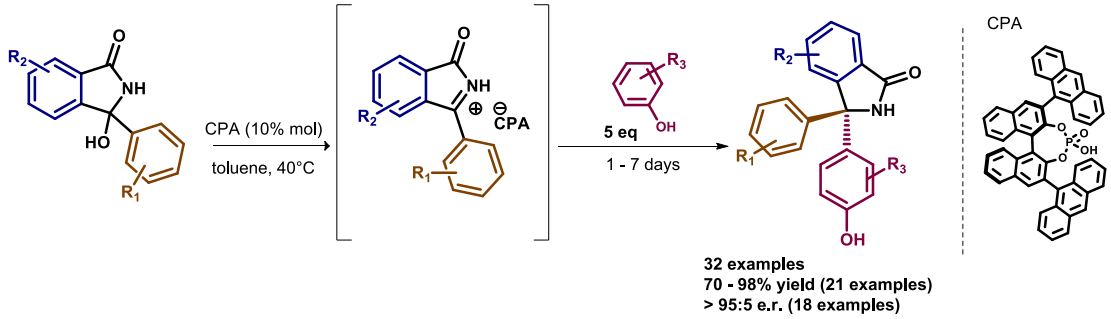
Stereoselective arylation of diaryl ketimines to afford products containing quaternary stereogenic centers bearing three aryl groups is challenging because of the steric hindrance on such stereocenters. The problem lies in the inherent difficulty for the catalyst to differentiate between two enantiotopic faces of the planar ketimine, due to the lack of sufficient steric difference between two aryl rings. Hence, only few notable examples of preparation of this class of optically active compounds have been reported thus far. In 2012, Hayashi and Nishimura developed an enantioselective arylation of *N*-sulfonyl diaryl ketimines with arylboroxines in the presence of a chiral rhodium complex.[1] Following this seminal work, several rhodium[2] and palladium[3] catalyzed enantioselective arylations of saccharine derived ketimines have been carried out. However, in the contrast to this elegant examples, there are no reports in literature for the preparation of such compounds in an organocatalytic fashion. Herein, we report a stereoselective arylation of *N*-acyl diariyl ketimines, mediated by chiral phosphoric acids (CPA). The success of this transformation lies in the *in situ* generation of the reactive diaryl ketiminium species from isoindolinone alcohols, making it susceptible for the reaction with phenols.[4] Various phenols reacted smoothly, enabling isoindolinone derivatives containing quaternary stereogenic center with three aryl substituents in high yields and enantioselectivities. Mechanism of stereochemical induction will be discussed.



Scheme 1. Stereoselective arylation of *N*-acil ketimine mediated by chiral phosphoric acid.

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Chemically engineered extracts of alpine plants: diversity-oriented approach

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Natural products are universally recognized for their structural and stereochemical diversity and complexity as they have been widely used to produce medicinal agents since ancient times. Despite the joint increasing use of combinatorial chemistry and high-throughput screenings (HTS) of synthetic molecular libraries within the past 20 years, natural products are still today a great bioactive compound supplier: from 1981 to 2019, about the half of all small-molecule FDA-approved drugs was inspired from Nature [1].

Therefore, in recent years, several approaches have been developed to create chemical libraries of highly diverse compounds starting from natural products: among them, the "Chemically Engineered Extracts" (CEE), pioneered in 2007 by Furlan *et al.* [2], simply consists of the direct derivatization of natural extracts by chemical modification. However, with this approach, the obtained mixtures suffer from a higher complexity as well as becoming more difficult to separate into pure compounds than the departure extracts in the majority of cases and being unsuitable for direct biological evaluations.

In this context, to overcome these difficulties (mainly the purification issues), we propose to combine for the first time chemical modification of natural extracts with solid-supported synthesis. Following a first work phase dedicated to the building of the proof-of-concept, the latter will be applied to extracts of high alpine plants which can biosynthesize specific molecules with various possible therapeutic interests because of a particularly stressful living environment. Next, rapid bioactivity evaluations of the modified extracts will be allowed and, after bio-guided fractionation, potentially original compounds could be isolated. For the proof-of-concept, phenolic compounds which were propargylated beforehand via a Williamson ether synthesis have been reacted with a solid-supported fragment possessing a precursor structure to the isocoumarine pattern, a well-known bioactive moiety. The latter can then be formed by cyclization, allowing in the same time the cleavage of the resin and the release of the final modified compounds.

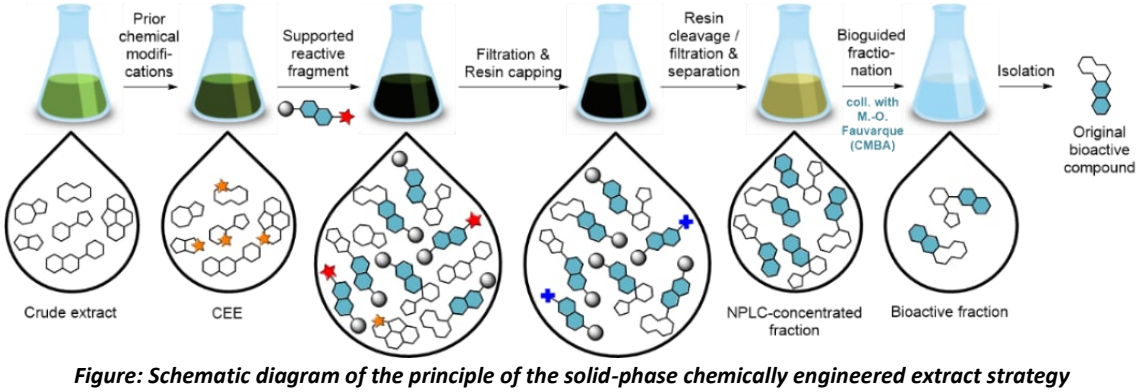

Figure: Schematic diagram of the principle of the solid-phase chemically engineered extract strategy

Thanks to the French Ministry of Higher Education, Research and Innovation and the Chemistry & Life Sciences Doctorate School (EDCSV) of the University Grenoble Alps (UGA) for the financing of the project by PhD scholarship; thanks to the NanoBio chemistry platform (ICMG UAR 2607) for granting access to facilities for MS, NMR analysis.

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Easy synthesis to a new, alpha helix mime

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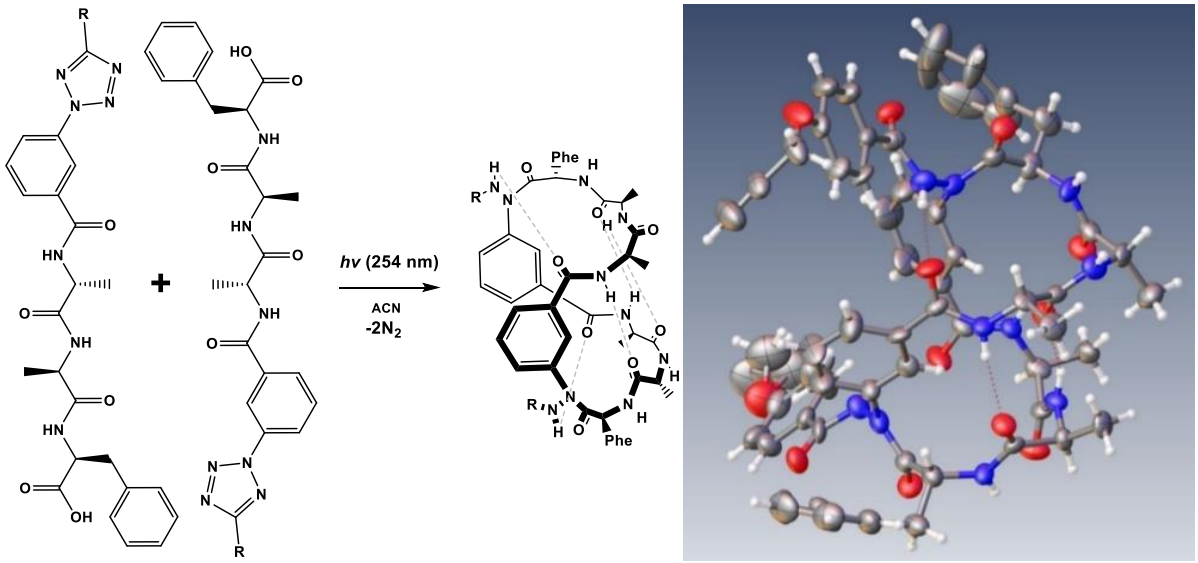
The Protein-Protein Interactions (PPI) are key to many biological functions [1]. Hα is widely present on PPI interfaces, and the interaction domain can involve shorts sequences [2]. The synthesis of shorts Hα, amongst other modulators, enables the development of new drug types [3]. However, Hα has a low stability when the peptides are short. Strategies such as staple [4], help to overcome these conformational stability issues.

This communication will report on the synthesis of a new Hα mime that are easily obtained by self di-oligomerization of pseudopeptides. By grafting a tetrazole photoactivable group [5], UV irradiation allowed the formation of the dimer cyclopseudopeptide in high selectivity and good yield. The conformation to the Hα structure was assigned by X ray, and their structure in solution by NMR. The reaction can accommodate different configurations and different types of residues carried by the amino acids.

We were able to construct a Hα mimicry scaffold, with mixed chirality and different amino acids. This method can open up new access to modulators targeting different PPI involving small alpha helix such as p53-MDM2 and p300-Hif1α [6]. This open the door to the design of new drugs that can be used to treat a wide range of diseases, including some forms of cancer.



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Straightforward Two Step Protocol for The Synthesis of Sulfonimidamides from Thionyl Chloride

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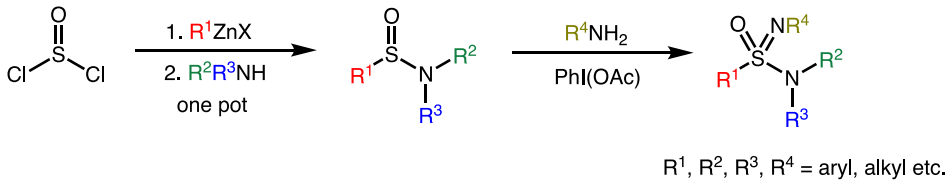
Sulfonimidamides are a promising class of compounds in medicinal chemistry as they offer a unique display of three different substituent around a tetrahedral chiral sulfur atom [1]. Also, they are believed to have suitable physicochemical characteristics to be employed as drugs. However, their utilization in drug discovery is hampered by the lack of efficient methods that would allow straightforward and robust introduction of various substituents on the sulfonimidamide skeleton. Despite a recent progress in the synthesis of sulfonimidamides, improvements in efficacy and robustness are desired for the wide spread application of this class of compounds [2].

Here, we present an efficient two step synthetic protocol that allows preparation of sulonimidamides with four different substituents from simple thionyl chloride (Scheme 1). The first step employs a novel one pot way of direct synthesis of sulfinamides from thionyl chloride, organozinc reagent and primary/secondary amine. Utilization of organozinc reagents is essential for the selective preparation of intermediate sulfinic chlorides over symmetric sulfoxides that are major products with more reactive organomagnesium/lithium reagents. Also, organozinc reagents enable larger functional group tolerance including esters, carbamates or nitriles. The second step uses addition of a nitrene derived from the corresponding amine/sulfonamide. We believe this method will allow the application of this class of compounds in physical or virtual library screening in drug discovery programs.



Scheme 1.

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MedChem-Relevant *gem*-Difluorocycloalkane Building Blocks and Their Impact on Physicochemical Properties

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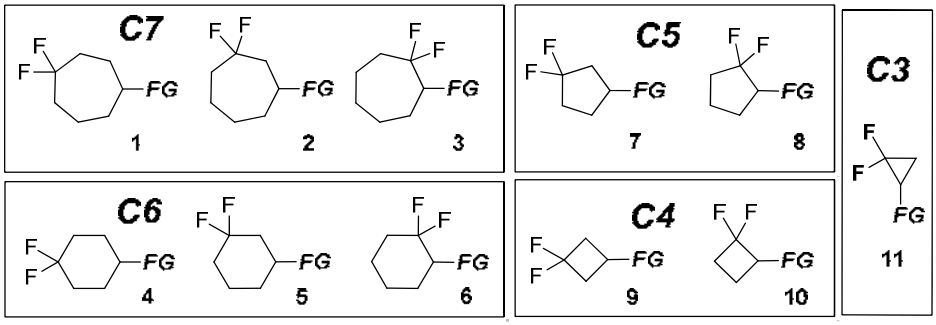
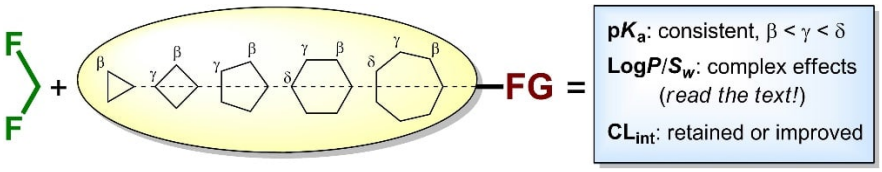
Fluorinated cycloalkane building blocks are useful structural motifs that become increasingly important in various areas, and most of all in drug discovery and agrochemistry. But, from the systematically enumerated functionalized gem-difluorocycloalkanes **1-11**, only the synthesis of 6-membered compounds type **6** (in a course of Maraviroc project) and, partially, cyclopropanes type **11** was industry developed. Also, the laboratory-scale synthesis of cyclobutanes type **9** was referenced. However, the multigram production of these compounds remained questionable. Recently, we elaborated chemical routes to the compounds types **1-11**, which can be promising for the further industrial scale-up. These investigations, as well as pioneering lab-scale approaches to the C7 **1-3** types compounds and cyclobutanes type **10** building blocks, will be discussed in the report.



FG = COOH, NH_2, OH, Br, $B(OAlk)_2$ etc.

Also, the effect of *gem*-diflurination on acidity/basicity (pK_a), lipophilicity (LogP), aqueous solubility (S_w), and metabolic stability (intrinsic clearance, CL_{int}) of functionalized C3−C7-cycloalkanes is established and compared to those of non-fluorinated and acyclic counterparts. While the pK_a values are varied similarly for the cyclic and acyclic series and can be explained by the inductive effect of the fluorine atoms, the LogP and S_w trends are more complex. The CL_{int} values are retained or slightly improved upon *gem*-difluorination. All these investigations will be discussed in the presentation.



Authors thanks Enamine Ltd and Prof. A. Tolmachev for the financial and technical support of the work.

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Preparation of cyclic carbonates and non-isocyanate polyurethanes (NIPUs) from bioderived feedstocks

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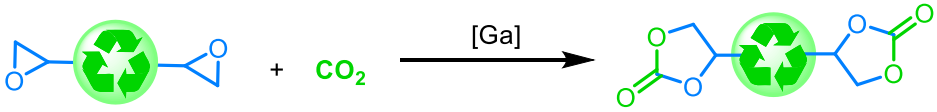
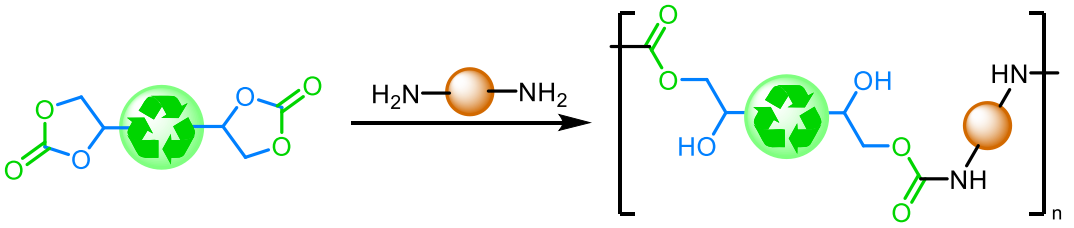
Nowadays, plastics play an invaluable part of our everyday lives and are as a result applied on an enormous scale. Two main issues arise from excessive use of plastics; one being the fact that traditional polymers, which form these plastics, are generally derived from petroleum feedstocks (which are limited) and the other being that they are usually difficult to degrade and recycle and thus remain in the environment long after the end of their useful life. Efforts are therefore focused on solving these two issues, by searching for bio-based monomers and creating more recyclable/biodegradable materials [1].

In addition, the use of CO_2 as a reagent is well established in organic synthesis, where it is considered a highly attractive renewable C1 building-block [2]. In particular, the reaction of CO_2 with high energy substrates, such as epoxides, under catalytic conditions to provide cyclic carbonates has gained a lot of attention. Our group has recently shown that gallium catalysts can be powerful mediators for this conversion [3]. In an attempt to apply these newly developed catalysts further, most recently we have become interested in the synthesis of cyclic carbonates from bio-derived feedstocks, using well established chemical transformations to realize the epoxide starting materials. When di-cyclic carbonates have been synthesized we have applied these in the synthesis of Non-Isocyanate PolyUrethanes (NIPUs), through the combination of these di-cyclic carbonates with di-amines. In this contribution we present our latest advances in the synthesis of bio-derived NIPUs, focusing on the design and use of novel monomers obtained from renewable feedstocks.



bioderived polyepoxides



non-isocyanate polyurethanes (NIPUs)

C.W. would like to thank the Comunidad de Madrid (Spain) for funding (Programa de Atracción de Talento 2019: Modalidad 1; Award number 2019-T1/AMB-13037, and CM/JIN/2021-018). We would like to also acknowledge funding from the Spanish Government (RTI2018-094840-BC31 and PID2020-113046RA-I00) and the Universidad de Alcalá (UAH-AE-2017-2).

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Total synthesis of (-)-agelastatin A *via* photochemical transformation of pyridinium salt and enzymatic resolution of aziridine

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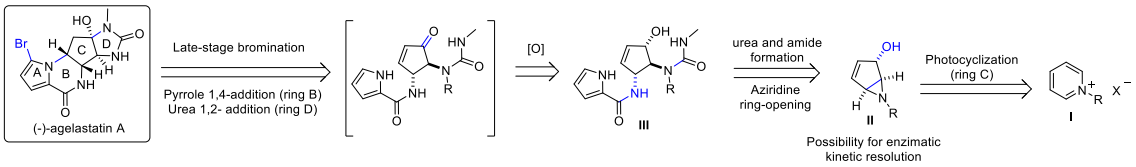
Agelastatin alkaloids have attracted scientific interest since the isolation of (-)-agelastatin A (AglA) from the sponge Agelas dendromorpha by Pietra et al. in 1993.[1] AglA shows remarkable cytotoxicity against a variety of tumor cells[2] and strong inhibition of osteopontin-mediated neoplastic transformation and metastasis.[3] Additionally, it displays high brine shrimp toxicity and insecticidal properties.[4] Since large quantities of AglA are problematic to obtain via natural sources, its total synthesis is highly desirable. Asymmetric synthesis is very challenging and reported procedures typically require laborious steps and protecting groups to construct the four contiguous stereocenters of the cyclopentane C-ring.[5] We have developed a new strategy (Scheme 1) that involves an early-stage photochemical transformation of pyridinium salts to bicyclic vinyl aziridines that originate, in one step, the AglA's C-ring core with the desired functionality and relative configuration. This process allowed the total synthesis of (-)-agelastatin A in only 12 steps with 4% overall yield, with the use of a single protective group.



Scheme 1: Retrosynthetic analysis of agelastatin A.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951996. The Farm-ID project PTDC/QUI-QOR/32008/2017 and Fundação para a Ciência e Tecnologia (FCT) is acknowledged for financial support to J. Vale (SFRH/BD/120119/2016).

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Synthesis of trifluoromethylated 4*H*-chromene derivatives via photocatalytic trifluoromethylation/oxidation/cyclization sequences of 2-vinyl phenols

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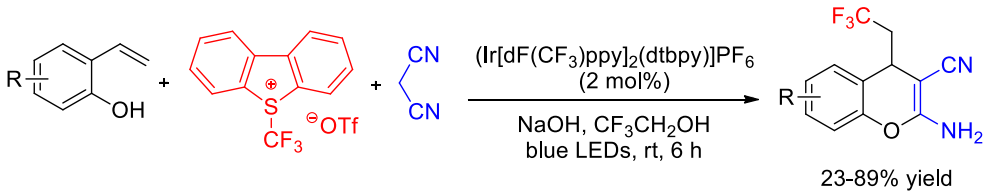
The introduction of a trifluoromethyl moiety into biologically active compounds usually leads to improvement of their physical properties and biological activities [1]. Due to the wide applications of these compounds, intensive efforts have been made to developing novel and practical synthetic methods. The radical trifluoromethylation to alkenes is among the most direct approaches for the construction of C–CF_3 bonds, which uses electrophilic and nucleophilic trifluoromethylation reagents in the presence of various types of reductants or oxidants. *ortho*-Quinone methides (*o*-QMs) are versatile synthons that are frequently used as 1,4-dipoles and Michael acceptors.

As part of the research program related to redox reactions and cyclization sequences, we recently reported intramolecular redox reactions [2] and radical addition and ring expansion reactions of alkenes with several radical sources under redox conditions [3]. In this presentation, visible light-mediated photocatalytic trifluoromethylation, single electron transfer (SET) oxidation, and cycloaddition cascades of 2-vinyl phenols with Umemoto's reagent and malononitrile were developed. This approach provided the multicomponent synthesis of trifluoromethylated 4*H*-chromenes via the *in situ* generation of *o*-quinone methides, followed by sequential cyclization [4].



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Explaining Regio-Divergent Vinylations with Vinylbenziodoxolone

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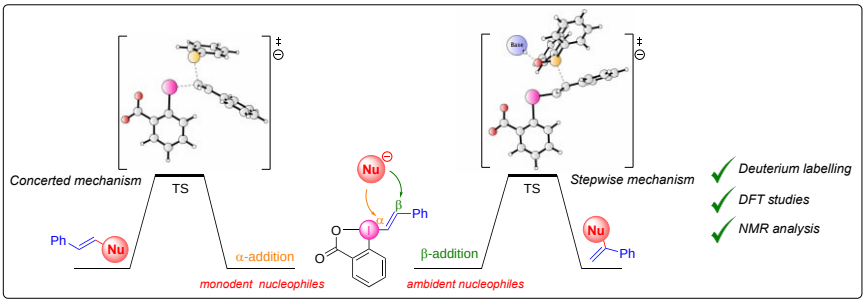
In recent years, several types of hypervalent iodine(III) reagents (HIR) have been demonstrated as efficient carbon ligand transfer reagents, e.g. in arylations with diaryliodonium salts and alkynylations with ethynylbenziodoxolones (EBX).[1] We have recently reported the synthesis and reactivity investigation of a novel class of iodine(III) reagents that we named vinylbenziodoxolones (VBX).[2] They have been identified as efficient electrophilic reagents under transition metal-free conditions as well as under transition metal-catalyzed and photocatalytic conditions in recent times.[3]

Two metal-free methodologies using VBX have been reported by our group. The regiochemistry of the products has been found to vary with the nucleophile class which showed an intriguing reactivity of this class of HIRs. The S-vinylation of thiols resulted in the formation of internal *E*-alkenes with retention of the configuration of the *E*-VBX reagent.[4] On the contrary, the vinylation of phosphine oxides and similar P-nucleophiles delivered the terminal alkenes with complete regioselectivity.[5]

Herein, the first mechanistic investigation of VBX vinylations is presented and makes use of NMR studies, deuterium labelling and DFT computational studies to rationalize the observed outcome.[6] While the S-vinylation was found to proceed through the ligand coupling mechanism typical of diaryliodonium salts,[7] the P-vinylations took place via a phosphinous acid-coordinated VBX complex, which underwent concerted deprotonation and Michael addition.[8] Subsequent base-assisted protonation and E2 elimination delivered the terminal alkene. The findings can be used to predict the regioselectivity in vinylations of other nucleophile classes.



Thanks to the financial support for this study which was provided through the Swedish Research Council (2019–04232). The computations were enabled by resources provided by the Swedish National Infrastructure for Computing (SNIC), partially funded by the Swedish Research Council through grant agreement no. 2018-05973.

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Selective α-Methylation of Aryl Ketones using Quaternary Ammonium salts as solid Methylating Agents

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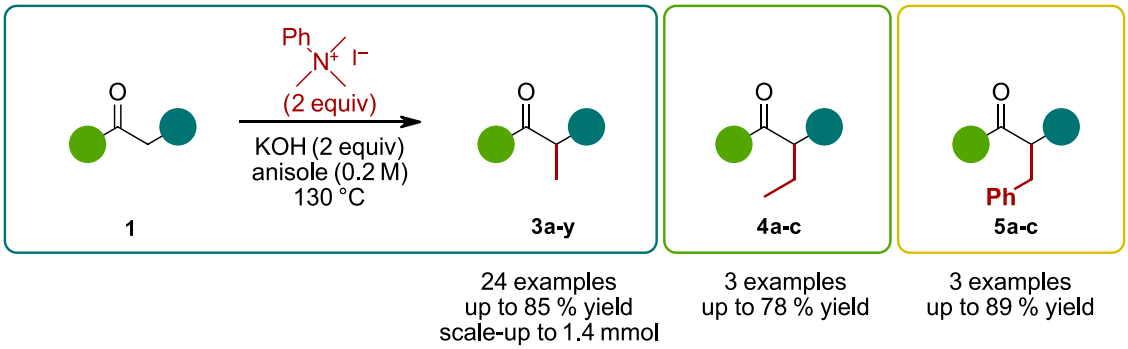
Incorporating a methyl group into small organic or bioactive molecules can positively affect their physical properties and biological effectiveness. The latter feature is commonly referred to as the "magic methyl effect". This renders the methyl group a prevalent structural motif in small-molecule drugs. Owing to its considerable impact, a late-stage introduction of a CH_3-group has become a particularly promising strategy in drug discovery. Hence, the development of efficient and new strategies for selective methylation attracts broad interest in medicinal chemistry and basic research, respectively. [1, 2]

Traditionally applied methylating agents often suffer from inconvenient physical properties (e.g., MeBr, b.p. 4 °C, MeI, b.p. 42 °C) or high toxicity (e.g., MeI, Me_2SO_4). Several organometallic reagents used for methylation (e.g., $MeB(OH)_2$, Me_4Sn, Me_3Al, MeMgCl, or Me_2Zn) are quite challenging to handle, as some are air sensitive, show low functional group tolerance or have to be freshly prepared. These toxicological and safety concerns encouraged us to search for a novel, safe, and easy to handle reagent for direct methylation.

In our recently published paper (scan QR-code for details), we described the use of phenyl trimethylammonium iodide ($PhMe_3NI$) as an alternative methylating agent for introducing a CH_3-group in α-position to a carbonyl group. Compared to conventional methylating agents, quaternary ammonium salts have the advantages of being nonvolatile, noncancerogenic, and easy-to-handle solids. This regioselective method is characterized by ease of operational setup, use of anisole as green solvent, and yields up to 85 %.[3]



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Selective Synthesis and Crystallization of Stereogenic Silicon Centers

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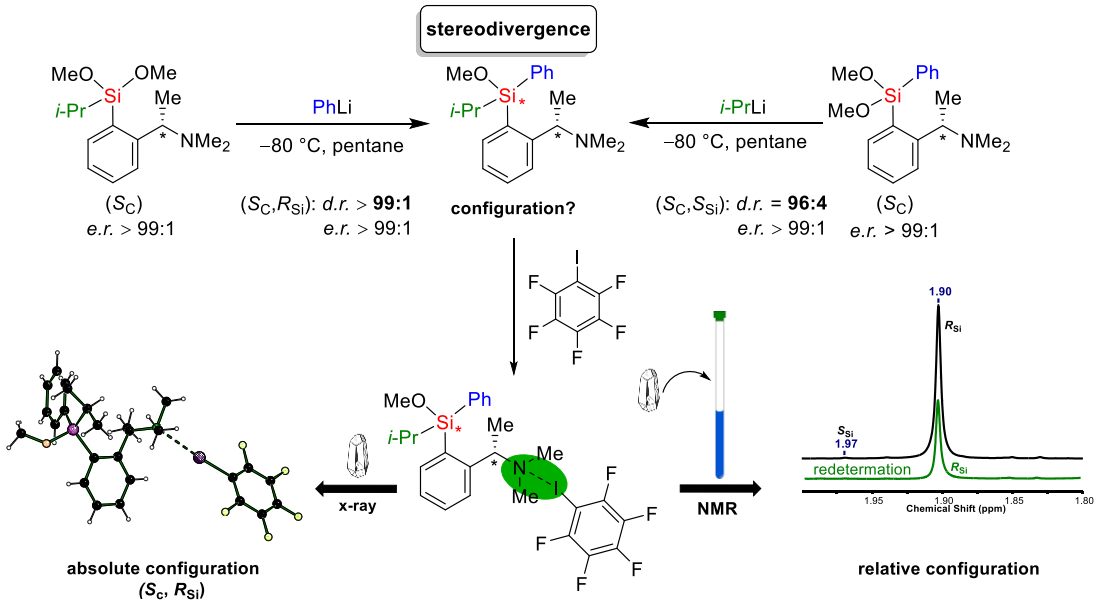
Multi-functionalized stereogenic silicon centers are interesting building blocks for chiral three-dimensional structures, catalysts, pharmaceuticals and chiral materials. The methods for constructing stereogenic silicon centers, compared to carbon are limited.[1] Using the substrate-induced asymmetric synthesis, it was possible to build Si-chiral alkoxysilanes in a stereoselective manner.

For the determination of absolute configuration by x-ray the *Halogen-Bond Method* could be used, which is a good alternative to covalent derivatizations (e.g. quaternization of amines). The big advantage of this method is that compared to covalent derivatization, non-covalent derivatizations can be reversed very easily. This also allows a fast redetermination of the compound without previous release of the educt via GC/MS, HPLC and NMR (e.g. for comparison of bulk material and crystal).



Scheme 1: Substrate-induced asymmetric synthesis of Si-chiral alkoxysilanes.

Halogen bonding (XB) is a special type of non-covalent interaction between a halogen atom (X) and an electron donor (D). XBs show a high analogy to hydrogen bonds and have a wide range of applications e. g. in liquid crystals, magnetic and conducting materials, and biological systems.[2] Perfluorinated halogen aromatic compounds show a high potential for crystallization with different amines by the formation of halogen bonds. Thus, XBs can be used as crystallization probes for sensitive functionalized amino-organosilanes and open up a new field of application.[3]

Thanks to *Deutsche Forschungsgemeinschaft* (DFG) for financial support.

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Substitutions of Si–N-functionalized silanes to alkoxysilanes using microwave radiation

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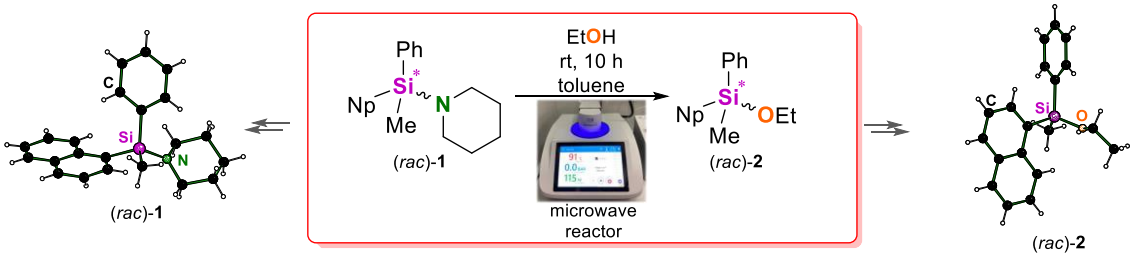
Aminosilanes (Si–N) represent central intermediates in silicon chemistry, which are of great importance in the modification of silicon surfaces. These compounds can be synthesized from industrially available methoxysilanes using lithium amides. This very well researched synthesis method can also be applied to the formation of Si–C bonds by using lithium alkyls.[1]

The most important functionalization of such Si–N-functionalized silanes is the substitution to alkoxysilanes (Si–O).[2] A well-known silylating agent is hexamethyldisilazane, which reacts with various alcohols. In contrast, aminosilanes with sterically more demanding substituents often lead to low yields in these reactions, which is due to the high kinetic barrier. Substitutions on (*rac*)-1-[methyl(naphthalen-1-yl)(phenyl)silyl]piperidine (**1**) with phenols as well as silanols show and confirm those low yields after long reaction times; other alcohols, like ethanol, do not show any conversion. Whereas substitutions on alkoxysilanes with the help of the lithium amides are possible, Si–N-functionalized silanes cannot be functionalized by using lithium alkoxides to synthesize the respective alkoxysilanes.

The synthetical access to various alkoxysilanes could be extended with the help of a new reaction method using microwave radiation. Amine functionalities on Si–N-functionalized silanes were selectively substituted with numerous alcohols (Scheme 1). The long reaction of the microwave-based substitutions can be explained by the decreased reactivity due to the large substituents at the silicon center, which could be improved by using more reactive Si–NH-functionalized compounds.[3] In addition, investigations are currently being carried out to transfer this new synthesis method to chiral systems. Moreover, the stereospecificity of microwave-based substitution reactions should be researched in detail in future experiments.



Scheme 1: Selective transformation of Si–N-functionalized silane **1** to ethoxysilane **2** performed by microwave radiation reactors.

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A halide-free, continuous-flow process for the synthesis of hydrophobic ionic liquids

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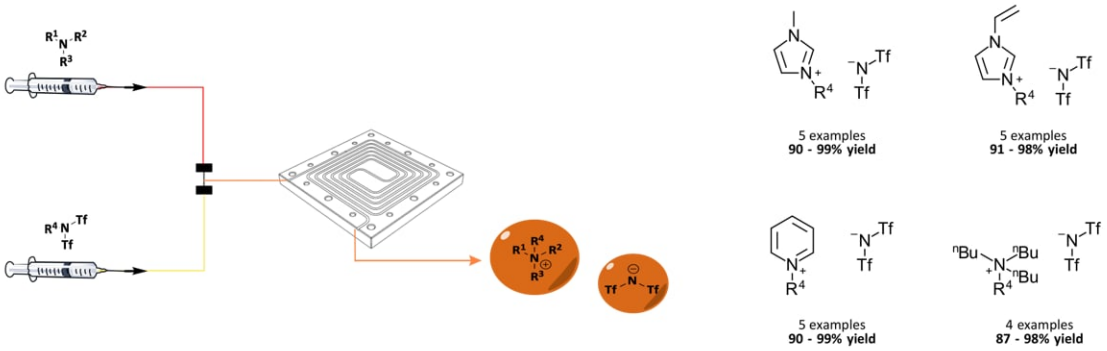
We present a novel approach for the halide-free, continuous-flow preparation of hydrophobic ionic liquids relying on the bis(trifluoromethanesulfonyl)imide (bistriflimide, NTf_2^-) anion [1]. The simple yet fast two-step synthetic route, which involves the formation of different alkyl bistriflimides ($RNTf_2$), followed by the quaternization with an amine nucleophile led to the desired ionic liquids in high yields and excellent purities without any by-product formation.

The variable alkyl chain (R^4) length, as well as the broad range of the applicable nucleophiles, offer considerable flexibility to the synthetic protocol. The quaternization can be performed under solvent-free conditions, while microwave irradiation can be applied as an alternative heating strategy, thus, providing a far more rapid synthetic process. Moreover, the homogeneous nature of these reactions allows the application of modern continuous-flow technologies. Given these advantages, the methodology can afford not just a fast and efficient alternative for the conventional synthesis of such compounds but reduce by-products, washing steps, and waste water formation. Moreover, the negligible halide content can provide a significantly broader application range for the IL products, especially in the field of material sciences where high purity and the absence of corrosive halide anions is required.



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Continuous-Flow Synthesis and Functionalization of Heterocycles Under Visible Light

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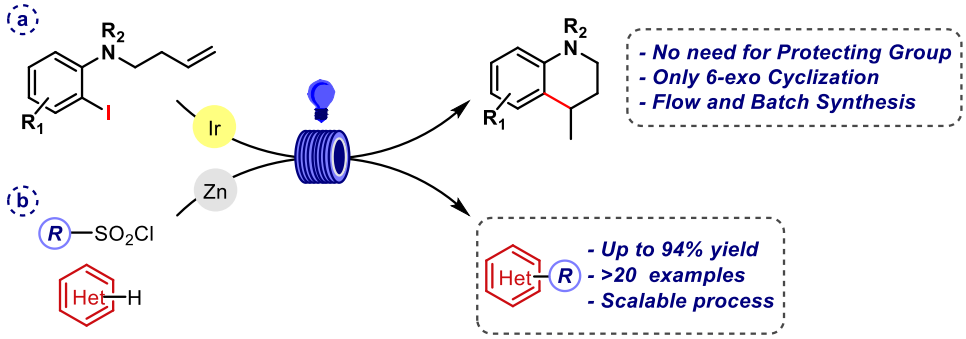
Over the last years, photoredox catalysis and light driven processes have been recognized as powerful tools for the synthesis and functionalization of biologically relevant heterocycles [1]. However, these methods face important drawbacks, such as scalability and light attenuation. In this regard, flow chemistry has currently gained huge attention thanks to the great benefits that it provides to the field [2]. Here, we present the photocatalytic flow synthesis of an important family of heterocycles (scheme 1a), and the continuous-flow in-situ generation of alkyl zinc sulfinates, furtherly employed for the visible light late-stage functionalization of heterocycles (scheme 1b).

Firstly, we describe the use of visible light and a photoredox catalyst for the cyclization of iodoaryl vinyl derivatives for the synthesis of tetrahydroquinolines (scheme 1a) [3]. This protocol presents mild reaction conditions and good functional group tolerance without *N*-protecting groups requirements. Furthermore, this methodology can be easily applied in continuous flow, making it scalable and taking advantage of the benefits this technique provides to photoredox catalysis. In a second project, we present a continuous-flow system for the in-situ generation of different alkyl zinc sulfinates [4]. Starting sulfonyl chlorides were pumped through a zinc column, and the corresponding zinc sulfinate was directly subjected to the visible light driven functionalization of relevant heterocycles. As a result, several cores such as quinoline or quinoxaline-2(1*H*)-ones were functionalized with a variety of alkyl radicals as benzyl, -CF_3 or -CF_2H, among others.



Scheme 1. a. Photocatalytic synthesis of tetrahydroquinolines. b. Continuous-flow generation of alkyl zinc sulfinates for the functionalization of heterocycles.

Financial support was provided by the Spanish Government (RTI2018-095038-B-I00), ''Comunidad de Madrid'', European Structural Funds (S2018/NMT-4367) and "Proyectos Sinérgicos I+D" (Y2020/NMT-6469). J. L. N. thanks "Comunidad de Madrid" for his industrial doctorate fellowship (IND2019/AMB-17142). M. J. G. thanks Spanish Government for her FPI predoctoral fellowship (PRE2019-090203).

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Metal-free and scalable alternatives for reduction of sulfoxides

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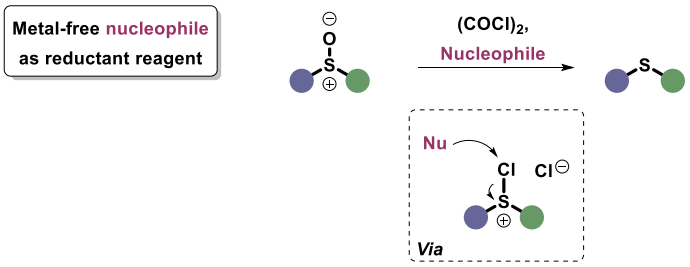
The chemistry of organosulfur is one of the most significant topics in organic synthesis nowadays.[1] For instance, sulfides are present in many biologically active molecules, and they are key intermediates for the synthesis of wide-ranging biological, pharmaceutical, and naturally occurring active molecules.[2] The deoxygenation of sulfoxides is among the most usual, efficient, and straightforward transformations to obtain the corresponding sulfides. During the last few decades, several methods for reducing sulfoxides into sulfides have been reported in the literature. Those methods are carried out using electrophilic reagents, Lewis acids, and transition metal complexes; unfortunately, most of those strategies clearly need polluting reagents or expensive heavy metals.[3] Furthermore, in 2020, we report the use of highly nucleophilic 1,3,5 trimethoxybenzene (TMB) as the reducing agent in the deoxygenation sulfoxides as a general and forthright new method.[4] In addition, other teams have been working on greener and scalable strategies in recent years; one example of a successful methodology is the electrochemical reduction of sulfoxides published by Guo, Wen and co-workers.[5] Regrettably, chromatographic purification is mandatory in all the cases described before, making them unsuitable for multigram scale preparations. Considering those difficulties, we have been interested in developing new metal-free and scalable strategies as alternative methods for reducing sulfoxides, minimizing problematic or polluting waste, and avoiding chromatographic purification. In that context, we present our advances on this topic.



Acknowledgments: This work was financially supported by Universidad de Los Andes, particularly the Faculty of Science (INV-2021-126-2269) and the Chemistry Department.

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Asymmetric synthesis of allenes from simple alkynes using novel chiral diselenide reagents

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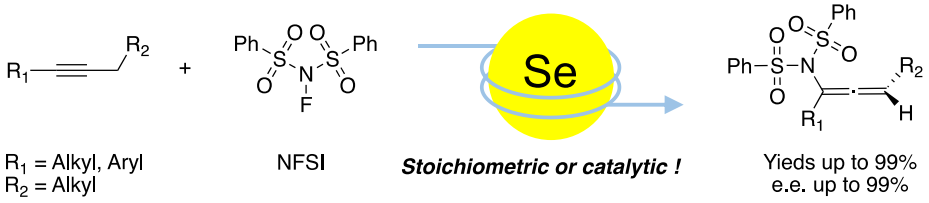
Allene chemistry has experienced a remarkable development in the past few decades. This is most certainly due to their synthetic potential in regio- and stereoselective C–C and C–X bond-forming transformations, as well as their occurrence in a variety of natural products and pharmacologically active compounds [1]. Most of the classical chemical reactions (additions, eliminations, substitutions or rearrangements) have been used toward their synthesis [2], and have led to an important number of methods. Despite this large variety of methodologies to access allenes, the direct synthesis of such motifs based non-metallic processes is still in its infancy [3].

To address this question, we have recently developed efficient novel chiral diselenides which can promote the asymmetric formation of allenes from simple non-activated alkynes in presence of N-Fluorobenzenesulfonimide (NFSI). The results of our efforts will be here presented for the first time, and will disclose the use of either stoichiometric or catalytic loadings of the chiral diselenides to generate a wide scope of trisubstituted allenes in both excellent yields (51 - 99 %) and enantiometric excesses (up to 99 %).



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Environmentally Friendly Phenol *O*-Arylation with Aryl(TMP)-Iodonium(III) Acetates

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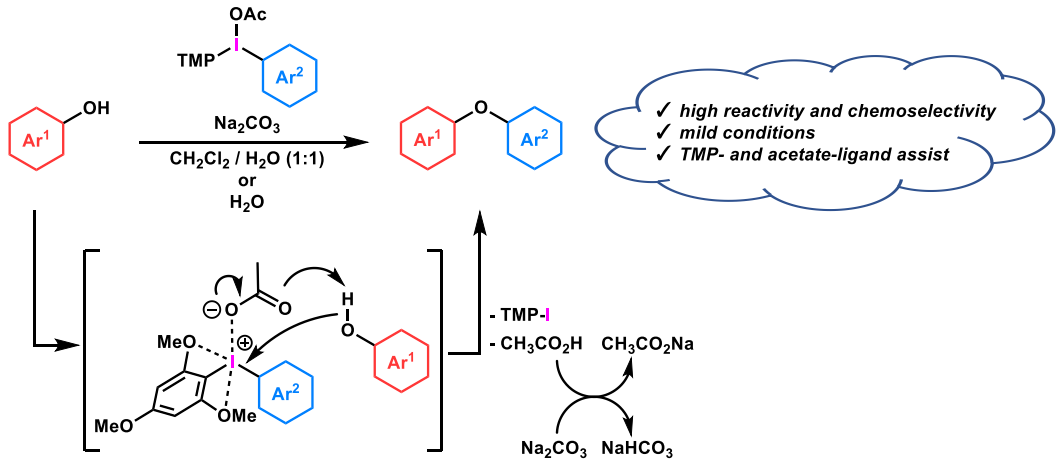
Diaryl ethers are important motifs in pharmaceutical and bioactive compounds. Classical diaryl ether synthetic methods are based on the metal-catalyzed *O*-arylation of phenols. However, these methods have limitations such as the need of transition metal catalyst and ligand, strong base, and high temperature. Therefore, phenol *O*-arylation without transition metal catalyst under mild conditions is highly beneficial. Recently, diaryliodonium(III) salts have been employed as an efficient arylating agent in the absence of transition metals. The first report of phenol *O*-arylation using diaryliodonium(III) salt was published in the 1950s[1a]. Also, an improved method for *O*-arylation with diaryliodonium(III) salts under mild conditions was developed by Olofsson's group[1b]. Gaunt and coworkers have noticed the crucial role of fluoride counterion of iodonium(III) salt in accelerating the phenol *O*-arylation process[1c]. More recently, Stuart group has reported the chemoselective arylation of aryl iodonium(III) tosylates containing trimethoxy(TMP)-group as a dummy ligand[1d].

We reported the efficient synthesis of aryl(TMP)-iodonium(III) acetates by reaction of aryliodine(III) diacetates with 1,3,5-trimethoxybenzene[2]. Interestingly, we found new synergistic effect to accelerate phenol *O*-arylation by TMP-ligand and acetate counterion of aryl(TMP)-iodonium(III) acetates[3]. The coordination of *ortho*-methoxy groups of TMP-ligand to the iodine(III) atom is the key to increase basicity of the acetate anion for activating the phenolic O-H group.

The broad reaction scope would enable the use of electron-rich, electron-poor, heterocyclic, sterically congested aryl(TMP)-iodonium(III) acetates, affording desired *O*-coupling products in high yields and excellent chemoselectivities.



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The Indium-Mediated Acyloxyallyation – A Tool for the Elongation of Aldoses Towards Higher-Carbon Sugars and Non-Natural Sugar Alcohols.

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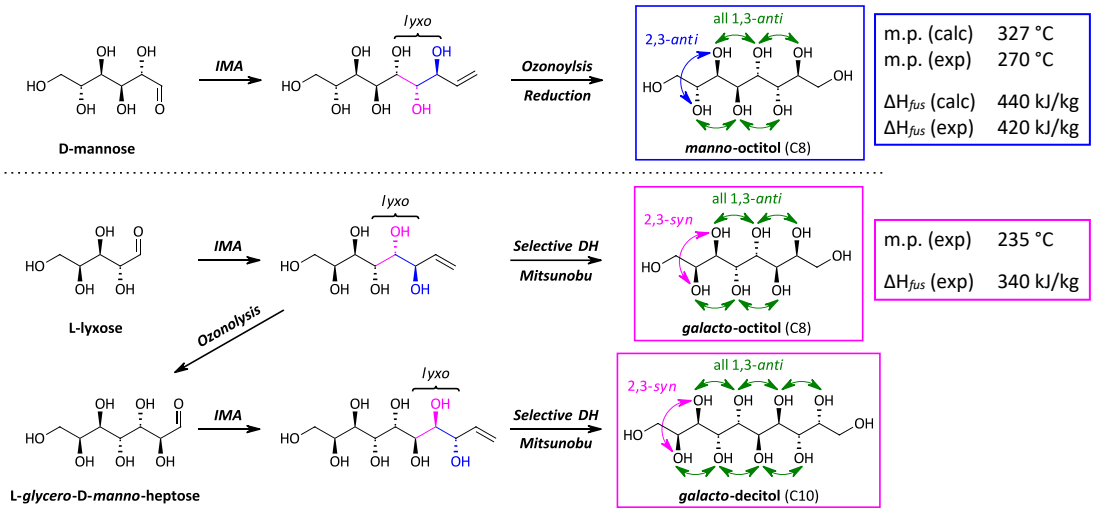
In carbohydrate chemistry, the synthesis of higher-carbon sugars and derivatives has been a challenge over decades. The addition of carbon atoms to the anomeric center of reducing sugars is often plagued by poor diastereoselectivity and most transformations require protection of the sugar. With the Indium-mediated acyloxyallylation (IMA) a method was developed and investigated in the last years, that allows direct elongation of unprotected aldoses by three carbons with high control of diastereoselectivity.[1,2]

In general, polyhydroxylated organic compounds are of high interest since they remain valuable for applications in various disciplines such as medicinal chemistry, material science or synthetic chemistry. Sugar alcohols, for example, can act as sugar mimics and chiral synthons and are therefore gaining popularity in the design of drugs and functional materials. Focusing on the latter, natural sugar alcohols like, e.g., erythritol or D-mannitol have been investigated intensively as potential phase change materials (PCMs) for thermal energy storage applications. With thermal storage densities of up to 350 kJ/kg, this substance class is considered as a promising candidate for thermal energy storage among organic materials.

Extraordinarily high thermal storage densities of up to 450-500 kJ/kg have been predicted for experimentally unknown non-natural sugar alcohols in a recent computational study.[3] These outstanding values were found for sugar alcohols that fulfil three structural criteria: a linear carbon backbone, an even number of carbon atoms and 1,3-*anti* configuration of all hydroxyl groups.

Based on the IMA as a tool for the elongation of reducing sugars in the required stereochemical fashion we developed an efficient strategy for the synthesis of non-natural sugar alcohols with more than six carbon atoms in the backbone that fulfil the stated rules. Our focus was on the synthesis of higher sugar alcohols with a *syn*-relationship between the two hydroxyl groups at the terminal stereocenters and a 1,3-*anti*-relationship of all hydroxyl groups, which we refer to as the "*galacto*-series". Furthermore, some of the investigated sugar alcohols with *manno*-configuration presented in the computational study [3] were accessible *via* IMA and the calculated values could be confirmed with experimental data.



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Novel DPPH-based compounds with redox properties

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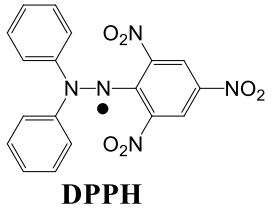
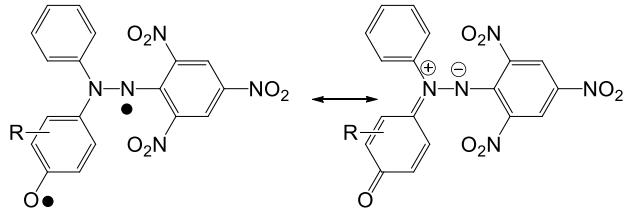
Hydrazyl free radicals, represented by key compound 2,2-diphenyl-1-(2,4,6-trinitrophenyl) hydrazyl, also known as DPPH, are a class of molecules that have been well studied and characterized in the literature over the past years. High stability of DPPH was explained by special structural characteristics, such as conjugation and steric hindrance. Moreover, push-pull effect of picryl moiety (as electron-acceptor) and diphenylamino moiety (as electron-donating) contribute to the high stability of DPPH. All mentioned above lead to easy handling of DPPH under usual conditions, such as light, humidity, air, or temperature, without losing its characteristics [1]. DPPH is used as a standard for ESR (Electron Spin Resonance) spectroscopy [2] and for studying the antioxidant properties of compounds [3].

Due to the high stability of DPPH free radical in solution or in the solid-state, the dimerization reaction doesn't appear spontaneously as it goes for other (unstable) radicals. In addition, derivatives of DPPH containing various other moieties, able, for example to yield betaines, could show unexpected properties. Our results disclose synthesis of novel DPPH-based compounds, containing phenol and phenyl bromide functionalities, including attempts to obtain the DPPH dimer. We present the difficulties encountered during the preparation strategies and their characterization in solution and solid-state. All synthesized compounds were characterized through NMR, UV-VIS and MS spectroscopy to confirm their identity.



DPPH



novel DPPH-based compounds

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Preparation and diene-transmissive Diels-Alder reactions of electron-poor [3]dendralenes

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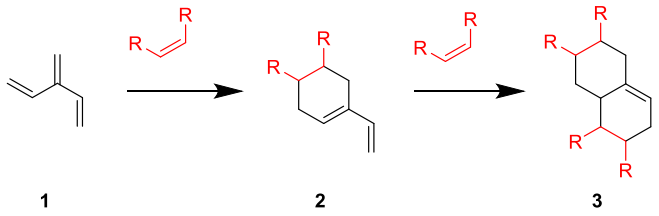
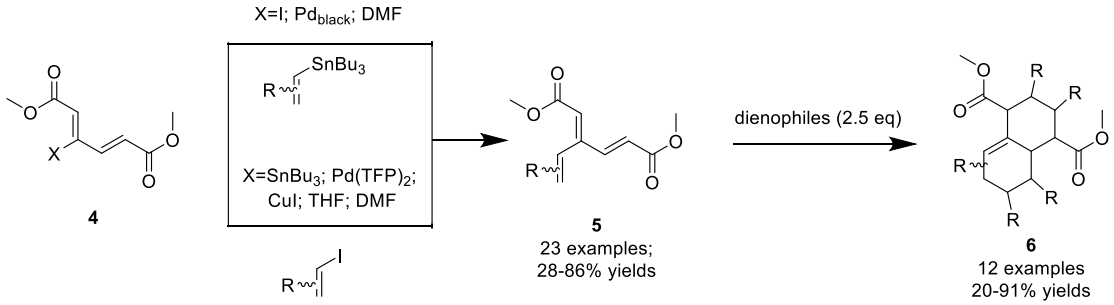
Dendralenes **1** (Scheme 1)[1] are a group of cross-conjugated olefins, which have enjoyed renaissance over the past few years thanks to the work of Sherburn et al.[2] Unlike other conjugated olefins, dendralenes are not limited to a single Diels-Alder (DA) cycloaddition. Cross-conjugation allows dendralenes to undergo multiple DA-reactions in diene-transmissive (DT) manner, where one cycloaddition furnishes a new conjugated diene subunit, which than can undergo another DA reaction (Scheme 1, **1**→**3**). Each DA reaction creates new six-membered ring with up to four new chiral centers. Thus, dendralenes can provide complex, polycyclic frameworks in one step.



Scheme 1. Diene-transmissive Diels-Alder reaction on [3]dendralenes

Our aim was to prepare a series of novel, electron-poor dendralenes (in contrast to generally electron-rich dendralenes, which are more common) and probe their reactivity in (DT)DA cycloadditions. The synthesis, was achieved in good yields with two variations of Stille coupling (Scheme 2)[3], providing us with a library of electron-poor [3]dendralenes **5**. Next, DTDAs, were accomplished with mostly high yields of DTDA products **6**. Unfortunately, our electron-poor dendralenes showed unusual selectivity for electron-poor dienophiles. This fact currently limits their further synthetic utilization. However, it is also an interesting example of atypical diene/dienophile pairing (poor-poor), which is in partial contrast with the general knowledge of DA reactions.



Scheme 2. Preparation and DTDA reaction of electron-poor dendralenes

This project is supported by the EFSA-CDN project (Reg. No. CZ.02.1.01/0.0/0.0/16_019/0000841) co-funded by the European Union.

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Fluorination of phenylacetic acids with a solvent-dependent selectivity switch

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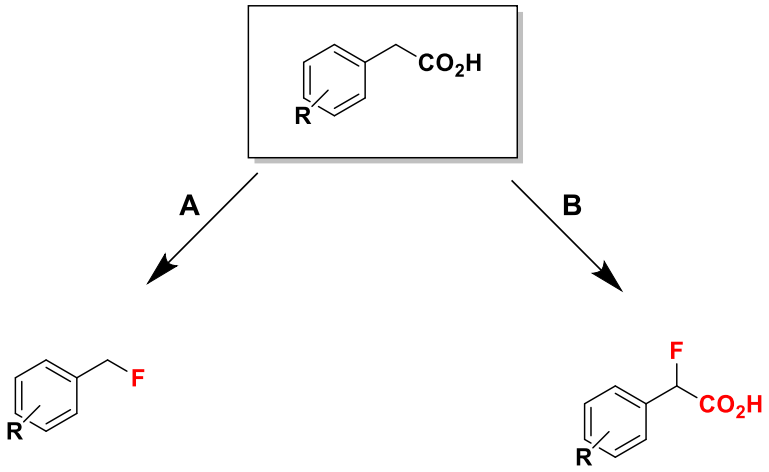
The fluorination of organic compounds is an appealing strategy to modulate the physicochemical properties of molecules without affecting their geometry. The small size of fluorine and its electronic properties enhance the metabolic stability and bioavailability of small molecules.[1, 2] As a consequence, fluorinated compounds are widely used in medicinal chemistry and agrochemistry, and convenient synthetic strategies for the introduction of fluorine on organic molecules are constantly under investigation.[3]

We present a novel, mild methodology for the fluorination of phenylacetic acid derivatives using a hitherto undisclosed activation of Selectfluor. Our strategy allows to perform either decarboxylative reactions that selectively result in the respective benzyl fluorides, or benzylic C-H fluorinations to obtain the corresponding α-fluoro carboxylic acids. The selectivity is controlled by simply changing the solvent. Both reactions use the same reagents and produce the respective products in high yields.



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Chiral phosphorus compounds by catalytic asymmetric C–P coupling

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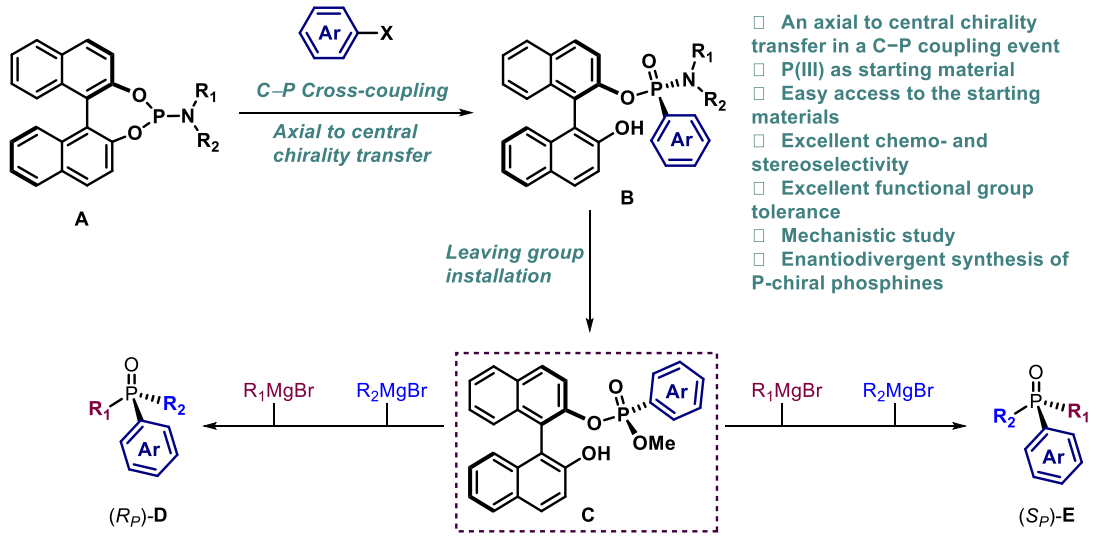
There has been growing interest in compounds that feature phosphorus stereocenters, not only in asymmetric catalysis but also for applications in materials science, agrochemistry, and drug discovery. In addition, they play an important role in oligonucleotide chemistry. Stereogenic phosphorus centers can be found in the structure of prodrugs or pharmaceutically active compounds. An illustrative example is Remdesivir, a drug that has recently gained much interest in light of the COVID -19 pandemic.

However, there are no versatile and flexible methods for synthesizing P-chiral phosphines, and their low commercial availability prevents them from finding practical applications. An attractive method for the preparation of these highly important P-chiral compounds is C–P cross-couplings catalyzed by transition metals in which an external chiral ligand has been used for chiral induction. Nonetheless, there are difficulties in these processes due to the direct competition between the initial and final phosphorus compounds and the metal catalysts, which reduces enantioselectivity.

In an alternative approach, BINOL-containing phosphoramidites (**A**) could be used as starting materials/ligands, along with halides for Pd-catalyzed P-arylation, which could then generate a P-chiral center (**B**), through axial to central chirality transfer. We have developed a general and divergent strategy for the preparation of P-chirogenic compounds based on a transition metal-catalyzed C–P cross-coupling involving the P-arylation of phosphoramidites with aryl halides and triflates.[1] This C–P reaction proceeds with high chemo- and stereoselectivity and accepts many functional groups such as halides, aniline, phenol, esters (-CO_2Et), ketones (-COMe), alkynes, as well as heterocycles common to drugs. Sequential substitutions at the phosphorus center of the aryl phosphoramidate formed after the P-arylation steps provide access to the hard-to-access enantioenriched monophosphines. Key to our methodology is its stereodivergent nature, which allows both enantiomers of a phosphine oxide to be prepared from a single phosphonate enantiomer. Another crucial factor in our preliminary mechanistic studies is the formation of a unique P-chiral aminophosphonium intermediate. The chemistry of chiral phosphonium salts remains to be explored in the field of phase transfer catalysts and organocatalysts.



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Copper-Catalyzed Oxy- and Amino- arylation of Unactivated Alkenes with Diaryliodonium Salts

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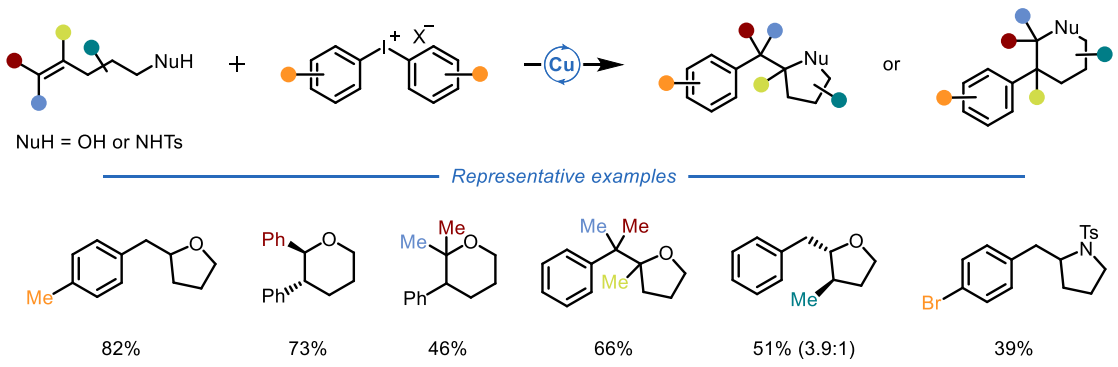
The synthesis of saturated heterocycles is of prime importance in modern synthetic chemistry as they are privileged scaffolds found in a variety of natural products and commonly used in medicinal chemistry [1].

Among all heterocycles, oxygen- and nitrogen-containing ones are the most widely found [2] and the development of new, catalytic and robust methods for the synthesis of such heterocycles based on the use of cheap and easily available starting building blocks remains of high interest since they are not that trivial to prepare. In this context, we have developed a new, efficient and broadly applicable arylative cyclization reaction from simple alkenes possessing an internal alcohol or amine which provides a direct access to 5- and 6-membered ring saturated heterocycles with high efficiency.

Our strategy for this alkene difunctionalization, based on previous reports by the Gaunt group on alkene arylations [3] and related cascade reactions [4,5], involves the easy activation of a diaryliodonium salt by a copper catalyst to generate a highly electrophilic arylcopper(III) intermediate. After addition onto the alkene and reductive elimination regenerating the copper catalyst, the resulting carbocation is finally trapped by the internal heteronucleophile to yield to the saturated heterocycle, in a single synthetic step.

A wide variety of tetrahydrofurans and pyrrolidines can be readily obtained with this process and tetrahydro-2*H*-pyrans can also be prepared in a divergent manner and depending on the substitution pattern of the starting alkene. The development of this process, including its optimization, scope and limitations and selectivity, will be discussed.



We gratefully thank the FNRS, the Fonds pour la formation à la Recherche dans l'Industrie et dans l'Agriculture (F.R.I.A.) and the Université libre de Bruxelles (ULB) for their material and financial support.

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The Double S_N2' Reaction

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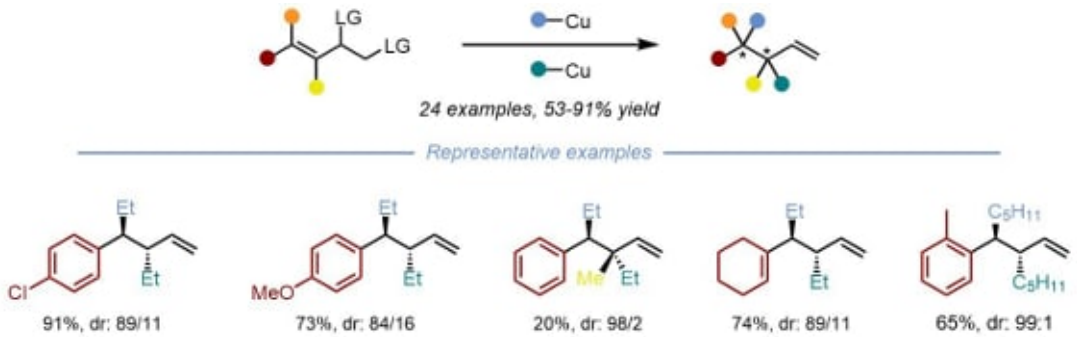
Organic chemistry is a central science with deep implications in many areas of sciences, notably in medicinal chemistry where organic molecules are still at the core of the majority of new drugs. While most of these drugs or drug candidates have been developed for decades based on aromatic scaffolds, mostly due to the development of palladium-catalyzed cross-coupling reactions expediting their synthesis, the scientific community has realized the strong limitations associated to these "flat" molecules and the strong need to "escape from flatland" [1]. In this perspective, the synthesis of more complex molecules by increasing the level of saturated chains has therefore become a necessity, which also means controlling the configuration of all stereochemical element, most drugs commercialized nowadays being single enantiomers [2].

While a number of efficient and robust methods exist for the installation of heteroatom-substituted stereogenic centers, such as the enantioselective reduction of ketones or imines, there are not that many reactions enabling the easy and reliable installation of all-carbon stereocenters from readily available starting materials, the enantioselective hydrogenation of alkenes being certainly the most utilized to date [3].

In this context, we have developed a new copper-mediated double S_N2' reaction in which two contiguous carbon stereocenters are formed starting from readily available enantiopure allylic diols in which the two alcohols are activated as leaving group. Interestingly, the stereoselectivity of the S_N2' reaction can be finely tuned by the nature of the alkene (*E* or *Z*) as well as the nature of the leaving group, non-coordinating group reacting in an *anti*-mode while coordinating ones favor *syn* S_N2' reactions [4,5].

The development of this reaction as well as its scope, limitations and models accounting for the stereoselectivity will be presented and discussed.



We gratefully thank the FNRS, the Fonds pour la formation à la Recherche dans l'Industrie et dans l'Agriculture (F.R.I.A.) and the Université libre de Bruxelles (ULB) for their material and financial support.

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Studies towards the synthesis of racemic 9*α*,10*β*-Bisangeloyloxy-7-*epi*-3*E*-agerafastin

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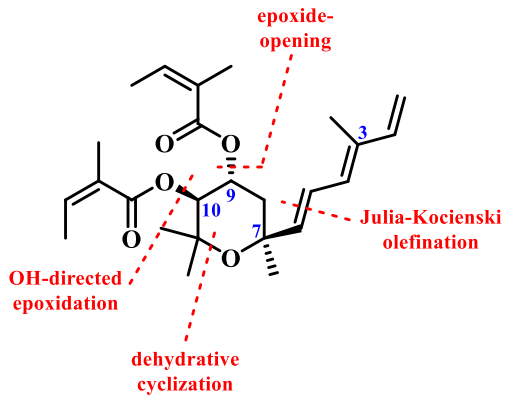
9*α*,10*β*-Bisangeloyloxy-7-*epi*-3*E*-agerafastin was isolated from the aerial parts of *Brickellia vernicosa* by BOHLMANN et al. [1]. Its structure features a highly substituted tetrahydropyrane core, a highly abundant scaffold in natural products and drugs. Especially the high substitution pattern at C7 and C11 poses an interesting synthetic challenge, as methods to obtain such highly substituted heterocycles are scarce. We envisioned overcoming this challenge by forming the corresponding dihydropyrane via a dehydrative cyclization [2].

Herein, we present our efforts towards the synthesis of racemic 9*α*,10*β*-Bisangeloyloxy-7-*epi*-3*E*-agerafastin. Our synthetic strategy comprises 15 steps, key steps being a CAN-mediated dehydrative cyclization [2] of a 2-ene-1,5-diol to form a key dihydropyrane intermediate, an OH-directed epoxidation aswell as a Julia-Kocienski olefination.



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Transition Metal-free Cyclization of Propargylic Amides to Oxazoles in Hexafluoroisopropanol

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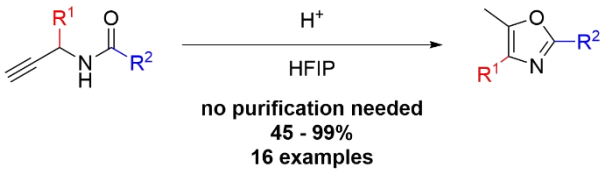
Today's chemistry often utilizes transition metals to catalyze reactions. These metals like palladium, copper or gold are precious resources which are rare, nonrenewable and involve complex mining and purification processes. Therefore it is desirable to reduce or substitute metals in synthesis. For gold this might be achieved by using a simple proton as it is isolobal to cationic gold(I) which is commonly used as catalyst.[1] However, difficulties arise when using H^+ as the reactions often require harsh conditions and are prone to side reactions.

Our goal was to develop an easily applicable transition metal free alternative to the gold-catalyzed cycloisomerization of propargylic amides to oxazoles published by Hashmi et al..[2] While there are examples in literature for acid-promoted cyclizations of propargylic amides, there is no efficient general protocol for a greater range of substrates.[3–5] As starting point we oriented ourselves by the work of Aubé et al.[6] who described catalytic Schmidt reactions in hexafluoroisopropanol promoted by the in situ generation of H^+.

To our delight the first reactions proceeded successfully. We optimized the method by employing Design of Experiments and could transform a broad range of substrates with yields up to 99%. Additionally the work-up procedure is quite simple since all components are volatile. The hydrochlorides are accessible by evaporation and the free oxazoles by basic extraction.



Scheme 1: H^+ promoted cyclization of propargylic amides to oxazoles.

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Total synthesis of +/- pestalactone C via tandem Pd-catalysis

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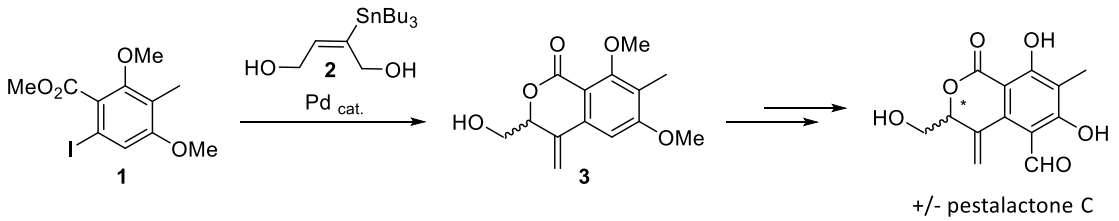
Pestalactone C was first isolated by Song and co-workers in 2017 from the solid cultures of the endophytic fungus *Pestalotiopsis sp.*, founded in the leaves of Chinese plant, *Photinia frasery*. The stereochemistry of the compound was determined as (*R*). Evaluation of antifungal activity showed growth inhibition of *Candida Glabrata* (MIC = 3,49 ± 0,21 µg/ml; MIC amphotericin B = 0,25 µg/ml) [1].

Two years later, Rivera-Chávez and co-workers isolated the (*S*)-enantiomer from the same fungal species. Interestingly, the (*S*)-isomer displayed a relatively strong inhibition of alfa-glucosidase (IC_{50} = 263,0 ± 5,9 µM) in comparison with acarbose as a positive control (IC_{50} = 604,4 ± 6,9 µM) [2].

The biological activity of both enantiomers led us to design a synthetic strategy based on the unique methodology, developed in our research group. The key step of pestalactone C synthesis includes palladium-catalyzed Migita-Stille coupling of iodoester **1** (Scheme 1) with stannylated diol **2**. Subsequent intramolecular Tsuji-Trost isomerization gives isochromanone **3** in a single reaction step [3].



Scheme 1

This study was supported by Charles University (SVV reg. No. 260 547 and GAUK reg. No. 205007), "Grant Schemes at CU" (reg. no. CZ.02.2.69/0.0/0.0/19_073/00169359) and Czech Science Foundation (reg. No. 22-19209S).

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Synthesis of new uracil derivatives through the generation of “uracilyne”

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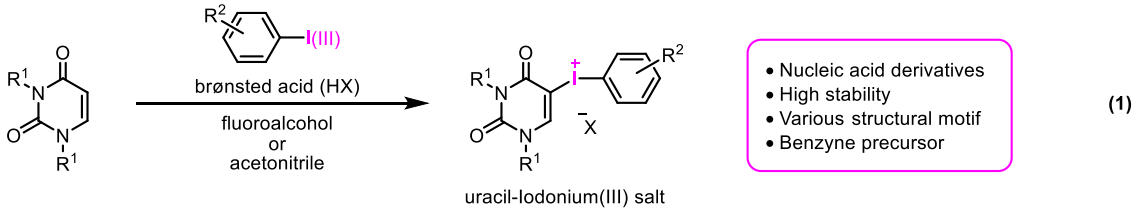
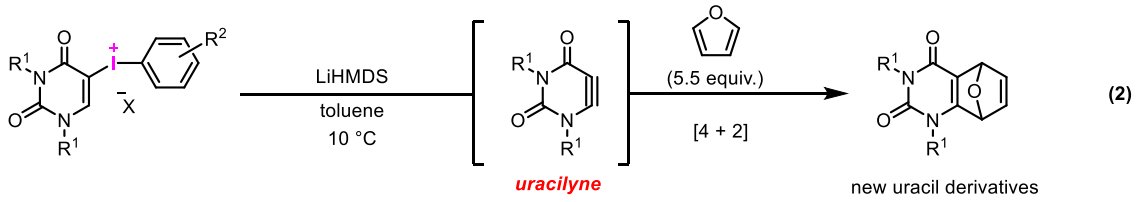
Nucleobases are important compounds included in many biological active substances. Uracil, which is one of the nucleobases, is an important structural unit for pharmaceutical and bioactive compounds. However, a limited number of studies have been reported on the methods for direct uracil C-H functionalization. A more efficient and complementary methodology is required for further advance of uracil functionalization and synthesis of new uracil derivatives.

The diaryliodonium (III) salts, which have two aryl groups and one counterion at trivalent iodine, is one of the most useful and important classes of hypervalent iodine(III) compounds in organic synthesis. In characteristics, the arene-iodine(III) bond is easy to cleavage and iodoarene group works as a super leaving group. Therefore, diaryliodonium(III) salts cause vicinal difunctionalization of C-I(III) and *ortho* C-H bonds and are used as reactive precursor for generation of benzynes [1]. The recent studies utilizing reactive heteroarynes with a distorted triple bond have gained specific interest as the efficient functionalization of heterocyclic compounds.

We recently reported the synthesis of uracil-iodonium(III) salts with various counterions as the reactive synthetic intermediates for coupling reactions and other transformations (Eq. 1). In this study, we found that the introduction of an electron-withdrawing group into the aryl moiety is beneficial for isolation and stabilization of uracil-iodonium(III) salts [2]. Furthermore, we investigated vicinal functionalization of heteroaryne analogue of uracil, which was generated by deprotonation of uracil-iodonium(III) salts using lithium bis(trimethylsilyl)amide (LiHMDS). The [4+2] cycloaddition products were obtained by trapping the heteroaryne analogue of uracil, as in “uracilyne”, with furan (Eq. 2) [3]. We have extended the reactivity of this active species, “uracilyne”, for the reaction with various substrates, wherein [3 + 2] and [2 + 2] cycloadditions as well as σ bond insertion reaction proceeded to afford corresponding functionalized uracil derivatives.



(1)



(2)

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Open-chain carbohydrate amides: synthesis, docking studies and acetylcholinesterase inhibition

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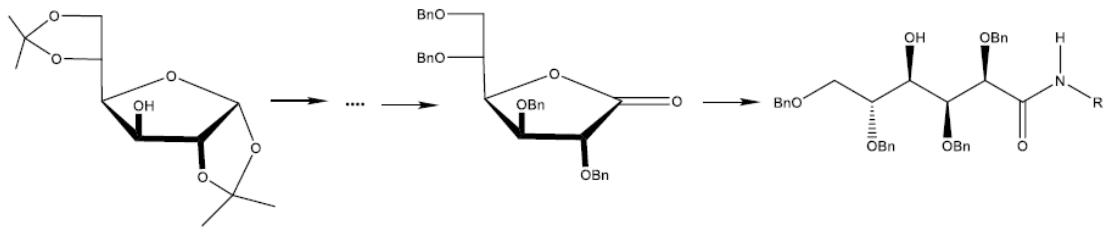
Acetylcholinesterase (AChE) is an important target for the symptomatic treatment of Alzheimer's disease (AD), a multifactorial syndrome not yet fully understood, causing memory loss, dementia, and ultimately death [1]. AChE inhibitors are the main stay drugs for early disease stages [2,3].

In this work we report on the development of a synthetic route to yield open chain sugar amides from commercially available carbohydrates. The synthetic pathway starts with diacetone glucose (DAG), which is converted into perbenzyl D-glucono-1,4-lactone in six steps. Reaction with aromatic or aliphatic amines in dichloromethane under reflux (0.5 h to 2 h) afforded the corresponding amides in high yield (80 – 95%) (Scheme 1). Bis(amidation) of a diamine was also accessed by this procedure in 3 h but reaction product was isolated in very low yield (13%). Docking studies and evaluation of acetylcholinesterase inhibition were carried out and the results will be disclosed.



Scheme 1. Synthesis of open-chain carbohydrate amides from diacetoneglucose.

Acknowledgements Fundação para a Ciência e a Tecnologia is gratefully acknowledged for the support of Centro de Química Estrutural (project UIDB/00100/2020), and of its Associate Laboratory Institute of Molecular Sciences (LA/P/0056/2020).

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Synthesis and characterization of red cyanine dyes with improved stability and solubility for color filter in micro OLED displays

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In the rapidly growing micro OLED display market, top emission structure of the display has advantages of enhanced optical properties attributed to high aperture ratio. Color filter in top emission OLED requires a low-temperature process to reduce thermal damage to emissive layer, which enable the dyes not suitable for conventional high-temperature process to be employed for the color filter fabrication.

Among various red dyes, cyanine dye exhibits strong optical absorption, while its relatively low stability limits their application. Therefore, we synthesized novel red cyanine dyes by introducing various substituents to increase stability and solubility[1]. Furthermore, their spectral property, stability and solubility in industrial solvent were examined to evaluate the dyes for dye-based color filter.

The synthesized dyes showed superior absorption property because of their characteristic charge transfer transition[2]. Also, they exhibited improved stability and solubility due to the introduced bulky functional group and counter anions[3]. In addition, the color filter layer was prepared based on the synthesized dye and its spectral properties were investigated. From the results, we expect that this study could contribute to the design and development of red cyanine dyes for the color filter in top emission OLED.

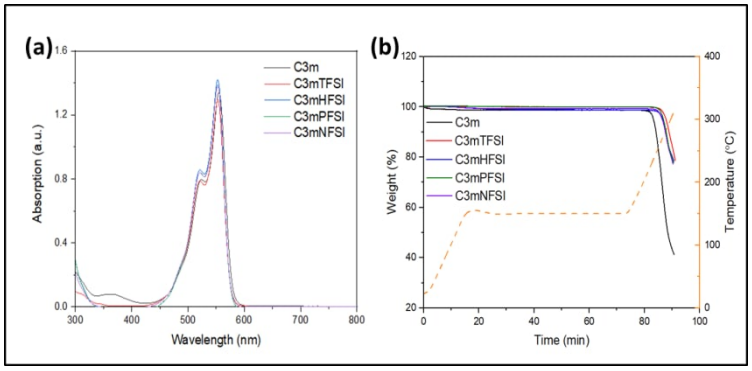

Figure 1. (a) Absorption spectra of the dye solutions dissolved in PGMEA and (b) TGA analysis of the synthesized dyes. Dyes were heated to 150 ℃, and held at the temperature for 1 hour, then further heated to 350 ℃.

This work was supported by the Industrial Technology Innovation Program (20016178, Development of dye-pigment hybrid color resists for ultra-high resolution over 4000PPI high-luminosity AR/VR displays) funded By the Ministry of Trade, Industry & Energy(MOTIE, Korea).

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Synthesis of highly functionalized six-membered carbocycles *via* strong acid mediated endocyclic C-C bond-cleavage of monocyclopropanated cyclopentadiene

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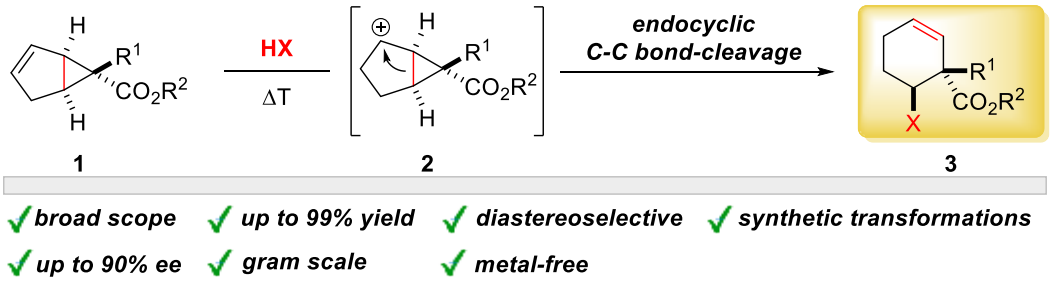
In recent years, various synthetic transformations utilizing activated donor-acceptor bicyclic cyclopropane systems involving chemo-, regio-, and stereoselective cleavage of an exocyclic cyclopropane C-C bond have been demonstrated. [1-3] In contrast, selective endocyclic C-C bond cleavage in bicyclic cyclopropanes remains a highly underexplored chemical space with only few reported examples. [4,5] In 2021 we developed a regio- and stereoselective synthetic route to highly functionalized tetrahydropyridine and dihydro-2H-pyran derivatives *via* the metal-free endocyclic ring-opening of monocyclopropanated pyrroles and furans. [4]

Since the scope of this endocyclic ring-opening was so far limited to heterocycles, we have here developed a method to achieve a highly chemo-, regio-, and stereoselective endocyclic C-C bond cleavage of bicyclic carbocycles. Mechanistically, we propose that the protonation of the double bond of monocyclopropanated carbocycle **1** by a strong acid occurs to form cyclopropylcarbinyl cation **2**, which then undergoes selective cleavage of the unactivated endocyclic cyclopropane C–C bond. After nucleophilic addition of the corresponding conjugated base of the utilized strong acid, cyclohexene compounds **3** are formed.



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Functionalization of Terminal Rings of Anthracene *via* Diels-Alder Reaction with Atypical Regioselectivity and Further Transformations

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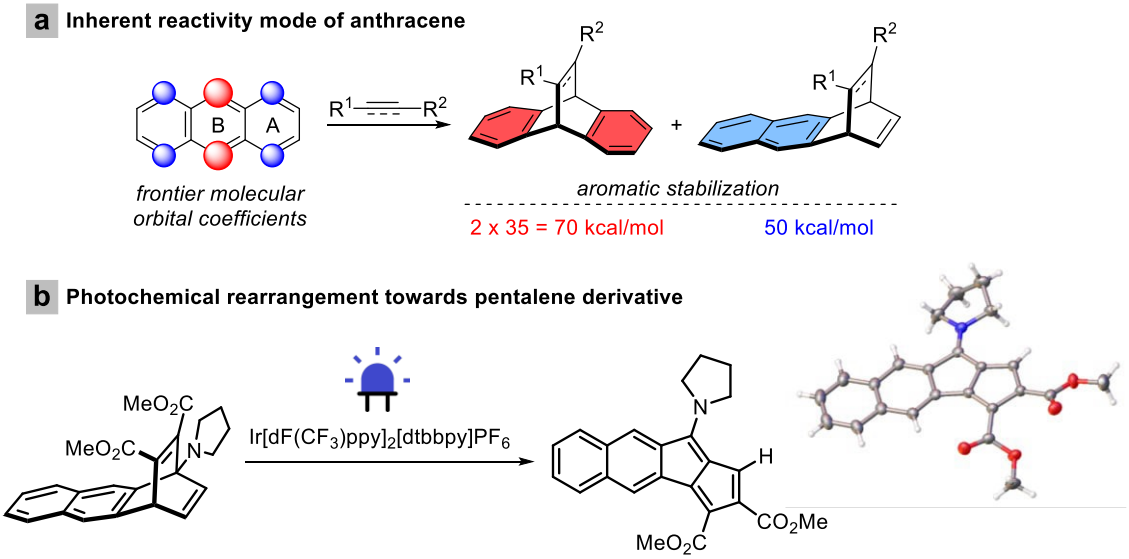
Anthracene exhibits a natural preference to undergo Diels-Alder reaction with dienophiles at their 9,10-positions (B-ring, Figure 1a) rather than their 1,4-positions (A-ring, Figure 1a), which is due to thermodynamic as well as kinetic factors.[1] Installation of voluminous and/or electron-withdrawing substituents at the 9- and 10-positions can shift this proclivity, thereby deactivating the central B-ring by steric and/or electronic means. This allows the corresponding cycloadducts with the terminal A-ring to be formed.[2] Only one example of an 9,10-unsubstituted anthracene with 1,4-selectivity has been reported thus far, involving an inclusion complex of a supramolecular octahedral organopalladium host.[3] Our group has achieved the heretofore unprecedented 1,4-selective [4+2]-cycloaddition of anthracenes by installing electron-donating substituents on the terminal rings without blocking or substituting the 9,10-positions.[4] The 1,4-products resulting from the aforementioned cycloadditions provide an excellent basis for further transformations. Of particular interest is the photochemical rearrangement of the bridged six-ring scaffold to an unsymmetrical pentalene derivative (Figure 1b). The mechanism of this transformation was investigated by both NMR and EPR spectroscopy. Moreover, optical properties of the anti-aromatic system, especially its peculiar behavior in an acidic medium, were investigated.



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Synthesis of new purine nucleosides and evaluation of their potential as copper chelators and anticholinesterase agents

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Alzheimer's disease (AD) is the most common form of dementia, being a multifactorial and degenerative pathology. The loss of cognitive functions, directly related to the progressive decline of the neurotransmitter acetylcholine (ACh), is one of the hallmarks of this disease, for which there is no efficient treatment [1,2]. Currently, the relief of AD's symptoms is achieved by the treatment with acetylcholinesterase (AChE) inhibitors, having recent studies showed that the long-term use of these drugs might lead to disease modifying effects [3].

Bivalent copper ions, at normal levels, play a crucial role in the regulation of neuronal functions and there are studies with statistical support showing that serum copper levels were higher in AD patients than in healthy controls [4]. Moreover, these ions were also found in some tumors [5].

Accordingly, the discovery of a compound with anticholinesterase and copper chelating activities would be an interesting challenge leading to dual target compounds against AD and, eventually, against some types of cancer. In this context, mannosylpurines synthesized in our group already shown a potent antibutyrylcholinesterase (BuChE) activity [6,7]. Aiming at the discovery of such multitarget drug candidates, we have synthesized a new series of mannosyl and rhamnosylpurines and evaluated copper chelation and cholinesterases' inhibition. The results obtained will be presented and discussed.

Fundação para a Ciência e a Tecnologia is gratefully acknowledged for the support of Centro de Química Estrutural (project UIDB/00100/2020) and Institute of Molecular Sciences (LA/P/0056/2020).

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Synthesis and ring-opening of sulfonylaziridine chiral to sulfonyloxzolidine

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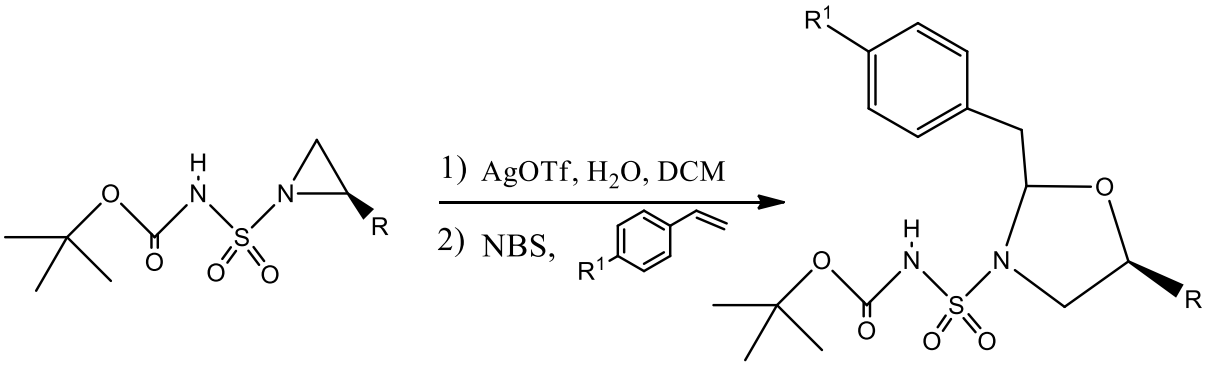
Abstract:

In this work, a new approch of the synthesis of sulfonylaziridine chiral was devloped, the desired aziridine resulting from the functional rearrangement of chlorosulfonyl isocyanate (ICS) by sequential interactions of carbamoline by adding *tert*-butanol to the isocyante function of the ICS, followed by sulfamoylation of the L-lysine ester by the base in an aprotic solvent. One pot synthesis of 1,3-oxazolidines derivatives was developed by ring opening of aziridine through geminal difunctionalization of vinyl arenes [1].

Key words: aziridines, oxazolidines, sulfonamides, difunctionalization.



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A fluorine-18 labelled difluorocarbene for PET ligand discovery

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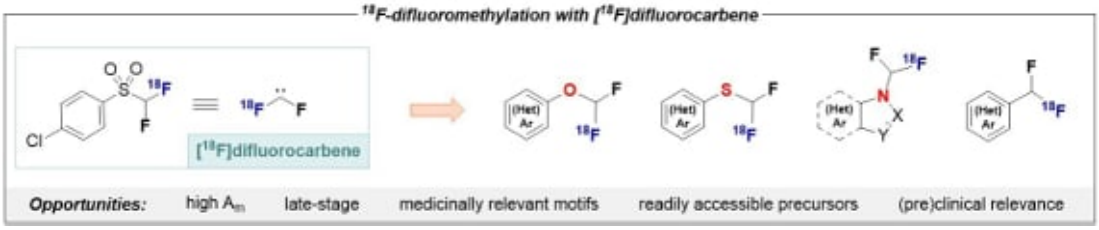
Positron Emission Tomography (PET) is a powerful molecular imaging technique, allowing for the interrogation of in vivo processes. It has found a range of applications including clinical diagnosis and therapy assessment, as well as drug discovery [1]. Tracers labelled with the radioisotope fluorine-18 are particularly privileged for PET applications, due to its favourable decay properties (97% β+ decay, 109.8 min half-life, 635 keV positron energy). This has led to the development of an array of highly effective methods to access radiofluorinated compounds, with a focus on the addition of fluorine-18 to aromatic and aliphatic scaffolds [2,3]. Despite these advances, currently available protocols to install valuable polyfluorinated motifs, such as [^{18}F]CF_2H, remain underdeveloped in comparison. The unique properties of this group have rendered its incorporation into various market and pipeline pharmaceuticals advantageous [4], but access to these compounds in radiolabelled form in high molar activity (A_m) remains an unsolved problem. This work unlocks this valuable radiochemical space by means of an ^{18}F-labelled reagent, which allows [^{18}F]difluorocarbene to be harnessed in a range of ^{18}F-difluoromethylation processes [5]. With the help of mechanistic insights, an optimal ^{18}F-reagent was designed that displayed excellent reactivity and crucially, was accessible in high A_m. Broad reactivity was observed in an array of reactions, including O–H, S–H and N–H insertions, cycloadditions and Pd-mediated cross-coupling with readily available reaction partners, such as ubiquitous (thio)phenols, N-heteroarenes and aryl boronic acids that are easy to install. The labelling of complex and bioactive molecules and radiotracers is demonstrated and the immediate relevance of this work to (pre)clinical studies is illustrated with a proof-of-concept in vivo study.



This research has been supported by the Engineering and Physical Sciences Research Council (EP/V013041/1, EP/T517811/1), Pfizer, Janssen, UCB, the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement (721902). J.F is grateful to the Centre for Doctoral Training in Synthesis for Biology and Medicine for a studentship, generously supported by GlaxoSmithKline, MSD, Syngenta and Vertex.

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Synthesis of hybrid polymer brush via combination of surface-initiated ring-opening metathesis polymerization and thiol-ene click reaction and its use in DNA hybridization

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In recent years, surface-initiated forms of controlled polymerization methods such as nitroxide-mediated polymeriza tion (NMP)[1], atom transfer radical polymer polymerization (ATRP)[2] reversible addition-fragmentation chain transfer (RAFT) polymerization[3] and ring opening metathesis polymerization (ROMP)[4] have been used to pro vide good versatility and functional group compatibility.

In this study, well-defined hyaluronated poly(exo-7-oxabicyclo[2.2.1]hept-5-en-2,3-dicarboxylic anhydride) [poly(EHDA)-HA] brushes on the hydroxyl terminated silicon (Si-OH) surface were prepared through the combination of surface-initiated ring-opening metathesis polymerization (ROMP) and thiol-ene click reaction. This process was realized in successive four steps: (i) formation of self-assembled monolayer of (3-aminopropyl)triethoxysilane on the Si-OH surface (Si-APTES), (ii) bonding of EHDA monomer to the Si-APTES surface, (iii) synthesis of poly(EHDA) brushes via surface-initiated ROMP and (iv) coupling of thiolated hyaluronic acid (Th-HA) to poly(EHDA) chains via thiol-ene click reaction. Surface wettability, surface morphology and chemical compositions of poly(EHDA)-HA brushes were characterized by contact angle measurements, atomic force, microscopy and X-ray photoelectron spectroscopy, respectively. Grafting density (σ, chains nm-2) and average distance between grafting points (D, nm) of the poly(EHDA) brushes were measured to be 0,50 chains nm-2 and 1,65 nm, independent of the [catalyst]/[monomer] ratios, which indicated that high grafting was created on the silicon substrate. However, low amounts of HA molecules were bonded to poly(EHDA) chains due to the high volume of Th-HA chains creating some steric hindrances.The biocompatibility of the brushes was determined by (3- (4,5-dimethylthiazol-2-yl) -2,5-diphenyl tetrazolium bromide) (MTT) cytotoxicity test. First, single stranded RNA molecules were attached to the poly(EHDA)-HA brushes, then hybridized with conjugated DNA probe and the surface was examined by Fluorescence Spectrum and Laser Scanning Confocal Microscope. As a result, the biocompatible property of poly(EHDA)-HA brushes could be useful a candidate for making advanced biological devices to control the behavior of biomolecules on surfaces.

Keywords: Exo-7-Oxabicyclo[2.2.1] Hept-5-en-2,3-Dicarboxylic Anhyride, Surface Initiated Ring-Opening Metathesis Polymerization (ROMP), Thiol-Ene Click Reaction, Grafting Density, DNA Hybridization

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Cyclodextrin derivatives and their synthesis

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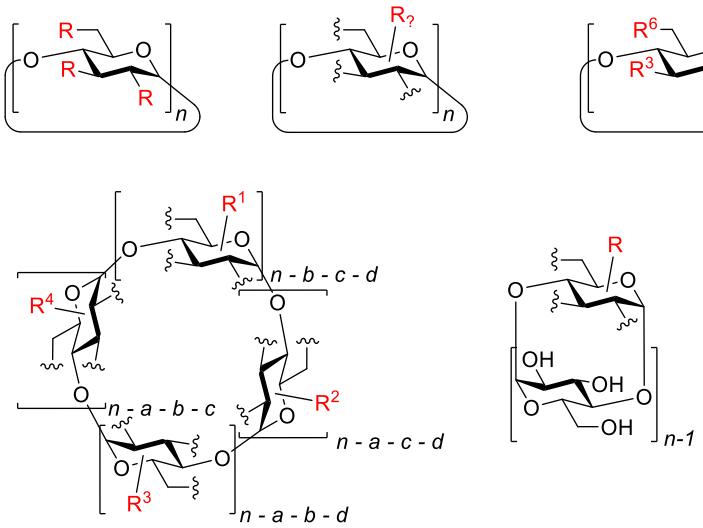
Cyclodextrins (CDs) are cyclic oligosaccharides containing in their molecule glucose units linked by an alpha-1->4 glycosidic bond. Their most significant feature is their lipophilic cavity capable of complexing various guests. If the native cyclodextrin is not suitable for a given application, its derivatives are synthesized (Figure 1). The reactivity of cyclodextrins is mainly related to the hydroxyl groups present. The three different hydroxyl groups on each of the glucose units make selective modification of cyclodextrins generally difficult because the hydroxyl groups compete with each other. Thus, the only consolation of an organic chemist remains some differences. In addition to the difference between the primary hydroxyl groups in positions 6 and the secondary ones in positions 2 and 3, there are also differences in acidity between them. The hydroxyl groups in positions 6 are the least acidic, while in positions 2 they are the most acidic. Selective modification of hydroxyl groups in positions 3 is thus the most difficult [1].

The presented research will be focused on the possibilities of synthesis of cyclodextrin derivatives, especially those which can serve as precursors for further synthesis. The research will show the current possibilities of cyclodextrin chemistry in the synthesis of individual derivatives using the most favourable procedures. At the same time, the research will draw attention to possible pitfalls in the synthesis. Finally, the research deals with some specific applications of cyclodextrin derivatives and opens the door to better understanding and their further possible uses.



n = 6, α-CD derivatives
n = 7, β-CD derivatives
n = 8, γ-CD derivatives

Figure 1. Groups of cyclodextrin derivatives.

This work was supported by the Ministry of Education, Youth and Sports of the Czech Republic and the European Union–European Structural and Investment Funds in the framework of the Operational Programme Research, Development and Education–project "Hybrid Materials for Hierarchical Structures" (HyHi, Reg. No. CZ.02.1.01/0.0/0.0/16_019/0000843).

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Zincate-Mediated Remote Functionalisation of *p*-Iodobenzyl Derivatives Through Metallotropy: Unprecedented Scope and Ubiquitous Influence of the 2-MeTHF on the Overall Process

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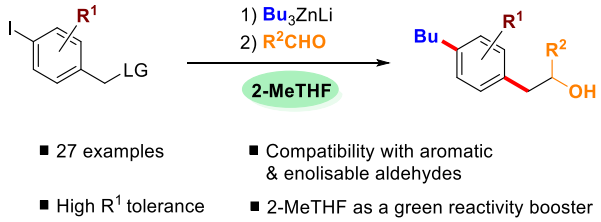
Metal-promoted remote functionalisation through internal induction is an efficient synthetic concept to swiftly access added-value molecular architectures with a high degree of structural diversity from simple and readily available substrates.[1] If perfectly implemented, such an approach leads to the selective functionalisation at a site away from a functional group initially interacting with the used reagent or catalyst. In this context, through-space metal migration[2] or intrinsic migration of the metal along a flexible carbon via unidirectional positional isomerisation sequence of a double C-C bond[3] are the most popular used internal communication processes between initiation and functionalisation sites. By contrast, metallotropic rearrangement[4] received very little attention from the synthetic community.

In this poster, we disclose the remote functionalisation of diversely decorated 4-iodobenzyl derivatives through metallotropy by using lithium tributylzincate as reagent and 2-MeTHF as solvent. The process leads to the selective formation of both a C(sp^3)-C(sp^2) and a C(sp^3)-C(sp^3) bond at sites localised at five atoms away from one another in a single operation and with a unique organometallic reagent. Compared with the literature precedent,[5] our reaction conditions allow reaching an unprecedented synthetic scope, both in terms of compatible substrates and electrophiles. The influence and the role of the eco-friendly solvent on key elementary steps of the overall transformation are discussed, namely (i) metalation step through I/Zn exchange, (ii) Bu 1,2-migration and (iii) generation od a benzyl zinc intermediate after dearomatisation / rearomatisation / metallotropy chain.



Thanks to the French "Agence Nationale de Recherche" (ANR-19-CE07-0032) for financial support and grants to A.P. The L2CM is grateful to F. Dupire (MASSLOR Platform) for mass spectrometry analyses as well as the "Plateforme de RMN de l'Institut Jean Barriol, Universite de Lorraine".

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μ-Oxo Hypervalent Iodine(III) Catalysis in Oxidative Aromatic C-N Couplings

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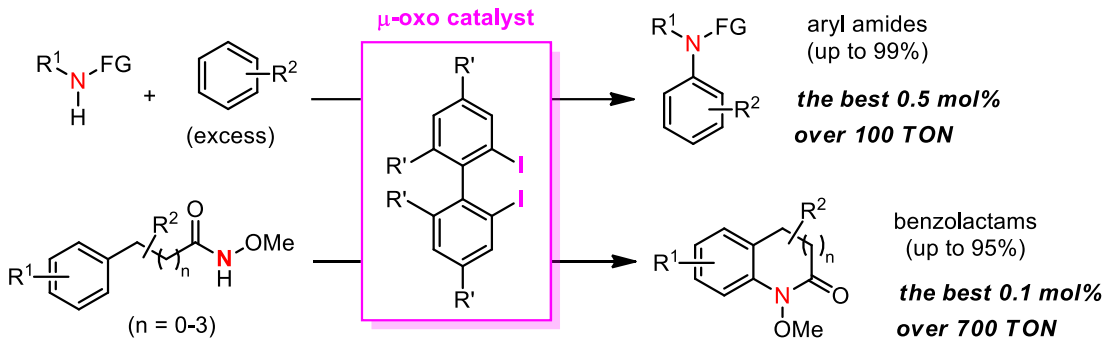
Hypervalent iodine reagent has become one of the promising tools in developing the dearomatization and oxidative coupling for aromatic compounds [1]. They have recently received significant attention in organic synthesis due to their low toxicity as well as the unique reactivities similar to the metal oxidants. On the other hand, stoichiometric amounts were always required for their use in these reactions, since discovery of the first hypervalent iodine compound (Willgerodt's reagent) more than 100 years ago. The catalytic utilization of hypervalent iodine reagent, in consideration of practical conceren, is a desired goal in 21st century.

In 2005, we reported the catalytic utilization of hypervalent iodine reagent for dearomatization of phenols and oxidative coupling of other aromatic compounds [2].

Herein, we would present the highly efficient hypervalent iodine catalytic strategy for the oxidative C-N bond forming dearomatizations and aromatic coupling reactions. The success key is our desinger μ-oxo hypervalent iodine catalysts, discovered by the extensive catalyst screening in developing asymmetric phenol dearomatizations [3]. The metal-free oxidative coupling initiated by the nitrogen atom activation, such as the oxidative amidation of aromatic rings, can smoothly proceed by this catalyst with very low catalyst loadings (less than 1 mol%) [4]. Recent investigation has revealed that our catalysts are applicable to a greener re-oxidizing system using peracetic acid (PAA), and electrolytic conditions for the oxidative aromatic C-N bond formations.



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Photochemical *in situ* Generation of Highly Reactive Alkyl Diazo Species

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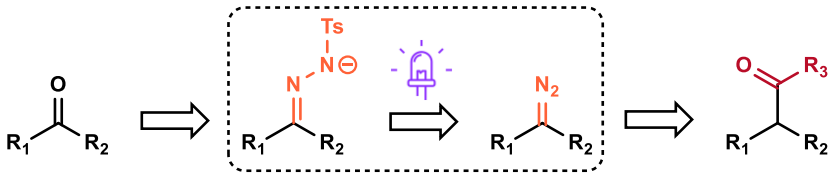
Ketones and aldehydes are one of the most prevalent functional groups in organic molecules. They are an essential part of many biologically active compounds, materials and can be used as one of the most basic organic building blocks for syntheses, especially polyketides. Therefore, gaining access to these groups is of high priority for organic synthetic chemists. While most approaches rely on oxidation or reduction of existing groups, combining carbon-carbon bond and carbonyl group formation is rather challenging, but offers great synthetic value. Thus, methods to directly access carbonyls by formal insertion into the aldehyde C–H bond have been topic of research over the last 100 years. Specifically, by combination of α-stabilized diazo compounds and transition metal catalysis β-keto esters can be generated from aldehydes. However, hazardous materials have to be isolated and handled and metal catalysis is still necessary, while the available scope of substrates is limited [1].

The associated risks can be eliminated by *in situ* generation of the active diazo species from hydrazones, but this brings new challenges such as long reaction times, high required temperatures and also limited suitable substrates. However, without the necessity to isolate the reactive compound, highly reactive unstabilized diazo compounds can be accessed and directly used for synthetic applications [2,3].

We developed a new system to safely and efficiently generate highly reactive unstabilized aliphatic diazo compounds *in situ*, by addition of base and light. Diazo species in this reaction participate effectively in C–H insertion of aldehydes, leading to the efficient synthesis of aldehydes and ketones. The reaction proceeds without the need of any transition-metal catalyst under light irradiation and features high functional group tolerance. More than 50 substrate examples demonstrate the broad applicability of this reaction sequence and these transformations are successfully performed on a gram-scale.



Scheme 1. Homologation by photolysis of tosylhydrazones and *in situ* generation of diazo compounds.

The project is partially funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - 426795949.

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Synthesis and photophysical properties of D-π-A aryl(thienyl)quinazoline fluorophores: the first step toward TADF materials

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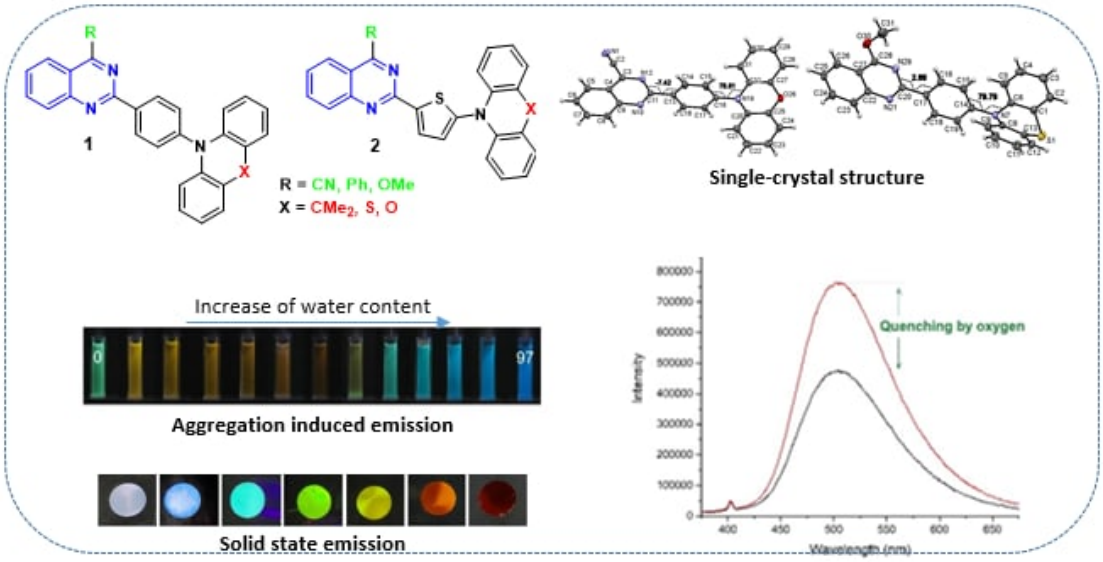
Over the past two decades, tremendous interest to OLED development has been increased from both academia and industry. Thermally activated delayed fluorescence (TADF) materials have received great attention due to their high performance and reduced cost.[1-4] OLEDs fabricated with quinazoline-based TADF emitter achieved good external quantum efficiency of ≈ 28% and current efficiency of 89.9 cd A^{-1}.[5]



Structures **1**, **2** based on 2-(thiophen-2-yl)quinazoline and 2-phenylquinazoline bearing an acridine, phenothiazine, or phenoxazine substituent have been developed. Target products were synthesized by Pd-catalyzed Buchwald-Hartwig cross-coupling reaction from the corresponding bromine derivative and dibenzoannulated azine. The effect of the substituent nature at position 4 of the quinazoline core on the photophysical properties was studied. The compounds demonstrated good quantum yields in solid state, aggregation induced emission properties, sensitivity to oxygen and emission solvatochromizm. The prospects for practical application of synthesized chromophores as TADF emitters were shown.

This work was supported by Russian Scientific Foundation (grant # 22-23-00006).

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Phosphonic acids from 1,2-benzoxaphosphorins and 1,2-benzoxaphosphorinphosphonates as analogues of bioactive compounds

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Phosphorus compounds have an extremely important and polyvalent functions, but their limited content and low solubility under physiological conditions are the reason for the growing interest in the synthesis of organophosphorus compounds.[1] The other direction is the study of their potential biological and physiological activity. Nowadays, organic synthesis is largely focused on obtaining analogues of important biomolecules and active substances that may have a regulatory or general effect on various metabolic pathways and physiological processes in organisms.

Selective dealkylation of the ester groups in 1,2-benzoxaphosphorins and 1,2-benzoxaphosphorine phosphonates presents the possibility of obtaining new representatives of phosphonic acids. The hydrolysis processes of the organophosphorus compounds for the synthesis of monophosphonic and diphosphonic acids show a dependence on the medium pH.[2] An alternative reaction is the dealkylation of phosphonate esters whereas the appropriate reagents are iodo-, bromo- and chlorotrimethylsilanes. The method is quantitative and allows the removal of alkyl groups in both anhydrous conditions and neutral medium in the presence of sensitive functional groups in the substrate.[3]

Acknowledgements: Authors are grateful to program "EUROPEAN SCIENTIFIC NETWORKS", funded by the Bulgarian Ministry of Education and Science as well the FNI project KP-06-M59/6 from 19/11/2021.

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Halohydrines as intermediates in the formation of enol phosphates and conjugate addition products with 2-Oxo-2H-1-benzopyrans

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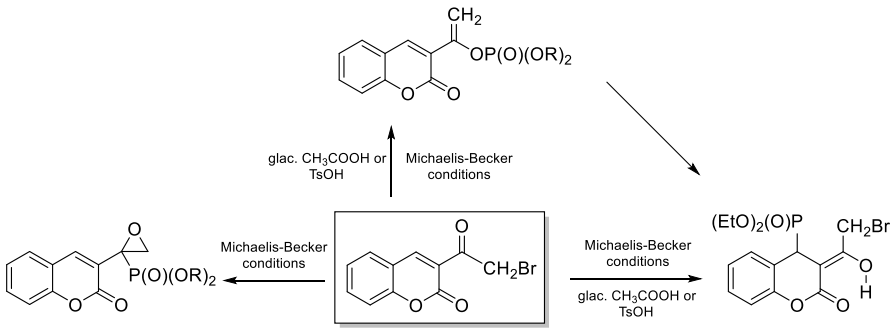
Phosphorus-containing coumarins have attracted much attention due to their wide biological activity due to the structural combination of benzopyrane and phosphonate or phosphate moieties. Among the known coumarins 3-(ω-bromoacetyl)coumarin plays a major role in the synthesis of divers bioactive compounds.

Transformations of 3-(ω-bromoacetyl)coumarin to enol phosphates, epoxy phosphonates and 1,4-addition products under Arbuzov and Michaelis-Becker reaction conditions as well as in the presence of glacial acetic acid or 4-toluenesulfonic acid were studied.[1,2] Among all, epoxy phosphonate esters have various applications in the synthesis of organic and bioactive compounds. They have attracted much interest due to their formation as intermediates under different reaction conditions and moreover have found broad application in the obtaining and modifying of some synthetic polymers.



Ring opening of coumarinyl-1,2-epoxy phosphonate esters under acidic conditions was performed. The chemical behavior of bromohydrins was examined under Michaelis-Becker reaction - conditions using dialkylphosphites.

Acknowledgements: Authors are grateful to program "EUROPEAN SCIENTIFIC NETWORKS", funded by the Bulgarian Ministry of Education and Science and the project № 80-10-28/10.05.2022 Sofia University "St. Kl. Ohridski".

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Ultrasound assisted homodimerization reactions of substituted 3-acetylcoumarins

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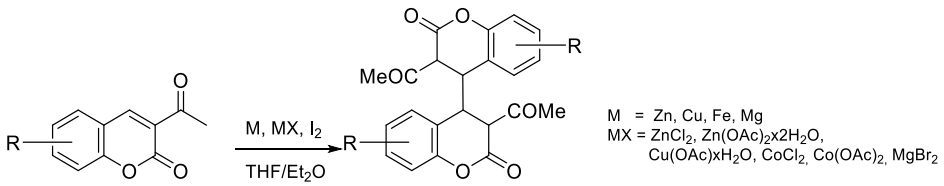
To develop effective anti-tumor drugs, many natural and synthetic biscoumarin derivatives have been examined and it has been found that they are involved in a number of biochemical processes. For example, some representatives of these heterocyclic group possess inhibitory action against number of enzymes such as kinases, telomerases, ureases, integrations, DNA polymerases, that plays a major role in the processes of tumor development and the spread of cancer cells.

Very few synthetic approaches are known in the literature to obtain biscoumarin structures, with most of the presented methods being multi-stage synthesis, electrochemical reduction, or electroreduction/hydration. The disadvantages of these methods are the long reaction time, the unsatisfactory yields, or the complex equipment necessary for the interaction.



1a **2a**

Here we present our research on the reaction condition optimization and new strategy to synthesize bis-3-acetylcoumarin as well as the progress on the preparation of substituted 3-acetylcoumarins' homodimers.

Acknowledgments: The authors are grateful to the Extreme Project within the program "EUROPEAN SCIENTIFIC NETWORKS", funded by the Bulgarian Ministry of Education and Science. This work was supported by National Science Fund project - KP-06-N-39/15 from 17.12.2019.

A Versatile Strategy for Isoindole N-oxides Synthesis by Palladium-Catalyzed C−H Activation of Aldonitrones

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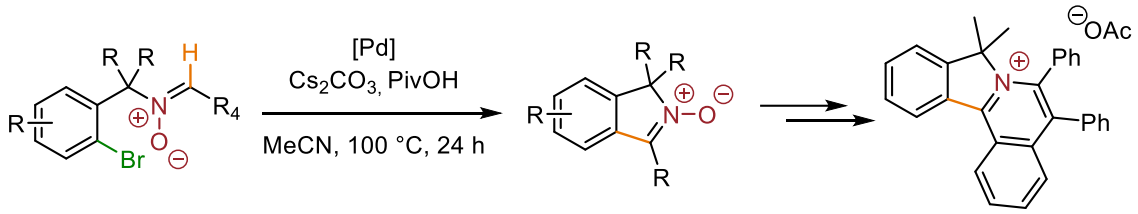
The isoindoles play an important role in the structural motif of natural and biologically active compounds.[1] However, the synthetic methodology of these compounds remains underexplored. In recent years, a few examples of isoindole *N*-oxide synthesis have been described: via metal-catalyzed activation or simple Michael addition.[2,3] Nevertheless, they are limited to specific substrates. Recently, we were focused on direct C−H functionalization of aldonitrones leading to diverse ketonitrones.[4] Based on our previous results, we decided to apply this atom-economical concept in the synthesis of isoindole *N*-oxides. The success was achieved by the use of a palladium-acid-based catalytic system. We prepared a broad spectrum of isoindole *N*-oxides in excellent yields and high functional group tolerance. The protocol was also found to be applicable to the synthesis of a complex isoindole *N*-oxide derived from (1*R*)-(-)-Myrtenal. Moreover, we demonstrated further modification of the nitrone moiety present in the isoindole *N*-oxide structure by the tandem rhodium-catalyzed C−H activation and subsequent 1,3-dipolar cycloaddition. To expand potential utility of this methodology, we also demonstrated the synthesis of novel 8*H*-isoindolo[1,2-*a*]isoquinolin-7-ium salt by simple derivatization of the ketonitrone structure. To gain mechanistic insight into the process of intramolecular C−H activation of aldonitrones we performed kinetic isotope effect (KIE) experiments.



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Rhodium (III)-Catalyzed C-H activation of Nitrones with Allyl Carbonates

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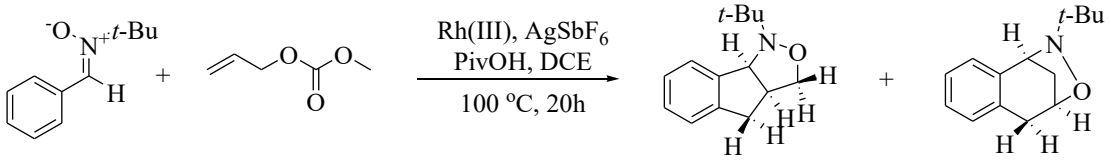
Among the most important processes in organic chemistry are reactions involving formation of new carbon-carbon bonds that make up the structural framework of the target organic compounds. In recent years, direct transition-metal-catalyzed arylation has undergone rapid development, becoming an excellent alternative to traditional cross-coupling reactions [1, 2]. Nitrones are highly useful and easily accessible compounds which are highly useful for synthesis of biologically important compounds such as β-lactams, unnatural aminoacids, alkaloids or amines [3]. They also serve as excellent directing groups for C-H activation of aryl rings [4]. Of particular interest are tandem processes involving nitrone-directed C-H activation and cross-coupling with allylic substrates, followed by intramolecular 1,3-dipolar cycloaddition [5]. We have developed an efficient corss-coupling intramolecular reaction (under cationic Rh(III) catalysis) of different aryl nitrones **1** with simple allyl carbonates **2** to obtain tircyclic heterocycles **3, 4**. We also aimed at the development of an asymetric variant of this process. The utility of our method is demonstrated by the formation of tricyclic heterocycles **3** as the main products.



1 **2** **3** **4**

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Silver-Promoted Direct Alkylation of Electron-rich (Hetero)arenes with Malonates

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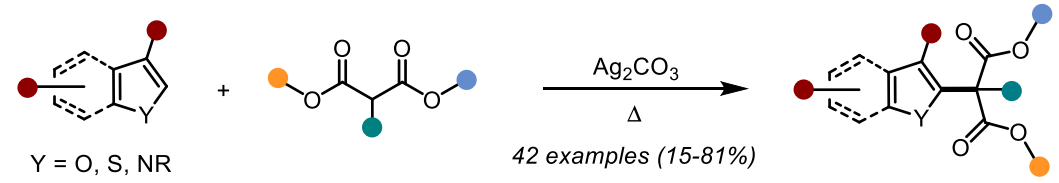
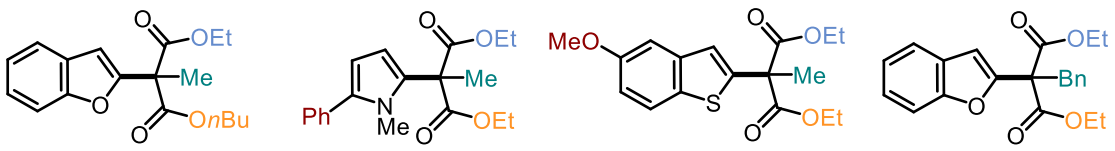
Regioselectively alkylated arenes are major starting materials and molecules relevant to most areas of science in which there is a need for small organic molecules. They are indeed used on a daily basis in the pharmaceutical, agrochemical and material sciences, and as building blocks for polymer chemistry or organic electronics. They also have had a profound effect in human health and many other sectors.

Despite their apparent simplicity, alkylated arenes are not that trivial to prepare, notably in terms of selectivity, efficiency and simplicity [1,2]. Therefore, novel synthetic methods for the efficient functionalization of (hetero)arenes are in ever-growing demand, alkylation protocols remaining one of the key transformations. While classical alkylation methods mostly rely on Friedel-Crafts protocols, Minisci-type radical additions, metalation processes or reactions involving substrate pre-functionalization, all exhibiting various challenges in terms of efficiency and selectivity, the direct functionalization via dehydrogenative cross-coupling remains rather restricted and understudied, despite an obvious potential [3,4].

With the objective to address these issues, we have developed a direct alkylation of electron-rich (hetero)arenes with simple, readily available and cheap malonate derivatives based on regenerable silver salts [5,6]. This procedure, that involves the activation of two C-H bonds, was found to be general and highly regioselective, and the respective products were smoothly submitted to late-stage modification steps. The development of this process and its scope and limitations, as well as its mechanism, will be discussed.



Representative examples



We gratefully thank the Federal Excellence of Science (EoS) program (BIOFACT, Grant No. O019618F), the Université libre de Bruxelles (ULB) and the Universiteit Antwerpen (UA).

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Total synthesis and enantioseparation of *(±)*-marinoaziridine B

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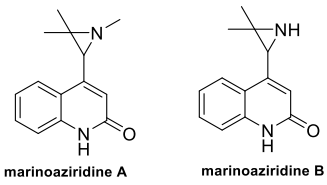
Marinoaziridines A and B (Figure 1a) are the first chiral aziridine-containing natural products isolated from Gram-negative bacteria from marine sediment [1]. Many aziridine-containing molecules demonstrate very useful pharmacological activity including anticancer, antibacterial, antimicrobial activity, etc. strongly indicating that the presence of the aziridine ring in natural as well as synthetic molecules is essential for such activities. Due to known activity as pharmacophore, aziridine moiety attracted considerable attention to medicinal and synthetic organic chemists [2,3]. Our research has been focused on the total synthesis of marinoaziridines A, B, and their derivatives with the determination of unknown absolute configuration and biological activity.

In this communication, we report the first total synthesis of racemic marinoaziridine B. Target compound was prepared in 6 steps by conventional reactions of organic synthesis. The route begins with the synthesis of two achiral fragments, which undergo a convergent coupling reaction of the achiral sulfur ylide derived from the sulfonium salt and the corresponding aldehyde to form the chiral epoxide as the key intermediate of our strategy. Regioselective ring-opening of the epoxide with sodium azide proceeded under acidic conditions to give the azidoalcohol which was then subjected to Staudinger reaction to give the desired marinoaziridine B. The conditions of enantioseparation of newly synthesized compound on polysaccharide chiral stationary phases based on amylose and cellulose derivatives were investigated using high performance liquid chromatography and supercritical fluid cromatography to perform the isolation of the enantiomers of marinoaziridine. The obtained results showed that the *Chiral ART Cellulose SC* stationary phase with selector cellulose *tris*-(3,5-dichlorophenylcarbamate) proved to be the best choice in the enantioseparation.

a) b)



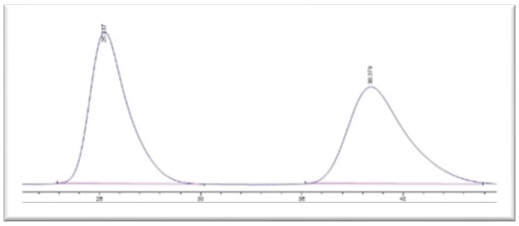


Figure 1. a) Structures of marinoaziridines A and B; b) HPLC enantioseparation of *(±)*-marinoaziridine B on *Chiral Art Cellulose SC* using dimethyl carbonate as a mobile phase.

ACKNOWLEDGEMENTS: The authors thank the Croatian Government and the European Union through the European Regional Development Fund - the Competitiveness and Cohesion Operational Programme (KK.01.1.1.01) for funding this research through the project Bioprospecting of the Adriatic Sea (KK.01.1.1.01.0002) granted to The Scientific Centre of Excellence for Marine Bioprospecting -BioProCro.

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Synthesis and enantioseparation of *syn*- and *anti*-3,5-disubstituted hydantoins by HPLC and SFC on immobilized polysaccharides-based chiral stationary phases

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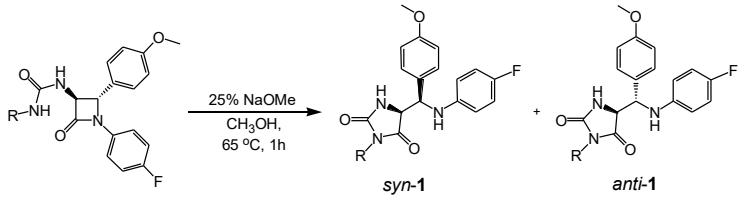
Imidazolidine-2,4-diones, also well known as hydantoins, are important heterocyclic compounds in organic chemistry [1]. The hydantoin moiety is an important structural scaffold present in a number of drugs (phenytoin, ethotoine, azimilide, dantrium, nilutamide, nitrofurantoin, etc) [2,3]. Hydantoin ring also constitute the core structure of various natural compounds from marine organisms but also from bacteria [3]. They display diverse and interesting pharmacological activities [2-5].

In conducted research the diastereomeric mixtures (*syn*- and *anti*-) of racemic 3,5-disubstituted hydantoins **1a-i** were synthesized *via* base-promoted intramolecular amidolysis of *trans*-β-lactam ureas in good yield, Scheme 1. The mixtures of diastereomeric hydantoins were then separated by preparative RP-HPLC. Each hydantoin product possesses two centers of chirality, one in the hydantoin ring and the other in the side chain.

The enantioseparation of synthesized *syn*- and *anti*-3,5-disubstituted hydantoins **1a-i** was investigated on three immobilized polysaccharide-based columns (CHIRAL ART Amylose-SA, CHIRAL ART Cellulose-SB, CHIRAL ART Cellulose-SC) by HPLC using *n*-hexane/2-propanol (90/10, v/v) or 100% dimethyl carbonate as mobile phases, respectively, and by SFC using CO_2/alcohol (methanol, ethanol, 2-propanol; 80/20, v/v) as a mobile phase. The chromatographic parameters, such as separation and resolution factors have indicated that Amylose-SA is more suitable for enantioseparation of the most analyzed *syn*- and *anti*-3,5-disubstituted hydantoins than Celullose-SB and Cellulose-SC in both HPLC and SFC modalities. All three tested columns showed better enantiorecognition ability toward *anti*-hydantoins compared to *syn*-hydantoins, both in HPLC and SFC modes. We have demonstrated that environmentally friendly solvent dimethyl carbonate can be efficiently used as the mobile phase in HPLC mode for enantioseparation of hydantoins on the immobilized polysaccharide-based chiral stationary phases.



1a, R = allyl-, *syn*/*anti* = 47.5:52.5
1b, R = hexyl-, *syn*/*anti* = 46.9:53.1
1c, R = cyclopentyl-, *syn*/*anti* = 48.2:51.8
1d, R = furfuryl-, *syn*/*anti* = 47.4:52.6
1e, R = $C_6H_5CH_2$-, *syn*/*anti* = 44.1:55.9
1f, R = 4-*tert*-Bu-C_6H_4-, *syn*/*anti* = 44.5:54.5
1g, R = 3-Cl-4-CH_3-C_6H_3-, *syn*/*anti* = 50:50
1h, R = 3,5-$(CH_3)_2$-C_6H_3, *syn*/*anti* = 51.0:49.0
1i, R= 2,6-$(CH_3)_2$-C_6H_3, *syn*/*anti* = 46.9:53.1

Scheme 1. Synthesis of racemic *syn*- and *anti*-3,5-disubstituted hydantoins **1**.

Acknowledgments: We would like to thank the Croatian Government and the European Union through the European Regional Development Fund - the Competitiveness and Cohesion Operational Programme (KK.01.1.1.01) for funding this research through the project Bioprospecting of the Adriatic Sea (KK.01.1.1.01.0002) granted to The Scientific Centre of Excellence for Marine Bioprospecting - BioProCro.

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Synthesis and investigation of hosting efficiency of emissive hydrazone-based macrocycles targeting fluorescent-based sensing applications

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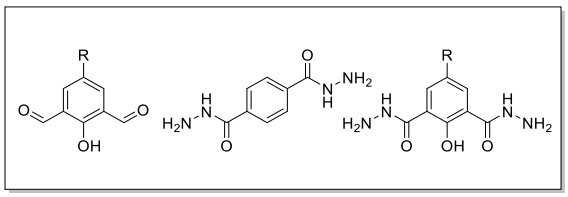
Macrocyclic compounds have attracted attention due to their evolution in structural design since first report of flexible crown ethers to rigid aromatic structures [1], mainly directed towards applications such as gas storage [2], separation technologies, catalysis, cation and anion sensors [3] or luminescent materials also useful for sensing. [4]

Dynamic chemistry has provided a useful tool for efficient identification and synthesis of macrocyclic hosts (synthetic receptors) through reversible imine, hydrazone or disulfide exchange reactions [5], enlarging the opportunities to develop structures with novel properties. Hydrazone-based macrocycles resulted using the principles of dynamic chemistry have been explored over the years for their formation under thermodynamic control and the possibility to be used as receptors for anions (F^-), metal ions (Ba^{2+}, Cd^{2+}) and organic small-molecules [5].

In this context, we used a pool of aldehyde and hydrazide building blocks to synthesize novel *N*-acylhydrazone macrocycles, investigate their structural features and the ability to encapsulate different guest molecules, from cations, anions and organic small molecules using NMR and HRMS. We noticed the ability of the macrocycles to emit light under irradiation and enhancement or quench of the luminescence by various guest molecules and we present the results we obtained in absorption and emission experiments.



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Tandem Diels-Alder-aza-Michael reaction - a new synthetic approach to rigid polycyclic guanidines

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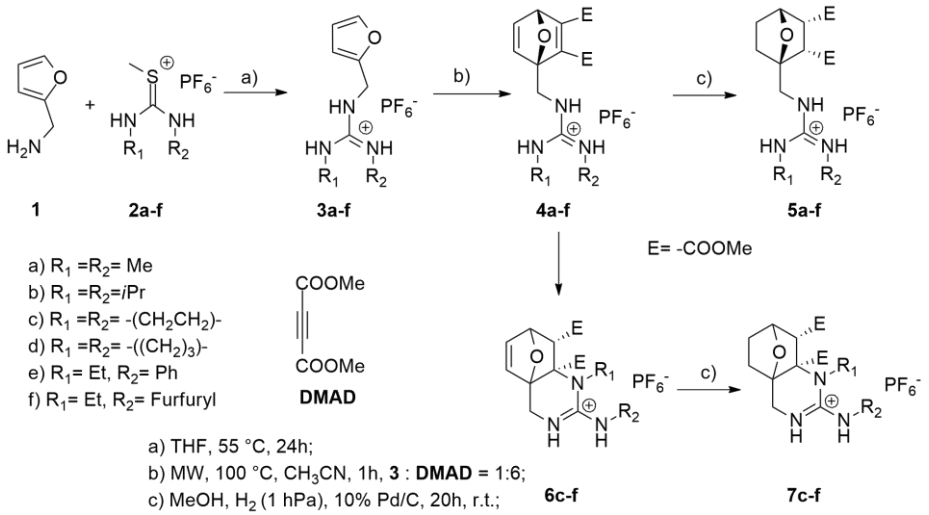
Oxanorbornane is bicyclic structural motif present in a variety of biological systems [1] and it can be used as glycomimetics [2], β-turn inducers [3], amphiphilic systems for drug delivery [4], etc. Such structures can be prepared by a variety of methods the main being cycloaddition/hydrogenation sequence starting from substituted furans [1]. This synthetic approach has a high atom economy and both of these steps in combination with easily available furan derivatives from biomass could be considered eco-friendly.

Herein, we report synthesis of a series of novel guanidine substituted oxanorbornanes by the cycloaddition/hydrogenation sequence. A special emphasis is laid on a tandem reaction encompassing cycloaddition/aza-Michael intramolecular addition what results in a formation of novel polycyclic guanidines. Efficiency of the intramolecular reaction is discussed in terms of the structural difference of the starting furfuryl guanidines **3a**-**3f**. To rationalize the experimental results, pK_a values as well as the reaction mechanisms were investigated by the DFT computational approach.



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Photoexcited Nitroarenes as Ozone & OsO_4 Surrogates

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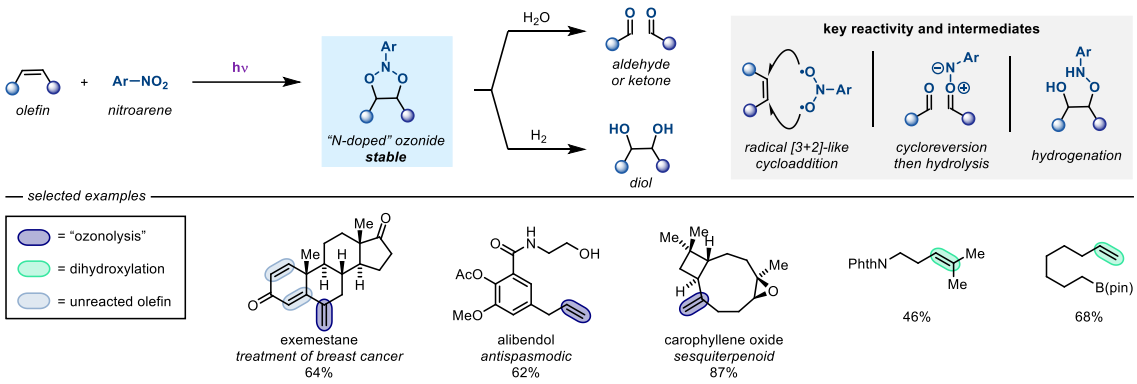
My PhD studies are focussed on the development of novel photochemical strategies for both the oxidative cleavage and dihydroxylation of olefins using photoexcited nitroarenes.

Olefin ozonolysis and dihydroxylation are two fundamental transformations in organic chemistry. Ozonolysis enables oxidative cleavage converting olefin feedstocks into valuable oxygenated materials. However, the explosive and uncontrolled reactivity of O_3 makes it restricted to specialised CROs and not applied to the oxidation of substrates containing multiple functionalities likes drugs and agrochemicals.

We have developed a novel approach to carry out this transformation by visible light irradiation of simple nitroarenes.[1] We have discovered that upon photoexcitation, the nitroarenes behave as ozone surrogates and undergo radical [3+2]-like cycloadditions with a broad range of olefins. While ozonides are explosive, the "*N*-doped" ozonide cycloadduct generated by our strategy is a stable solid and undergoes cycloreversion and hydrolysis to the resulting carbonyl products. This strategy has provided the first example of a "dosable" reagent displaying the same reactivity as ozone, and has been applied to the selective and high-yielding oxidative cleavage of complex and bio-active materials.

Furthermore, the "*N*-doped" ozonide cycloadducts can be converted to the corresponding 1,2-diols by hydrogenation in the presence of Pd/C.[2]

I will discuss the key mechanistic blueprints of these novel olefin functionalisation processes, highlight the broad scope currently developed, and explain the ability of these processes to discriminate between olefins in complex structures.



[1] Manuscript currently under review in *Nature*. (2) Manuscript in preparation.

A study on cyanine dyes coordinated with bis(fluorosulfonyl)imide anions for color filter of ultra-high resolution OLED display

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Recently, as ultra-high resolution OLED display is demanding top emission structure, color filter layer should be fabricated below 100°C to reduce thermal damage. The relatively low-temperature process allows use of dyes with moderate stability, not available in high-temperature process. In this study, we synthesized four novel red cyanine dyes[1] by introducing bis(fluorosulfonyl)imide counter anions for the color filter of ultra-high resolution OLED. The synthesized dyes coordinated with anions were identified by 1H, 19F NMR analysis and cold spray-LC-TOF-MC. In addition, stability and optical property of the dyes were analyzed through TGA and UV-vis spectroscopy respectively, and solubility in industrial solvent was measured. The dyes showed narrow and strong absorption as well as improved stability and solubility compared to conventional cyanine dye. The improved photo-stability is might be attributed to stabilizing and large shielding effects of weakly coordinating anions from the singlet oxygen[2,3]. Furthermore, the color filter was fabricated with the dye with excellent properties and its spectral property was investigated. From the results, it is expected that the dye could be one of the promising candidates as a red colorant for the color filter of ultra-high resolution OLED display.

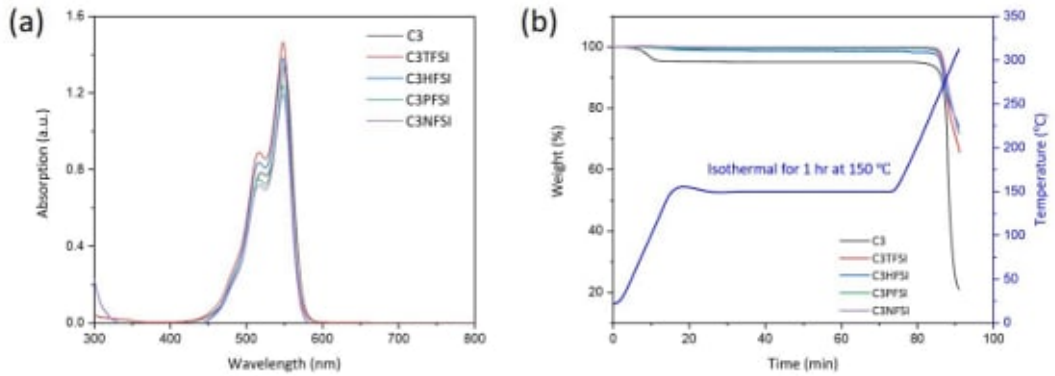

Figure. (a) Absorption spectra and (b) TGA curves of cyanine dye(C3) and synthesized dyes(C3TFSI, C3HFSI, C3PFSI, C3NFSI).

Thanks to This work was supported by the Industrial Technology Innovation Program (20016178, Development of dye-pigment hybrid color resists for ultra high resolution over 4000PPI high-luminosity AR/VR displays) funded By the Ministry of Trade, Industry & Energy(MOTIE, Korea).

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Chemoselective CuAAC Reaction using Miscibility Difference in Water

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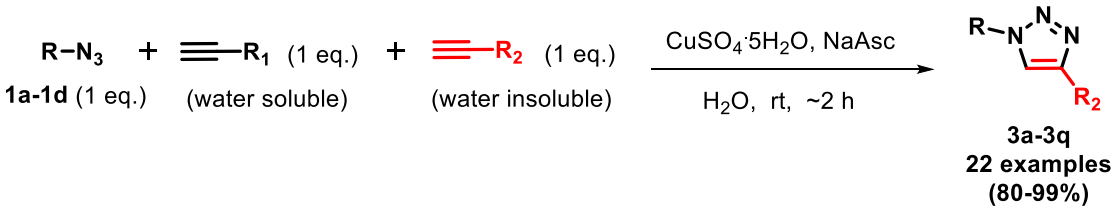
The copper-catalyzed azide-alkyne 1,3-cycloaddition (CuAAC) reaction has received enormous attention as a powerful tool to form 1,4-disubstituted-1,2,3-triazoles easily and conveniently. Recent research on CuAAC reaction have endeavored to improve a method for synthesizing chemoselective triazole by using the difference in reactivity or chelation effect between the azide and alkyne groups [1,2]. Several groups have employed diyne substrates by introducing a temporary masking group on one of the alkyne groups [3]. In addition, a combination of the CuAAC and SPAAC (strain-promoted azide-alkyne cycloaddition) reactions can make it possible to control the chemoselectivity [4].

This study conducted a simple competitive reaction of hydrophilic/hydrophobic alkynes with water using miscibility difference to accomplish the chemoselective CuAAC reaction. We focused on the hydrophobic interactions between nonpolar reactants in water, which can improve chemical reactivity [5]. When both a hydrophilic and a hydrophobic alkyne existed, organic azides primarily reacted with the hydrophobic alkyne due to the hydrophobic effect on water. As a result, chemoselective triazole could be obtained under the typical $CuSO_4$/sodium ascorbate catalytic system. This synthetic strategy is an eco-friendly method that can synthesize chemoselective triazole in the water, so it is expected to apply to various fields.



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THIOUREA BASED TRITOPIC ACCEPTORS FOR HALOGEN BONDING

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Halogen bonding has been a known phenomenon for a long time, but the actual definition of the halogen bond was given not until 2013 by IUPAC [1]. The research about halogen bonding has grown almost exponentially in the last decade, there is still lots to discover, for example in the fields of supramolecular chemistry, molecular recognition, material sciences, crystal engineering and medicinal chemistry. Earlier studies have shown that small commercially available thiourea based compounds can act as halogen bonding acceptors and form easily crystallizable complexes, for example with different diiodotetrafluorobenzenes [2-3]. Inspired by this we wanted to design and synthesize multidental halogen-bonding acceptor molecules and study their halogen bonding properties with x-ray diffraction. Intermediate isothiocyanate products of our chosen synthesis path are usually synthesized with primary amines reacting with thiophosgene, but we decide to use less toxic reagents and carry out the synthesis with potassium thiocyanate and two different brominated 2,4,6-trialkyl-1,3,5-tris(bromomethyl)benzenes [4]. During the synthesis we found out that thiocyanate can react two different ways, either forming wanted isothiocyanate product or thiocyanate side product. Considering these findings, we decided to perform series of test reactions to understand better the behavior of thiocyanate in this reaction.

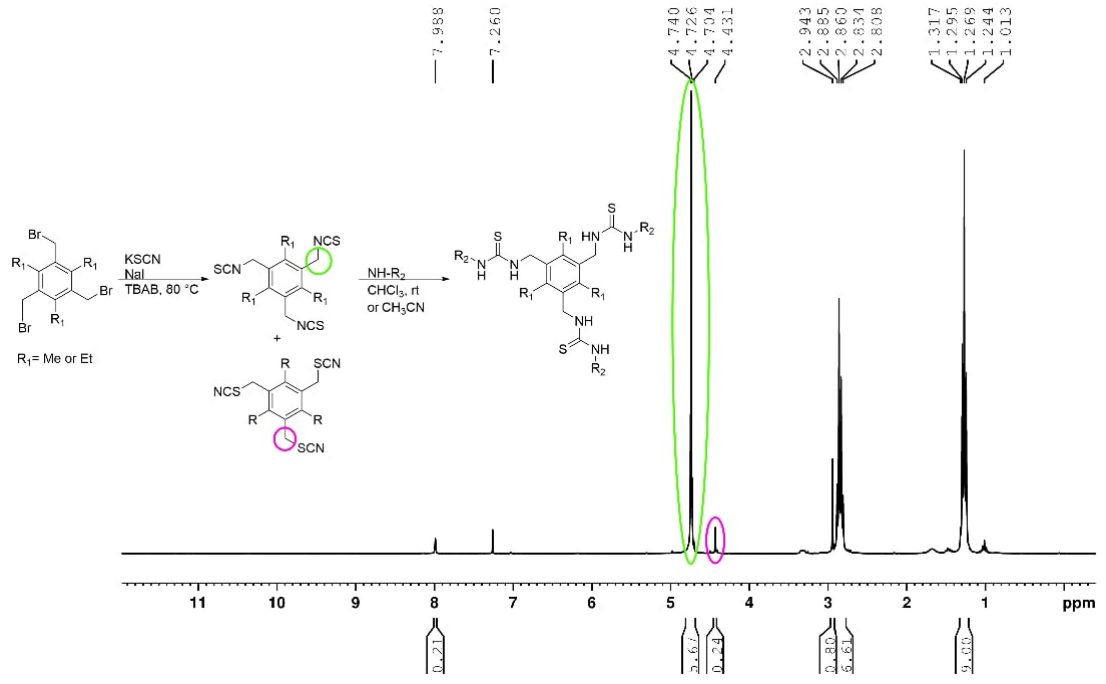

Figure 1. Reaction path of tritopic halogen bonding acceptors and ^{1}H NMR spectra of intermediate product showing side product formation.

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Cyclodextrin polymeric fibers

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Fiber materials are currently a very effective tool in tissue engineering that uses them to create tissue scaffolds. Therefore, one of the challenges today is to modify the fibers with bioactive molecules to make them more effective in this area. However, in order to functionize fibers from conventionally spun polymers, it is usually necessary to optimize this step for each bioactive substance separately[1]. Cyclodextrins are already commonly used as carriers of bioactive substances and can fulfill this function even if they are part of the fibrous material[2–4]. The possibility of cyclodextrins to be modified by many different bioactive compounds is not only easy but also fast[5]. Therefore, the preparation of cyclodextrin fibers represents a way to prepare a fully functional and at the same time universal material usable for the scaffolds. Although such materials are already being prepared, toxic substances (e.g. epichlorohydrin) are used for their synthesis[6]. This project is focused on the preparation of fibers composed of cyclodextrins crosslinked with citric acid, i.e. substances of natural origin.

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CO2-mediated monoacylation of symmetric diamines

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Symmetrical diamines are important but under-utilized substrates for conjugation of different residues due to the high selectivity of bis-amide formation when activated acid chlorides acylation agents are used. We demonstrate the strong affinity of diamines towards CO2 as an effective inhibitor of the di-acylation. This inhibition effect is prevalent in different low dielectic constant solvents and indifferent towards diamine carbon chain length. The practical application of CO2-mediated unsymmetric acylation is shown with various acylation agents.

Facile microwave-assisted syntheses of *N*-functionalized pyrrolidine-fused chlorins

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Chlorins are ubiquitous tetrapyrrole macrocycles, a class of natural pigments so important for life on earth. Chlorins are typically obtained by derivatization of porphyrins through hydrogenation, cycloaddition, and annulation approaches [1]. 1,3-Dipolar cycloaddition reactions offer a very simple and useful method for the preparation of chlorins with five-membered rings and this approach has been successfully applied to many porphyrins and analogues [2,3]. Reaction of glycine with paraformaldehyde yields an azomethine ylide that can react at the β,β'-pyrrolic double bonds of the porphyrin macrocycle resulting in a pyrrolidine-fused chlorin bearing a secondary nucleophilic amine (**C1**, figure 1) with great potential for bio-imaging [4] and bioconjugate synthesis [5].

Encouraged by these recent works [4, 5], we pursued research involving the microwave assisted *N*-alkylation of the pyrrolidine-fused chlorin **C1** (and its corresponding Zn(II) complex) with 1,4-diiodobutane (**C2**), methyl 4-(bromomethyl)benzoate (**C3**), *N*-(2-bromoethyl)phthalimide (**C4**), 2-bromoethylamine hydrochloride (**C5**) and dansyl chloride (**C6**) to obtain functional pyrrolidine-fused chlorins (figure 1). It was possible to obtain the *N*-substituted chlorins within 5 to 30 minutes at 60–80 °C and with yields between 47 and 89%. Because of the simplicity of this approach, we believe it will enable the access to a wide library of custom-tailored *N*-functionalized chlorins.

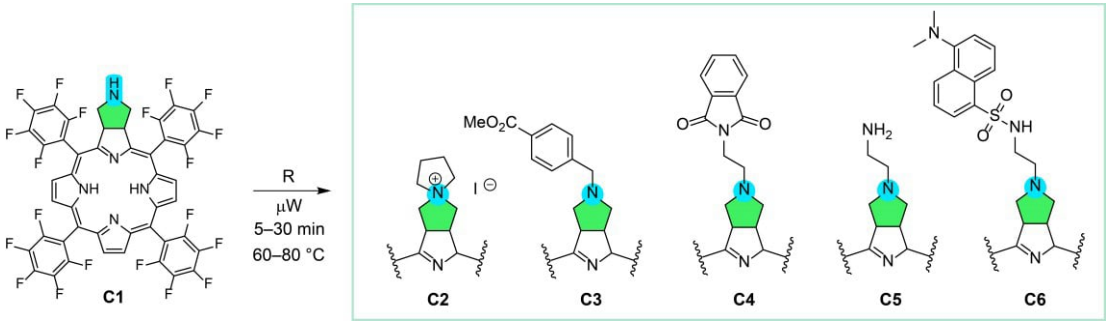

Figure 1 – MW-assisted *N*-alkylation of chlorin **C1** with R = 1,4-diiodobutane, **C2**; R = methyl 4-(bromomethyl)benzoate, **C3**; R = *N*-(2-bromoethyl)phthalimide, **C4**; R = 2-bromoethylamine hydrochloride, **C5** and R = dansyl chloride, **C6**.

This work received financial support from the project EXPL/QUI-OUT/1554/2021. We also thank National Funds (FCT/MCTES), under the Partnership Agreement PT2020 through projects NORTE-07-0162-FEDER-000048, UIDB/50006/2020, UIDP/50006/2020 and the project PTDC/QUI-QOR/29426/2017 (X-Sensors). J. Almeida acknowledges FCT and ESF (European Social Fund) through POCH (Programa Operacional Capital Humano) for his PhD grants (PD/BD/142868/2018 and COVID/BD/152681/2022). A. M. G. Silva thanks FCT for funding through program DL 57/2016 – Norma transitória. The research team would like to thank the valuable contribution from Alexandre Seabra and Rodrigo Monteiro.

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Nickel-Catalyzed Asymmetric Synthesis of α-Arylbenzamides

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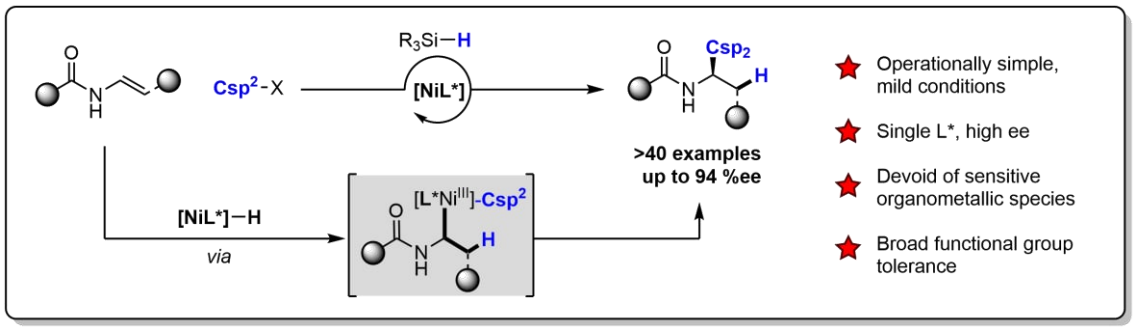
α-Arylbenzamides are ubiquitous motifs in bioactive molecules such as anti-cancer agents, SARS-CoV PLpro inhibitors and anti-depressants among many others. Access to enantiomerically enriched versions of these motifs is nonetheless far from straightforward. Known methods, such as C-N couplings between carboxylic acid derivatives and chiral α-aryl substituted amines, hydrogenations of vinyl benzamides, or opening of N-acylaziridines often suffer from a limited reaction scope, relatively harsh conditions and risk of epimerization. Recently, a mild Ni/photoredox dual catalyzed α-arylation of benzamides has been realized [1]. Alternatively, a three-component formal hydroarylation reaction involving readily available vinylbenzamides, arene halides and an H source can be employed.

Here, we present a highly efficient hydroarylation of *N*-vinyl benzamides under chiral Ni-catalysis allowing for the mild and operationally simple synthesis of enantioenriched α-arylbenzamides [2]: In continuation of our group's efforts in the difunctionalisation of olefins [3,4], we envisioned the activation of a silane with nickel in combination with a chiral bisimidazoline ligand to produce, upon addition to the double bond of *N*-vinyl benzamides, a chiral Csp^3-Ni(I) intermediate. Further, aryl halide precursors are activated via oxidative addition, forming a chiral alkylaryl-Ni(III) complex outcompeting the potential direct reduction of the Csp^2-X precursors. The C-C bond-forming reductive elimination occurs regioselectively at the internal position of the olefin delivering the new stereogenic center with high levels of stereocontrol. Control experiments and DFT studies were performed to gain insights into the reaction mechanism and confirmed the beneficial neighbouring effect by the amide group.

With over 40 examples we could successfully demonstrate the efficiency of our approach yielding a broad variety of the desired chiral amides in good yields and with high stereoselectivity. Subsequent derivatization of the target molecules enables the straightforward assembly of pharmacologically relevant scaffolds.



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Unified Bioinspired Approaches toward complex pyrazinoquinazoline alkaloids total synthesis

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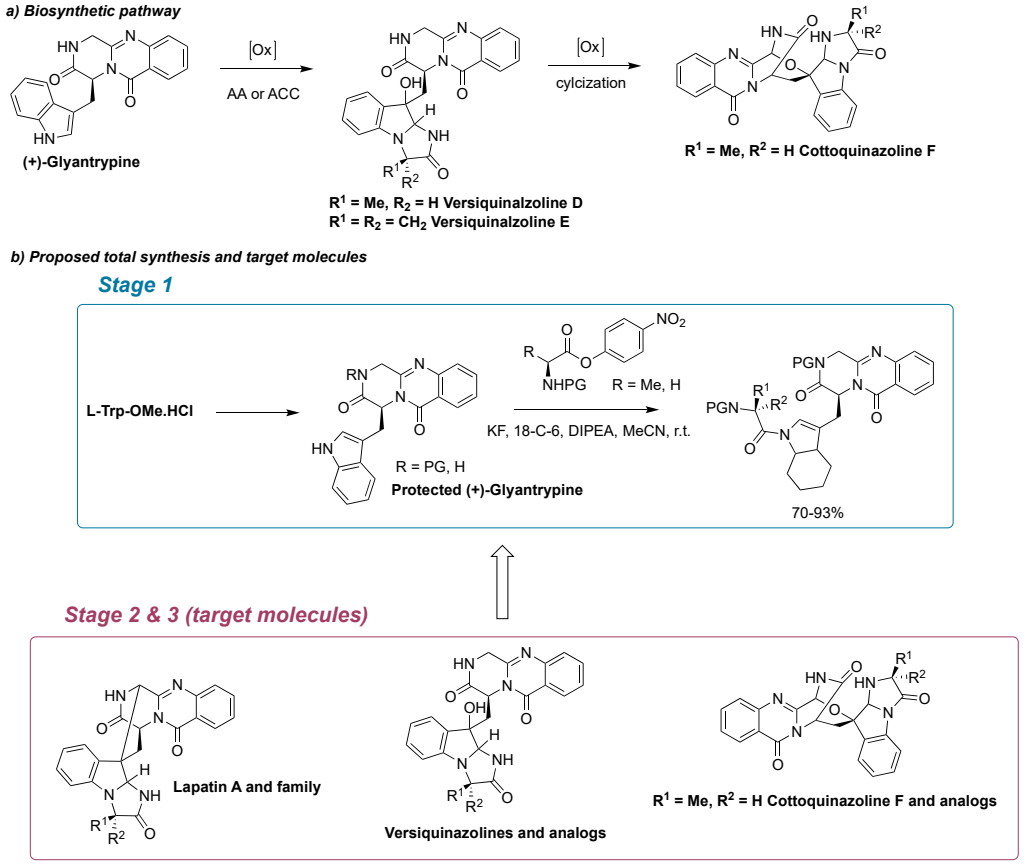
The pyrazino[2,1-b]quinazoline-3,6-dione motif is the core fragment found in many terrestrial and marine fungal metabolites showing interesting biological properties and therefore might serve as powerful chemotherapeutic agents [1, 2]. (+)-Glyantrypine, which contains such motif, was proposed as the biosynthetic precursor of numerous of them [2] (scheme 1). The biosynthetic studies support that through an intermolecular condensation with amino acids followed by further oxidation-cyclisation Versiquinazolines D and E are obtained. The total synthesis of Fumiquinazolines family, slightly differing from glyantrypine-based alkaloids in structure, has been achieved by Snider and Zeng but involved long 13-16 step synthesis [3]. Our proposed total synthesis for the Versiquinazolines D and E, Cottoquinazoline F and Lapatin A families consists of a bioinspired diversity-generating three-stage approach (scheme 1): sysnthesis of (+)-glyantrypine and its acylation with diverse protected amino acids (stage 1) followed by bioinspired oxidation/amination strategy (stage 2), base-mediated oxygenation and substitutive cyclization (stage 3).



Scheme 1. a) Biosynthetic pathways to Versiquinazolines D, E, Cottoquinazoline F, b) Total synthesis strategy and target molecules.

This work is supported by the Grant Agency of Czech Republic (GA ČR) (Project: 21-30730S) and IOCB (RVO:61388963).

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New derivatives procedures for determination of biogenic amines in food after lactic acid fermentation

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Biogenic amines (BAs) are nitrogen compounds formed mainly by the decarboxylation of amino acids or the amination and transamination of aldehydes and ketones. BAs can be found in all foods that contain proteins or free amino acids, including fish, meat, dairy, wine, beer, vegetables, fruits, nuts, and chocolate. In unfermented foods, the presence of biogenic amines is generally undesirable and may suggest the appearance of unwanted microorganisms. On the other hand, many types of microbes can be expected in fermented foods, some of which are capable of producing Bas.

BAs are food components capable of causing adverse toxicological reactions and poisoning harmful to health. It is important to develop fast and effective methods for their quantitative analysis in food. Most of the biogenic amines in their structure do not contain chromophore groups that would allow direct analysis using the RP-HPLC method with a spectrophotometric or fluorimetric detector. Therefore it is essential to convert the amines into appropriate derivatives.

In the presented research, the synthesis of reagents reacting with BAs was developed. Apart from enabling their analysis by RP-HPLC, they are also soluble in water. As a result, after the amines are reacted with the reagent, the reaction mixture can be analyzed directly by RP-HPLC without isolation of products and undesirable compounds affecting the chromatographic separation process.

The developed reagents are sulfonates of benzaldehyde which lead to the formation of imine products. The halogenphenyl sulfonates are the second proposed group of reagents that form derivatives of BAs by the nucleophilic substitution on the aromatic ring.

Financial assistance
The work was financed entirely by the project "Initiative of Excellence - Debuts" project number: 4101: 00000066.

Enhancing Bicyclic-Aziridines Potential Through Enzymatic Kinetic Resolution in Flow

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The demand for enantiomerically pure compounds in the pharmaceutical industry increases the complexity of the synthetic routes. Among the methodologies to obtain enantiopure compounds, lipase mediated kinetic resolution offers a green process, with a well-established route, distinct advantages of high activity, selectivity, and mild operating conditions. [1]

α-hydroxycyclopenteno-aziridines (bicyclic-aziridines) are an intermediary to achieve molecules with biological properties such as functionalized aminocyclopentitols (*e.g.,* peramivir, ticagrelor, neplanocin A and trehazolin).[2] The bicyclic-aziridines are obtained in a racemic mixture through a photochemical transformation of pyridinium salts, for which we developed a flow reactor for gram-scale preparation. [3] These bicyclic-aziridines have a free secondary alcohol in their structure, allowing for an enzymatic kinetic resolution, which could be achieved by using Novozym 435, an immobilized lipase, CAL B. The obtention of enantiopure bicyclic-aziridines unlocks synthetic routes to complex chiral structures.

We herein disclose the enzymatic kinetic resolution of two bicyclic-aziridines: allyl bicyclic-aziridine and butyl bicyclic-aziridine, from early batch studies to flow (Figure 1 (B,D) and (C, E)).
We successfully obtained with short residence times (*S*)-allyl bicyclic-aziridine 98% enantiomeric excess (*ee*) and 46% isolated yield (Figure 1(C)), as well the obtention of (*R*)-butyl bicyclic-aziridine acetate in 95% *ee* and 20% isolated yield (Figure 1(B)).

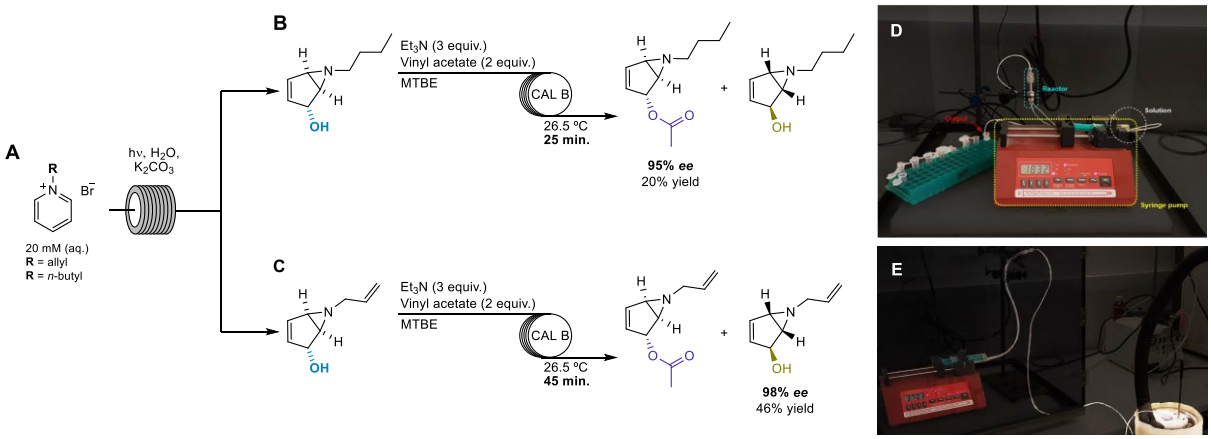

Figure 1. Obtention of enantiomeric pure bicyclic-aziridines: (A) Photochemical transformation of pyridinium salts in flow; Enzymatic kinetic resolution of (B) butyl-bicyclic -aziridine and (C) allyl-bicyclic -aziridine. Flow setup of enzymatic kinetic resolution (D) and (E).

Thanks to Fundação para a Ciência e Tecnologia (FCT) for financial support (2021.06598.BD, PTDC/QUI-QOR/32008/2017, UIDB/04138/2020 and UIDP/04138/2020). The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951996.

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Sustainable and highly controlled aryl couplings revealed by systematic assessment of photoactivatable linkers

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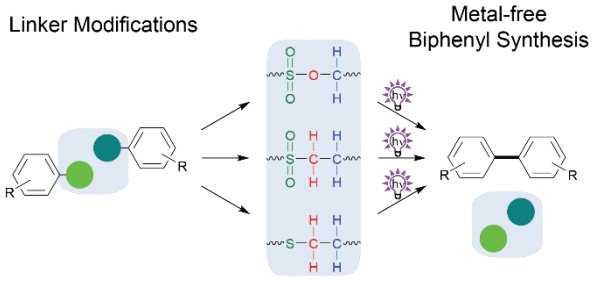
The controlled synthesis of biphenyls, which play a prominent role in pharmaceuticals, agrochemicals, and liquid crystals, typically requires hazardous organometallic reagents, aryl halides, and heavy metal catalysts. We recently reported a metal-free, photochemical alternative ("photosplicing") for the selective preparation of a wide range of pharmaceutically important biphenyls.[1] Whereas the traceless sulfonamide linker enables and controls the aryl coupling, unwanted toxic byproducts are released. Therefore, we designed over 25 different temporary linkers and tested them for their suitability for the photosplicing reaction in a flow reactor. We found that a surprisingly high number of functional groups enable light-induced aryl fusion and identified a number of linkers for environmentally friendly procedures. We also report that a thiol-ene (click) – photosplicing sequence enables a convenient route to biaryls such as liquid crystals. This work sheds light on thus far neglected photochemistry of temporary linkers, reduces toxic byproducts, and expands the available starting materials for metal-free biphenyl synthesis.[2]



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Electrochemical reduction of C-S bonds

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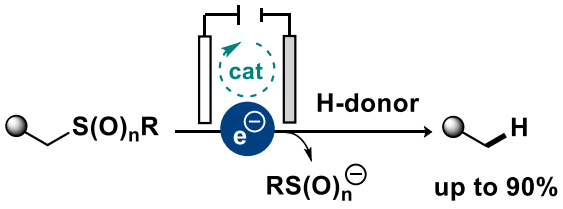
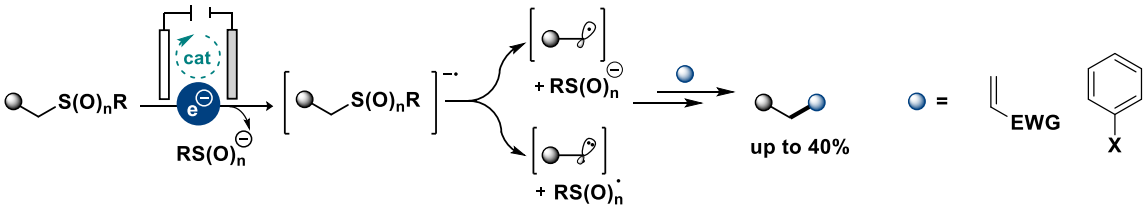
We target the formation of C-centered radicals via electrochemical reduction cleaving C-S bonds that is promoted by the use of a metal complex. Cleaving the bond in the presence of a hydrogen donor results in the alkane product, with results up to 90%.



The formed reaction intermediate can also be captured in a C-C bond forming reaction, with preliminary results up to 40%. Which intermedate that is formed seems to be highly substrate dependent.



Lewis Base-Brønsted Acid Co-catalyzed Morita-Baylis-Hillman Reaction of Cyclic Sulfamidate Imines

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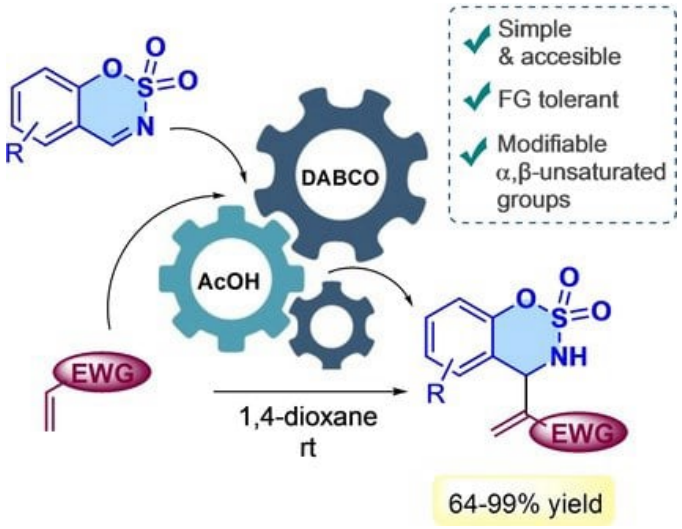
Cyclic sulfamidate imines have received increasing attention as very promising precursors for the synthesis of heterocyclic compounds that possess important biological activities.[1] Therefore, the development of new efficient organocatalytic methods for the synthesis of cyclic sulfamidate derivatives with construction of a new carbon-carbon bond between the α-position of an activated imine is still extremely desirable. Additionally, despite advances in the synthesis of sulfamidates bearing α,β-unsaturated moieties, the Morita-Baylis-Hillman reaction of cyclic sulfamidate imines[2] with simple acrylate-type Michael acceptors remains unexplored.

Within the project,[3] a highly efficient Lewis base-Brønsted acid co-catalyzed Morita-Baylis-Hillman reaction of cyclic sulfamidate imines with acrylate-type Michael acceptors by combination of DABCO and acetic acid as equimolar co-catalytic system has been developed. The described approach allows a straightforward access to a variety of 6-membered ring sulfamidates and a sultam derivative bearing α,β-unsaturated chains, involving a wide range of acrylates, as well as acrylonitrile and methyl vinyl ketone. The synthetic utility of the method was finally demonstrated by performing a gram scale reaction and further functionalization of the MBH-adducts.



The German Academic Exchange Service (DAAD) is gratefully acknowledged for generous support.

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A Metal-free Multicomponent Strategy for Amidine Synthesis

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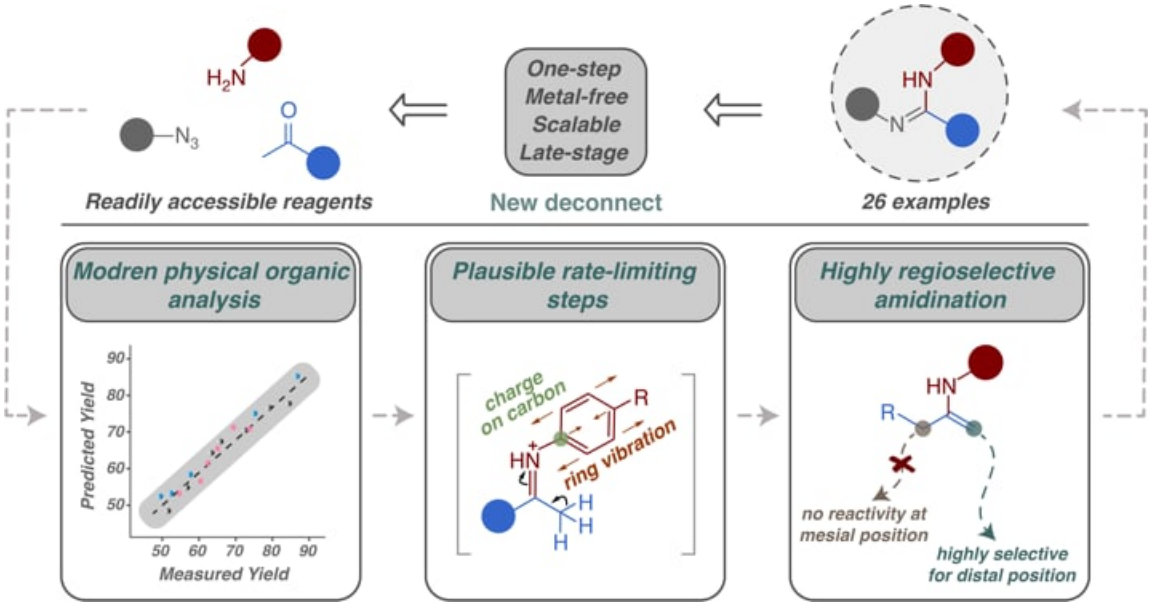
a) Ben-Gurion University of the Negev; b) Institute of Chemical Research of Catalonia (ICIQ)

ABSTRACT: Amidines are a ubiquitous class of bioactive compounds found in a wide variety of natural products; thus, efficient strategies for their preparation are in great demand. Specifically, their common structural core decorated with three substituents, set amidines as perfect candidates for multicomponent synthesis. Herein, we present a highly modular metal free multicomponent strategy for the synthesis of sulfonyl amidines. This work was focused on selecting readily accessible reagents to facilitate the *in situ* formation of enamines by the addition of amines to ketones. These components were coupled with azides to provide a broad reaction scope with respect to all three coupling partners. Aromatic and aliphatic amines and ketones were tolerated under our reaction conditions. Likewise, the presence of a methyl group on the ketone was critical to reactivity, which was leveraged for the design of a highly regioselective reaction with aliphatic ketones. A biologically active compound was successfully synthesized in one step, demonstrating the practical utility of our methodology. Finally, the postulated mechanism was investigated and supported both experimentally and by means of a multivariate statistical model.



Constitutional Dynamic Networks of Covalent Organic Macrocycles and Cages: Self-Sorting and Orthogonal Switching

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1)Institut de Science et d'Ingénierie Supramoléculaires (ISIS), Université de Strasbourg, France ; 2)Lehn Institute of Functional Materials, School of Chemistry, Sun Yat-sen University, China

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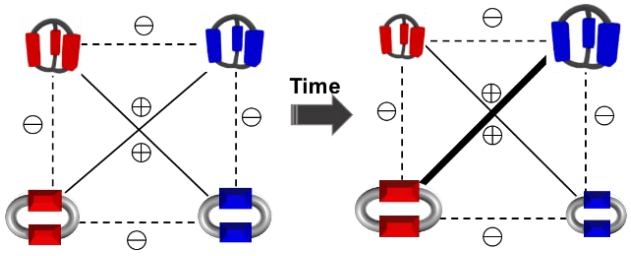
Self-sorting is chemical process that screens the permutations and combinations of different components. It selects as well the optimal ones to generate specific organized structures, which present thermodynamically optimal constitutions and could be involved in particular molecular recognition processes. Reversible dynamic connections, dynamic covalent bonds or dynamic non-covalent interactions are the possible chemical "vehicles" that allow error corrections during the formation of the self-sorted entity. These complex transformations selectively give access to the generation of the thermodynamically favored constituents from multicomponent libraries.

Here, we present the simultaneous generation of macrocycles and macrobicycles which are based on reversible imine bond formation from dynamic covalent libraries (DCLs). By operating through both kinetic and thermodynamic properties, self-sorting systems are allowed to reveal the occurrence of kinetic switching via component exchange in the course of the formation of macrocycles and macrobicyclic cages. This behavior endows an orthogonal amplification and switching among constituents in the diagonal of their associated [2×2] constitutional dynamic networks (CDNs).



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A 3D oxalate-bridged [$Cu^{II}Fe^{II}$] network as a photocatalyst and precursor for the preparation of $CuFe_2O_4$ spinel oxide

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In recent years, great efforts have been made to develop new metal-organic frameworks (MOFs) and coordination polymers (CPs) with photocatalytic potential, especially with respect to the development of photocatalysts for organic pollutant degradation, CO_2 reduction, and water splitting for H_2 production. Compared to conventional metal oxide semiconductors, well-defined and tailored structures of MOFs offer great advantages for understanding the structure-activity relationship. Their high porosity enables the exposure of active sites for catalysis and facilitates the transport of substrates by creating short migration paths for charge carriers prior to their reaction with substrates, thus improving electron-hole separation.[1]

The use of heterometallic complexes or frameworks containing more than one metal as single source precursors provides simplified synthetic routes through one-step thermal decomposition to form mixed metal oxide materials. The advantage of a solid phase transition is the retention of the elemental composition defined by the molecular precursor with only a loss of volatile decomposition products – allowing excellent stoichiometric control of the intermetallic ratio in the oxide products. It is known that the release of organic gases affects the particle size and porosity of the produced oxide; a higher content of organics in the starting materials allows larger porosity and smaller particle sizes in the decomposition products. In addition, control of the heating rate is important to control decomposition and avoid melting/vaporisation of molecular species that can occur with rapid heating. High temperatures also determine the crystallinity, particle size and porosity of the produced materials, limiting the ability to develop specific properties for applications. By using lower synthesis temperatures, oxides with small particle sizes and large surface areas can be produced.[2]

Since it is known that Fe–O clusters can be directly excited by visible light[3], leading to more efficient use of solar energy, and that compounds with iron are much cheaper due to the abundant Fe element on Earth, an oxalate-bridged heterometallic coordination polymer $[Cu^{II}(H_2O)(terpy)Fe^{II}_2(C_2O_4)_3]_n$ (terpy = 2,2′:6′,2″-terpyridine) with a three-dimensional (3D) network[4], was tested as a photocatalyst for the photodegradation of Rhodamine B (RhB) and methylene blue (MB). The optical band gap and photocatalytic activities were studied in detail.

This 3D network $[Cu^{II}Fe^{II}_2(H_2O)(terpy)(C_2O_4)_3]_n$ was also tested as a single molecular precursor for the preparation of spinel oxide $CuFe_2O_4$ due to the suitable metal ratio. The oxalate group, $C_2O_4^{2-}$, easily decomposes at low temperatures into gaseous CO_2 and CO, and therefore the oxalate-based solids can serve as suitable precursors for oxides. The (micro)structural, optical and photocatalytic properties of the (nano)crystalline spinel $CuFe_2O_4$ samples, prepared for the first time by a simple molecular precursor-to-material route, were presented.

ACKNOWLEDGEMENTS: This work has been supported by the Croatian Science Foundation under the project IP-2019-04-5742.

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The influence of alkyl-substituted ammonium cations on the structural arrangements and proton conductivity of the oxalate-based compounds of iron(III)

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Proton conductivity has recently been considered as a new functionality of the metal-organic compounds because they are crystalline, can be designed and tuned in structure and properties, and have high porosity. The simplest method to introduce proton carriers is to incorporate a counterion such as hydronium (H_3O^+), ammonium [NH_4^+, $(CH_3)_2NH_2^+$,...] or an anion (SO_4^{2-}), resulting in charged compounds. The counterions form the hydrogen bonds with the guest water or other constituents of compound, creating proton-conducting pathways composed of hydrogen-bond networks. Conductivity can also be achieved by introducing functionalized structural components such as non-coordinated functional groups in organic ligands (e.g., -OH, -NH_2, -COOH or -SO_3H) or by coordinating a metal center with functional molecules as H_2O, EtOH, and imidazole [1].

A very important role in the design and synthesis of multifunctional materials belongs to the oxalate moiety, $C_2O_4^{2-}$, due to its various possibilities of coordination to metal centres and its ability to mediate electronic effects between paramagnetic metal ions. Homo- and heterometallic oxalate-based compounds are being intensively studied not only for their magnetic properties but also, more recently for their proton-conducting properties. The proton conductive materials must have good water and chemical durability under the influence of humidity and temperature, and in general, oxalate-based systems have regular structures and stable frameworks. Further, the oxygen atoms of the oxalate group can construct complex hydrogen-bonded networks with water, which are more than suitable for proton conduction [2].

In our previous work, we reported a one-dimensional (1D) oxalate-bridged coordination polymer of iron(III) with the formula $\{[NH(CH_3)(C_2H_5)_2][FeCl_2(C_2O_4)]\}_n$ (**1**), which has hydrogen-bonded cationic diethylmethylammonium moieties leading to a very high room-temperature proton conductivity and exceptional humidity-sensing properties [2.70×10^{-4} $(\Omega\ cm)^{-1}$ under 93% relative humidity conditions] [3]. Motivated by this result, we explored the proton conduction behaviour of the novel oxalate-based compounds of iron(III) ion, of different dimensionality and nuclearity, containing different alkyl ammonium cationic components introduced as proton carriers: 1D $\{[NH(CH_3)_2(C_2H_5)][FeCl_2(C_2O_4)]\cdot H_2O\}_n$ (**2**) and $\{[N(CH_3)(C_2H_5)_3][FeCl_2(C_2O_4)]\}_n$ (**3**), and mononuclear $(NH_4)_2[Fe(H_2O)Cl_3(C_2O_4)]\cdot H_2O$ (**4**). Although high proton conductivity is often found in 2D and 3D oxalate-based assemblies, the low-dimensional structures can exhibit excellent proton conductivity properties *via* the hydrogen-bonding chain because a low void space can be advantageous for proton hopping.

Acknowledgements

This work has been funded by the Croatian Science Foundation under project number IP-2019-04-5742.

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Metal-organic adsorbents to enable water decontamination from persistent and mobile organic compounds

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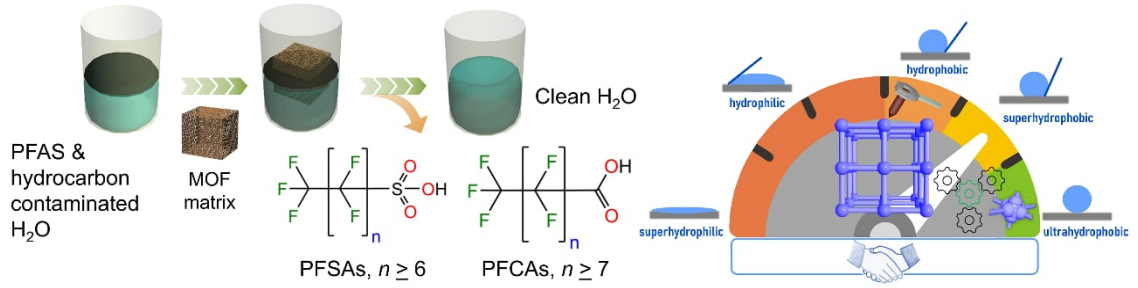
Hydrophobic metal-organic frameworks (HMOFs) and their composites are primed to enable trace scavenging of "forever" toxins, per- and polyfluoroalkyl substances (PFAS), from drinking water. Our interest in this area is closely aligned with the UN Sustainable Development Goals 3, "Good Health and Well-being" and 6, "Clean Water and Sanitation" [1]. It also addresses Stockholm convention regulations on restricted contaminants in drinking water. PFAS, such as perfluorooctanoic acid (PFOA), perfluorooctanesulfonate (PFOS), and ammonium perfluoro-2-propoxypropionate (GenX) contaminate ground and surface waters to affect hundreds of millions of people worldwide. Concerns about PFOA's ecological persistence, bioaccumulation and health effects prompted its global phase-out, but other PFAS, such as GenX and ADONA (4,8-dioxa-3H-perfluorononanoate) soon replaced it. However, removal of these replacement PFAS by conventional/advanced treatments is negligible.

Albeit poor performance, granular/powdered activated carbon, GAC/PAC is the state-of-the-art adsorbent used by the current remediation technologies. However, its low affinity and ineffectiveness to capture short-chain PFAS toxins have motivated research of suitable structured solid adsorbents, such as MOFs. We have thus far designed and studied two families of regenerable (and stable) HMOF physisorbents that offer benchmark PFAS removal at lab-scale. Our yet-unpublished research focuses upon the development and study of the next generation of HMOFs and their hybrid composites in order to set new performance benchmarks versus the state-of-the-art PFAS-adsorbents, GAC/PAC. In this pursuit, PFAS adsorption isotherms are recorded to determine the structure-function relationships of platforms of HMOFs. This study offers insights into which HMOF functionalization routes elicit optimal electrocatalytic efficiencies and surface wetting traits. Liquid chromatography is used for PFAS signal separation coupled with mass spectrometry for accurate composition/concentration measurements via direct sample injection. Record-high PFAS removal efficiencies (> 2-3 times over GAC) have been realized.



Scheme 1. Schematic illustration of the proposed PFAS contaminants' scavenging (left); distinct wetting characteristics of MOFs/MOF derived composites culminate in different static water contact angles (right) [2].

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Novel copper-based/C composites: synthesis, morpho-structural characterization, and electrochemical properties

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(Poly)saccharides represent ideal natural sources for the green hydrothermal synthesis of carbonaceous materials due to their natural occurrence, low cost, degradability, and non-toxicity [1]. Their unique properties, such as relative stability, availability, and high functional group content, make these compounds suitable candidates for the preparation of valuable hydrothermal carbons (HCs). The carbonization of polysaccharides under mild hydrothermal conditions can lead to the formation of hydrothermal carbons with different shapes and sizes [2], which can then be combined with metal nanoparticles to form composites with interesting physical and chemical properties.

Copper oxides and/or copper-based nanoparticles have extensive uses in various fields, owing to their attractive properties such as biocompatibility, surface activity, and high electrical conductivity [3]. Copper-based nanomaterials have been widely used for the development of electrochemical sensors with low detection limits and good signal amplification [4]. Therefore, this study aimed to synthesize a new class of copper-based/C composites and investigate their morpho-structural and electrochemical properties. The copper-carbon composites were prepared by a simple one-pot hydro-/solvothermal method using mono- and polysaccharides, glucose (G), chitosan (CS), and carrageenan (CR), respectively as sources for the carbonaceous support.

Different morphologies and compositions of the copper-based/C composites were obtained depending on the carbohydrate type, copper source, and solvent (water or diol) used. Thus, when glucose and carrageenan were employed, spherical morphologies of the carbonaceous support were obtained, and the copper species (copper or cuprous oxide, Cu_2O particles) were deposed/embedded onto/into the carbonaceous material (Fig. 1A). Conversely, the hydro-/solvothermal carbonization of chitosan afforded a carbonaceous matrix with a polymeric-like pattern, having the copper/Cu_2O particles agglomerated on its surface (Fig. 1B). We investigated the use of the as-obtained copper-based/C composites for the electroanalytical sensing of various analytes, and the results are due to be discussed.

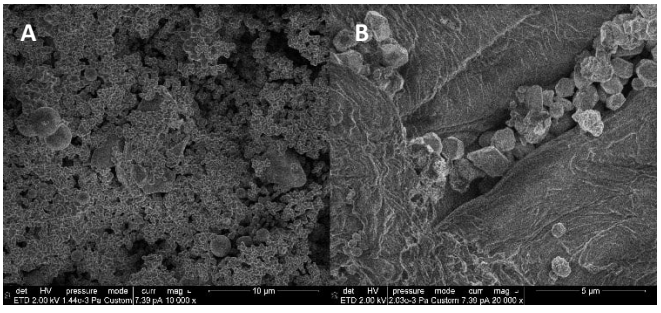

Fig. 1. (A) SEM image of copper-based/glucose composite synthesized using water (B) SEM image of copper-based/chitosan composite synthesized using ethylene glycol

Thanks to the Romanian Ministry of Education and Research, CNCS-UEFISCDI for supporting this work, project number PN-III-P4-ID-PCE-2020-2324.

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Robust iron(IV) and manganese(IV) clathrochelate complexes and their application in water oxidation catalysis

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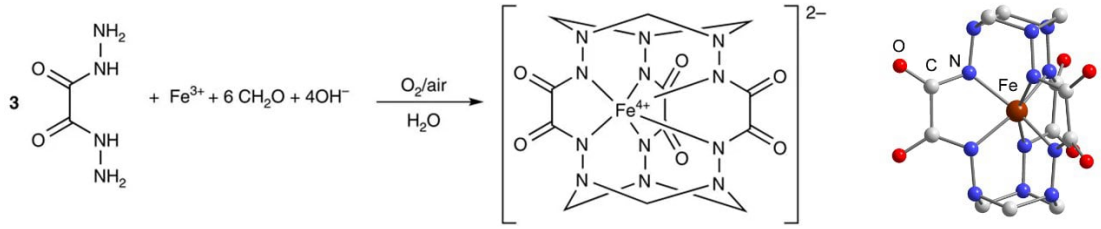
In nature, iron occurs in its stable forms either as the native metal or in its compounds in the +2 or +3 (low-valent) oxidation states. High-valent iron (+4, +5, +6) compounds are not formed spontaneously at ambient conditions; and those obtained synthetically are usually not stable in polar solvents. High-valent iron exists as reactive transient species in the catalytic cycles of many haem and non-haem iron enzymes as well as in important industrial (Haber–Bosch synthesis), laboratory and environmental (Fenton reaction) catalytic processes. We have recently reported unprecedented iron(IV) complexes formed in water by air oxidation (see the reaction scheme below) [1]. The complexes can exist indefinitely at ambient conditions without any sign of decomposition in water and in the solid state. Cyclic voltammograms of their aqueous solutions show a reversible Fe^{V}/Fe^{IV} redox couple followed by a catalytic water oxidation wave [2]. Using one-electron oxidant $[Ru(bpy)_3]^{3+}$ we were able to trap and identify a catalytic relevant intermediate, in which iron exhibits oxidation state +5 and spin S = 1/2. The intermediate Fe^{V} complex was characterised using UV-Vis, EPR, Mössbaer spectroscopy and ESI-MS. Our catalytic studies show that the high-valent iron complexes are efficient water oxidation catalysts [3]. In a ruthenium dye photo-oxidant system, the complexes attain more than 300 turnovers. To the best of our knowledge, it is the highest TON observed for mononuclear iron complexes in photochemical water oxidation. The synthetic versatility of clathrochelate complexes provides one avenue to fine tune their redox and catalytic properties.

Our further studies show that this ligand environment can be also used to stabilise high oxidation states of other transition metals (e.g., Cu^{3+}, Mn^{4+}, etc.). We have isolated a manganese(IV) clathrochelate with S = 3/2, which has a similar crystal structure [4]. The complex is stable in water and organic solvents. It can be easily oxidised to the Mn^{V} state either chemically or electrochemically. Its studies in redox catalysis are currently ongoing.



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Peripherally functionalized supramolecular grids and their post synthetic functionalization

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Supramolecular grids are long known class of multinuclear coordination compounds.[1] Their main feature is the very regular rectangular shape and multicomponent constitution. The first assigns them for potential use in nanoelectronics and surface engineering. The second suggests their implications in multivalency studies.

However, regardless of their high potential the results and application reports are still lacking. For the surface application this is caused by their unfavorable, perpendicular to surface, configuration. In the case of multivalence it is because of the lack of functionalization protocols, which currently also often have detrimental effects on the grid self-assembly as such.

We believe that the dynamic covalent chemistry together with subtle modifications of ligands' skeleton offers an answer and solution to most of the current problems. The proof of concept of this approach has been recently published by the group of prof. Lehn.[2][3] Here we would like to present a simplified protocol that leads to the aldehyde and amine functionalized grids and their successful post synthetic functionalization through imine bond formation. (Figure 1) Furthermore, we have used compatibly functionalized grids to form higher oligomeric species through DCC chemistry. These oligomers can be interesting for bottom-up formation of so called "grids of grids", a regular extended 2D arrays with high utility in nanoelectronics and alternative data storage concepts.[1][3]

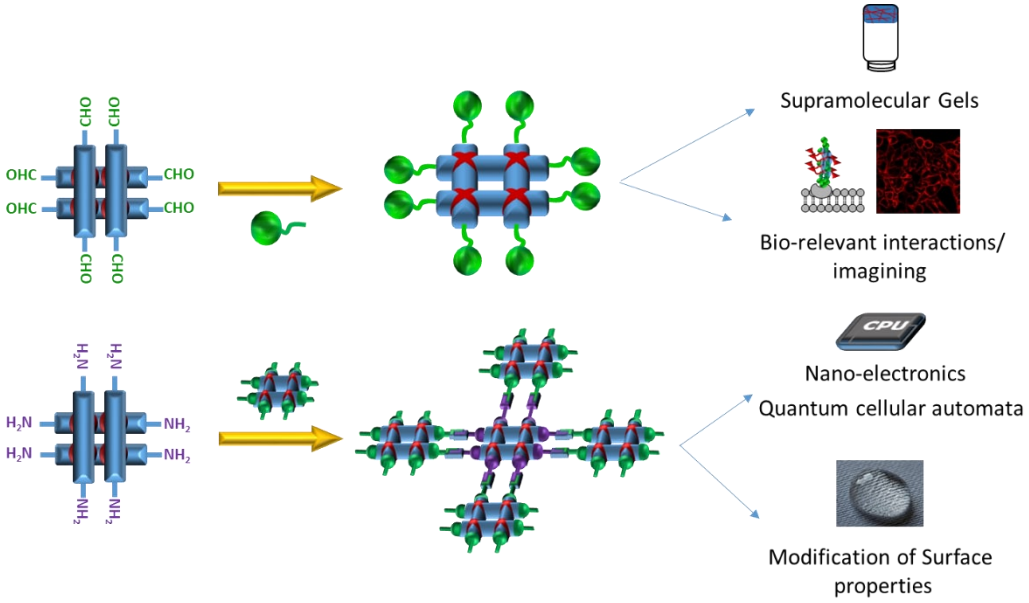

Figure 1: Depiction of amine and aldehyde peripherally functionalized grids; their decoration (Top) and oligomerization towards "grids of grids" array (Bottom).

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Dynamic single-crystal-to-single-crystal transformations on a novel octamolybdate/{Cu(cyclam)} porous framework: X-ray monitoring of cluster isomerization and intramolecular metal migrations

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The combination of polyoxometalates with metalorganic complexes of macrocyclic N4-tetradentate ligands constitutes a powerful method to obtain extended open frameworks [1]. The hydrothermal reaction involving a molybdate source and $\{Cu(cyclam)\}^{2+}$ complexes (cyclam = 1,4,8,11-tetraazacyclotetradecane) results in the hybrid $[\{Cu(cyclam)\}_3(Mo_8O_{27})]\cdot 14H_2O$ (**1**) framework, which exhibits an unprecedented octamolybdate anion. Each polyanion is covalently linked to six neighboring clusters through octahedral {Cu(cyclam)} metalorganic units, which leads to an extended porous framework with interconnected square-like voids where the hydration molecules are hosted. Thermal evacuation of guest solvent molecules via two sequential single-crystal-to-single-crystal transformations affords two anhydrous phases $[(Cu(cyclam)][\{Cu(cyclam)\}_2(Mo_8O_{27})]$ (**2**) and $[\{Cu(cyclam)\}_3(Mo_8O_{27})]$ (**3**) at 50 and 120 °C, respectively. These thermally-triggered phase transitions imply not only modifications in the crystal packing and coordination geometry of the Cu centers, but also changes in the octamolybdate cluster, with remarkable rearrangements in the Mo-O bonding scheme. This leads to two additional unprecedented clusters (Figure 1) in which the penta-coordinated addenda metal unit in **1** turns to display a tetra-coordinated geometry. Both anhydrous phases exhibit accessible micropores with potential applicability in gas sorption. Nevertheless, preliminary studies reveal that only **3** (cross section ca. 8.5 x 8.5 A^2) is able to adsorb CO_2 and N_2 with a S_{BET} = 250.7 m^2/g, which is quite high for POM-based structures. Hydration of **3** upon exposure to open atmosphere implies further condensation of the constituent molybdate units, resulting in the well-known $\{\gamma\text{-}Mo_8O_{26}(OH)_2\}$ polyanion [2]. The structure of $[\{Cu(cyclam)\}_3(Mo_6O_{26}(OH)_2)]\cdot 12H_2O$ (**4**) also presents a covalent open network with water filled interconnected channels. In contrast, **2** is rapidly hydrated to lead to $[\{Cu(cyclam)\}_3(Mo_8O_{27})]\cdot 13H_2O$ (**5**), which exhibits the same polyanion found **1**.

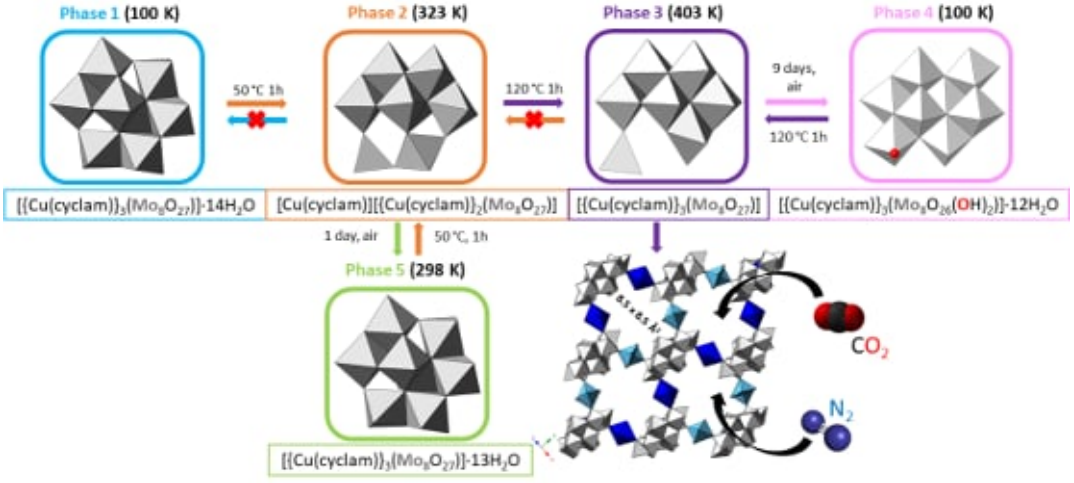

Figure 1. Solid-state isomerization of octamolybdate anions in compounds **1-5** and representation of crystal packing of **3** with accessible pores for CO_2 and N_2 gas sorption.

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Reactivity Increase of Organolithium Reagents using Amines as Ligands

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Due to the highly polarized C–Li bond, alkyllithium compounds (RLi) exhibit a high tendency to form aggregates which induce a strong structure-reactivity relationship. To use these reagents efficiently, a profound knowledge of the formed structures is inevitable. By the addition of donor bases, e. g. nitrogen ligands or donating solvents, a deaggregation can be achieved, which increases the reactivity of the RLi/additive system.[1] Commonly used chelating nitrogen ligands or donating solvents, such as thf or diethyl ether, have limitations regarding to the reaction temperature.[2] Reactions must be carried out at low temperatures (T < –30 °C), otherwise side reactions or decomposition of the ligand can occur. Therefore, alternative ligands are of great interest, which have to be stable against the lithiumalkyl even at higher temperatures and also should be able to form accessible aggregates.[3] Due to the higher stability of cyclic and bicyclic amines, these have a high potential to be used at higher temperatures and thus enable a new substrate spectrum.[4]

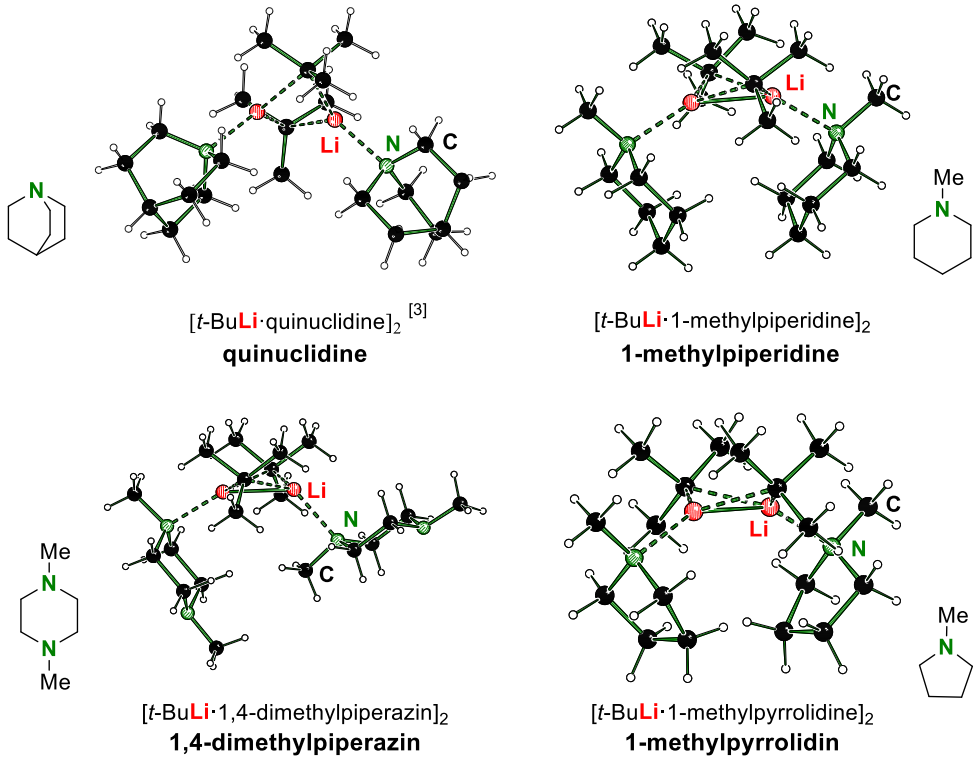

Figure 1 : Dimeric organolithium aggregates containing *tert*-butyllithium and quinuclidine [3], 1-methylpiperidine, 1,4-dimethylpiperazine, 1-methylpyrrolidine.

We are greatful to thank *Deutsche Forschungsgemeinschaft* (DFG) for financial support.

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Selective Formation of Mixed Metal Sulphur Complexes of Copper(I) and d^{10} Transition Metals

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Copper(I) halide complexes show a tetrahedral complex geometry due to the d^{10}-configuration of the metal. Sulphur ligands, like thioethers, form dimeric $[Cu_2(\mu_2\text{-}X)_2]$ or tetrameric $[Cu_4(\mu_3\text{-}X)_4]$ (X = Cl, Br, I) units. However, if the desired complex motive differs from these oligomeric structures, the usage of copper(I) halides is heavily limited. Most commonly copper salts with weak coordinating anions, like BF_4^-, PF_6^- or ClO_4^- as starting material are utilized.[1–3]

Herein, we now present the formation and characterisation of the dimeric copper(I) halide complexes **2a–c** (X = Cl, Br, I) starting from the neutral silyl thioether **1**. By treating these complexes with a d^{10}-transition metal salt, we were able to dissociate the strong Cu–X bond, destroying the $[Cu_2(\mu_2\text{-}X)_2]$ complex motive and leaving the weaker Cu–S contact intact. The resulting complexes **3a–h** consist of a separated ion pair, in which the copper(I) cation is tetrahedral coordinated by two chelate ligands of **1** and a butterfly shaped d^{10}-metal halide dianion. Complexes **3a–h** are one of a few examples and especially interesting because of their simple, yet elegant way to form mixed metal complexes with thioligands.

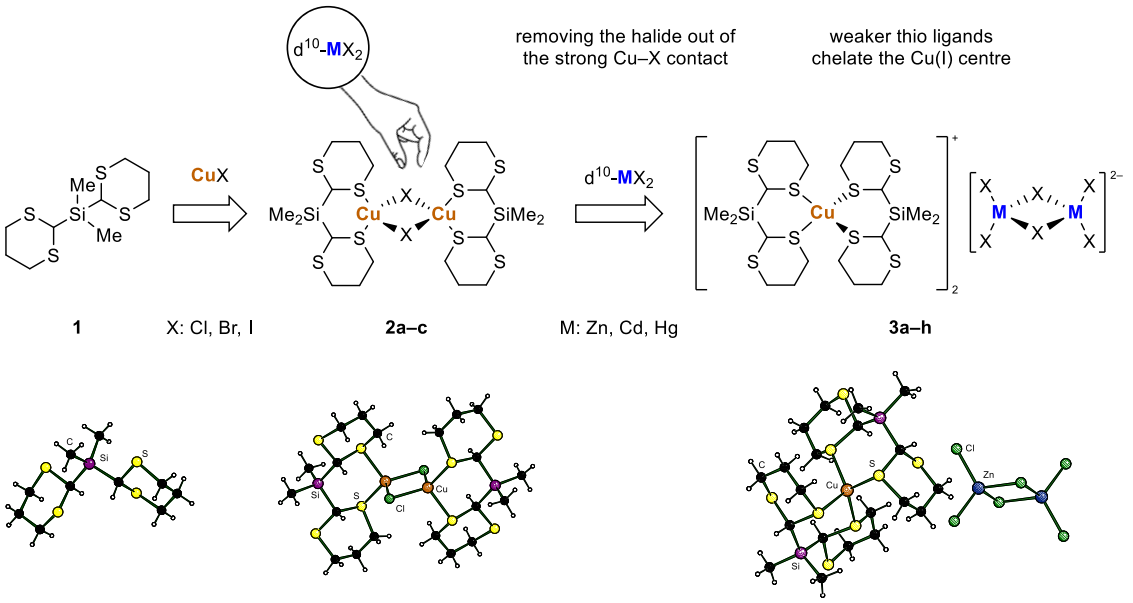

Figure 1: Selective formation of mixed metal complexes of copper(I) and d^{10} transition metals by removing the halide from the dimeric copper(I) complexes **2a–c**.

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Combining Coordination Chemistry and Carbolithiation

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Living anionic polymerization initiated by lithium alkyls is a well-known pathway to highly defined polymers. Especially, styrene and its derivatives can be polymerized successfully with high control of the polymeric features.[1] By using functionalized initiators, it can be ensured that each polymer chain carries the functionalization, which represents an advantage over ω-functionalization.[1] With aid of this method we want to report two interesting approaches which may allow new synthetic pathways for metallopolymers. (*R*,*R*)-TMCDA (**1**) and 2-(dimethylaminomethyl)pyridine (**2**) showed promising applicability as anionic initiators in the model carbolithiation reaction, as they were successfully lithiated and subsequently added to 1,1-diphenylethylene. Moreover, both ligands provide a further characteristic as bidentate ligands. Due to their chelating properties, by post-polymerization functionalization, the (*R*,*R*)-TMCDA addition product **3** coordinated to $ZnCl_2$, whereas **2** itself was able to form transition metal complexes of rhenium, ruthenium, silver and palladium. So that this ligand can be used for pre-polymerization functionalization.

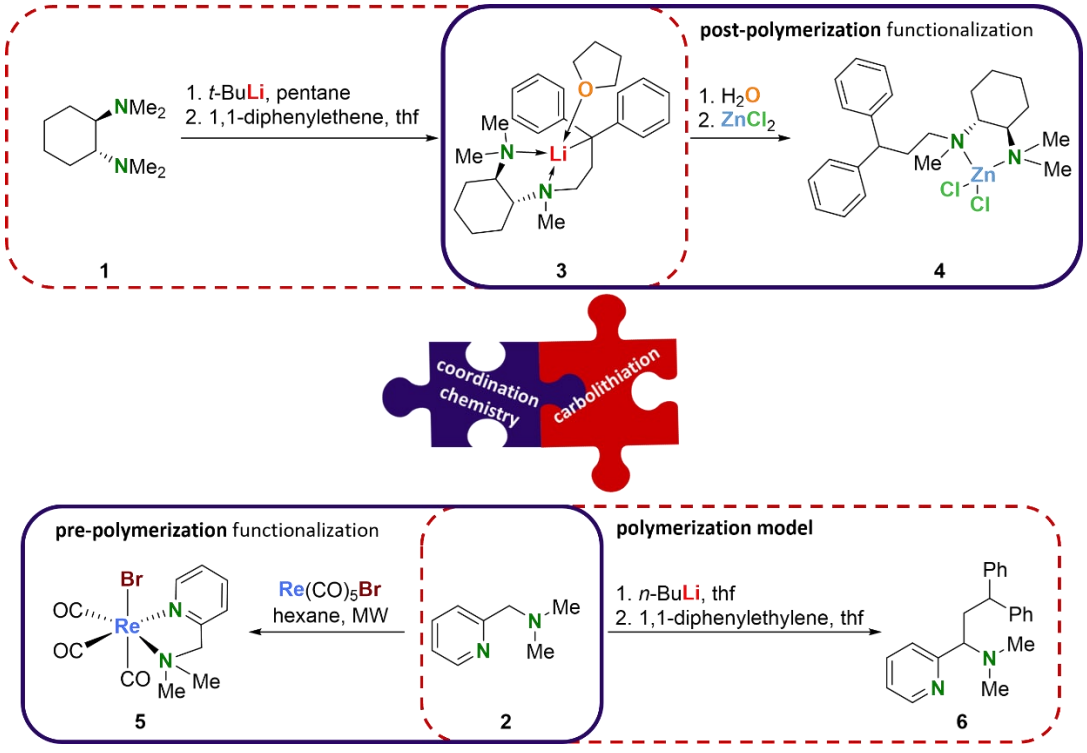

Figure 1: The two approaches to combine coordination chemistry with carbolithiations exemplarly shown with (*R*,*R*)-TMCDA (**1**) and 2-(Dimethylaminomethyl)pyridine (**2**).

The possibility to combine coordination chemistry and carbolithiation allows an access to defined polymers as ligands for transition metal complexes. Thereby, this approach offers a wide variety of promising applications (e.g. catalysis), which aim to be discovered in future research.

Thanks to Studienstiftung des deutschen Volkes for financial support.

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Insights into the Deprotonation Mechanism of Superbases using an Aminomethylferrocene based Lochmann-Schlosser Base

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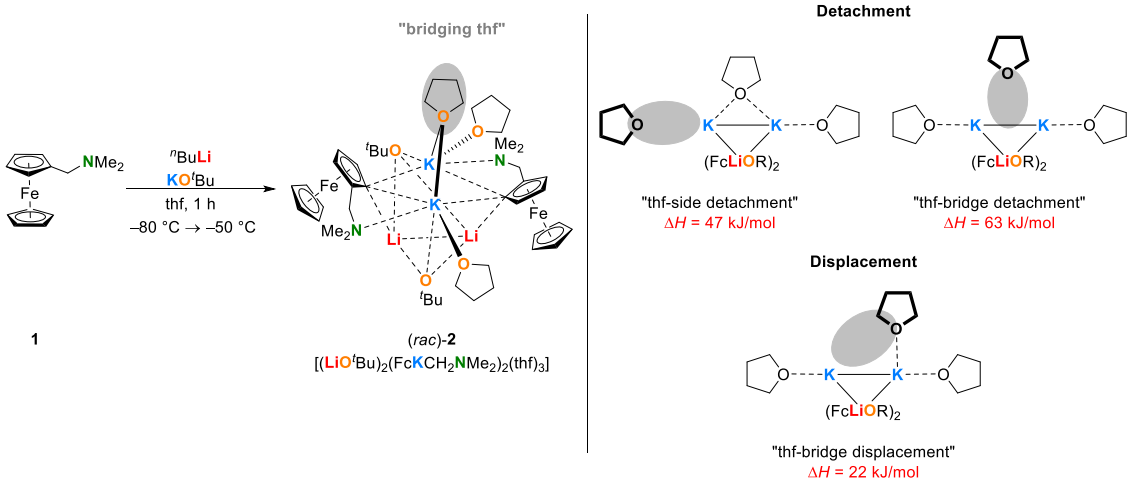
Lochmann-Schlosser bases are valuable tools in organometallic and organic chemistry. They can be used, e.g., for the regioselective synthesis of pharmaceuticals. [1] Since its discovery by its namesakes in the last century, the mechanism is still under investigation. [2] The structure of one reactive intermediate could be elucidated by isolating the crystallization product of benzene treated with a mixture of KO^{t}Bu and ^{n}BuLi. [3]

By deprotonation of *N,N*-dimethylaminomethylferrocene (**1**) with KO^{t}Bu and ^{n}BuLi at –80 °C and subsequent storage at given temperature, yellow blocks were formed. X-ray structural elucidation revealed the structure of (*rac*)-**2**. The coordination sphere of the potassium center is saturated by the amino handles and by two thf molecules each. The unique feature here is that one thf molecule bridges the potassium cations. Deprotonation reactions initially proceed via pre-coordination of the substrate at the metal center, for which a coordination site must be free. It was assumed that the coordination site is cleared by the detachment of a thf molecule. However, the bridging thf molecule gives reason to believe that simple displacement of the thf molecule initiates the coordination site release. To verify this, quantum chemical calculations of the detachment and displacement of the thf molecules were performed. The results show that the energy barrier of the displacement is lower than that of the detachments and therefore this is the potential reaction pathway. Furthermore, due to the planar chirality of this system, an enantiomerically pure superbase can be synthesized, possibly undergoing an asymmetric deprotonation reaction.



Scheme 1: Synthesis of (*rac*)-**2** and quantum chemical calculations of the detachment and displacement of thf molecules at the theory level M062X/def2svp.

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Imine derivatives of POSS as ligands complexing lanthanide cations

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Polyhedral Oligomeric Silsesquioxanes (POSSs) are an organosilicon species with the general formula $[RSiO_{1.5}]_n$, where *n* is the total number of silicon atoms and *R* is the functional group. Silicon atoms can be bonded with different substituents, from the simplest hydrogen atom to specific organic arms[1]. This makes these species the group of hybrid materials combining the properties of inorganic silica and organic substituents. POSS can be substituted with reactive groups on one, several, or all corners. This affects their reactivity and the nature of using them[2].

POSSs are cage-type compounds made of a silicon-oxygen core with a size of 1-3 nm, which makes them classified as nanoparticles and, at the same time, the smallest model of silica that can be obtained[3]. There are cages of 6, 8, 10, and even 12 silicon atoms connected by oxygen bridges. T_8 cages are most often used in the research. They can be obtained with higher efficiency than other POSS types and relatively easily isolated from the post-reaction mixture[4].

The work aimed to synthesize new imine derivatives of mono-POSS, which could be obtained in the condensation reaction of primary amines and aldehydes[5]. Condensation reaction was carried out using 3-aminopropylheptaisobutyl POSS and aromatic aldehydes. First, the new imine POSSs were obtained with substituted benzaldehyde and naphthaldehyde. Then, the resulting compounds were used as ligands coordinating the lanthanide cations, such as erbium(III) and gadolinium(III). All compounds were characterized by NMR and IR spectroscopy, elemental analysis, and X-ray crystallography[6].

This work was financially supported by the National Science Centre, Poland (Grant No. 2020/39/B/ST4/00910).

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Disubstituted T_8-type cage-like silsesquioxanes: are they possible to obtain?

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Fully condensed T_8-type polyhedral oligomeric silsesquioxanes (POSSs) with a basic cage-like structure of the general formula $(RSiO_{3/2})_8$ (where R is an organic group) belong to the group of organosilicon compounds. Their substituents can be divided into reactive or non-reactive, and depending on their selection, the compound will have different properties and reactivity [1].
Due to their cubic symmetry, easy synthesis methods, and good thermal stability, POSS with T_8-type architectures have gained the most recognition. Regarding the R groups, the well-developed compounds are either homogeneous, where labile organic groups substitute all silicon atoms ($[R_8Si_8O_{12}]$) or monosubstituted ($[R'R_7Si_8O_{12}]$) with only one reactive side arm [2].

Recently, attempts have been made in the literature to synthesize disubstituted POSS ($[R'_2R_6Si_8O_{12}]$), but the published results of the experiment were inconclusive [3-4]. Lack of experimental data, incomplete NMR spectra, and receiving the only *para*-disubstituted product made us revisit the synthesis and characterization of the obtained compounds. We tried to repeat the synthetic route by corner-opening monosubstituted POSS and then by corner-capping reaction with selected silane. The resulting species have been characterized using spectroscopic methods. Furthermore, the theoretical calculations were conducted to check which position (*ortho*, *meta*, *para*) the opening of the monosubstituted cage is most privileged. All structures presented in this poster were fully optimized at the B3LYP-D3/6-31g(d) (hybrid density functional with D3 damping function to include dispersion) level of theory in the gas phase [5-7]. All optimizations were carried out in Gaussian16, Rev.C.O1 set of codes [8].

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Titanium(IV) amino alkoxides: From academic curiosity to industrial application

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Amino alcohol derivatives of tin hold high potential as catalysts for polyurethane formation [1]. Titanium and tin show similar covalent (Sn: 1.40 Å, Ti: 1.36 Å) and van der Waals radii (Sn: 2.42 Å, Ti: 2.46 Å). This inspired us to synthesize amino alcohol derivatives of titanium and to investigate their capacity as catalysts for the reaction mentioned above. The reactions of Ti(O*i*Pr)$_4$ with a variety of different amino alcohols gave the corresponding Ti(IV) spirocyclic compounds *spiro*-[R''N(CH$_2$CRR'O)$_2$]$_2$Ti. In course of these syntheses, we also obtained both the trinuclear and hexanuclear titanium oxoclusters **A** and **B**, respectively. The trinuclear cluster **A** can be interpreted as a product of the partial hydrolysis and subsequent condensation of the intermediate MeN(CH$_2$CHCF$_3$O)$_2$Ti(O-iPr)$_2$ giving MeN(CH$_2$CHCF$_3$O)$_2$Ti(O-*i*Pr)O(*i*PrO)Ti(OCF$_3$HCCH$_2$)$_2$NMe. Complexation of the latter with Ti(O-*i*Pr)$_4$ via intermolecular O→Ti coordination stabilizes the latter giving the cluster. All compounds were characterized by *state of the art* analytical methods. We also report studies on the reactivity and catalytic activity of selected compounds presented on this poster.

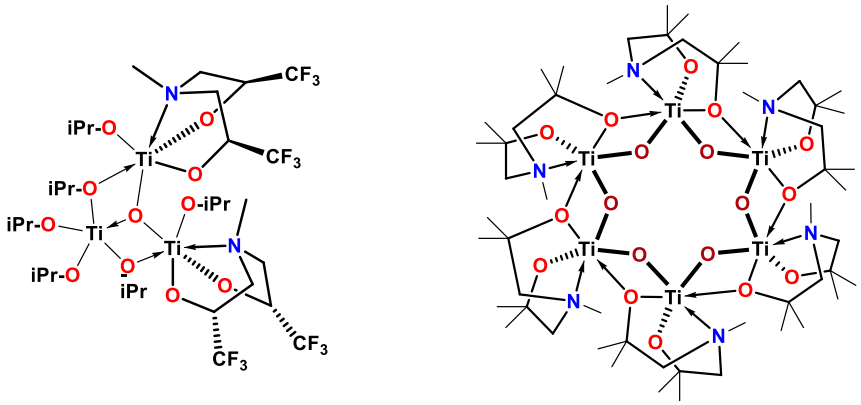

Figure 1. Schematic drawing of the tri- and hexanuclear titanium oxoclusters **A** and **B**.

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Silylation of Mixed Polyanionic Si_xGe_{9-x} *Zintl*-Clusters – Synthesis, Structure and Dynamics

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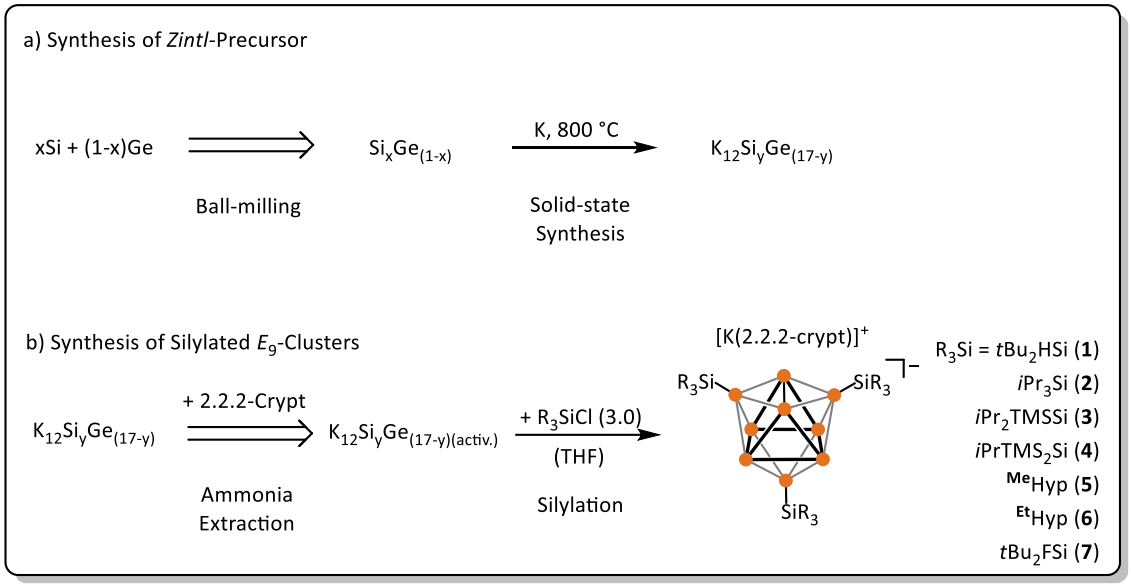
The *Zintl* precursor K_4Ge_9 can be easily silylated in the presence of various chlorosilanes.[1] Starting from these monoanionic, trisilylated species, further charge reduction can be achieved by reaction with different electrophiles e.g. alkyl halides or acyl chlorides. As described for unsubstituted tertel element cluster, these species exhibit a pronounced dynamic behaviour.[2] In contrast to ^{29}Si, the heavier homologue ^{73}Ge bears unfavourable NMR-properties allowing only the periphery of the respective clusters to be studied. Thus, the detailed mechanism of the molecular rearrangement remains unclear. Recently, a reliable synthetic access to trisilylated, nineatomic silicon clusters *via* extraction of $K_{12}Si_{17}$ from liquid ammonia was found.[3,4] Hence, in this work we started to transfer this synthetic approach to ternary $K_{12}Si_yGe_{(17-y)}$ *Zintl* precursors. The corresponding activated phases can be further transformed into the trisilylated, binary $[(R_3Si)_3(Si_zGe_{(9-z)})]^-$ clusters (**1-7**). ^{29}Si-NMR spectroscopy showed a size-dependent dynamic character of the respective monoanions. Due to the reduced symmetry of the cluster framework, this rearrangement could be investigated now.



Synthetic pathway to trisilylated, binary $[(R_3Si)_3(Si_zGe_{(9-z)}]^-$ clusters. a) Synthesis of the ternary *Zintl*-precursor $K_{12}Si_yGe_{(17-y)}$ *via* solid state reaction; b) Synthesis of trissilylated E_9 clusters *via* activation in liquid ammonia and silylation of the protonated intermediate.

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Synthesis and Catalytic Activity of Phosphorylated Ten-Atomic [Ge_9Ni] Clusters

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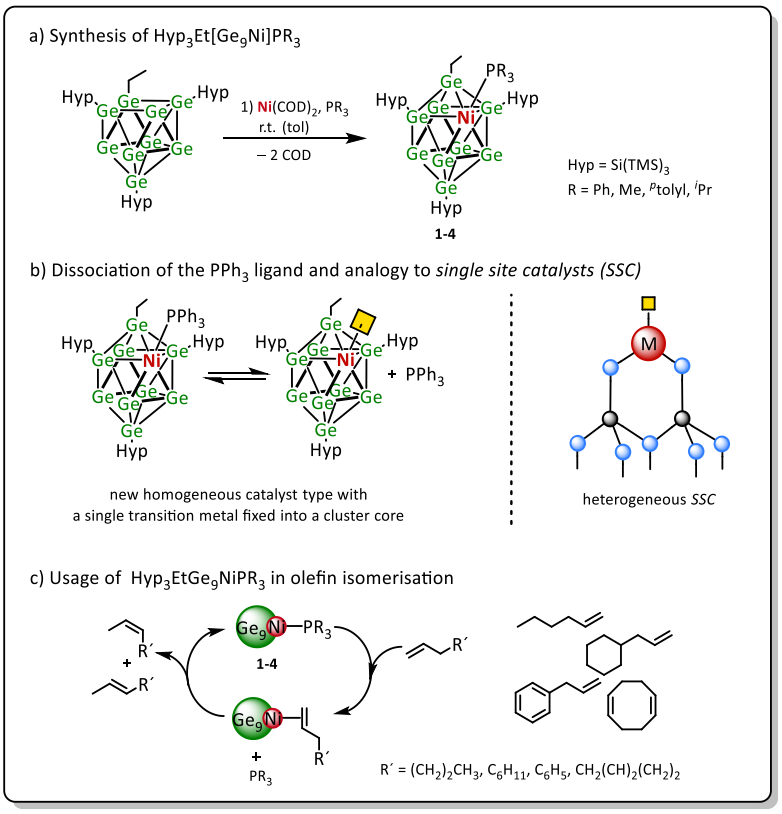
Single site catalysts are known to catalyse a wide range of different reactions, whereby these usually take place heterogeneously. The active centre of these catalysts consists of one or few atoms (*single sites*), which are fixed on a wide variety of support materials.[1] In contrast to this, metalated *Zintl*-clusters, as a new type of such catalysts, could react in a homogeneous way. By reacting [Hyp_3EtGe_9] with $(PPh_3)_2Ni$-||, $Hyp_3Et[Ge_9Ni]PPh_3$ (**1**) as neutral ten-atomic [Ge_9Ni] clusters, possessing an pronounced dynamic behaviour, could have been gained. In this context, the PPh_3 ligand dissociates from the nickel atom at higher temperatures generating a vacant binding site at the transition metal. This fact makes them promising candidates for catalytic applications. Due to unfavourable synthetic access of the starting nickel complex $(PPh_3)_2Ni$-||, we looked for a simpler synthetic approach to build up such clusters.[2] In doing so, we succeeded in developing a synthetic strategy allowing the variation of the phosphine ligands and could obtain four different clusters $Hyp_3Et[Ge_9Ni]PR_3$ with R = Ph, Me, ^{p}tolyl and ^{i}Pr (**1-4**), whereby **2** and **4** could have been crystallized from hexane. Since the hydrogenation of cyclooctadiene with a transition metal decorated *Zintl*-cluster is known,[3] we investigated the catalytic activity of our newly obtained ten-atomic [Ge_9Ni] clusters. In doing so, we could successfully isomerise different olefins, whereby the reaction velocity and yields depend on the bound phosphine ligand.



a) Synthetic route to neutral ten-atomic [Ge_9Ni]-clusters with different phosphine ligands; b) analogy of newly obtained [Ge_9Ni]-clusters with *single site catalysts* c) Postulated catalytic cycle for olefin isomerization by $Hyp_3Et[Ge_9Ni]PR_3$ (R = Ph, Me, ^{p}tolyl, ^{i}Pr).

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A new look at molecular and electronic structure of homoleptic diiron(II,II) complexes with *N,N*-bidentate ligands: Combined experimental and theoretical study

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Transition metal complexes incorporating the metal-metal (M-M) bond are a subject of widespread interest driven by several perspectives, including fundamental curiosity and potential applications in heterogeneous or enzymatic catalysis and small molecules activation. Among the most intensively developed groups of the M-M bonded compounds are paddlewheel-type binuclear complexes supported by appropriate bridging ligands such as amidinates.[1] This class of complexes generally shows strong metal-metal interactions, leading to a low-spin bimetallic core, often with a multiple bonding between metal atoms. However, metal-metal bonded bimetallic compounds containing iron or cobalt centres generally show a high-spin ground state, challenging the common wisdom according to which strong metal-metal interactions should be antiferromagnetic. While the majority of high-performance single molecular magnets (SMMs) achieve their high ground state by superexchange coupling mechanism at low temperatures, the Fe-Fe bonded complexes may be an alternative pathway to the design of SMMs combining high spin ground state even at room temperature due to the direct overlap of the metal valence orbitals with significant magnetic anisotropy.

Herein, we present our examinations concerning the metal-metal interactions in high-spin diiron formamidinates $[Fe_2(\mu\text{-DPhF})_4]$ (DPhF = *N,N'*-diphenylformamidinate) and $[Fe(\mu\text{-DTolF})_3Fe(\kappa^2\text{-DTolF})]$ (DTolF = *N,N'*-di(*p*-tolyl)formamidinate), and an influence of their molecular structures on a slow magnetic relaxation.[3] Particularly, we show how subtle changes in the character of aromatic subunit *N,N'*-diarylformamidinate ligand can dramatically affect the molecular and electronic structure of diiron Fe-Fe bonded complexes. Thus, a minor alteration in the ligand system, *i.e.* switching from phenyl to *p*-tolyl *N*-substituted formamidinate ligand, results in major structure change – the formation of an unprecedented non-centrosymmetric complex $[Fe(\mu\text{-DTolF})_3Fe(\kappa^2\text{-DTolF})]$ incorporating variously coordinated *N,N*-bidentate symmetric ligands. Finally, we also provide a new ground state electronic structure of diiron formamidinate complexes $[Fe_2(\mu\text{-DPhF})_4]$ and $[Fe(\mu\text{-DTolF})_3Fe(\kappa^2\text{-DTolF})]$ based on both combined high-level *ab-initio* calculations, and supported by magnetic measurements, Mössbauer spectroscopy, and cyclic voltammetry. The reported study sets the stage for further advances in the fundamental chemistry of metal-metal bonded complexes and their applications in catalysis and molecular magnetic materials.

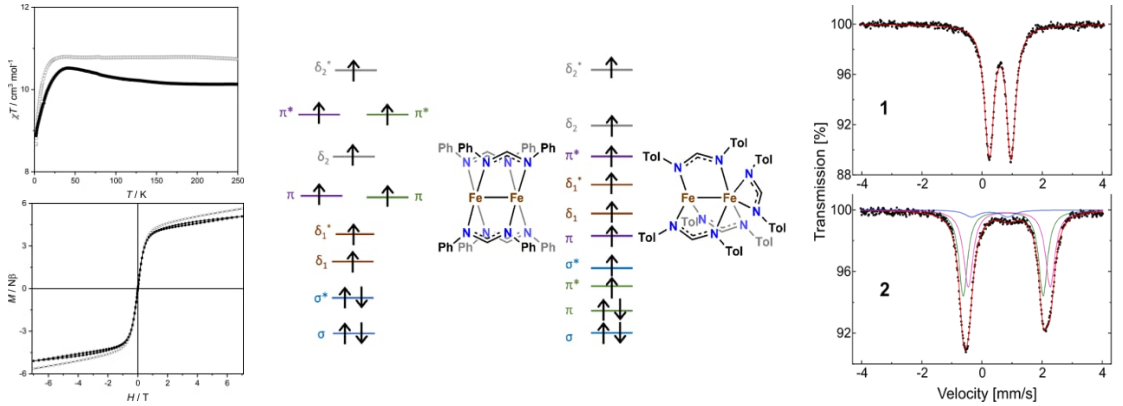

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Photo-induced size control and selective guest binding of Pd_2L_4 coordination cages

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Abstract: Due to the inner space by skeletal structures, coordination cages act as a powerful tool for studying the confined effect. The control of structure and functions of coordination compounds by external stimuli has been a key strategy for the stabilization of reactants, catalysis, drug delivery systems. Among various stimuli (e.g. pH, temperature, electrochemical or chemical input), light-triggered supramolecular systems have many advantages: waste-free, rapid process, and a high degree of photoconversion. The group of Fujita reported the photoswitching behavior of azobenzene-based compounds underwent significant geometry conversion and dipole moment shifts in the structure. Clever group has studied on chirality induction of coordination cages consisting of dithienylethene (DTE) link. Nevertheless, the development of light-responsive supramolecules has proven to be a highly challenging topic. Hereby, we present Pd_2L_4 coordination cages based on a diazocine moiety. *Cis*-form of diazocine is stable and isomerized to *trans*-form by UV irradiation, showing significant changes in molecular dimensions.

Acknowledgement
This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (2021R1C1C1013037).

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Cisplatin−based platinum(IV) conjugates immobilized in mesoporous silica SBA-15 prove highly potent against different breast cancer cell lines

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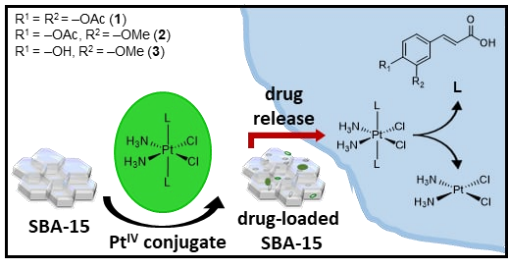
In spite of strides made in diagnostics and treatment, female breast cancer has surpassed lung cancer as the foremost commonly diagnosed cancer and it accounts for most cancer-related deaths among women around the world [1]. Drug-resistance and severe side effects are the leading causes for restricted clinical efficiency of used chemotherapeutics including the platinum(II)-based agent cisplatin. Preparation of platinum(IV) complexes has emerged as an attractive approach for overcoming these drawbacks due to the higher stability of these complexes as well as the possibility to introduce biologically active ligands in their axial positions constructing multifunctional prodrugs [2]. Use of nanoparticles as drug delivery systems is another approach towards chemotherapeutics with reduced toxicity relying on the advantage of nanoparticles to accumulate in larger amounts, along with the respective cargo (therapeutic drug), in tumor tissues through passive targeting based on the enhanced permeability and retention effect (EPR effect) [3].

Aiming to develop anticancer drugs with higher activity and reduced toxicity, we combined the two approaches: preparation of platinum(IV) complexes and loading them into the nontoxic, mesoporous silica nanoparticles (MSNs) SBA-15 [4]. The platinum(IV) conjugates are based on a cisplatin scaffold bearing in the axial positions derivatives of the naturally occurring phenolic acids, caffeic and ferulic acid. These acids have attracted attention as potential chemopreventive and chemotherapeutic agents due to various biological and pharmacological activities they possess including antioxidant, anti-inflammatory, anticancer, antimicrobial, antiviral, antithrombotic and hepatoprotective effects [5]. The three platinum(IV) conjugates prepared are: cisplatin–acetyl-protected caffeic acid conjugate (**1**), cisplatin–acetyl-protected ferulic acid conjugate (**2**) and cisplatin–ferulic acid conjugate (**3**). Upon loading them into mesoporous silica SBA-15, the MSNs SBA-15|**1**, SBA-15|**2** and SBA-15|**3** were afforded accordingly.



The cytotoxicity of all conjugates and MSNs was assessed in a panel of four breast cancer cell lines (MDA-MB-468, HCC1937, MCF-7 and BT-474) with distinctive characteristics and sensitivities towards cisplatin. The free platinum(IV) conjugates **1** and **2** demonstrated comparable (MDA-MB-468 and HCC1937) or higher (MCF-7 and BT-474) activity with respect to cisplatin, whereas **3** was found less active against all four cell lines. Upon immobilization, however, all conjugates showed superior antiproliferative activity with markedly increased cytotoxicity compared to cisplatin. The most dramatic enhancement of the antiproliferative activity was observed against the estrogen/progesterone-positive (ER/PR-positive) cell line BT-474 causing invasive ductal breast cancer resistant to the standard treatment with the ER-antagonist tamoxifen. In this case, more than 1000-fold decrease in the IC_{50} value was observed for the drug-loaded MSNs, with SBA-15|**1** being the most potent nanomaterial.

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Amino – functionalized Supermagnetic Fe_3O_4 Nanoparticles. Synthesis and interaction with the silver ion

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Magnetic nanoparticles are a class of nanomaterials that can be manipulated using a magnetic field. Materials such as Fe_3O_4 behave like ferromagnetic in an induced magnetic field, but after subtracting this field, they do not exhibit any magnetic assets. This phenomenon is called supermagnetism. Those nanoparticles commonly consist of magnetic elements, for example: iron, nickel, and cobalt and their chemical compounds. The preparation methods are critical in determining the iron oxide nanoparticles size and size distribution, morphology, magnetism, and surface functionality. These particles have shown attractive properties in catalysis, biomedicine, magnetic resonance imaging, data storage and environmental water treatment remediation, and thus have attracted broad research interests [1].

Nanoparticles have shown great potential in the removal of heavy metal ions from water [2] by surface modification with chelating ligands. In this case, the bound ions can easily be removed by an external magnetic field. The ability to transfer ions and molecules between solutions may be particularly useful in the development of new analytical methods with high sensitivity. Magnetic isolation is a promising way to specifically trap analytes from a complex environmental or biochemical sample.

This work describes the synthesis of magnetic Fe_3O_4 nanoparticles using the modified co-precipitation method and their modification with aminosilanes of various chain lengths and the number of amino groups. The obtained structures were characterized using Fourier Transform Infrared Spectroscopy, Dynamic and Electrophoretic Light Scattering, and Scanning Electron Microscopy.

The objective of the work was also to develop a technique of investigation nanoparticles with potentiometric titration methods using a silver-silver electrode. The presented technique was used to determine the ability to coordinate silver and the total adsorption of silver on the surface of nanoparticles [Fig 1.]. The adsorption was described by using the Freundlich and Langmuir isotherms.

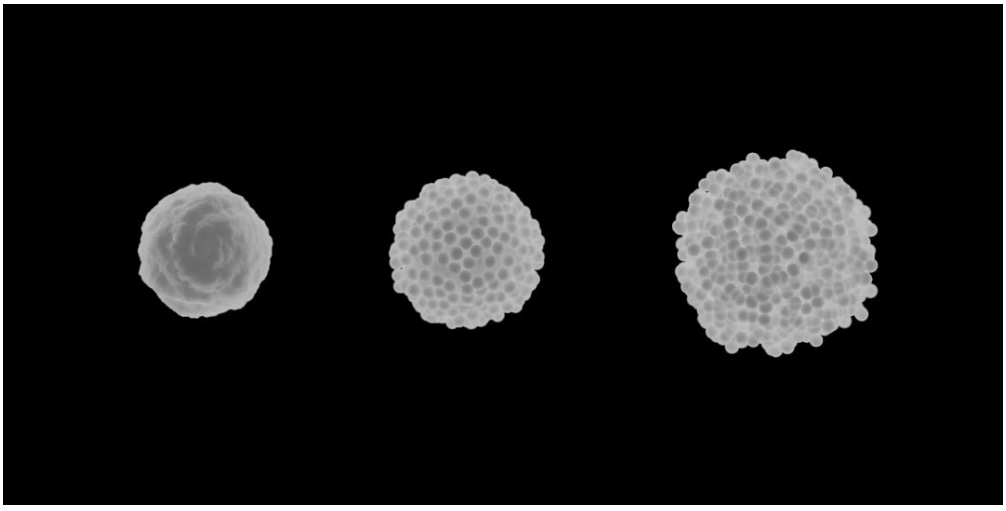

Fig 1. The graphic shows from the left a pure nanoparticle, a nanoparticle coordinating silver ions in a monolayer, a nanoparticle adsorbing silver in a polylayers

This research was financially supported by the University of Gdansk - Project Supporting young Scientists and PhD students (grant No. BMN 539-T050-B039-22)

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Alkylaluminium derivatives of *o*-substituted benzoic acids: synthesis, structure and reactivity

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Group 13 organometallic complexes, often considered as exemplary compounds of main group organometallics, are of fundamental and practical importance due to their extraordinary structural diversity and a significant number of applications. Hence, attempts to gain an in-depth understanding of the multi-faceted chemistry of Group 13 organometallics are continually vital for the development of new reagents and catalysts or building units for modern functional materials [1]. Particularly, both the reactivity of octet-compliant compounds and the bonding situation in electron-rich hypervalent molecules are still a topic of constant debate [2]. A large number of studies have been directed to understand better the factors controlling the formation and stability of higher coordinate Group 13 complexes. However, none of them offers a comprehensive view on this subject. Another intriguing issue concerns the role that non-covalent interactions have in the properties of the title organometallics. Noncovalent interactions are common and influential forces that affect the primary and secondary coordination spheres as various second-sphere interactions often operate in concert with the primary donor-acceptor bonds and can lead to complexities in the structure of metal complexes, stabilize reactive species or lower activation barriers.

In this work, we focused on the synthesis and structure characterization of novel alkylaluminium complexes supported by (*O, X*)-type anionic ligands (X = N or S), which are derivatives of *o*-substituted benzoic acids. Reactions of AlR_3 (R – alkyl substituent) with selected pro-ligands in non-coordinating solvent lead to the formation of a number of oligonuclear alkylaluminium carboxylate complexes of different molecular structures. The resulting compounds were fully characterized using spectroscopic techniques (including Diffusion-Ordered) and single crystal X-ray diffraction studies. In addition, the optical properties of obtained compounds were studied. Moreover, the reactivity studies towards selected strong Lewis bases revealed uncommon products and structural motifs.

The authors gratefully acknowledge the National Science Centre, Poland (grant OPUS 2020/37/B/ST4/03310) for financial support.

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Time-dependent Self-assembly of Copper(II) Coordination Compounds: New Catalysts for Mild Oxidative Functionalization of Alkanes

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Copper-based catalysis represents a recognized and sustainable alternative to many important organic transformations that traditionally involve significantly more expensive metal-containing catalysts. Despite intensive research on copper-based catalytic systems for hydrocarbon functionalization, most of them have limitations in terms of activity, selectivity, and sustainability, or require the synthesis of expensive ligands and the use of unfavorable reaction conditions.

The present study describes the self-assembly generation of new Cu(II) coordination compounds from an aqueous-medium reaction mixture composed of copper(II) nitrate, H_3bes biobuffer (*N*,*N*-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid), ammonia and benzenecarboxylic acid, namely 4-methoxybenzoic (Hfmba) or 4-chlorobenzoic (Hfcba) acid. Two products were isolated from each reaction, namely 1D coordination polymers $[Cu_3(\mu_3\text{-}OH)_2(\mu\text{-fmba})_2(fmba)_2(H_2O)_2]_n$ (**1**) or $[Cu_2(\mu\text{-}OH)_2(\mu\text{-fcba})_2]_n$ (**2**) and discrete tetracopper(II) rings $[Cu_4(\mu\text{-Hbes})_3(\mu\text{-}H_2bes)(\mu\text{-fmba})]\cdot 2H_2O$ (**3**) or $[Cu_4(\mu\text{-Hbes})_3(\mu\text{-}H_2bes)(\mu\text{-fcba})]\cdot 4H_2O$ (**4**), respectively. The compounds were obtained as microcrystalline air-stable solids and characterized by standard methods, including the single-crystal X-ray diffraction [1].

Catalytic activity of **1**–**4** was investigated in two model reactions: (a) mild oxidation of saturated hydrocarbons with hydrogen peroxide to form alcohols and ketones, and (b) mild carboxylation of alkanes with carbon monoxide, water and peroxodisulfate to generate carboxylic acids. Effects of different parameters were studied, including an effect of acid co-catalyst and various selectivity parameters. Apart from notable catalytic activity, this study showcases a novel time-dependent synthetic strategy for the self-assembly of two different Cu(II) compounds from the same reaction mixture.

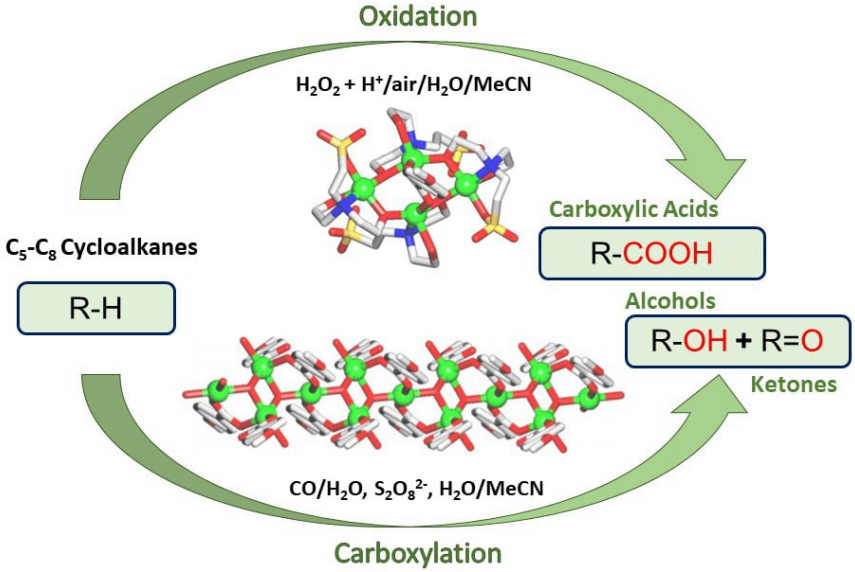

Figure 1. Model Cu-catalyzed hydrocarbon oxidation and carboxylation reactions.

This work has been supported by the Foundation for Science and Technology (FCT) (grant PD/BD/150418/2019 and projects LA/P/0056/2020, UIDB/00100/2020, UIDP/00100/2020, PTDC/QUI-QIN/3898/2020, CEECIND/03708/2017, LISBOA-01-0145-FEDER-029697).

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Sustainable development of a novel rosamine loaded metal-organic framework as a powerful fluorescent nanoplatform for sensing of Cu(II)

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Copper (Cu) is a vital trace metal that plays a crucial role in many biological systems that govern the human body. In excess, free Cu ions can cause abnormal cellular events that are believed to be linked to many neurodegenerative diseases including Wilson's, Menkes, Alzheimer's and Parkinson's diseases. Therefore, it is of utmost importance the development of new and improved sensors for monitoring different Cu sources, such as industrial sources of waste, water pipes and drinking water [1].

Over the last 10 years, metal-organic frameworks (MOFs) have proven to be powerful platforms for many applications including catalysis, adsorption, and particularly as sensory materials capable of accurately and selectively monitoring many analytes of interest [2,3]. Thanks to their porous structure, MOFs exhibit unique characteristics that make them excellent chemical sensors. The present work intends to develop fluorescent materials that can overcome some of the limitations of organic dyes, such as self-quenching caused by aggregation and their low water stability, while maintaining their sensory capability to detect and quantify harmful substances accurately and selectively.

With this in mind, we developed, via several different strategies, new composite materials that combine the interesting properties of MOFs, namely UiO-66, with the sensory capability of rosamine dyes. The results revealed that the *in-situ* incorporation of the rosamine dye plays a crucial role in the sensory capability of the nanoplatform here reported. Thereby, we applied sustainable methodologies, namely the use of recycled polyethylene terephthalate (PET) and alternative heating methodologies, such as microwave and ohmic heating [4]. The developed synthetic strategies and the sensory properties of the resulting materials will be presented and discussed.

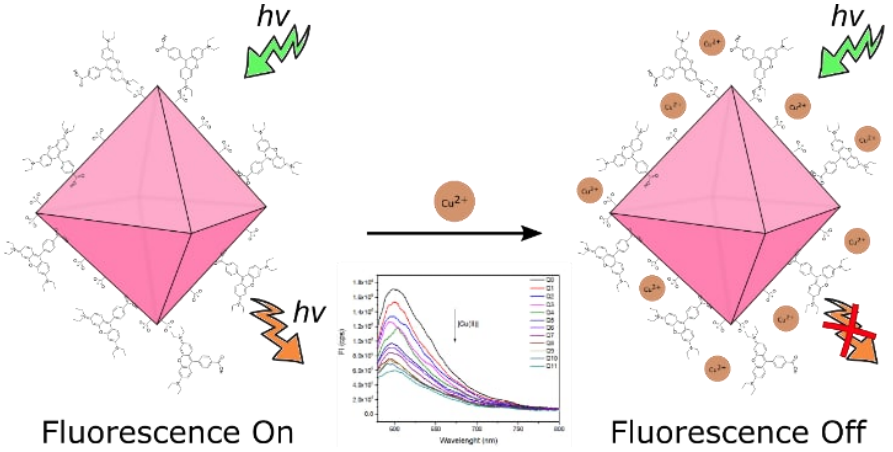

Figure 1- Schematic diagram of the fluorescence detection mechanism.

Acknowledgments: This work received financial support from National Funds (FCT/MCTES), under the Partnership Agreement PT2020 through projects NORTE-07-0162-FEDER-000048, UIDB /50006/2020, UIDP/50006/2020, the projects PTDC/QUI-QIN/28142/2017, PTDC/QUI-QOR/29426/2017 and EXPL/QUI-OUT/1554/2021.

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Preparation of porphyrin derivatives of Tröger's and spiro-Tröger's base

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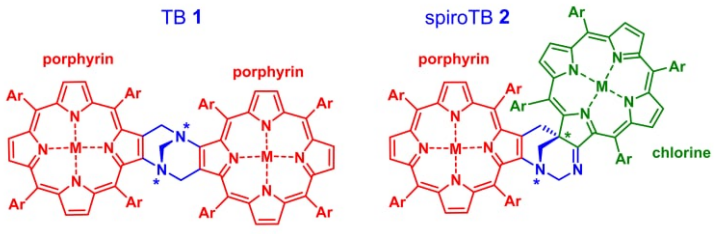
In 2012 we have discovered that the formation of porphyrin Tröger's base (TB) **1a-Ni$_2$** is accompanied by the formation of spiro-Tröger's base (spiroTB) **2a-Ni$_2$** (see figure) [1]. To this date, only five spiroTB derivatives have been described [1-3] from which only the **2a-Ni$_2$** derivative contains a porphyrin core in its structure [1]. SpiroTB derivatives and their properties are therefore rather unknown. Porphyrin spiroTB **2** is an interesting molecule, as it has a dramatically different molecular shape from the porphyrin TB **1**, and therefore should have different physicochemical properties (e.g., chiral recognition properties). In addition, by the formation of a spiroTB **2**, one porphyrin core is transformed into a chlorine core. Due to the presence of chlorine in the spiroTB molecule, a new absorption band at around 625 nm appears in the absorption spectrum. This absorption band is close to the area of the so-called phototherapeutic window (650-850 nm) of the electromagnetic radiation spectra, which indicates the possibility of the use of spiroTB **2** derivatives for various applications, such as photodynamic therapy [4].

We have prepared a series of porphyrin spiroTB **2** derivatives and their TB **1** analogues with different *meso*-aryl substitutions (Ar = Ph (**a**), 3-MeO-Ph (**b**), or 4-MeO-Ph (**c**)) in a form of nickel(II) complexes (M = Ni) or in form of free bases (M = 2H). Free bases of porphyrin spiroTB derivatives **2** were prepared for the first time. All the prepared compounds were isolated and characterized by NMR spectroscopy and HRMS and UV-Vis spectrometry. Due to the high relative molecular mass of the prepared compounds (M_R > 1287) and due to the hindered rotation of *meso*-aryl substituents, the NMR spectra of obtained compounds were rather complicated and had to be measured at temperatures exceeding 140°C. UV-Vis spectra were compared with respect to the presence of complexed metal in the porphyrin core and the effect of the *meso*-aryl substitution. In the case of spiroTB derivatives **2b-H$_4$** and **2c-H$_4$**, intensive absorption bands have been observed at 675 nm (area of the phototherapeutic window), indicating the possibility of their use in photodynamic therapy. In the case of nickel(II) complexes, enantioseparations were performed using HPLC analysis on a chiral stationary phase. In general, enantiomers of spiroTB **2** derivatives have shown higher resolution in comparison to TB **1** derivatives, indicating the possibility of their use for chiral applications. In addition, preparative enantioseparation of spiroTB **2** enantiomers was performed for the first time.



1a-Ni$_2$: Ar = Ph, M = Ni
1a-H$_4$: Ar = Ph, M = 2H
1b-Ni$_2$: Ar = 3-MeO-Ph, M = Ni
1b-H$_4$: Ar = 3-MeO-Ph, M = 2H
1c-H$_4$: Ar = 3-OH-Ph, M = 2H

2a-Ni$_2$: Ar = Ph, M = Ni
2a-H$_4$: Ar = Ph, M = 2H
2b-Ni$_2$: Ar = 3-MeO-Ph, M = Ni
2b-H$_4$: Ar = 3-MeO-Ph, M = 2H
2c-H$_4$: Ar = 3-OH-Ph, M = 2H

Financial support from the grant of Specific university research – grant No. A2_FCHI_2021_019 and from the MSMT LTAUSA19065 grant is gratefully acknowledged.

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Bioactive Metal-Organic Networks for Antimicrobial Applications

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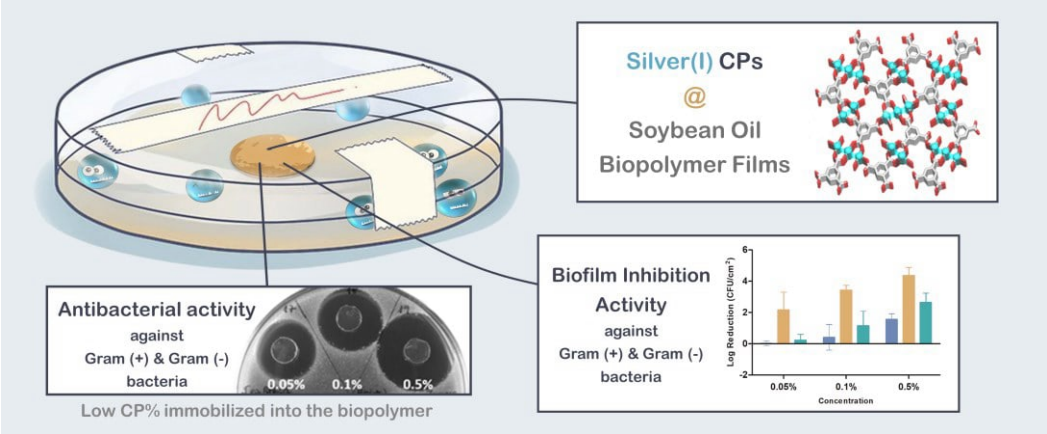
This presentation will highlight our recent research on the self-assembly synthesis, crystallization methods, structural features and applications of a wide diversity of functional metal-organic architectures, including bioactive metal-organic frameworks (bioMOFs), coordination polymers (bioCPs) and derived materials with potent antimicrobial properties [1,2]. The following topics will be discussed:

(1) Self-assembly generation and structural diversity of silver(I) and copper(II) coordination polymers derived from carboxylic acids and aminoalcohols.
(2) Application of these compounds as efficient antimicrobials against different types of Gram-positive and Gram-negative bacteria, and bacterial biofilms.
(3) Design of bioCP-doped polymer films, based on epoxidized soybean oil acrylate (ESOA) or potato starch (PS) as model biopolymer materials.
(4) Antibacterial and biofilm inhibition activity of the obtained biopolymer films as a function of bioCP dopant type and loading, biopolymer matrix, and metal ion release rates (Fig. 1).

This multidisciplinary study expands antimicrobial use of bioactive coordination polymers [3] and hybrid biopolymer materials obtained from renewable biofeedstocks such as soybean oil and potato starch.



All the coauthors of the cited references are gratefully acknowledged. Financial support is provided by the FCT (PTDC/QUI-QIN/29697/2017, LA/P/0056/2020, UIDB/00100/2020, Portugal).

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Systematic investigation of the influence of electronic substituents on dinuclear gold(I) amidinates: Synthesis, characterisation and photoluminescence studies

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Dinuclear gold(I) compounds are of great interest due to aurophilic interactions which influence their photophysical properties. We report on the capability of ligands with various electronic properties and their influence on gold(I)-gold(I) interactions. Therefore, various *para* substituted N,N'-bis(2,6-dimethylphenyl)formamidinate ligands (**L^1-L^6** *p*RXylForm) (Xyl = 2,6-dimethylphenyl, Form = formamidinate) were treated with Au(tht)Cl (tht = tetrahydrothiophene) to give the corresponding gold(I) compounds [*p*RXylForm$_2$Au$_2$] (R = -OMe (**1**), -Me (**2**), -Ph (**3**), -H (**4**), -SMe (**5**), -CO$_2$Me (**6**)) via a salt metathesis reaction.[1, 2] All complexes show distinct aurophilic interactions and intense luminescence properties at low temperatures (77 K). Alignment with the Hammett parameter σ_p revealed trends for the ^{1}H and ^{13}C NMR spectra. This indicates the influence of different donor-acceptor strength on the ligand system and were confirmed with calculated orbital energies. Photophysical investigations show lifetimes in millisecond range, indicating phosphorescent processes and revealed a redshift with decreasing donor ability of the substituents in solid state.

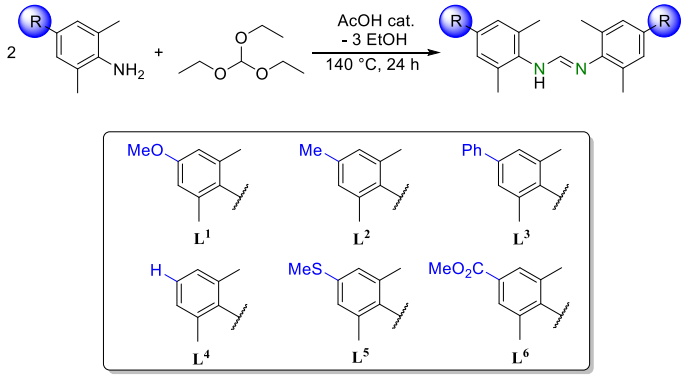

Figure 1: Synthesis of the amidine ligands **L^1-L^6**.

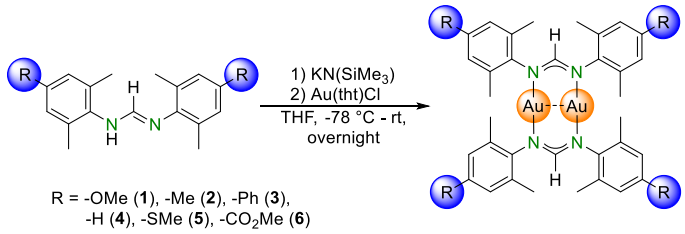

Figure 2: Synthesis of the gold complexes **1**–**6**.

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Photodissociation studies of half-sandwich type Ru(II) complexes containing different (N,N) chelates

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Ru(II)-based complexes have drawn great attention as photoactivatable compounds owing to their potential anticancer activity and tunable photophysical properties. Local activation of a complex in cancer cells provides a noninvasive, powerful method to reduce toxic side-effects due to offering spatial and kinetic control over the administered prodrug. In recent years, Ru(II) polypyridyl complexes with octahedral/distorted octahedral geometry have emerged as promising candidates for both PDT and PACT; TLD1433 the first Ru(II)-based photosensitizer for PDT has already entered human clinical trials [1,2]. Another large family of Ru(II)-based compounds, half-sandwich type Ru(II) arene complexes with the general $[(\eta^6\text{-arene})Ru(XY)Z)]^{n+}$ formula (where XY is a bidentate while Z is a monodentate ligand) also show attractive prospects in photoactivated chemotherapy as they can covalently bind to DNA after photoinduced ligand dissociation involving monofunctional coordinative and intercalative modes [1,3].

As the activity of Ru(II) containing PACT compounds is strongly related to the efficiency of ligand release, numerous works have been devoted to study the effect of the different half-sandwich type moieties (arene, chelating and monodentate ligand) on the photochemical behaviour. Investigation of kinetically inert, mononuclear $[(\eta^6\text{-arene})Ru(N,N)Z]^{2+}$ complexes (where (N,N) is a chelating, Z is a pyridine or pyridine derivative) revealed that the monodentate ligand can selectively dissociate upon exciting with UV or white light [4]. However, irreversible decomposition – most probably linked to the arene loss - has been published nowadays for the $[(\eta^6\text{-arene})Ru(N,N)(H_2O)]^{2+}$ and $[(\eta^5\text{-Cp*})Rh(N,N)(H_2O)]^{2+}$ type complexes when exposed to light [5].

In this work, we have studied $[(\eta^6\text{-}p\text{-cym})Ru(N,N)DMAP]^{2+}$ (DMAP = 4-dimethylaminopyridine) complexes to get a deeper insight into the steric demand and electronic properties of the incorporated (N,N) donor ligands on photoactivation. We have synthesized some of the above mentioned Ru(II) complexes with systematic variation of chelators such as ethylenediamine (en), 2-picolylamine (pic) and 1-10-phenanthroline (phen). These ligands can form 5-membered (N,N) chelates containing aliphatic, aliphatic-aromatic or aromatic nitrogens, which may influence the photochemical reactivity of the complexes.
This contribution summarises the results obtained. X-ray structure of $[(\eta^6\text{-}p\text{-cym})Ru(pic)(DMAP)](PF_6)_2$ will also be reported.

The authors would like to thank the Hungarian Scientific Research Fund (MEC_R 141258) for the financial support.

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2D and 3D silver(I) metal-organic architectures assembled from 1,3,5-triaza-7-phosphaadamantane-7-oxide and 1,3,5-triaza-7-phosphaadamantane-7-sulfate: synthesis, structural features, and antimicrobial activity

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Coordination polymers (CPs) and metal-organic frameworks(MOFs) represent a rapidly evolving class of coordination compounds. The applicability of these materials in various fields is vast (including gas absorption, drug delivery, target therapies, etc.), and new possibilities for their use in other areas are constantly being discovered. The appropriate choice and arrangement of inorganic and organic building blocks open up the possibility of creating new materials with fascinating metal-organic architectures and functional properties. Therefore, a fruitful direction consists of using a mixed ligand synthesis strategy that includes carboxylate and aminophosphine building blocks with O,O-, N,O-, P,N-, and N,S-donor sites [1,2].

Herein, we report two novel 2D and 3D silver(I) carboxylate-based coordination polymers driven by water-soluble cagelike aminophosphine derivatives, namely 1,3,5-triaza-7-phosphaadamantane-7-oxide (PTA=O) and 1,3,5-triazaphosphaadamantane-7-sulfate (PTA=S) (Figure 1). In this poster communication, we will discuss the aspects of the synthesis, structural features, and biological activity of the obtained coordination polymers.

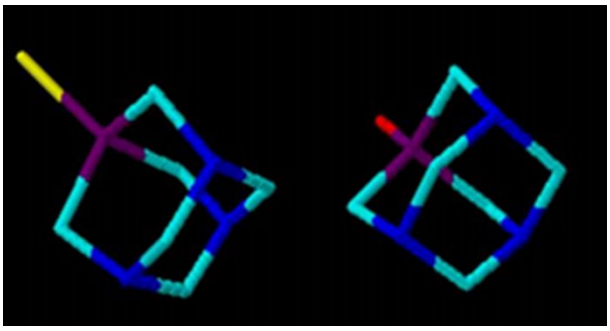

Figure 1. 1,3,5-triaza-7-phosphaadamantane-7-oxide (PTA=O) and 1,3,5-triazaphosphaadamantane-7-sulfate (PTA=S).

We thank the National Science Center (Grant No. 2019/35/D/ST5/01155, Poland) for financial support. AMK acknowledges the FCT (PTDC/QUI-QIN/29697/2017, LA/P/0056/2020, UIDB/00100/2020, Portugal).

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Group-4 metal based MOFs. Adsorption and catalytic properties of EHU-30 family

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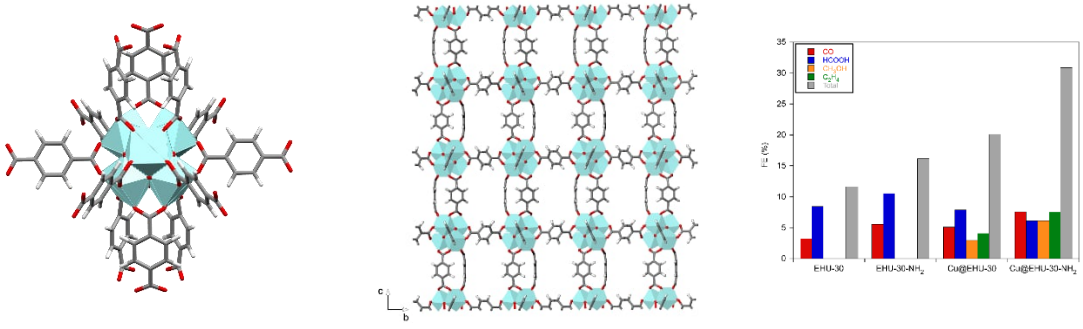
Since its discovery in 2008, the paradigmatic UiO-66 can be regarded as the germ that has prompted the chemistry of group-4 metals (Ti, Zr, Hf) based metal-organic frameworks (MOFs). Their interest arises from their outstanding thermal and chemical stability, which has promoted to test them in applications in which many common MOFs collapse. However, the tightness of their building blocks and bond strength make it tough to access new topologies, but the use of well-selected structure directing agents and harsh synthesis conditions allowed us to isolate the first polymorph of UiO-66, named EHU-30,[1] and their Zr- and Hf- based amino-functionalized analogous: EHU-30-NH_2(M) and EHU-30-NHR(M) (M: Zr, Hf; R: 2-carboxypropyl).[2] The crystal structure analysis reveals 8-connected [$Zr_6O_4OH_4(OOC)_{12}$] secondary building units (Figure 1a) linked into a polymeric framework with **hex**-type topology (Figure 1b) and superior porosity to that of their polymorphic counterparts.

Taking into account the relevance of MOFs in greenhouse gas capture and utilization and in water harvesting technologies, we have explored CO_2 and water-vapour adsorption of the polymorphic phases by means of experimental and computational resources, showing that the amino functionalization makes the EHU-30 series more prone to adsorb these species.[2] To further study their potential applications, we have doped them with copper(II) and analysed their performance on the electroreduction of CO_2 towards value-added products. The analyses suggest that the Cu(II) doping takes place through a transmetalation reaction and show how the amino function enhanced the yield of the process, while the incorporation of Cu(II) turns the product selectivity toward more reduced species (Figure 1c).[3]



(a) (b) (c)

Figure 1. (a) Hexameric cluster of EHU-30 showing the disposition of the ligands, (b) three-dimensional packing of EHU-30 showing the connection of the hexagonal layers, and (c) faradaic efficiency (FE) as function of the EHU-30 based electrocatalysts.

Thanks to Spanish Ministry of Science and Innovation (PID2019-108028GB-C21). Technical and human support provided by SGIker (UPV/EHU, MICINN, GV/EJ, and ESF) is also acknowledged.

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Bioinspired Catalysis And Hydrogen Technologies: When Nanosciences And Electrocatalysis Flow Together

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Transitioning toward a post-oil society (as part of the the so-called ecological transition) is a major challenge for our modern economies and will require new efficient, stable and cheap catalytic materials based on abundant elements. Specific hurdles relate to the storage of electrical or solar power as fuels and/or chemicals, and the conversion of chemical energy into electrical power in fuel cells. These alternative energy processes will all involve multielectron-multiproton reactions, the kinetics of which are inherently sluggish unless driven by catalysts. The structure of the active sites of enzymes involved in bioenergetic processes can inspire the design of active, stable and cost-effective catalysts [1]. In particular hydrogenase enzymes compete with platinum as catalysts for H_2/H^+ interconversion and such an activity can be reproduced in synthetic mimics [2], the performance of which can be benchmarked in "catalytic Tafel plots" [3]. However, for these materials to reach maturity, the benefits of such bioinspired systems must be combined with practical technological requirements. We will show how the immobilization of biomimics onto surfaces allows the preparation of electrode materials approaching industrial current densities and compatible with existing PEM electrolysis technology [4-9], allowing for the assembly of noble-metal free H_2/O_2 fuel cells.

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Polyelectorlyte complexes of substituted macrocycles and native DNA in the assembly of electrochemical (bio)sensors

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Supramolecular chemistry offers new opportunities for the development of artificial receptors able to efficient binding of various substrates and influence their interaction within common biochemical paths. Such systems find growing application in design of drug delivery systems, tests, biosensors etc. Due to multiple non-covalent binding, supramolecular structures can be easily adapted to the specific structure of a natural counterpart and provide universal approaches to recognition of specific targets based on general principles of recognition and self-assembling. Macrocyclic platforms on the thiacalixarene and pillararene core are considered as most promising candidates for design of such materials due to easy functionalization of the substituents, their pre-organized steric structure, rather simple introduction of functionalities required for recognition of biomolecules and tuning properties important for sensing, e.g., hydrophobicity, self-assembling ability, charge separation, electrochemical activity etc. In this work, the tool of electrochemistry was successfully applied for the investigation of new polyelectrolyte complexes consisting of DNA and derivatives of thiacalix[4]arene and pillar[5]arene bearing anionic (carboxylic) or cationic (primary amino and quaternary ammonia) groups. As was shown, variation of the macrocycle structure allowed assembling electrochemical sensors and biosensors for determination of the DNA binding species and for detection of specific DNA interactions with predictable characteristics.

Polyelectrolyte complexes consisted of alternating layers of macrocyclic receptors and native DNA obtained by consecutive drop casting of the reactants on the glassy carbon electrode. Assembling progress was monitored by the cyclic voltammetry and electrochemical impedance spectroscopy. The role of steric and electrostatic factors in the complex formation and in the recognition functions were assessed using redox probes (ferricyanide, methylene green, hydroquinone) able to the reversible electron exchange and to response to the specific DNA reactions with model intercalators. Variation of the thiacalix[4]arene configuration (cone, partial cone and 1,3-alternate) resulted in remarkable changes of the signals. The role of underlying surface was characterized for different modifiers (polymers and carbon nanomaterials) deposited on the electrode prior to the polyelectrolyte assembling. The results showed that interactions between the terminal functional groups of the macrocycles and phosphate residues of the DNA backbone have crucial importance for the biochemical specific interactions with DNA molecules. Directed selection of the macrocycle structure (configuration, spacers of the substituents, terminal functional groups) and conditions for the polyelectrolyte complex assembling (underlying surface, number of layers, nature of redox probe) made it possible to alter the sensitivity (slope of calibration curve) and diminish the limit of detection of doxorubicin as model intercalator to picomolar concentrations. Besides, the comparison of the results obtained with the redox probes different in their charge and mechanism of DNA interactions allowed discriminating the DNA damaging factors (thermal denaturing and reactive oxygen species damage). This offers broad opportunities for application of such polyelectrolyte complexes in the assembly of biosensors intended for the determination of drug residues, estimation of DNA damaging factors and preliminary assessment of antioxidant capacity of the foodstuffs based on their protecting effect in DNA damage by Fenton reagent. Electrochemical biosensors with voltammetric and impedimetric response were tested on spiked samples of urine and blood serum containing doxorubicin, as well as on the quality assessment of appropriate medicines (doxorubicin-LANS) and tea fusions.

Financial support of Russian Science Foundation (grant No 21-73-20067) is gratefully acknowledged.

DNA-ferrocene as two-step-mechanophore

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Since many years, researchers are interested in sandwich-type complexes that can be used in various areas like in catalysis, in electrochemistry, in agrochemical applications or for the production of pharmaceuticals and flavours.[1, 2] Recently, we have shown that ferrocene can be used as a mechanophore in polymers, hence as preferential breaking point in poly methyl-acrylate and polyurethane.[3]

We have now introduced additional functionality by associating the ferrocene moieties via a linker [4] to a DNA duplex. Embedding such an entity into a polymer is expected to give rise to a two-step mechanophore [5] (Figure 1) in which first the H-bonds of DNA, and then the sandwich-complex are cleaved as increasing force is exerted. Mismatches that have been introduced in the DNA pairing, have an influence on the mechanical strength of the mechanophore.

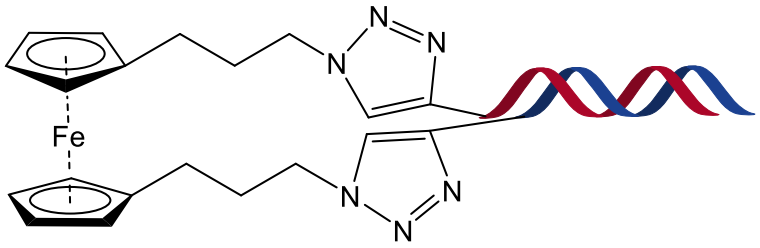

Figure 1: Ferrocene linked to DNA

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Photocyclization to form new cell permeable cyclodepsipeptides

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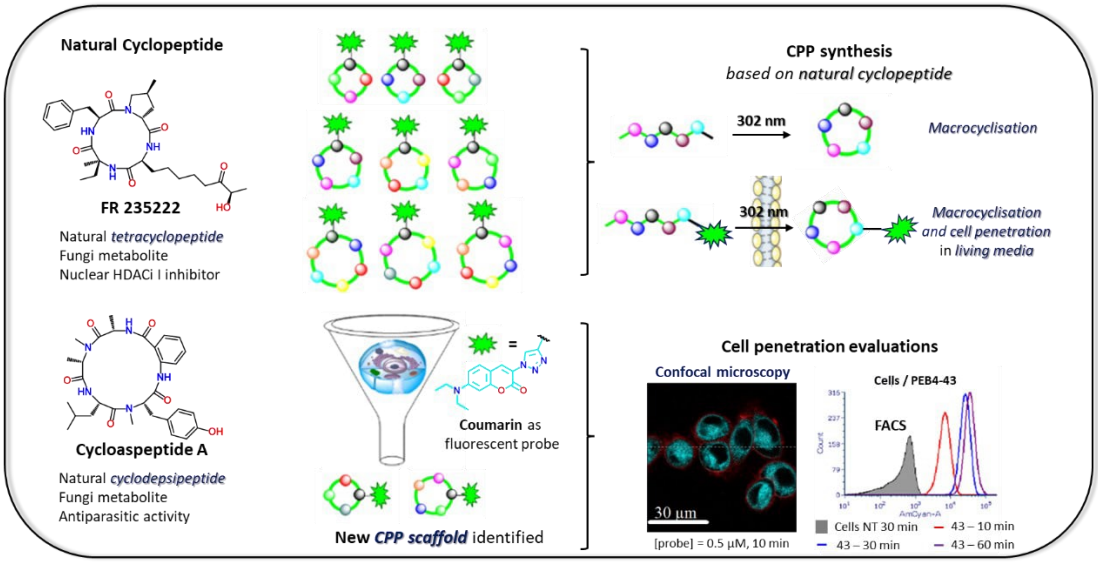
One of the challenges for a drug is to be able to cross the physiological barriers that separate it from its target. The inability to cross the cell membrane is often the reason that drugs are limited in their effect. An emerging strategy is the use of cell penetrating agents such as cyclopeptides to transport it into the cell.[1,2] Recently, we have shown that a small cyclotetrapeptide inspired by the natural product FR235222 can deliver a fluorescent probe both in the cytosolic and nuclear compartments.[3,4] Natural cyclopeptide and cyclodepsipeptide effectors can be a source of inspiration for integrating various and new structural motifs into the cell penetrating scaffold.[2,5]

In this communication, we wish to present our latest work concerning the research and discovery of new cell penetrating agents. Indeed, we have identified small uncharged cyclodepsipeptides with improved cell penetration efficacy. We have also developed a new method of light-induced macrocyclization to control internalization in the cell in a spatio-temporal manner. The photocyclization experiment carried out in biological medium shows that macrocyclization can occurs in the biological environment under UV light at 302 nm which confers a large scope of application to this new cell penetrating vector.



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Donor atom preference of metal ions with biological relevance to construct heterobimetallic complexes having likely hypoxia activation

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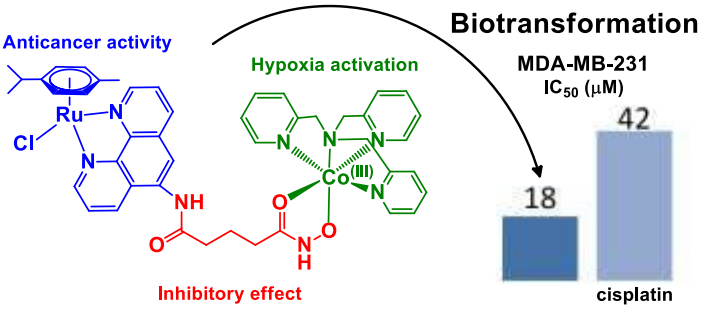
Pt(II)-based anticancer agents currently used for the treatment of some type of cancers suffer from lack of selectivity therefore there is an urgent need to develop novel metal compounds with higher selectivity and with less side effects. Higher selectivity might be achieved by considering the differences between healthy and cancer cells/tissues. Among these differences hypoxia in cancer tissues results in a reductive environment allowing e.g. inert Co(III) complexes to selectively be reduced [1] and to release biomolecules with various (e.g. anticancer, metalloenzyme inhibitory, iron(III) sequestering) properties. Incorporation into of these chaperon Co(III) complexes another metal ions with proven anticancer potential may result in further advantage and improved biological activity.

Ambidentate ligands may serve as useful building blocks for heterobimetallic complexes with various properties. In an ongoing project to develop cobalt(III)-platinum group metal (Co/PGM) complexes with likely hypoxia activation and selective anticancer activity various ligands incorporating separate O and N donor sets have synthesized and characterized. Although a $[Co(4N)]^{3+}$ ion (4N = tripodal 4N donor (tren, tpa) or 2x2N (phen, bpy, en, ampy)) with two vacant coordination sites is considered as a hard metal entity while PGMs are known to behave as soft metal ions their preference to coordinate to the above chelating sets needs to be explored for the successful solid phase synthesis of the desired Co/PGM complexes or to foresee the fate of the prepared solids after administration.



This contribution will summarize some of our latest results obtained on the metal ion binding capabilities of different type of ambidentate chelating ligands with various (N,N) and (O,O) chelating sets using the combination of pH-potentiometry, NMR and ESI-TOF-MS techniques in aqueous solution [2-9].

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Unlocking the recognition of the immunomodulatory human macrophage galactose C-type lectin

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Glycans have an important role on immune modulation.[1] The human macrophage galactose C-type lectin (MGL) is the only C-type lectin present on immune cells with a marked sugar specificity for N-acetylgalactosamine (α- or β-GalNAc) [2]. MGL recognizes GalNAc containing structures that can be present in pathogens, self-glycoproteins, and tumour cells, which makes of MGL a modulator of distinct immune cell responses. Herein, our latest advances in unlocking the structural and dynamic features behind the fine specificity and recognition of MGL will be described.

By following an integrative and multidisciplinary approach, which combines glycopeptide synthesis and molecular biology protocols, with biophysical and structural techniques with special focus on nuclear magnetic resonance spectroscopy (NMR), we revealed that the structure of the carbohydrate recognition domain (CRD) of MGL is highly dynamic and is strongly dependent of the structure and presentation of the precise GalNAc-containing antigen [3-5]. This plasticity of MGL-CRD perfectly agrees with the ability of MGL-CRD to accommodate different GalNAc-containing ligands and might explain the capacity of MGL to produce distinct immune responses (tolerance vs immunity) depending on the nature of the GalNAc-containing structure. Furthermore, the molecular recognition of distinct mucin-1 tumour-associated carbohydrate antigens, common in several tumours, by MGL was also investigated, and our data also pinpoints the ability of MGL to discriminate different tumour-associated antigens.

The authors acknowledge FCT-Portugal for funding projects: IF/00780/2015, PTDC/QUI-OUT/2586/2020, UCIBIO project UIDP/04378/2020 and UIDB/04378/2020 and Associate Laboratory Institute for Health and Bioeconomy - i4HB project LA/P/0140/2020). FM and H.C. thanks FCT for the CEEC contract 2020.00233.CEECIND and 2020.03261.CEECIND, respectively. A.D. acknowledges the PhD grant PD/BD/142847/2018 under the PTNMRPhD Program (PD00065/2013). The NMR spectrometers are part of the National NMR Facility supported by FCT-Portugal (ROTEIRO/0031/2013- PINFRA/22161/2016, cofinanced by FEDER through COMPETE 2020, POCI and PORL and FCT through PIDDAC). F.M. and J.J.B. acknowledge the COST Action GLYCONanoProbes (CA18132).

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Structural features and health effects of water-soluble organic matter from atmospheric fine particulate matter

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Fine atmospheric particulate matter ($PM_{2.5}$, < 2.5 µm) exposure has been recognized as a key public health issue, being linked with increased risks of lung cancer, cardiovascular, and respiratory diseases [1]. Moreover, PM exposure has been shown to affect the immune system, leading to an increased susceptibility to infections and pathogens, or exacerbating pre-existent lung diseases [2]. The main mechanisms through which $PM_{2.5}$ can affect the human health, include the induction of reactive oxygen species (ROS) , the triggering or exacerbation of an inflammatory response, and PM-related direct cytotoxicity, with these effects mostly affecting lung cells [1]. These toxicological effects are associated with $PM_{2.5}$ concentration, and its composition in metals and solvent-extractable organics [3,4]. Although not receiving much attention, the ubiquitous water-soluble organic matter (WSOM) present in $PM_{2.5}$ has been recognized as capable of mediating ROS generation [5,6]. Furthermore, WSOM can account for a significant portion of $PM_{2.5}$ mass. Hence, it is important to better understand the impacts of exposure to this $PM_{2.5}$ fraction.

In this work, we highlight the link between the structural features of daytime and nighttime $PM_{2.5}$ WSOM samples and their effects on lung macrophages [6]. We show how the structural features of WSOM samples differ between day and night periods and between seasons. These fractions did not induce the generation of ROS on exposed lung macrophages and were in fact capable to inhibit bacterial lipopolysaccharide-triggered ROS generation in exposed cells. We also observed that this $PM_{2.5}$ fraction induced a moderate inflammatory state in exposed macrophages in acute exposure setups, whereas in chronic exposure setups, the cells presented an impaired capacity to respond to subsequent strong pro-inflammatory stimuli. This indicates that chronic exposure could compromise the lung macrophages capacity to manage harmful pathogens, thus increasing infection susceptibility [6]. Finally, the ongoing research on the mechanisms of aerosol WSOM-induced respiratory diseases will be also addressed.

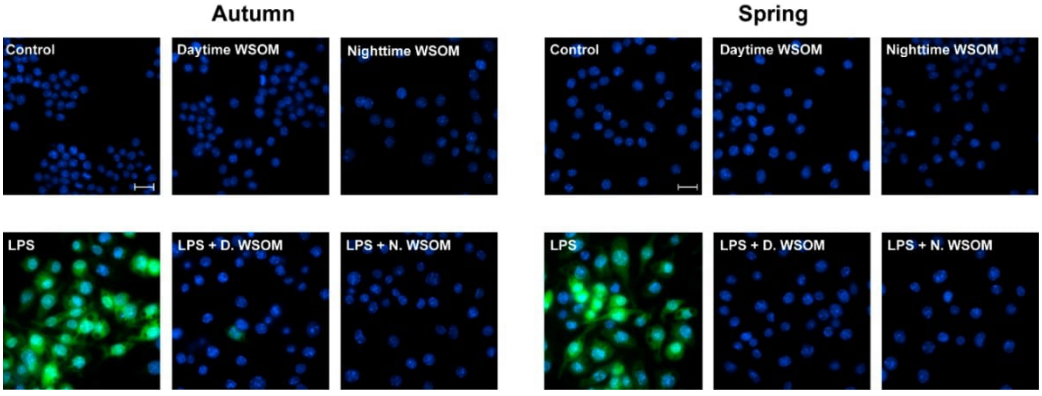

Figure 1. ROS production and modulation of LPS-induced oxidative stress by WSOM extracts on lung macrophages. H_2DCFDA (green) and Hoechst (blue) were used to label ROS and the nuclei, respectively. Reprinted (adapted) with permission from Almeida et al. Environmental Science & Technology 2020 54 (2), 1082-1091. DOI: 10.1021/acs.est.9b04596. Copyright 2020 American Chemical Society.

Financial support to CESAM by FCT/MCTES (UIDP/50017/2020+UIDB/50017/2020+LA/P/0094/2020), and iBiMED (UIDB/04501/2020) through national funds is acknowledged. FCT/MEC and the ESF are acknowledged for a PhD grant (2020.05804.BD). This work was supported by project AMBIEnCE (PTDC/CTA-AMB/28582/2017) funded by FEDER, through COMPETE2020, and by national funds, through FCT/MCTES. The Surface Ocean-Lower Atmosphere Study (SOLAS) project is also acknowledged for endorsing the AMBIEnCE project.

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A traceless strategy for the cytosolic delivery of proteins *via* thiol-mediated uptake

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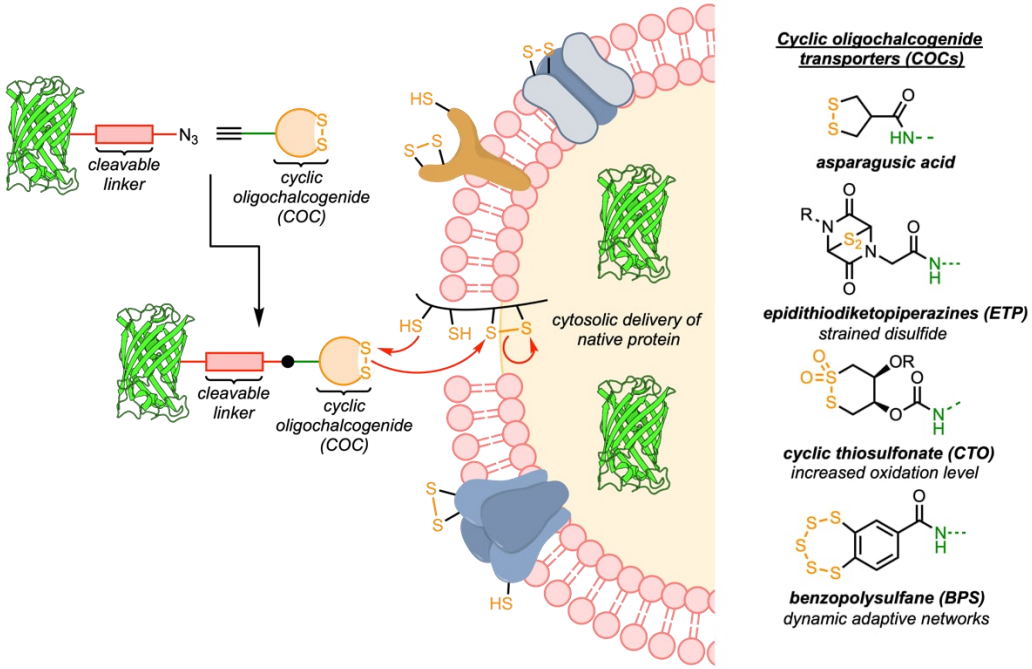
Thiol-mediated uptake is a term used to denote the enhanced cellular uptake observed for substrates bearing chalcogenides, typically disulfides, capable of engaging in dynamic covalent exchange cascades, with characteristic uptake inhibition from thiol-reactive reagents.[1] A number of transporters have been developed to exploit this pathway into the cell, such as cell-penetrating polydisulfides and small molecule cyclic oligochalcogenide (COC) transporters, and cargoes ranging in size from small molecule fluorophores to liposomes and polymersomes up to 400 nm in diameter.[1] Recent studies with oxidised cyclic thiosulfonates and the dynamic adaptive networks formed by benzopolysulfanes have demonstrated the potential of more exotic sulfur chemistries for enhancing thiol-mediated uptake.[2][3]

Due to their vital role in the proper functioning of the cell, proteins provide a potent class of potential therapeutic agents; however as most proteins are unable to cross the cellular membrane without modification, the majority are limited to targets at the cell surface.[5] Numerous delivery strategies have been developed to allow proteins to access the cytosol, however many suffer from issues such as endosomal entrapment.[5]

To develop a general approach for the cytosolic delivery of native proteins *via* thiol-mediated uptake, a cleavable linker was developed for the functionalisation of protein cargoes with an azide for subsequent derivatisation with COC-alkyne transporters. A selection of COC transporter units were screened to maximise cytosolic protein delivery, and the generality of the method was verified by delivery of proteins of a broad mass range. Finally, characteristic inhibition with thiol-reactive reagents provided conclusive experimental evidence for thiol-mediated uptake.



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Sharing compounds across Europe: EU-OPENSCREEN as the European research infrastructure for chemical biology

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The quality of a screening collection is one of the most critical factors of success in drug discovery. Academic compound collections often predominantly consist of compounds that are commercially available, but proprietary compounds synthesized by academic chemists as well as natural products represent a rich, untapped source for novel chemical diversity. In order to make the invaluable chemistry accessible to a broader scientific community and to allow chemists to uncover novel bioactivities of their compounds, EU-OPENSCREEN offers chemists the opportunity to make their compounds available, in a regulated and transparent framework, to a wider community of biologists, who screen these compounds in suitable bioassays. By doing so, chemists can expose their compounds to a broad range of different biological/drug targets to screen for unknown bioactivities of their compounds, which would otherwise not be feasible in individual one-to-one-collaborations. Once a compound has been identified as an active hit compound, a research collaboration between the chemist (who submitted the compound) and the biologist (who developed the bioassay) can be initiated.

The European research infrastructure EU-OPENSCREEN aims to support projects in early drug discovery. Through its more than 20 academic partner institutes across Europe, it offers complementary expertise and instrumentation for the development of novel chemical research tools for the Life Sciences community. EU-OPENSCREEN partner sites jointly use a unique diversity compound collection containing commercial as well as proprietary compounds submitted by chemists from all over Europe. The primary screening data will be made available to the scientific community through its open-access European Chemical Biology Database.

Here we will present this unique pre-competitive compound sharing model and explain the opportunities and benefits for chemists to make their compounds available to a broader scientific community. We will discuss this collaborative model in the context of collaborative initiatives, which aim to accelerate chemical biology and early chemical biology in academia.

This project receives funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 823893.

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Expanding enzymes' abilities with redox-dismantlable synthetic organometallic catalysts

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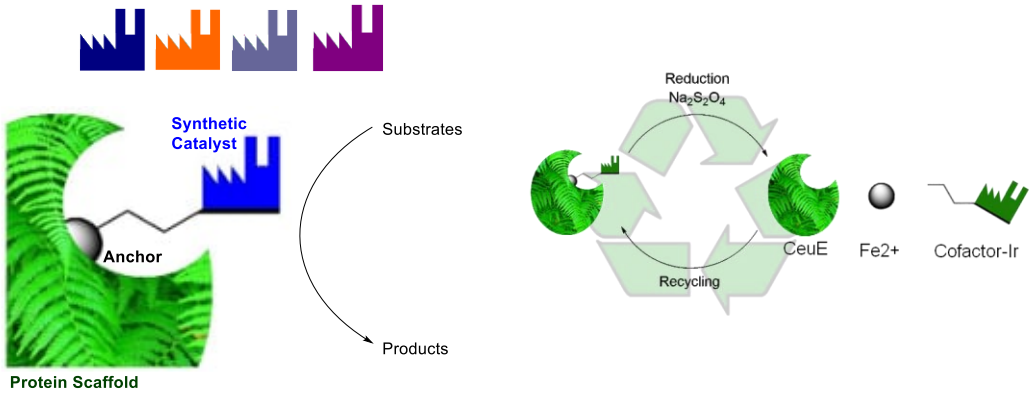
Being able to do chemistry in a more environment-friendly fashion is one of the main challenges every chemist is facing, and one of the best and the most evident way to do so is to use Nature's tools: enzymes. Enzymes are amongst the most selective and efficient catalysts we know, being able to transform large quantities of chemicals, with high TurnOver Numbers (TON) and with surgical precision. However, the high selectivity of these enzymes can also be a major disadvantage, as they are usually limited to a limited number of substrates and reactions, and their large size makes them difficult to modify. To broaden their range of action whilst taking advantage of their numerous qualities, Artificial Metalloenzymes were developed, merging natural enzymes with synthetic organometallic catalysts to obtain chimeric catalysts, able to perform unknown-to-nature reactions with the precision and the TONs of natural enzymes.[1] The work I will be presenting is about building such hybrid catalysts from a protein (CeuE) and various metallic catalysts, held together by an iron based releasable linker.[2] Such assembly allows the full electrochemical dismantling, recycling and repurposing of every part of the ArM, and could be used as a versatile platform to perform diverse chemical transformations in a multipurpose flow reactor, such as imine and ketone reductions, Diels Alder reaction and Grubbs metathesis.



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The nitrosylation of Vitamin B12 derivatives. What is the role of interaction between Vitamin B12 derivatives and selected intracellular antioxidants in NO/NO$^-$ chemistry?

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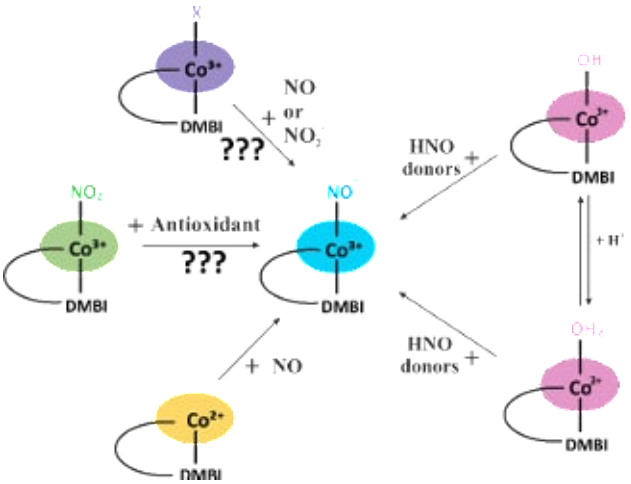
Nitric oxide (NO) and nitroxyl (HNO/NO$^-$), the product of the one-electron reduction of NO, are highly reactive molecules that are known to play an important role in physiological processes. Many of the mentioned activities involve the reactions of NO or HNO/NO$^-$ with biological molecules, oxygen or superoxide, as well as with metal complexes.

Over 20 years ago it was shown that interaction between the reduced form of Vitamin B12 and nitric oxide leads to the formation of the complex that is known as nitrosylcobalamin (CblNO) [1]. Studies on the formation of nitrosylcobalamin, as well as chemistry and biochemistry of this compound, were the subject of intensive research over the past years. Numerous studies demonstrated that CblNO can also be formed as a product of the interaction of Vitamin B12 derivatives and HNO/NO$^-$ donors like Piloty's acid, Angeli's salt or NONOates [2-4]. However, despite the numerous detailed studies, it is still questionable whether it is possible to obtain nitrosylcobalamin (CblNO) intracellularly via nitrocobalamin ($CblNO_2$) reduction.

The subject of the present research focused on the investigation of reactions involved in the formation of Vitamin B12 nitrosyl derivatives, viz. nitrosylcobalamin (CblNO). The concept included studies on the interaction between Vitamin B12 derivatives and selected biologically relevant antioxidants in aqueous solution. Additional studies involved the reaction of Vitamin B12 derivatives with NO and nitrite (NO_2^-). The mentioned reactions were studied by spectroscopic and kinetic techniques that enable elucidation of the molecular mechanism of the observed processes.



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Factors governing the competition between Sr^{2+} and Ca^{2+} in biological systems. Implications for strontium therapy

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Strontium (in the form of soluble salts) is used in medicine and pharmacology as a diagnostic or therapeutic agent. Its medicinal use stems from its ability to closely mimic calcium, thus following the calcium-specific pathways in the body involving cell signaling and bone formation. Both Ca^{2+} and Sr^{2+} are doubly charged "hard" cations with similar physicochemical properties and strong preference toward oxygen-containing "hard" ligands. Their ionic radii are similar as well, differing by only 0.18/0.15 Å in hexacoordinated/heptacoordinated complexes, respectively. Both dications are characterized with flexible coordination/hydration spheres comprising 6 to 9 ligands, and exhibit strong boneseeking properties in humans.

Although much information has been accumulated on the role of strontium as a calcium mimetic in biology and medicine, a systematic study delineating the key factors governing the competition between the two dications is still lacking, thus leaving several intriguing questions: (1) Can Sr^{2+} displace Ca^{2+} in calcium-binding proteins, and if so, how efficiently can it do so? (2) Which Ca^{2+}-binding sites are more prone to Sr^{2+} substitution? (3) Which characteristics of the host protein are the major determinant of the Sr^{2+} vs. Ca^{2+} competition?

Here, we attempt to address these questions by studying the Ca^{2+}/Sr^{2+} competition in calcium-binding sites (modeled in accordance with the X-ray structures of Ca^{2+} proteins) by employing density functional theory (DFT) calculations combined with polarizable continuum model (PCM) computations. We systematically evaluate how the rivalry between the two cations depends on the coordination/hydration number, the chemical type, number, denticity and charge of the protein ligands ligating the dication. We also assessed the effect of the secondshell interactions, as well as the rigidity and solvent exposure of the binding pocket. The findings of this work, which are consistent with available experimental data, help delineate the key determinants of selectivity of Ca^{2+} over Sr^{2+} in calcium proteins.

Acknowledgement: Todor Dudev is supported by the Bilateral Bulgaria-Russia Research Grant KP-06-Russia/30–2019.

Panoramic overview of unconventional approaches to detect chiral information

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The concept of inherent chirality has gained considerable attention due to the possible synthesis of π-conjugated monomers that can be employed for preparing chiral electrode surfaces after electrooligomerization [1]. These materials have been used in enantiorecognition measurements involving chiral analytes, resulting in high selectivity based on diastereomeric interactions between the deposited enantiopure antipode and the probes dissolved in solution. In this context the high enantioselectivity of such chiral surfaces was used in combination with the mechanical and electrical properties of polypyrrole (Ppy) films to develop three new straightforward read-outs for the absolute on-off recognition of enantiomers of a chiral probe in solution; i) electromechanical deformation (a) [2], ii) electrochemically induced light emission (b) [3] and iii) self-induced enantioselective trajectories (c) [4]. These new approaches allow to convert chiral information present at the molecular level into macroscopic actuation, light emission or controlled trajectories. Furthermore, such systems allow correlating the output signal with the concentration of the enantiomers present in solution, even in the case of mixtures containing different ratios of the molecular antipodes.

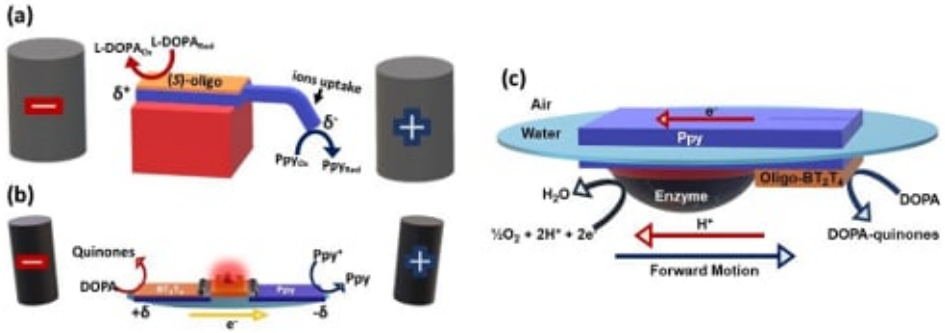

Figure. Three straightforward read-out concepts for the absolute on-off recognition of enantiomers.

This work has been funded by the European Research Council (ERC) under the HORIZON-ERC-2021 program (grant agreement no 101040798, ERC Starting Grant CHEIR)

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Rare metals catalyse a potentially prebiotic carbon fixation pathway

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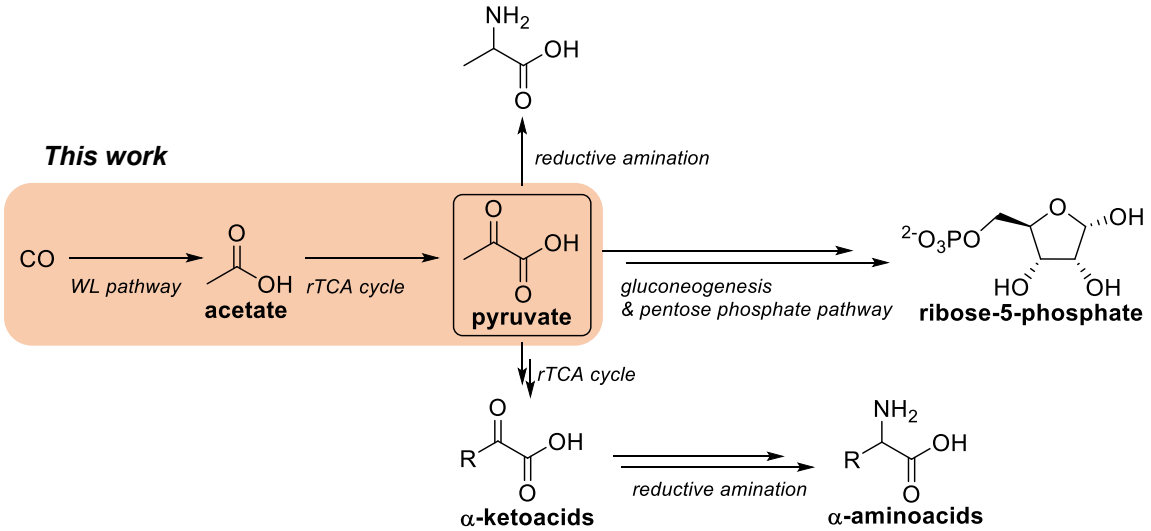
Metabolism is a complex self-organised network of enzyme-catalysed reactions. Enzymes are made from metabolites, yet, at the time of life's origins, enzymes had not evolved. How then did metabolism begin and why is it the way that it is? To answer this question, our lab explores the hypothesis that prebiotic chemistry roughly mirrored biochemistry using metals and minerals as precursors to enzymes.

The reductive acetyl-CoA pathway, also known as the Wood–Ljungdahl (WL) pathway, is believed to be the most ancient biological carbon fixation pathway [1,2]. It reduces carbon dioxide to acetate and to pyruvate, a key metabolite that is the entry point of gluconeogenesis and a precursor of other keto and amino acids. Recent work has demonstrated nonenzymatic versions of this pathway using metallic iron or H_2 gas as reductant, the latter under heterogeneous catalysis with all reactions happening on the surface [3,4]. Although remarkable, the flux through this nonenzymatic pathway is low. It is also unclear how entirely surface-bound reactions might have been replaced by enzyme catalysts. It is therefore worthwhile to explore alternative nonenzymatic versions of the acetyl-CoA pathway.

Although absent from modern metalloenzymes, some rare transition metals possess very high catalytic activity and might have played a crucial early role in chemical self-organization on early Earth. Rare metals would have been later replaced by more abundant metal catalysts once the synthesis of complex organic ligands could enable the catalytic activity of the latter, allowing the chemistry to persist in a wider variety of environments. Here we show a homogeneous rhodium catalysed analogue of the acetyl-CoA pathway.



Emilie Werner thanks the ENS for a PhD fellowship. This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program.

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Synthesis of a responsive paraCEST contrast agent for the magnetic resonance imaging of sulfatase-expressing tumors

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Paramagnetic Chemical Exchange Saturation Transfer (paraCEST) is an emerging Magnetic Resonance Imaging (MRI) modality in medical diagnostics. It enables sensitive and non-invasive imaging of important factors, such as pH, temperature, enzyme activity and receptor expression[1], by employing lanthanide complexes as imaging agents to enable selective water signal saturation (Fig. 1). Molecular engineering of those complexes can be used for the design of responsive paraCEST imaging agents.[1] Here we describe the synthesis and initial evaluation of ParaCEST contrast agents activated by sulfatases, which could serve for the detection of hormone-dependent breast tumours, where sulfatase are overexpressed.[2,3]

Responsive paraCEST imaging agents should only be activated upon enzymatic conversion to ensure that the imaging signal is enhanced in the areas of enzyme overexpression. The design principle of such activatable paraCEST contrast agents is the unmasking, upon enzymatic cleavage of the parent complex, of a functional group bearing exchangeable protons that can be selectively saturated. Fig. 1 presents our design of a sulfatase-responsive paraCEST agent 1-Yb, featuring an enzymatic cleavage site, connected through a self-immolative linker to the lanthanide complex. In the presence of sulfatase, the sulfate group of 1-Yb is hydrolysed and the resulting molecule undergoes 1,6-elimination, leading to the final compound 3-Yb, which features exchangeable protons for CEST imaging. Amine 3-Yb has been confirmed to be an active paraCEST imaging agent [4,5], which supports our molecular design

The poster will present the successful design, synthesis and evaluation of two molecules: complex 1-Yb as the ''off'' contrast agent, and complex 3-Yb as the ''active'' contrast agent, i.e., a model compound to study the paraCEST performance of the product of the enzymatic reaction. Initial studies have confirmed that 1, in the presence of sulfatase, is converted to 3, providing a key proof-of-principle for our molecular design. The studies on complexation of Ytterbium and evaluation of the resulting complexes with NMR-Z will also be presented.

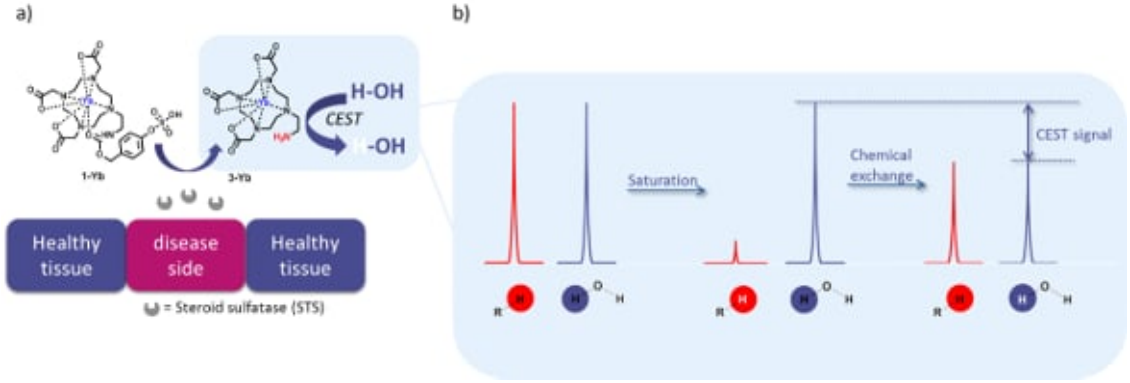

Figure 1. The concept of sulfatase-activated paraCEST imaging agents. A) The exchangeable proton in the imaging agent (red) is masked by a protecting group that is removed through the catalytic action of a sulfatase, which is overexpressed in the area of interest. B) The CEST signal is created via the selective saturation of the protons of the contrast agent (red protons) and their concurrent chemical exchange with the water protons. In this pocess, the water signal is reduced, giving rise to the CEST signal.

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Mechanisms of Action of the Abiogenic Silver (I), Strontium (II), and Gallium (III) in Medicine. Insights from a Computational Study

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Organism evolution has lasted about 3–4 billion years. As a consequence, about 40 % of all known to date proteins contain metal co-factors. "Native", or "biogenic" metal species of different oxidation state (Na^{+}, K^{+}, Mg^{2+}, Ca^{2+}, Zn^{2+}, Mn^{2+}, $Fe^{2+/3+}$, $Co^{2+/3+}$, Ni^{2+} and $Cu^{+/2+}$) have been chosen to participate in key biological processes. On the other end stand toxins like mercury and lead, which poison the recipient by competing with the natural co-factors for binding the essential proteins. As a third example, however, should be outlined some abiogenic metal species, which exert a curative effect on the host organism, and are, therefore, applied in medicine as novel drugs. Such are silver (Ag^{+}), strontium (Sr^{2+}), and gallium (Ga^{3+}). The current study investigates their ability to compete with the native cuprous (Cu^{+}), calcium (Ca^{2+}), and ferric (Fe^{3+}) cations, respectively, by exploiting the methods of the computational chemistry.

Nowadays, silver finds broad application in many areas of medicinal use, e.g. being added to dressings of burn wounds as a concomitant therapy of skin ulcers, as a potential water disinfectant, or even in ophthalmology as an active component in eye drops. Strontium prevents the destruction of bones and contributes to their restoration. Sr^{2+} salt of ranelic acid is a medication (under the names Protelos, Protos, Strontium ranelate Aristo) used for treatment of osteoporosis in postmenopausal women and very elderly patients. Gallium, in its cationic form (Ga^{3+}), is well known for its anticancer activity. Nonetheless, recent experimental studies have considered the employment of gallium as a promising "Trojan horse" strategy against pathogenic microorganisms. Herewith, we set on a quest for deciphering the most acclaimed mechanisms of therapeutic action of the aforementioned metal cations at atomic level. The obtained results shed light on the intimate mechanisms of metal recognition, thus revealing key factors governing the processes of native/abiogenic metal rivalry. This approach serves not only for explaining already existing experimental findings, but also as a first step in designing/engineering novel drug molecules of potential therapeutic value.

Key Words: computational chemistry, DFT, gallium, metal selectivity, silver, strontium, therapeutic effect

Diamidophosphate (DAP) as a Potential Prebiotic Source of Amino Acids and Their Oligomers

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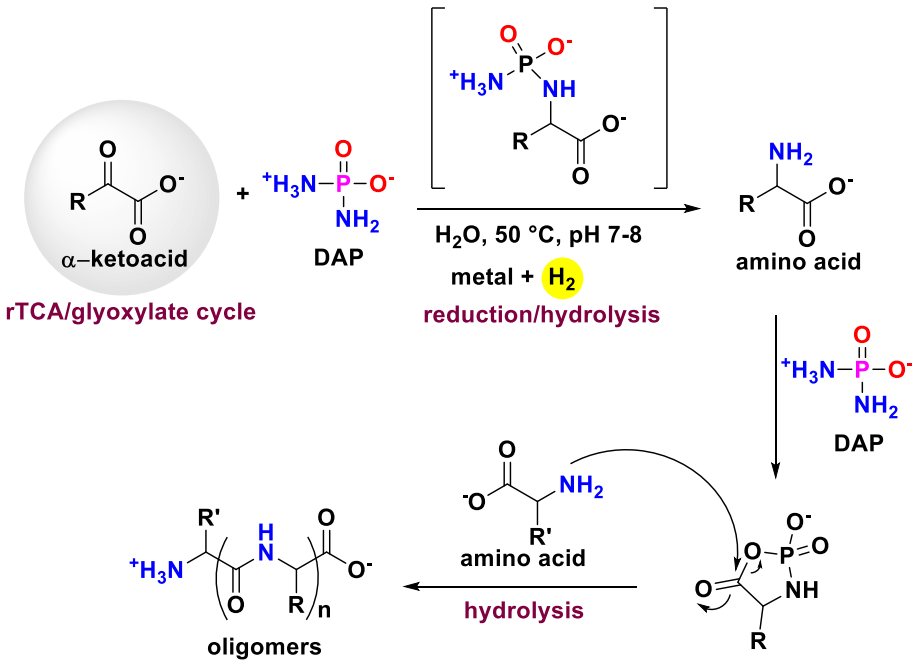
The synthesis of amino acids and their subsequent oligomerisation to form peptides in water are crucial steps for the origin of life. In biochemistry, several amino acids are biosynthesized by formal reductive amination of an α-keto acid, either through direct reductive amination with ammonia or through transamination. However, previous reports on prebiotic amino acid synthesis via reductive amination are not always realistic (extreme pH, highly concentrated ammonia, etc.) or require environments which are incompatible with the consequential generation of the corresponding oligomers.[1]

We demonstrate that DAP (diamidophosphate), a plausible prebiotic reagent obtained from the reaction of inorganic phosphates and ammonia,[2,3] serves as ammonia donor for the transition metal catalysed reductive amination employing H_2 as reducing agent in a plausible prebiotic environment. Additionally, DAP acts as a phosphorylating agent to enable the oligomerisation of amino acids under the same reaction conditions. Thus, in a single pot experiment, oligopeptides can be obtained from α-keto acids in low to moderate yields.



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Continuous electro-chlorination (CEC) Cell Efficiency of Chlorine Production

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Continuous electro-chlorination (CEC) can be used to produce free chlorine (Cl_2/HClO/ClO^-) from electrolysis of an aqueous salt solution (here, sodium chloride). CEC is available as an on-site technology and the produced free chlorine can be used for industrial purposes (Micangeli, et al., 2013; Migliorini & Meinardi, 2005; Pulido, 2005) and/or small-scale applications for disinfecting water, e.g. swimming pools, remote locations and for use in emergency contexts (Fuqua, 2010; Larson, et al., 2017).

To study the performance of CEC for chlorine production in a laboratory-scale cell, salt solutions containing 25, 50 and 100 mg L^{-1} Cl^- as NaCl were electrolysed. The two electrodes in the CEC cell were connected to a 100 W DC power supply with voltage capacity ranging from 0 to 60 V, and the salt solution was pumped through the cell. The electrodes were titanium plates coated with a Ti/Rh/Ru oxide layer. A 2 mm gap separated the anode from the cathode. The electro-oxidation of chloride showed a strong positive correlation between chlorine production and chloride concentration and electric potential (voltage) and an inverse correlation between chlorine production and flow rate.

The optimum operating conditions for chlorine production were observed at higher feed chloride concentrations, higher electric potentials and lower flow rates. The univariate analysis of variance between-subjects factors indicated that there are significant effects of chloride concentration, flow rate and electric potential on chlorine production (p-value < 0.01). The optimum cell performance efficiency occurred at lower feed chloride concentrations, lower electric potentials and higher flow rates. The cell performance is mainly affected by the active surface of the electrodes, the current density and the ion combinations in the feed water.

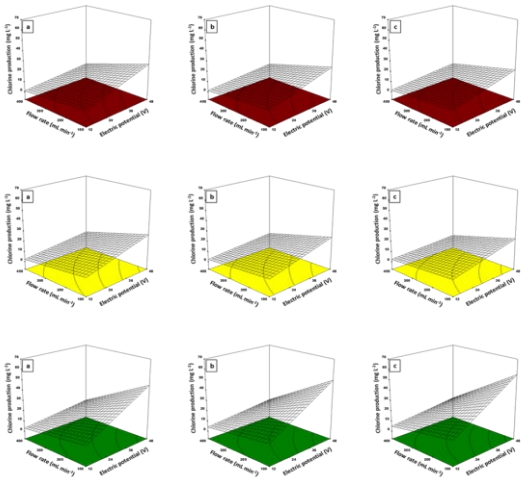

Figure 1: Response surface and contour plots of chlorine production in the presence of various ions with respect to electric potential and flow rate; (a) 0.5 mM (b) 1 mM (c) 2 mM sulfate (top) ammonium (middle) bicarbonate (bottom)

As showed the highest chlorine production is observed by increasing individual ion concentrations and voltage and lower flow rate. The different effects on chlorine production were observed from the different ions. In the present of sulfate and ammonium ions, chlorine production decreased, but a reverse effect was observed from bicarbonate ion, where chlorine formation increased (Figure 1). Specifically, in the presence of sulfate and ammonium ions, reductions of chlorine production up to on average 30% and 25%, respectively, in comparison with the feed chloride (100 mg L^{-1}) only solution were observed.

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Toward a non-enzymatic analogue of gluconeogenesis

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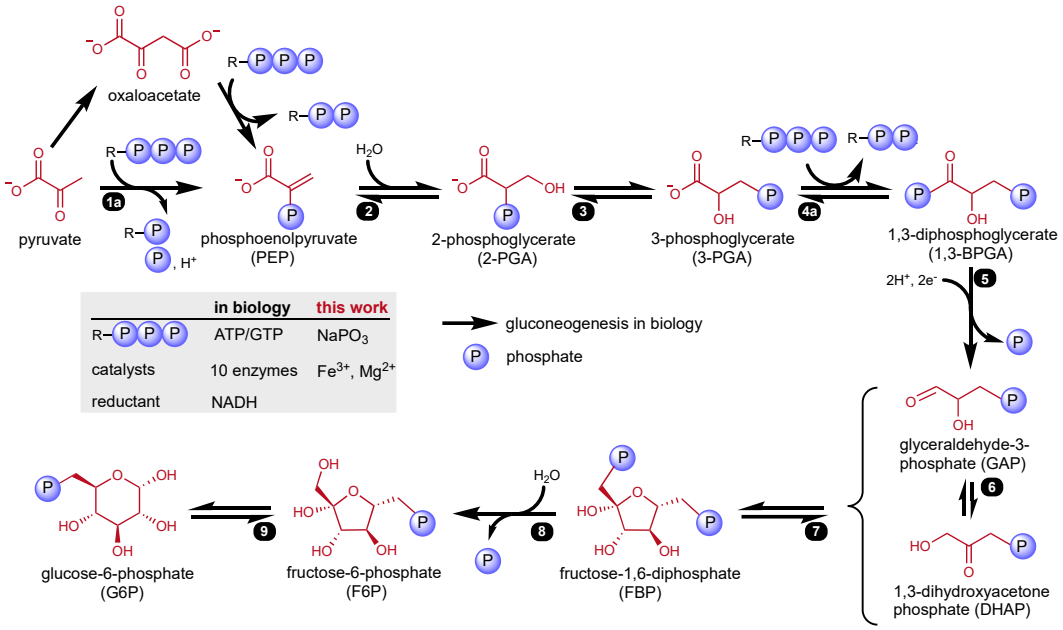
One of life's fundamental classes of molecules are the sugars, which store energy and scaffold genetic molecules. Explaining the origin of sugars is therefore critical to solving the origin of life mystery. Classically, the prebiotic synthesis of sugars was focused on the formose reaction (the polymerization of formaldehyde) or, more recently, on the Kiliani-Fisher homologation of aldehydes with cyanide. However, nature does not use such chemistry and leaves no trace that it ever did. Thus, these two approaches do not explain how and why carbohydrate metabolism works the way it does. In biology, sugars are made through the gluconeogenesis pathway, which starts from pyruvate, and requires a more complex chemistry (phosphorylated intermediates, cofactors and ATP-dependent steps). However, few steps of gluconeogenesis have known non-enzymatic variants [1,2]. To understand the origin of this pathway, we set out to develop a one-pot non-enzymatic analogue of gluconeogenesis using mineral catalysts. To achieve this goal, we started by focusing on one reaction at a time and systematically screened a variety of conditions (phosphate source, minerals, temperature, pH, additives) to identify those that enable the reactions in the absence of enzymes. NMR, HPLC, and mass spectroscopy were used to analyse the reaction products.



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VISIBLE LIGHT-PROMOTED BIOORTHOGONAL PHOTOCATALYSIS

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Biological chemistry allows to understand the cellular and molecular mechanisms related to biological functions, essential for the treatment of many diseases. Furthermore, being able to manipulate, monitor and transform cellular behavior is key to the development of modern medicine. However, interfering with cellular functions is not a trivial task and requires the development of new tools to carry out the transformations in a bioorthogonal and selective manner, under the complex environment of biological systems. Towards this goal, an exciting novel field of research which combines photochemistry and bioorthogonal methods has been recently born, opening the way to photobioorthogonal chemistry.

Herein, we describe our preliminary contributions in this new area, from early work on designing new bioorthogonal photo-promoted processes to recent advances in exporting the reaction to live settings. Specifically, we are currently investigating the possibility of performing different visible light promoted reactions in either water or more complex biological settings. The intermolecular processes involve the formation of C-C and C-heteroatom bonds to obtain interesting structures such as phenanthrenes [1], benzothiophenes [2] and coumarins [3]. As a source of aryl radicals we have selected diazonium salts, whose biocompatibility has already been demonstrated.

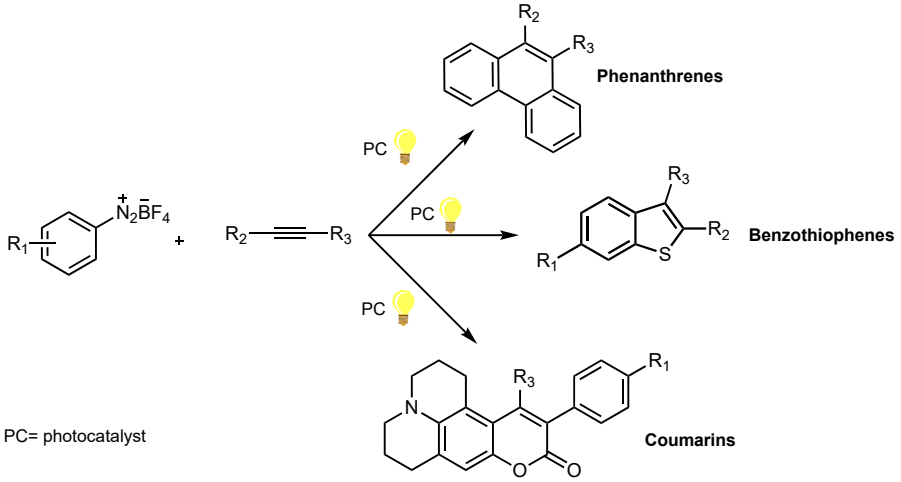

Figure I Examples of photocatalyzed transformations.

The performance of different photocatalysts has been explored, from organic compounds to metal complexes, along with the use of a variety of sources of light. Substrates can be employed in the millimolar range, although a slow addition of the diazonium salt is required in order to obtain excellent yields. Moreover, the transformation tolerates physiological temperature and open-air atmosphere. Ongoing research is mainly focused on the translation of these reactions to live settings.

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Detection of glucose-derived D- and L-lactate in erythrocytes and cancer cells by use of a chiral NMR shift reagent

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Excessive lactate production, a hallmark of cancer, is largely formed by reduction of pyruvate via lactate dehydrogenase (LDH) to L-lactate. Although D-lactate can also be produced from glucose via the methylglyoxal pathway, less is known about the amount of D-lactate produced in cancer cells. Lactate can be detected in vivo by 1H NMR spectroscopy but the methyl resonances from D-and L-lactate overlap so the relative amounts of these two isomers cannot be measured directly. However, in the presence of the chiral paramagnetic NMR shift reagent Yb1(Figure), the NMR signals of the two stereoisomers of lactate are fully resolved [1]. Production of D-lactate from glucose in freshly isolated red blood cells was first demonstrated using Yb1, followed by two different cancer cell lines with high GLO1 expression (H1648 and H 1395) which were selected for the study from a panel of over 80 well-characterized human NSCLC cell lines. Cells were grown and a small volume of extracellular fluid was collected and mixed with Yb1 for analysis by 1H NMR spectroscopy. The effect of incubation with glucose and methylglyoxal was studied in each case by determining the (L-lac/D-lac) ration by NMR. Although the biological role of D-lactate is uncertain this method for monitoring D-lactate production could provide new insights into the biological roles of D- versus L-lactate in cancer metabolism. This NMR techniques could potentially be applied in vivo to image D- and L-lactate production in tumors using either magnetic resonance spectroscopy (MRS) or CEST [2]

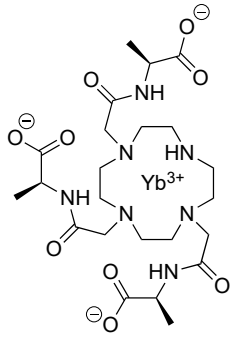

Figure. The chemical structure of Yb1= YbDO3A-(L-alanylamide) drawn as the (S)-isomer.

We thank the National Institutes of Health (CA115531 and EB02584), the Robert A. Welch Foundation (AT-584), a Fulbright visiting scholarship for CFGCG and the Coimbra Chemistry Centre (UID/QUI/00313/2019 and POCI-01-0145-FEDER-027996) of the University of Coimbra for finantial support.

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Changes in the secondary structure of lysozyme after complexation with ferulic acid

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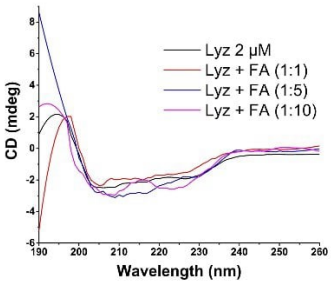
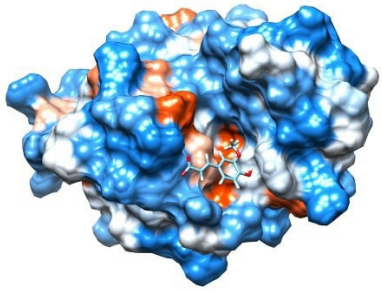
Lysozyme (Lyz, EC 3.2.1.17) is a globular, ubiquitous and thermolabile protein, with high enzymatic and bacteriostatic activity, which exists widely in nature [1]. Egg whites are a natural source of Lyz that makes up about 3 to 4% of its total protein [2]. However, it can trigger very serious allergic reactions, especially in babies and children. It is known that the interactions between phenolic compounds and proteins can cause changes in the native structure of proteins, with the formation of complexes [3]. Thus, in this work, the effect of the interactions of egg Lyz with ferulic acid (FA) was evaluated on the protein secondary structure.

The Lyz solutions in 50mM phosphate buffer, pH 7.40, were incubated for 10 min, at 310K and analyzed by Circular Dichroism (CD) in the range of 190-260 nm. The molar ratio between Lyz (2 µM) and FA were 1:1, 1:5, 1:10, respectively [4]. The CD spectra (**Figure 1 - A**) and the data from the CDSSTR software analysis showed that the increase in the concentration of FA (0 µM, 2 µM, 10 µM and 20 µM, respectively) resulted in an increase in the α-helix content of Lys from 44% to 48%, 50%, and 52% respectively, after the formation of the complexes Lyz-FA, as well as an increase in the stability of α-helix [5]. In addition, molecular docking (Swissdock Software and UCSF Chimera 1.14) (**Figure 1 - B**) of FA with Lyz also indicated the formation of hydrogen bonds in the complexes Lyz-FA ($\Delta G° = -28$ kJ mol^{-1}). Therefore, the interactions between Lyz and FA, promoted changes in the secondary structure of the protein that may have a consequence on its conformational structure and functional properties.

A





B

Figure 1: A - CD spectra of Lyz (2µM) with FA solutions; **B** - Molecular docking: Surface hydrophobicity (blue - hydrophilic regions, orange – hydrophobic regions, white - neutral regions).

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Immobilisation of a redox-reversible artificial metalloenzyme on nitrilotriacetic acid-modified gold electrodes

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Artificial metalloenzymes (ArMs) represent an exciting and rapidly expanding field of biocatalysis. The integration of an organometallic catalyst into a protein scaffold opens up opportunities for carrying out new-to-nature chemical transformations in a biocompatible environment. An ArM based on a non-covalent interaction between the protein scaffold and an anchor-catalyst conjugate, comprising a periplasmic binding protein of C. *jejuni*, CeuE and its cognate iron(III) siderophore complex bonded to an iridium-based imine reduction catalyst, has been developed.[1] The design exploits the reversible iron-siderophore binding mechanism for the recycling of the protein through the dissociation of the anchor-catalyst conjugate from the CeuE scaffold, facilitated by the chemically induced reduction of the iron(III) centre.

We are exploring the scope for the immobilisation of this hybrid catalyst onto gold electrodes modified with self-assembled monolayers (SAMs) of metallated (M^{+2}) nitrilotriacetic acid (NTA) groups.[2] The immobilisation based on the specific interaction between an M^{+2}-NTA complex and a His-tagged protein is proposed to facilitate flow-chemistry catalysis and the recycling and recovery of both disassembled components simultaneously following a successful catalytic reaction. The successful immobilisation of a catalytically-active ArM on a conducting surface opens up the scope for the employment of an electrochemical trigger to control the disassembly of the ArM. This will enable a more precisely controlled release of the anchor-catalyst conjugate from the immobilised protein scaffold, allowing the development of more complex arrays capable of ArM disassembly with high spatial and temporal control.

This work describes our efforts to modify the gold electrodes with SAM-NTAs and characterise the subsequent immobilisation of CeuE-His utilising a quartz crystal microbalance with dissipation monitoring (QCM-D) and complementary electrochemical techniques, such as impedance spectroscopy (EIS). We also outline our attempts at monitoring the release of the anchor-catalyst conjugate from the gold immobilised ArM following the reduction of the iron(III) centre.

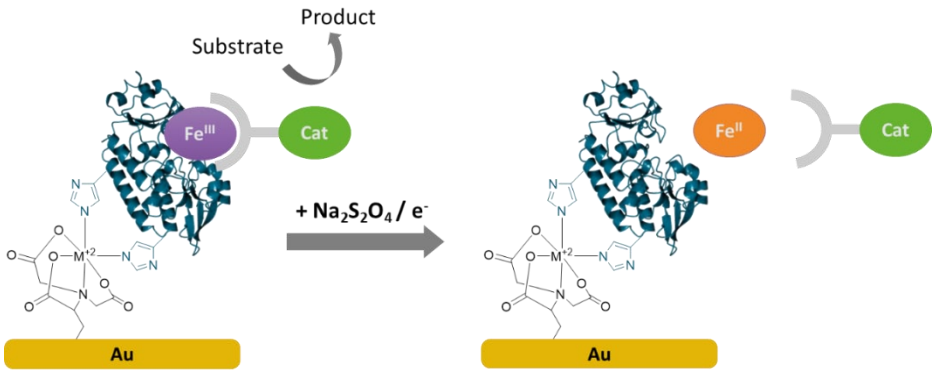

Figure 1. A schematic representation of a catalytically active ArM immobilised on a gold electrode through the interaction between the metal NTA complex and the two imidazoles of a terminal His-tag. The change in the iron oxidation state of the anchor is highlighted upon the release of the anchor-catalyst conjugate from the protein scaffold either through a chemical or electrochemical trigger.

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The Ser220Cys polymorphism of the β2-adrenergic receptor can influence interactions with G proteins

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The β2 adrenergic receptor (β2-AR) is a type of G protein-coupled receptor (GPCR) which represent the largest class of membrane receptors, with more than 800 members identified in the human genome. As confirmed by in vitro and clinical studies, individual variations in physiological responses, expression and function of β2-AR, as well as individual differences in response to drugs may relate to polymorphic variants of the receptor. The main aim of the current work was to check whether the Ser220Cys polymorphism can significantly influence of the structure- or thermodynamics-mediated function. Residue 220 is located close to the Gs/β2-AR interface created during the β2-AR-Gs coupling. For this reason, this polymorphism seems to potentially significant for β2-AR-mediated signaling. Our study relied on both atomistic and coarse-grained molecular dynamics simulations performed in the presence of explicit solvent.

From perspective of thermodynamically-driven influence, we have found that the energies involved in the β2-AR is highly insufficient to significantly alter the absolute binding energy associated with Gs-β2-AR coupling. However, some non-negligible structural alterations, induced by the Ser220Cys polymorphism have been found in the intracellular region of the receptor (ICL1, ICL2 and ICL3), being the interface for the contact with Gs protein. A series of molecular switches acting through Cys220, Val216, Gln224, Lys227 and Glu268 and leading to conformational rearrangements within the intracellular part of ICL3 and TM6 has been identified. The rearrangements can propagate to ICL2 and ICL1 through interactions mediated by e.g. Glu225 and Tyr141. All these conformational movements are essentially absent in the case of β2-AR^{Ser220}, thus, they can be ascribed to the polymorphism-induced consequences. Judging from the RMSD comparison against the β2-AR-Gs complex, the β2-AR^{Ser220} polymorph structure is more compatible with the Gs-bound receptor.

In conclusion, the current results indicate that the polymorphism-dependent functionality of the β2-adrenergic receptor is not correlated with any simple energetic characteristic including e.g. changes in the affinity to the Gs protein. On the other hand, the Ser220Cys polymorphism-induced alterations of the local protein conformation have sufficient magnitude to be considered in terms of the structural basis of the considered phenomena.

Acknowledgments: This research was funded by the National Science Centre, Poland (contract financed in 2019–2021 under Project Opus, No. 2017/25/B/NZ7/02654).

Toward Multifunctional Dynamic Covalent Polymers for siRNA Delivery

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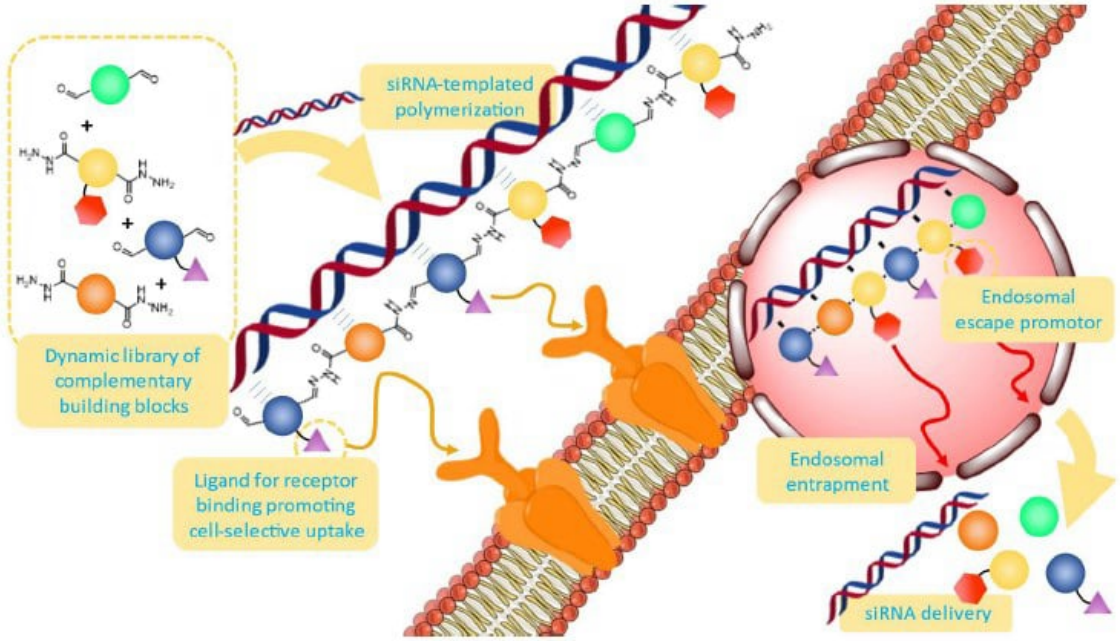
Dynamic Covalent Polymers (DCPs) are emerging as promising vectors for gene delivery.[1],[2],[3] In a previous work,[4] we showed that a dynamic library of complementary cationic peptides can undergo a siRNA-templated polymerization through acylhydrazone and oxime ligations leading to the formation of a glycosylated DCP which in turn trigger cell-selective uptake and siRNA delivery.

However, despite a good overall activity, endosomal entrapment was evidenced and probably limits the potential of this 1st generation of clickable DCPs. Therefore, we set out to develop a new generation of multifunctional DCPs. We report in this communication the design and synthesis of modified peptide bishydrazides having a free N-terminal position in which new functional groups such as short endosomolytic peptides have been placed. SiRNA complexation studies were carried out by gel electrophoresis and confirm that these polyacylhydrazone DCPs are formed by templated polymerization while also revealing a non-innocent role of this pending group. Finally, our first efforts to assess the potential of this new generation of DCPs for the delivery of siRNA on live cells will be presented.



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Unconventional Cleavage mechanism of mRNA XBP1 by IRE1 RNase

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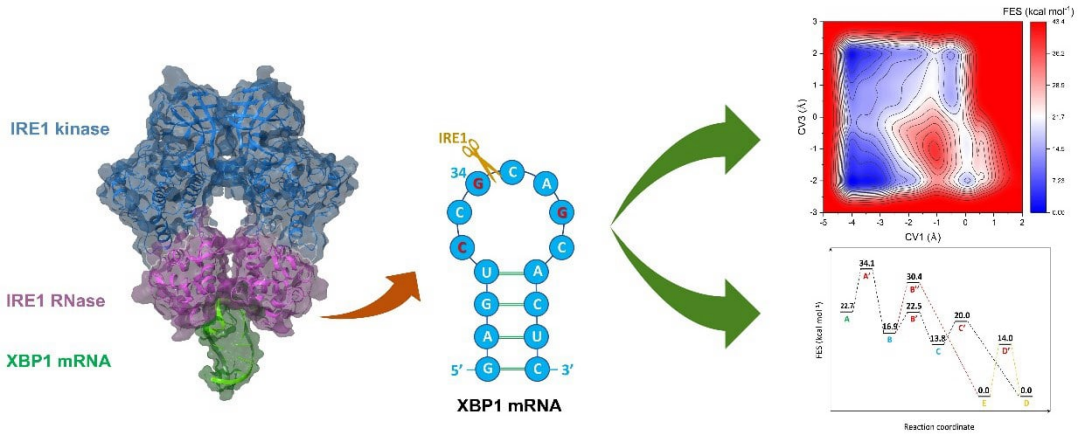
Inositol Requiring Enzyme 1α (IRE1), a kinase/endoribonuclease protein spanning the endoplasmic reticulum (ER) membrane, is a mediator of the unfolded protein response (UPR) [1,2]. Accumulation of improperly folded proteins in the ER causes IRE1 oligomerization and trans-autophosphorylation which activates its RNase domain. IRE1 RNase excises a 26-nucleotide intron from X-Box Binding Protein 1 (XBP1) mRNA whose fragments are then ligated by the tRNA ligase RtcB to yield the XBP1s mRNA that is translated into a potent transcription factor controlling UPR target genes. The atomistic details underlying the mRNA XBP1 cleavage mechanism by IRE1 remain undetermined. In silico methodologies were herein employed to construct a reliable IRE1 back-to-back dimer and mRNA XBP1 single stem-loop complex to investigate the cleavage mechanism [2]. Protein-RNA molecular docking along with a series of restrained atomistic molecular dynamics (MD) simulations were applied to construct and refine the IRE1/XBP1 mRNA complex. A series of well-converged Quantum Mechanics Molecular Mechanics Well-Tempered Metadynamics (QMMM WT-MetaD) simulations were conducted to accurately estimate the free energy profile of the cleavage mechanism and to determine intermediates and transition state structures.

Based on our findings, the cleavage reaction occurs via (a) proton transfer from O2' to the Nε atom of H910 (GB) that activates the nucleophilic attack to the scissile phosphate atom, leading to the formation of the pentavalent di-anionic phosphate intermediate; (b) subsequent proton transfer from the hydroxyl group of Y892 (GA) to the ready-to-leave O5' atom; and (c) formation of the product. In agreement with experimental evidence [3], an alternative reaction path with activation energy significantly higher can also take place (*i.e.*, 13.5 kcal mol^{-1} vs 5.6 kcal mol^{-1}, respectively, compared to the main reaction path), in which XBP1 mRNA cleavage proceeds without direct contribution of the GA in the proton transfer to the leaving O5' atom. This study brings unique atomistic insights into the cleavage mechanism of mRNA XBP1 by IRE1 which sheds light on the path of developing new therapeutic agents to modulate the UPR signaling.



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Electro-fermentation as a tool to control microbial fermentations with electrochemical systems

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Electrobiotechnologies, such electro-fermentation (EF), use electroactive microorganisms that can exchange electrons extracellularly with a solid electrode [1,2]. In EF, electrodes are introduced into fermentation environments to improve microbial cell growth and density, or to increase the production yield of targeted products [1]. Within this context, our aim is to study the influence of small electric currents on the biotechnological revalorization of carbon-rich food wastes into value-added products (e.g., organic acids, bioethanol), using microorganisms (bacteria and yeasts).

Initially, we used lactic acid bacteria (LAB) under EF conditions in optimized fermentation media. Recent examples with some LAB strains have shown efficient direct or indirect extracellular electron transfer with carbon electrodes [3]. We used *Lactobacillus plantarum* and *L. casei* with and without soluble redox mediators (i.e., ferricyanide, hydroquinone and menadione) in model media (controlled composition). The redox mediators were initially tested by cyclic voltammetry (Fig. 1) in 10 mM phosphate buffer (pH=7.0), using carbon screen printed electrodes (Methrohm, Dropsens) and the PGSTAT204 potentiostat/galvanostat (Methrohm, Autolab).

We ran triplicate experiments for each LAB strain, and we monitored the pH, microorganisms' viability, and wet biomass. We found no significant differences between polarized (electrochemically controlled) and non-polarized conditions. We also quantified the fermentation products: tartaric, malic, lactic, citric, succinic, fumaric, and butyric acids, using HPLC. Here, we could see notable differences in terms of yields and products ratios, depending on the value of the applied potentials and the nature and concentration of the used soluble charge transfer mediator.

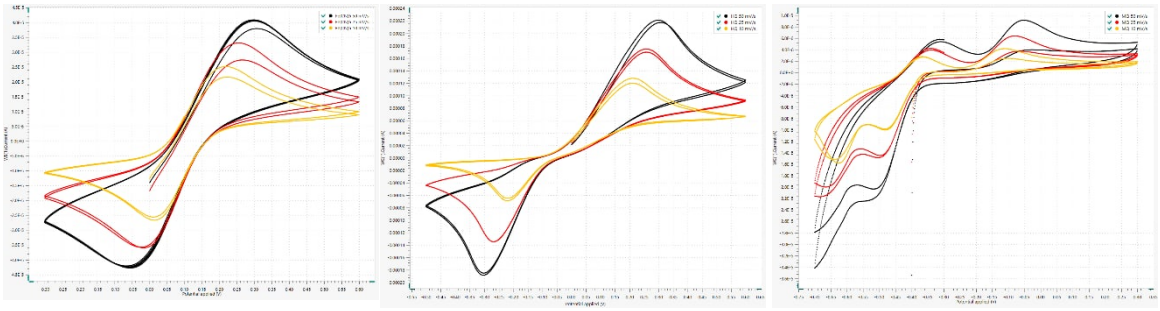

Fig. 1. Cyclic voltamogrammms for ferro/ferricyanide, hydroquinone and menadione.

Acknowledgements: This work was supported by a grant of the Ministry of Research and Innovation, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2019-0067.

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Nucleophile-N(5)-adducts to flavins and flavinium salts – intermediates in organocatalytic umpolung systems

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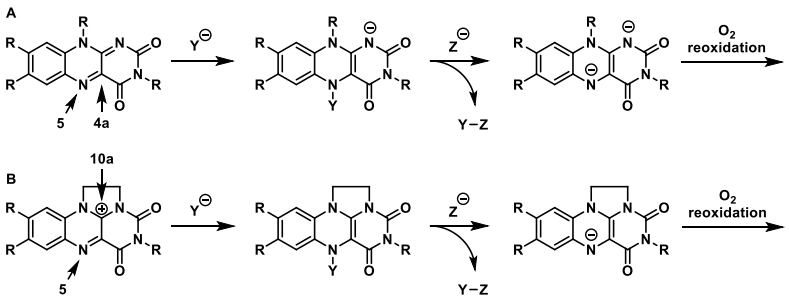
Flavins (**A**) are naturally occurring compounds with electrophilic nature and ability to bind nucleophiles. Their derivatives, N^1,N^{10}-ethylene-bridged flavinium salts (**B**) have even better ability to form the adducts. The addition of nucleophiles can take place at various positions. Interesting ones are adducts to a nitrogen atom at position 5. In most cases, formation of adduct is a reversible process, which enables its employment in biological and artificial catalytic systems. For example, flavin-N(5)-adducts, in a form of $FADH_2$ and flavin-N(5)-oxide, are intermediates in biological catalytic redox systems [1]. Metabolisms of nitroalkanes [2] and alkyl-dihydroxyacetone phosphate [3] are based on flavin adducts of carbanions. Besides, there are many other N(5)-adducts involved in biological and artificial catalytic systems. The most common are adducts to carbon at position 4a of neutral flavins (adducts of sulfides, hydroxide and hydroperoxide) and 10a of N^1,N^{10}-ethylene-bridged flavinium salts (adducts of hydroxide and hydroperoxide) [4].

Research of our group has been focused on the flavin adducts, conditions of their formation, their properties, reactivity, and role in organocatalysis. We have described several catalytic systems utilizing various adducts. These are sulfoxidation (based on 4a and 10a hydroperoxide adducts) [5], Mitsunobu reaction (based on N(5) phosphine adducts) [6] and oxidative denitrification (based on N(5) nitroalkanide adducts). All these systems have one essential feature in common: There is an umpolung of the nucleophile. Its addition to the flavin activates it for reaction with another nucleophile. Flavin acts as an electron acceptor and then it is reoxidized, usually by molecular oxygen. (Scheme 1)

In the presentation, we will focus on systematic investigation of flavin adducts, mainly on their properties and reactivity, ability of various flavins to form them and regioselectivity of various nucleophiles while binding to different positions at flavin structure. The study is performed using experimental techniques and quantum calculations.



Scheme 1. Umpolung of nucleophiles via formation of N(5)-adduct of flavin (**A**) and flavinium salt (**B**).

This work was supported by Czech Science Foundation (reg. No. 21-14179S) and by IGA of VŠCHT (No. 110 88 2122). Authors thank for financial support.

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Glucans: From spent yeast to an ingredient with skin repair properties

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The valorisation of byproducts produced throughout already established fermentation processes is part of an emergent integrated approach to improve overall industrial sustainability, promote circular economy and create additional commercial value. Among the various side streams generated throughout the fermentation process, spent yeast stands out as a primary target for valorization since it contains a wide number of biomolecules with commercial potential, especially polysaccharides. Glucans, a complex polysaccharide composed by α/ß links of glucose units, are present in the yeast cell wall and are attracting attention for its potential as a cosmeceutical ingredient. β-Glucans in particular, have been reported to have specific properties that could be of interest to promote overall skin health, as well as to prevent age-related signs, such as antioxidant and anti-inflammatory activity, photoprotective capacity, ability to stimulate certain aging-related molecules (i.e., collagen or hyaluronic acid) or by interacting with our immune system [1,2]. Additionally, β-Glucans from *Saccharomyces cerevisiae* have already demonstrated great *in vitro* wound healing capacity in its insoluble form [3]. These reported properties represent a huge catalyst to make use of spent yeast to extract this biomolecule and therefore apply it as a cosmeceutical. Thus, we developed a chemical extraction method to isolate and purify insoluble glucans, focusing on the β-Glucan content, from two different strains of *S. cerevisiae*: a genetically modified strain (GMO) spent yeast, obtained from an industrial fermentation process, and a wild strain (CEN.PK2), produced through lab-scale fermentations. Two purified insoluble extracts were tested using in vitro and ex vivo methodologies for wound healing capacity. According with the results obtained, both glucan extracts are capable of promoting wound closure, demonstrating wound healing capacity.

Thanks to Amyris for providing the spent yeast used for this study. This work was financially supported by Amyris Bio Products Portugal Unipessoal Lda and Escola Superior de Biotecnologia – Universidade Católica Portuguesa through Alchemy project – Capturing high value from industrial fermentation bio products (POCI-01-0247-FEDER-027578). We would also like to thank the FCT project UIDB/50016/2020.

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MNTR PROTEINS AS MANGANESE METALLOSENZORS IN *BACILUS SUBTILUS* AND *MYCOBACTERIUM TUBERCULOSIS*

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Manganese ions (Mn^{2+}) are essential for bacteria since they are necessary for basic cellular processes such as DNA replication and resistance to oxidative stress. On the other hand, manganese ions are toxic for the cell if present in high concentrations. Therefore, bacteria must have sensitive cellular mechanisms through which manganese homeostasis is regulated.[1] Often, such mechanisms in (pathogenic) bacteria differ from those in eukaryotes, which makes them a potential target for the development of novel antibiotics. An example of such a pathogenic bacterium is *Mycobacterium tuberculosis* whose manganese homeostasis is regulated by the MntR transcription factor.[2] A similar mechanism is present in the nonpathogenic bacterium *Bacillus subtilis*, where the MntR transcriptional factor regulates cellular concentrations of manganese (Mn^{2+}) ions.

In the first step, both MntR proteins, from *B. subtilis* and *M. tuberculosis*, were studied using computational methods. Starting from available crystal structures, MntR proteins in different forms were prepared for molecular dynamics (MD) simulations. Since hydrogen bond networks present in the protein structure might have an important role in the protein's molecular mechanisms, different approaches for adding polar hydrogen atoms were used. The prepared systems were subjected to extensive all-atom molecular dynamics simulations in order to explore their structural and dynamical properties. Computational results will serve as a starting point to design experimental research aiming to reveal the molecular mechanism(s) of the studied manganese metallosensors.

This work was supported by the Croatian Science Foundation project "Manganese metallosensors" IP-2020-02-3446.

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Manganese binding reduces the available conformational space in the MntR protein from *Bacillus subtilis*

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The MntR protein from *Bacillus subtilis* is a transcriptional repressor which is activated for DNA binding by manganese ions (Mn^{2+}).[1] There are more than a dozen crystal structures of this protein available in the PDB, both with and without manganese (II) ions, as well as with various other ligands and mutations. However, the differences between the apo- and manganese-bound crystal structures are minor [2] and not sufficient to fully explain the possible allosteric mechanism by which manganese binding modulates the DNA affinity of the MntR protein.

Therefore, molecular dynamics (MD) simulations on the µs simulation time scale of different forms of the protein, manganese-bound and apo forms, were conducted. The obtained results suggest that manganese binding doesn't significantly change the structure of the protein, as much as it limits the size of the available conformational space of the protein. The manganese-bound protein adopts a narrow range of conformations with the DNA-binding helices in a relatively fixed orientation. On the other hand, the apo protein, although transiently achieving this conformation, adopts a variety of different conformations. These results are evident from statistical analyses, such as principal component analysis and clustering, and from visualization of the trajectory.

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Gaining insight into structure-activity relationship of natural products – Synthesis of vincamine derivatives and investigation of their bioactivities

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Vincamine, the main alkaloid of *Vinca minor*, exhibits vasodilatory, neuroprotective and nootropic activities, therefore being sold as dietary supplement in the US. [1] Additionally, vincamine is known to be able to interact with transferrin receptors, thus regulating the iron (Fe) uptake through the blood-brain-barrier. On the other hand, the excretion of Fe ions is facilitated by the metabolite vincaminic acid. Due to these properties vincamine is of pharmacological interest. In particular it could also be used as treatment for Alzheimer's or Parkinson's disease. [2; 3] Mechanisms by which vincamine interacts in the brain are still not fully elucidated. Therefore, it is of great importance to determine which parts of the chemical structure are responsible for its remarkable bioactivities.

For this purpose, different vincamine analogues or substructures were synthesized to be further on used in biological assays. The synthetic route involved the composition of various aldehydes via already established routes, namely the reduction of nitriles and esters with DIBAL-H yielding several compounds in good yields. The resulting substances were then used in Pictet-Spengler reactions with tryptamine to form the tetrahydro β-carboline (THBC) core structure. Subsequently, cyclization reactions were performed to obtain the vincamine derivatives in moderate to good yields although the cyclization only took place at the non-aromatic nitrogen atom. Additional difficulties arose at introducing more sophisticated functionalities like an α-keto ester moiety. Nevertheless, feeding experiments using larvae of *Spodoptera littoralis* were conducted with the successfully synthesized vincamine analogues. The determination of growth inhibition resulted in effects in the range of 27% to 40% after four and 32% to 55% after six days at the highest concentration.

Whereas the synthetic route mentioned above was successful to obtain rather simple derivatives, more complex structures are needed to get further insight in structure-activity relationship of vincamine. Therefore, reactions like ozonolysis of terminal double bonds or other synthetic methods could be used to generate highly functionalized aldehydes. Additionally, a protecting group strategy for the secondary amine in the aliphatic ring should be investigated to be able to control the reaction site for the second cyclization step. Successfully implementing a protecting group should result in the possibility of forcing the ring closure at the indole nitrogen.

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Isonitriles as a potential new class of anti-malarials? – Synthesis of natural product-derived isonitriles and binding studies

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Malaria, still one of the most devastating diseases in the world, is caused by the parasite *Plasmodium* which is transmitted by *Anopheles* mosquitos. Especially, in the less developed regions in the southern hemisphere this disease is hardly containable and hence problematic. One reason for this problem might be increasing resistances against commonly used anti-malarials, such as chloroquine and artemisinin-based combination therapies. New drugs are required to counteract this issue. [1] A novel potential class may be marine natural diterpene isocyanides, since distinct anti-plasmodial activity by binding to heme (key-step of used drugs) was already revealed. [2]

In this work, therefore, the aim was to investigate smaller synthetic isocyanides mainly based on monoterpenoid and carbohydrate scaffolds. In case of the monoterpenoids two steps were conducted to obtain the desired isonitriles. Starting from ketones, a Leuckart reaction was performed which led to the corresponding formamides. They were then converted into isocyanides by dehydration. Other additional ketones were functionalized in an analogous manner. Protection and deprotection steps were required for carbohydrates prior to functionalization. Possible anti-malarial properties of these products were further assessed spectroscopically.

Initial binding studies between several synthesized isonitriles and heme were conducted applying UV-Vis and NMR spectroscopy to evaluate if binding occurs and to gather information on the binding mode, respectively. Moreover, the stoichiometry was determined via mass spectrometry. Monoterpenoid isonitriles based on norbornane scaffolds do not seem to be ideal binding partners for heme, since no complexes could be identified so far. In contrast, structures based on menthane scaffolds, indeed, show abilities of binding heme coordinatively with a 1:1 (compound/heme) stoichiometry, although steric properties appear to have a major influence on the affinity. Additionally, 1:1 as well as 2:1 complexes could be observed using functionalized glucose and acetyl-adamantane. Preliminary results of NMR studies also support the assumption of the presence of a 2:1 complex. Future *in vitro* assays will give further insight of these compounds' potential and promising activity.

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Inhibition of Thiol-Mediated Uptake with Pnictogen-Expanded Cascade Exchangers

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Thiol-mediated uptake is an efficient method to directly deliver biological substrates into the cytosol of cells. Dynamic covalent cascade exchangers (CAXs) such as cyclic oligochalcogenides and disulfides have been developed as excellent transporters. The inhibition of thiol-mediated uptake has been attractive because thiol-disulfide exchange plays a key role in the mechanism of many viral entries. More recently, new type of CAXs including cyclic thiosulfonates and oligophosphorothioates have been identified as candidate inhibitors of thiol-mediated uptake and viral entry as well as transporters. Here, we introduced pnictogen-expanded cascades exchangers (p-CAXs) by inserting pnictogen relays into active cyclic disulfides. p-CAX with Bi (III), dithiabismepane, and As (III), aminophenyl-dithiarsinae, efficiently inhibit thiol-mediated cytosolic delivery with fluorescent CAX reporters. In addition, they showed the inhibition of SARS-CoV-2 lentivirus cellular entry at concentrations of 10 µM or lower. Dynamic covalent exchange with p-CAXs was supported by crystal structures, computational studies, and exchange kinetics. This study provides a deeper understanding into the mechanism of thiol-mediated uptake and leads to promising investigations with regard to drug delivery, release, and discovery.



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Bioleaching and chemical leaching of nickel laterite using *Burkholderia* sp.

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Nickel (Ni) is a metal that has many industrial applications, nowadays mainly in lithium-nickel-cobalt-aluminium (LiNiCoAl) and lithium-nickel-manganese-cobalt (LiNiMnCo) batteries. A high demand for Ni is expected in the next twenty years due the electric vehicles' boom. Within this sector alone, the forecast global demand to increase by 2.6Mt Ni to 2040, up from only 92kt Ni in 2020 with an average price of approximately US$15,521/t [1].

Interest in low-grade Ni-laterite ores has increased in recent years; however, the laterite process has proven technically difficult and costly, and the development of alternative low-cost biotechnologies for Ni solubilization has been encouraged [2,3].

Biohydrometallurgy is an interesting alternative that can be used to recover metals from lateritic ores on a massive scale, and it has already been utilized to recover metals from sulfide deposits [4,5]. The majority of current Ni-laterite microbial leaching research is focused on the utilization of heterotrophic fungi, such as *Aspergillus* sp. and *Penicillium* sp. as well as the chemolithotrophic bacteria *Acidithiobacillus* sp. [3,6]

In this context, for the first time, a sample of Brazilian saprolite magnesium-rich Ni-laterite ore was subjected to microbial bioleaching using a heterotrophic *Burkholderia* sp. strain. The effects of glucose concentration (5-15 %, w/v), Ni-laterite ore concentration (0.25-0.75 %, w/v), and cultivation period (14-42 days) on the biocatalytic leaching of the ore were initially tested in flasks to obtain the optimum conditions for the *Burkholderia* sp. Then chemical leaching was applied as a comparison to bioleaching, using different organic acids.

The variable more important for Ni-laterite bioleaching was the glucose concentration (x1). Bioleaching batch experiments demonstrated that about 87% Ni (7.5 mg Ni/g ore) were solubilized by *Burkholderia* sp. after 42 days. Chemical leaching experiments showed that hydroxycarboxylic acids could dissolve Ni from a Brazilian Ni-laterite ore. The Ni extraction (%) rates decreased according organic acid molecular weight: citric acid (68%) > lactic acid (23%) > acetic acid (10%). This study's significance is that it has opened up an opportunity for the potential application of potassium-solubilizing bacterial strains to process low-grade Ni-laterite ores.

H.L. Carpen thanks the PIBIC/CNPq/CETEM for the scholarship granted.

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Design, Synthesis, and Biological Evaluation of a Novel VEGFR-2 Inhibitor Based on a 1,2,5-Oxadiazole-2-oxide Scaffold with MAPK Signaling Pathway Inhibition

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Abstract: Over the past few decades, the development of broad-spectrum anticancer agents with anti-angiogenic activity has witnessed considerable progress. In this paper, a new series of pyrazolo[3,4-d]pyrimidines based on a phenylfuroxan scaffold are designed, synthesized, and evaluated, in terms of their anticancer activities. NCI-60 cell one-dose screening revealed that compounds 12a–c and 14a had the best MGI%, among the tested compounds. The target fluorinated compound 12b, as the most active one, showed better anticancer activity compared to the reference drug sorafenib, with IC50 values of 11.5, 11.6, and 13 µM against HepG-2, A2780CP, and MDA-MB-231 cell lines, respectively. Furthermore, compound 12b (IC50 = 0.092 µM) had VEGFR-2 inhibitory activity comparable to that of the standard inhibitor sorafenib (IC50 = 0.049 µM). Furthermore, the ability of compound 12b in modulating MAPK signaling pathways was investigated. It was found to decrease the level of total ERK and its phosphorylated form, as well as leading to down-regulation of metalloproteinase MMP-9 and over-expression of p21 and p27, thus leading to subG1 cell cycle arrest and, thus, induction of apoptosis. Additionally, compound 12b decreased the rate of wound healing in absence of serum, in comparison to DMSO-treated cells, providing a significant impact on metastasis inhibition. The quantitative RT-PCR results for E-cadherin and N-cadherin showed lower expression of the neuronal N-cadherin and increased expression of epithelial E-cadherin, indicating the ability of 12b to suppress metastasis. Furthermore, 12b-treated HepG2 cells expressed a low level of anti-apoptotic Bcl-2 and over-expressed proapoptotic Bax genes, respectively. Using the DAF-FM DA fluorescence probe, compound 12b produced NO intracellularly as efficiently as the reference drug JS-K. In silico molecular docking studies showed a structural similarity through an overlay of 12b with sorafenib. Interestingly, the drug-likeness properties of compound 12b met the expectations of Pfizer's rule for the design of new drug candidates. Therefore, this study presents a novel anticancer lead compound that is worthy of further investigation and activity improvement.

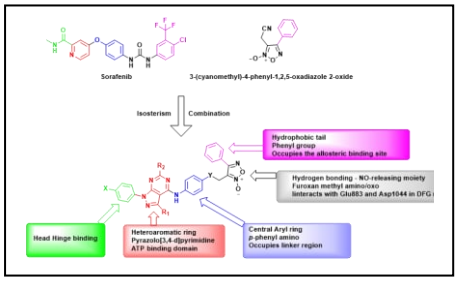

Figure 1. Rational design for target compounds.

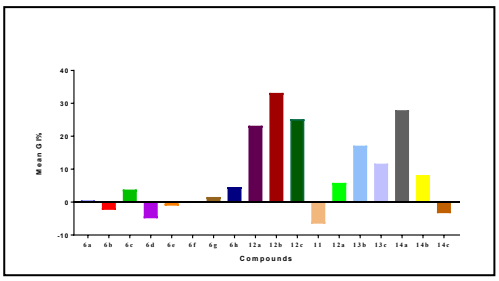

Figure 2. Mean GI% of compounds **6a–h, 12a–c, 11, 13a–c**, and **14a-c** against NCI-59 cell line panel.

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Why not nucleosides in meteorites? An approach based on mechanochemical studies

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The detection of organic molecules in extraterrestrial bodies leads to some proposals focused on the extraterrestrial input of relevant compounds for the emergence of life on our planet [1]. Nevertheless, these extraterrestrial bodies encounter very harsh conditions which can induce chemical transformations in the molecules within them. Besides thermal heating and friction [2], mechanochemistry, which uses mechanical energy as a driving force for chemical transformations, can play an important role in the reactivity of organic molecules in those extraterrestrial materials. For instance, carbonaceous chondrites meteorites are a portion of an asteroid that was able to cross Earth´s atmosphere and land on the Earth´s crust. Despite the wide variety of organic molecules detected in meteorite samples, ribonucleosides were never identified, as opposed to corresponding components, such as ribose and nucleobases [1, 3]. Previously studies indicated that ribose could be degraded by mechanochemistry in the presence of carbonate ions [4]. In this way, the degradation of ribonucleosides to nucleobases could be simulated by mechanochemistry, in presence of carbonate ions and transition metals, explaining in this way, the lack of ribonucleosides in meteorite samples, since carbonate could be formed by oxidation of organic matter and transition metals that are abundant in extraterrestrial bodies. In addition, to reinforce this possibility, the degradation mechanism promoted by carbonate ions and metals can be addressed with computational models, by DFT/TDDFT methodologies, modeling the structures of ribonucleosides, their degradation products, and reactive intermediates. Preliminary results show the degradation of guanosine into guanine by mechanochemistry, intensified by carbonate ions and transition metals, such as nickel. This model compared with a real asteroid sample without mechanochemical activity (Bennu, from OSIRIS-Rex mission or Ryugo, from Hayabusa2 mission) explains our suggestion that ribonucleosides could be detected in asteroids. Furthermore, by relating the shock energy with atmospheric composition, it would be possible to extrapolate to the prebiotic era, whether ribonucleosides could be transported directly to Earth, thus proving that the direct synthesis of ribonucleosides by reaction of ribose and nucleobases is not a favorable step for the prebiological evolution of life, and that life may have started at different points in the Universe, not exclusive to planet Earth.

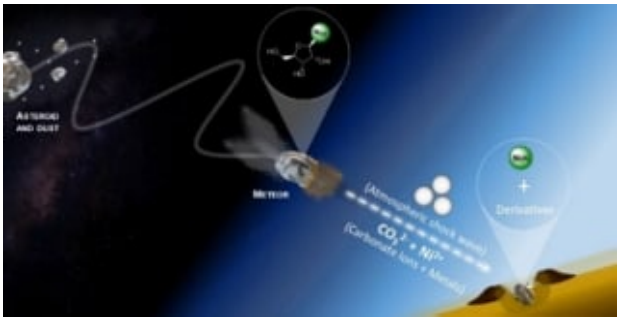

Figure 1 - Degradation model of ribonucleosides in their respective nucleobases and analogs by the action of mechanochemistry, intensified by carbonate ions and metals

This work has been carried out with financial aid of the FCT (Portugal) (Projects number UIDB/00100/2020, UIDP/00100/2020 and IMS -LA/P/0056/2020).

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Synthesis and characterization of pegylated Er^{3+} and Nd^{3+} doped yttrium oxide nanoparticles

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Lanthanide-doped yttrium oxide nanoparticles can display selective upconversion properties, such as NIR to shorter NIR, visible (blue, green and red) and UV. Thus, it is possible to irradiate them by using NIR excitation light, exploiting the "optical transparency window" (in the near-infrared (NIR) of 700−1100 nm) of biological tissues, obtaining deeper light penetration and reduced photodamage effects [1].

The syntheses of Er^{3+} and Nd^{3+} doped Y_2O_3 nanoparticles ($Er:Y_2O_3$ and $Nd:Y_2O_3$) were carried out according to [2] in which PAAC as template and urea to obtain a basic environment were added to a solution containing the nitrates of yttrium and/or Er/Nd nearly to the boiling point. The $Er:Y_2O_3$ and $Nd:Y_2O_3$ were characterized by different techniques: SEM, TEM, RAMAN, RBS and EDX. The SEM micrographs show that both $Er:Y_2O_3$ and $Nd:Y_2O_3$ nanoparticles are highly dispersed with dimensions of the order of few tens of nanometers. The TEM microphotographs and the related diffraction pattern proves that both samples are polycrystalline, whereas the RAMAN spectra demonstrate that the phase crystalline of the samples is cubic. Both RBS and EDX data show that both samples have the same stoichiometric ratios made in the starting solutions. The photoluminescence measurements show that either $Er:Y_2O_3$ and $Nd:Y_2O_3$ nanoparticles have the luminescence properties required and also show upconversion luminescence.

The nanophophors were also properly functionalized by a pegylation procedure in order to suppress unwanted reactions of the nanoparticles with the components of blood stream, making the systems biocompatible, and also rendering the particles themselves "soluble" in water and well dispersed. The pegylated nanoparticles show the same morphological and optical characteristics of the naked ones.

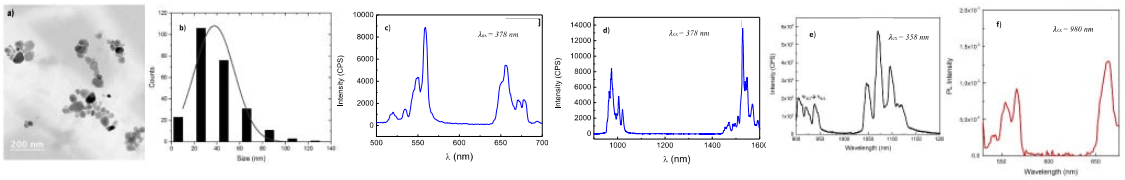

Figure: a) TEM micrographs of Er:Y2O3 nanoparticles and b) their size distribution. c) PL spectrum of Er:Y2O3 (Vis) and d) PL spectrum of Er:Y2O3 (IR). e) PL spectrum of Nd:Y2O3 nanoparticles and f) upconversion luminescence of Er:Y2O3 nanoparticles.

Acknowledgements We thank Università di Catania PIAno di InCEntivi per la RIcerca di Ateneo - PIA.CE.RI. 2020/2022" - linea 2 - Progetto di ricerca intra-dipartimentale Phototeranostic and MIcrovescicle Recognition Nanostructures under electromagnetic Activation (Piano per la Ricerca di Ateneo Linea di Intervento 2) for financial support.

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Development of dyes/tracers for the analysis of different kidney functions

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Chronic kidney diseases (CKDs) affect a huge population world-wide, where most of these patients do not know they are suffering from a CKD until the later stage. At this point, the treatment options available often lead to poor quality of life without full recovery of the kidney's functioning. The current clinical diagnostic techniques are expensive, cumbersome, invasive and many-a-times not accurate. This creates a need for an early detection way [1].

GFR is till this date the most used parameter for diagnosing kidney diseases [2]. Nevertheless, tubular secretion and reabsorption play as much a role in healthy functioning of the kidney as does the filtration. The primary focus of this study has been to synthesise novel fluorescent markers for evaluating the three physiological processes of the kidneys. This would help diagnosing function-/location-specific abnormalities in kidneys. These dyes are tested altogether to be able to evaluate the three kidney functions at the same time using a transcutaneous device. The detection can be done in parallel with multiple LEDs, or successively. Since the ideal goal would be to measure all the kidney parameters together in a patient, the absorbance and emission wavelength for each marker is designed to be significantly different to evaluate each function distinctly. The markers have been designed in the blue-green region of the visible light, red region, and the near-infrared region of the electromagnetic spectrum. This paves way for a wholesome, rapid, and non-invasive technique for kidney diagnosis at an early stage.

In addition to the functional analysis of renal functions, this study also involves the development of dyes that are compatible for use with whole animal perfusion-fixation protocols to facilitate imaging of intact kidneys ex vivo. This further allows study of disease progression by means of histology [3].

Together, these studies pave way for an early, wholesome, rapid, and non-invasive technique for kidney diagnosis.

Acknowledgements: This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 813839.







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Computational discovery of compounds against Parkinson´s Disease through pharmacophore directed docking

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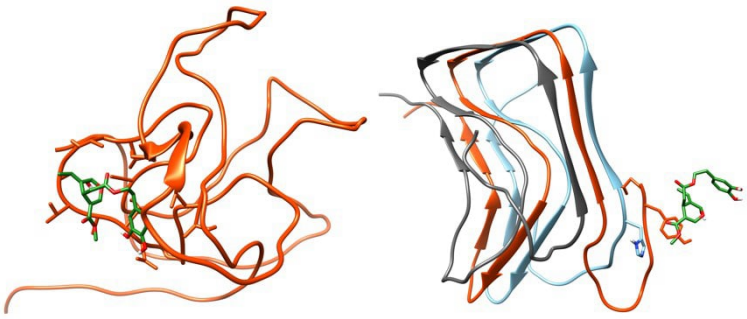
Although the specific causes of Parkinson's disease are not fully understood, abnormal aggregation of the protein α-synuclein is known to be one of the main factors triggering toxicity and degeneration in dopaminergic neurons. Despite the fact that there are currently palliative treatments for the motor manifestations of this disease, the real challenge remains to discover how the progression of the disease can be blocked or at least slowed down by therapies aimed at reducing, through one way or another, the misfolding of α-synuclein. We present here the theoretical results of a bigger, multidisciplinary project, aimed at analyzing the effect of a phenolic compounds of the olive tree (namely oleuropein aglycone, OA) on the aggregation and toxicity of α-synuclein, as well as on mechanisms that can modulate this process, such as molecular chaperones.

It is already known that OA interferes with α-synuclein aggregation into amyloid fibrils [1], although it is not clear if OA impedes the aggregation or breaks the fibrils already formed. Thus, we have performed long molecular dynamics calculations (4 runs of 500 ns) using the ff14IDPSFF force field [2], which improves the conformer sampling of intrinsically disordered proteins, on both a system composed of one copy of full length α-synuclein together with one molecule of OA, and a trimer composed of 3 copies of ordered (β-sheet) α-synuclein, as shown in the figure below (residues 30-100). An analysis of these trajectories through clustering of the zones of α-synuclein explored by OA allows us to classify possible interaction sites and rank them according to H-bond interactions and MMGBSA free binding energies, from which the possible pharmacophores are obtained. These pharmacophores will be used in a pharmacophore directed docking of compounds included in the EU-OPENSCREEN´s Compound Collections [3].



The author would like to thank the Junta de Andalucía (Programa Operativo FEDER Andalucía 2014-2020 REF. 1380736) and Universidad de Jaén (Acción 1).

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On the Role of Simple Polyphenols in the Aggregation of Parkinson's Disease Related Peptides

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Abstract

Protein aggregation is implicated in several neurodegenerative diseases, including Parkinson's Disease (PD). PD's etiology has been associated with the formation of cytotoxic oligomers of which α -synuclein (α-syn), a 140 amino acid intrinsically disordered protein mainly expressed in the central nervous system, is the primary component. While several small molecules have shown some aggregation inhibition activity *in vitro* there is still no approved drug that can disrupt and/or inhibit the formation of these aggregates in PD and other proteinopathies. Furthermore, the action mechanism of some of these aggregation inhibitors remains poorly understood. Herein, we compare the effect of a protein denaturant (urea) with that of archetypal aggregation inhibitors in the solvation and binding of model peptides from the non-amyloid-β component (NAC), a highly hydrophobic and amyloidogenic domain of α-syn.

Submicron polystyrene particles affect on the colorectal adenocarcinoma cell line DLD-1

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Submicron polymer particles (SPPs) are defined as plastic molecules smaller than 5 mm in diameter [1]. Polymers have become a serious concern for the life and health safety of living organisms, as their presence in the ecosystem becomes more and more evident. Human activity is the main cause of the environment's contamination with plastics. SPPs are still a very undervalued subject of study. Scientists are not fully aware of the effects that SPPs have on humans, as that due to their small size they can overcome many biological barriers and enter into circulation, which is not possible with larger sized microplastics.

It is crucial to clarify the manner of SPPs' interaction on humans. To obtain that, two fundamental characteristics of SPPs must be taken into consideration: the size/shape and loads, which are the most effective in terms of internalization by cells. In this work, we focused our attention on two sizes of two types of polystyrene: 100 nm neutral polystyrene (PS-100) and 200 nm neutral polystyrene (PS-200), as well as 100 nm polystyrene with amino groups (PS-NH_2-100) and 200 nm polystyrene with amino groups (PS-NH_2-200).

The effect of 24-h exposures of DLD-1 cells to polystyrene particles at different concentrations (0 – 1000 μg/ml) was studied. The MTT assay was conducted to evaluate the viability of polymer-treated cells. The surface charge and zeta potential of cells were determined by performing micro-electrophoretic assessments on samples using the Electrophoretic Light Scattering technique. The measurements were performed from pH 2 to 10 using 0.9% NaCl as a supporting electrolyte, titrated to the desired pH with concentrated HCl or NaOH.

The treatment of DLD-1 cells with PS-100, PS-200, PS-NH_2-100 and PS-NH_2-100 particles in various concentrations caused evident dose-dependent cell viability changes. Based on the results obtained by the DLS technique, exposure of human colorectal adenocarcinoma cells with SPPs decreased the negative surface charge at high pH values in comparison to the non-treated controls. No significant adjustments were observed between the surface charge density values in DLD-1 cells after treatment with polymers at low pH values. Also, no shifts in the isoelectric point values of the whole analyzed cell membranes were detected.

Our findings demonstrate that SPPs treatment induces variations in DLD-1 cells' electrical parameters. However, a more detailed analysis of SPPs' effects is still mandatory to comprehensively clarify the nature of these compounds in colorectal adenocarcinoma cells. The future increase of the data's quantity on submicron particles existing in the human organism will provide a greater understanding of such data in terms of whether effects are likely to be seen at plausible exposures.

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A combined chemistry and biophysics approach to understanding the tear film lipid layer

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The tear film lipid layer (TFLL) is a biological membrane that stabilizes the tear film and protects the ocular surface from drying [1]. The TFLL is secreted by the Meibomian glands and is mainly composed from non-polar wax esters and cholesterol esters [2]. In addition to the non-polar lipid species, polar lipids such as *O*-acyl-ω-hydroxy fatty acids (OAHFAs) and diesters (DiEs) have been suggested to play an important role in TFLL function [3]. The relationship between TFLL function and composition is still not fully understood, although a close connection to ocular surface diseases has been established [4]. Understanding how the different lipid classes generate and sustain the function of the TFLL is therefore essential going forward.

We have been studying the biophysical profiles of key lipid classes through the use of chemically synthesized molecular probes in order to shed light on their possible roles in the TFLL. We have already identified lipid species which contribute to specific functions of the TFLL and showcased how the interactions of different lipid classes may alter the behavior displayed by individual components [5,6]. At the conference, our latest results on the synthesis and biophysical characterization of TFLL lipid species will be showcased.

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DNA Biosensors For Capacitive Detection Of Viral RNA

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Abstract: The emergence of the coronavirus disease in 2019 (COVID-19) highlighted the need for rapid, accurate and massive virus detection techniques to control the widespread of infectious diseases. Epidemic-causing mosquito-borne viruses such as Dengue, Zika or Chinkungunya, are under tight surveillance by sanitary organizations, as they may be next to emerge on the global stage [1]. In Europe, although those viruses circulation is up to now limited, concerns have been raised about the recent emergence of Tiger mosquitos [2]. Monitoring potential arboviruses in the mosquitoes' established populations is of great interest for European health organizations to stay one step ahead.

We suggest an approach to address the limitations of current detection procedures using a low-cost and highly responsive biosensor, which would remove the need for biomedical personnel and advanced laboratory infrastructures. The biological samples could be taken from humans or any viral hosts and be processed to detect a variety of viruses. Most viral detection techniques require the immobilization of biomolecules on a sensor surface. Silica-based materials are ideal sensor plateform for viruses due to their inexpensiveness, ease of functionalization and good temperature and mechanical stability [3].

We herein disclose various surface conjugation strategies for the immobilization of single-strand DNA (ssDNA) probes on silica-based slides. Amide-bond coupling and copper-free click chemistry, through the use of dibenzoannulated cyclooctyne moieties, were considered to covalently attach the DNA at the surface. The density of the ssDNA probes immobilized and their distance to the surface are known to play a major role on the efficacy of hybridization events [4]. Therefore, variation of size and branching degree is investigated for optimal sensor sensitivity (Figure 1). The resulting sensing platforms will be assessed for SARS-CoV-2 and Zika detection. Fluorescence and bioimpedance measurements were chosen for the detection of the hybrization events between the viral RNA strands from the biological samples and the immobilized ssDNA strands.

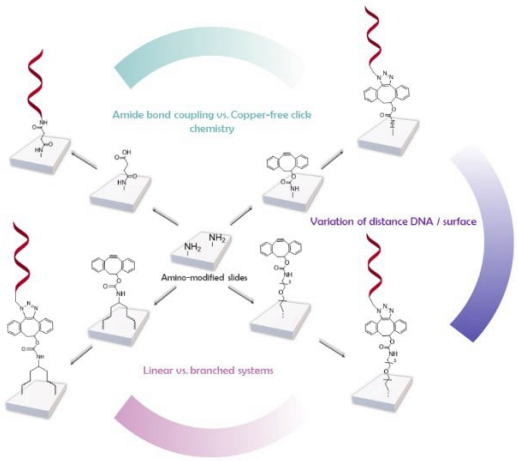

Figure 1. Various immobilization strategies of ssDNA probes on silica-based material to tailor their orientation and density. Dibenzoannulated cyclooctyne moieties was chosen for the copper-free click chemistry attachment of DNA strands.

We are grateful for financial support by the Swiss Confederation in the form of an Innosuisse grant 38934.1 IP-LS and the Swiss National Science Foundation via a NRP 78 grant 4078P0_198265.

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Discovery of Small-Molecule Antidotes for *B. asper* Viper's Venom

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In 2017, snakebite envenoming was recognized as a neglected tropical disease (NTD). As overpopulation in tropical countries kept increasing, rural communities began expanding territories, which resulted in the occupation of venomous snakes habitats for agricultural purposes. Consequently, snakebite envenoming became a daily issue for those communities. Estimations point out that this NTD annually causes over 2.7 million accidents and more than 100 thousand deaths.

Nowadays, the only cure available to address this illness is an antibody-based antivenom, which consists of administering antibodies produced by large mammals' immune systems as a response to the injected venom. This treatment is highly costly, needs cold storage conditions, inpatient administration and several doses. Finally, it can lead to several failures, due to its high specificity regarding the snake species. Given these limitations, there is an urgent need to develop a new kind of antivenom treatment. To fulfill this necessity, this work characterizes the mode of action of several small-molecule potential antidotes in order to accelerate the discovery of new antidotes against the *Bothrops asper* viper's venom. This viper is responsible for more than 80% of snakebite envenoming cases in South America and is known for its aggressive behavior.

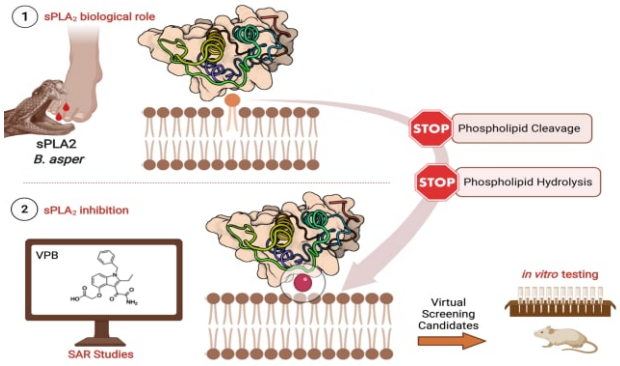
Proteomic analysis of viper venoms revealed that its composition is very complex, comprising up to 100 components, mostly of proteinaceous nature. However, two types of enzyme proteins stand out as potential drug targets, because they are highly expressed and toxic– the metalloproteinases and the phospholipases A_2 ($sPLA_2$).

This work focuses on the $sPLA_2$ because it presents a highly conserved binding site and represents almost 30% of the *B. asper* viper's venom. Furthermore, it is responsible for the venom myotoxicity. When bound to the victim's cell membranes, a hydrophobic channel is created and the active site of the enzyme is exposed. It then cleaves the cell membrane phospholipids. A calcium cofactor coordinates with the substrate and guarantees its efficient hydrolysis. Our goal is to find an $sPLA_2$ competitive inhibitor that binds to the Ca^{2+} ion and competes with its natural substrate to impede or drastically reduce the $sPLA_2$ enzymatic rate.

To reach this goal, we started by gathering data from *in vitro* experiments of 18 known $sPLA_2$ inhibitors. Afterwards, we performed molecular docking calculations and molecular dynamics simulations in order to establish the enzyme-ligand structural-activity relationship. The results showed that despite the differences in chemical properties and scaffolds, each inhibitor contained a similar pattern of interactions that assisted its binding to the $sPLA_2$.

Then, we did a virtual screening of a chemical library of drugs that had already participated in clinical trials in the past to find inhibitors for repurposing to $sPLA_2$, a strategic approach to speed up the drug discovery process and reduce the financial cost. Ultimately, we picked the best compounds for *in vitro* testing, based on the $sPLA_2$ protocol that was previously assessed.

To our knowledge this is the first structural study performed on $sPLA_2$ that comprises chemical diversity and responds to the structural complementarity between the ligand and the enzyme.



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A New Strategy to Induce Self-assembly with A Carbodiimide-fueled Reaction Cycle

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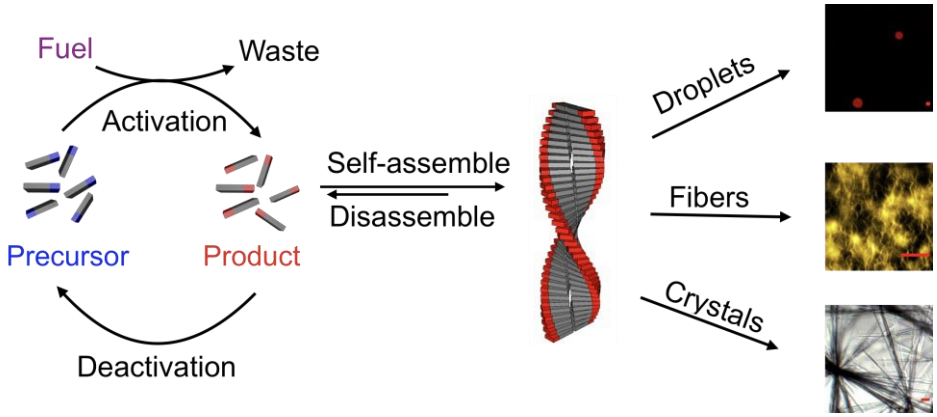
In living systems self-assemblies are out-of-equilibrium and are mostly driven by chemical reaction cycles where high-energy molecules are irreversibly consumed such as GTP for the self-assembly of microtubules or ATP for the actin self-assembly [1,2]. Man-made examples exist but remain relatively rare due to the lack of chemical reaction cycles leading to dissipative self-assemblies. Here we introduce a new chemical reaction cycle fueled by a carbodiimide to induce dissipative self-assembly. This new reaction cycle is efficient to form the transient product and is robust to operate under a wide range of conditions, such as under different pH, temperatures, and concentrations. It is also versatile to apply to potential precursors and drive reachable kind of self-assemblies, like droplets, fibers and crystals. Its robustness, versatility and ability of inducing dissipative self-assemblies open the scope of its applications. We anticipate that our new reaction cycle can provide more possibilities for dissipative self-assembly systems and further aid to develop autonomous materials with life-like properties.



Scheme 1. Schematic representation of a chemically fueled reaction cycle coupled to self-assembly. Activation and deactivation regulate the self-assembly behavior of a building block. Our new reaction cycle can drive reachable kind of self-assemblies, like droplets, fibers and crystals. All scale bars correspond to 5 µm.

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Fenoterol and its analogues as potential new drugs in the heart failure therapy: a molecular modeling and *in vivo* zebrafish study

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Cardiovascular diseases are one of the leading causes of death worldwide. Using the animal models is the main approach to design and test novel therapies. In particular, zebrafish has been proven to be a powerful tool in research on new potential drugs designed for the treatment of heart failure. Small size, optical transparency, and rapid external development allow for the *in vivo* high-throughput screening of substances that modulate heart parameters.

In the current study, we investigated a series of full and selective agonists of β2-adrenergic receptor (β2-AR): (*R*,*R*)-fenoterol ((*R*,*R*)-Fen), (*S*,*S*)-fenoterol and its analogues, e.g. (*R*,*R*)-4-metoxy-naphtyl-fenoterol ((*R,R*)-MNFen), and (*R*,*R*)-4-metoxy-fenoterol ((*R*,*R*)-MFen) with respect to the elicited mortality, changes in heart rate, and morphological alterations in zebrafish larvae according to Fish Embryo Acute Toxicity Test.

In vivo studies showed a series of significant differences between fenoterols in terms of their toxicity, effects on the heart rate and zebrafish mobility. (*R*,*R*)-Fen reduces heart rate starting from the concentration of 2.5 mM (2.23 times lower than LC_{50}); (*R*,*R*)-MFen exhibits the same effect starting from 0.25 mM (20.84 times lower than LC_{50}); (*R*,*R*)-MNFen reduces heart rate at 0.25 mM, thus, the corresponding dose is 2.6 times lower than LC_{50}. (*R*,*R*)-MFen suppress heart rate at the widest range of concentrations indicating higher cardiotoxicity. Moreover, all drugs increase coiling activity in 24 hpf (hours post fertilization) embryos. Crucially, zebrafish mimicked the response of the human heart to cardiovascular drugs. The greater part of impaired cardiovascular parameters and cardiac abnormalities were alleviated, confirming the functionality of human heart medications in zebrafish.

The results of in vivo studies can be interpreted in terms of molecular interactions accompanying to binding ligands to the receptor molecule. Docking simulations (AutoDock Vina) revealed that all tested agonists occupy the orthosteric binding site of zebrafish β2-AR by forming the number of interactions that are critical for agonist-induced activation. Within this site, agonists interact primarily with $D^{3.32}$, $S^{5.42}$, $S^{5.43}$, $S^{5.46}$, $N^{6.55}$, $F^{7.35}$, $N^{7.39}$, similarly to the human β2-AR. Additionally, docking revealed the structural differences between fenoterols in binding to subtypes A and B of the zebrafish β2-AR and stereoselective effects present during ligand binding.

In our view, the results emphasize that a zebrafish platform may rapidly reveal the cardiotoxic property and provide an objective indication of cardioprotection of tested substances. Zebrafish may thereby serve as a complementary system to rodent models.

Acknowledgments: This research was funded by the National Science Centre, Poland (contract financed in 2019–2021 under Project Opus, No. 2017/25/B/NZ7/02654).

Total synthesis and characterization of tear film wax- and cholesteryl esters

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The tear film lipid layer (TFLL) is a unique biological membrane that covers the ocular surface, forming the outermost layer of the tear film. It stabilizes the tear film and plays a major role in the maintenance of ocular surface health [1]. The TFLL is secreted by the Meibomian glands and has a highly specific composition, consisting of wax esters (WEs), cholesteryl esters (CEs), *O*-acyl-ω-hydroxy fatty acids (OAHFAs), type I-St and type II diesters, triglycerides, and free cholesterol [2–6]. Roughly 75–95% of the entire TFLL lipidome consists of WEs and CEs.

Isolation of individual components from tears is, however, time-consuming and challenging, which makes studies on their biophysical profiles scarce. Additonally, previous studies have been conducted on simplified structural analogs. The synthetic preparation of authentic species is therefore warranted. We have recently reported on the total synthesis and properties of a TFLL-related OAHFA and its diesters [7]. At the conference, the results on the total synthesis and structural characterization of authentic TFLL C26:0-WEs and CEs will be presented.

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Fumiquinazoline analogues: Synthesis, antibacterial activity and assessment of potential as efflux pump inhibitors

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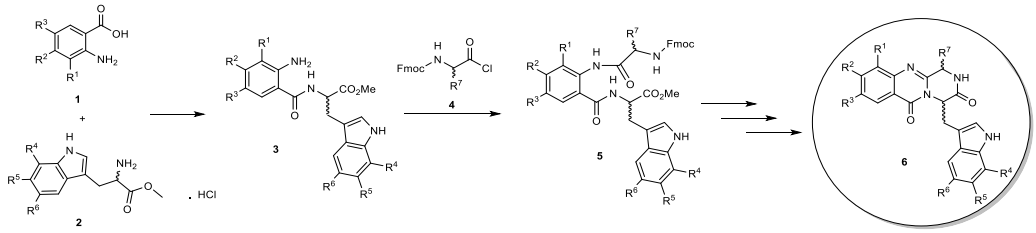
Drug resistance has reached critical levels, posing a public health challenge with extensive economic, and societal implications. Thus, the development of antimicrobial new compounds that can be useful to overcome resistance mechanisms is a priority in the current society [1]. One of the most common causes of antimicrobial resistance is the overexpression of efflux pumps that render the antibiotics ineffective by expelling them from the microorganism [2]. Fumiquinazolines and derivatives are a chemical family of alkaloids that have shown potential for the development of new antimicrobial agents [3, 4]. In our group, both natural and synthetic derivatives showed promising antibacterial activities in both reference and resistance strains [5,6].

In this work, we aim to synthesize new fumiquinazoline analogues, evaluate their antibacterial potential, and investigate their ability to act as efflux pump inhibitors. Herein, we present the multi-step synthesis [7] of a small library of fumiquinazoline derivatives (Scheme 1), comprising two naturally occurring alkaloids and several new derivatives. Molecular structure elucidation was achieved through high-resolution mass spectrometry (HRMS) and nuclear magnetic resonance (NMR) techniques. To assess the antibacterial activity, the minimum inhibitory concentration (MIC) of each compound against a panel of clinically relevant bacterial species was determined and a preliminary synergism study with known antibiotics was made; several compounds were active against the tested Gram-positive bacteria. It is worth highlighting the promising activities of one of the novel alkaloids against methicillin-resistant *Staphylococcus aureus* (MRSA) (MIC = 8 µg/mL) and against vancomycin-resistant *Enterococcus faecalis* (VRE) (MIC = 32 µg/mL). Additionally, the compounds were screened for their potential as efflux pump inhibitors using the ethidium bromide accumulation assay as well as for their anti-biofilm capacity with some of the alkaloids showing promising results.



Scheme 1 *Multistep synthetic pathway towards the obtainment of fumiquinazoline analogues.*

Acknowledgments: This research was supported by national funds through FCT (Foundation for Science and Technology) within the scope of Base Funding UIDB/04423/2020 and UIDP/04423/2020 (CIIMAR, Group of Natural Products and Medicinal Chemistry), projects EXPL/CTA-AMB/0810/2021, PTDC/CTA-AMB/0853/2021 and CHIRALBIO ACTIVE-PI-3RL-IINFACTS-2019 and by the Norte Portugal Regional Operational Programme (NORTE 2020), under the PORTUGAL 2020 Partnership Agreement and through the ERDF, as a result of the project ATLANTIDA (reference NORTE-01-0145-FEDER-000040). Mariana C. Almeida acknowledges the BYT+ 2020/2021 scholarship to CIIMAR (Master Student Scholarship) and the PhD grant (2021.05224.BD) to FCT.

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The zeta potential changes of *Escherichia Coli* membranes by the exposure to nonfuctionalized and functionalized polystyrene nanoparticles of various sizes

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Among many scientific topics being investigated throughout this decade, plastic takes the spotlight as probably the most controversial one. Studies have confirmed the occurrence of microplastics (*abbrev.* MPs, smaller than 5 µm) and nanoplastics (*abbrev.* NPs, smaller than 100 nm) in almost every area of our lives, namely in food products, air, water and soil [1]. These findings have been paired up with research that confirmed uptake of plastic particles into living cells. Such a gruesome scenario led to a crucial need to know more about those small anthropological polymer molecules that are entering our organisms. Recently, a study confirmed the existence of microparticles of various plastics in the human bloodstream [1,2].

The goal of this study was to assess the influence of plain, nonfunctionalized and functionalized, with amine groups attached to the surface of the material, polystyrene molecules, of sizes equal to 100 and 200 nm, on the membranes of *Escherichia Coli*. Plastic particles were chosen for these tests on a merit that polystyrene (PS) is one of the most commonly used synthetic polymers and thus its presence in the environment is high. To more thoroughly represent various plastics currently present in the ecosystem, both functionalized and nonfunctionalized particles of different sizes were chosen. *Escherichia Coli* is a Gram-negative bacteria that is living in our intestines [3]. It too can be exposed to the various concentration of plastic particles, with human organism, due to the food contamination. The electrokinetic potential of cell membranes was determined in this study. This electrical parameter can be used to assess what is happening on the surface, as well as inside the bacteria. The membrane is the essential part of the cell and changes to its parameters can picture a response of a whole cell to e.g. external substances.

In our measurements, the Electrophoretic Light Scattering technique of Metasizer Nano ZS apparatus was used. *Escherichia Coli* (PCM 2857) used in the study came from the Polish Collection of Microorganisms. The bacteria were dispersed in the electrolyte solution (0.3 mmol/dm^3 NaCl) and plastic particles of various concentrations were added to them. The concentrations of 0.002, 0.01, 0.1, and 0.5 mg/mL of polystyrene were investigated. The measurements were done in the function of pH, in the range 2-11. Additionally, for the concentration of 0.1 mg/ml tests considering the time of the exposure were performed. The measurements were done after 0.5, 1, 3, and 5h of exposure, all in the function of pH.

Acquired data showed the occurrence of changes to the electrokinetic potential values of *Escherichia Coli* membranes due to the exposure to polystyrene particles. Existence of the function groups on the surface of the polymers, time of the exposure and concentration of plastic was shown to have an influence on the magnitude of effects caused by PS to the bacteria.

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Electrophoretic Light Scattering technique for electrical characterization of liposomes mimicking microbial membranes upon interaction with phenolic acids and their metal complexes

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Biological membranes play an essential role in the regulation of electrochemical processes occurring in living organisms, and this regulation is dependent on their structure. Because systematic studies are impeded by the complexity of the natural membranes, simplified, well-defined models are used. Electrochemical methods, in particular Electrophoretic Light Scattering (ELS), may be very helpful in the characterization of properties of model lipid membranes such as liposomes [1].

Caffeic (CA) and p-coumaric (p-CA) acids are phenolic compounds with various biological functions, such as antioxidant, anti-inflammatory, antimicrobial and anticancer activities [2]. In addition, their metal complexes play fundamental roles in biological systems. Nevertheless, research on the properties of CA or p-CA with lanthanide metal ions is very scarce, and little to no information is known about these particular systems.

Gadolinium is rare earth that occurs primarily in the +3 oxidation state. It has complex environmental chemistry that includes the potential for complex formation with a variety of organic and inorganic ligands, surface sorption and hydrolysis, co-precipitation and precipitation. Due to the use of Gd3+ in magnetic resonance imaging and manufacturing, large quantities of gadolinium have been released into the environment. Gd3+ can be extremely toxic under some circumstances, and an investigation of its chemistry in the environment is warranted [3].

The goal of this study was to assess the influence of Gd3+, and its complexes with CA and p-CA, on the surface charge and zeta potential of liposomes formed from phospholipids prevalent in cell surfaces of fungi, Gram-positive and Gram-negative bacteria. The values of the electrical parameters were determined by performing micro-electrophoretic assessments on samples using ELS. The measurements were conducted with the Zetasizer Nano ZS apparatus, in the pH range from 2 to 10. The liposomes were suspended in the tested solutions and allowed to interact with the solution components for 1 h at room temperature. 0.2 $mol \cdot dm^{-3}$ KCl solutions containing phenolic acid (CA or p-CA), Gd3+, or Gd3+ with the appropriate amount of phenolic acid, at a 1:1 metal to ligand molar ratio, at *ca.* 10^{-3} $mol \cdot dm^{-3}$ were used. Suspended liposomes were then titrated to the desired pH with strong acid and strong base solutions, which were prepared with NaCl to keep the strength of the ionic solution constant. Six measurements were made (each covering 100–200 series for a duration of 5 seconds) for each pH value for each sample. The experiments were repeated three times with similar results.

Our results indicate that changes of electrical parameters occurring during the modelling of microbial surfaces in the presence of complexes of phenolic acids and gadolinium may be useful for the interpretation of antibacterial properties of these complexes.

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An MS multi-omics approach to drug repurposing - unravelling hidden mechanisms of drug action

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Drug development can proceed by de novo drug design, rational drug modification, or, as it happens more often recently, by drug repurposing. In the latter approach, any given drug can be tested for use towards a target different from the original one. Off-site drug action and adverse drug reactions can be good indicators of drugs worthy of repurposing.

Montelukast (MTK, Singulair) is routinely used for asthma management. MTK displays sporadic peripheric side-effects, which promptly resolve upon stopping the treatment, but is also associated with mild-to-severe neuropsychiatric effects, particularly in children. Interestingly, MTK is being considered as an alternative therapy towards Alzheimer's Disease.

In order to reconcile the central nervous system (CNS) adverse reactions to MTK with its repurposing for a neurodegenerative condition, we performed a multi-omics multi-system MS-based evaluation of the pathways involved in the response to MTK administration using an *in vitro* embryonic chicken neuron model and an *in vivo* approach using a rodent model. Taking advantage of the high-resolution mass spectrometry equipment installed at CQE Mass Spectrometry Lab, full untargeted metabolomics and proteomics approaches were used to study both models' response to MTK.

Results clearly show that MTK treatment is associated with an hyperactivation of the HPA axis, leading to a dysregulation of neurotransmitter-dependent pathways, establishing a clear relation between MTK and the described adverse reactions on the CNS. Furthermore, proteomics data also suggest that MTK influences endopeptidase activity, apoptotic processes, and cell death.

In parallel, thiol-based oxidative stress-protection pathways were found shifted towards an increased global oxidative status. This result correlates with the identification of an MTK-glutathione adduct formed by both enzymatic and non-enzymatic pathways, also completely characterized by HRMS in this work.

To conclude, the network connectivity between both omics approaches supports the relation between metabolites and proteins in pathways influenced by montelukast.

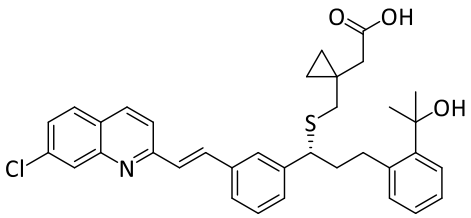

Figure 1. Chemical structure of montelukast.

Acknowledgments: Centro de Química Estrutural is a Research Unit funded by Fundação para a Ciência e Tecnologia through projects UIDB/00100/2020 and UIDP/00100/2020. Institute of Molecular Sciences is an Associate Laboratory funded by FCT through project LA/P/0056/2020. This work was partially funded through FCT grants SAICTPAC/0019/2015 and PTDC/QUI-QAN/32242/2017 and through the Portuguese Mass Spectrometry Network (RNEM-LISBOA-01-0145- FEDER-022125). CFM also thanks FCT for a PhD fellowship (PD/BD/143128/2019 and COVID/BD/152559/2022).

Silica-based imprinted particles as adenovirus scavengers

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Molecularly imprinted polymers (MIPs) are synthetic affinity matrices that can recognize a specific target molecule and even entire organisms, like viruses. The technique of molecular imprinting is based on mimicking natural interactions and allows the formation of specific binding sites within a polymer matrix. Synthesis strategies can be tailored to the used target molecule and desired applications [1]. In this study, core-shell particles combining silica cores with surface imprinting techniques were synthesized for selective binding of human adenovirus type 5. The polymer particles with organosilane-based shells provided an ideal surface for virus binding after a monomer screening for selection of appropriate surface functionalities. Imprinted particles have higher stability and lower production costs compared to natural receptors. High binding capacities were obtained and rebinding of virus to the imprinted particles was investigated in presence of protein blocking agents, like BSA and skim milk. In addition, elution conditions for extraction of the virus from the particles were optimized and high recoveries were obtained with a sodium chloride high salt buffer. The viruses were not removed from the particles by washing steps with PBS indicating strong virus binding to the polymeric layer [2].

Furthermore, the particles were applied for adenovirus extraction from complex matrices. Therefore, cell culture supernatant was used, and the virus showed high affinity towards the particles unaffected by the present matrix components. Amount of adenovirus was quantified by qPCR. Additionally, virus binding to the particles was confirmed by SEM and viruses are visible on the imprinted particles after staining with osmium tetroxide. In contrast, the matrix proteins mainly remained in the supernatant, as confirmed by UV-Vis and SDS-PAGE analysis, and the viruses were successfully removed from the matrix. Imprinted polymers can therefore be used for virus extraction in biological samples, like cell culture supernatants, as well as for virus enrichment steps or virus purification processes.

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Histidine, Leucine and Isoleucine as dietary supplements. Formation of N-Nitrosocompounds

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Besides being the basis for protein synthesis, amino acids have an important role in most biological processes, some of them cannot be synthesized by the human body, so they must be ingested into the diet. We will focus this study in Histidine, Isoleucine and Leucine, amino acids highly consumed as dietary supplements to which are attributed benefits in the immune system, tissue repair and increased energy levels, among others. When these amino acids are consumed they can react with nitrite – a food additive commonly used to inhibit the growth of C. botulinum – in the acidic medium of the stomach, to nitroso compounds [1]. Nitrosation of amino acids with a primary amino group is particularly interesting since their products are unstable and lead to the formation of direct-acting alkylating agents such as β-propiolactone and β-butyrolactone [2-3], which have been classified by the International Agency for Research on Cancer within the group of substances possibly carcinogenic to humans (2B) [4].

The present work was carried out using a strong excess of amino acid concentrations compared to sodium nitrite concentrations, keeping pH and temperature constant in a range from 2.0 to 4.5 and from 293.15 K to 313.15 K, respectively. A quartz cuvette was used as a reactor for spectrophotometric monitoring carried out at 371nm, the wavelength corresponding to one of the maximum absorptions of the HNO_2/NO_2^- system (henceforth nitrite), in which no interference of the other species present in the reaction medium is observed.

For the analysis of the obtained data, both the integration method and the initial rate method were used. It was found a second order with respect to the nitrite concentration and first order with respect to the amino acid concentration, according to the following rate equation:

$$v = k_3[AA][Nit]^2$$

In the study at different pH values, it was observed a strong dependence of the experimental rate constant k_3 with the pH, as well as a higher effectiveness of the nitrosation at pHs around 2.5. The thermodynamic study allowed the calculation of the activation parameters of the reaction.

The following conclusions have been obtained: i) a nitrosation reaction occurred to all three amino acids evaluated, founding the most effective process at values close to gastric pH; ii) the second order with respect to the nitrite concentration involved N_2O_3 as the main nitrosating agent; iii) the study of the dependence of k_3 on pH has allowed to propose the reaction mechanism and to obtain the rate constants associated with the slow steps.

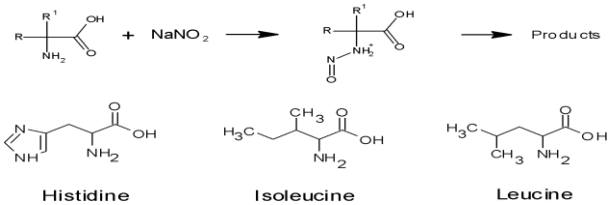

Fig 1. Scheme of the primary amino acid nitrosation reaction. Chemical structures of the amino acids studied.

Thanks to the University of Salamanca (Own programs: 19K125/463AC01). Scholarship program for doctoral studies at the University of Salamanca for Latin American students.

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In vitro gastrointestinal digestion of purified anthocyanins enhances cytotoxicity in colon cancer

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Anthocyanins represent a versatile subclass of flavonoids, a class of polyphenols, which fundamentally consists of two aromatic rings bonded together by a heterocyclic oxygen-centered ring, forming a C6-C3-C6 carbon chain. Knowing their chemistry is crucial in understanding the mechanisms by which anthocyanins are digested. Naturally, anthocyanins are found in fruits and vegetables in a glycosylated form, which means that their aglycone nucleus has attached one or more sugar radicals [1]. The reason for the glycosylation process is to increase the stability of the compounds, both in food and biological matrices [2]. As they cross the gastro-intestinal tract, anthocyanins change not only their confirmation due to pH, but also structure due to special reactions mediated by digestive tract enzymes.

Therefore, the first objective of this study was to evaluate the biotransformation of anthocyanin-rich fraction from 3 different sources having different aglycon or type of sugar substitution after digestion using a static digestion (SD) model. Samples underwent digestion via the SD model and LC-ESI-MS was used to assess anthocyanin profiles and antioxidant capacity measures following simulated digestive processes. The second objective was to compare the effects of intestinal digests of the analyzed samples (chokeberry, black carrot, red cabbage) on the cytotoxicity and cell viability on the human colon cancer DLD-1cell line.

After simulated digestion, LC-ESI-MS confirmed the identification of anthocyanins and also other compounds in all three samples. The total anthocyanin concentration was higher in red cabbage compared to chokeberry and red grapes. Chokeberry intestinal digests showed greater potency to induce cytotoxicity and decrease viability of DLD-1 cells. The IC50 values for the combination treatment were 5,89 µg/mL for chokeberry, for red cabbage the calculated IC50 was 9,72 µg/mL and respectively 16,65 µg/mL for red grapes. Those values being very low comparing to the available literature data regarding nondigested tested extracts.

The current study presents the effect of digested anthocyanin-rich fraction from red cabbage, chokeberry and red grapes on the cytotoxicity and cell viability on the human colon cancer DLD-1cell line.
The results indicate major variations in the pattern of anthocyanin breakdown and release during digestion of analyzed samples. The anthocyanin-rich fraction of chokeberry demonstrates the most effective effect in vitro.
The in vitro assays results suggest that digested anthocyanin-rich fraction have a higher bioaccessibility and antioxidant capacity than the nondigested anthocyanin-rich fraction frequently reported in literature.

Acknowledgments: This research was funded by The Executive Unit for Financing Higher Education, Research, Development and Innovation (UEFISCDI), grant number PN-III-P1-1.1-TE-2019-0960

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New composites incorporating silver(I) coordination polymers and their antibacterial and antiviral potential

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Contamination by microorganisms, especially of bacterial and viral origin, has a tremendous impact on everyday life and public health. In particular, there is an alarming problem of bacterial resistance for various strains of *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, which explains an urgent need for new antibacterial therapeutics and disinfectants [1]. Moreover, viral infections, especially those caused by Adenovirus 36 (Adv-36), are considered an additional factor responsible for the development of obesity [2,3]. Therefore, to address these global health threats, urgent investment in developing new advanced materials capable of combating bacterial resistance and averting the development of surface-attached microorganisms is required.

In particular, the surface microbicidal approach realized with starch biopolymers doped with metal-based biocides drives increasing research attention. Such materials may become ideal candidates for creating antimicrobial packaging and surfaces, microbe resistant materials, and different personal health care products.

Following our recent interest in the design of novel antimicrobial and antiviral silver(I) coordination polymers [3], the present work describes the assembly, characterization, and antimicrobial performance of new composites Ag-CP@AHSP. These are based on bioactive silver(I) coordination polymers (bioCPs) used as dopants of acid hydrolyzed polymer starch (AHSP). The obtained composites widen a growing family of hybrid bioactive materials with prospective topical antimicrobial applications.

We thank the National Science Center (Grant No. 2019/35/D/ST5/01155, Poland) for financial support. AMK acknowledges the FCT (PTDC/QUI-QIN/29697/2017, LA/P/0056/2020, UIDB/00100/2020, Portugal).

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Ectomycorrhizal fungi alleviate high temperature stress in pedunculate oak (*Q.robur)* through modulation of polyamine metabolism

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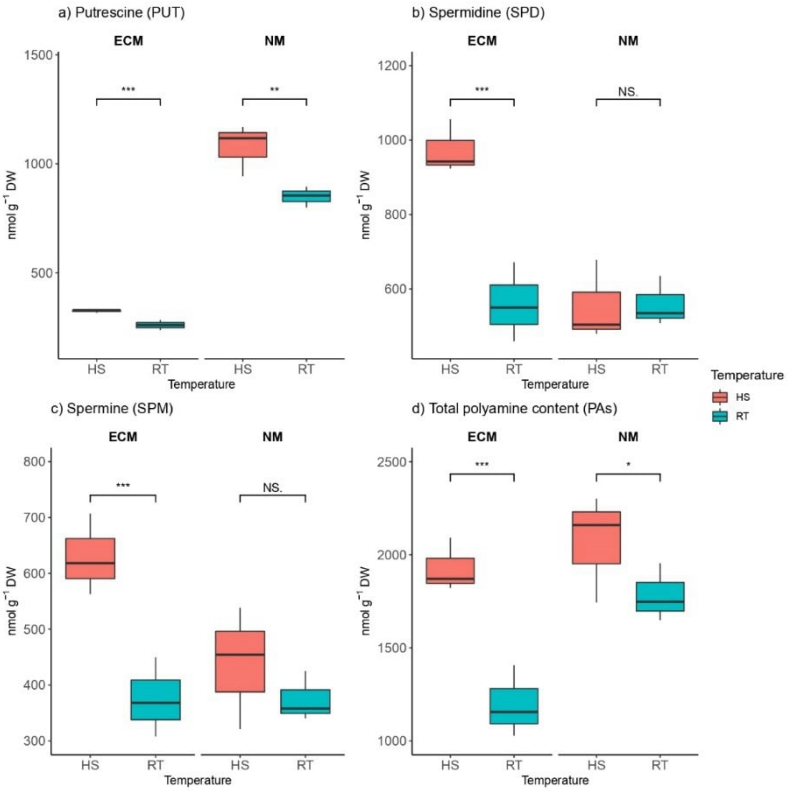
Arbuscular mycorrhizal fungi (AMF) are well known as protective agent during abiotic stress in plants, particularly high temperature stress. One of the suggested mechanisms is that AMF regulates photosystem II heterogeneity during exposure to high temperature [1]. On the other hand, less in known about potential of ectomycorrhizal fungi to mitigate high temperature stress in the host plant. Polyamines stand for very important markers of both-abiotic and biotic stress in plants and due to their polycationic structure, they also act as the membranes stability factors as well as antioxidants, but they are also known to affect synthesis of heat shock proteins (HSP) under heat stress by buffering the cell membrane integrity [2]. Furthermore, it has been proven that AMF modulates plants polyamine metabolism during the induced drought in trifoliate orange [3], while the effects of ectomycorrhizal fungi on polyamine amounts in plants are not thoroughly elucidated yet. Therefore, the main aim of this study was to assess how ectomycorrhizal fungi affect foliar polyamine accumulation during heat stress. For that reason, pedunculate oak seedlings (*Q. robur L.*) were germinated from acorns and inoculated with commercial inoculum ECTOVIT (Symbiom, Checz Republic) that consisted from spores and basidiocarps of five ectomycorrhizal species, whereas only one species, *Scleroderma citrinum* was identified by molecular characterization from the oak root tips. After plants were fully developed, both non-mycorrhized controls as well as mycorrhized oak seedlings were exposed to short-time heat stress for 72h (40°C, humidity 80%) in a programmable climate chamber. Amounts of individual polyamines were assessed and compared in total at four treatments: plants inoculated with ectomycorrhizal inoculum (ECM) exposed to heat stress (HS) and those grown only at the room temperature (RT) vs non-mycorrhized controls exposed to HS and those grown at the room temperature (RT) in a climate chamber. Amounts of three main foliar polyamines (putrescine, spermine and spermidine) were quantified by using high performance liquid chromatography (HPLC) coupled with fluorescent detection after derivatization of polyamines with dansyl-chloride [4]. Heat stress upregulated biosynthesis of spermidine (Spd) and spermine (Spm) in the similar manner in plants inoculated with ECM comparing to non-mycorrhized plants. During heat stress, Spd and Spm content were significantly higher in ECM inoculated plants (ca. 940 nmol g^{-1} DW and 630 nmol g^{-1} DW for Spd and Spm, respectively), while these compounds in non-mycorrhized oak seedlings ranged from ca. 510 to ca. 550 nmol g^{-1} DW for Spd and between ca. 350 to ca. 450 nmol g^{-1} DW for Spm. This study confirms that ectomycorrhizal fungi prime oak plants with polyamines (Spm and Spd), which consequently contribute to mitigation of heat-induced stress in oak seedlings.



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Cyclolinopeptides in Linseed Oil

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Abstract

Flaxseed (linseed) is a cultivar of the spring flowering annual plant flax (Linum usitatissimum) from the Linaceae family. Derivatives of this plant are widely used as food and as health products. In recent years, natural hydrophobic cyclic peptides isolated from flaxseed and flaxseed oil, better known as the cyclolinopeptides (CLPs), seized the attention of the scientific community due to their role in inhibition of osteoclast differentiation, or having antimalarial, immunosuppressive, and anti-tumour activities, as well as their prospect in nanotechnology and in the biomedical sector. This study describes the detection, identification, and measurement of CLPs in the samples obtained from nine different flaxseed oil manufacturers. For the first time Q Exactive Hybrid Quadrupole-Orbitrap Mass Spectrometry was used for CLPs identification together with RP-HPLC. The routine analyses were done using RP chromatography measuring the absorption spectra and fluorescence detection for identifying tryptophan containing peptides using the native fluorescence of tryptophan. In addition, existing protocols used for CLPs extraction were optimized and improved in fast and cost-efficient way. For the first time, 12 CLPs were separated using methanol/water as eluent with the RP-HPLC. Finally, the stability and degradation of individual CLPs in the respective flaxseed oil were examined over a period of 60 days at different temperatures. Using HPLC-MS 15 CLPs were identified in total in the different flaxseed oils. The characterization of the peptides via HPLC-MS highlighted two types of CLPs profiles with a substantial variation in the concentration and composition of CLPs per manufacturer, probably related to the plant cultivar. Among the observed CLPs, CLP-O, CLP-N and CLP-B were the least stable, while CLP-C and CLP-A were the most stable peptides. However, it is important to highlight a gradual degradation of most of the examined CLPs over time, even at the room temperature.

Structural, dynamic, and self-assembly properties of gluten peptides in complex solutions and interaction with intestinal-like epithelial membrane models

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Clinical manifestations of Celiac Disease (CD) - an immune-mediated enteropathy triggered by dietary gluten intake - are thought to be pathogenetically related to the ongoing duodenal mucosal inflammation [1]. Nevertheless, there are still many mechanistic gaps regarding the immunomodulatory action of gluten proteins in CD, most of which caused by the lack of valid experimental models faithfully expressing the molecular signatures characteristic of CD and consequent knowledge about the pathways driving gluten peptide uptake by intestinal epithelial cells. *In vivo*, this interaction causes a primary impairment of villi in the small intestine, increases epithelial permeability and allows the entry of immunogenic gluten peptides from the gut lumen to the lamina propria. So far, no specific cell receptor has been identified [2]. Recently, it has been hypothesized that membrane composition and organization, rather than a specific cell receptor, drive the entry of gluten peptides in intestinal epithelial cells.

Peptide-membrane interactions play critical roles in many cellular and organismal functions, including protection from infection, remodeling of membranes, signaling, and ion transport. Peptides interact with membranes in a variety of ways: some associate with membrane surfaces in either intrinsically disordered conformations or well-defined secondary structures. Peptides with sufficient hydrophobicity can also insert vertically as transmembrane monomers, and many associate further into membrane-spanning helical bundles. Indeed, some peptides progress through each of these stages in the process of forming oligomeric bundles. In each case, the structure of the peptide and cell membrane represent a delicate balance between peptide-membrane and peptide-peptide interactions, the latter of which have already shown to occur for gluten peptides in Milli Q water, without considering the influence of extracellular salts and intracellular crowding molecules [4].

In this study, the structural, dynamic, and self-assembly properties of gluten peptides in complex solutions have been probed by both Dynamic Light Scattering and Nuclear Magnetic Resonance, including analysis of conformational changes, oligomerization state and hydrodynamic behavior. The interaction of gluten peptides with intestinal epithelial cell-like liposomes has also been probed. Overall, such multi-technological approach provides critical clues for understanding fundamental biological unknown in CD as well as the physical-chemical basis behind gluten peptides recognition and intestinal cytotoxicity.

This work was funded by national funds provided by Fundação para a Ciência e Tecnologia (FCT) through the project UID/QUI/50006/2019 and AgriFood XXI project (NORTE-01-0145-FEDER-000041), co-financed by European Regional Development Fund (ERDF), through the NORTE 2020 (Programa Operacional Regional do Norte 2014/2020). The authors would also like to acknowledge FCT for the research project grant (PTDC/OCE-ETA/32287/2017) as well as the FEDER-Interreg España-Portugal program (I377_IBERPHENOL_6_E).

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Fabric Phase Sorptive Extraction: A Universal Sample Preparation Technology for Drug Discovery Investigations Directly from Whole Blood

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Preclinical and clinical studies in drug discovery and development processes involve a series of experiments including pharmacokinetics (PK), pharmacodynamics (PD), toxicokinetics (TK), and therapeutic drug monitoring (TDM). Due to the enormous complexity of whole blood, either plasma or serum are used in preclinical and clinical research as the proxy for whole blood. During the transformation of whole blood into plasma or serum, prior to the extraction of targeted drug(s) and their metabolites using conventional sample preparation techniques such as solid phase extraction (SPE) and liquid-liquid extraction (LLE), a significant portion of the analytical information often disappears, resulting in questionable data in these critical studies. Fabric phase sorptive extraction (FPSE) has offered a paradigm shift approach in sample preparation for preclinical and clinical research. FPSE innovatively combines the benefits of solid phase extraction (SPE) (exhaustive extraction) and solid phase microextraction (equilibrium extraction) into a single sample preparation technology platform. FPSE utilizes a flexible and permeable fabric substrate, coated with sol-gel sorbents as the extraction membrane. This uniquely designed extraction membrane is capable of quantitatively extracting target analyte(s) directly from whole blood. Special geometry of FPSE membrane (flexible, flat, and permeable) and sponge-like porous architecture of sol-gel sorbents promote rapid analyte transfer between the bulk sample matrix and the extraction membrane, resulting in a near exhaustive extraction within a fraction of time generally required for other comparable sample preparation techniques.

FPSE is particularly suitable for analysing target analytes e.g., drug residues, metabolites, and disease biomarkers directly from whole blood without requiring protein precipitation or other pre-extraction sample cleaning/manipulation. FPSE is carried out by direct insertion of FPSE membrane into the sample container holding the pristine, unmodified whole blood. A Teflon coated magnetic stir bar can be used to diffuse the sample matrix. After extracting the target analyte(s) from the whole blood sample, FPSE membrane is exposed to a small volume of organic/organo-aqueous solvent for eluting the extracted analyte(s). Low viscosity of organic solvent, capillary force of the fabric support and sponge-like porous sol-gel network allow fast diffusion of organic solvent into the FPSE membrane for quick and complete recovery of the extracted analyte(s). As a result, FPSE eliminates time consuming and error prone solvent evaporation and sample reconstitution step often considered as an integral part of solid phase extraction/liquid-liquid extraction workflow. During the elution/back-extraction, any protein or matrix interferents adhered to the FPSE membrane precipitates out and a final centrifugation of the resulting solution prior to injecting into the analytical instrument ensures clean particle-free highly concentrated target analyte(s).

Fabric phase sorptive extraction has already developed a large number of high performance sol-gel sorbents specifically suitable for polar drugs/metabolites/disease biomarkers. These high-efficiency sol-gel sorbents have been found equally effective for analytes possesing wide range of polarity. Consequently, searching for the drug residues and their metabolites from whole blood in presence of numerous endogenous and exogenous interferents is no longer a wishful thinking but an achievable reality.

In the current talk, some fascinating data on bioanalytical sample preparation using FPSE will be presented.

Keywords: fabric phase sorptive extraction, metabolomics sample preparation, whole blood analysis, green analytical chemistry

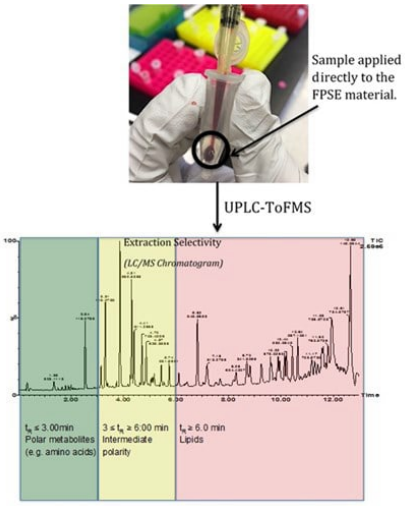

Figure 1. LC-MS chromatogram demonstrating broad range of metabolites extraction from 50 µL whole blood using fabric phase sorptive extraction.

N-based silane coupling agents for application in silica/SSBR/BR hybrid composite systems

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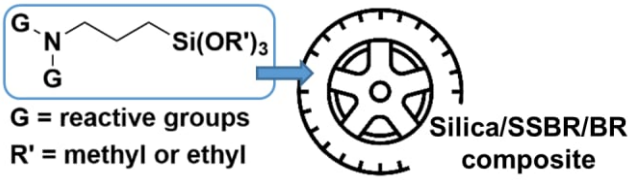
Silica/rubber nanocomposites are promising materials for the production of "green tires" because of their excellently low rolling resistance and reduced amount of carbon footprint [1]. In this communication, synthetic pathways for *N*-containing silane coupling agents (**SCA**s) as filler dispersants in silica/SSBR/BR systems are shown. The synthesized **SCA**s were mixed with bis(triethoxysilylpropyl)tetrasulfide (TESPT), and then the subsequent mixtures were examined in silica/SSBR/BR rubber vulcanization compositions. Mechanodynamic and viscoelastic properties of the obtained vulcanizates were measured and discussed, in reference to the composite sample based on TESPT only.



The work was supported by grant no. POWR.03.02.00-00-I020/17 co-financed by the European Union through the European Social Fund under the Operational Program Knowledge Education Development.

This work was financed by Synthos Generation – a scholarship program dedicated to students and PhD candidates organized by Synthos company.

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Si-Cl reduction as a route to obtain dendritic systems with silsesquioxane cores

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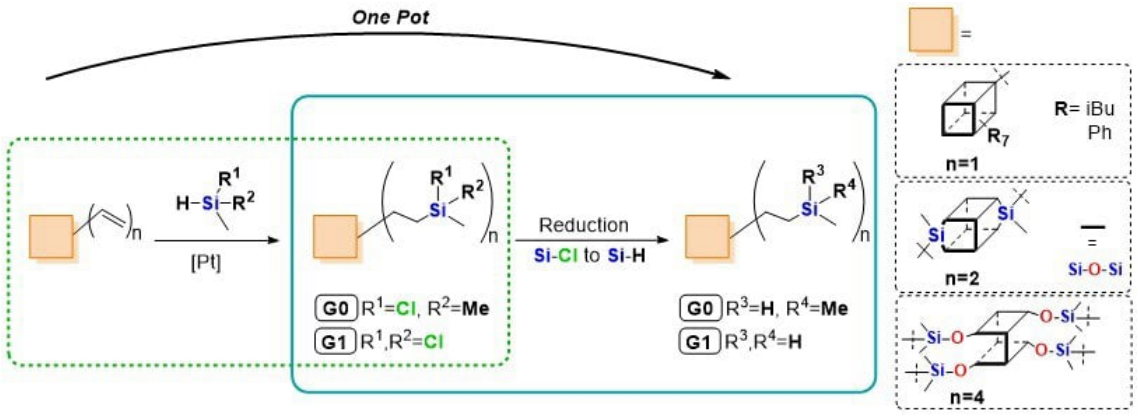
Dendrimers are branched, polymeric systems with well-defined structures. They are built of multifunctional core and attached branched dendritic arms. Their properties depend on the number and type of terminal groups, e.g. -NH_2, -COOH, -OH. They are used i. a. in supramolecular chemistry, medicine (e.g. as drug delivery systems), catalysis or in the synthesis of nanoparticles [1]. The immanent components of denrimers are organosilicon compounds, e.g. carbosilanes. Possible synthetic pathways are e.g. based on a sequence hydrosilylation reaction followed by Grignard reaction [2].

Organosilicon molecules also include the group of specific systems, i.e. silsesquioxanes (SQs) – organo-inorganic compounds. There are several types of SQs: random, ladder, cage and partial cage structures [3]. In particular, octafunctional silsesquioxanes have been used as dendrimer cores, due to the high functionality being obtained with a small number of synthetic steps. However, the reports on the formation of mono-T_8 and double-decker silsesquioxane as cores of dendritic systems are rare an their synthetic routes to be obtained are analogous to those for carbosilanes or octa-T_8 silsesquioxane cores [4,5].

The aim of the research was to obtain dendritic systems with different silsesquioxane cores (mono-T_8 and double-decker silsesquioxane) by a sequence of hydrosilylation process with subsequent reduction. In the course of these studies, the best reducing factor was selected, enabling the formation of desired systems with the highest efficiency [6].



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Developing a self-healing bio-based material halogen bond

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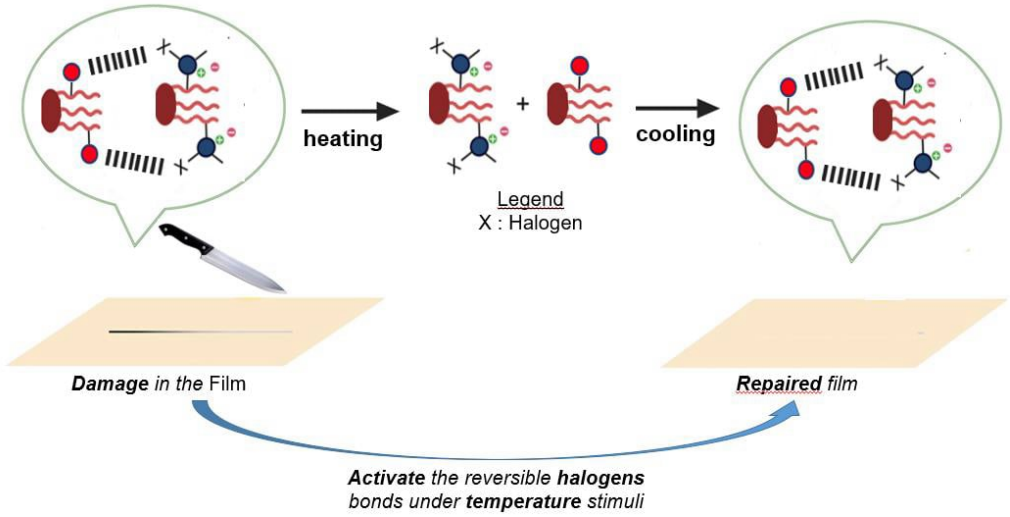
Self-healing materials are a class of intelligent materials that have the ability to repair damages caused by mechanical wear and tear over time. Different supramolecular interactions have already been used to prepare this type of materials such as the non-covalent hydrogen bonding. [1] An interesting alternative is represented by halogen bonding (XB): this phenomenon occurs when there is a clear attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity, and a nucleophilic region in another, or the same, molecular entity. [2] XB is an emerging non-covalent interaction to design novel supramolecular assemblies. Though similar to the more familiar hydrogen bonding, four primary differences between these two interactions make halogen bonding a unique tool for molecular recognition and the design of functional materials: high directionality, tunable interaction strength, hydrophobicity and large donor atom size.[3] For the moment, halogen bonding have not been sufficiently developed to obtain self-healing materials, despite all the inherent benefits. In this context, we propose a bio-based self-healing material with halogen bonds.

In this study, we prepare a self-healing material based on epoxidized linseed oil having XBs active under temperature stimuli as shown in the figure below. The order of the strength of halogen bonding is I > Br > Cl > F for the respective halogens.[4] In order to achieve this material, we combined several steps: chemical modification, chemical grafting and *N*-alkylation to obtain an ionic liquid (this latter depleting the halogen atom of the system in electrons). [5] Moreover, mixing the XB-acceptor ionic liquid (electron-poor), with a second epoxidized linseed oil modified with an electrodonating group, provide a material with enhanced mechanical properties. Finally, the self-healing properties will be assessed under temperature stimuli.



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Growth kinetics modeling of seedless, one-pot synthesized gold nanostars for probebased lateral flow immunochromatographic assay

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Gold nanostars (AuNS) are seen as promising candidates due to their physicochemical properties like morphology, size and surface plasmon resonance which provide high sensitivity for biosensing applications to develop rapid Lateral Flow Immunochromatographic Assay (LFIA). Herein, we present the microscopic and spectroscopic analysis of evolution of gold nanostars which are synthesized without using any surfactants and seeding method. In this one-pot approach precursors used are gold chloride trihydrate and reducing agent N-2-hydroxyethyl piperazine-N-2-ethane sulphonic acid (HEPES) buffer. Ratios of the precursors used gave rise to the formation of nanostars with distinct core sizes and arm lengths. Alterations in size and shape during growth were examined by collecting aliquots at different time intervals which were subjected to dynamic light scattering (DLS) zeta sizer and scanning electron microscope (SEM). The change in color and spectra during the reaction was monitored by a UV-Vis spectrophotometer which correlates with the formation of stable, anisotropic star-shaped particles within the size range of 20-40 nm. After physiochemical characterization, the nanostars were surfacefunctionalized with an azide group, polyethylene glycol (PEG) and carboxylic acid group for enhanced bioconjugation with mycotoxin antibodies. For better detection and imaging, these AuNS-labelled with antibodies are attached with fluorescent molecule 6-chloro-4-methyl umbelliferone which binds actively with the azide group. The modified nano-moieties tagged with antibodies are applied on the test line on LFIA strips used in detecting mycotoxins in food samples.

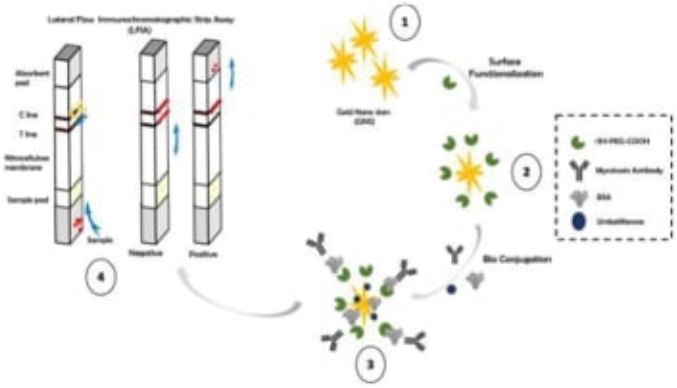

Figure1: Schematic for employing surface functionalized gold nanostars in lateral flow immunochromatographic assay

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The influence of water-based diketopyrrolopyrrole supramolecular architectures on photocatalysed sulfoxidation reactions

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The combination of a chromophore unit and an amino acid side chain provides a molecular template that promotes assembly into supramolecular architectures that can in turn be used for photo-responsive applications.[1, 2] In this work, we have synthesized four dithiophene-diketopyrrolopyrrole (DTDPP) based amphiphiles with phenylalanine (F), valine (V), leucine (L) and alanine (A) amino acid side chains (Figure 1a).[3] The self-assembly of these molecules into supramolecular architectures is carried out in an aqueous environment and triggered by a change in pH. This process allows for the formation of various aggregated systems depending on the amino acid used, the concentration of the DTDPP amphiphile, and the phase (sol vs gel) and the pH (high pH vs low pH) of the system.

This work exhibits the use of the DTDPP supramolecular systems as photocatalysts by using visible-light irradiation (Figure 1b). In the presence of an oxygen atmosphere, the DTDPP photocatalyst transforms oxygen molecules into singlet oxygen; which is a stronger oxidant for the sulfide. The process is highly selective for the oxidation to the sulfoxide product over the double oxidation to the sulfone product.

Screening a range of pH values for the DTDPP sol phases showed an increase in thioanisole conversion at pH values below the pK_a, although the pH differences did not result in significant conversion changes across the range. The reactions of different sulfide substrates with DTDPP sols and gels were also tested and showed that the sulfides have different selectivity for the DTDPP systems for the best conversion.

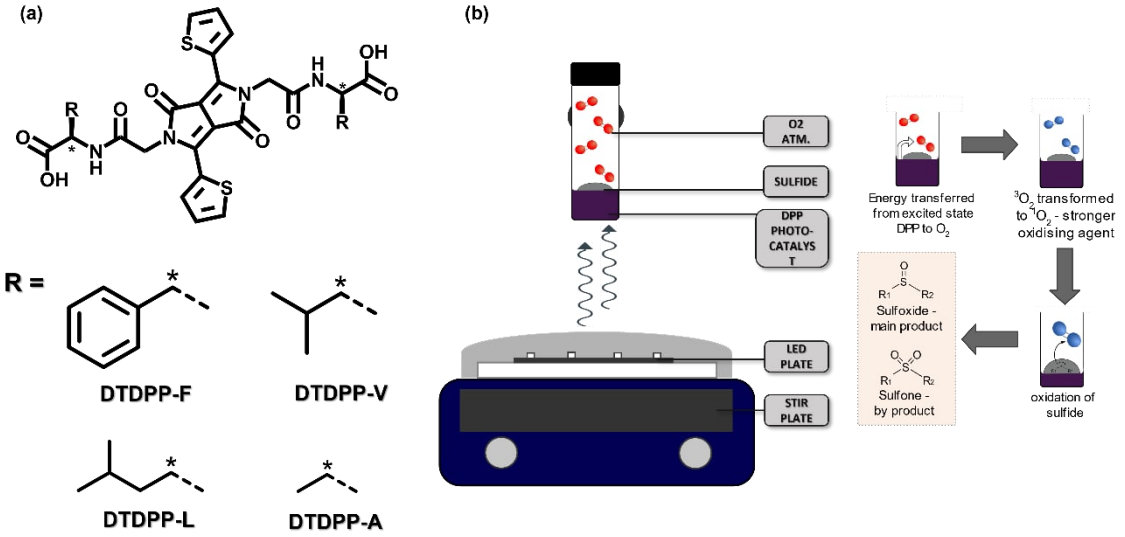

Figure 1. (a) The DTDPP amphiphiles. (b) The photocatalysis setup and the mechanism for the sulfoxidation reaction.

VG and DA thank the Leverhulme Trust (RPG-2019-165) for funding. AB thanks the Royal Society and TATA for a University Research Fellowship.

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Phase and morphology change of $CePO_4$ obtained by microwave-assisted hydrothermal method: a study of the synthesis time and solvents used

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Cerium phosphate ($CePO_4$) is a member of the lanthanide orthophosphate family, in which cerium as a rare earth element and its 4f transitions exhibit peculiar characteristics in terms of optical properties (luminescence) and allied to the phosphate group give it characteristics of biocompatibility and high electron transfer for catalytic and sensors properties [1]. This way, there is great interest in the research of these compounds due to the its versatility in different applications [2]. Alterations in the synthesis can present significant changes in its structural, morphological and electronic characteristics [3][4]. In this study, the main objective was to investigate the crystal structure, morphology and electronic properties of $CePO_4$ nanoparticles synthesized by the microwave-assisted hydrothermal method, varying the radiation exposure time by 2^n (n = 2, 4, 8, 16, 32 and 64 minutes) and the solvente type used (water and ethanol). The samples were characterized by X-Ray Diffraction (XRD), Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM), absorption spectroscopy in the ultraviolet-visible region - diffuse reflectance mode (DRS), Raman scattering (Raman) and Photoluminescence. According to the XRD patterns analyses, it was possible to observe a gradual change in the crystal structure of $CePO_4$. In shorter times of exposure to microwave radiation, powders with a monoclinic structure and P21/n space group, indexed by ICSD form N°027860, were obtained. At longer times, the hexagonal phase and space group P6222 (ICSD °027859) were observed. The micrographs obtained via SEM and TEM showed clusters of nanoparticles with heterogeneous morphology similar to nanowires, nanorods and nanoplates. In addition, a reduction in the size of the nanoparticles was also seen when replacing the water for ethanol solvent. DRS analyses showed that the synthesized powders present E_{gap} between 1.6 and 1.8 eV. Raman spectra analyses, the active modes of greater intensity were identified, suggesting that the powders are structurally ordered at long range. PL results, broad bands were observed in the blue region between 2.7 to 1.9 eV, using a 355 nm laser (Cobolt/Zouk). The results indicate that by varying the exposure time to microwave radiation and the solvent used it is possible to change the crystalline structure, morphology and intensity of emission in photoluminescence, helping to better understand the behavior of these structures for future applications using surface chemistry.

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Contractile frameworks of optically commanded switches: towards a mechanized nano-sponge

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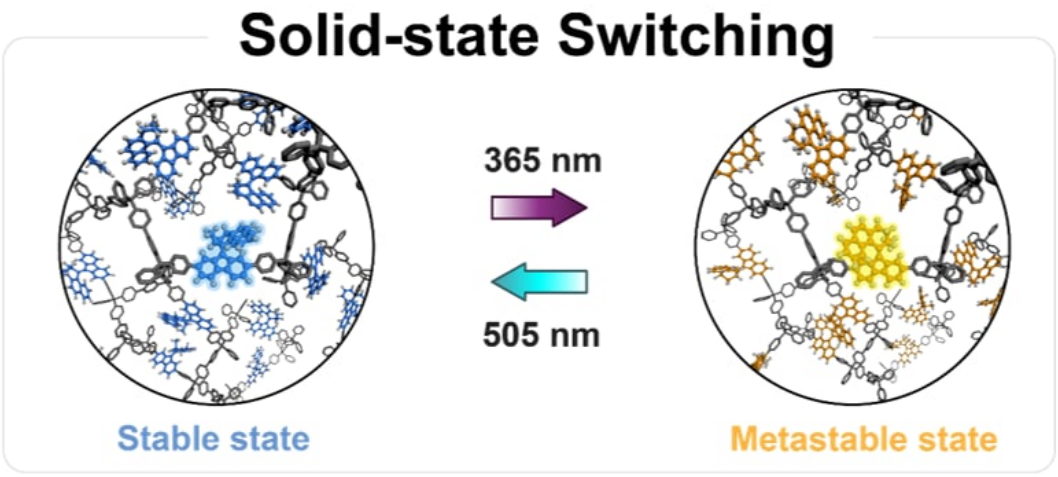
Dynamic porous materials combine the rigidity of the material scaffold with the flexibility of the individual components or the entire network, giving rise to adaptive and responsive structures.[1-3] Integration of photoswitchable molecules into porous solids provides a non-invasive handle to control the porosity functions and properties these materials with high spatial-temporal precision. However, apart from rare examples[4-7], photochemical isomerization in these systems is restricted to the individual responsive units and is neither further propagated nor amplified by the cooperative action within the material framework. Limited light-penetration depth originating from the high concentration of the photoswitches and lack of cooperative effects amplifying their nanoscale motion pose a significant limitation to development of these materials. Here we demonstrate a highly porous photoswitchable framework prepared by Yamamoto homo-coupling of multi-arm photoswitchable monomers. The framework exhibits a highly selective reversible photoisomerization of the embedded overcrowded-alkene in a bulk material accompanied by amplification of the light-triggered nanoscale motion of the photoswitch from micro to mesoporous region.



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Less is more: application-driven organometallic approach for the synthesis of zinc oxide nanocrystals

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Semiconductor nanocrystals have been gaining tremendous attention over the past two decades. In an exceptional way, they combine both the physicochemical peculiarity of molecules and optoelectronic properties of semiconductors. Zinc oxide nanocrystals (ZnO NCs), otherwise known as quantum dots (QDs) (i.e. NCs up to 10 nm in diameter), are now considered to be one of the most promising semiconductor metal oxides. Their unique physicochemical properties strongly depend on the applied synthetic procedure. In this regard, wet chemical approaches, especially the sol-gel method, play a dominant role among the synthetic routes leading to ZnO NCs. Nevertheless, this kinetically controlled process is difficult to terminate at the desired stage of the particle growth, hence it results in batch-to-batch quality. An attractive alternative to the classical sol-gel technique is wet-chemical organometallic approach. For instance, the preparation of high-quality and isotropic ZnO NCs has been significantly advanced by our research group due to the introduction of a one-pot self-supporting organometallic (OSSOM) procedure via the controlled exposition of an easy-to-prepare [EtZnX]-type precursor (where X-monoanionic organic ligand) solution to air, which leads to well-passivated, bio-safe colloidal ZnO NCs coated with monoanionic X-type ligands.[1,2]

However, the use of long-chain organic ligands can be particularly disadvantageous in the context of possible technological applications. For instance, the research on ZnO-based solar cells modules demonstrated that an atomic-scale control of the ZnO NC surface and the reduced organic surface modifier content are critically important for the potential use of these NCs as electron transfer layer for solar cells and other particle-based light-emitting devices.[3] Therefore, there is continuous interest in searching for efficient and well-reproducible synthetic strategies that exclude the use of additional long-chain capping ligands to minimize energy barriers, enable efficient charge transfer, and afford bio-safe and colloidal ZnO NCs with the stable organic-inorganic interface. For this reason, we introduced short-chain neutral molecules – sulfoxides (i.e. ligands commonly used in coordination chemistry) as an effective and easily removable L-type stabilizing agents for the preparation of ZnO NCs with reduced organic layer, which makes them a great candidate for applications such as electron-transporting layer in photovoltaics and photocatalysis. These results may pave the way for further study on environmentally friendly, stable, highly efficient perovskite solar cells and more advanced energy harvesting devices.

The authors acknowledge the Priority Research Areas (POB) funding (Materials Technologies-2:Start) (M.W-P., M.J.).

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Supramolecular Synthon Promiscuity in Phosphoric Acid–Dihydrogen Phosphate Ionic Cocrystals

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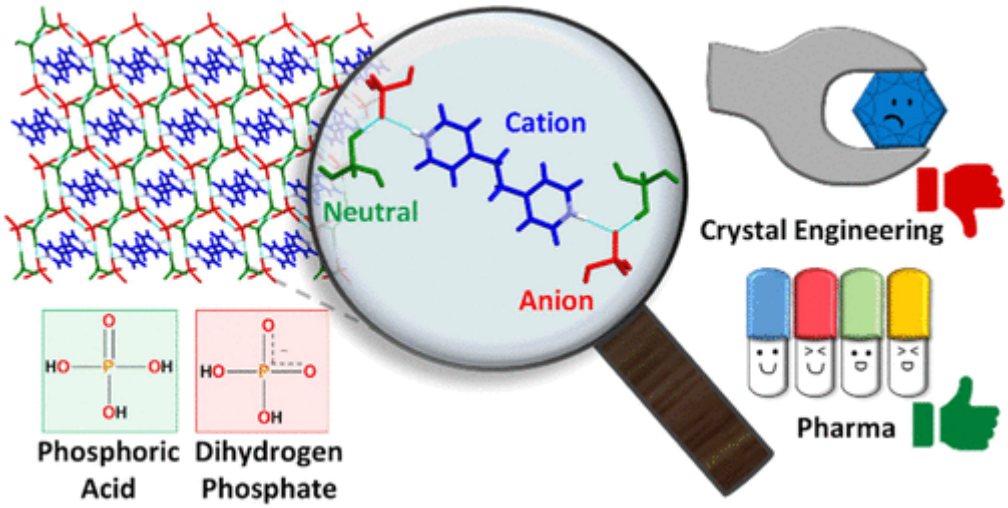
The majority of active pharmaceutical ingredients (APIs) studied as lead candidates in drug development exhibit with poor aqueous solubility, which typically results in such APIs being poorly absorbed and exhibiting low bioavailability. Salts and pharmaceutical cocrystals can address low solubility and other relevant physicochemical properties of APIs. Pharmaceutical cocrystals are amenable to design through crystal engineering because supramolecular synthons, especially those sustained by hydrogen bonds, can be anticipated through computational modelling or Cambridge Structural Database (CSD) mining.
In this contribution, we report a combined experimental and CSD study on a class of ionic cocrystals containing ionic cocrystals composed of dihydrogen phosphate (DHP) salts and phosphoric acid (PA). These are present in marketed drug product, but remains understudied from a crystal engineering perspective. Ten novel DHP:PA ionic cocrystals were prepared from nine organic bases and one anticonvulsant API, lamotrigine. From the resulting crystal structures and a CSD search of previously reported DHP:PA ionic cocrystals, 46 distinct hydrogen bonding motifs (HBMs) have been identified between DHP anions, PA molecules, and, in some cases, water molecules. Our results indicate that although DHP:PA ionic cocrystals are a challenge from a crystal engineering perspective, they are formed reliably and, given that phosphoric acid is a pharmaceutically acceptable coformer, this makes them relevant to pharmaceutical science.



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Application of stone cutting sludge in the preparation of alginate films with potential antimicrobial activity

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The stone processing industry generates a significant amount of waste in the form of stone sludge. This by-product is difficult to recover and it is often landfilled, presenting an economical and environmental challenge.[1,2] The total or partial recycling of this sludge can minimise the negative economic and environmental impacts associated with this industry. For instance, stone sludge can be directly used in the preparation of concrete or bricks. The stone sludge, especially from carbonate rock, can also be valorised by the preparation of alginate-based protective films and coatings. The work presented herein focuses on the reuse of carbonate stone sludge as a precursor of a hardening agent for alginate films, due to the high concentration of calcium ions present. This hardening agent was obtained by dissolution of the sludge with an appropriate mineral acid such as HCl. The alginate films prepared by casting/solvent evaporation were then treated with this hardening solution to obtain a hardened and insoluble alginate film. The preparation of alginates modified chemically with amino acids and amino sugars was also attempted, using 5-chloromethylsalicylaldehyde as covalent grafting agent. The objective the chemical modification was to obtain films with enhanced antioxidant and antimicrobial properties. In addition, preliminary evaluation of antimicrobial activity of the prepared film by contact inhibition against filamentous fungi is being carried out. Furthermore, chemical and morphological analysis of the prepared films is also under way.

This work was financially supported by LA/P/0045/2020 (ALiCE), UIDB/50020/2020 and UIDP/50020/2020 (LSRE-LCM), funded by national funds through FCT/MCTES (PIDDAC) and by FCT - Fundação para a Ciência e a Tecnologia, I.P., within the scope of the project MARE (UIDB/04292/2020 and UIDP/04292/2020) and also through the project INOVMINERAL 4.0 – Tecnologias Avançadas e Software para os recursos Minerais, project number 46083, cofinanced by FEDER – Fundo Europeu de Desenvolvimento Regional, in the scope of the Programa Portugal 2020, COMPETE 2020 – Programa Operacional. This study also had the support of national funds through Fundação para a Ciência e Tecnologia (FCT), under the project LA/P/0069/2020 granted to the Associate Laboratory ARNET. L. Côrte-Real acknowledges FCT for projects UIDB/00100/2020, UIDP/00100/2020, LA/P/0056/2020, and Programa Operacional Regional de Lisboa 2020. Mafalda Guedes acknowledges FCT under contract UIDB/04540/2020, through CeFEMA.

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Low Dimensional Magnetism in Ordered Perovskite and Ruddlesden-Popper Variants

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Perovskites and their myriad of structural permutations have long been studied for their intriguing properties and interplay of degrees of freedom, both chemical and physical.[1] While, generally three dimensional in nature, perovskites can provide multiple means of access to low dimensional properties as well. In this poster, new results in three different directions pertaining to this concept will be presented. The first and most common approach, is the use of the Ruddlesden-Popper and similar phases, which effectively separate perovskite-like layers with interlaced *A*O layers, rendering them primarily two dimensional. Here, several new cation-ordered[2] iridate and rhodate Ruddlesden-Popper phases will be presented. The second approach is that of orbital order using Cu^{2+} in the double perovskite structure[3] to yield in-plane only square lattice like magnetic interactions (e.g. Ba_2CuWO_6). New compounds produced by substitution series and high pressure methods will be shown. The third is that of vacancy ordering. By ordering of vacancies in combination with cation ordering, hexagonal perovskite phases can be reduced to well separated triangular two dimensional magnets with variable spin sizes and frustration.[4] Again, new compounds will be shown. In all three directions, primarily crystallographic and magnetometry data on these new inorganic transition metal oxides will be presented.

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Assessment of the impact of polystyrene nanoparticles on *Stevia rebaudiana* plants grown in vitro

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Polystyrene nanoplastics (NPs) are emerging pollutants of global importance. They are small enough to be ingested by a wide range of organisms and they can be uptaken by plants. Therefore, deeper understandings of the impact of these pollutants to agro-eco-systems, as well as cost-effective methods for their detection are required [1].

The aim of this work is the determination of toxicity levels of polystyrene NPs for *Stevia rebaudiana* plant, as well the development of a rapid (in order of minutes) and cost-effective methodology, based on Visible-Near-Infrared (Vis-NIR) and Raman hyperspectral imaging (HSI) for the direct detection and quantification of NP accumulation in plant tissue.

Our research is focused on potential risks associated to polystyrene NPs exposure to plants. We have assessed the accumulation of polystyrene NPs in *Stevia rebaudiana* grown in vitro, and its impact on plant growth, morphology and on a series of plant metabolites (chlorophylls and carotenoids). The plants were exposed to polystyrene NPs (26 nm) at concentrations up to 250 mg/L.

A positive impact on *Stevia rebaudiana* in the presence of low concentrations of polystyrene NPs was observed. The NPs stimulated photosynthesis at low concentration (<10 mg/L). However, at 100 mg/L concentration a clear suppression in photosynthesis was observed. The root morphology and plant length are adversely affected by NPs and, with almost complete inhibition at doses of 250 mg/L of polystyrene NPs.

The *Stevia rebaudiana* metabolites were quantified using High-Performance Liquid Chromatography (HPLC). The concentrations of chlorophyll A and B, lutein, zeaxanthin, and beta-carotene showed the same trend upon exposure to increased polystyrene NP levels. Their concentrations increased up to the 250 mg/L NPs dose, more exactly, the concentration of all the investigated analytes increased twofold, compared to controls.

HSI provides beside the optical image of micro-objects a spectral (Vis-NIR extinction or Raman), in each pixel of the map, at a limit of 0.5 µm spatial resolution. The impact of NPs on the plant length and root as well as plant weight can be assigned to a stress response of the plant.

The major economic impact of the developed methodology for imaging, lies in its applicability for screening food matrices at large scale, in order to detect contaminations such as polystyrene NPs, ensuring thus an important tool for food safety and security.

Acknowledgements: This work was supported by two grants of the Romanian National Authority for Scientific Research and Innovation, CNCS-UEFISCDI, project number PN-III-P1-1.1-TE-2021-1585 and PN-III-P4-ID-PCE-2020-1847

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Formulation of colloidal nanosystems with Au/Ag and citrus essential oils

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Essential oils (EOs) are aromatic volatile oily liquids extracted from different parts of plants. EOs are known to possess various functional properties, including: antioxidant, antimicrobial, antidiabetic, anti-inflammatory, antiproliferative, antidepressant, antipyretic, antitussive, insect repellent, and so on. Citrus essential oils (CEOs) are approved by the FDA as "generally recognized as safe". CEOs are used in food industry as flavoring agents but they are also good source of natural antimicrobials that can fulfil both food industry and consumers' safety requirements.

Nonetheless, EOs widespread use and marketing are still restricted due to their sensitivity to environmental factors (light, temperature, oxygen, water), high volatility, low water solubility, uneven dispersibility as well as pronounced influence on the organoleptic attributes of the food system. The aim of the present study was to limit the above-mentioned shortcomings and to facilitate the use of CEOs as antimicrobials and antioxidant agents by the synthesis of colloidal Au and Ag nanosystems using CEOs (AuNPs and AgNPs). The developed colloidal nanosystems are expected to enhance the physical stability and the bioactivity of CEOs.

The colloidal nanosystems synthesized in this study involved the reduction of Au^{3+} and Ag^{+} ions to Au^{0} and Ag^{0}, in the form of nanoparticles, using CEOs as reducing agent. For this purpose, essential oils of lemon, lime, orange, grapefruit and tangerine were used. The reduction of Au^{3+} ions was carried out at boiling temperatures, while the reduction of Ag^{+} ions was possible at room temperature [1]. The confirmation of nanoparticle synthesis was assessed based on their characteristic UV-Vis spectra.

For the morphological characterization of the nanosystems, dynamic light scattering (DLS) experiments were performed, which facilitated the determination of the average diameter of the nanostructures. Also, the Zeta potential values of the synthesized NPs were measured, providing information on the stability of nanostructures. According to the obtained data, the NPs have average diameters between 13.58 and 22.65 nm and are characterized by Zeta potential values between -44.7 mV and -62.2 mV, suggesting a very good stability. The most stable colloidal nanosystems were those obtained by reduction with lime (Zeta -62.2 mV) and tangerine (Zeta -59.4 mV) oils. The antioxidant and antimicrobial activity of the colloidal nanosystems were assessed by the DPPH method and by the microdilution method respectively, evaluating the minimum inhibitory concentration (MIC) against *Staphylococcus aureus* (ATCC 49444), *Pseudomonas aeruginosa* (ATCC 27853), *Salmonella enteritidis*, *Candida albicans* (ATCC 102310), *Candida parapsilosis* (ATCC 22019).

The results showed that the developed nanosystems are stable and at the same time, they generate a synergy of the bioactivities of the CEOs and nanoparticles.

Acknowledgment: This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS - UEFISCDI, project number PN-III-P4-ID-PCE-2020-1847, within PNCDI III.

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Insight into the Formation Mechanism of ZrO_2 and HfO_2 Nanocrystals; towards Size-Tunable Syntheses

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One can nowadays readily generate monodispersed colloidal nanocrystals, but a retrosynthetic analysis is still not possible since the underlying mechanism is often poorly understood. A genuine mechanistic model can provide fundamental scientific interpretation to the chemical system and initiate evolution in synthetic strategies. In this work, we unknot the formation mechanism during the surfactant-assisted non-aqueous synthesis of zirconia and hafnia nanocrystals. First, we identify the active precursor species in the reaction mixture using a powerful combination of nuclear magnetic resonance (NMR) spectroscopy, *in situ* X-ray pair distribution function (PDF) analysis, gas chromatography (GC-FID), and density functional theory (DFT) calculations. We further monitor how the reaction mixture decomposes using solution NMR and gas chromatography, and we find that $ZrCl_4$ is formed as a by-product of the reaction, limiting the reaction yield. The reaction proceeds via two competing mechanisms: E1 elimination (dominating) and S_N1 substitution (minor). It's worth noting that the reaction follows a different synthetic path from the earlier proposed mechanistic model. With the newly obtained insight, we adapted the synthesis to optimize the yield and gain control over the size.[1] After elucidating the precursor chemistry, we turned to nucleation and growth mechanism. X-ray scattering techniques (pair distribution function analysis and small-angle scattering) were chosen for investigating the atomic-scale structural evolution and particle concentration estimation. A thorough understanding of the crystal structure of the nanoparticles will serve to formulate a structure-function correlation. The combined outcome of the precursor chemistry and the crystal growth will enable the rational design and synthesis of complex oxide nanocrystals which will serve as valuable building blocks in material science.

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Neighbour-based characterization to reconstruct the intrinsic dynamics of supramolecular self-assembled structures

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Self-assembled supramolecular structures are macromolecules composed by fundamental sub-units, that interact via non-covalent bonds and, under certain conditions, assemble spontaneously into complex objects. Due to the reversible nature of the interactions between their building blocks, these supramolecular structures are characterized by inner nontrivial dynamics, which contributes to define their global behaviour and makes them useful in applications like materials development [1].

Molecular Dynamics (MD) and especially Coarse-Grained MD (GC-MD), provide a fast way to computationally reproduce the behaviour of self-assembled systems. By simulating the dynamics of these building-blocks, both the whole structure motion and their rearrangement within the macromolecule are tracked [2], thereby exploring temporal and spatial scales that could not be easily accessed through experiments. Moreover, the analysis of the simulated trajectories by means of statistical and clustering techniques, allows to extrapolate information on the whole structure and insights about the mechanisms that governs the inner dynamics behaviour [3].

Here we propose an exploratory analysis that aims at characterizing the intrinsic properties of supramolecular structures, like phase coexistence and chemical features, by focusing on the behaviour of their constituent units along the dynamics. The key idea is to extract information about the inner dynamics of a supramolecular assembly by following the changes in terms of neighbour environments around each molecule within the structure. First, we collect the contact identities of each sub-unit with each other's, and we analyse, from a probabilistic point of view, the frequencies of contacts between each pair of assembling units along their dynamics. The resulting distributions are classified according to an unsupervised clustering technique. In such way, each cluster identifies a region where molecules behave on average similarly in terms of variability of neighbourhoods. Second, we combine such average approach, with the temporal evolution of the local changes during time. The latter analysis gives information about the evolution of the neighbouring environment of each building blocks along the dynamics, and it provides insights about the mobility of the molecules among the clusters.

As case studies, we investigated different type of chemically relevant supramolecular assemblies, like micelles, lipid bilayers, and fibres, and we applied the described approaches to obtain reliable information of the intrinsic dynamics. Indeed, we identified clusters in both mono component and multi component systems, providing crucial information like topological defects for fibres, coexistence in lipid bilayers, and pattern identification in bi-component micelles. Supported by our preliminary results, we believe that the approach here presented, although simple, could be successfully employed in the context of supramolecular science helping to elucidate the behaviour of these kinds of systems.

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Precise control over nanoparticle synthesis through supramolecular preorganization

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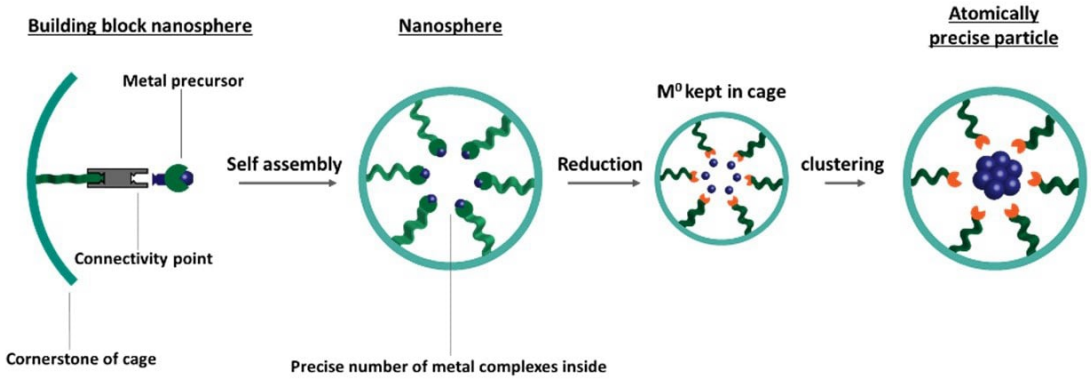
Our group is specialized in the preorganization of homogeneous catalysts by means of supramolecular self-assembly. Up till now, the strategy of supramolecular confinement was primarily used for achieving unique activity and selectivity in catalysis. It was found that under hydrogenative conditions the complexes themselves were reduced, which posed a new question: Could supramolecular self-assembly of metal complexes be a powerful tool to create a defined system before/during the preparation of nanoparticles? This way, the particles could nucleate and grow in an isolated confined space, thereby achieving ultimate control over the size and composition of the particle.



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Novel Sr doped titanate nanowires/*g*-C_3N_4 photocatalytic active films for photo-assisted degradation of emergent pollutants

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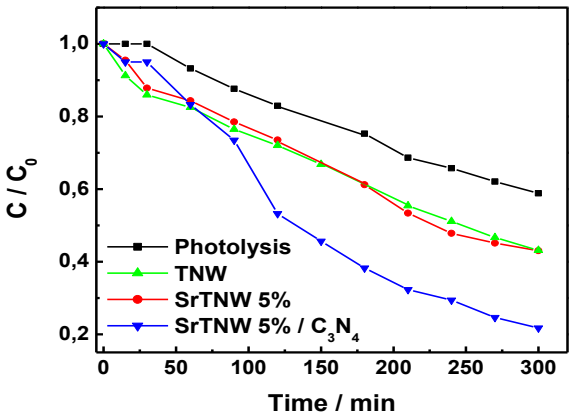
In face of the environmental impact caused by organic pollutants in water, including pharmaceutical and personal care products (PPCPs), it becomes evident that there is an increasing demand to research for new photocatalytic nanomaterials for the efficient removal of these pollutants. A wide variety of semiconductor materials has been studied, as TiO_2 nanoparticles, but the low efficiency of this class of materials in the visible region has been obstructing their large-scale application. In this context, titanate nanowires (TNW), have been proposed as excellent alternatives due to their superior surface area and ion-exchange ability. It is also possible to improve further the photocatalytic properties of such materials by improving the visible radiation absorption and/or by reducing the photogenerated charge carriers' recombination. The doping of TNW with transition metals have been described as an excellent methodology to attain this objective [1,2].

In this work, TNW modified by Sr doping (1% and 5%), were synthesized using a hydrothermal approach. For the photocatalytic tests, distinct amounts of SrTNW particles were immobilized on an FTO surface using a layer by layer method. A final layer of exfoliated *g*-C_3N_4 was applied aiming to improve the photocatalytic performance and stability of the photoactive film for recycling. After characterization, the photocatalytic ability of the nanocomposite films was further studied, under visible light, for the degradation of an emergent pollutant, caffeine. The obtained results indicate that SrTNW is a promising catalyst for caffeine photo-assisted oxidation and the layer of *g*-C_3N_4 clearly improves the performance of the film. The best catalytic results were obtained for the film composed of 2 layers of SrTNW and 1 layer of g-C_3N_4.



Photocatalytic degradation profile of a caffeine 5 ppm solution, under visible irradiation.

This work was supported by Fundação de Ciência e Tecnologia (FCT) and NAWA under a 2019 Portugal-Poland Bilateral Cooperation Project; This work was also funded by FCT through projects UIDB/00100/2020, UIDP/00100/2020 (CQE) and LA/P/0056/2020 (IMS). V.C. Ferreira acknowledges the financial support from FCT, DL57/2450 contract.

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Nanostructure in 1-alkyl-3-methylimidazolium cations combined with alkyl-sulfonate anions Homologous Series

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Many biomedical applications and physical-chemical functionalities, such as detergency, surface-activity agency and oil recovery, emerge from the addition and use of sulfonate groups in polymers. *In vitro* studies, the introduction of sulfonated groups revealed enhanced adhesion, spreading, proliferation, and osteo-differentiation in living cells [1]. Additionally, the sulfonate-bearing components had anti-inflammatory properties, and antibacterial activity [1]. Therefore, one of the fields where sulfonate compounds thrive are the medical applications. Moreover, poly(sulfobetaines) present special properties such as antifouling, antimicrobial, strong hydration properties and good biocompatibility that lead to their use in nanotechnology, water remediation, hydrometallurgy, the oil industry and biological and medical fields [2]. Furthermore, another area where sulfonate groups are used is in chemical modification of compounds in order to modify regioselectivity and enhance strength of cellular bonding [3]. Lastly, they often act as surfactants and gels [4].

For that matter, ionic liquids combining 1-alkyl-3-methylimidazolium cations, $[C_nC_1im]^+$, with alkyl-sulfonate anions, $[C_nSO_3]^-$, have been studied in large simulation boxes containing 1200 ion pairs at 425 K. The ionic liquid molecular ions were modeled using the CL&P atomistic force field [5,6]. The combination of these ions enables the analysis of the effect of the sulfonate group in such ionic liquids, whilst exploring the influence of the increase of alkyl-chain length in the cation and in the anion, simultaneously.

This contribution will be crucial to unravel the nature of the interactions and structure in different ionic compounds containing not only sulfonate groups, but also different sizes of the non-polar domain. To that effect, several analyses, including structural characterizations, ranging from structure factors, *S(q)*, to radial distribution functions, *g(r)*, aggregation analysis, including probability distribution functions, $P(n_a)$, and average number of contact neighbors, N_i, and spatial distribution functions, SDF, attained from molecular dynamics (MD) simulations are obtained and discussed regarding their interactions and organization in bulk.

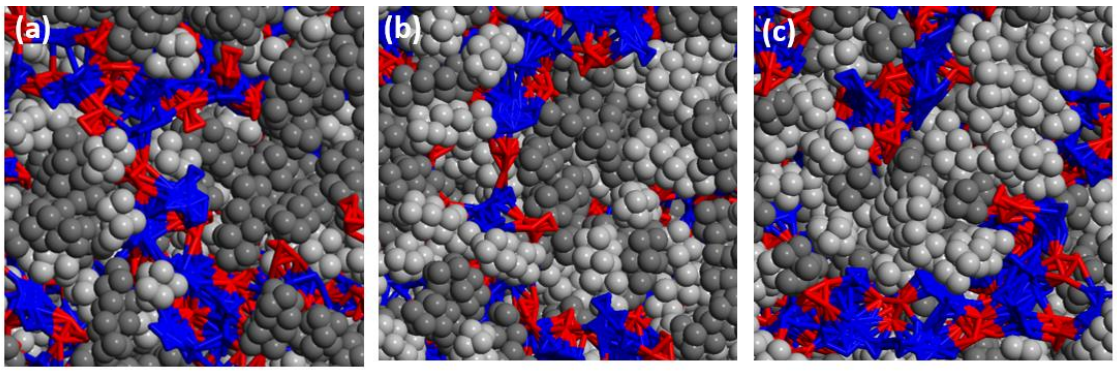

Figure 1. Snapshots of the MD simulation box performed for $[C_4C_1im][C_8SO_3]$ (left), $[C_8C_1im][C_8SO_3]$ (middle) and $[C_8C_1im][C_4SO_3]$ (right). The blue and red colors depict the polar part of the cations (imidazolium ring) and anions (sulfonate group), respectively, and the light grey and dark grey colors represent the nonpolar alkyl chain of the cations and the anions, respectively.

The authors thank Fundação para a Ciência e Tecnologia, FCT/MCTES (Portugal) for financial support through CEEC contracts (IST-ID/100/2018 to K.S. and IST-ID/93/2018 to A.A.F.) and through projects UIDB/00100/2020 e UIDP/00100/2020, LA/P/0056/2020 and PTDC/QUI-QFI/29527/2017 (including a grant for H. M.).

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Tuning the gelation ability of a shared scaffold by inserting fluorine atoms

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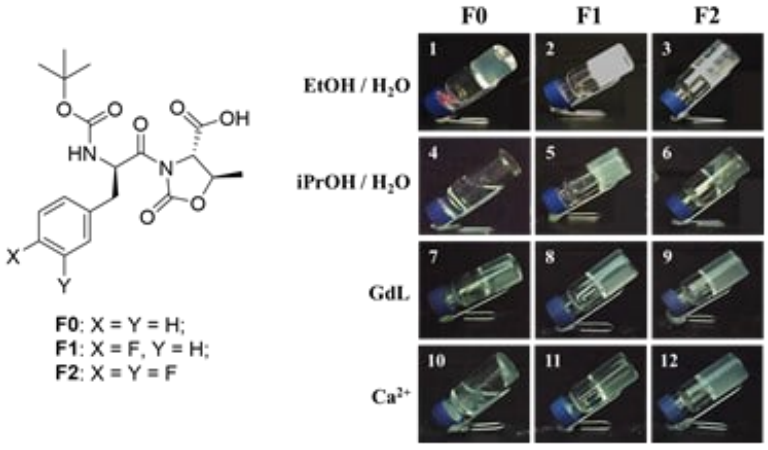
Low-molecular-weight (LMW) gelators are small molecules able to form gels, that are materials able to support their own weight when subjected to gravity. During the gelation process, the gelator molecules are firstly dissolved in a suitable medium, then after the addition of a trigger, they start to form fibres that entangle together and form the gel matrix. It is possible to design new LMW gelators, following few guidelines. Among them, the insertion of moieties able to form weak bonds like H-bonds and hydrophobic interactions is a common strategy.

However, predicting if a molecule can form a gel is not straightforward. Among all the possible weak interactions, π-π stacking plays a pivotal role in governing the gelation process [1]. As halogen atoms usually enhance π interactions and allow the formation of additional weak bonds [2], their insertion on aromatic rings is another strategy to improve the gelling ability of a molecule [3].

We studied three molecules, sharing the same scaffold with a different number of fluorine atoms on a phenyl ring (figure): Boc-^{D}Phe(F_n)-^{L}Oxd-OH (**F0**: n = 0; **F1**: n = 1; **F2**: n = 2). These molecules were tested for the formation of hydrogels under different conditions in EtOH:H_2O mixture in 3:7 ratio, in ^{i}PrOH:H_2O mixture in 3:7 ratio, in H_2O with GdL, and in H_2O with the addition of calcium ions.

Most of the gels display a broad range of transparency in the visible region. This property is very useful for optical and biomedical applications. The rheological properties and the morphology of these gels were analysed to compare the stiffness and the structure of the materials obtained [4].



Left: chemical structure of the three gelators synthesised; right: gelling outcomes of the three molecules tested with different methodologies.

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Resorc[4]arene-functionalized MWCNTs for the development of high selective and sensitive immunosensors

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One of the main problems in the development of immunosensors is to overcome the complexity of binding antibodies onto the sensor surface, thus leading to a loss of sensitivity.[1] For this reason, in the last twenty years, macrocyclic species such as calix[4]arene has been used for the site-directed immobilization of antibodies in the correct end-on orientation.[2] In the last years, due to their configuration and unique molecular recognition properties, resorcinol-based cyclooligomes, namely resorc[4]arenes,[3] have been used for the development of highly sensitive immunosensors.[4] In this project, new resorc[4]arene-based derivatives have been designed and synthesized for covalent grafting by nucleophilic substitution or cycloaddition of multi-walled carbon nanotubes, a versatile material endowed with great electric properties, high electroactive surface area and biocompatibility.[5] The prepared materials have been fully characterized by both morphological (FE-SEM and AFM) and spectroscopical (XPS) techniques before the construction of the immunosensors. Finally, the modified electrodes have been characterized by DPV and CV and IgG antibodies for the SARS-CoV-2 spike protein S1 (SPS1) were immobilized on their surface. The developed immunodevice was then employed in the analysis of SPS1 standard solutions as a proof of concept for COVID-19 immunosensor.

Thanks to MIUR (Ministry of Education University and Research) under Grant number 2017SXBSX$ (PRIN project 2017); MIUR under the Excellence Departments Grant to the Department of Chemistry and Technology of Drugs; MIUR under PON (Piano Operativo Nazionale) Grant number ARS01_00432 (PROGEMA) and Sapienza University of Rome under Grant “Progetti Ateneo 2019”.

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Ionic composites of starch and chitosan as drug delivery systems

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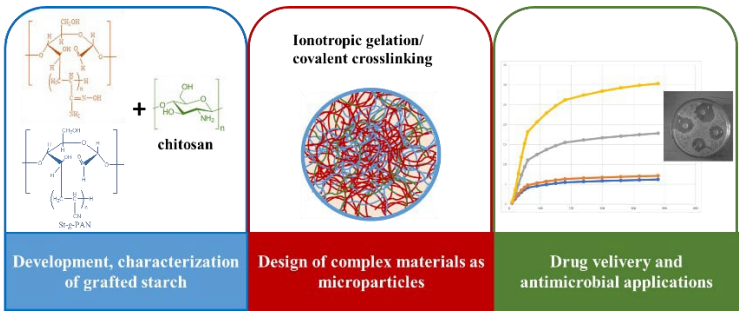
Recently, the composition between the different groups of polysaccharides gives broad characteristics in drug release and carrier systems [1]. Starch and chitosan are naturally abundant polysaccharides which are generally non-toxic, available from renewable sources, and suitable for drug delivery system [2]. Starch is the most used polysaccharide by the pharmaceutical companies due to its physicochemical properties and functional characteristics. In recent years, starch was evaluated as one of the most important candidates for the preparation of the new drug delivery system due to its smart features such as renewable property, abundant in nature, low cost, good availability, and the possibility of the preparation from the variety of products. The high tendency towards retrogradation, insolubility in cold water, sensitivity to shearing, a tendency to aggregation, and settling in the aqueous medium are some of the native starch drawbacks. The drug delivery system distributes drugs to the target site in a precise manner and it has always been the focus of the formulation scientists in the pharmaceutical industry. The smart and intelligent polymer concept is gaining ground for more than a couple of decades to maximize the therapeutic utility of drugs with minimization of side effects [3]. Ionic composites are a special class of composites materials, with porous structures and with application in various domain. Depinding on sizes can be macro-beads or nano-beads. They could be obtained from different organic or inorganic components. Ionic composites derived from polysaccharides attracted a strong interest in the last decades.

Therefore, we developed ionic composites by ionotropic gelation/covalent crosslinking of a mixture composed of starch and chitosan composite beads. The surface of ionic composites is relatively dense, the morphology is characterized by interconnected pores and the average diameter of pores around 2 nm. The combination between natural polymers in the design of new ionic composites could combine the chemical stability at different values of pH, specific to the each involved polymer, with other special properties of natural polymers such as bioadhesion, biocompatibility, biodegradability and antimicrobial activity. The investigation of the potential applications of the of microparticle as drug delivery systems or antimicrobial materials was also investigated.



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α-Helically enhanced synthetic peptides derived from ACE2 as potential SARS-CoV-2-Spike inhibitors

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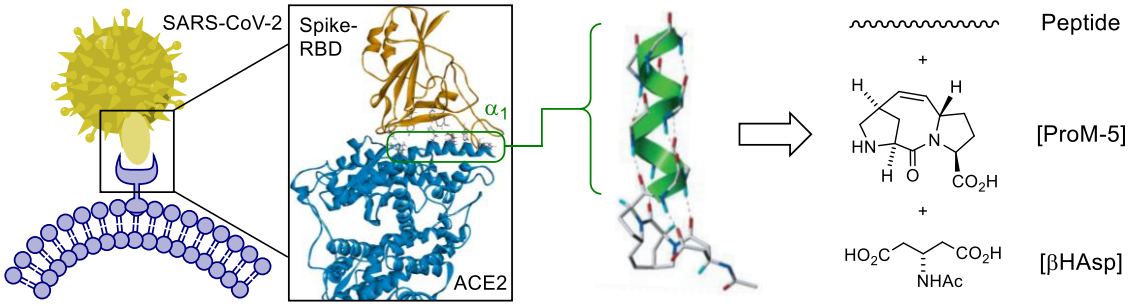
Cell entry of SARS-CoV-2 is initiated by binding of the viral Spike protein to the α1-helix motif of human angiotensin-converting enzyme 2 (ACE2) [1]. Small-molecular peptides that mimic the α1 motif could therefore act as inhibitors for this interaction. However, maintaining a helical conformation in peptides derived from secondary structures is difficult because the stabilizing effects present in proteins are often lost in shorter sequences. To tackle this problem, a toolkit of Proline-derived Modules (ProMs), consisting of rigidified diproline units was developed, which can induce conformational preorganization in small peptides. While the focus of our ProM research has been on mimicking PPII-helical peptides to inhibit the EVH1 domain [2], we have also made a construct of β-homoaspartic acid (β-HAsp) and ProM-5 that can induce an α-helix in short peptides when used as an *N*-cap [3]. This α-helix inducing effect of ProM-5 was initially demonstrated for idealized short peptides and has now been applied to a more complex biological system by attempting to mimic the α1-helix found in ACE2, as a proof of our concept and as a first step towards a therapeutic strategy for COVID-19.

The α-helix-inducing effect of our Ac[β-HAsp][ProM-5] *N*-cap was clearly demonstrated by comparison with peptides containing no *N*-cap or an Ac[β-HAsp]PP unit as *N*-cap. However, an even greater increase in helicity (of up to 63%) was achieved by additionally replacing non-binding amino acids with alanine, what is an established strategy in the preparation of helical peptides [4].

Binding affinities were measured by microscale thermophoresis for all peptides prepared, and significant binding to the SARS-CoV-2 Spike protein was observed for all peptides with a ProM-5 containing *N*-cap. Interestingly, the binding affinities did not correlate with the helical content of the peptides, and best binding affinities (≤ 1 µM) were observed for some peptides *N*-capped by Ac[β-HAsp]PP.



Acknowledgement: We thank Prof. Dr. Christian Hackenberger and Dr. Daniel Lauster for councelling and assistance with binding affinity measurements as well as the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - Project-ID 411422114 - GRK 2550 (RELOC) for funding.

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Immobilization of acid glycoprotein on magnetic nanoparticles coated with starch

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Albumin (HSA) and α_1-acid glycoprotein (AGP) are the most important proteins in human blood serum. One of their key functions is to binding and transporting exogenous and endogenous substances such as drugs [1]. The α_1-acid glycoprotein molecule contains a single polypeptide chain composed of a protein core (183 amino acids) and five branched glycan chains [2]. After albumin, AGP is the main protein binding and transporting drugs, mainly of an alkaline nature.The study of drug-protein interactions is of key importance in pharmacology, especially in the case of newly synthesized active substances with the expected pharmacological activity. Protein-bound drugs are pharmacologically inactive - only the free, unbound fraction of the drug is active. Traditional methods of determining the basic pharmacokinetic parameter, which is the degree of drug binding, are characterized by high difficulty of implementation and low repeatability due to the complicated process of separating the protein from the supernatant. An alternative method is to immobilize the protein on a support that would be easy to separate from the reaction mixture and at the same time allow the protein to remain active [3].

The main objective of the research was to obtain magnetic nanoparticles coated with chemically modified biopolymers that will have highly reactive functional groups capable of effectively immobilizing glycoproteins without losing their ability to bind active substances. The first phase of the project involved the synthesis of starch-coated magnetic nanoparticles by in situ co-precipitation. In the next step, the polymer was chemically modified, which led to the production of dialdehyde starch, which was then coupled with 3-aminophenylboronic acid. The obtained materials consist of a magnetite core covered with starch enriched in dihydroxyboryl groups. The obtained materials were fully characterized (scanning electron microscopy, transmission electron microscopy, XRD, thermal analysis, and ATR-FTIR analysis). The obtained materials were used for the immobilization of acid α_1-glycoprotein.

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Heavy metals and associated health risks in wild edible mushrooms: Bioconcentration factors and consumer health implications

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Abstract. In recent years, edible mushroom consumption has increased in the human diet. It is well known that some species accumulate toxic/carcinogenic metals in a quite high concentration, both in unpolluted and polluted areas. The literature showed that the content of heavy metals is intensified for polluted areas mushrooms compared to ones from unpolluted rural or forest sites, which usually have been taken as background values. On the other hand, the relationship between the grown substrate contamination and content of toxic element in a mushroom is not tight enough to allow universal usage of each mushroom species as a reliable bioindicator. This research aims to investigate the heavy metals accumulation (*i.e*., Cd, Cr, Cu, Ni, and Pb) in the fruiting bodies of six indigenous wild edible mushrooms including *Agaricus bisporus, Agaricus campestris, Armillaria mellea, Boletus edulis, Macrolepiota excoriate*, and *Macrolepiota procera*, in relation to various factors, such as the growth substrate, the sampling site, the species and the morphological part (*i.e*., cap and stipe) and their possible toxicological implications. Heavy metal concentrations in mushroom (228 samples) and soil (114 samples) were determined by Inductively Coupled Plasma - Mass Spectrometry (ICP-MS). At the end of these analyses, it was concluded that *Macrolepiota procera* accumulates more Cd and Cr, *Macrolepiota excoriata* accumulates Cu, *Boletus edulis* accumulates Ni and *Armillaria mellea* accumulates Pb, in relation to the underlying soils. There were statistically significant differences between the stipe and cap (*i.e.*, in the cap subsamples of *Macrolepiota procera*, the accumulation factor for Cd was five-times higher than in the stipe subsamples). Toxic/carcinogenic metal concentrations were compared to levels set by legislation and data reported in the literature. The bioconcentration factor and daily intake of toxic metals related to the consumption of these mushrooms with negative consequences on human health, especially on young people, were investigated as well. In the current study, it was noteworthy that the translocation of heavy metals in the anatomical part of the fruiting body (*i.e*., cap and stipe). The results show that the accumulation of highly toxic metals from soil takes place substantially through the stipe to the cap of the studied mushrooms. In this respect, it implies a plausible conclusion concerning the presence of various compounds that can transport these metals *via* the stipe and selectively bind them largely to the cap of selected mushrooms. In addition, can be recommended that consumption of studied mushrooms (*e.g., Agaricus bisporus* and *Boletus edulis*) is not a toxicological risk for adults –as far as Cd content is concerned; although the species *Agaricus campestris*, *Armillaria mellea*, *Boletus edulis*, *Macrolepiota excoriata* or *Macrolepiota procera* should not be consumed by children.

Acknowledgments: This work was supported by the Ministry of Research, Innovation and Digitization, (Institutional Development Projects - RDI Excellence Financing Projects, PDI-PFE), project ID 584/2021-2024.

Carboranyl analogues of the non-steroidal anti-inflammatory drug mefenamic acid

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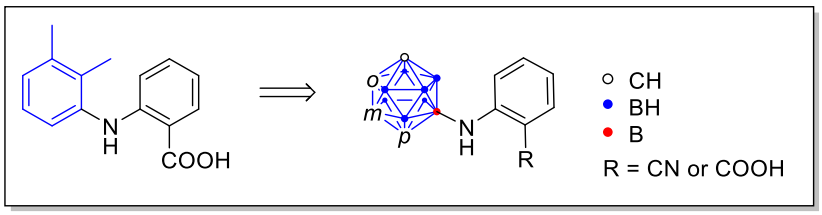
Mefenamic acid is a nonsteroidal anti-inflammatory drug (NSAID) with a wide range of pharmacological activities. It is used to treat muscular aches, menstrual cramps, headache, dental pain and as a painkiller after surgeries. Based on its structure, it is a derivative of *N*-aryl anthranilic acid and belongs to the class of fenamic acids [1,2]. Like other NSAIDs, mefenamic acid inhibits the synthesis of prostaglandins by blocking the active site of cyclooxygenase (COX) [3]. COX is an enzyme that exists in two isoforms: as COX-1, moderating the homeostatic processes in the organism, and as COX-2, inducing pain, fever and inflammation [4]. Even though they are responsible for different effects, they both are homodimeric integral membrane proteins with a high degree of homology. Thus, many NSAIDs, including mefenamic acid, are non-selective in their mode of action [5]. Beside the mentioned homology, the active site of COX-2 is about 20% bigger than that of COX-1. Therefore, one strategy to enhance COX-2 selectivity is by increasing the size of the NSAIDs, e.g. by replacing the phenyl ring with a carborane moiety [6,7].

Mefenamic acid like many other NSAIDs blocks non-selectively both isoforms, resulting in many unwanted side effects. To improve the COX-2 selectivity of the drugs, carborane analogues of well-established NSAIDs were prepared [7,8]. Herein, carborane analogues of mefenamic acid will be presented, containing the *ortho, meta* and *para* isomer cluster. Following a three-step synthesis: Halogenation, B–N coupling of the halo-carborane via Palladium (Pd) catalyst and in the end the hydrolysis of the nitrile derivatives under acidic conditions the titled compounds were synthesized from good to excellent yields. Furthermore, they were fully characterized and also tested for their potential as COX inhibitors and cytotoxic properties.



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Application of the versatile reactivity of 5-aminotetrazole scaffold in the synthesis of biologically active compounds

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Compounds containing 5-aminotetrazole moiety have been investigated for the application in different fields of chemistry [1]. Particularly their potential in the medicinal chemistry was shown. These studies indicated that this heterocyclic motif could be a great starting point for developing various drugs and agents with diverse chemotherapeutic properties [2].

In this study, we report the synthesis of a library of 5-aminotetrazole derivatives obtained by exploiting versatile reactivity [3] of this scaffold. Reactions of 5-aminotetrazole with alkyl-halides in the presence of a base gave mixture of N1- and N2- substituted derivatives which were separated by column chromatography. Furthermore, N-arylation of exocyclic amino-group of 1-substituted-1*H*-tetrazole-5-amines was studied in the presence of a palladium catalyst. In order to show the applicability of the synthesized 5-aminotetrazole derivatives inhibition of filamentation of *C. albicans* was investigated. Several derivatives showed very good activity against disseminated candidiasis, as well as good selectivity. Additionally, we determined that some 5-aminotetrazole derivatives improve the antifungal efficacy of the clinical drugs meaning that they could be used in combination therapy [4].

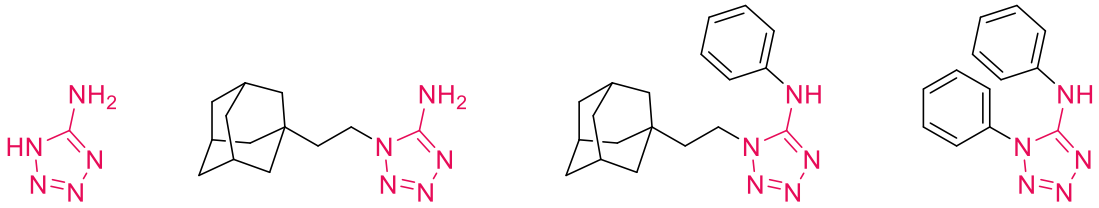

Figure 1. 5-Aminotetrazole and selected 5-aminotetrazole derivatives

This research was financially supported by the Ministry of Education, Science, and Technological Development of Republic of Serbia (contract numbers: 451-03-68/2022-14/200168, 451-03-68/2022-14/200288, 451-03-68/2022-14/200026, 451-03-68/2022-14/200042) and Serbian Academy of Sciences and Arts under strategic projects programme-grant agreement no. 01-2019-F65.

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Double-Decker Silsesquioxanes as Hybrid Molecular Building Blocks: Synthesis and Bioapplication

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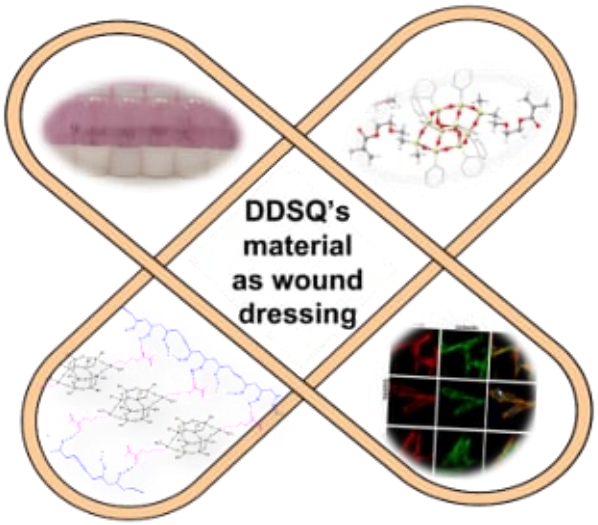
Hybrid inorganic-organic nanostructures figure prominently in the development of new technologies, constituting substrates for a wide range of new materials, among others, such as polymers [1], sensors [2], fuel cells [3], semiconductors [4], catalysts [5], and biomaterials [6]. A fascinating feature that distinguishes them from other compounds is the **synergism of their properties**. An example of such derivatives is **oligomeric silsesquioxanes**. **Organic functional** groups ensure flexibility and reactivity, and a **siloxane core** guarantees high thermal and mechanical resistance of the material [7][8].

We focused on the chemistry of the selected "**Double-Decker Silsesquioxanes" (DDSQ)** as an example of the hybrid molecular building blocks for various applications. Methods for the synthesis and **separation of isomers** of hydroxyalkyl-DDSQ derivatives have been developed [9]. Moreover, the obtained derivatives were used as starting materials for the preparation of **methacrylate derivatives**, which were then used as (i) components of **composites** that can be used in **wound healing dressings [10]**; (ii) monomer for the preparation of DDSQ-modified **polymethacrylate** materials exhibiting the **high thermal stability**.



The authors express their gratitude to the National Science Center, Poland (Grant No. 2020/39/B/ST4/00910) for financial support.

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Valsartan-Catechol Deep Eutectic System: A thermoanalytical study

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Valsartan (VAL) is an antihypertensive drug classified by the Biopharmaceutical Classification System as a class II drug, which means that VAL has low aqueous solubility and high intestinal permeability [1]. Thus, studying strategies to improve its solubility is necessary to increase its bioavailability. Eutectic mixtures consist of two distinct solid phases in a proportion that has the lowest melting temperature observed for mixtures of the compounds considered [2]. These mixtures have shown promise in improving the properties of drugs [3]. Additionally, recently some eutectic mixtures began to be studied as Deep Eutectic Solvents (DES), which represent eutectics that present a considerable decrease in the melting point compared to the predicted for systems that form an ideal liquid mixture [4]. Furthermore, coamorphous are homogeneous multicomponent amorphous systems that exhibit kinetic stability due to intermolecular interactions between the components or to mixing effects [5]. In this work, VAL was milled with catechol (CAT) that was used as a coformer, via mechanochemistry. The resulting powder was characterized by Differential Scanning Calorimetry (DSC), infrared spectroscopy (IR), and powder X-ray diffraction (PXRD). The binary phase diagram of the VAL-CAT system, Figure 1a, was constructed and shows a decrease in liquidus and solidus, when compared to the theoretical (dashed line) melting point, of about 40°C which suggests the formation of a deep eutectic system (DES). The second DSC heating curve reveals an amorphous system. A graph, Figure 1b, showing glass transition temperature (Tg) vs molar fraction ratios of the drug was constructed using experimental and calculated Tg temperatures (Gordon-Taylor equation), and shows a positive deviation between the 0.1 to 0.6 molar fractions, which suggests that the system has interactions between the components. PXRD and infrared data confirm eutectic mixtures and for the sample obtained by melt cooling, amorphous system, band deviation confirm the intermolecular interactions between VAL and CAT.

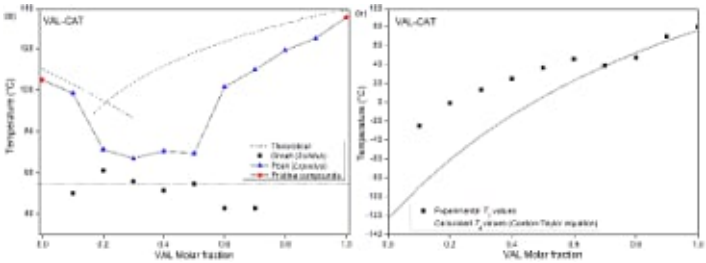

Figure 1 (a) Binary phase diagram of VAL-CAT system and (b) Glass transitions temperatures (T_g) as a function of molar ratios of VAL

This work was possible thanks to the scholarship granted from the Brazilian Federal Agency for Support and Evaluation of Graduate Education (CAPES), in the scope of the Program CAPES-PrInt, process number 88887.310463/2018-00, Mobility number 88887.571008/2020-00. It was also supported by national funds through FCT – Fundação para a Ciência e a Tecnologia, I.P., under the project UIDB/00313/2020.

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CycloSiFA: The Next Generation of Silicon-Based Fluoride Acceptors for Positron Emission Tomography (PET)

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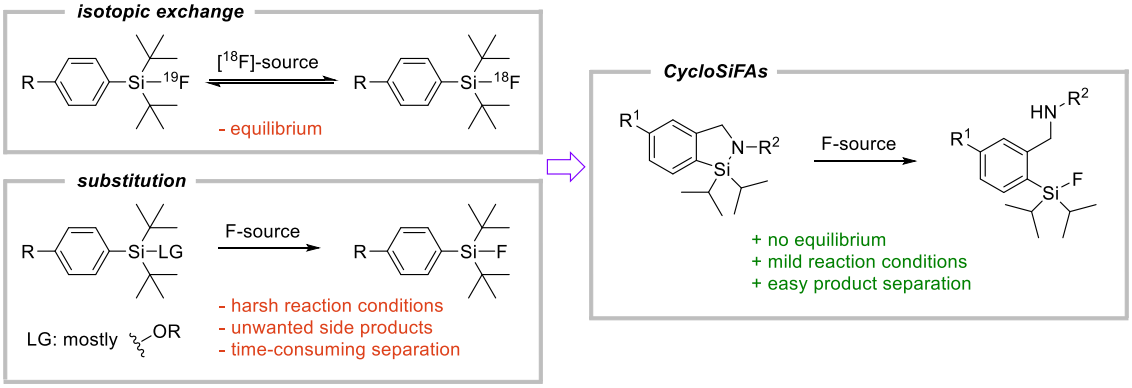
The development of positron emission tomography (PET) can be considered as one of the most important advances in modern imaging techniques in the field of nuclear medicine.[1] Combination of PET and computed tomography allows the morphological and functional visualization of tissue.[2]

As radiotracers labeled with radioactive isotopes, a wide variety of compound classes can be used in diagnostics. A still relatively new and promising variant represent the silicon-based fluoride acceptors (SiFAs). These building blocks were first synthesized in 2006 by the working groups SCHIRRMACHER and JURKSCHAT and can be labeled under mild reaction conditions by isotopic exchange of naturally occurring ^{19}F with ^{18}F.[3] The only drawback is that the isotopic exchange is an equilibrium reaction and a large excess of radioactive ^{18}F is required to obtain good radiochemical yields.

Another approach uses substitution of a leaving group on the silicon atom to incorporate ^{18}F. Generally, a Si–O-bond is cleaved, but this concept is not used in practice because high temperatures and time-consuming separation are required to yield a useful radiotracer.[4]

This project focuses on the synthesis of new CycloSiFA derivatives that are expected to combine the advantages of both labeling technologies. The molecules contain a Si–N-bond which is stable under standard conditions but can be cleaved under mild conditions using various fluoride sources in a non-equilibrium reaction. The leaving group remains in the labeled radiotracer and does not need to be removed. In addition, the lack of side product formation also contributes to the ease of separation. The CycloSiFA derivatives could be bound to biomolecules such as proteins or peptides via click reactions before labeling and serve as an on-demand library for PET diagnostics. Radiochemical labeling of selected CycloSiFAs is currently underway.



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Investigation of Leoligin Derivatives as NF-κB Inhibitory Agents

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The natural compound leoligin [1] a furan-type lignan and a secondary metabolite found in the roots of edelweiss (*Leontopodium nivale* ssp. *alpinum*) was discovered as an interesting compound with anti-inflammmatory pharmacological activity profile [2-5]. Among other effects, it acts as a weak NF-κB inhibitor.

The transcription factor NF-κB is an essential mediator of inflammation; thus, the identification of compounds that interfere with the NF-κB signaling pathway is an important topic. The natural products leoligin and 5-methoxyleoligin have served as a starting point for the development of NF-κB inhibitors. Using our modular total synthesis method of leoligin, modifications at two positions were undertaken and the effects of these modifications on the biological activity were investigated. The first modification concerned the ester functionality, where it was found that variations in this position have a significant influence, with bulky esters lacking Michael-acceptor properties being favored. Additionally, the substituents on the aryl group in position 2 of the tetrahydrofuran scaffold can vary to some extent, where it was found that a 3,4-dimethoxy and a 4-fluoro substitution pattern show comparable inhibitory efficiency.



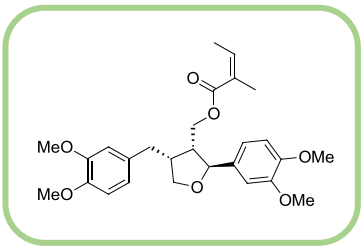

Figure 1. Leoligin, the major lignan isolated from *L. nivale ssp. alpimum*.

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Lipophilic dopamine derivatives prevent cold damage to cells

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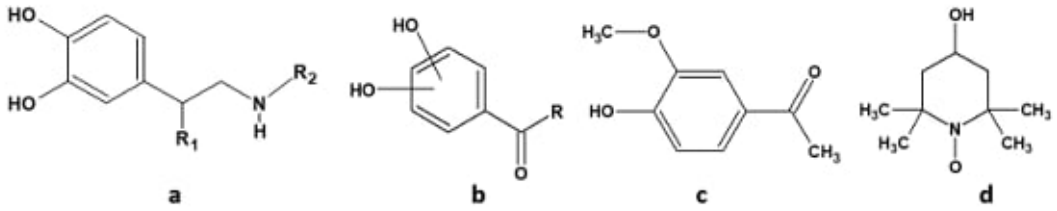
Endothelial cells are particularly prone to damage during cold ischemia, which occurs if donor organs are stored before transplantation. The compromised barrier function significantly increases the risk for failure of the xenograft. It is therefore highly desirable to develop strategies that protect cells from cold damage. Approaches described in the literature include usage of carbon monoxide releasing metal complexes or chelation of iron.

While dopamine has traditionally been used in the context of kidney transplantation, the scientific basis for this practice has been largely unclear. Cold storage of cells leads to uncoupling of the mitochondrial respiratory chain with concomitant formation of reactive oxygen species that damage the cell [1]. In a cell culture model using human umbilical vein endothelial cells, the protective effect of substances can be studied by measuring e.g. LDH leakage into the medium. In this model, both dopamine and dobutamine, though triggering different receptors, were protective [2], whereas the NADPH oxidase inhibitor apocynin and the superoxide dismutase mimic tempol were ineffective. These findings initiated the design of a range of compounds that are structurally related to dopamine. Efficacy was evaluated on the basis of EC_{50} values derived from the cell culture model.

Results indicate that efficacy of some compounds is much higher than that observed for dopamine and is largely linked to the reducing property of the compounds. Strongly reducing substances had EC_{50} values in the low µM range, whereas weak reductants did not exhibit significant protective action. Furthermore, lipohilicity also correlates with efficacy. No other structural prerequisites were found, indicating that the effect is not mediated by any receptor. Interestingly, cell protection by the novel compounds is fully independent from hemodynamic action as shown in a rat model. Thus the novel derivatives may be used for pretreatment of organ donors with very little risk for undesired effects.



Structures of compounds investigated: dopamine derivatives (**a**), dihydroxy phenyl derivatives (**b**), apocynin (**c**) and tempol (**d**)

Thanks to the students that contributed as part of their student projects, among them Nadine Ruh, Steffen Roth and Miriam Wagner.

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The specificity of interaction of Zn(II), and Ni(II) with the α5 domain from mycobacterial SmtB and BigR4 transcription regulators

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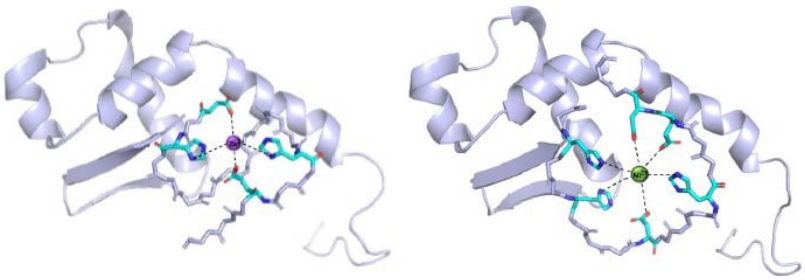
Mycobacterium tuberculosis (Mtb) is the infectious agent of tuberculosis (TB), a disease that continues to overwhelm health systems, despite the existence of combination therapy and the widespread use of an anti-TB vaccine. Considering the rapidly growing number of multi-drug resistant TB, a new method of TB treatment is needed. One of the most promising targets for novel antimicrobial therapies against mycobacterium strains is metal-sensing transcriptional regulators (e.g., ArsR-like). Mammalian immune system response to mycobacterial infection includes i.a. increasing (up to toxic levels) the concentration of Zn(II) and other divalent metal ions in phagosomes vesicles. The mycobacterial SmtB protein - one of the metal-dependent transcription regulators of the ArsR/SmtB family, allows bacteria to survive in challenging environments by dissociating from DNA in the presence of high concentrations of metals, activating the expression of metal efflux proteins. [1].

This work aims to identify and characterize the coordination site of the metal-ligands interaction and to determine the effect of mutations of studied systems of not only crucial for bioactivity zinc but also nickel ion to the zinc-binding domain from SmtB (M. tuberculosis) and BigR4 (homolog of SmtB from M. smegmatis, non-pathogenic mycobacterial strain). The chosen ligands are α5 zinc ion binding domains of SmtB/BigR4 proteins and two particular mutants of BigR4.

The results show that all the peptides form equimolar complexes with zinc and nickel ions. The BigR4 protein domain is more stable than the SmtB with both metals. Histidine mutations affect the stability of complexes and coordination modes of the metal ions differently. Exchanging one of the His into Ala causes a decrease in the stability of Ni(II) complexes [2]. However, surprisingly, that mutation in zinc systems causes an increase in the stability of complexes that we investigated and discussed more in our work [3]. The results of this study could lead us to better understand the role of the critical mycobacterial virulence factor – SmtB – especially as a manager of metal ions uptake and transport – and therefore, be a significant input to the overall comprehension process of Mycobacteria bacteria virulence.



The proposed model of the SmtB protein complex with (A) zinc and (B) nickel ions.

Financial support by the National Science Centre (UMO-2017/26/D/ST5/00372) is gratefully acknowledged.

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Iron (II) clathrochelates – synthesis and spectral characterisation of the first fluorescein tagged derivative

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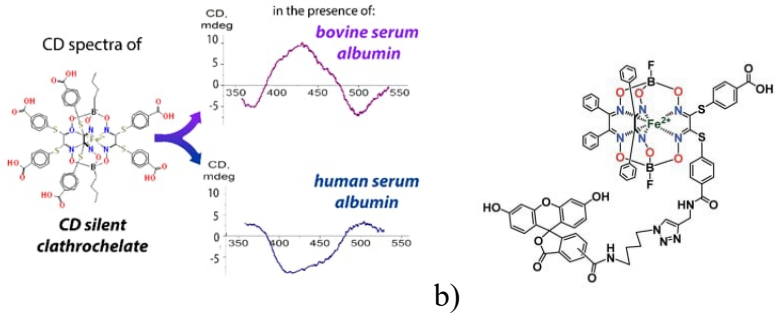
Biological macromolecules exhibiting inherent chirality are able to induce asymmetry of achiral organic and coordination compounds, and therefore, may cause an appearance of a signal in their CD spectra. These ICD bands are very sensitive to the arrangement of the binding sites of hosting biomolecules. [1] As a result, the chirality of small molecules gained upon their binding to proteins may reflect both the structural alterations and the conformation transitions of proteins (to be observed via changes in the ICD spectra). Clathrochelates are metal-centered compounds because their caging (encapsulating) ligands do not exist in the metal-free form due to thermodynamic reasons. [2]

We have obtained fluorescein-tagged iron(II) cage complex using a two-step synthetic procedure. There were no evidence for strong supramolecular host–guest interactions between BSA and the tested compounds but addition of BSA or HSA to deacetylated iron(II) clathrochelate caused the appearance of strong clathrochelate-based ICD outputs. Subcellular uptake of the fluorescein-tagged molecules was visualized using fluorescence microscopy. [3]

The designed fluorescently active cage complexes seem to be prospective molecular probes for studies of subcellular localization. Newly designed and prepared fluorescent clathrochelates can give new insights into the mechanism of bioactivity of clathrochelate-based drug candidates, which are promising therapeutically active compounds to fight viral, neurodegenerative, and cancerous diseases.



a) b)

Fig. 1 a) Mode of action of prepared clathroprobes. b) Deprotected macrobicyclic derivative with iron(II) clathrochelate molecule with the single acylated fluorescein group.

Acknowledgements: The project leading to these results has received funding from the European Union's Horizon 2020 Research and Innovation Programme under the Marie Skłodowska-Curie grant agreement no. 778245.

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Polymeric systems as carriers of fluorinated curcumin analogues exhibit anticancer activity

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Turmeric is one of the ingredients in spice curry and has been consumed for medicinal purposes for thousands of years [1]. It has long been used in traditional Indian and Chinese preparations for treating various diseases. Recently, curcumin has received increasing attention due to its anticancer, antimicrobial, anti-inflammatory, and anti-aging activities, confirmed by numerous *in vitro* and *in vivo* studies. However, the transfer of curcumin *from bench to bedside* is limited by poor water solubility related to its hydrophobic nature and rapid metabolism [2]. Thus, the structural modification of curcumin is an important approach to overcoming these drawbacks [3]. Several new derivatives with enhanced anticancer activity and improved pharmacokinetic properties have been synthesized. On the other hand, a promising way to improve the bioavailability of water-insoluble compounds is to use nanoparticles as carriers [3,4]. Several delivery systems, e.g., lipid-based and polymeric nanoparticles, micelles, nanogels, and cyclodextrin, were used for curcumin encapsulation. Thus, the combination of both strategies: chemical modification and nanotechnology, can enhance the therapeutic activity of curcumin.

Herein, we report the synthesis of novel symmetrical curcuminoids that are difluorinated at the active methylene position and bearing fluorines in the phenyl rings. Fluorine substitution might prevent oxidative metabolism, improve bioavailability, and increase the binding affinity to a target protein [5]. Moreover, the BF_2 group inserted into the methylene position might increase cytotoxic activity [6]. The anticancer activity was evaluated in two bladder cancer cell lines: 5637 and SCaBER. Our novel curcumin derivatives decreased cells viability more efficiently compared to curcumin. Thus, to increase the stability and improve physicochemical properties, the selected compounds were loaded into polymeric carriers based on poly(lactide-co-glycolide) (PLGA). Further studies were performed to describe their physicochemical properties and biological activity.

The National Science Center has financially supported this research (grant number 2019/35/B/NZ7/01165).

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Synthesis of open-cage silsesquioxanes containing methacrylates as sidearms

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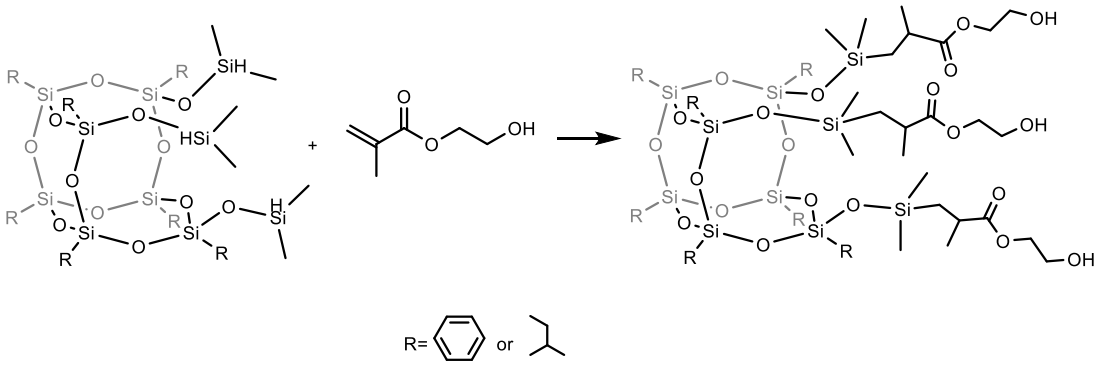
In recent years, polyhedral oligomeric silsesquioxanes (POSS) have been gaining popularity in science. Such a significant interest is mainly due to the organic-inorganic architecture responsible for the unique properties of hybrid materials [1]. Cage-like silsesquioxanes are used mainly in the chemistry of biomaterials [2], catalysis [3], optoelectronics [4], and the production of cosmetics [5].

One of the processes often used to modify the compounds obtained is their functionalization. This process allows the structure of the original material to be preserved while gaining new properties [6]. For example, one of the functionalization methods of polyhedral oligomeric silsesquioxanes is based on hydrosilylation reaction [7], which has been used in this research to obtain novel open-cage silsesquioxanes containing methacrylate as sidearms.

Two types of open-cage silsesquioxanes and 2-hydroxyethyl methacrylate were used as substrates to prepare silsesquioxane derivatives (Scheme 1). Due to their properties, methacrylates are widely used in medical applications to produce specific materials [8]. Thanks to the hydrosilylation reaction, new, undescribed open-cage silsesquioxane derivatives were obtained, which constitute an excellent basis for new composite materials. The combination of the properties of both compounds can lead to the production of a material that has many potential applications.

The aim of the study is to present the synthesis of new polyhedral oligomeric silsesquioxanes derivatives. The obtained products were characterized with the use of ^{1}H, ^{13}C, ^{29}Si NMR, FT-IR, and elemental analysis.



Scheme 1 *Hydrosilylation reaction of open-cage silsesquioxanes with 2-hydroxyethyl methacrylate.*

This work was financially supported by the National Science Centre, Poland (Grant No. 2020/39/B/ST4/00910).

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Chitosan-based materials featuring multiscale anisotropy for wider tissue engineering perspectives

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We present the design of new graphene oxide composites based on chitosan modified with fatty acids, that resulted in amphiphilic structures with increased morphological and structural variability. Chitosan-fatty acid derivatives are synthesized via N,O-acylation of chitosan with palmitic and lauric acid. Obtained co-polymer assembled in core-shell-like items were further crosslinked with genipin and composited with graphene oxide.

The FTIR technique was used to demonstrate the modification and to chemically characterize novel materials. DLS, SEM and contact angle measurements were used to investigate the surface attributes of the samples, which revealed that hydrophobic components linked into chitosan macromolecules resulted in an increase in both surface roughness and water contact angle values. Nanoindentation tests highlighted notable durotaxis gradient in-depth due to polysaccharide / fatty acid self-organization and also as a result of graphene sheets embedment. Graphene oxide containing materials were more stable in phosphate buffer saline and lyzozime incubation and swelled less due to additional physical interactions developing among the composited building blocks.

Finally, preliminary viability, cytotoxicity and inflammatory response tests revealed that all chitosan-fatty acid composite derivatives were promising while in vitro protein adsorption assay indicated a potential antifouling activity of the composites. Our findings show that the proposed synthesis, notably the graphene oxide/chitosan-fatty acids composite derivatives, have the potential to be used as risk-free durable and stable substrates with heterogeneous architecture in biomedical applications.

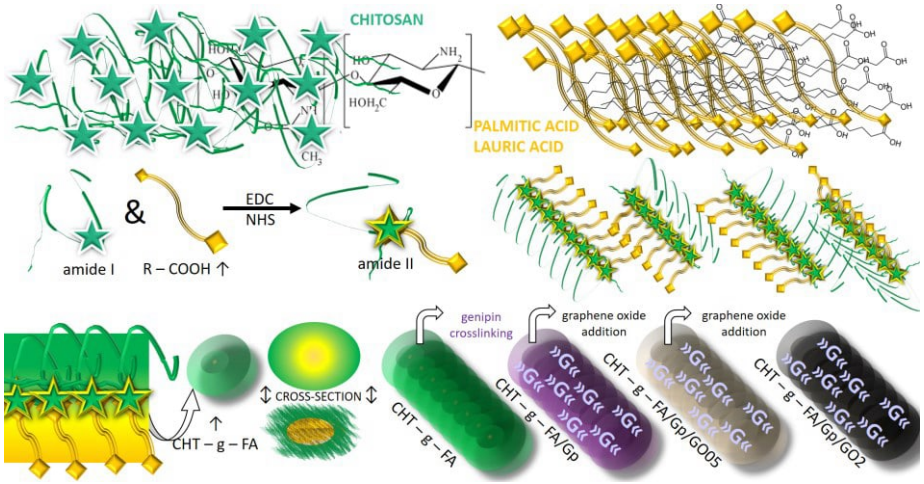

Figure 1. Schematic representation of chitosan modification, crosslinking and graphene oxide reinforcement

This work was supported by a grant of the National Authority for Scientific Research and Innovation, Operational Program Competitiveness Axis 1-Section E Program cofinanced from European Regional Development Fund "Investments for Your Future" under Project no. 154/25.11.2016, P_37_221/2015 MySMIS code 108117.

Synthesis of novel sclareol derivatives and evaluation of their anticancer activity

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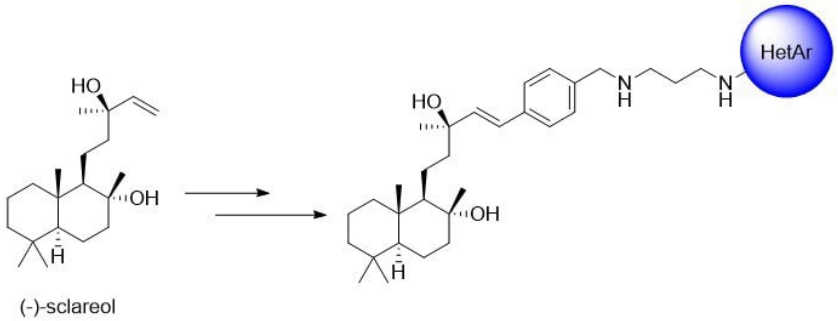
Sclareol is a labdane diterpenoid found in clary sage (*Salvia sclarea* L.) with various biological activities, most notably anticancer and cytotoxic activity [1]. There are several examples of synthetic derivatives of sclareol with antischistosomal [2], antifungal [3], and anticancer activity [4]. Since it is known that modifications of biologically active molecules can lead to the improvement of physicochemical properties and modes of interactions with target cells, we have envisioned the derivatization of sclareol to obtain molecules with more potent cytotoxic activity.

Sclareol used as a starting material in this research was isolated from Clary sage harvested in Bulgaria. New compounds were obtained by derivatization of sclareol at its $\Delta^{14,15}$ double bond using oxidative Heck coupling catalyzed by palladium-acetate with copper(II)-acetate as oxidant, followed by the introduction of different diamine-moieties. Finally, the terminal amino-group was coupled with a nitrogen-rich heterocycle to obtain desired compounds. During the course of the synthesis, both tertiary and tertiary allylic hydroxyl groups remained unchanged, which was of particular interest, since it was shown that the tertiary allylic group is crucial for the biological activity of sclareol.

Synthesized compounds were tested on human cancer cell lines, primarily glioblastoma cells. It was shown that certain derivatives have caused a significant reduction of glioblastoma cell viability at low concentrations. Moreover, some derivatives inhibited cell membrane transporter P-glycoprotein (P-gp) responsible for multidrug resistance and increased accumulation of doxorubicin to the same extent as tariquidar (a well-known P-gp inhibitor). Most importantly, novel molecules exhibited more potent biological activity than sclareol itself.



(-)-sclareol

This research was financially supported by the Ministry of Education, Science, and Technological Development of the Republic of Serbia (contract numbers: 451-03-68/2022-14/200168, 451-03-68/2022-14/200026, 451-03-68/2022-14/200007).

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Purely hybrid organosilane (nano)fibres for possible applications in medicine

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There is a whole range of fibrous materials used in regenerative medicine. However, the organic polymers-based nanomaterials (such as PVA, PVB, PCL and many others) developed over the last decade still have many limitations and thus offer potential for the development of various types of new inorganic, organic and/or hybrid organic-inorganic scaffolds[1,2].

Our work is focused on the preparation of purely hybrid organic-inorganic fibrous materials with suitable properties such as mechanical and thermal resistance, flexibility, biocompatibility and biodispersity in the human body. These unique fibrous materials are prepared thanks to the interconnection of organic chemistry, acid catalysed sol-gel method and variouselectrospinning techniques. Thus a fine layer of smooth homogenous fibres without the presence of harmful additives and with a high molar content of hybrid precursor inside the silica matrix together with additional features belonging to the incorporated organic molecule(s) may be obtained[3,4].

According to the preliminary results, these fibrous layers are cytocompatible with multiple cell lines such as fibroblasts, stem cells or fetal neuronal cells and show huge potential for regenerative medicine applications.

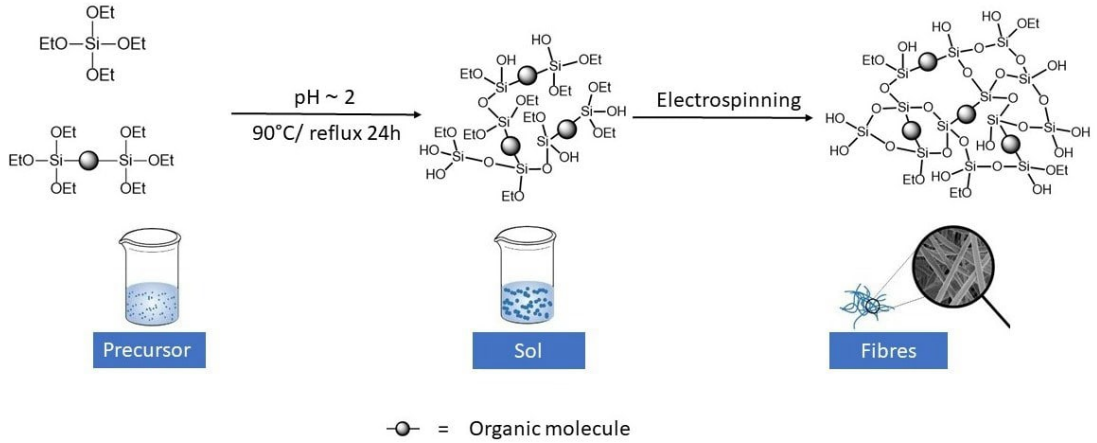

Figure 1. Schematic illustration of one-pot synthesis leading from hybrid organosilane precursors into the (nano)fibres by the sol-gel process

This work was supported by the Student Grant Competition of the Technical University of Liberec under project No. SGS-2022-4059 and the European Union - European Structural and Investment Funds in the framework of the Operational Programme Research, Development and Education project "Hybrid Materials for Hierarchical Structures (HyHi)", Reg. No. CZ.02.1.01/0.0/0.0/16_019/0000843.

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Development of a Lateral Flow Assay for Quantification of Amitriptyline

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Amitriptyline is an antidepressant for which therapeutic drug monitoring would be beneficial to ensure patients receive the correct dose [1]. Conventional analytical methods are expensive and time-consuming, thus point-of-care testing with a cheap and fast method is necessary. Lateral flow assays are well-established analytical tools for this task as they are cost-effective, easy to handle, and provide a result within a few minutes.

For therapeutic drug monitoring of amitriptyline, a lateral flow assay that provides a quantitative result is needed. As amitriptyline is a small molecule, the binding inhibition assay is a suitable method. For the development of such an assay, the recognition element has to be carefully selected. Different methods of binding the detection antibody to gold nanoparticles are compared using quality control analytics based on UV/Vis spectroscopy and dynamic light scattering. The most appropriate conjugate is selected on the basis of yield, stability, and the performance on lateral flow assays. To determine the suitability of the lateral flow assay for therapeutic drug monitoring, cross reactivities are investigated, and calibrations are carried out (Figure 1a).

To overcome the limited reproducibility of lateral flow assays, the strips used are structured in parallel channels (Figure 1b), enabling replicate measurements. A deep learning based software automatically finds and evaluates the biosensor colour spots. The colour intensities in calibration experiments show the suitability of the conjugates for a quantitative binding inhibition test and provide a minimum detectable concentration required for therapeutic drug monitoring. Results for optimum conjugate and details for evaluation and calibration will be given.

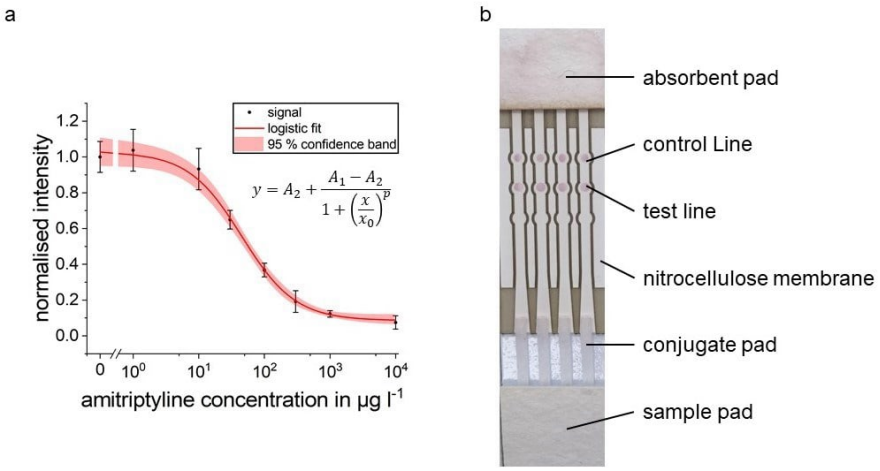

Figure 1: a) calibration curve, b) test strip with parallel channels

This work was supported by the Bundesministerium für Wirtschaft und Energie within the project 'On-Chip kalibrierender Biosensor für kleine Analyten im Bereich POCT und Umweltanalytik', IGF-Vorhaben Nr. 20949 N/2.

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Synthesis and biological activity of hydroxy-substituted *N*-benzimidazole carboxamides

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It has been widely demonstrated that oxidative stress participates in all stages of chemical carcinogenesis. Since antioxidants are known by their function in protecting the human body against damage by reactive oxygen species (ROS) as well as by inhibiting ROS-relayed reactions, there has been tremendous and constant growing interest for the searching of novel natural or synthetic organic molecules as potential antioxidants. Being one of the well-known privileged building substructures in medicinal chemistry, benzimidazoles derivatives can be promising candidates as antioxidants. Among versatile pharmacological features, the most important ones for the rational design of novel bioactive compounds are antitumor, antimicrobial, antiviral, antioxidative and anti-inflammatory activities [1,2].

All compounds were prepared by conventional reactions of organic synthesis as well as by microwave assisted reactions [3]. Targeted benzimidazole-2-carboxamides were synthesized by removal of methoxy protecting groups by using BBr_3 in absolute dichloromethane at −75 °C, or by removal of benzyloxy protecting groups by Pd/C catalytic hydrogenation in methanol to afford the corresponding deprotected derivatives.

All newly prepared compounds were screened for their antioxidant capacity using several spectroscopic methods as well as antiproliferative activity on several human cancer cells *in vitro.* To explore the antioxidative potency of benzimidazole-2-carboxamides we developed 3D-QSAR models and used them for computational prediction of antioxidative activity of the presented compounds.

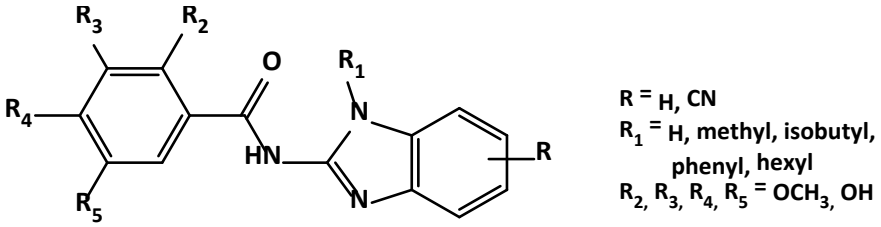

Figure 1. Hydroxy-substituted *N*-benzimidazole carboxamides

Acknowledgments: This work was funded by the Croatian Science Foundation (project IP-2018-01-4379).

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Synthesis, antiproliferative activity and DNA binding of amino and amido substituted pentacyclic benzimidazole derivatives

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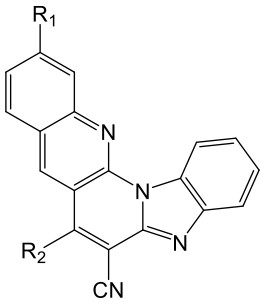
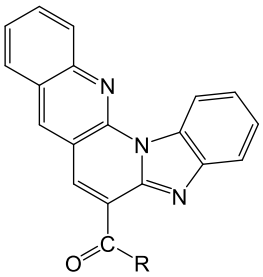
Benzimidazoles and their azino-fused derivatives are important and fundamental structural motifs in medicinal chemistry found in a variety of bioactive natural and numerous synthetic medical and biochemical agents, which possess different chemical and pharmacological features [1]. Quinoline-fused tetracyclic benzimidazoles, recently prepared and published in our research group, have shown to be a very promising class of antiproliferative agents and intercalators [2]. Importantly, due to the structural similarity of with naturally occurring nucleotides, benzimidazole derivatives can easily interact with biomolecules like DNA, RNA or proteins in living systems. DNA molecule is still one of the principal targets in anticancer drug development strategies since it has a central role in many life processes.

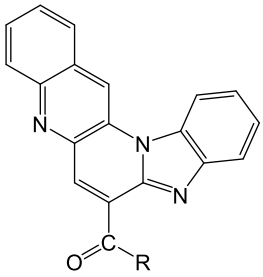
Pentacyclic compounds were prepared by conventional reactions of organic synthesis as well as by photochemical and microwave assisted reactions [1-3]. Targeted amino substituted benzimidazole derivatives obtained in the uncatalyzed microwave assisted amination from corresponding halogeno substituted precursors, while amido substituted derivatives obtained in the reaction of corresponding pentacyclic acyl chlorides and chosen amines. All prepared compounds were tested for their antiproliferative activity *in vitro* on several human cancer cells. A few compounds showed very strong activity in submicromolar range of inhibitory concentrations and thus, were chosen to study their DNA binding as possible mechanism of biological action.



R_1 = H, $CH_2CH(CH_3)_2$, $(CH_2)_3N(CH_3)_2$, piperidine, piperazine
R_2 = H, $CH_2CH(CH_3)_2$, $(CH_2)_3N(CH_3)_2$, piperidine, piperazine



R = $NH(CH_2)_3N(CH_3)_2$, piperidine



R = $NHCH_2CH(CH_3)_2$ piperidine

Figure 1. Pentacyclic benzimidazole derivatives

Acknowledgments: This work was funded by the Croatian Science Foundation under the project IP-2018-01- 4379.

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Synthesis and biological activity of newly designed 2-benzothienyl and 2-bithieny amidino-substituted benzazole derivatives

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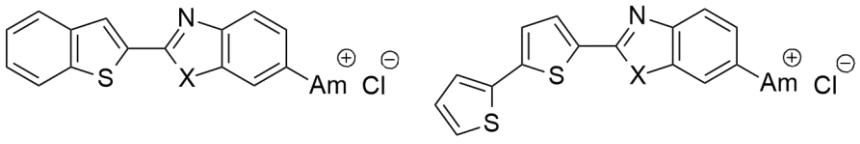
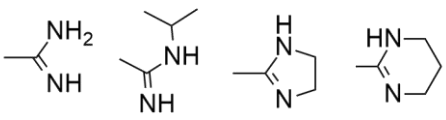
It is well known that cationic amidines, placed usually at the termini of the molecule, are structural parts of numerous compounds of biological interest. Their main function is the interaction with potential biological targets and formation of the stable complex with biological molecules. On the other hand, benzimidazoles and benzothiazoles as one of the most important heterocyclic nitrogen scaffolds have great biological importance and thus become unavoidable structural motifs in the rational design of novel drugs. In our recent studies we have proved that by engrafting amidine extremities as positively charged substituents at the end of the heteroaromatic substructures we could significantly improve the antiproliferative [1, 2] as well as antitrypanosomal activities [3].

Herein we present the synthesis of newly designed 2-benzothienyl and 2-bithienyl benzimidazole/benzothiazole derivatives bearing either acyclic unsubstituted and isopropyl amidine moiety, as well as cyclic 2-imidazolinyl and 3,4,5,6-tetrahydropyrimidin-2-yl amidine moiety. All prepared compounds were tested for their antiproliferative activity on six human cancer cell lines (HCT116, H460, MCF-7, PC3, HeLa, SW620) and non-tumour cell line HEK 293, while antitrypanosomal activity was tested on protozoan parasite *Trypanosoma brucei.* Some of tested compounds showed strong and selective antiproliferative activity against H 460 cells in submicromolar range of inhibitory concentrations. Obtained results revealed that benzothiazole derivatives were more active in comparison to their benzimidazole analogues. Additionally, we can conclude that also the type of the amidine group has strong influence on the biological activity.



X = S, NH

Am = 

Thanks to Croatian Science Foundation, project IP-2018-01-4379 for financial support of this work

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Synthesis and in vitro anthelmintic activity evaluation of some new guanidinobenzimidazole derivatives

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Helminthic infections, caused by roundworms from the genus Trichinella, lead to serious health and economic problems worldwide. Humans become infected after consumption of meat products contaminated with Trichinella larvae [1]. The benzimidazole anthelmintics albendazole and mebendazole are the main drugs for the treatment of trichinellosis [2] but the therapy is far from perfect as these drugs are active against the intestinal adult Trichinella parasites but much less active against encapsulated larvae in muscles. Moreover, these anthelmintic agents have limited bioavailability and a high degree of resistance [3]. So, there is an intense need for the development of new effective anti-Trichinella drugs with less toxicity and are free from adverse effects.

Here, we present a new series of guanidinobenzimidazole derivatives, prepared by a one-step synthesis, in short reaction times, and with high yields. The structures of the targeted compounds were confirmed by IR, 1H NMR, and 13C NMR spectra. In addition, the molecular geometry and electron structure of these molecules were theoretically evaluated using density functional theory (DFT) methods.

The larvicidal effects of the newly synthesized benzimidazoles on encapsulated muscular larvae of *Trichinella spiralis* were studied *in vitro*. Biological assay results indicated that the compounds in the tested concentrations (50 μg/mL and 100 μg/ml) exhibited moderate activity. Similar to our previous results [4], the benzimidazole derivatives containing hydroxyl groups in their molecule showed the highest efficacy on the viability of the parasite larvae.

Acknowledgments

The work is realized as a part of National Program "EUROPEAN SCIENTIFIC NETWORKS" of Ministry of Science and Education of Bulgaria, project "Drug molecule" D01-278/05.10.2020

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Glucose-powered Janus nanomotors for active anticancer drug delivery

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Self-propelled and bio-inspired nano- and micromotors are a promising field in the biomedical area, specifically in anticancer therapy due to their ability to enhance tumor reach, tumor infiltration and tumor cell internalization. However, these devices still have disadvantages that limit their real application. The main problem lies in the use of toxic and exogenous fuels for living beings to produce their movement. The most commonly employed is hydrogen peroxide, at high concentrations to achieve high levels of diffusion or velocity in nanoparticles.[1-3] Herein, we describe a new versatile nanomotor capable of both self-propulsion and drug delivery for "smart" cancer therapy. It consists of a Janus-type nanoparticle with two opposing faces, a platinum (Pt) nanoparticle and a mesoporous silica nanoparticle (MSN), unified in the same nanodevice. The MSN face acts as a container for the anticancer drug doxorubicin (DOXO). In addition, the surface of the MSN is decorated with the enzyme glucose oxidase (GOx), bound by amide bonds. The GOx enzyme acts as a "molecular gate" controlling the specific intracellular delivery of DOXO and as a trigger to initiate the propulsion reaction, converting the abundant glucose present in the tumor microenvironment into gluconic acid and hydrogen peroxide (H_2O_2). The platinum face is responsible for autonomous motion by catalytically decomposing the H_2O_2 produced by the GOx into water and oxygen (gas), Figure 1. The advantages of the Janus Pt-MSN (DOXO)-GOx nanomotor lie in the bioavailability and non-toxicity of glucose in tumors and in its geometry, which enhances their diffusive motion. After structurally and functionally characterization of the developed nanomotors, their anticancer properties were tested in a HeLa tumor cell culture, tumor spheroids, and in an *in vivo* mice xenograft model. The results obtained showed a high capacity for three-dimensional tumor infiltration and cell internalization resulting in a controlled DOXO release, promoting a significant tumor size reduction. In summary, this innovative and versatile nanotechnology could suppose a great advance in anticancer therapy employing biocompatible self-propelled nanoparticles.

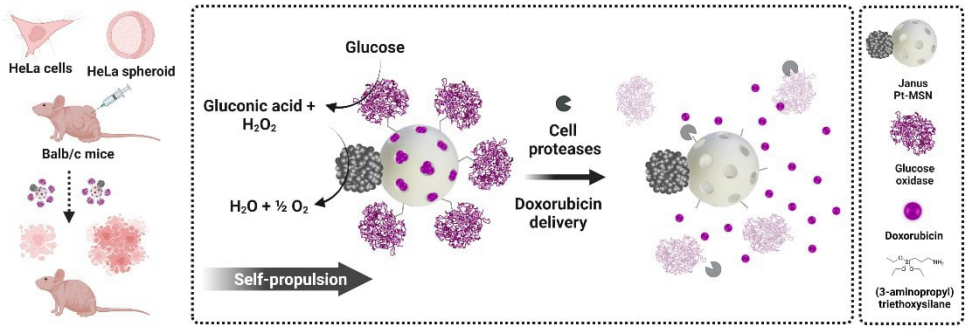

Figure 1. Representation of glucose-powered Janus Pt-MSN nanomotor for active anticancer drug delivery in HeLa tumor cell culture, tumor spheroids, and in a balb/c mice model.

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Addressing the principle of polypharmacology in cancer therapy – Carborane-containing drugs as dual enzyme inhibitors

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Multi-target drug design has significantly drawn attention within in the past two decades. The treatment of complex inflammatory processes including various types of cancer requires tremendous effort in developing drugs acting on more than one target [1]. Besides conventional chemotherapy and radiotherapy, the selective inhibition of tumour-inducing enzymes that catalyse the biosynthesis of important signal mediators (e.g. eicosanoids), subsequently enabling tumour cell proliferation, represents another promising approach for cancer therapy [2,3]. Our strategy focuses on the incorporation of metabolically stable, sterically demanding and highly hydrophobic carborane moieties into existing dual inhibitors of cycloxygenase-2 (COX-2) and 5-lipoxygenase (5-LO) that are key enzymes in the biosynthesis of prostaglandins and leukotrienes [4-6].

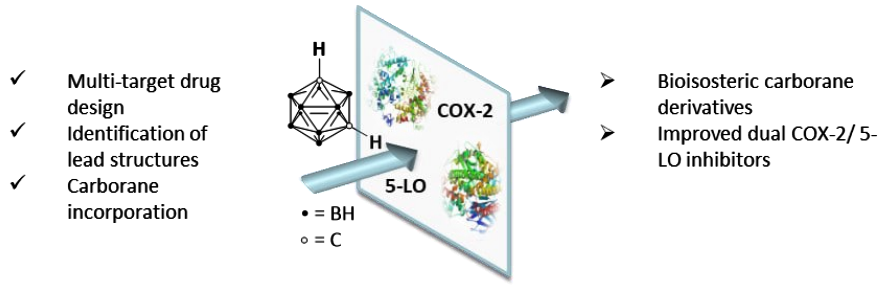

Figure 1: General principle of our research on carborane-based dual COX-2/5-LO inhibitors.

Potential carborane-based dual COX-2/5-LO inhibitors were synthesised and fully characterised by typical physico-chemical methods. After subsequent determination of their stability in suitable biological media, dual COX-2/5-LO inhibitors and their corresponding carborane analogues were tested *in vitro* on melanoma and colon carcinoma cancer cell lines to determine their cytotoxicity [5]. Additionally, their inhibitory potential on COX-2 and 5-LO in cell-based as well as enzyme-based assays was studied [5,6]. Finally, these experiments were complemented by *in silico* studies, namely molecular docking, to derive their structure-activity relationship.

Thanks to the European Social Fund (ESF), the Research Academy Leipzig (RAL) and the Graduate School BuildMoNa for financial support and for giving the opportunity to present these scientific results.

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Analogues of the phorbazole natural products

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The phorbazole family of natural products are polychlorinated heterocyclic secondary metabolites that comprise of a phenol, an oxazole and a pyrrole (**Figure 1**). Phorbazole A-D were isolated from the marine sponge *Phorbas aff. Clathrata* [1] off the South African coast, while phorbazole E and F were found in the Indo-Pacific marine mollusk *Aldisa andersoni*.[2]

As of date, no bioactivity has been reported for phorbazole B-D. However, reports suggest that phorbazole A and two new phorbazoles, 9-chloro-phorbazole D (phorbazole E) and *N*1-methyl-phorbazole A (phorbazole F) is involved in chemical defence, and that these analogues have shown promising *in vitro* growth inhibition of human cancer cells.[2,3]

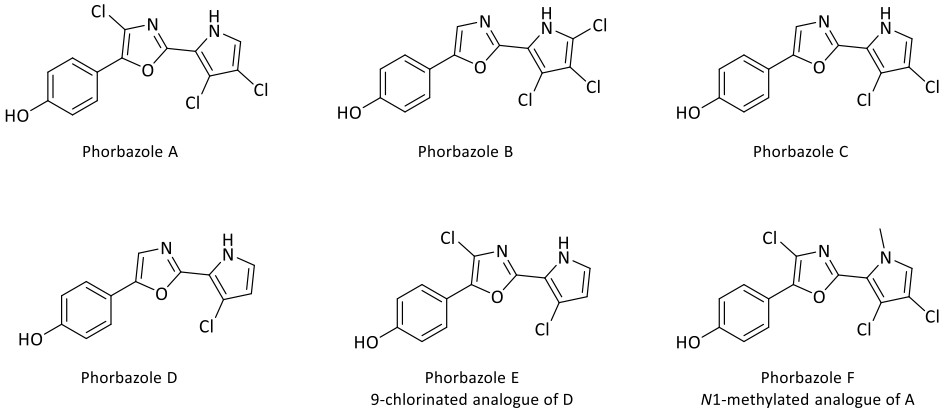

Figure 1. The phorbazole family of natural products.

We have prepared a series of phorbazole analogues and investigated their biological activity. Results from these efforts will be discussed.

This work was supported by the University of Bergen and Meltzers Høyskolefond.

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Design, synthesis and Biological evaluation of New, glycolipid-based Toll-Like Receptor 4 (TLR4) Modulators

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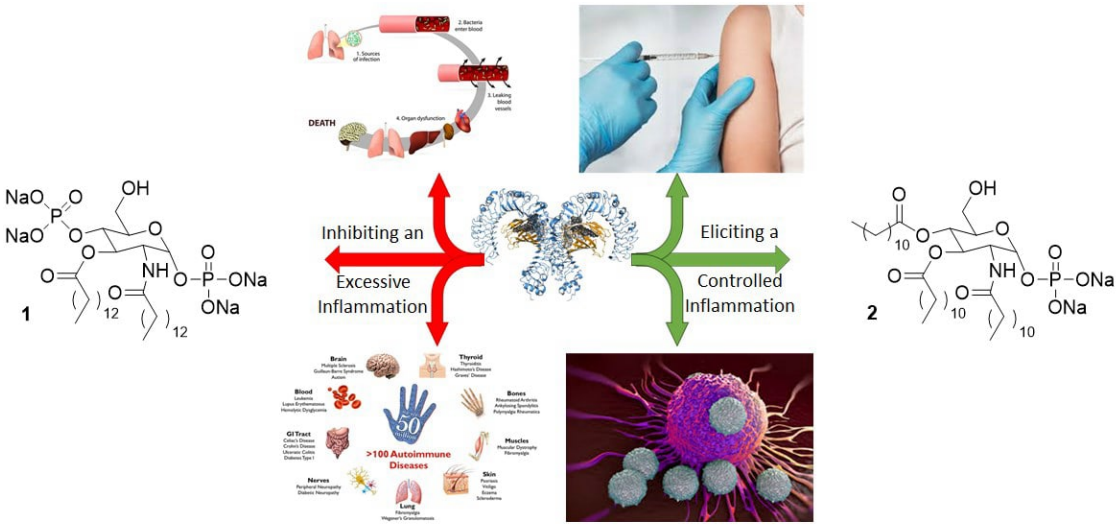
Innate Immunity is the first defense line in multicellular organisms against internal or external threats. It acts through inflammation, triggered by the recognition of specific Pathogen or Damage Associated Molecular Patterns (PAMPs or DAMPs) by specific pattern-recognition receptors (PRRs). Toll-Like Receptor 4 (TLR4) is one of the most important PRRs, and it responds to gram-negative bacteria lipopolysaccharide (LPS).[1]

TLR4 modulation is emerging as an important therapeutic approach in several clinical settings: TLR4 inhibition has a potent anti-inflammatory effect; on the other hand, TLR4 mild activation can be used to stimulate immunity in vaccine adjuvants or to develop cancer immunotherapeutic drugs.[2,3]

We present here rationally designed lipid A analogues based on a monosaccharide structure that are active in binding MD-2/TLR4, thus activating or inhibiting LPS/TLR4 or DAMP/TLR4 signalling. We also present synthesis optimization of TLR4 modulators, with the aim of producing versatile synthetic intermediates and reducing the number of synthetic steps to efficiently scale the synthesis up for industrial purposes.



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Encapsulation of fungicide agents of nitroeugenol derivatives in interpolyelectrolyte complexes chitosan based. A physicochemical study

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The interpolyelectrolyte complexes (PECs) are a type of nanoaggregates widely used in several fields mainly as carriers or reservoirs of bioactive molecules. These systems are formed by anionic and cationic polyelectrolytes [1]. These structures are highlighted for being capable of generating two environments in just one structure: hydrophilic and hydrophobic environments. These characteristics are very attractive since it is possible encapsulates compounds soluble in organic solvent to be applied in aqueous medium. In this sense, a serie of nitro-eugenol derivatives (NEd) has been tested against *Botrytis cinerea*, previously and, the results showed promissing effects against this fungus.

Here it is presents two new formulations environmentally friendly of a series of PEC chitosan based, with the incorporation of synthetic nitro-eugenol derivatives (NEd) to be applied as a potential biofungicide (Figure 1). These formulations were constituted by chitosan, which was used as cationic polyelectrolyte, meanwhile copolymers of maleic anhydride-α-olefins (1-hexene; 1-octene) family were used as anionic polyelectrolytes. The results showed that the PECs systems were successfully obtained. The incorporation of NEds in PECs were effectively carried out. The physichemical characterizations showed that the structure of anionic polyelectrolyte influences in the encapsulation of the NEds.

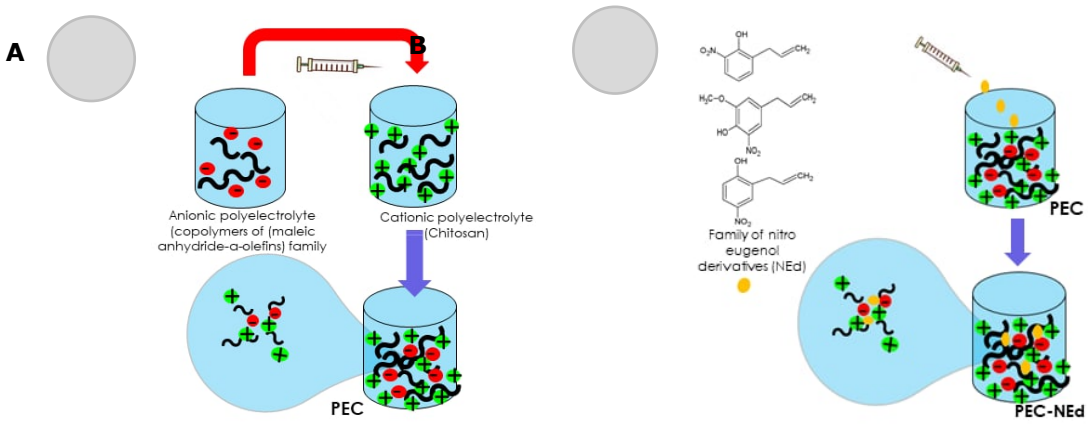

Figure 1. Schematic description of the preparation of PECs-NEDs. A) PEC formation and B) Incorporation of NEd on PEC for PEC-NEd formation.

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Design, Synthesis and Antitumor activities of novel α, β-unsaturated ketones molecules: EGFR inhibition by molecular modeling study

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The term cancer refers to a collection of diseases in which abnormal growth of cells is present with the potential to spread into or invade adjacent tissues.[1] The most common cancer therapy is chemotherapy, however cytotoxic effects on healthy cells may contribute to substantial side effects. The endothelial growth factor receptor (EGFR) kinase enzyme is overexpressed in several cancers.[2] It is possible to inhibit EGFR kinase enzyme in cancer treatment, with the use of small chemical synthesized molecules such as erlotinib, neratinib, sorafenib and crizotinib.[3] Similarly, α,β-unsaturated ketones, such as curcumin which are prevalent natural products have exhibited diverse biological activity. Drugs containing the core structure of curcumin having α, β unsaturated ketone moiety have numerous biological applications, including EGFR inhibition, and anti-cancerous and anti-oxidant properties.[4]

Keeping all the above points in mind, we designed and synthesized a small α,β-unsaturated ketones molecule i.e. 2-benzylidene-3-oxobutnamide, and it's derivative with good solubility under physiological conditions. These derivatives exhibited potent anti-cancerous activities against 5 cancer cell lines : A549, HCT116, SiHa, C33A, SW620 (IC_{50} = 2 to 8 µg/ml) . Molecular docking studies indicated that EGFR is the potential target of the molecules. In molecular modeling studies, one of the derivatives exhibited excellent binding towards EGFR (binding energy: -7.5 Kcal/mol) compared with erlotinib (binding energy: -6.9 Kcal/mol) which show similar interaction. Also, In the hemolysis assay, the compounds showed excellent hemocompatibility. Thus, these small molecules with potent activity against cancer cells were identified. *In- vitro* studies on their biological target are being carried out.

Acknowledgements

We thank the Department of Biotechnology IIT Madras, India for providing facilities to conduct the research work. We thank Innovative Project IC&SR , IIT Madras Chennai, India for a grant of 2 lakhs/year in the years 2019-20. Ankur thanks to Half Time Research Assistantship (HTRA), MHRD , India for fellowship.

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Fluoride-mediated breaking of Oxygen-Silicon bonds (FOSi)-method for radiolabeling of peptides

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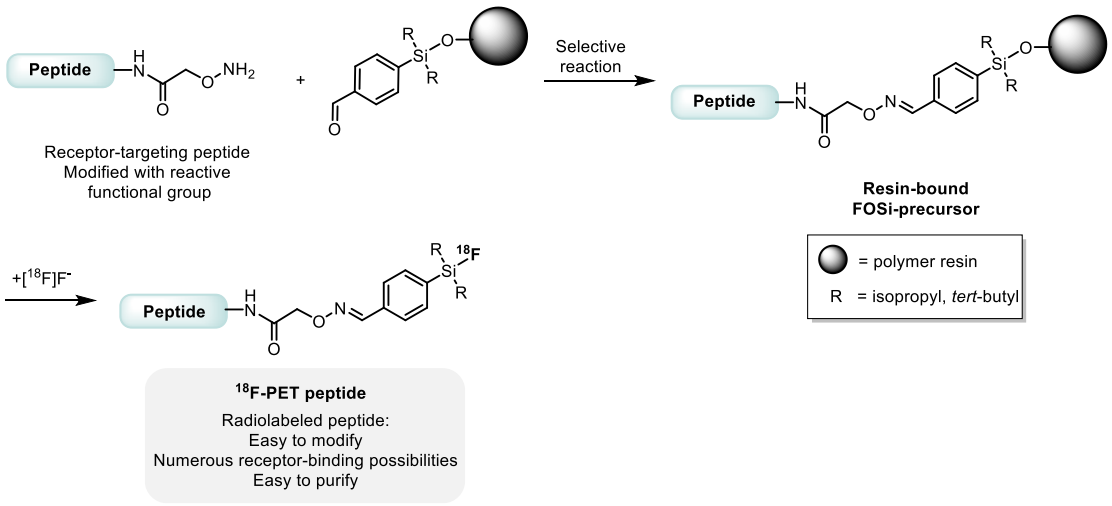
In the past 20 years, fluorosilanes have been studied as potential labeling synthons for ^{18}F-PET imaging.[1-3] In 2006, Schirrmacher *et al.*[4] reported on how differently sized alkyl and aryl groups on the silicon atom influenced hydrolytic stability of fluorosilanes. This formed the basis for the well-established "silicon-fluoride acceptor" (SiFA)-method, which is based on isotopic exchange, developed by Wängler et al.[5] This work inspired us to develop a new method for radiolabeling of bioactive molecules. Our research is towards a new method for ^{18}F-radiolabeling of peptides that will be devoid of the problems associated with existing methods (e.g. low radiochemical yield, difficulty of purification). Our approach is based on direct fluorination through breaking an oxygen-silicon bond within a molecule that is attached to a solid support (Scheme 1). This method will ensure fast production of highly desirable peptide-based PET-tracers with high chemical purity and high specific activity. Silicon is more electropositive than oxygen, thus nucleophilic attack from fluoride occurs on silicon leading to the formation of a Si-F bond, which releases the peptide from the solid support. The small size of the fluoride anion allows for a rapid cleavage of the oxygen-silicon bond with formation of the strong Si-F bond as an additional driving force.



Scheme 1. The concept of fluoride-mediated breaking of oxygen-silicon bonds

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Dextrans, pullulan and lentinan, new scaffold materials for use as hydrogels in tissue engineering

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Gel-like biomaterials play a key role as backbone materials in regenerative medicine.[1,2] Hydrogels based on biomacromolecules are developing increasing importance as scaffold materials due to their natural origin and biocompatible properties, especially in the field of tissue engineering.[3,4] In recent years, we have synthetically expanded the structural space of polysaccharides for the formation of hydrogels and their use in tissue engineering, both in terms of the choice of natural polysaccharides as well as the use of chemical processes for hydrogel formation.[5,6]

Despite the fact that selected polysaccharides such as hyaluronic acid are well established, little is known, how these polysaccharides can be chemically altered to create hydrogels under controlled conditions. In this work we present a small library of chemically modified polysaccharides (such as dextran, pullulan and lentinan) which are used for a divergent approach to achieve biomedical relevant hydrogels. In this case the crosslinking is based on thio ether formation between thiol modified donor and vinylsulfone or maleimide modified acceptor components. After succesful synthesis of the linker systems and coupling at the polysaccharides, hydrogel formation takes place under physiological conditions. We extended the study by coupling small molecules like adhesion factors for increasing biocompatibility and dye for further studies. The different hydrogels were studied to their rheological properties, water up take, their permeability, biodegrability and their cytotoxicity. With this results in hand we generated potential material for biomedical applications.

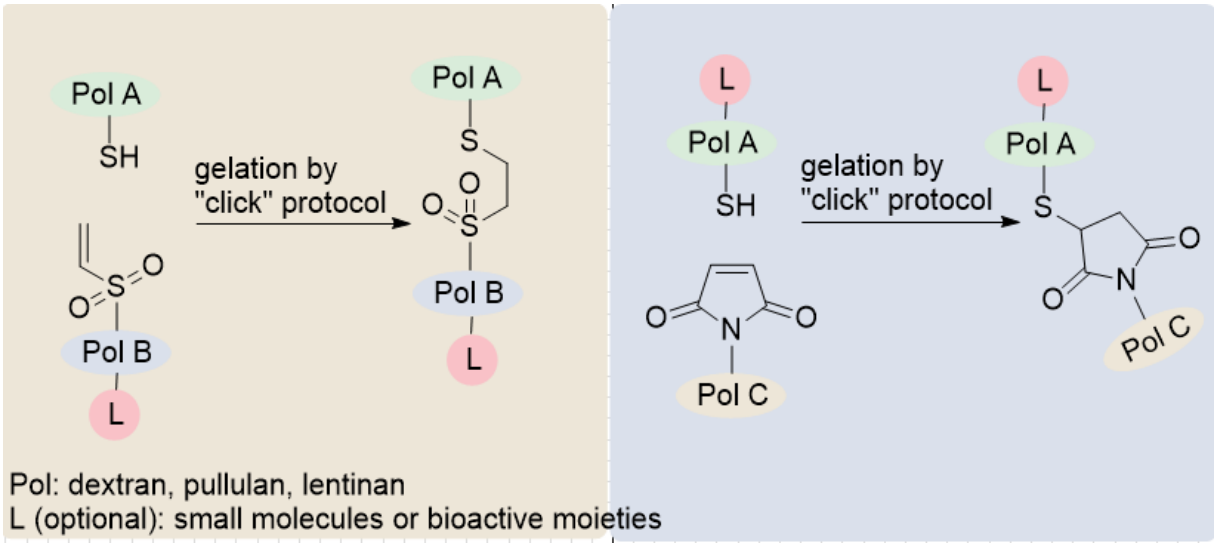

Figure 1

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In-Silico Tools for Analysis of Protein-Ligand Interactions I: Atom-specific Energy Decomposition Analysis

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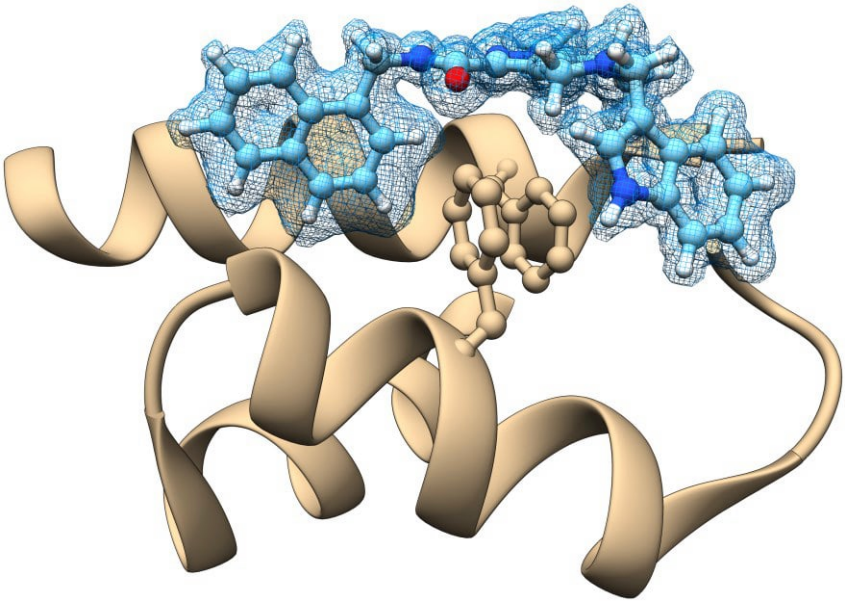
Energy Decomposition Analysis (EDA) is a valuable tool in quantum chemistry that allows one to understand the physical basis of interactions between molecules. Several algorithms have been put forth over the years, bringing out different views over the forces that bind molecules.[1-8] Most of these methods are compatible with Hartree-Fock or density functional theory, then the system size that may effectively be tackled is reasonably reduced. Treating systems of biological interest is completely out of question. Nevertheless, EDA algorithms would prove extremely helpful for medicinal chemists and structural biologists in their efforts to develop ligands into effective drug-lead candidates: a more systematic view over the effects of certain structural modifications on the protein-ligand interactions.

Here we present an extension of the van der Vaart-Merz EDA,[9,10] fully compatible with semi-empirical quantum chemistry. Due to the reduced computational cost, our new algorithm may be applied to large chemical systems, *e.g.*, of biological interest. We furthermore make our EDA atom specific.[10,11] This allows us to assemble powerful interaction specific maps, which bring a deep understanding of the particular role of certain atoms/functional groups for the interactions with the biological target. The new semi-empirical EDA[12] is available from our in-house semi-empirical package, *ULYSSES*.[13]



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In-Silico Tools for Analysis of Protein-Ligand Interactions: In-Pocket Optimization and a new Energy Decomposition Analysis

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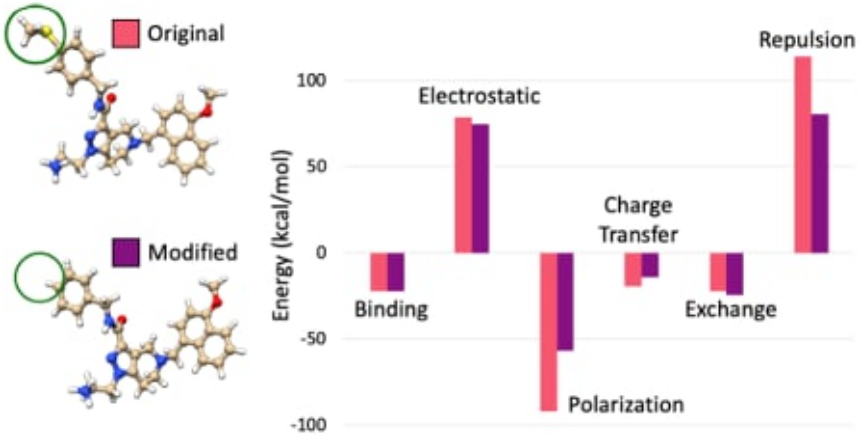
The protein-ligand complex forms the basis of structure-based drug design [1] Though available through different methods, the geometry of these macromolecular complexes is not a direct observable to the experimentalist. Electronic densities, chemical shifts or the Coulomb potentials are. Resolution and inconsistencies in the models converting experimental data into relative atomic coordinates may result in less qualitative structures. Quite often, molecular fragments or even full molecules may be distorted.

Understanding how protein and ligand interact allows medicinal chemists and structural biologists to optimize ligands according to protein. Techniques used to understand which interactions are at interplay include scaffold hopping and protein mutation. However, the results of modifications are commonly unpredictable, and binding may be lost. The result is a slow, low-success-rate and expensive endeavor. In our efforts to bring forward rational drug design, we introduce two computational tools within our in-house quantum chemical package, ULYSSES [2]. These parallel *in-silico* the techniques of protein mutation and scaffold hopping.

In-pocket optimization uses bias potentials [3-5], which allow the minimization of strain due to limitations of experimental data, while effectively retaining a specific conformation. It is a simple, yet highly efficient algorithm that may be coupled to any computational method in molecular physics. In-pocket optimization may be employed on ligands and proteins alike. By running targeted optimizations, it opens the doors to the quantification of group specific tension and the generation of scaffold hopped new ligands. These may be obtained with the maximum experimental information available to the computational scientist.

Energy Decomposition Analysis (EDA) [6], the theoretical equivalent to protein mutation, further enhances the potential of in-pocket optimization. Running a series of wavefunction optimizations, one decomposes the protein-ligand binding energy into several contributions, which go from pure electrostatics, polarization, repulsion, charge transfer, (electron) exchange, dispersion and solvation. Our EDA module is furthermore able to split each of these contributions into atom-atom or fragment-based interactions, which quantifies the contribution of different molecular groups for each type of interaction.



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Tailor-Made, Self-Healing Hydrogels For Biomedical Applications

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3D cell cultivation plays an invaluable role in a broad variety of applications in the medical field, especially in cell culture and tissue engineering. In recent years, research interest had been focused on modulating hydrogels as a cell cultivation platform.[1] Hydrogels are 3-dimensional, water-swollen networks of crosslinked polymers with mechanical properties that are similar to natural tissues.[2]

In order to control stem cell differentiation and enable cell migration, the elasticity compliance between cells and their hydrogel matrix is an important factor.[3–6] However, it remains a challenge to stabilize cells mechanically while enabling their mobility as they evolve.[7]

A promising solution for this problem are reversibly crosslinked hydrogels in which polymer chains are connected by physical interactions. In this study, biocompatible and reversible crosslinks are designed on the basis of host-guest interactions between the host molecule β-cyclodextrin (β-CD) and the guest molecule adamantane. By mixing adamantane-modified and β-CD-modified polymers in an aqueous medium, fast gel formation takes place. The permanent association and dissociation process of the two complexing molecules renders the hydrogel self-healing and therefore provides a flexible environment for cells (Figure 1).
Composition and dispersity of the polymers was controlled by NMR and SEC, respectively. Varying the crosslinker concentration had a strong influence on the mechanical properties of the generated materials. In particular, rheological characterization by amplitude and frequency sweeps showed enhanced stiffness and elasticity of the hydrogels with increasing crosslinking density. Thus, by changing the amount of adamantane and β-CD in the polymer, the elastic modulus can be fine-tuned to study how cells respond to defined mechanical inputs. Moreover, step-strain measurements demonstrated the self-healing properties of the hydrogels.
Cell viability assays in presence of the host and guest polymers using COS7 cells confirmed the very good biocompatibility of the system components. Hence, these tailor-made, self-healing, elastic hydrogels present a very promising approach for basic cell biological investigations and applications in tissue engineering.

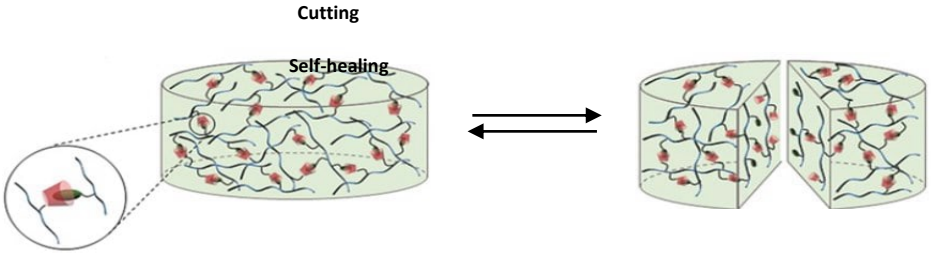

Figure 1: Cutting and self-healing of a host-guest hydrogel.[8]

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AI driven drug discovery using MD and structural data

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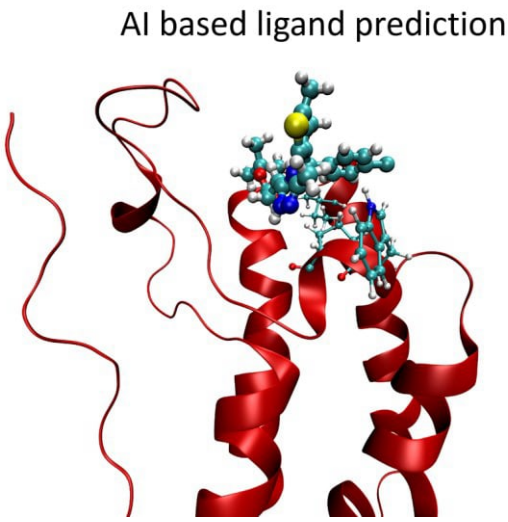
In silico approaches to predict small molecules for rational drug design rely on methods that calculate the binding affinity. Such approaches to estimate the binding free energy are either computationally too costly to screen large ligand libraries or make crude approximations in case of docking scores. We are tackling computational drug design with an AI approach that reverses the problem. We no longer require a given ligand molecule that is placed into the protein pocket in order to calculate an affinity but we ask the protein what ligand it would like to interact with in a predefined volume. The model is not only able to perform predictions based on structural data but also extends to dynamical, MD derived traces and thus incorporates structural adjustments and entropic effects. With such an approach e.g. the optimization process of a given ligand for experimental validation can be highly facilitated. The AI model will be an extremely valid tool for computer aided drug discovery and bioinformatics.



Preparation of 3,5-difluoro-2,4,6-tris(perfluorophenoxy)benzaldehyde for the synthesis and characterization of BODIPY (meso-trisperfluorophenoxyphenyl)

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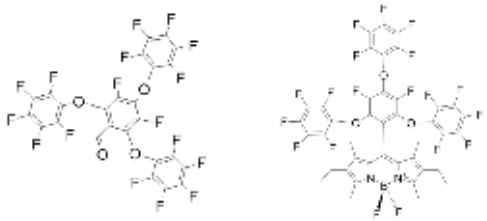
Photodynamic therapy (PDT) is currently used to treat malignancies and premalignant tumors. It is based on the accumulation of a photosensitizing molecule (PS) which, when excited by light at a proper wavelength, reacts with oxygen and generates oxidizing species (radicals, singlet oxygen, triplet species) in the target tissues, leading to cell death [1, 2].

BODIPY derivatives are relevant molecules in photovoltaic materials [3, 4] and fluorescent sensors [5, 6]. They are now emerging as photosensitizer candidates for photodynamic therapy, particularly halogenated derivatives with high triplet quantum yield [6-7].

The work aims to synthesize the BODIPY (*10-(3,5-difluoro-2,4,6-tris(perfluorophenoxy)phenyl)-2,8-diethyl-5,5-difluoro-1,3,7,9-tetramethyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-4-ium-5-uide*) and investigate its effect on lung cancer cells as a PDT agent. The aldehyde (3,5-difluoro-2,4,6 tris(perfluorophenoxy) benzaldehyde (1) was prepared from pentafluorobenzaldehyde and was converted to BODIPY (2) (scheme 1). The compounds were characterized by standard analytical techniques, including Uv-Vis spectroscopy, ^{1}H, ^{13}C, ^{19}F, ^{11}B NMR spectroscopies, and mass spectrometry.



(1) (2)

Scheme1:(3,5-difluoro-2,4,6tris(perfluorophenoxy)benzaldehyde and BODIPY (10-(3,5-difluoro-2,4,6 tris(perfluorophenoxy)phenyl-2,8-diethyl-5,5-difluoro-1,3,7,9-tetramethyl-5H-dipyrrolo[1,2-c:2',1'-f] [1,3,2] diazaborinin-4-ium-5-uide)

The results of the above compounds in PDT essays on several lines of lung cancer cells will be presented and discussed in the poster presentation.

Acknowledgments: The authors thank the Chemistry Department of the University of Coimbra and Institute of Biophysics and Institute for Clinical and Biomedical Research (iCBR).

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Targeting selective butyrylcholinesterase inhibition with purine nucleosides

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Alzheimer's disease (AD) is the most common form of senile dementia. Current treatment options rely mainly on inhibitors of cholinesterases. However, such treatment options are not effective in preventing disease progression. While acetylcholinesterase (AChE) activity decreases in specific brain regions as disease progresses, butyrylcholinesterase (BChE) activity is upregulated, making it an interesting target for drug discovery. Also, it has been demonstrated that selective inhibition of BChE improved memory, cognitive functions and learning abilities in mice.[1] Both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) present an interesting therapeutic target to tackle AD.
Over the years our research group has focused on a purine nucleoside scaffold and developed a new family of highly selective and potent cholinesterases inhibitors, the most active one presented a k_i = 50 nM for BChE showing an extraordinary selectivity (selectivity factor of 340) over acetylcholinesterase inhibition.[2] These promising results encouraged us to further investigate the role of glycosyl structure and configuration in promoting selective inhibition of BChE. Synthetic approaches to either glycosyl regioselective protection or deoxygenation followed by synthesis of the corresponding purine nucleosides are now presented affording promising analogues of the lead nucleoside, bearing a perbenzyl protected α-d-manosyl N^7 linked to a 2-acetamido-6-chloropurine.

Acknowledgement The European Union is gratefully acknowledged for the support of the project entitled "Diagnostic and Drug Discovery Initiative for Alzheimer's Disease" (D3i4AD), FP7-PEOPLE-2013-IAPP, GA 612347. The authors also thank the Portuguese Foundation for Science and Technology (FCT) for the PhD scholarship attributed to VC (SFRH/BD/90359/2012) and for the support of Centro de Química Estrutural (project UIDB/00100/2020). The Dirección General de Investigación of Spain (CTQ2016-78703-P), the Junta de Andalucía (FQM134), and FEDER (501100008530) are also acknowledged for financial support.

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Innovative methods for determine psychotropic substance and it's metabolites for clinical and forensic purpose

Renata Wietecha-Posłuszny

Novel aspect: Innovative methodology using small amount of biological materials

Abstract: The subject of this work is an overview of selected methods of sample preparation and analysis, in particular effective extraction techniques used for the isolation of psychoactive substances from biological materials used in toxicological-forensic analyzes. The process of preparing a sample for analysis is one of the first and critical stages of its analysis, which regardless of further phases of proceeding with the sample, determines the quality and reliability of the results of chemical analysis. It is assumed that the sample preparation stage is the source of approx. 60% of the sum of all errors committed during the entire analytical course. Therefore, the sample preparation step is absolutely crucial for the results of analysis of organic compounds in such complex matrices as human body fluids or tissues. The most popular technique for cleaning biological samples is the extraction process, which allows the isolation of analysts from the primary matrix, and then their transport to the so-called secondary matrix. During this process, the composition of the sample matrix is significantly simplified and is often more suitable for the further analysis. Moreover toxicological and forensic analysis covers the analysis of traces found direct at crime scenes. Blood stains are one of the traces most frequently encountered in forensic practice. Due to their potential role as crime evidence, their analysis ought to be performed fast and with the use of minimally contact and minimally destructive methods. The application of spectroscopic methods: Hyperspectral Imaging in the VIS-NIR and SWIR range, and DiP Mass Spectrometry, in the toxicological and forensic analysis of blood samples for the purposes of blood stains' age determination and qualitative analysis of benzodiazepines were presented.

Acknowledgments:
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Harmonic nanoparticles functionalization with proteins for cancer active targeting

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Nowadays, cancer is a major health burden and has become the second leading cause of death in industrialized countries. Cancer mortality can be reduced through early detection and appropriate selective treatment. Respectively, traditional imaging techniques and cancer treatments lack sensitivity for early detection and show poor specificity, causing adverse side effects.[1] Nanomedicine has emerged as an optimal tool to support early diagnosis and targeted tumor therapy. Stimuli-responsive nanocarriers allow the simultaneous imaging, controlled release of payloads and active targeting, for a theranostic approach.[2]

We herein propose novel strategies for the surface functionalization of harmonic nanoparticles (HNPs, e.g. $LiNbO_3$, LNO), known for their efficient non-linear optical response by generation of second and third harmonic signals upon ultrafast laser irradiation.[3] These NPs can be functionalized with i) imaging probes for multimodal imaging; ii) photocaged cargos for controlled drug delivery; and iii) targeting ligands for active targeting of neoplastic cells and tumor sites. In this project, an inorganic silica-based coating was first achieved on LNO NPs to improve their biocompatibility and decorate their surface with reactive carboxyl groups. These were post-functionalized through amide bond covalent conjugation to avidin and neutravidin. Several quantification methods, such as fluorescence spectroscopy and BCA assays, were implemented to quantify the amount of grafted protein and assess the residual ability of the protein to subsequently bind biotinylated ligands. Finally, first attempts at immobilization of anti-EGFR biotinylated antibodies to the surface of avidin-functionalized NPs and characterization of the resulting conjugates are presented.

The long-term perspective of this project is to use protein-coated nanoparticles as theranostic nanoplatforms, focusing on the active targeting feature, through the use of monoclonal antibodies. Several grafting strategies, apart from avidin-biotin biotechnology, will be investigated. Overall, these nanocarriers, decorated with targeting ligands, anti-cancer drugs and imaging probes, will potentially combine early detection and *in vivo* cancer treatment.

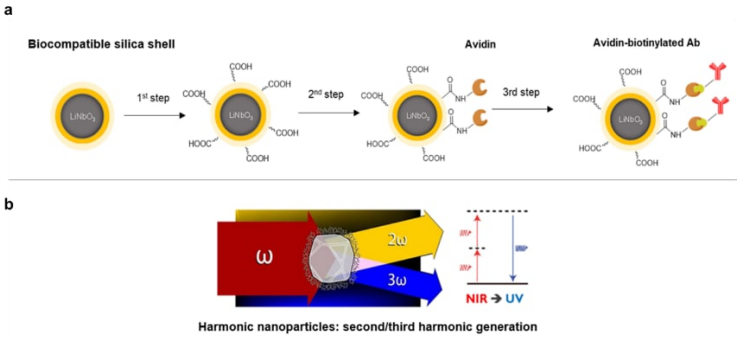

Figure. a) Schematic representation of protein functionalization steps of harmonic nanoparticles for cancer active targeting. b) Non-linear optical properties of harmonic nanoparticles: second/third harmonic generation.

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Fabrication of bovine serum albumin based biocomposite for the protein sensing application

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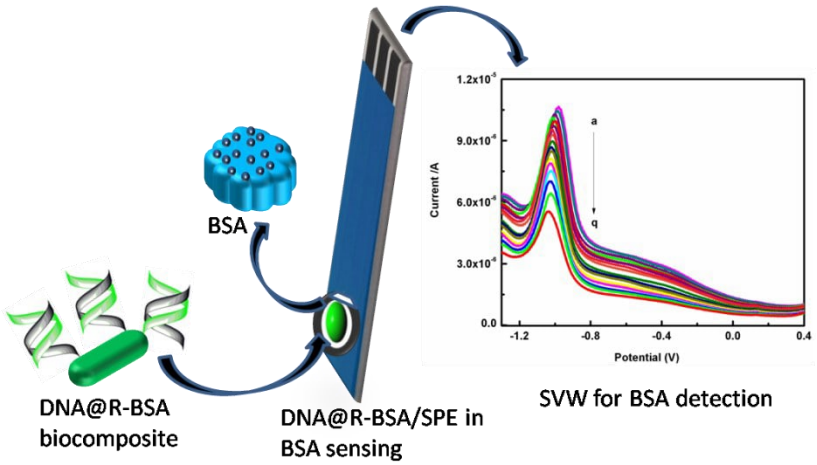
Recently, the increase in interest of protein detection based on electrocatalysis of biomolecules has garnered greater attention for signal transduction filed [1, 2]. Here, the DNA modified Bovine serum albumin microcapsules (DNA@R-BSA) utilized in the protein detection. To achieve effective biocomposite, the functionalities of BSA were tuned by using Sodium borohydrate as a reducing agent at pH 7.2. Therefore, the presence of certain amount of positive amino acid residues in negative protein results the adsorption towards DNA due to electrostatic interaction. The structural modification of BSA and adsorption with DNA further characterized by Scanning Electron microscopy, X-ray Diffraction (XRD) analysis, Fourier Transform-Infrared (FT-IR) spectroscopy. The prepared biocomposite of DNA@R-BSA is utilized as selective probes for the detection of BSA by recording Square Wave Voltammetry (SWV) signals. The synergistic effect caused from –OH, –COOH and thiol groups of R-BSA and thymine group, sugar molecules and phosphate groups of DNA are responsible for sensitive detection of amino acid residues in BSA protein. The sensitivity of the hybrid biosensor was significantly improved the BSA detection over a wide concentration range from 1×10^{-20} g/mL to 1×10^{-4} g/mL with a very low detection limit of 2.18×10^{-21} g/mL The results confirm the DNA modified R-BSA based strategy may have potential applications for the detection of protein content in real time application.



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Functionalization of harmonic nanoparticles with lanthanide chelates for multimodal imaging applications

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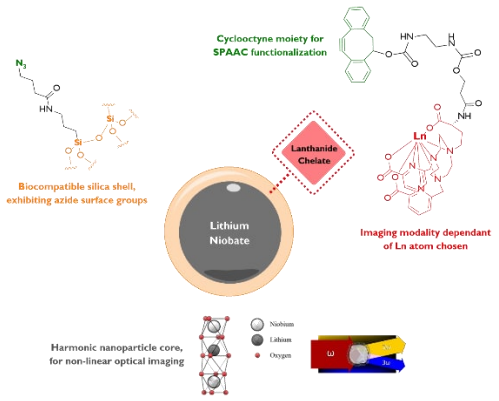
Nanomaterials have attracted high interest in the biomedical field for their numerous favorable properties, including their large surface area, their potential for multi-functionalization, and their long blood circulation time compared to small molecules. [1] Nanoscale systems integrating multiple imaging modalities allow for precise diagnosis, which could serve in the field of oncology to detect malignancies at an early stage of their development and thus increase the success rate of therapeutic interventions. The inherent shortcomings of individual imaging techniques can be overcome by their synergistic combination within a single nanoparticle platform, thereby providing simultaneously high spatial resolution, penetration depth and sensitivity.

Harmonic nanoparticles (HNPs), are metal oxide nanomaterials characterized by a crystalline structure lacking inversion symmetry (e.g $LiNbO_3$, LNO). This unique property allows them to exhibit a non-linear optical response by generating second- and third- harmonic signals upon laser irradiation, with long-term photostability and spectral flexibility. [2] These materials have thus emerged as attractive novel probes for optical bioimaging. Although advances in the field of optical imaging are now giving access to penetration depths in the order of the millimeter thanks to new laser sources, [3] this modality is still not adapted for whole-body imaging. Magnetic resonance imaging (MRI) and X-ray computed tomography (CT) are more adapted for the acquisition of anatomical pictures due to their high tissue penetration capacity. [4]

We aim at functionalizing LNO HNPs with various lanthanide chelates to explore their multimodal capabilities. LNO HNPs are first coated in a silica shell using a water-in-oil microemulsion approach to improve their biocompatibility and display surface reactive azides for post-functionalization. The lanthanide chelates, designed with a cyclooctyne moiety, are then grafted on the coated LNO HNPs by strain-promoted azide-alkyne cycloaddition (SPAAC). Through the variation of the lanthanide atom, different imaging modalities can be achieved such as MRI with gadolinium, CT with ytterbium, and various luminescence wavelengths with europium and terbium. We thus aim at producing multimodal HNPs with complementary capabilities for cancer diagnosis.



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Aryl piperazine ligands as novel 5-lipoxygenase inhibitors. Biological and computational studies

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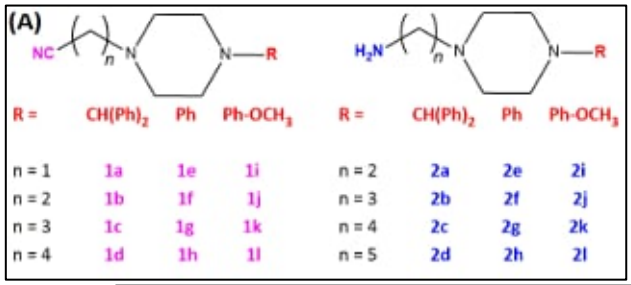
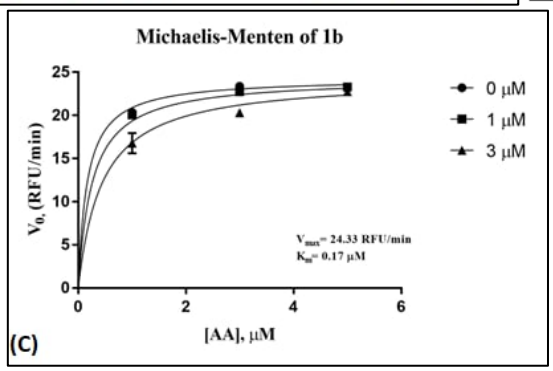
Inflammation is a natural response of the immune system to injuries or infections in the body. Diverse inflammation mediators such as leukotrienes (LTs) are biosynthesized during the process, for example through the catalytic activity of the 5-lipoxygenase (5-LOX) enzyme.[1] The LTs are involved in some diseases, such as Covid-19.[2] Different compounds have been described in the literature as 5-LOX inhibitors, such as the well-known zileuton, a drug accepted by the FDA for its use in the treatment of asthma, but its prolonged use causes liver toxicity. In the search for promising non-toxic 5-LOX inhibitors, compounds that possess a piperazine fragment have shown properties like anti-inflammatories. We present a new family of aryl piperazine ligands and their biological evaluation against 5-LOX.



(B)

Ligand	IC_{50} (μM)	Ligand	IC_{50} (μM)
1a	15.05	**2b**	8.63
1b	2.34	**2c**	5.3
1g	2.25	**2f**	2.45
1h	6.62	**2g**	3.27
1j	23.36	**2h**	5.89
1k	3.04	**2i**	9.12



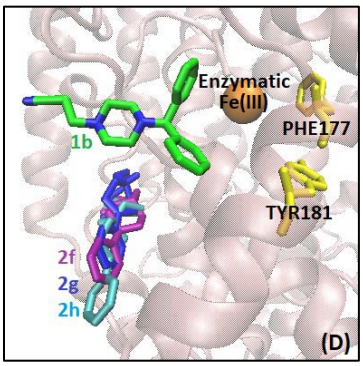


Figure 1. Ligands synthesized and evaluated in this work **(A)**. Most representative ligands and their IC_{50} values **(B)**. Michaelis-Menten plots of **1b** inhibition against 5-LOX **(C)**. Docking studies (*Active Site of 5-LOX*) of ligands **1b**, and **2f-2h (D)**.

The IC_{50} was determined. The most representative results are shown in **Figure 1.B**. In general, both the cyano and the amino derivatives presented engaging inhibitory activities. Additionally, the ligand **1b** showed a mixed mechanism, with a K_i for 5-LOX of 1.77 ± 0.46 μM. Therefore, **1b** could bind both the free enzyme and the enzyme-substrate complex.

Also, computational studies were carried out. All the aryl piperazine ligands showed optimal binding energies in the active site of 5-LOX (-4.0 to -7.5 Kcal/mol). Interestingly, ligand **1b** was located even closer to this enzymatic region where we can find the residues **Phe177** and **Tyr181** (**Figure 1.D.**), which have been reported as a mobile lid that controls the access of the substrate to the catalytic iron.[3] This suggests that **1b** could prevent the entry of arachidonic acid by blocking access to the active site. These results are supported by the *in-vitro* assay, where we determined that **1b** is a mixed inhibitor.

S.T. acknowledges to Proyecto POSTDOC_DICYT, Código 022141MC_POSTDOC (M.M.), Vicerrectoría de Investigación, Desarrollo e Innovación, Universidad de Santiago de Chile; and FONDECYT Chile No. 1200378 (C.M.).

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Synthesis and characterization of Iron-based Metal-Organic Frameworks from terephthalic acid derivates for Cancer Photodiagnostic and Magnetic Hyperthermia Therapy

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Metal-organic frameworks (MOFs) are inorganic-organic solids constituted by a wide range of metal ions or clusters and organic linkers. These components are linked through coordination bonds forming porous crystalline structures, which can acquire different dimensionalities. The type of metal ion and organic ligand influence the topology of the MOFs as well as their chemical functionality. [1,2] This choice also affects its adsorption properties and the interactions with other molecules. These materials have applicability in catalysis, gas storage, selective molecular adsorption, and separation. Due to their high surface area, easy synthesis pores with different sizes and good chemical stability become MOFs more attractive in areas related to medicine, especially in biosensing, imaging, and drug delivery. [3]

Magnetic Hyperthermia Therapy (MHT) is an alternative approach for cancer treatment based on the use of magnetic nanoparticles to generate heat when exposed to an alternating magnetic field (AMF). The effect is an increase in the temperature in the tissue, resulting in cancer cell death. The heat production will depend on the magnetic behaviour of the material used. [4]

In this context, we synthesized and characterized iron-based metal-organic frameworks from terephthalic acid derivates for future applications in cancer photodiagnosis and magnetic hyperthermia therapy.

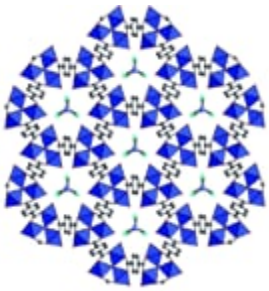

Figure 1. Structure of MOF-235 (Fe, blue; O, red; Cl, teal; C, grey).[5]

Using the solvothermal method, the samples were prepared using a Teflon reactor in an oven. After cooling at room temperature, the crystals were collected, washed, and dried. Using single crystal and powder X-ray diffraction, the structures were determined. The thermal, microscopic, and magnetic properties will be presented and discussed in this presentation.

Thanks to ChemMat PhD program from the Fundação para a Ciência e Tecnologia (FCT, MEC, Portugal) for their general financial support (PD/BD/150440/2019) (SFRH/BPD/103103/2014), and to Centro de Química (UID/QUI/00313/2013) of University of Coimbra. The authors thank also to C2TN, (UID/Multi/04349/2019) (IST, UL) and Trace Analysis and Imaging Laboratory (TAIL-UC) funded under QREN-Mais Centro Project ICT_2009_02_012_1890.

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Synthesis and characterization of "ferroleutón", the first organometallic complex of the drug zileuton: *in-silico* and *in-vitro* studies against human 5-Lipoxygenase

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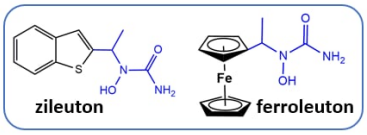
Chronic inflammation caused by overexpression of 5-lipoxygenase enzyme (5-LOX) has become a major health problem worldwide because it contributes to the development of cancer, autoimmune and neurodegenerative diseases.[1] 5-LOX present a non-heme iron into its catalityc site (varies between inactive ferrous (Fe(II)) and active ferric (Fe(III)) states), for which inhibitors have been designed to interfere with the metabolization of the substrate (arachidonic acid to leukotrienes), which have been classified according to their mechanisms of action like redox, iron chelating, non-redox and allosteric inhibitors (eg NDGA, zileuton, ZD-2138, AKBA, respectively), and of which only zileuton has been approved by FDA, however, adverse effects such as, hepatotoxicity associated with benzothiophene fragment, have motivated the design of new structures maintaining the pharmacophore fragment N-hydroxyurea.[2]

In that context, organometallic compounds have stood out for their better activity against biological receptors, presenting applicability as anticancer, antifungal, antibacterial, among others, highlighting ferrocene ($Fe(\eta^5\text{-}C_5H_5)_2$, sandwich complex), due to its well-defined electronic properties (reversible redox pair Fe(III)/Fe(II)), synthetic adaptability, low toxicity, stability in air and in aqueous media, have given great applicability in biological media.[3]

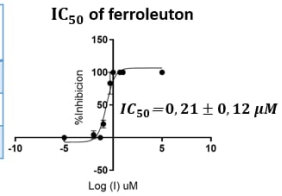
With regard to the aforementioned, this work presents the synthesis and characterization of a new complex derived from ferrocene, functionalized with the N-hydroxyurea pharmacophore unit of the inhibitor zileuton, a complex which we have named ferroleuton. IC_{50} values in the micromolar order of ferroleuton (IC_{50}=0.21 µM) showed a positive effect after incorporation of the organometallic fragment ($IC_{50\ zileuton}$=0.92 µM). Docking and molecular dynamics showed a preferentially coordinating mechanism, in the same way that has been described for its analog zileuton. Additionally, antioxidant capacity and electrochemical studies (in organic solvente and buffer) indicated a possible mechanism of enzymatic deactivation mediated by a redox pathway, in addition to the aforementioned chelating mechanism.



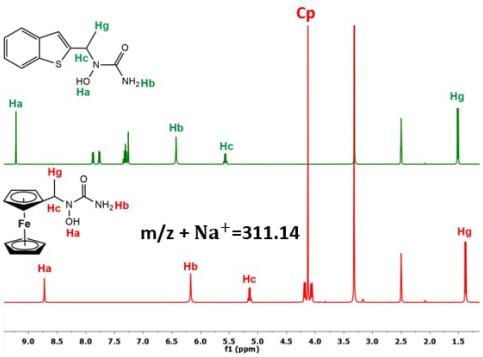
Biological evaluation

Compound	% inhibition	IC_{50} (μM)	$DPPH$ (%)
zileuton	75.5	0.92	65.2
ferroleuton	100	0.21	95.4
Trolox	n.d	n.d	96.5

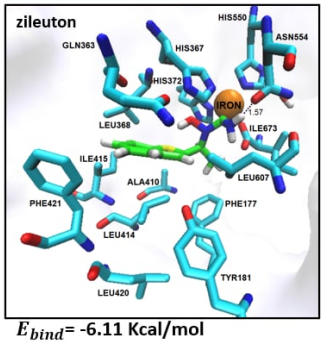
n.d: not determined



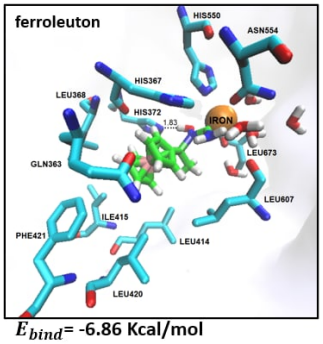
Characterization



in-silico studies



E_{bind}= -6.11 Kcal/mol



E_{bind}= -6.86 Kcal/mol

Acknowledge: FONDECYT-Chile 1200378 (C.M.) and 1191130 (F.G.); FONDECYT-Postdoctoral 3200644 (EF).

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New Concept for the Development of a Thermal Release Strategy of *locked nucleic acids* for Gene Therapy

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The increasing incidence of cardiac insufficiency represents a serious health problem in our population. The healing of heart tissue after a heart attack (myocardial infarction) often causes large areas of scarring. [1] Due to these scars in the heart tissue, cardiac insufficiency can develop. New approaches for therapy development are non-coding ribonucleic acids (ncRNAs). These code for molecules that are not translated into proteins but often have a gene-regulatory effect. This includes RNA molecules with a length of about 21 nucleotides (microRNAs) and the long non-coding RNAs (lncRNAs). [2]

To improve the delivery of antisense oligonucleotides (ASO) targeting ncRNAs to cardiac cells, aim of this work is to design new polymer-based superparamagnetic iron oxide nanoparticles (SPIONs). [3] The idea behind is to couple a modified ASO named locked nucleic acid (LNA) to the nanoparticle by a newly designed linker allowing a heat-dependent release of LNAs. Therefore, it is necessary to choose nanoparticles that are biocompatible, generate and release heat by setting an alternating magnetic field (AMF) and that can be easily functionalized. [4] A functionalization represents a connection point to the LNA and enables an increasing number of active binding sites thus a dose-reduction might be possible. This connection has to be stable while transported through the organism but precisely cleavable at the site of action. Hence, a thermolabile conjugate is used that releases the LNA at a certain temperature when inducing an AMF, whereas the linker molecule itself is not supposed to have any toxic or side effects. [5,6] The most promising candidates of nanoparticles with polymer coating as well as different conjugates that fulfil the requirements were separately tested *in vitro* regarding cell viability and toxicity. When auspicious nanoparticle systems have been selected, the coupling of the individual parts will be approached. Prior to animal experiments, the coupled nanoparticles will be fully characterized *in vitro* to determine the efficiency of LNA release and ncRNA knockdown in a dose-dependent manner in addition to the tolerance of the nanoparticle-based therapeutic approach.

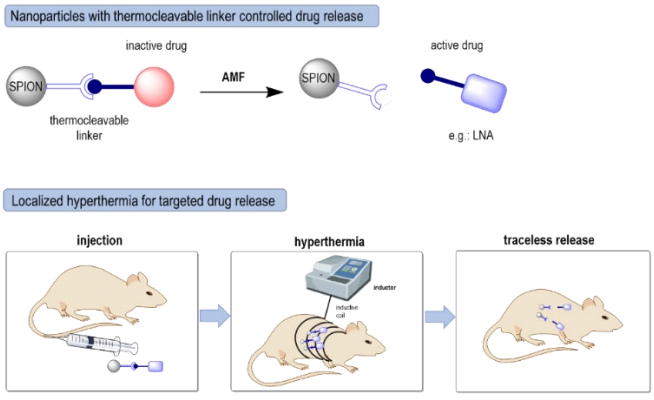

Figure 1: Schematic representation of nanoparticles with thermocleavable linker controlled drug release (top) and localized hyperthermia treatment for targeted drug release (bottom).

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Insights into the cytotoxic properties of fluorescent silver camphorimine complexes for bone cancer therapy

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Bone diseases are a serious health concern due to the impact they have in the quality of life [1]. In the case of bone cancer (BC), treatment strategies are sometimes compromised by inflammatory processes that decrease its efficiency. Therefore, alternatives that concomitantly encompass anti-inflammatory and/or anti-cancer properties are most welcome to improve cancer bone treatment efficiency.

Conventional treatment of BC consists of a combination of surgery and chemotherapy (*e.g.* doxorubicin, cisplatin). However, these drugs induce severe side effects and resistance and no anti infection effects. Based on the antimicrobial properties of silver camphorimine complexes, we now address their anticancer activity towards bone cancer cells (HOS). Two complexes $[Ag(NO_3)L^A]$ (**1**) and $[Ag(NO_3)(L^B)_2]$ (**2**) were selected and synthesized [2,3] and their chemical, morphological and anticancer properties against bone osteosarcoma HOS cells [4] evaluated. The possibility of building of a drug delivery platform for targeting therapy towards bone cancer using hydroxyapatite (HAP) composites is under assessment. The choice of HAP is due to its ability to act as a drug carrier and present excellent biocompatibility. [5]

The morphology and homogeneity of the complexes (**1**, **2**) were studied by SEM and elemental analysis. The cytotoxicity towards HOS cell lines was assessed through evaluation of their IC_{50} values after 24h exposure. Both compounds display high cytotoxic activity (**1**, IC_{50}, 3.08±0.9 µM; **2**, IC_{50}, 12.7±4.5 µM), although **1** performs slightly better than **2**. Protocols for the identification of cellular uptake by fluorescence spectroscopic techniques based on the intrinsic fluorescence of the complexes are under development.

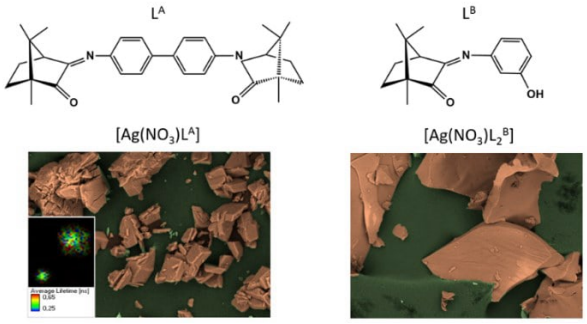

Figure 1 – SEM and fluorescence images of the complexes **1** and **2**, respectively.

Acknowledgments: Fundação para a Ciência e Tecnologia-FCT, through CQE (UIDB/0100/2020, UIDP/00100/2020) and Institute of Molecular Sciences (LA/P/0056/2020) projects and a PhD Grant to Joana Costa (UI/BD/152244/2021).

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Glycoconjugates as potential delivery agents for Boron Neutron Capture Therapy

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Boron neutron capture therapy (BNCT) is a non-invasive cancer targeting therapy. The working principle of BNCT is based on the cell-destructive effect achieved when boron-10 atoms are irradiated with low energy thermal neutrons [1]. The bottleneck of BNCT thus far have been the neutron sources, however, with the recent development of accelerator-based neutron sources and their implementation in clinics, this has redirected the focus to the optimization of boron-10 delivery agents for BNCT.

We have focused our efforts on the development of a GLUT1-targeting strategy to BNCT [2,3]. This approach may yet outperform the current delivery strategies in clinical use. Our preliminary studies on the biochemical premises of the approach support these thoughts (Figure 1.). At the conference we will present our recent work on the synthesis and assessment of *ortho*-carboranylmethyl glycoconjugates.

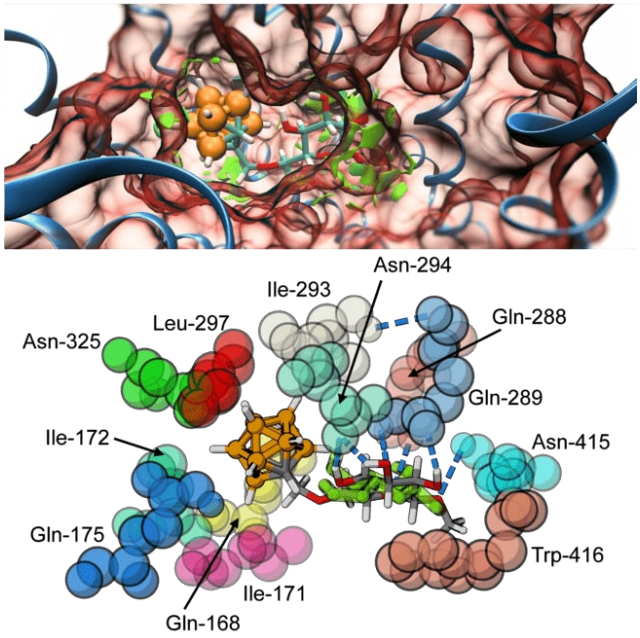

Figure 1. Computational studies emphasizing the molecular recognition events unfolding between the transporter and the ligand.

We would like to thank the Jane and Aatos Erkko foundation, the Chemistry and Molecular Sciences graduate school, the Finnish Pharmaceutical society, the Cancer foundation, the Ruth and Nils-Erik Stenbäck foundation, the University of Helsinki research funds and Orion Research Foundation for financial support.

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Redesigning Clozapine for the Potential Treatment of Melanoma Brain Metastases

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The drug approval process is divided into different phases in order to prove the safety and dosage of novel drugs, by repurposing already approved drugs the first phase of the process can be skipped, cutting down the time and monetary costs.
In the last years, it has been proven that several antipsychotic medications have a cytotoxic effect on cancerous cells, by stopping the G0/G1 phase and by doing so reducing the proliferation rate or can be used as chemo/radiosensitizers by avoiding drug efflux.[1]

Clozapine, a treatment-resistant schizophrenia treatment, whose drug target resides in the brain has also been proven to have this cytotoxic effect on cancerous cells.[2] Since its drug target resides in the brain, the small lipophilic molecule needs to cross the blood-brain barrier (BBB) to have an effect. Clozapine can be used as a PET tracer when radiolabeled to study the BBB crossing and the interaction with the drug target.

Clozapine was tested on three human Melanoma Brain Metastases (MBM) cell lines and an astrocyte cell line. The total synthesis of Clozapine was redesigned to permit a Structure-Activity relationship (SAR) study of several analogues and the testing of the analogues on the same four cell lines. The redesign of the total synthesis of Clozapine and the development of analogues allows the late-stage functionalization by introducing $[^{11}C]CH_3I$ into the structures to further study the biological activity, both *in vitro* and *in vivo.*

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Resveratrol theranostic microsystems designed for *in vitro* laser-induced treatment in diabetic retinopathy

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An enormous burden on the healthcare system is caused by eye diseases that affect people's quality of life. Diabetic retinopathy (DR), one of the most common eye pathologies, can be triggered by high blood sugar levels that affect the retina. Unfortunately, the current treatments with anti-VEGF agents (bevacizumab, ranibizumab, aflibercept) or corticosteroids associated with laser photocoagulation manifest side effects that can harm patient health. In this context, the development of targeted delivery systems is necessary.

The aim of this study was to create a microsystem which targets the VEGF protein in the human retina and allows a controlled and local release of resveratrol (Rv), a polyphenol with therapeutic potential, using an external source of non-invasive irradiation. The delivery microsystem was created by the Layer-by-Layer technique. Alternate layers of polystyrene sulfonate (PSS) and polyethyleneimine (PEI) polymers were added on to a calcium carbonate core, containing inside Rv. Fluorescein isothiocyanate (FITC) and gold nanoparticles entered the microcapsule structure and their surface was decorated with anti-VEGF antibodies.

A spherical shape, an average size of 2.5 µm and an encapsulation efficiency of 100% were obtained. Using confocal fluorescence microscopy, the internalization and localization of the microcapsules were monitored inside D407 human retinal pigmented epithelial cells. Ex-vivo irradiation at 785nm and 808nm demonstrated good photothermal performance of the microsystem. Cell viability, as measured by WTS-1 reagent, was significantly increased in Rv-treated glucose-induced stress cells after applying a dose of 10 µl of Rv.

In conclusion, our results reveal a new possible therapeutic approach in diabetic retinopathy management.

Acknowledgement: This research was funded by the Romanian National Authority for Scientific Research, CNDI - UEFISCDI, project number PN-III-P2-2.1-PED-2019-4558, contract no. PED 369/2020.

New 5(6)-methyl-1*H*-benzimidazol-2-yl hydrazones: synthesis, combined evaluation of the anthelminthic and antioxidant activity and performed quantum-chemical calculations

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Parasitic infections in humans, caused by parasites of the genus *Trichinella* play a significant role in human pathology and are widespread in tropical or subtropical countries [1]. The chemotherapy is the main direction in the control of parasitic morbidity due to the lack of antiparasitic vaccines but the arsenal of anthelmintic drugs is small [2]. In many cases due to this disease there is tissue damages and immune system dysfunction that could be related to decrease of the antioxidant capacity of the organism and presence of oxidative stress [3]. Therefore, antioxidants are expected to help protecting the hosts against the injurious factors. The benzimidazoles are a large chemical family widely used in veterinary and human medicine to treat helminthic infections such as the benzimidazole carbamates (Albendazole and Mebendazole) [4] as well as an appropriate structural platform for antioxidant discovery efforts.

In view of the above mentioned, we present the design and synthesis of new benzimidazole derivatives that combine anthelmintic and antioxidant actions in one molecule. The synthesis of the 5(6)-methyl-1*H*-benzimidazol-2-yl hydrazones was achieved by a multi-step reaction pathway by using o-phenylenediamine, hydrazine hydrate and broad series of hydroxyl- and methoxyl-arylaldehydes as reagents.

The anthelmintic activity of the target hydrazones was evaluated *in vitro* on encapsulated *Trichinella spiralis larvae* in concentrations 50 μg/mL and 100 μg/mL incubated after 24 h and 48 h. Compounds containing two or three hydroxyl groups demonstrated the strongest effect (100 % effectiveness) after 24 hours incubation period in both concentrations.

The antioxidant and radical scavenging properties of the new designed compounds were studied *in vitro* towards stable free radicals – ABTS and DPPH. The potency of the compounds to decrease the oxidative molecular damage of biologically important molecules in model systems using as oxidisable substrate deoxyribose and lecithin has been determined. The tested compounds demonstrated potent radical scavenging activity (RSA%) in all systems.

The molecular structure and tautomeric isomers were analyzed by density functional theory (DFT) calculations. In addition, several mechanisms of radical scavenging activity (HAT, SET and RAF) were evaluated. The ability of the studied compounds to deactivate different free radicals were modelled by transition states involving attack by •OCH3, •OOH and •OOCH3, at all reactive site. It was also found that the predicted activities of the studied compounds are in good correlation with the experimentally observed antiradical activity.

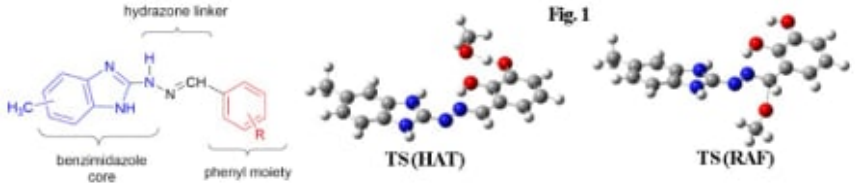

Fig. 1

Thanks are due to the National Science Fund of Bulgaria, Contract КП-06-Н39/4, for financial support of this work.

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Innovative drug-loaded scaffolds for post operatory infections treatment

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Currently, bone affections have become a severe problem for healthcare systems worldwide because of the increased number of cases. The usual treatment method is to use bone transplant procedures using allografts and autografts. Considering that a surgical procedure is needed, a new problem derives from the use of bone grafts: the potential postoperative infections [1][2]. Recently, composite hybrid scaffolds have attained a great interest for drug-delivery applications because of the biocompatibility of the polymeric matrix and because of the organophilic character of the clay used in the material. Montmorillonite (MMT) is a smectite group of minerals with a layered structure. This layered structure reinforces the material`s mechanical properties and allows antibiotics to be easily intercalated into its structure and released over time [3].

The present study aims to develop a freeze-dried scaffold based on MMT/gentamycin sulfate/biocompatible polymers for the treatment of post operatory infections. The biopolymers used for the scaffolds were chitosan (CS) and gelatin. To obtain the systems, the gentamycin sulfate in different concentrations (5% or 10% wt.) was first intercalated into the MMT layers by inflation method [4]. The functionalized MMT powders were further dispersed into the polymer solutions: 2% wt. CS solution in acetic acid 2%, or 2% wt. gelatin solution in water. The obtained mixtures were cross-linked with glutaraldehyde aqueous solution 1% wt., maintained over night at 4°C, then freeze-dried. The powders and obtained scaffolds were morphological and structural characterized by means of X-ray diffraction, scanning electron microscopy, and Fourier transformed infrared spectroscopy. Also, the absorption capacity of the porous scaffolds was assessed in simulated body fluid.

Based on preliminary results, the obtained scaffolds can be considered prospective materials for use in the treatment of post operatory infections.

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19-Oxygenated steroidal D-homo lactones: synthesis, *in silico* ADME and *in vitro* screening of binding affinity to ER, AR or aromatase

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Breast cancer is one of the leading causes of death in women worldwide, and treatment options include surgical removal, chemotherapy and radiotherapy. In addition, because 80% of breast cancers are estrogen-dependent, hormonal therapy is often applied to inhibit cancer cell proliferation stimulated by estrogens. Hormonal therapy is achieved using antiestrogens and/or cytochrome P450 aromatase inhibitors. The aim of this research was to synthesize potent steroid inhibitors of aromatase that do not possess hormonal activity. Taking into account the structures of known potent inhibitors as well as the structure of the aromatase active site, we synthesized and tested a series of 19-oxygenated steroidal D-homo lactones. The starting compounds for synthesis were previously synthesized steroidal halohydrines [1, 2]. In the first synthetic steps, these compounds were transformed into 6,19-epoxy derivatives, that by reductive opening provided 19-hydroxy products, further subjected to oxidative transformations. Eight novel 19-oxygenated steroidal D-homo lactones were synthesized and their *in silico* ADME properties were determined using the SwissADME online tool. *In vitro* cytotoxicity of the synthesized steroid derivatives was tested using an MTT assay on six tumor and one normal human cell line. Furthermore, the relative binding affinities of each 19-oxygenated steroidal D-homo lactone to the ligand-binding domains (LBDs) of androgen receptor (AR) and estrogen receptor (ER) α and β isoforms, was measured using a fluorescence-based assay in yeast [3]. None of the compounds showed significant binding to the LBDs of the tested steroid hormone receptors at 10 μM. Since aromatase inhibition is clinically approved for the treatment of breast cancer in postmenopausal women, we also evaluated binding of one steroid derivative for recombinant aromatase by monitoring Soret band shifts upon addition of ligand. Addition of ligand induced a red-shift in the Soret band maximum, consistent with type II spectral changes characteristic for aromatase inhibitors. Together our results suggest that 19-oxygenated steroidal D-homo lactones have potential for the treatment of hormone-dependent cancers.

The authors acknowledge financial support of the Ministry of Education, Science and Technological Development of the Republic of Serbia (Grant No. 451-03-9/2021-14/ 200125). This presentation is also sponsored by the Faculty of Sciences award for the best young scientist.

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Studies towards the Development of Small Molecule Inhibitors of Chorismate Synthase (CS)

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The shikimate pathway plays a crucial role for the biosynthesis of aromatic amino acids, alkaloids and plant pigments, in prokaryotes, fungi and plants. The central metabolite chorismate is synthesized through seven enzymatic steps starting from erythrose-4-phosphate and phosphophenol pyruvate, which cannot be bypassed through any other enzyme. Therefore, inhibition of the shikimate pathway can lead to cell death, thus accounting for its toxicity against prokaryotes, fungi and plants. The fact, that the shikimate pathway is absent in mammals makes it a promising target for the development of antibiotics and fungicides. Recent investigations by Seixas and coworkers [1] using a combination of virtual screening and molecular dynamics revealed potent inhibitors for *Paracoccidioides brasiliensis*, which feature a naphthalene backbone. Recombinant *in vitro* and *in vivo* chorismate synthase binding to *P. brasiliensis* was confirmed for the identified hit compound. [1,2]

In this work we aim to take advantage of the previously identified hit compound in order to improve their affinity to chorismate synthase through structural modifications. Following this, we want to establish a structure-activity-relationship (SAR) around a certain chemotype and develop more affine compounds. Therefore, we synthesized first generation inhibitors with K_d values up to 19 µM. To further improve their affinity we want to develop a new second generation of small molecule inhibitors, which will also be tested in biological experiments (inhibition, binding, crystallization, *in vitro*, as well as cytotoxity studies), thus enabling to assess their pharmacological potential.

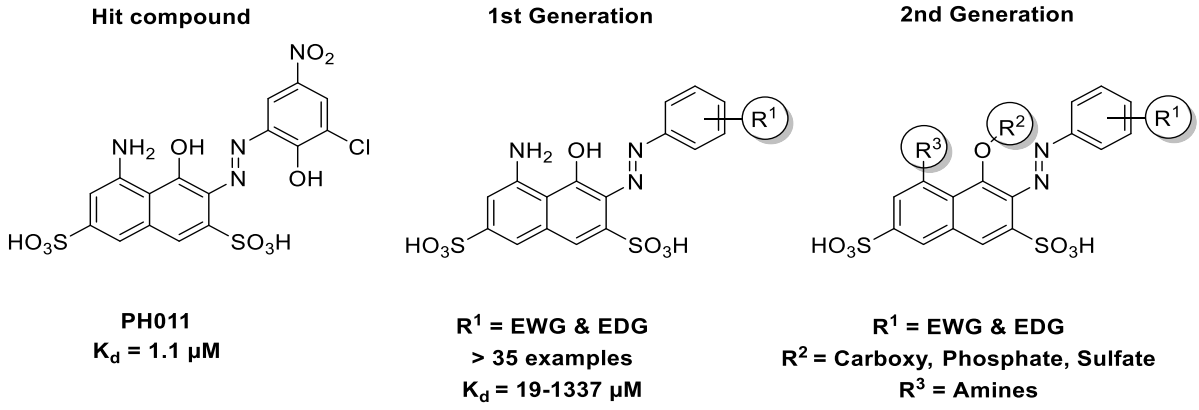

Figure 1. Hit structures [1] and planned structural modifications to improve their affinity to CS.

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Innovation in the Development of Polyphenol C-Glucosides with Disease-Modifying Effects against Alzheimer's Disease

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Alzheimer's Disease (AD) and other dementias are ranked by the World Health Organization as the 7th leading cause of death worldwide [1]. Around 55.2 million people are currently living with dementia and this number is expected to rise to 78 million people by 2030 [1,2]. Despite this disconcerting estimate, only one disease-modifying drug — the monoclonal antibody aducanumab — is currently approved to treat AD.

In the search for new lead molecules suitable for further development, our group has been focusing on the potential of carbohydrate-based molecules against several relevant molecular targets for AD. Based on the well-established role of the binding between the cellular prion protein (PrP^C) and Aβ oligomers (Aβo) for the activation of Fyn kinase and subsequent tau hyperphosphorylation in the brain [3], we herein report the rational design, synthesis, and structural optimization leading up to the discovery of *N*-methylpiperazinyl flavones and their *C*-glucosyl derivatives as protein-protein interaction (PPI) inhibitors against PrP^C-Aβo [4-6]. Furthermore, the identification of small *C*-glucosyl polyphenols as the first sugar-containing inhibitors of Aβo-induced Fyn activation and tau hyperphosphorylation will be explored, including the physicochemical properties that make them good candidates for pharmaceutical development [7].

Importantly, because many planar lipophilic polyphenols are Pan-Assay Interference CompoundS (PAINS), we were also interested in clarifying whether *C*-glucosyl polyphenols lead to unspecific alterations of cell membrane properties. Our results show, for the first time, that well-known membrane disruptors such as resveratrol and genistein lose their ability to reduce membrane dipole potential when linked to a glucosyl moiety through a C-C bond [8], suggesting that our *C*-glucosides should not raise any concerns regarding membrane-related PAINS-type behavior.

The work presented in this communication highlights the promising disease-modifying effects displayed by *C*-glucosyl polyphenols in the context of AD, and explores the role of the sugar moiety not only in tuning bioactivity in a favorable way but also in conferring protection against unwanted aglycone-induced membrane perturbing effects.

Centro de Química Estrutural is a Research Unit funded by Fundação para a Ciência e Tecnologia through projects UIDB/00100/2020 and UIDP/00100/2020. Institute of Molecular Sciences is an Associate Laboratory funded by FCT through project LA/P/0056/2020. A.M. Matos thanks CQE for her PhD Scientific Researcher contract.

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"Ferrocenyl chalcones as novel and potent inhibitors of 5-hLOX. Synthesis, biological and computational studies"

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Organometallic complexes have proven to be an attractive and excellent alternative for the design of new metallodrugs, showing that incorporating an organometallic fragment improves or enhances the biological activity of different organic candidates in different biological targets [1]. However, few studies of organometallic complexes in inflammatory processes have been explored and reported despite this important advantage. [1,2] Therefore, in the search for new inhibitors of the activity of the inflammatory enzyme 5-lipoxygenase, a family of organometallic chalcones (**2a-c**) and their respective organic analogs (**1a-c**) were evaluated as potential anti-inflammatory candidates.

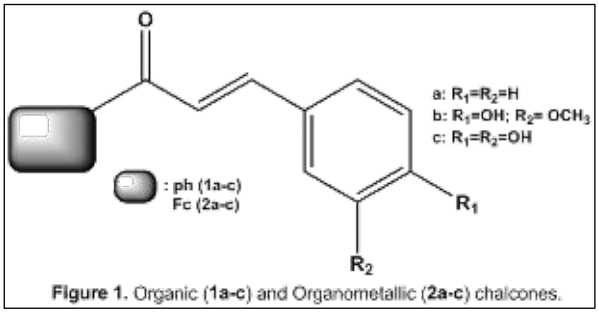

Figure 1. Organic (**1a-c**) and Organometallic (**2a-c**) chalcones.

A docking study between the ferrocenyl chalcones (**2a-c**), their organic analogs (**1a-c**), and 5-hLOX were carried out. Our findings exhibited an interesting affinity to the protein, with binding energy values between -4.2 and -5.3 kcal/mol for the organic chalcones **1a-c**, and between -5.5 and -6.5 kcal/mol for the ferrocenyl chalcones **2a-c**. Additionally, the inhibitory activity of **1a** and **2a** was determined. Our results showed a potent inhibitory activity for **2a** with an IC_{50} value of 0.4 ± 0.08 μM, while its organic analog **1a** exhibited a 100-fold higher IC_{50} value (Figure 2). In addition, **2a** showed binding energy of -6.07 kcal/mol at the catalytic site of 5-hLOX, where the ferrocenyl fragment was oriented towards the catalytic iron of the enzyme, suggesting a possible redox mechanism. Our attractive results motivate us to continue evaluating the in vitro activity of these derivatives to correlate our theoretical and experimental data.

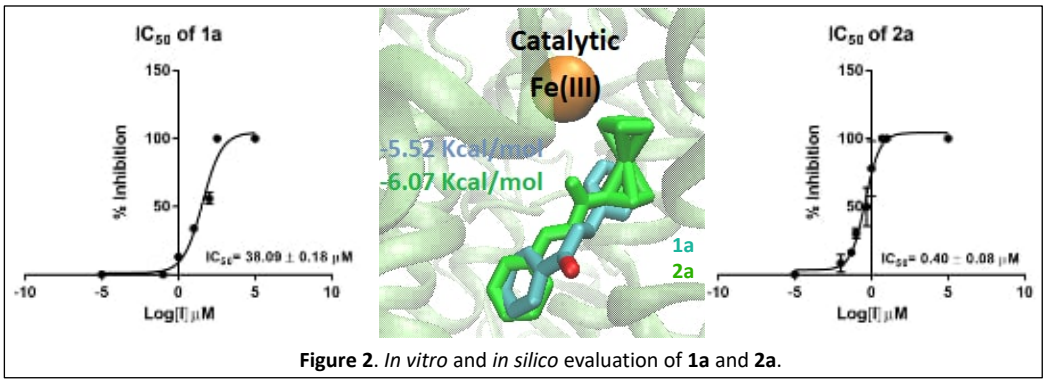

Figure 2. *In vitro* and *in silico* evaluation of **1a** and **2a**.

Acknowledgment: MMO thanks for Project POSTDOC_DICYT 022241_MC Postdoc, Vicerrectoría de Investigación, Desarrollo e Innovación and FONDECYT Nº 1200378 (C.M).

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Preparation of copper complexes from benzimidazole-2-yl hydrazones containing salicylic moiety and cytotoxicity study

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The metal complexes of benzimidazolyl Shiff bases and hydrazones have been found to display promising biological activities such as antimicrobial and anticancer [1-3]. Recently Cu and Zn complexes of benzimidazolyl Shiff bases were synthesized and showed enhanced cytotoxicity in regard to the ligand on different human cancer cells, HepG2, SK-MEL-1, HT018, HeLa, and MDA-MB 231 [1]. Transition metal complexes with benzimidazolyl-2-hydrazones of o-hydroxybenzaldehydes and ketones displayed antibacterial activities against B. subtilis, B. stearothermophilus, E. coli and S. typhi [3].

Herein we report the synthesis of Cu(II) complexes from benzimidazole-2-yl hydrazones containing salicylic moiety and the evaluation of their cytotoxicity towards mouse fibroblasts CCL-1 and cancer cell lines MCF-7 (ER-positive breast adenocarcinoma) and AR-230 (chronic myeloid leukemia). The complexes were obtained from the benzimidazolyl ligands and copper chloride as precursors by sonification and heating in ethanol medium. The structure of the complexes was established by elemental analysis, spectroscopic (IR and Raman) and SEM-EDS methods. The possible coordination modes, structural and vibrational characteristics were investigated by also quntum-chemical calculations. The gathered data have shown that the complexes were formed by coordination of one benzimidazole molecule to one copper atom (Figure 1):

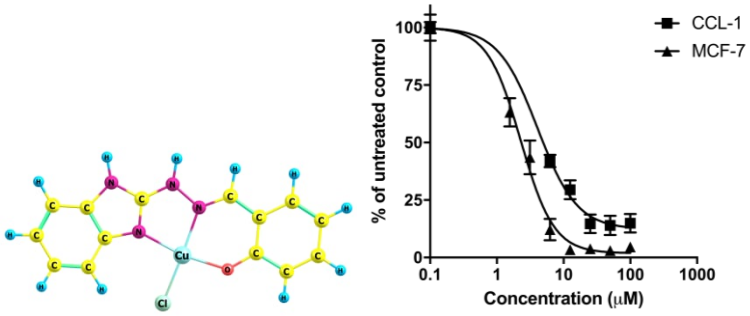

Figure 1.

The antiproliferative activity to MCF-7, AR-230 and CCL-1 cancer cell lines was evaluated using MTT test and demonstrated a potent antiproliferative effect for the studied complexes towards MCF-7 cells, with IC_{50} 2-8 μM.

The authors thank to the National Science Fund of Bulgaria, Contract КП-06-Н39/4, for financial support. Equipment of INFRAMAT (Research Infrastructure from National roadmap of Bulgaria), supported by the Bulgarian Ministry of Education and Science was used in a part of the present investigations.

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Finding potential anti-MRSA compounds targeting PBP2a

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a critical worldwide concern that requires new treatment and management approaches. MRSA is a major cause of nosocomial infections, with a high mortality rate due to multi-resistance to β-lactams. MRSA resistance is related to the acquisition of a PBP2a-coding *mecA* gene; the mecA protein has low affinity to β-lactams, meaning that cell wall peptidoglycan formation is not blocked, and bacteria survive[1], [2]. *S. aureus* PBP2a adopts a closed active site conformation, inaccessible for β-lactams. This reduced susceptibility to β-lactams is related to both PBP2a changes at a serine nucleophile in the active site and to the presence of a loop protecting the active site from inhibitors. The conformational change of this loop is regulated by an allosteric site distal from the active site, which becomes accessible only when the allosteric site is occupied[2]. Thus, there is a pressing need for innovative antibiotics to control resistance in these strains.

In this work, a structure-based computational molecular docking screening approach was applied with Autodock Vina, using the X-ray structures of both closed and open PBP2a conformations (PDB ID 1vqq and 3zg0, respectively). Different ring size lactams, fluorenone, flavone and quinazolinone derivatives were tested as possible inhibitors for both catalytic and allosteric sites. Known specific inhibitors were also tested. Molecular dynamics simulations using GROMACS software were deployed to understand whether binding of natural substrate and most promising hit compounds can induce protein conformational changes.

Known inhibitor, L-695256, with best results to the target protein presented affinities of -6.2 kcal.mol^{-1} for the allosteric site in the native PBP2a and -9.4 kcal.mol^{-1} for active site of acylated PBP2a protein (PDB:3zg0). Promising hit compounds tested in this work presented significant improvements in affinity for both catalytic sites, for instance, -8.1 kcal.mol^{-1} for the allosteric site in the native PBP2a (PDB:1vqq) and -12.1 kcal.mol^{-1} for active site of acylated PBP2a protein (PDB:3zg0). Hit compounds maintained the expected interactions to the protein has known inhibitors. These obtained lower binding energies for these interesting scaffolds present significant improvements in affinity for both sites. Moreover, binding of one of the most promising hit compounds to the allosteric site induce protein conformational change and subsequently to a more accessible catalytic residue.

These results indicate that tested compounds are promising hits targeting PBP2a protein from MRSA, contributing towards their potential use to overcome β-lactam resistance. Currently, more molecular dynamics simulations are being deployed to understand whether the binding of other hit compounds to the allosteric site can induce protein conformational change, contributing to a more accessible active site.

Acknowledgments: This work was funded through Research Grant PTDC/QUI-QAN/32242/2017 (MMM). PCR is an FCT-funded PhD student (UI/BD/152269/2021). Part of this work is funded through Rede Nacional de Computação Avançada (FCT/CPCA/2021/01). Centro de Química Estrutural is a Research Unit funded by Fundação para a Ciência e Tecnologia through projects UIDB/00100/2020 and UIDP/00100/2020. Institute of Molecular Sciences is an Associate Laboratory funded by FCT through project LA/P/0056/2020.

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Amaryllidaceae-type alkaloid derivatives as ABCB1 inhibitors in resistant human colon adenocarcinoma cancer cells and synergistic interaction with doxorubicin

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The increasing occurrence of multidrug resistance (MDR) is the major obstacle to cancer chemotherapy. One of the most important MDR mechanisms is the overexpression of ABC drug transporter proteins, namely P-glycoprotein (P-gp). Modulation of P-gp is among the most promising approaches for overcoming MDR.
Aiming at generating a small library of anticancer compounds for overcoming multidrug resistance, in the present study, lycorine, the major Amaryllidaceae-type alkaloid isolated from *Pancratium maritimum,* was derivatized. Thirty-two new derivatives were obtained by the chemical derivatization of hydroxyl groups of lycorine into carbamates. The structure of the compounds was established by NMR experiments, including 2D NMR (COSY, HMQC, and HMBC).
The compounds were evaluated as MDR reversers, through functional and chemosensitivity assays, in resistant human colon adenocarcinoma cancer cells (Colo 320), overexpressing P-gp. Significant inhibition of P-gp efflux activity was observed for some derivatives at non-cytotoxic concentrations. The effect on the ATPase activity of the strongest modulators showed that the compounds behaved as inhibitors. In drug combination assays, most of the compounds showed strong synergistic interactions with doxorubicin. Moreover, some derivatives showed a selective antiproliferative effect toward resistant cells, having a collateral sensitivity effect.

Keywords: *Pancratium maritimum*, Amaryllidaceae alkaloids, multidrug resistance, P-glycoprotein.

Acknowledgments: We thank the Fundação para a Ciência e Tecnologia for financial support in Portugal (Projects PTDC/MED-QUI/30591/2017 and Ph.D. grant SFRH/BD/130348/2017).

A Molecular Dynamics approach for unveiling the nanosegregation of novel biocompatible ILs and their aqueous solutions

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The great interest on Ionic Liquids (ILs) prompted reports not only highlighting their outstanding performance, but also issues related to the toxicity and biodegradability of the most common and studied cations and anions [1]. Notwithstanding, ILs made-up with natural substances, such as the Choline (Ch) cation and Amino-Acid (AA) anions, are usually less toxic and more biodegradable [1]. In this context, our research group has recently proposed the use of peptides (Pep) as anions [2,3], which exponentially expands this family of green solvents.

Since the nano-segregations of the novel ChPep and their aqueous solutions arose as a possible explanation for some observed phenomena during their application [2,3], contributing to constructing knowledge on this topic became the inspiration of this work. To this end, we tackled a classical Molecular Dynamics (MD) approach using the OPLS-AA force field but with a self-developed charge assignation, similarly to previous works [4], and the re-parametrization of the most relevant dihedrals.

After a preliminary outlook, using peptides chains up to 3 residues of glycine (Gly) for configuring anions returns Ch-based ILs that present a continuous polar domain in the bulk characterized by a complex hydrogen bonding network. Notwithstanding, if the phenylalanine (Phe) is employed instead (up to only dipeptides), both ChPhe and ChPhePhe present two continuous phases, polar and apolar. The forces ruling the formation of the apolar domains seem to be complicated: each Phenyl ring (Phe_r) is surrounded by 1 Ch, which suggests the presence of π-cation complexes, but the solvophobic effect of the polar network and the internal electrostatic stabilization of the Phe_r-Phe_r aggregate may have their impact too. As a result, Phe_r-Phe_r complexes presents some residual unfavourable stacked configuration, some of the offset stacked and mainly the more stable edge-to-face orientation. When dealing with ChPep dilutions, water seems to be dispersed into the polar network acting as a hydrogen bonding intermediator that ends separating the ions. For the 5 studied ILs, the aggregate distribution of charge centres suggests that each ion pair starts being isolated about an $80\%_{n/n}$ while each ion pairs is broken from ~$96\%_{n/n}$ on. Moreover, it appears that water facilitates the organization of the Phe_r in ChP and especially in ChPP since the relative orientation in Phe_r-Phe_r evolves towards the more favourable edge to face configuration. In fact, while ChPP with $96\%_{n/n}$ of H_2O presents ~0.5 cations close to the anion charged centre, each Phe_r has about ~4 Phe_r from ~2 neighbour anions, which highlights the importance of apolar aggregation in such conditions.

Finally, we believe that these results may contribute to explaining future performances of these ChPep.

L.M., A.A.F., J.N.C.L. and K.S. acknowledge FCT/MCTES for contracts and projects UIDB/00100/2020, UIDP/00100/2020 LA/P/0056/2020 Lisboa/01/0145/FEDER/028367 and PTDC/QUI-QFI/29527/2017. L.M. thanks Universidade de Vigo for the Margarita Salas post-doctoral contract financed by the Spanish Ministry of Universities with NextGenerationEU founds. L.M. and M.A.S. acknowledge Xunta de Galicia and ERDF for funding through ED431C 2021-43.

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Bisubstrate-based inhibitors of n-terminal acetyl transferases

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N-terminal acetylation is a ubiquitous co- or post-translational protein modification occurring on more than 80% of human proteins [1]. This biochemical reaction is catalyzed by N-terminal acetyl transferases (NATs) enzyme family and consists of the transfer of the acetyl group from acetyl coenzyme A to the N-terminal amino group. Nt-acetylation results in a multitude of cellular effects and controls a myriad of biological processes.

Despite being such a common protein modification- there are still pending questions in the NAT field which require potent inhibitors to facilitate further inquiries.

A number of bisubstrate inhibitors of NAT enzymes have been prepared by covalently linking coenzyme A to a short peptide carrying an N-terminal bromoacetyl group resulting in a thioether acetyl linker moiety between the two substrate parts [2-4]. X-Ray crystal structures of several NATs in complex with these bisubstrate inhibitors have shed light on the active sites, reaction mechanism of N-terminal acetylation and substrate specificity of various NAT members.

Although undeniably powerful tools for studying NATs, the inability of bisubstrate inhibitors to cross cell membranes severely hampers the range of experiments that can be conducted. To get access to cell-permeable NAT inhibitors, we are appending bisubstrate inhibitors onto targeting moieties that can facilitate shuttling into cells. Aiming for folic acid receptor-specific targeted delivery, we have investigated synthetic strategies to produce selectively labelled folic acid-bisubstrate inhibitor conjugates. Toward this end, we have explored into using the lysine side chain on bisubstrate inhibitors as an anchoring site for folic acid, either directly or via a cleavable dipeptidic linker. Results of these endeavors will be presented.

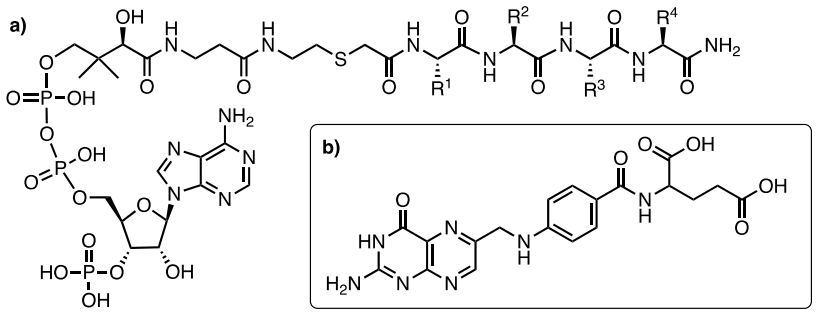

Figure 1. Structures of a) generalized bisubstrate inhibitor and b) folic acid

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Anti-inflammatory studies of succinimides with cyclic-ketoester derivatives using in-vitro, in-vivo, in-silico and phlogistic models

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Inflammation, being a well-known and complex pathological condition is always a challenge to the human health. This research work was designed for a rationale based anti-inflammatory studies on β-ketoester derivatives of N-ary succinimides. The compounds (**A-D**) were synthesized by organocatalytic Michael addition. The compounds were initially screened for *in vitro* 5-lipoxygenase (5-LOX) and cyclooxygenase (COX-2) assays. For the *in vivo* activity, carrageenan induced paw edema and arachidonic acid induced ear edema tests were used. Furthermore, different *in vivo* pathways like prostaglandins E_2, histamine, leukotriene and bradykinin were studied. The results were supported with molecular docking studies. Among the compounds, **D** (ethyl 1-(1-benzyl-2,5-dioxopyrrolidin-3-yl)-2-oxocyclohexane-1-carboxylate) at concentration of 1000 µg/ml showed significant inhibitory effects of 83.67% and 78.12% against COX-2 and 5-LOX in comparison to Celecoxib and Zileuton respectively. Similarly, compound **D** also showed excellent *in vivo* anti-inflammatory potential. Amongst all the compounds, **D** demonstrated excellent (55.92±2.95%) anti-inflammatory potential at maximum tested dose (100 mg/kg) which accomplished the highest significance at 4^{th}h following the carrageenan insertion and stayed considerable (***P<0.001) till the 5th h of test sample injection. Compound **D** also exhibited excellent percent inhibition (63.81±2.24%) at the highest dose in arachidonic acid induced ear inflammation. On the basis of *in vivo* and *in vitro* results, compound **D** was subjected to various inflammation causing agents such as histamine, prostaglandins E_2, bradykinin, and leukotriene via mouse paw edema test. Compound **D** revealed moderate effect (28.10±1.64 %) against histamine-induced-paw edema while non-significant result (9.72±3.125%) was marked for bradykinin pathway. Compound **D** showed significant against edematogenic consequence of prostaglandinE_2 (56.28–72.03%) and leukotriene (55.13±2.25%) induced inflammation. In summary, our findings recommended that compound **D** possesses double acting anti-inflammatory properties inhibiting both COX and LOX pathways. Binding orientations and energy values computed via docking simulations support the results of the experimental *in vitro* evaluation.

Modulation effect on tubulin polymerization and cytotoxicity studies of 1H-benzimidazole-2-yl and 5(6)-methyl-1H-benzimidazole-2-yl hydrazones

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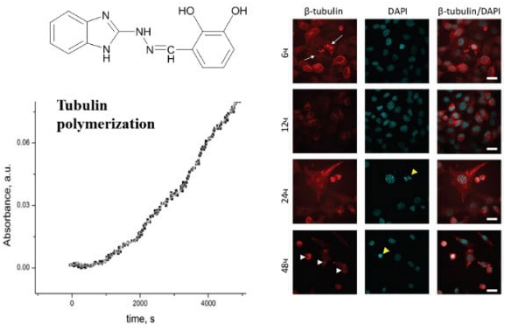
Recently some benzimidazolyl-2-hydrazones of fluoro-, hydroxy- and methoxy- substituted benzaldehydes and 1,3-benzodioxole-5-carbaldehyde were synthesized and have shown potent anthelmintic activity against isolated muscle larvae of *T. spiralis* as well as moderate antiproliferative activity against MCF-7 breast cancer cells [1]. The antiparasitic and anticancer effects were correlated to the ability of the compounds to interfere with tubulin polymerization [1].

As continuation of this study, a broader series of 1H-benzimidazol-2-yl and (6)-methyl-1H-benzimidazole-2-yl hydrazones with varying pattern of hydroxyl and methoxyl substituents in the phenyl ring was synthesized and their cytotoxicity on *MCF-7* (ER-positive breast adenocarcinoma), *AR-230* (chronic myeloid leukemia) and *3T3* (mouse fibroblasts) cell lines was evaluated. The tested 1H-benzimidazole-2-yl hydrazones showed excellent to moderate cytotoxic effect towards the cancer cell lines, accompanied in several cases by low cytotoxicity towards the *3T3* cells.

The ability of the compounds to interfere with tubulin polymerization was evaluated *in vitro* on porcine tubulin by spectrophotometric monitoring at 350 nm and compared to those of nocodazole and paclitaxel as reference. It was found that the compounds are able to modulate the polymerization of tubulin at different extend depending on their molecular structure. Some of them induced a decrease in the tubulin polymerization rate similarly to the microtubule inhibitor nocodazole, while other compounds did not show a lag period (nucleation time). Based on these combined results, the most promising compounds – containing two hydroxyl or three methoxyl substituents in the phenyl ring in combination with methyl or no substituent in the benzimidazole fragment, were selected for further evaluation of their antiproliferative effect on *MDA-MB-231* cell line (breast cancer) and immunofluorescent study on the mictrotubule assembly and cell nuclei morphology. The interaction of the 1H-benzimidazol-2-yl and (6)-methyl-1H-benzimidazole-2-yl hydrazones with tubulin was explored by molecular docking at the colchicine binding site and provided useful insights on the structure-activity relationship.



This work has been financially supported by the National Science Fund of Bulgaria, Contract КП-06-Н39/4. Research equipment of Distributed Research Infrastructure INFRAMAT, part of Bulgarian National Roadmap for Research Infrastructures, supported by Bulgarian Ministry of Education and Science was used in a part of this investigation.

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Reversion of drug resistance – a carboranic approach

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Multidrug resistance (MDR) is a major obstacle in the clinical treatment of many tumours that develop resistance to various drugs and, thus, lead often to failure of chemotherapies. MDR has been associated with overexpression of membrane-bound ATP binding cassette (ABC) carrier proteins, which are known to actively release anticancer drugs from the cytoplasm, reducing intracellular drug concentrations below therapeutic levels.[1] ABCG2, also known as breast cancer resistance protein (BCRP), is one of the three ABC members related with resistance in cancer treatment, therefore being a potential target for drug-based reversion of MDR. With the focus on selective inhibition of ABC-mediated excretion of chemotherapeutics, the efficacy of cancer treatments shall be enhanced. It is important to mention that no ABCG2 inhibitor has shown clinical significance to date.[2]

Icosahedral carboranes (*closo*-dicarbadodecaboranes) remain an interesting class of compounds, exhibiting beneficial properties for drug design. By virtue of their inorganic nature (enhanced biological stability), hydrophobicity, and steric demands, carboranes open up exciting possibilities as pharmacophores for known biological targets.[3] Therefore, combining the benefits of carboranes with structural characteristics of known ABCG2 inhibitors and substrates, novel carboranyl derivatives were evaluated *in silico*, followed by synthesis and testing their inhibitory efficacy and their ability to reverse chemotherapy resistance in ABCG2 overexpressing cancer cell lines.

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Exploiting the Warburg effect to target mutant p53: synthesis of tryptophanol-derived oxazoloisoindolinones glucoconjugates

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The tumor suppressor protein p53 plays a pivotal role in maintaining genomic stability in response to cellular stress [1]. This protein is a high interest target in cancer research as it is inactivated by mutation in more than half of all human cancers. In the last years, our research group has been developed novel oxazoloisoindolinone-based small molecules able to reactivate mutant p53 (mutp53) functions with excellent pharmacological properties [2]. Another hallmark of neoplastic transformation is the metabolic reprogramming, known as Warburg effect, characterized by increased carbohydrate uptake and overexpression of glycolytic enzymes and glucose transporters (GLUTs) [3]. Additionally, mutp53 can foment the Warburg effect by promoting the GLUT translocation to plasma membrane [4]. Therefore, we envisioned to exploit the Warburg effect to enhance the selectivity and pharmacokinetic properties of our tryptophanol-derived oxazoloisoindolinones by glycoconjugation with GLUT substrates (i.e., D-glucose and D-galactose). The target compounds were prepared by stereoselective cyclocondensation reaction of enantiopure tryptophanol with several achiral oxoacids, followed by *N*-indole functionalization via introduction of non-cleavable (i.e., saturated alkyl chain and triazole nucleus) and cleavable (i.e., paramethoxybenzyl, imine, dialkylalkoxysilane bonds) linkers. Further, the chemical stability in biological media and the anti-proliferative activity of the compounds will be assessed in vitro against mutp53-expressing cell lines and non-transformed cells to determine the selectivity index.

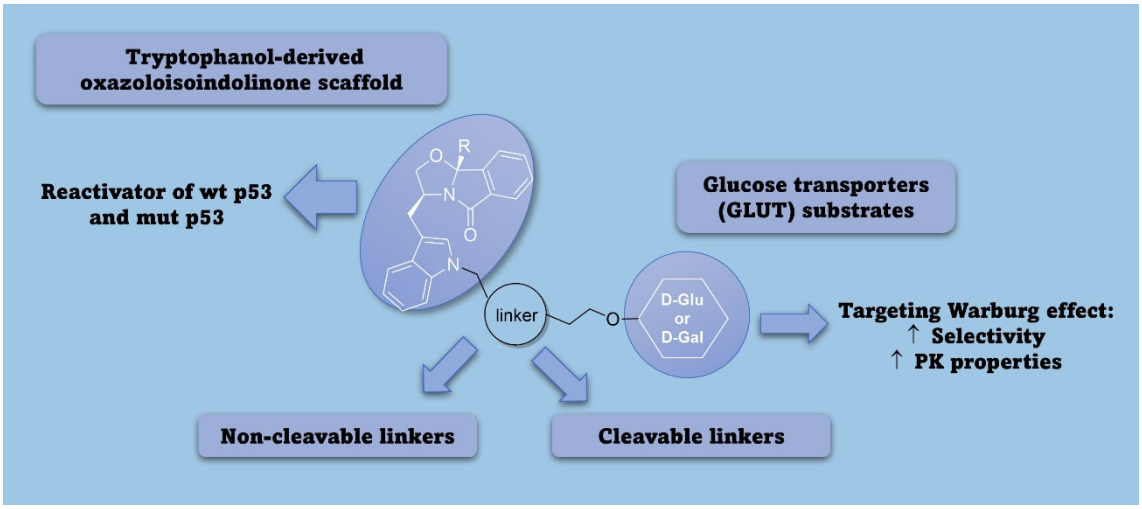

Figure 1. General structure of tryptophanol-derived oxazoloisoindolinone glycoconjugates.

ACKNOWLEDGMENTS: We thank PT national funds (FCT/MCTES, Fundação para a Ciência e Tecnologia and Ministério da Ciência, Tecnologia e Ensino Superior) the funding through grants PTDC/QUI-QOR/1304/2020 and the research institute iMed.ULisboa (UIDB/04138/2020).

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[1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones containing aryl and heteroaryl fragments at 2-position: synthesis, structural characterization, antiproliferative and radical scavenging activity

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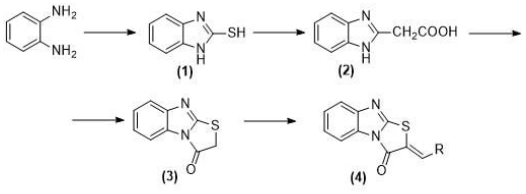
Benzimidazole heterocycle system is very important pharmacophore and privileged structure in the medicinal chemistry. Its derivatives exert various biological activities such as antioxidant and anticancer. The benzimidazole ring system exists in the structure of many antiparasitic, anthelmintic, antifungal, antiviral and antitumor drugs [1]. 2-Substituted-[1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones have demonstrated previously promising anthelmintic, antimicrobial and radical scavenging activity [2,3].

This motivated us to further synthesize an extended series of 1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones containing aryl and heteroaryl fragments at 2-position and evaluate their radical scavenging ability and antiproliferative effect. The synthesis was carried out through 5 steps: the first step comprised the synthesis of benzimidazolethiol scaffold **1**, from which at the next step benzimidazolethioacetic acid **2** was obtained. Then the thioacetic acid was transformed into benzimidazolethiazoleone **3** and finally in the last step the hydroxy- and methoxy-substituted aromatic and heteroaromatic rings were introduced and the target [1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones 4 were afforded (Scheme 1). The preferred structure of the compounds was established with theoretical computations. The more stable conformation of the exocyclic double bond is Z, and for compounds with a heterocyclic moiety in which rotation around the C-C bond to the aryl moiety results in different conformers, the s-cis isomer is more advantageous.

The radical scavenging activity was tested *in vitro* on lecithin, deoxyribose, ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) and DPPH (2,2-diphenyl-1-picrylhydrazyl) assays. The antiproliferative effect was studied on MCF-7 (ER-positive breast adenocarcinoma), AR-230 (chronic myeloid leukemia) and HeLa (cervical cancer) cell lines as well as 3T3 cells (mouse fibroblasts).



Scheme 1 Scheme of synthesis.

Thanks to Scientific Research Fund, project KP-06-H39 / 4 for the financial support. In part of the research, INFRAMAT equipment (Research Infrastructure from the National Road Map of the Republic of Bulgaria) was used, supported by the funds of Contract DO1-284 / 17.12.2019 with the Ministry of Education and Science.

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Supercritical CO_2 applied on the production of liposomal dry powder formulations suitable for the treatment of inflammatory lung diseases

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Chronic obstructive pulmonary disease, asthma, and cystic fibrosis are the most common chronic neutrophilic inflammatory lung diseases, requiring high doses of anti-inflammatory drugs. Unfortunately, a long-term systemic therapy with the common medicines such as corticosteroids can provoke adverse effects such as osteoporosis, adrenal suppression, diabetes, and cardiovascular diseases [1]. Biopharmaceuticals and flavonoids with anti-inflammatory properties can overcome those drawbacks and provide healthier patient treatment. PEGylated liposomes, owing to their physical and chemical features, can carry hydrophilic and hydrophobic drugs, like biopharmaceuticals and flavonoids, respectively, circulating in the bloodstream up to 24 h [2]. Yet, due to their limited stability in suspension upon storage that might limit their use, it is advantageous to convert them into solid dosage forms. Therefore, using a green technology like supercritical CO_2-assisted spray-drying (SASD), the liposomal suspension is converted into dry powder formulations capable of administration via different routes, including the lungs. In this work, liposomes, encapsulating 5(6)- carboxyfluorescein (CF) as a marker of the internal aqueous phase, were produced and then dried using the SASD [3]. After resuspension in water to remove the excipient, CF encapsulation efficiency remained above 95 %. In parallel, a flavonoid (FLAV) was incorporated into liposomes, achieving an incorporation efficiency of 66 %. Powders showed a mass median aerodynamic diameter and a fine particle fraction suitable to be inhaled. The CF-loaded liposomal dry powder formulations were submitted to storage stability assays at relative humidity of 4 %, 50 %, and 78 % for 30 days. Results showed that the dry powder formulations were able to maintain liposome stability at relative humidity of 4 % and 50 % at 20 °C for 30 days. This work is a proof-of-concept that highlights the innovative potential of supercritical CO_2-assisted spray-drying for converting liposomes into liposomal dry powder formulations**.** The challenges faced with regards to the storage stability of hydrophilic loaded liposomal formulations were surmounted through the production of solid form dosages using the supercritical fluid drying method with optimized ratios of excipients. The aerodynamic performance of the dry powders showed to be suitable for inhalation. Our findings point to promising synergies between pharmaceutical and chemical technologies in the search for effective alternative liposome storage techniques that forgo the need for cold chain storage, being able to target the lungs.

Acknowledgments

This work received financial support from PT national funds (FCT/MCTES, Fundação para a Ciência e Tecnologia and Ministério da Ciência, Tecnologia e Ensino Superior) through the projects UIDB/50006/2020 & UIDP/50006/2020, UIDB/00667/2020, UID/DTP/04138/2020 & UIDP/04138/2020, UIDB/50011/2020 & UIDP/50011/2020. C.C. thanks FCT (Fundação para a Ciência e Tecnologia) and ESF (European Social Fund) through POCH (Programa Operacional Capital Humano) for her PhD grant ref. PD/BD/142880/2018 and the project PD/00184/2012-PDQS. The authors are grateful to Prof. M. F. Martins, Prof. M. Dionísio e Dr A. B. Pereiro for the Laser® Thermohygrometer data logger, differential scanning calorimetry and Karl-Fischer titration facilities.

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Green Synthesis of Novel Benzoxazole Derivatives with Antitumoral Potential

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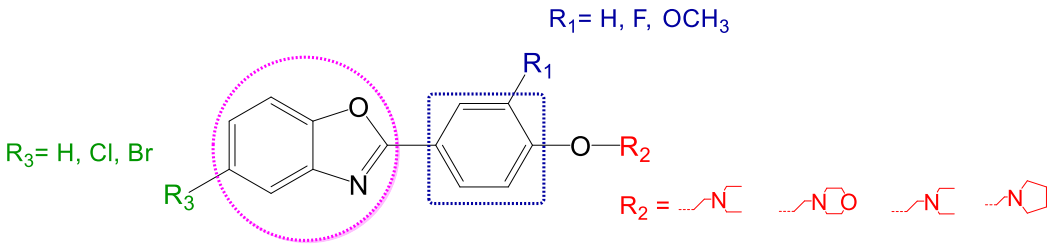
The low survivability associated with lung cancer is a clear indication of the need for more effective drugs, particularly those that act on targets or pathways of greater relevance to the disease [1]. Benzoxazole is a privileged scaffold that represents a promising class of heterocycles and the backbone of many bioactive compounds and possess antitumor activity. In recent times, much progress has been made to develop benzoxazole derivatives into clinical candidates. The growing importance of benzoxazole derivatives as therapetuic anticancer agents has fuelled the development of benzoxazole based drugs.

Trends in environmentally friendly and sustainable process development during past years are abridged involving the use of alternative organic synthesis including mechanochemistry, ultrasound or microwave irradiation and greener organic solvents. Conventional organic solvents are not only hazardous to the environment but also show acute and chronic toxicity, carcinogenicity, ecological toxicity and non-biodegradability. Deep eutectic solvents (DES) have emerged as an interesting type of ionic liquid and have proven useful as an environmentally benign sustainable alternative to the conventional organic solvents in synthetic chemistry to increase the efficiency of organic transformations.

Herein we present the synthesis of novel benzoxazole derivatives substituted at position 2 with disubstituted phenyl moiety by using mechanochemical and microwave reactions as well as application of different DES, and their cytostatic and antibacterial evaluations. 4-O-alkylated benzaldehydes, as key precursors for the synthesis of target benzoxazole derivatives, were prepared in DES (ChCl/glycerol) with K_2CO_3 as a base and subsequent mechanochemical reactions with 2-aminophenole were afforded corresponding Schiff bases. Microwave assisted cyclization reaction of Schiff bases with NaCN in ethanol gave target 2-(3,4-disubstitutedphenyl)benzoxazole derivatives. The novel benzoxazole derivatives were evaluated against tumor cell lines (Capan-1, NCI-H460, DND-41, K- 562, Z-138) and on the growth of gram-positive and gram-negative bacterial strains. Of all tested compounds benzoxazole derivatives with 4-(*N,N*-diethylethoxy)phenyl substituent showed the most pronounced activity against lung carcinoma cell lines (NCI-H460, IC_{50}=0.4-1.4 µM), while 2-(4-(2-morpholinoethoxy)phenyl)benzoxazole showed considerable activities against pancreatic adenocarcinoma (Capan-1, IC_{50}=2 µM), colorectal carcinoma (HCT-116, IC_{50}=5.7 µM), glioblastoma (Ln229, IC_{50}=2.2 µM) and lung carcionoma (NCI-H460, IC_{50}=1.3 µM) cell lines.



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Synthesis of phosphoglycoglycerols

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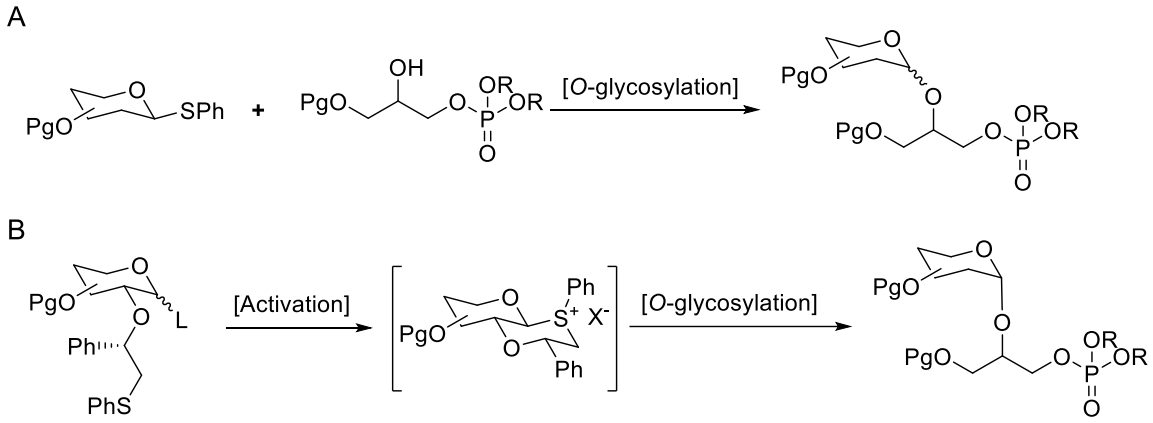
Phosphoglycoglycerols (PGG) are constituents of cell walls and membranes and have a variety of roles in an organisms' metabolism.[1] Natural products of this kind are reported to have a multitude of bioactivities, such as antibiotic [2] and anti-inflammatory.[3] In this work, two synthetic pathways were envisaged to achieve the desired PGG structures. The first is a traditional glycosyl bond formation pathway, while the second addresses a stereospecific pathway aiming to obtain solely the a anomer. The first uses a benzyl galactose derivative on reaction with a phosphoglycerol unit (Scheme 1A) and for the latter, a chiral auxiliary unit was synthetized and coupled to the carbohydrate moiety at the C-2 (Scheme 1B). The purpose is that after activating the C-1 a semi-stable intermediary linked to the b position is formed *in situ*, directing the attack of the glycerol nucleophile to the a position.[4]



Scheme 1 Synthetic pathways for the synthesis of PGG. A – traditional synthesis; B – stereospecific synthesis.

This work was also supported by the Associate Laboratory for Green Chemistry - LAQV which is financed by national funds from FCT/MCTES (UIDB/50006/2020 and UIDP/50006/2020). FCT/MCTES is also acknowledged for the National NMR Facility Network (ROTEIRO/0031/2013-PINFRA/22161/2016, co-financed by FEDER through COMPETE 2020, POCI, PORL, and FCT through PIDDAC) and PhD grant UI/BD/151271/2021

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An Unexpected Loss of Chirality: Challenges in the Synthesis of an Aminopyrrolidine core

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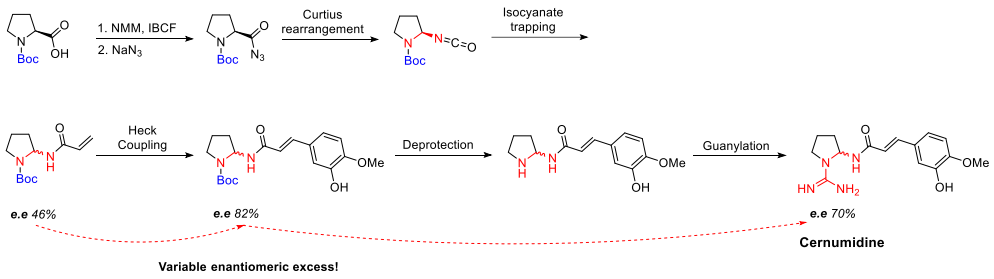
Cernumidine is a natural alkaloid isolated from the leaves of Solanum cernuum Vell [1], a plant that grows naturally in the southern regions of Brazil, where it is widely used in folk medicine [2,3]. Although Cernumidine showed a positive optical rotation, the X-ray crystallography analysis revealed the presence of a racemic entity.

Biologically, Cernumidine has the potential to inhibit the production of IL-8 (Interleukin-8) produced by the HT-29 cells from colon carcinoma [1] and the proliferation of bladder cancer cells [3]. Chemically, although with only one stereogenic center, its aminal-guanidine core (highlighted in red) presents a unique synthetic challenge.

We initially envisioned, what we thought to be, an enantioselective approach for the synthesis of Cernumidine and derivatives. Having the Curtius rearrangement as the key step (Scheme 1), the aminal core formation would be achieved while preserving the stereogenic center. However, here we will present our preliminary experimental and computational results on the complex system responsible for the substrate-dependent enantiomeric excess (ee) changes on this aminal core during distinct stages of the synthesis.



Scheme 1: Synthetic route to the synthesis of cernumidine and the aminopyrrolidine nucleus.

Thanks to the Associate Laboratory for Green Chemistry—LAQV which is financed by national funds from FCT/MCTES (UIDB/5'006/2020 and UIDP/50183/2020). FCT/MCTES is also acknowledged for the National NMR Facility Network (ROTEIRO/0031/2013-PINFRA/22161/2016. Rafael Rippel acknowledges the PhD grant SFRH/BD/136692/2018 from Fundação para a Ciência e Tecnologia.

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Phytochemical, Proximate Elemental and Anti-diabeticStudies of the Methanol Rhizome Extractof *Curcuma Longa* and its column fractions on normal and diabetic rats

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ABSTRACT

The explosion in human population has made it almost impossible for modern health facilities to meet health demands all over the world, thus putting more demands on the use of natural herbal remedies. Accordingly, the World Health Organization in a number of resolutions emphasized the need to ensure the quality control of plant products by using modern techniques and applying suitable standards. Thus, this paper seeks to validate the phytoconstituents, proximate contents and anti-diabetic potential of methanol extract of *Curcuma longa* on diabetic and non diabetic rats.A mass of 1000 grams (1kg) of the mashed *Curcuma longa* rhizomes was extracted exhaustively using maceration technique for seven days with 85% methanol. The extract was concentrated to dryness on air and the resulting mass was weighed, labelled and kept in a desiccator. The methanol crude extract of the rhizome of *Curcuma longa* was subjected to column chromatography using the graded elution protocol through suitably mixed solvent system ($CHCl_3$:CH_3OH.The eluate with same R_f value were pooled together and evaporated to dryness and was further subjected to hyperglycaemic evaluation. Proximate and elemental content of the plant was also evaluated by using standard method. The results revealed that the methanol extract of *Curcuma longa*and its column fractions contained bioactive compounds such as flavonoids terpenoids, alkaloids, saponins, phlabotannins and steroids capable of eliciting anti-diabetic effect in diabetic rats. Also elemental content analysis indicates that the plan has various element in different concentrations. The result of Proximate Analysis of *Curcuma longa* shows that the turmeric contains 80.00% moisture, 3.03% ash, 1.96 % crude fibre and 0.81 % fat. It also contains 1.82 % crude protein and 12.38 % carbohydrate. The result of its proximate and elemental analyses implies that it's a good source of protein, fibre, carbohydrate and phytominerals. Conclusively, the findings of this study revealed that methanolic extract of the*Cucurma longa*, contained pharmacologically active phytoconstituents with significant anti-diabetic effects, thus, scientifically backing to the local use of the its rhizomes as plant-drug for diabetic management.

Keywords: Phytochemical, Anti-diabetic; hypoglycaemia, Methanol.

N,N-dimethylglycine-amantadine – synthesis and biological activity (antiparkinson)

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ABSTRACT: NMDA receptor blockade can improve L-DOPA-induced dyskinesias in Parkinson's disease (PD) patients. Amantadine is well-tolerated and effective antiparkinsonian agent, was recently found to possess NMDA antagonistic properties [1]. Oxidative damage, may contribute to dopaminergic neurodegeneration in the substantia nigra of patients with PD [2]. N, N-Dimethylglycine (DMG) (also known as vitamin B15 or pangamic acid) acts as an antioxidant, extending the lifespan of animal cells through protection from oxidation [3]. In this study we synthesized and tested *in vivo* the newly obtained compound N,N-Dimethylglycine-Amantadine (DMG-Am) for antiparkinsonian activity. MPTP (1-methyl-4–phenyl-1,2,3, 6-tetrahydropyridine) is widely used neurotoxin as an experimental model which mimics some Parkinson's disease-like symptoms [4]. The neuroprotective capacity of new amantadine derivative DMG-Am was evaluated by its potential to ameliorate the behavioral changes induced by the toxin. Our experimental results showed that DMG-Am applied for 12 consecutive days, 5 days simultaneously and 7 days after MPTP restored motor and memory performance of the animals to the control level, indication of beneficial protective effect of this compound. In DMG-Am treated group the motor and memory behavior of the animals were as in the control group.

Acknowledgments

The work is realized with the financial support of KP-06-Russia/7- 2019

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Artificial Intelligence Approaches for Antibiotic Discovery

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Artificial intelligence (AI) has the potential to outperform humans and revolutionize our world. In this talk, I will describe our efforts using AI to develop computational approaches for antibiotic design and discovery. Computers can already be programmed for superhuman pattern recognition of images and text. In order for machines to discover novel antibiotics, they have to first be trained to sort through the many characteristics of molecules and determine which properties should be retained, suppressed, or enhanced to optimize antimicrobial activity. Said differently, machines need to be able to understand, read, write, and eventually create new molecules. I will discuss how we trained a computer to execute a fitness function following a Darwinian algorithm of evolution to select for molecular structures that interact with bacterial membranes, yielding the first artificial antimicrobials that kill bacteria both in vitro and in relevant animal models. My lab has also developed pattern recognition algorithms to mine the human proteome, identifying throughout the body thousands of antibiotics encoded in proteins with unrelated biological function, and has applied computational tools to successfully reprogram venoms into novel antimicrobials. Computer-generated designs and innovations at the intersection between machine and human intelligence may help to replenish our arsenal of effective drugs, providing much-needed solutions to global health problems caused by infectious diseases.

Multivalent Self-Assembled drug delivery system for combined treatment of Advanced Colorectal Cancer Therapy

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Colorectal cancer is one of the most diagnosed cancers in the world; in fact, it is the third most common cancer diagnosed in the United States, and worldwide, it represents the second leading cause of cancer death. [1]

There are different types of treatment for patients with colorectal cancer, depending on the stage at the time of the diagnosis. A first line therapy for advanced metastatic colorectal cancer (mCRC) is represented by the co-administration of 5-Fluorouracil (5FU) and the prodrug Irinotecan (IRI), a soluble derivative of SN38.[2]

Because of the low water solubility and high chemical lability of SN38, as well as the low degree of conversion of IRI to the active SN38 in vivo, researches are focused on the discovery of innovative strategies that allow the direct administration of the SN38. Furthermore, on the basis of recent clinical trials, the correct ratio between the two drugs must be considered in order to obtain more effective treatments using lower doses and reducing the side effects.

The objective of this work is the development of a small library of multivalent drug delivery systems with hetero- and homo-bivalent structured molecules, designed in order to test their ability to form nanostructures in aqueous media (fig.1). All the systems are based on a scaffold to which the hydrophobic SN38 and a hydrophilic polyethylene glycol (PEG) are conjugated through a trifunctional platform. All these systems can also be modified with different target moieties and an oligomer of Floxuridie (5FdU), an antimetabolite tumor drug with similar 5FU mechanism of action.

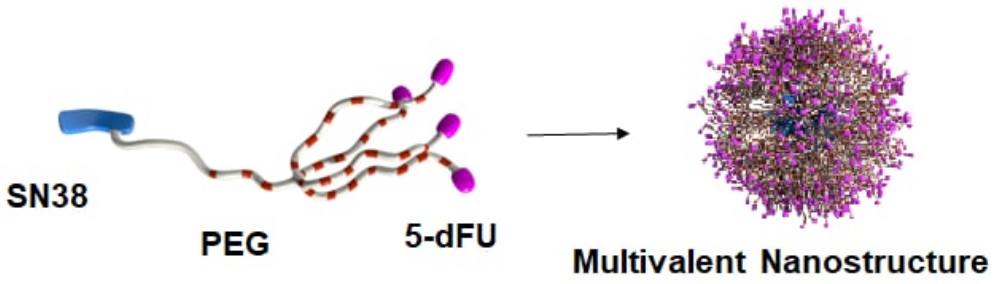

Figure 1. Simplified structure of multivalent nanoparticle for combined therapy.

Once the synthesis of all the conjugates will be completed and characterized, their self-assembly ability will be evaluated together with their stability in physiological conditions.

Acknowledgment: This research was funded by MCIN/AEI/ 10.13039/501100011033 and by "ERDF A way of making Europe" (grant number RTI2018-093831-B-I00 and CIBER BBN (CB06/01/074)

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Photosensitive packaging materials for microorganism photoinactivation

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The management of infectious diseases has been so far one of the biggest challenges for science and healthcare systems. One of the leading causes of infection is the consumption of contaminated food, which affects millions of people worldwide and leads to more than 400,000 annual deaths. [1] In this regard, there is an increased interest in designing new packaging materials to help preserve food's properties, increase their shelf-life and prevent microorganism contamination. [2] One possible approach to this problem is the use of materials containing photosensitive molecules, which can inactivate bacteria through irradiation with an appropriate light, in a process called photodynamic inactivation (PDI). [3]

Herein, we present our recent studies on the incorporation of the natural non-toxic photosensitizer curcumin in a polylactic acid (PLA) matrix (Figure 1), aiming its potential use as a packing material. Through the solvent casting method, thin PLA films were prepared containing up to 30% curcumin load, and characterized using differential scanning calorimetry (DSC), thermogravimetry (TG), polarized light thermomicroscopy (PLTM), fourier-transform infrared spectroscopy (FTIR) and X-Ray powder diffraction (XRPD). The combined results from these techniques gave interesting insights on the semi-crystalline nature of these materials. Additionally, these films showed a promising *Staphyloccocus aureus* photoinactivation, with up to 99.99% antimicrobial reduction, after irradiation with a blue LED (23.5 J/cm^2). Their good physicochemical properties combined with high microbicide activity demonstrate the potential of PLA-Curcumin films as next-generation packaging materials, capable of curbing infections by food contamination.

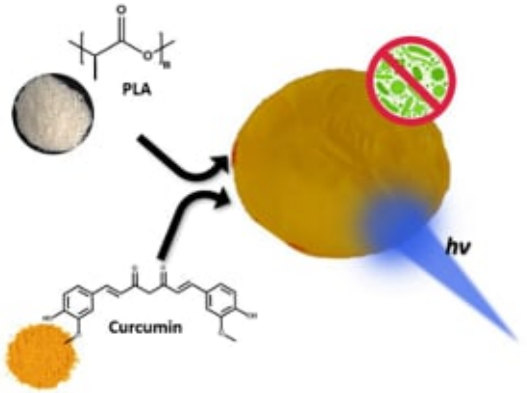

Figure 1: Photosensitive PLA-Curcumin films for the inactivation of bacteria.

The authors acknowledge the funding by FCT, QREN/FEDER for project UIDB/00313/2020. Furthermore, they acknowledge IAPMAI-PRR funding (Produtec R3, 2022) and UC-Santander for "Prémios Semente de Investigação interdisciplinar" funding (CO2BioFilter). We thank BIO4PLAS for supplying the PLA materials, lab TAIL-UC for the TG studies and lab UCQFarma for the XRPD studies.

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Fe–N–C Electrocatalysts in the Oxygen and Nitrogen Cycles in Alkaline Media: The Role of Iron Carbide[1]

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Iron- and nitrogen-doped carbons (Fe–N–C) are fast-rising stars in electrocatalysis. Fe-N-C drive reactions in the oxygen/water cycle (reduction and evolution of O_2, H_2O_2 and H_2),[2–8] the nitrogen cycle (oxidation of hydrazine and urea,[9–12] reduction of N_2 and NO_x[13–15]), and the carbon cycle (CO_2 reduction[16,17]). Their tunability and low cost make them attractive for energy devices such as fuel cells, electrolyzers and batteries.

Yet the mechanisms by which Fe–N–C electrocatalysts operate are obscured by their compositional and structural complexity. When iron, nitrogen and carbon precursors are heated to 500–1000 °C in inert atmosphere, an array of potential electrocatalytic sites forms in the resulting carbon (Figure 1):[18–21] carbon edges or defects;[22,23] nitrogen dopants at various positions;[24,25] carbon-embedded metal–organic moieties (e.g. Fe–N_x),[26]; and iron-based inorganic particles, bare or graphite-coated.[27–30] Iron carbide (Fe_3C) is found in nearly all pyrolytic Fe–N–C materials, including the most catalytically active ones.[28–36] Its role in catalysis remains murky, despite detailed investigations: some identify Fe_3C as a central catalytical component,[30–36] while others maintain it is a useless by-product of the pyrolysis.[37–41] The discussion is clouded by the broad variety of Fe_3C particle sizes, shapes, and carbon environments found in pyrolytic carbons, and by the challenge of preparing Fe_3C-free control materials. Eliminating iron from the pyrolysis mixture prevents Fe_3C formation and often leads to lower electrocatalytic activities, thus suggesting Fe_3C is active.[30–32] However, the absence of iron during pyrolysis also abolishes catalytic Fe–N_x sites[20,42] and degrades electrochemically-relevant carbon properties such as graphitization,[43] micropore etching[44] and pore templating.[45] Alternatively, Fe_3C-free controls can be obtained by acid leaching of the Fe_3C particles. Some observed that leaching increased catalytic currents,[37–40] indicating they are merely a pore-blocking nuisance, while others reported a current decrease, suggesting Fe_3C is catalytically active.[34–36] However, most leaching procedures employed oxidizing oxoacids (H_2SO_4, HNO_3) at high temperatures (60–100 °C), probably damaging the carbon[40,46] and demetallating Fe–N_x sites,[47,48] not allowing true comparison between the materials.

We now report a direct investigation on the role of iron carbides to electrocatalysis in the oxygen and nitrogen cycles in alkaline media. We examine the typical Fe_3C phases found in pyrolytic Fe–(N)–C materials, by systematically assessing a broad range of particle sizes and carbon environments in five different Fe_3C-rich carbon materials. Then, we remove the Fe_3C by a mild, non-oxidizing washing procedure, allowing us to determine the true contribution of Fe_3C without destroying other sites. The carbide-rich and washed materials are tested as electrocatalysts towards the oxygen reduction reaction (ORR) and the hydrazine oxidation reaction (HzOR), two representative and important reactions in the oxygen and nitrogen cycles, respectively. Finally, DFT calculations of oxygen- and nitrogen-cycle reactions on bare Fe_3C corroborate and extend the experimental findings.

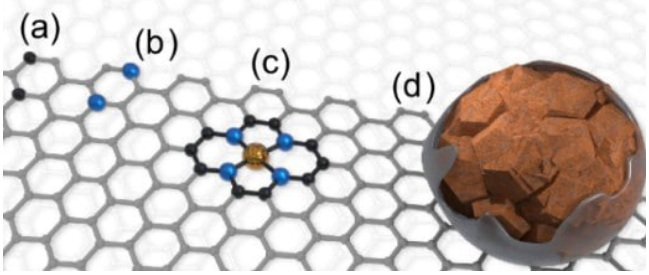

Figure 1. Four possible active sites in Fe–N–C electrocatalysts: (a) carbon atoms, (b) nitrogen atoms, (c) Fe–Nx moieties, (d) Fe_3C particles.

Thanks to Israel Science Foundation (grant 2430/19), the Grand Technion Energy Program, and the Ministry of Energy (graduate scholarship program) for financial support, and Prof. Lior Kornblum and Prof. Charlotte Vogt (Technion) for helpful advice.

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Metal-free mesoporous graphitic carbon nitride for visible-light-driven photoredox trifluoromethylation of (hetero)aromatics under flow conditions

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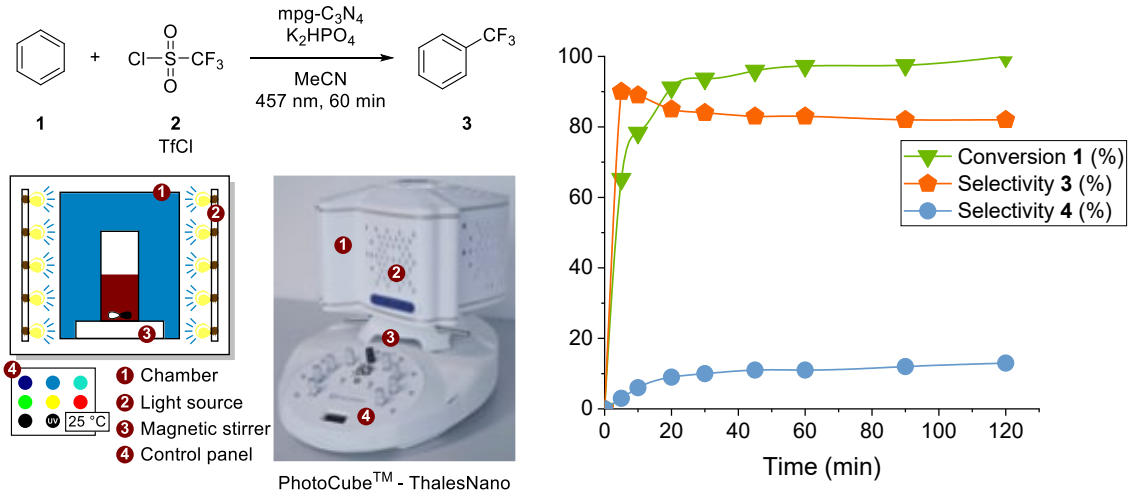
The introduction of fluorine and trifluoromethyl groups is an important step in pharmaceutical and fine chemical manufacturing, due to the positive role of this moiety on the physical and biological properties of many drugs. However, this reaction is still suboptimal due to the requirement of harsh conditions and dangerous reagents. [1] The radical mechanism of the reaction suggests the possibility to employ a light-driven approach for trifluoromethylation reaction. Herein, the synthesis of trifluoromethylated compounds using different innovative C_3N_4 heterogeneous photocatalysts is presented. [2] The kinetics and the impact of process conditions on the reaction progress have been investigated, providing detailed information about the photocatalytic mechanism. Under optimized conditions a solution of the aromatic compound, K_2HPO_4, and TfCl in acetonitrile was stirred for 60 min using a 457 nm light wavelength in the PhotoCube™ apparatus. Particularly, the catalyst effect on the conversion and selectivity has been investigated using metal-free carbon nitride (mesoporous graphitic, nanosheet, and graphitic materials) with tuned specific surface area. These tests show that the higher is the catalyst surface area, the higher is the selectivity for the desired product. Moreover, the reaction rate is improved by the increasing surface area. Finally, the reaction scope has been extended to different aromatic substrates, proving the flexibility of our protocol, and the process has been performed also in continuous-flow conditions, confirming the role of flow chemistry as enabling technology for photocatalytic reactions. [3]



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Cobalt pincer complexes - selective and efficient catalysts for the dehydrogenative coupling of alkynylsilanes with primary and secondary hydrosilanes

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The metal-catalyzed dehydrogenative silylation constitutes the most atom-efficient strategy for the functionalization of multiple bonds of unsaturated compounds by a silicon atom. The corresponding transformation is applicable in laboratory and industrial scale providing protective groups for reactive moieties as well as giving themselves versatile building blocks used in many fields of material chemistry. Among well-investigated methodologies for silylation of triple bond, approaches that have employed hydrosilanes are considered to be the most straightforward, convenient, and environmentally benign. By far, developed strategies for dehydrogenative silylation of terminal alkynes with hydrosilanes have been mediated by various heterogeneous and homogeneous transition metal catalysts, alkali metal oxides, hydroxides, alkoxides, and even hydrides. Unfortunately, high temperature, formation of side-products, or a large amount of the catalyst concentration are the biggest disadvantages of these protocols and allow to get all the desired products with moderate selectivities and efficiencies. On the other hand, several articles describe the use of also earth-abundant metal complexes as catalysts in organosilicon synthesis. The low cost of the preparation of the earth-abundant catalysts associated with the high catalytic activity are the favorable features of this solution. [1–3]

In the light of these facts, we present in the communication our new approach for extremely selective and efficient dehydrogenative silylation of alkynylsilanes with hydrosilanes catalysed by inexpensive and easy to obtained cobalt complexes. A wide scope of symmetrical and unsymmetrical products, which synthesis might be challenging via alternative methodologies, was received under mild conditions with high isolated yields. What is more, during intensified research it turned out that mono-substituted silanes played a dual role as reagents and pre-catalyst activators, and no additional bases were needed. Taking all this, our strategy constitutes a very accessible and competitive tactic in organosilicon synthesis among previously established reports.[4]

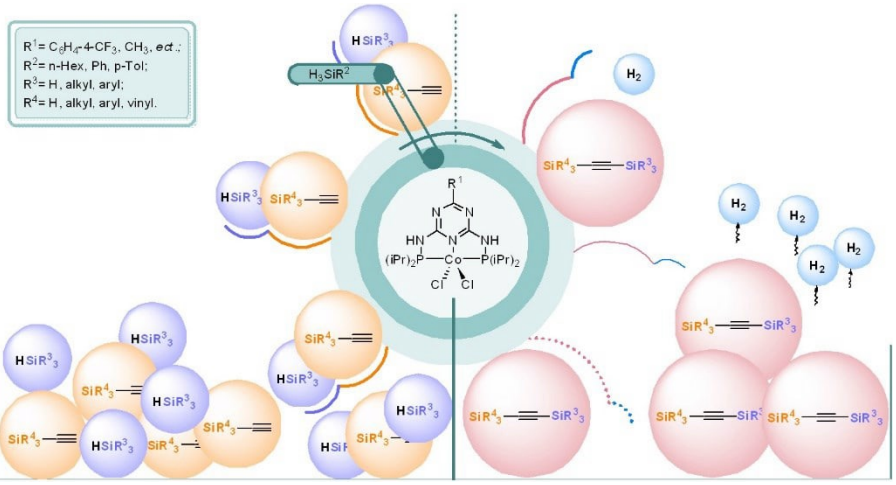

Fig. 1. Our Co-mediated approach for the synthesis of bis(silyl)acetylenes

Acknowledgments

The work was supported by grant no. POWR.03.02.00-00-I020/17 co-financed by the European Union through the European Social Fund under the Operational Program Knowledge Education Development and National Science Centre Grant UMO-2018/30/E/ST5/00045.

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Synthesis of nanoparticles and thin film of Cu_2ZnSnS_4 by hydrothermal method and its application as Congo Red photocatalyst

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The textile, food and pharmaceutical industries are expanding daily worldwide, they are located within the most polluting industries due to the fact that wastewater is discharged into watercourses with high concentrations of dyes and traces of drugs. Many of these compounds are stable to light and biodegradation, being considered as emerging organic contaminants [1]. Advanced oxidation processes (AOPs) emerge as an effective alternative for the removal and elimination of this type of contaminants. Heterogeneous photocatalysis has been extensively studied as it is an efficient, low-cost and durable method. As the main photocatalyst, TiO_2 has been used for the degradation of a large number of dyes and drugs. The disadvantage of TiO_2 is its absorption in the UV region of the solar spectrum [2]. On the other hand, quaternary chalcogenides based on Cu_2SnZnX_4 (X = S, Se) are a possible alternative due to their narrow band gap (ca. between 0.8 to 1.5 eV depending on the phase considered), low cost, abundance of its constituent elements in the earth's crust and its low toxicity. As a photocatalyst, CZTS has shown good results in the treatment of some emerging organic pollutants, but studies are scarce [3].

The objective of this research was to synthesize Cu_2SnZnS_4 (CZTS) through of a low-cost hydrothermal method and evaluate it as a potential photo-catalyst in the photo-degradation process of Congo Red.

The synthesis of the nanoparticle in suspension and film onto FTO was carried out using a mixture of: 2 mmol $CuCl_2$, 1 mmol $ZnCl_2$, 1 mmol $SnCl_2$ and 4 mmol CH_4N_2S in a Teflon reactor at 180°C for 72 h. Characterization was performed through scanning electron microscopy (SEM), X-ray diffraction (XRD) and UV VIS spectroscopy. Photo-degradation monitoring was carried out employing a UV VIS spectrophotometer.

The results show that photodegradation of 55% of the dye can be obtained after 4h of exposure to polychromatic light, which represents an advance since the use of CZTS as a photocatalyst in the degradation of Congo Red dye is being studied for the first time.

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Basic heterogeneous catalysts for the production of Biodiesel

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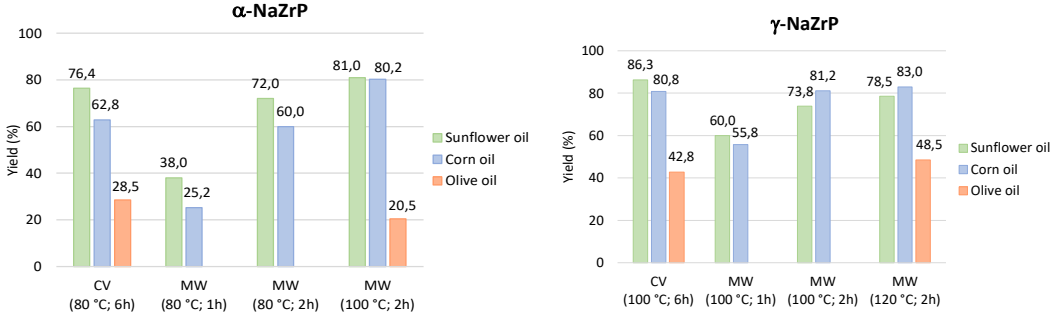
The world of today is facing significant changes due to the incorrect human behavior that is severely jeopardizing precious resources for future generations. As such, the search for renewable and safer resources for unlimited usage is now mandatory. An alternative fuel must be economically competitive, environmentally acceptable and readily available.

Biodiesel is a good alternative and its production can be performed in the presence of acidic, basic and enzymatic catalysts. As homogeneous catalysts present several disadvantages the use of heterogeneous catalysts including the tetravalent metal phosphates and phosphonates [1] have received an increasing attention in the last decades [2,3].

Our work started with the synthesis, characterization and catalytic evaluation of the α- and γ-zirconium phosphates (α- and γ-ZrP) and the correspondent sodium exchanged phosphates (α-NaZrP and γ-NaZrP) in the transesterification reaction of sunflower oil using the conventional reflux method (CV). The fatty acid methyl esters (FAMEs) formed with α-NaZrP and γ-NaZrP were identified by GC-MS and quantified by GC. The best yields were obtained after varying sequentially the molar ratio methanol:oil, temperature, mass ratio catalyst:oil and reaction time. Then, the former best reaction conditions achieved with the sunflower oil were tested in the transesterification reaction of corn and olive oil.



After the above results, the transesterification reactions of the sunflower, corn and olive oils were performed by the microwave assisted method (MW). With this method, only the temperature and reaction time parameters were studied. The best yields were obtained after 2 hours of reaction at 100ºC with the α-NaZrP and after 2 hours of reaction at 120ºC with the γ-NaZrP for the three oils.

No FAMEs were observed with α- and γ-ZrP or in the blank reactions either with the sunflower, corn and olive oils.

As can be confirmed by the two graphics, very good results were achieved using the MW considering that the reaction time was substantially decreased for both situations compared with the CV, which implies a considerable decrease in energy consumption.

The structure of the catalysts and the optimization of the reaction conditions will be discussed in detail during the presentation.

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How oriented external electric fields modulate reactivity

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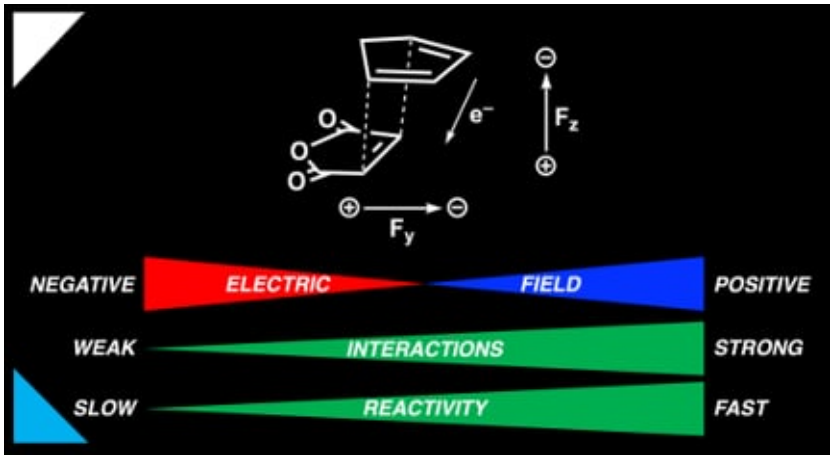
A judiciously oriented external electric field (OEEF) can catalyze a range of reactions and can even induce *endo*/*exo* stereoselectivity of cycloaddition reactions [1, 2]. We studied the Diels-Alder reaction between cyclopentadiene and maleic anhydride using quantitative activation strain and Kohn-Sham molecular orbital theory to pinpoint the origin of these catalytic and stereoselective effects [3].

Our quantitative model reveals that an OEEF along the reaction axis induces an enhanced electrostatic and orbital interaction between the reactants, which in turn lowers the reaction barrier. The stronger electrostatic interaction originates from an increased electron density difference between the reactants at the reactive center, while the enhanced orbital interaction arises from the promoted normal electron demand donor–acceptor interaction driven by the OEEF. An OEEF perpendicular to the plane of the reaction axis solely stabilizes the *exo* pathway of this reaction while the *endo* pathway remains unaltered and efficiently steers the *endo*/*exo* stereoselectivity.



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Investigation of Zeolite-based Water Sorbents for the Sorption-Enhanced CO_2 Hydrogenation to Methanol

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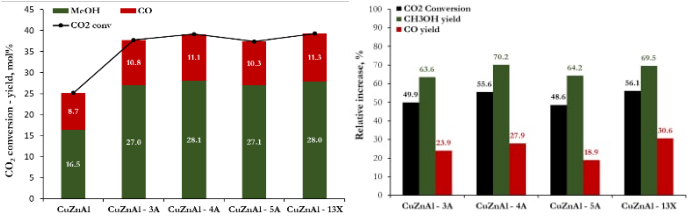
Methanol production via CO_2 hydrogenation is thermodynamically favored at high pressures and low temperatures, conditions under which the methanol yield is limited to low levels due to the high stability of CO_2 and slow reaction kinetics. We have previously shown, both computationally [1] and experimentally [2], that water sorbent addition can considerably increase the methanol yield (up to 130%). Requirements for an efficient solid sorbent are high water sorption capacity and selectivity at reaction conditions, low regeneration temperature and high stability in consecutive sorption-regeneration cycles. In this work, we investigate the use of zeolites as efficient water sorbents in the sorption enhanced CO_2 hydrogenation reaction. In particular, the performance of four different solid sorbents, namely zeolites 3A, 4A, 5A and 13X, was assessed under different operating conditions in multiple reaction-regeneration cycles of CO_2 hydrogenation over a commercial $Cu/ZnO/Al_2O_3$ catalyst.

The addition of the zeolites leads in all cases to a prominent increase in CO_2 conversion and CH_3OH yield. As the reaction proceeds with time, the sorbent becomes gradually saturated, the enhancement effect reduces and the system eventually reaches the same steady state as the conventional process. Under the employed operating conditions, the sorption enhancement effect has a duration of ~ 60 min. In the presence of the zeolites, the integral CO_2 conversion for 120 min reaction time increases by 49-56%. The respective increase in the integral CH_3OH yield lies in a higher range (63-70%), indicating that the water sorption preferentially enhances the production of methanol. Comparison of the performance of the different zeolites (see figure below) shows that the highest enhancement is exhibited by zeolites 4A and 13X. This can be related to the higher water sorption capacity of these two zeolites at 250°C, as reported in literature [3].

The effect of the reaction temperature (225–275°C) and regeneration temperature (275-300°C) was assessed over a $Cu/ZnO/Al_2O_3$-zeolite 13X mixture. The temperature of the hydrogenation reaction strongly affects both activity and product distribution in conventional and sorption enhanced CO_2 hydrogenation. Highest methanol production in 120 min reaction time is achieved at 275°C, due to the significant increase in activity under these reaction conditions. However, the highest sorption enhancement occurs at 225°C, where the methanol yield increases by 115% compared to the conventional process. Increasing the regeneration temperature from 275°C to 300°C has a negligible impact on the process performance.

Finally, stability was examined by running three consecutive sorption-regeneration cycles. Zeolite 4A presents the highest stability, retaining more than 89% of its initial performance, while zeolite 13X the highest deactivation. Analysis of the liquid obtained from the regeneration step reveals that the zeolites adsorb, not only water, but also part of the produced methanol.

Overall, zeolite-based water sorbents constitute promising materials for the sorption-enhanced CO_2 hydrogenation to methanol. Zeolite 4A exhibits the optimum performance, both in terms of activity and stability, increasing the methanol yield by 70% during the sorption enhancement step.



This research has been co-financed by the European Regional Development Fund of the European Union and Greek national funds through the Operational Program Competitiveness, Entrepreneurship and Innovation, under the call RESEARCH – CREATE – INNOVATE (project code: T1EDK-01532).

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Catalytic purification of waste water by gold-phosphorene nanohybrids

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Phosphorene is the single layer derivative of layered Black Phosphorus (BP), which is a member of a layered material family with anisotropic properties and with a layer-dependent bandgap. In comparison with graphene - the typical reference single layer material, phosphorene is significantly more reactive, and its reactivity can be applied for the autogenous reduction of gold ions to the metallic gold nanoparticles supported by phosphorene sheets (Au/BP). Phosphorene, as well as gold, are well-known oxidation catalysts, which are essential in organic synthesis, and catalytic treatment and purification of industrial wastewaters. The treatment of organic contaminants in water from chemical industry exhibit serious problem, and its treatment is a challenge for catalysis. Here we show a high catalytic activity of the gold-phosphorene nanohybrid [1] (Au/BP) for wet oxidation of acrylic acid and industrial-like wastewater with complex composition. Further, the prepared nanohybrid showed high stability, which is the crucial feature for an application of layered materials. The stability is caused by a presence of gold, which modified the electronic structure of the phosphorene surface. The Au/BP stability opens the utilization of the easy-accessible surface of 2D material for the preparation of 2D material supported metal catalysts.

The research leading to these results was supported by the European Structural and Investment Funds, OP RDE-funded project 'CHEMFELLS IV' (No. CZ.02.2.69/0.0/0.0/20_079/0017899).

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Designing zeolite ZSM-5 based catalysts by 3D-Printing for Methanol Dehydration to Dimethyl Ether

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Despite the large impact three-dimensional (3D) printing has on various sectors, its application in catalyst design is still at an early stage [1]. By utilizing the prospects of this technology, it is possible to design structured catalytic materials with optimized geometries for maximizing catalytic activity and improving mass and heat transfer phenomena. Catalyst design via 3D printing can prove extremely useful in applications that require bifunctional catalysts, such as one-step conversion of CO_2 to dimethyl ether (DME), which requires both metal and acidic active sites.

In this study, we explore the possibility of using zeolite ZSM-5 based 3D-printed catalysts for the dehydration of CH_3OH to DME. Zeolite ZSM-5 was chosen as reference material, due to its high acidity that catalyzes the dehydration reaction [2]. Based on manufacturing restrictions and printing technology capabilities, different catalyst configurations were designed in CAD and were investigated in terms of hydraulic behavior and pressure drop, and the optimum design was selected. Two routes were then followed for the preparation of the 3D printed catalysts; the indirect and the direct route. In the indirect method, sacrificial templates were printed and were then post-modified to prepare the final catalysts using ZSM-zeolite powder mixed with sodium silicate solution that acts as binder and is required to provide plasticity for the formulation of a homogenous paste. The template filling was conducted by mechanically pressing the paste into the template. The samples were then dried and calcined under air flow to achieve template removal. In the direct 3D printing, the ZSM-5 powder was mixed with the binders (betonite and methyl cellulose) with the use of distilled water using a mortar. The paste was loaded in the syringe of a high-resolution 3D printer and controlled selective deposition of the material was performed via the Direct Ink Writing (DIW) method. Pure ZSM-5 powder was also used for comparison reasons.

The 3D printed zeolites were characterized to determined their textural properties (BET), crystallinity (XRD) and acidity (FT-IR pyridine). Characterization was also performed to the ZSM-5 powder for comparison reasons. The ZSM-5 powder has a high surface area and a high number of Lewis and Brönsted acid sites. The monoliths prepared via the indirect method have significantly lower surface area and acidity, the latter probably due to the use of basic sodium silicate material as binder. The directly printed ZSM-5 zeolites retain on the other hand both their textural and acidic properties.

Finally, the catalytic performance of the ZSM-5 powder and the ZSM-5 based 3D printed materials in the methanol dehydration to DME was assessed in a continuous high-pressure dual fixed-bed reactor unit. The results highlight the promising performance of the 3D printed ZSM-5 catalysts prepared via direct printing, which demonstrate good catalytic performance and stability.

The research project was supported by the Hellenic Foundation for Research and Innovation (H.F.R.I.) under the "1st Call for H.F.R.I. Research Projects to support Faculty Members & Researchers and the Procurement of High-and the procurement of high-cost research equipment grant" (Project Number: HFRI-FM17-62).

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Coordinating solvents as novel selectivity enhancers on the direct synthesis of hydrogen peroxide for palladium catalysts supported on ion-exchangers

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The direct synthesis (DS) of hydrogen peroxide (HP) has become a hot topic in heterogeneous catalysis since 1990s, as it turned out to be the more promising strategy to replace the anthraquinone process in the exploitation of HP as oxidant in chemical manufacturing. [1-3] The main issue that still prevents the application of the DS is the selectivity of the catalysts, typically supported nanostructured palladium and palladium alloys, as water is the thermodynamically most favored product. Common selectivity enhancers are mineral acids combined with chloride or bromide ions, but corrosion issues prevent their industrial application.[4] Like halides, acetonitrile (ACN) behaves as a good ligand to Pd(II), but is not corrosive to metal components. Based on this similarity we have investigated the effect on palladium catalysts of ACN as the co-solvent, in addition to pure methanol.

As a general trend, ACN poisons the catalyst bringing to a lower hydrogen conversion, but at the same time, it leads to a selectivity enhancement with catalysts supported on ion-exchangers such as sulfonic polystyrene/divinylbenzene (Fig.1) resins or zeolites. In semi-batch experiments with very long time-on-stream (ca. 48 h), the ACN-promoted catalysts present an increase of the HP productivity with a lower hydrogen consumption, with a consequent remarkable increase in the HP selectivity.

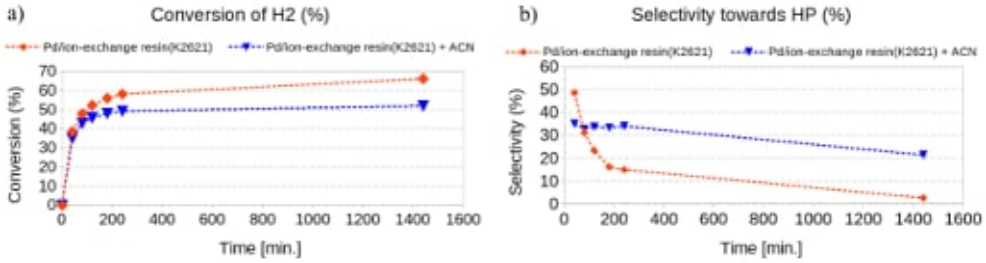

Fig. 1: a) Conversion of H_2 and b) selectivity towards HP of Pd/K2621 in methanol (red squares) and methanol with 10% v/v of ACN (blue triangles).

Catalyst characterization with XPS and HR-TEM revealed that ACN leads to a significant oxidation of Pd and nanoparticles reconstruction, leading to the formation of both smaller and bigger nanoparticles. The reconstruction of the metal phase that occurs between solid and liquid phases is compatible with a release-and-capture mechanism, based on the leaching of Pd in the form of palladium(II) complexes with ACN. As these complexes are positively charged, it can be assumed that they can interact with ion-exchange functionalities of the supports, which keep them anchored to catalyst, preventing the leaching into the solution. Furthermore, these species can be reduced, forming further nanoparticles or growing the existing ones, according to TEM.

The continuous reconstruction of the metal phase likely affects the most active sites, that are responsible for undesired hydrogenation reactions, hence the overall effect is a lower hydrogen conversion with a higher selectivity. The first investigation of the effect of ACN in a continuous system has been performed in a trickle-bed reactor (TBR). The preliminary results suggest that the effect of ACN is quite different when compared to a semi-batch reactor, as the presence of the co-solvent does not change the HP productivity on catalysts supported on zeolites. However, the hydrogen consumption is lower and the production of water is remarkably suppressed, leading to an overall increase of the HP selectivity.

Thanks to: We are grateful to Dr. Marcello Marelli for his contribution with TEM characterization of the catalysts. This research was funded by University of Padova, BIRD projectP-DiSC#03BIRD2020-UNIPD

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CO_2 methanation reaction using MgF_2-NiF_2 binary fluorides

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Nickel-containing catalysts are applied on a large scale in chemical industry in many reactions of organic synthesis including methanation reactions. Increasing content of CO_2 in the Earth atmosphere is a serious problem in the world. As the ubiquitous emission of CO_2 contributes to global warming and pollution, the utilization of waste CO_2 has become an urgent problem [1]. The most popular catalyst for CO_2 methanation is nickel supported on different metal oxides. It is high activity, high CH_4 selectivity, and a low cost [2]. The most frequently used nickel-containing catalyst is Raney nickel.

The MgF_2-NiF_2 binary fluorides used in our research were prepared by the precipitation from a solution of a mixture of nickel nitrate(V) and magnesium nitrate(V) with an aqueous solution of ammonium fluoride. The obtained precipitate of binary fluorides was reduced with hydrogen atmosphere at 500°C. As a result of it, a part of NiF_2 undergoes reduction to metallic nickel, whereas MgF_2 is stable in this conditions and no reduction of this compound was observed. Magnesium fluoride makes a support on which the nickel metal is deposited.

The catalysts were tested using TPR-H_2, XRD, BET methods. After reduction at 500°C , these catalysts have metallic nickel, large surface area and mezopores. The obtained catalysts have been studied in the CO_2 methanation reaction. All binary fluorides are active and show high reaction conversion. The catalyst containing 85 mol% of NiF_2 and 15 mol% of MgF_2 (MgNi85) was the most active and its activity exceeded that of a commercial Raney nickel catalyst. The best activity was obtained at temperatures of 400°C and 450°C (Figure 1). It also has high reaction selectivity.

The way of nickel catalyst synthesis developed in this study is very simple, because it does not require the introduction of a support and enables a precise control of nickel metal content. The NiF_2-MgF_2 catalyst, in contradistinction to Raney nickel, is not pyrophoric and can be stored in air for a long time.

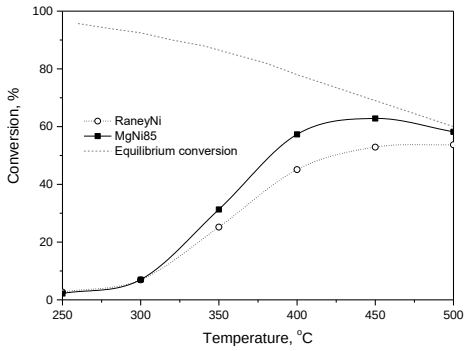

Figure 1. CO_2 methanation conversion for MgNi85 and Raney nickel.

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Synthesis optimization of precursors of nature-based bactericides: alliin and its derivates

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In this day and age, a resistance to antibiotics is becoming a more significant issue. Allium plants such as garlic or onion developed a self-protective mechanism against pathogens and microorganisms. Sulfur compounds are the main ones responsible for this mechanism. One of the advantages of these compounds is their fast degradation rate, which prevents the development of bacterial resistance [1,2]. In this work, we focused on one of them, allicin. We aimed to prepare and optimize the synthesis of allicin precursors, namely alliin and its derivates, methiin, ethiin, and propiin (fig. 1).

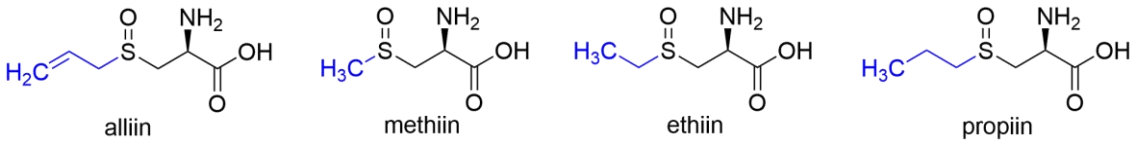

Figure 1: Structure of precursors

The preparation of these precursors is a two-step synthesis. In the first step, L-cysteine is alkylated to the corresponding *S*-alkyl-L-cysteine. The second step involves oxidation with hydrogen peroxide to (±)-L-sulfoxide. The tested parameters included temperature, type and amount of catalyst, and the molar ratio of starting materials for the alkylation step. The chosen catalysts were sodium hydroxide solution, ammonium hydroxide solution, and sodium. Several oxidation agents were tested in the case of oxidation, particularly hydrogen peroxide and tetraisopropyl orthotitanate with tert-butyl hydroperoxide. Furthermore, the effect of the amount of oxidation agent and temperature on the reaction course was observed. All of the above mentioned precursors have been successfully prepared, and in follow-up research will be used for the topical application.

This work was supported from the OP RDE registration no.: CZ.02.2.69/0.0/0.0/19_073/0016928“, funded by the ESF.

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New mesoporous organosilica with controllable morphologies: Their design, synthesis and applications as nanocatalysts for organic transformations under green and sustainable conditions

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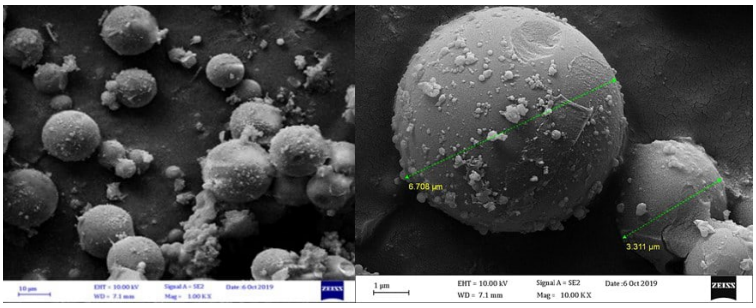
The design and facile preparation of nanomaterials (NMs) with suitable functional groups, active centres as well as definite morphologies for high-technology applications has received great attention in recent decades. These high-technology NMs can be used in different areas such as catalysis, smart medicine/drug delivery and formulations, sensors and microelectronic devices, gas storage, optical applications, adsorbents, chromatography, etc. Mesoporous silica materials (MSMs) have received significant attention from both academia and industry as an important class of NMs. The unique features of MSMs include the regular mesoporous structure and tunable surface properties as well as adjustable pore size, which guarantee their widespread applications in drug delivery, gas storage, heterogeneous catalysis, adsorption, batteries, and optical devices[1].

Periodic mesoporous organosilicas (PMOs) are an important group of hybrid inorganic–organic MSMs that have organosilane bridges in their pore walls. The high loading speed, uniform dispersion of organic groups within the framework, different surface characteristics and possibility of anchoring suitable functional groups make PMO materials unique compared to other organosilica materials for different applications. Recently, PMOs with different organic bridges and pore sizes as well as porous structures and morphologies have been successfully synthesized. However, there is still room to design and prepare new PMOs with appropriate physicochemical properties for definite applications including heterogeneous catalysis[1-5].



In continuation of our interest to develop MSMs and especially PMOs for promoting different organic transformations or CO2 capture, herein we wish to report the synthesis of a new PMOs with uniform particle size and high purity using simple, inexpensive and green methods.

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Synthesis of organometallic compounds - green approach to chemistry

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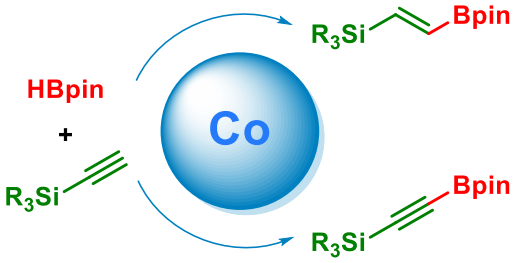
Modern advanced organic synthesis highly exploits the unique properties of organometalloid compounds to synthesize a variety of organic derivatives.[1] Moreover, in addition to being used as precursors in the synthesis, they are themselves valuable resources for the preparation of intelligent materials, polymers, catalysts, or bioactive molecules.[2]

However, the synthesis of organometallic compounds based on conventional methods generates large amounts of by-products, often toxic or corrosive. Importantly, they also tend to use dangerous and moisture-sensitive organolithium and organomagnesium compounds, therefore complicating applied experimental techniques.[3] On the other hand, catalytic methodologies allow avoiding some of these issues at the expense of their high price associated with the use of precious metals.[4] Therefore, the current trend in chemistry is towards the development and use of catalytic synthesis methods based on low-cost main groups or earth-abundant metals.[5]

In my poster communication, I will present a method for the synthesis of unsaturated boronic ester derivatives, which are valuable synthons in organic synthesis. The featured procedure represents a green, solvent-free, and high atom economy approach to chemistry, using low-cost cobalt pincer complexes.



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Bridging Pyridine-Oxazoline Ligands: Synthesis and Enantioselective Catalytic Applications

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Pyridine-oxazoline (PYOX) ligands are frequently used in asymmetric catalytic reactions due to their ease of synthesis from pyridine derivatives and inexpensive chiral amino alcohols. The importance of this class of chiral ligands has been realised since the 1980's and, the last five years have seen them return to prominence through several new asymmetric transformations [1]. The structural diversity of these ligands is widespread, with the functionalisation of the pyridine and oxazoline moieties previously achieved [2]. Yet, there are limited reports on the functionalisation of a carbon bridging the pyridine and oxazoline [3,4].

A key S_NAr alkylation reaction, expanding on previous research in conjunction with Roche Ltd., [5] has been utilised as the starting point toward the synthesis of novel bridging PYOX ligands. (Figure 1) Ten ligands were prepared in two steps, from 2-pyridyl alkylnitriles followed by their conversion to oxazolines in the presence of chiral amino alcohols and the Lewis acid, zinc chloride. The relative reactivity of related halopyridines to the reaction was examined. The synthetic utility of the method is enhanced by its simplicity, scalability, and its toleration of variation in the nitrile, halopyridine and amino alcohol starting materials. Catalysts based on these ligands were applied to several asymmetric catalytic reactions, including allylic alkylation, Alder-Ene, cyclopropanation, and Henry. The results demonstrate that the substituent located on the bridging carbon has a significant impact on the enantioselectivities and reaction conversions.

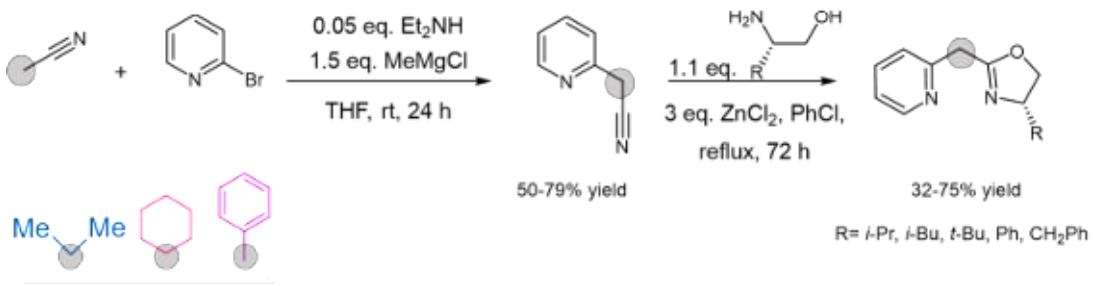

Figure 1: Two-step synthesis of bridging PYOX ligands.

Financial support from the College of Science, NUI Galway is gratefully acknowledged.

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CO_2 methanation over mesoporous silica supported Ni catalysts

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The major impact of the increasing CO_2 emissions on the environment has compelled the scientific community to research for solutions in order to diminish its effects. One solution might be the transformation of this greenhouse gas, through different technologies, in valuable chemicals like methane, methanol or syngas. This might be a compelling measure for the chemical and energy companies and even the scientific communities to find better strategies for sustainable use of resources. One feasible technology to add value to CO_2 is its hydrogen reduction to CH_4 also known as CO_2 methanation. This catalytic process has been investigated over a large variety of metal catalysts, like Ni, Ru, Rh, Cu [1]. Ni based catalysts although exhibit high catalytic activity in the methanation reaction do present a major drawback in catalytic stability.

Due to their large specific surface area, ordered mesoporous channels, and high hydrothermal stability the silica mesoporous materials (SBA 15, FDU 15, MCM 41) might enhance the dispersion of active metal nanoparticles and especially might significantly increase their stabilization inside the channels, improving thus the catalytic performances [2].

In this context, this research has investigated a series of metal-based catalyst support on different mesoporous silica structures (SBA 15, FDU 15). The mesoporous silicas were selected to have pores with narrow size distribution and of different values (3-5 nm for SBA 15 and 7-8 nm for FDU 15) and were prepared by solvothermal methods. The catalysts were prepared through three different approaches: wet impregnation, double solvent and melting impregnation, and tested in CO_2 methanation in a temperature range of 100-500°C under atmospheric pressure. The as prepared catalysts underwent different characterizations (SEM-TEM, BET, XRD) in order to investigate the preservation of ordered mesoporous structure, the encapsulation of NiNPs inside the pores and the crystalline structure of components. The functional characterization (thermo-programmed desorption techniques) investigated the metal support interaction with direct implication on the catalytic performance towards CO_2 methanation.

The characterization results show that the melting impregnation was the method which provide materials with high dispersed NiNPs placed inside the silica channels.

The outcome of the catalytic tests revealed the important influence of the preparation method and of the support nature upon catalytic results. For catalysts with most of NiNPs stabilized inside the pores high catalytic activity was obtained that even at low temperature (350°C). CO_2 conversions above 80% were obtained for Ni/SBA 15 at 450°C. The major product is CH_4; low concentrations of CO were also observed. The catalysts are stable for 8h time on stream and no carbon deposition has been observed.

In summary, the results obtained might present a significant contribution in developing highly active and stable catalysts for CO_2 methanation.

Thanks to NO Grants 2014 - 2021, under Project contract no. 13/2020.

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CO_2 valorization as synthesis gas by combined reforming of biogas

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The reaction between CO_2 and CH_4 (methane dry reforming - DRM), although possible and appealing at first sight since both molecules are recognized to have important green house effect, has a series of major drawbacks when it comes to practical applications. The most important one is the rapid catalyst deactivation by carbon formation and accumulation on the catalyst's active sites, besides the formation of syngas with low hydrogen content. By addition of water (combined steam and dry reforming of methane - CSDRM), carbon deposition is significantly suppressed, and hydrogen content in the products is increased, resulting a syngas with better qualities. Methane and carbon dioxide are also the main components of the purified biogas, so its valorization by syngas production would be of particular interest, both economically and environmentally. In this presentation the results of CSDRM for the production of a high-quality syngas, with H_2:CO ratio of 2:1 will be discussed. Ni was selected as active phase because it is affordable and active for reformation reactions, and alumina with bi-modal pore structure promoted with La_2O_3 and CeO_2 as support. Both promoters are expected to positively influence the CO_2 reformation reactions due to their basic nature (La_2O_3), and redox and oxygen storage properties (CeO_2).

Catalysts were prepared using a template-free method by co-precipitation of $Al(NO_3)_3$, $Ni(NO_3)_2$, $Ce(NO_3)_3$ or $La(NO_3)_3$ with NaOH solution, followed by reflux for 24h, filtration and drying at 100°C for 12h [1]. The target concentration for both Ni and promoters was 10wt.%. The catalyst precursor was further calcined in Ar at 450°C for 3h, and reduced in H_2 at 650°C. Catalysts were characterized by XRD, N_2 adsorption-desorption isotherms (BET), TPR, STEM, H_2-TPD, and CO_2-TPD. Catalysts were tested for CSDRM in a fixed-bed reactor, under atmospheric pressure, at 600°C-700°C.

All catalysts present bi-modal pores structure and similar total surface area (Table 1). TEM images revealed that both La_2O_3 and CeO_2 are very well dispersed on the surface, no visible island of these oxides being identified. The addition of promoters significantly increases the Ni surface area, proving that NiNPs are better dispersed and stabilized. TPD revealed that addition of promoters increases the interaction of NiNPs with the support. CO_2 conversion is improved for $Ni/CeO_2/Al_2O_3$ and $Ni/La_2O_3/Al_2O_3$, compared to Ni/Al_2O_3, but no significant differences were observed between the promoted catalysts. Besides the dispersion of NiNPs, the intervention of La_2O_3 and CeO_2 in CSDRM is based on different mechanisms: lanthana enhanced the surface basicity, increasing thus the surface affinity for CO_2 activation, while ceria's redox properties generate oxygen active species during the catalytic process, which contribute to improved water adsorption and transformation of carbonaceous intermediate species in reaction products [2]. Although by different mechanisms, the catalytic results are similar for both promoters. Carbon deposition is very low for all studied catalysts.

Table 1. Structural characteristics of catalysts.

Catalyst	S_{tot} (m^2/g)	d_{pore} (nm)	$d_{Ni\text{-}XRD}$ (nm)	S_{Ni} (m^2/g)	X_{CO2} (%)	H_2:CO
Ni/Al_2O_3	220	4, 8	6.5	2.3	59	2.2
$Ni/CeO_2/Al_2O_3$	208	4, 9	5	4.3	70	2.3
$Ni/La_2O_3/Al_2O_3$	215	4, 9	-	6.9	70	2.3

S_{tot} – total surface area, d_{pore} – pores diameter, $d_{Ni\text{-}XRD}$ – nickel crystallite size, S_{Ni} – nickel surface area calculated from H_2-TPD, X_{CO2} – CO_2 conversion at 650°C.

Thanks to NO Grants 2014 - 2021, Project contract no. 13/2020.

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Selective hydrogenation of cinnamaldehyde on low loading of noble metal based catalysts

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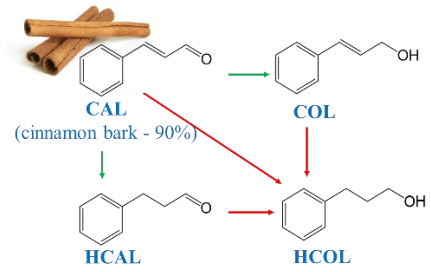
Unsaturated alcohols/aldehydes are platform molecules largely used in the chemical, food or pharmaceutical industries, especially in drugs design [1] and are produced by the chemoselective reduction of unsaturated carbonyl compounds. A representative molecule for α,β-unsaturated aldehydes is cinnamaldehyde (CAL), a naturally occurring organic compound (90% in cinnamon bark). The chemoselective reduction of CAL to the corresponding unsaturated reaction products, cinnamyl alcohol (COL) or hydrocinnamaldehyde (HCAL) as represented in Scheme 1, by using suitable heterogeneous catalysts is highly desirable since the traditional homogeneous synthesis procedure is hazardous and generates waste [2,3].

Herein, heterogeneous catalysts with low noble metal content (max. 0.5% noble metal mixture – e.g. 0.25 % Au - 0.25% Ir or 0.4% Au - 0.1% Pd) were prepared by their deposition-precipitation on mesoporous TiO_2@UVM7 support. The presence of the titanium oxide ensures a strong metal-support interaction by electron transfer from the support to the noble metal [4] and favors the preferential adsorption of the C=O group. The materials were thoroughly characterized by XRD, adsorption-desorption isotherms of N_2, XPS, FTIR and UV-VIS spectroscopies, electronic microscopy (SEM/TEM) and H_2-TPD in order to establish their textural, structural and morphological properties.

TiO_2@UVM7 is a bimodal support containing Ti and Si oxides prepared by the "atrane route", with a very high specific surface area (SSA) ~ 1150 m^2/g; the further noble metal deposition induces a very low decrease of the SSA (max. 10 %) indicating a well dispersion of the noble metal. Moreover, X- ray diffraction data revealed that the support structure is maintained after the deposition procedure.

The as-prepared catalysts were tested in the hydrogenation of CAL and the best results were obtained on 0.4% Au – 0.1% Pd/TiO_2@UVM7, with 88% yield to HCAL (Figure 1) and total conversion of the substrate. From the characterization data and the catalytic activity, we can infer that Pd is mainly responsible for the high conversion, while Au contribution resulted in high selectivity toward HCAL.



Scheme 1. Cinnamaldehyde hydrogenation – main reaction products

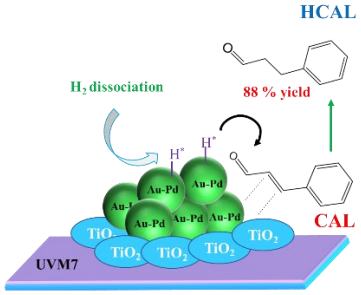


Figure 1. Chemoselective reduction of CAL to HCAL on Au-Pd/TiO_2/UVM7

This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS - UEFISCDI, PD 77/2020, PN-III-P1-1.1-PD-2019-1092, within PNCDI III.

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Development of an air-stable Co(III)-complex for the use in photocatalytic water splitting

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The establishment of renewable resources becomes more important with the constantly use of fossil fuels and their impact on the environmental pollution. The interest in energy supplies such as molecular hydrogen (H_2) significantly increased due to their utilisation of water splitting and using solar power as the energy source.[1] In this context finding a suitable Photosensitizer (PS) is of high interest, common complexes are transition metal complexes (TMCs) consisting of Ru^{II}, Os^{II} and Ir^{II}. The attempt is to find an inexpensive and earth-abundant metal, therefore the first-row transition metals (TM) become a considerable solution, like for instance cobalt.[2,3]

A qualified PS should possess a long-lived metal-to-ligand charge transfer (MLCT) excited state, which enables the electron transfer to the catalytic cycle of the water splitting mechanism. Unfortunately, cobalt bears a small ligand field splitting causing a fast deactivation of the MLCT into the low-lying metal-centered (MC) state. One method to elongate the lifetime is to destabilise the MC-state with strong σ- donor ligands and remodel the octahedral geometry. Contrariwise the MLCT-state stabilises with π- aceptor ligands or by an electronic delocalisation.[2] In this work a Co^{III}-complex with strong σ-donor characteristics is synthesised, using the well-known *N*-heterocyclic carbenes (NHCs) to destabilise the MC-state and extend the MLCT-lifetime. Apart from this, the backbone is being modified to analyse the changes in the UV/Vis absorption and emission spectroscopy. [2,3]

Herein we report a Co^{III}-NHC-complex (figure 1) with a functional group in the backbone. The UV/Vis-spectra shows absorptions from 220 nm to 500 nm and emissions at 315 nm and 357 nm. Further plans are to include the investigation of the Co^{III}-species and their characteristics more with a changing backbone functionality and eventually extending the moieties. The aim is the implementation of the complex into the water splitting catalytic cycle.

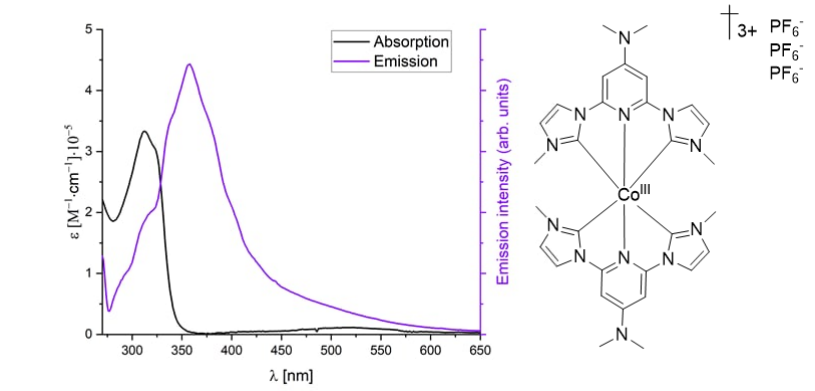

Figure 1: Absorption (black) spectrum of $Co^{III}(BIP^{NMe2})2$ in MeCN. Deareated emission (purple) after excitation at 250 nm. The synthesised Co^{III}-complex is shown next to the spectra.

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Synthesis of Water-soluble Randomly Methylated Cyclodextrin-NHC-gold Complexes

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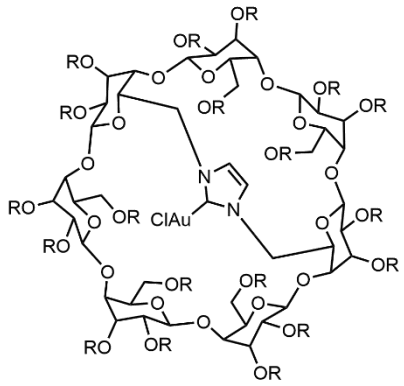
For the sustainable chemistry the avoidance of solvents, atomically economical reactions, and the use of water as solvent are important issues. This requires the development of reactive, selective, and recyclable homogeneous catalysts.

One approach relies on the use of cyclodextrins as ligands. These cyclic oligosaccharides, which are obtained by enzymatic degradation of starch from renewable raw materials, are therefore available in large quantities at low cost. The basic structure forms a hollow truncated cone, with a hydrophobic chiral cavity and a hydrophilic shell.[1] They easily form host-guest complexes and can transfer their chirality to a hydrophobic substrate during catalysis.[2,3] Due to the natural chirality, a complex stereoselective synthesis is not necessary, in contrast to many industrially used ligands.

Native β-cyclodextrins have a low solubility in water because the free hydroxy groups form intramolecular hydrogen bonds along the cyclodextrin. This effect can be interrupted by complete methylation. However, to create a good compromise between water solubility and organosolubility, partially methylated cyclodextrins will be synthesised in this work.[4] Connected with *N*-heterocyclic carbenes, which have proven to be good ligands to many transition metals with their strong σ-donor and weak π-acceptor properties, they form enantioselective and recyclable catalysts, as shown e.g. by Sollogoub and Krause.[2,3]

In the work of Sollogoub and Krause, bridged cyclodextrins and cyclodextrins whose catalytic centre is in close spatial proximity to the carvity showed good to very good enantioselectivity.[2,3] In this work, symmetrically bridged cyclodextrins and unilaterally linked cyclodextrins with random methylation are to be prepared following the work of Sollogoub and Menuel.[2,5] In addition, other catalysts will be prepared that are characterised by a long and flexible linker so that the catalytic gold centre can extend into its own or another cyclodextrin carvity. The host-guest properties are investigated with the help of ion mobility spectrometry and NMR spectroscopy.



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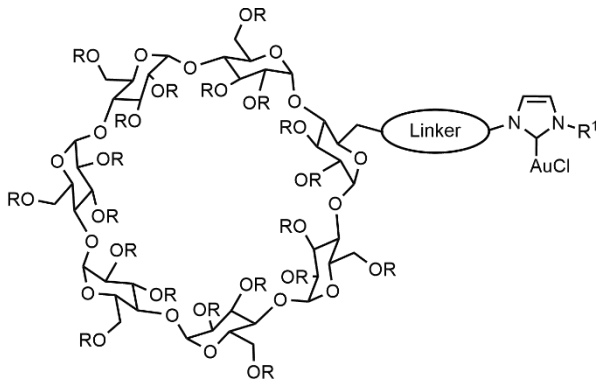

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Synthesis of CuO-$Ce_xZr_{1-x}O_2$ catalysts for combustion of volatile organic compounds

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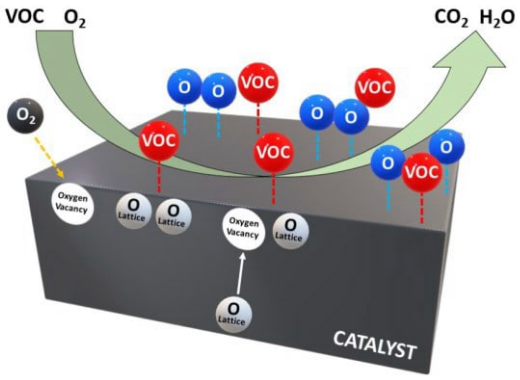
Volatile organic compounds (VOCs), which by definition are organic compounds with a boiling point ≤ 250 °C at atmospheric pressure, are amongst the major contributors to global air pollution. VOCs are emitted from a wide variety of sources and play an important role in aerosol, photochemical smog and ground-level ozone formation, hence contributing to global climate change. Besides their impact on the environment, VOCs also pose a threat towards human health, since many VOCs are carcinogenic, mutagenic and teratogenic. Due to their toxic nature, strict regulations regarding VOCs emissions have been implemented. To comply with these regulations, efficient techniques of VOCs elimination from poluted air, including adsorption, membrane separation, thermal oxidation, (photo)catalytic combustion, have attracted extensive research. From these methods, catalytic combustion is believed to be the most promising due to its low cost, low operational temperature (200 – 500 °C) and limited formation of by-products.[1]

At present, noble metal based catalysts are considered to be the most efficient for the VOCs abatement. However, the high cost of these materials has led scientific research towards exploring cheaper transition metal oxide containing catalysts. Ceria and cerium based materials have been widely used in catalytic processes (CO-PROX, automotive three-way-catalysis, water-gas shift reaction, etc.) owing to their high redox activity and oxygen storage capacity (OSC). The latter is caused by the presence of lattice defects in the crystal structure, which induce oxygen mobility. As a result, besides Langmuir-Hinshelwood (L-H) and Eley-Rideal (E-R) also Mars-van Krevelen (MVK) mechanisms can be activated in the oxidation reactions. Hence, this is why ceria and cerium based materials are of specific interest for the VOCs combustion.

According to literature, the OSC of the widely used ceria can be enhanced significantly by incorporating zirconium ions in the crystal lattice. The smaller size of a Zr^{4+} cation (ionic radii of 0.84 Å compared to 0.97 Å for Ce^{4+}) modifies the cubic fluorite structure of CeO2, which results in an enhanced OSC and oxygen mobility, improving the redox properties of the material.[2] Moreover, the addition of zirconia also improves the thermal stability of ceria. Therefore, in this research focus is put on the synthesis of Ce/Zr-oxide based catalysts for the VOCs combustion.

In an attempt to enhance the VOCs combustion properties of Ce/Zr-oxide based materials, specific amounts of Cu were added. Cu is cheap, has good redox properties and is known to have a strong synergistic effect with CeO_2. In addition, the activity of CuO/CeO_2 catalysts depends on the CuO dispersion and/or on the extent of interaction with the support.[3] Therefore, in this research Cu was deposited by using a water based ammonia driven deposition precipitation method, which ensures a strong metal-support interaction and high stability of the deposited CuO sites.[4] The influence of the catalyst composition CuO-$Ce_xZr_{1-x}O_2$ (x = 0; 0.25; 0.5; 0.75; 1) on the properties of active phase and its catalytic performance in the toluene combustion was studied.



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Synthesis of cuprous oxide nanoparticles and their application as methylene blue photodegrader

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The dye industry is one of the most important in the world, supplying its products mainly to the textile industry. In this context, the textile industry represents a global pollution problem, according to studies this industry is among the first 6 places of the most polluting industries around the planet due to the discharge or accidental dumping of contaminated wastewater into the courses. of water. These effluents are characterized by having an intense color, high chemical oxygen demand (COD) and pH that varies between values of 2 to 10. For this reason, it is of great importance to look for methods of decomposition of these species, in view of the fact that the water is a vital resource for society.

Various methods have been used for the reduction or degradation of these colorants in water, such as adsorption on activated carbon, chemical coagulation, Fenton, photolytic degradation, reverse osmosis, enzymatic treatment, microbial degradation, etc. [1,2], however, these techniques have drawbacks, such as high cost of treatment and equipment, harmful UV radiation and sludge generation (which must be treated in a second stage). To counteract these problems, photocatalytic or electrocatalyst methods have been used for the oxidation of dyes and other organic species present in aquifer flows [2,3].

Based on the above, the present work aims to study the photocatalyst properties of cuprous oxide nanoparticles for the degradation of methylene blue. The nanoparticles were chemically synthesized by adding 0.1 M $Cu(CH_3COO)_2 \cdot H_2O$ and 0.2 M NaOH, in a volume of 100 mL. After 5 minutes, 0.1M L-ascorbic acid was added, resulting in a color change from blue through green, yellow, orange to brick red. After that, the nanoparticles are washed and centrifuged, repeatedly. Finally, what is obtained is dried, obtaining a fine powder. The structures were characterized by SEM showing a cube morphology and XRD confirmed the presence of the Cu_2O phase. The initial tests as a photodegrader were carried out at a concentration of 5 ppm of dye with the nanoparticles immersed in the solution by suspension. The preliminary results show a degradation of 58 and 75% at 60 and 90 minutes, respectively, of irradiation with the sunlight lamp, in addition, the attenuation of the initial coloration is observed.

Acknowledgments
The autors, especially PhD.(C) Francisco Figueredo are grateful the financial support of ANID, Beca Doctorado Nacional N°21202131 also to the Pontificia Universidad Católica de Valparaíso, Beneficiario Beca Postgrado 2019 and the Dr. Paula Grez to DI-PUCV with the project N °125.789.

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Enzymatic synthesis of fructose fatty acid esters using oleic acid as acyl donor and lipase cross-linked enzyme aggregates as biocatalyst

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Sugar fatty acid esters (SFAE) are biocompatible nonionic surfactants widely used in the food, cosmetic and pharmaceutical industries [1]. Moreover, SEAEs have gained attention thanks to their anti-bacterial and antifungal activity, while they are also reported as insecticides and miticides [2]. They can be synthesized enzymatically and offer many advantages over chemical synthesis [3].

Lipase-catalyzed acylation of sugars with activated carboxylic esters in organic solvents is well documented in the literature [4], and this one-step enzymatic strategy has been extended to SFAE synthesis, providing a promising approach for cleaner production, thus gained widespread popularity [5]. When catalyzed by lipases, sugars can be acylated by esterification with fatty acids or transesterification with active carboxylic acid esters to produce SFAEs. Both reactions must be carried out in a non-aqueous medium to prevent any possible hydrolysis of the ester product. Enzymatic methods have been shown to outperform the currently dominant chemical synthesis in terms of mild reaction conditions, simple operational procedures, excellent regioselectivity, high productivity, and easy product isolation[6].

In this study, we present our results on the enzymatic reaction between fructose and oleic acid mainly but also the influence of various parameters such as the reaction time, the solvent, the chain length of the fatty acid, the molar ratio between sugar and fatty acid, and the initial amount of water in the medium. Where possible, we will model the curves obtained in order to provide industrially important kinetic data. We give analytical conditions allowing a fast follow-up of the reaction.

This work was generously supported by The General Directorate for Scientific Research and Technological Development (DG-RSDT), Algerian Ministry of Scientific Research.

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Light-Induced Homolysis of Copper(II)-carboxylates

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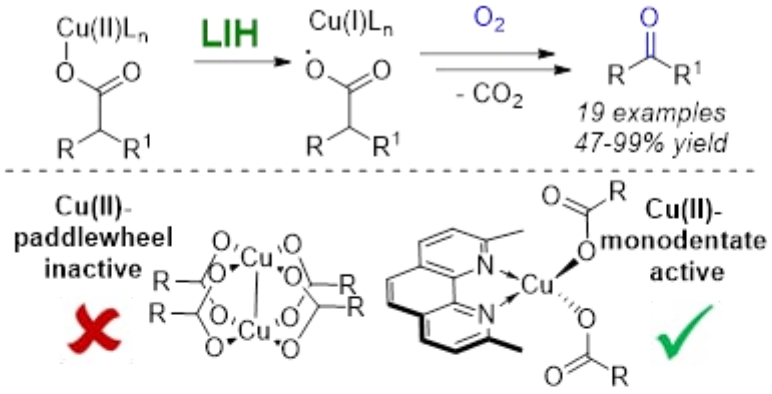
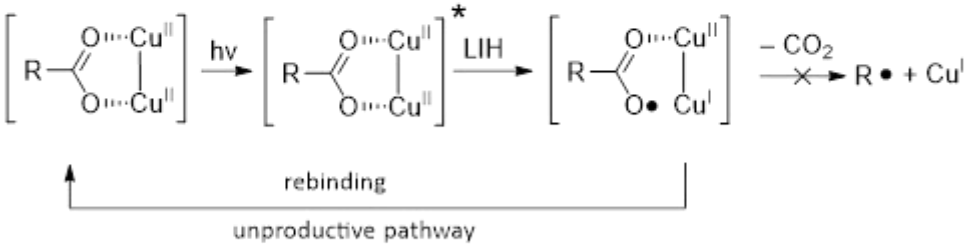
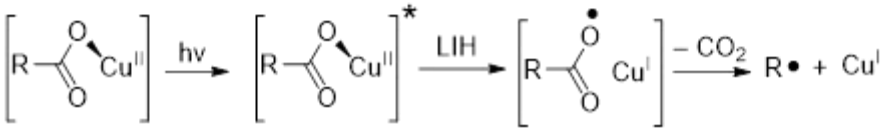
Showcasing the concept of light-induced homolysis for the generation of radicals, the Cu^{II}-photocatalyzed decarboxylative oxygenation of carboxylic acids with molecular oxygen as the terminal oxidant is described [1]. Two Cu^{II}carboxylate complexes with different coordination geometries were synthesized and characterized by X-ray analysis, correlating their structure with their ability to initiate light-induced decarboxylations.



a) Rebound mechanism (dinucelar paddlee-wheel type Cu(II)-carboxylates)



b) Homolytic cleavage mechanism (monodentate Cu(II)-carboxylates)



Further, several mechanistic investigations were carried out, e.g. UV-Vis absorption spectra, solution-phase IR spectra as well as EPR studies supporting the light-induced homolysis of monodentate Cu^{II}-carboxylate, rather than paddle-wheel type chelation. The method can be successfully applied to nonsteroidal anti-inflammatory drugs (NSAIDs) such as felbinac, ibuprofen, or naproxen delivering the corresponding decarboxylated products in high yields. Also, cyclohexyl substituted carboxylic acids could be converted to corresponding cyclohexanones.

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Copper(I)-photocatalyzed Bromo-(nitromethylation) of Olefins and Synthetic Applications

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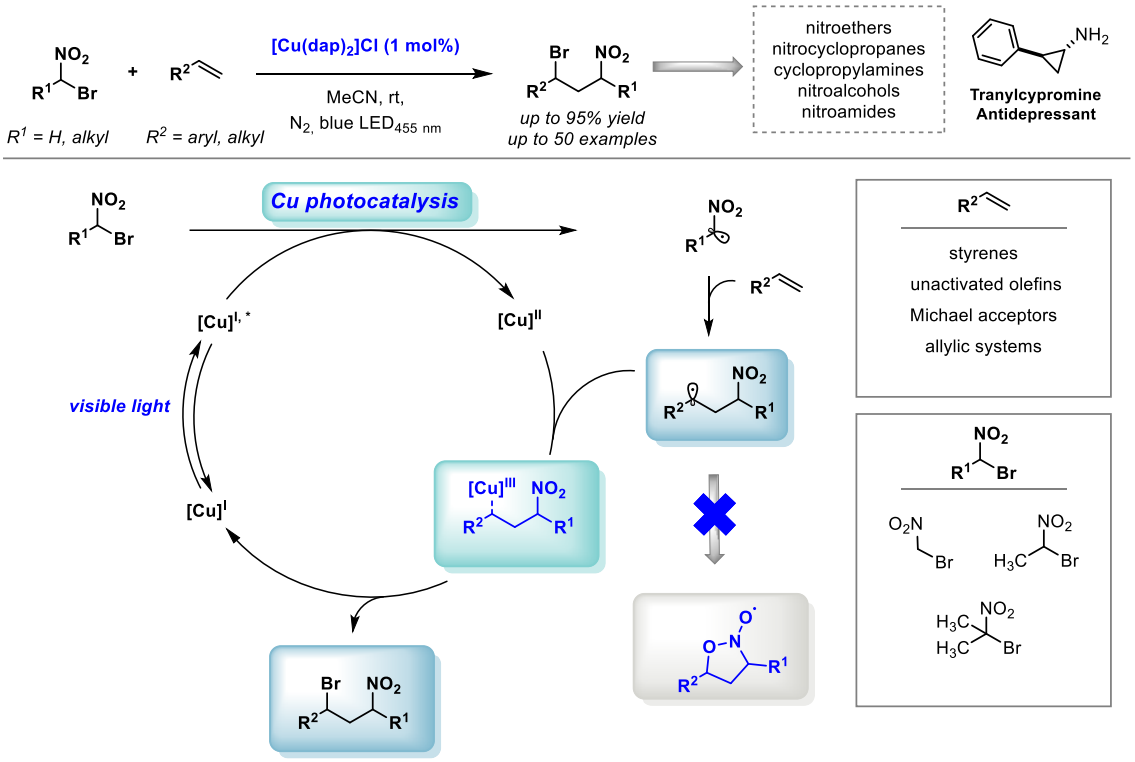
We developed a new method for the atom transfer radical addition (ATRA) of bromonitromethane-derivatives with styrenes and unactivated alkenes to obtain highly functionalized products with a vast potential for further synthetic applications such as the access to cyclopropylamines. Although a complementary ATRA reaction has been previously reported applying iridium [1], we can show that the exchange of iridium towards a copper-based photocatalyst offers not only the ability to use a more abundant and environmentally friendly catalyst as well as an enhancement of the scope and yields, but it also proceeds through an altered radical intermediate and therefore via a different reaction mechanism.



The method works well for an array of olefin structures such as styrenes, unactivated olefins, allylic systems, and Michael acceptors. Furthermore, the protocol can be applied for late-stage functionalization of bioactive molecules, as well as upscaling to gram quantities of product. The obtained products could be transformed into various valuable structures such as nitroethers, -alcohols, and -amides as well as nitrocyclopropanes and by further reduction into aminocyclopropanes such as the antidepressant tranylcypromine.

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Synthesis of novel functional polyolefins

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Polyolefins have become prominent in the everyday life. Organic polymers excel in chemical and mechanical properties, energy efficiency, are economically and ecologically attractive materials, and continue to experience an ever-growing demand in a wide range of applications [1,2]. Nonetheless, polyolefins are hydrophobic and their application in blending, adhesion, and dyeing remains difficult due to a lack of polar organic groups. Therefore, the synthesis of tailored polyolefins with reactive units and functionality is a key target [3-4]. Among the large group of known organic polymers, polybutadiene is a versatile and convenient starting material for further functionalization thanks to the high content of readily accessible double bonds revealing reactivity in a wide spectrum of stoichiometric and catalytic transformations. Therefore, butadiene-based polymers seem to be excellent precursors for the synthesis of organofunctional polymers [5].

In this contribution, efficient methodologies for the synthesis of novel organofunctional polymers are proposed. It includes the synthesis of two novel polymeric precursors, bearing hydrosilyl or alkyne moieties and their subsequent transformation through catalytic reactions. The developed synthetic strategy enables incorporation of a wide variety of functional units into the polymer chains, which cannot be introduced through conventional polymerization protocols [6-7].

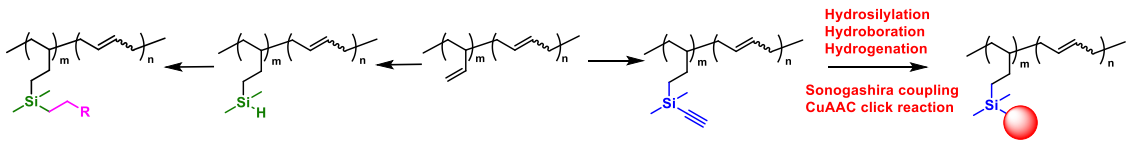

Figure 1. Novel organofunctional polymers

Acknowledgments

The authors wish to thank the National Science Centre, Poland, for their financial support under project UMO-2019/32/C/ST4/00178

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Pd-catalyzed allylic substitution between C-based nucleophiles and Bicylcic Aziridines

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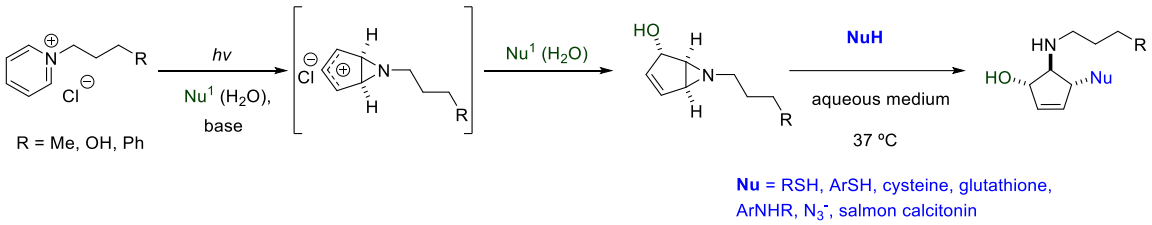
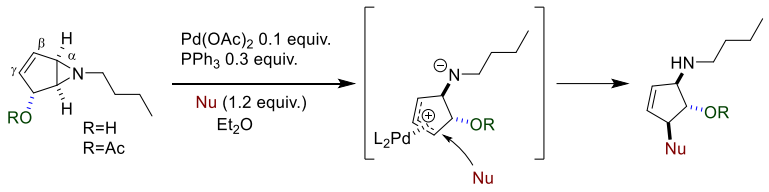
A short route for the synthesis of these structures is the photochemical transformation of pyridinium salts to bicyclic-aziridines. The photochemical rearrangement forms a *cis*-fused cyclopenteno-aziridine allylic cation which reacts stereospecifically with poor nucleophiles/solvent devising a stable bicyclic-aziridine containing a new C-Nu bond in *trans*-position (Scheme 1).[2] In 2016, We reported the ring opening of these aziridines structures by performing a S_N2 reaction with nucleophiles such as azides, anilines, and thiols, forming new carbon-heteroatom bonds (Scheme 1).[3]



Scheme 1. Photochemical transformation of pyridinium salt and an example of ring opening

Considering the peculiar structure of the above described α-oxycyclopenten-aziridines in connection with our long-standing interest in Pd-catalyzed allylations, we were intrigued by the thought of investigating the behaviour of such cyclic substrates against soft carbon-based pro-nucleophiles under Pd(0) catalysis. Within this framework, we recently developed a palladium-catalyzed ring opening of vinyl aziridines. This process proceeds takes place through η^3-allylpalladium complex formation via aziridine cleavage, and γ-reactivity of carbon-based nucleophiles leading to new carbon-carbon bonds (Scheme 2).[4] In this line, will be described recent efforts on the enantioselective opening of the aziridine via Pd catalysis.



Scheme 2. Palladium catalysis followed by nucleophilic attack

Acknowledgements: This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951996 *Biomass4Synthons.* We also thank the Fundação para a Ciência e Tecnologia for financial support (PhD grant 2020.04589.BD) and project (PTDC/QUI-QOR/32008/2017 and PESSOA 2018/2019 (Proc. 441.00 França and PHC PESSOA 2018 No 40875QJ)

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Plasma Catalytic Dry Reforming of Methane: How Material Properties Influence Conversion and Kinetics – The PlasMaCatDESIGN Project

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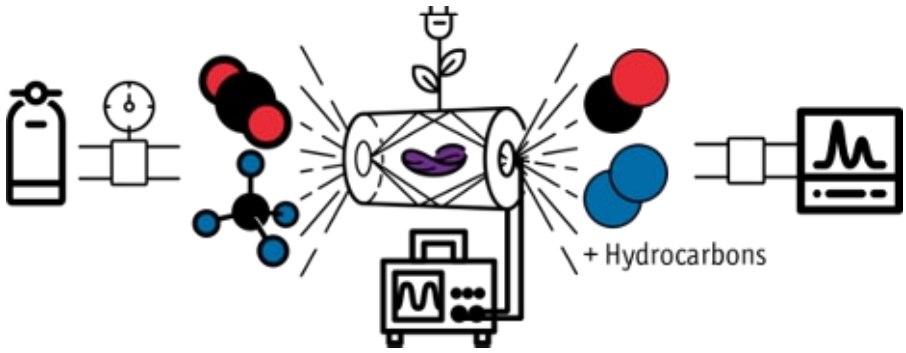
Although much research is being conducted on plasma-assisted heterogeneously catalysed CO2 conversion and some general concepts and literature data are available, systematic and detailed knowledge of the impact of material properties with respect to catalytic control (efficiency, space time yield and selectivity) in the plasma is currently insufficient[1]. Recent literature is starting to fill in some gaps through detailed catalyst characterization[2-4], but the study of the impact of material properties on the kinetics of the overall CO2 conversion reactions are often missing In the PlasMaCatDESIGN project, we aim to study material-activity correlations through controlled and systematic catalyst synthesis and detailed characterization, not only linking reagent conversion and product selectivity/yield, but also reaction kinetics, to catalyst properties. This knowledge is necessary to allow crucially needed knowledge-based catalyst design.

An essential part of this project is thus the systematic and controlled synthesis of catalytic materials, structured at different length scales (from macro to nano). These materials are thoroughly characterized using typical methods, e.g., XRD, N2-sorption, SEM(-EDX), TGA-MS, NH3-TPD, CO2-TPD, CH4-TPD, DRIFTS and Raman, before and after plasma catalysis. For plasma catalysis, less common methods such as Hg intrusion porosimetry, TPO-MS, TPR-MS, and cyclic TPR-TPO/TPO-TPR are also employed.

A coaxial dielectric barrier discharge (DBD) reactor is employed to perform the plasma catalytic conversion of CH4 and CO2 (known as dry reforming of methane; DRM). It is the simple geometry of a coaxial DBD set-up that allows for use of catalysts in the plasma discharge. The plasma catalytic process is studied using a GC to study conversion and selectivity/yield, thermocouples are inserted before and after the plasma to measure the overall gas temperature and several electrical components are used to evaluate the plasma power, current, Lissajous figure shape, number of discharges per half cycle and the transported charge per discharge in function of the applied voltage and AC frequency[5]. Results show a clear impact of the catalytic element applied. Both positive and negative impact on conversion, selectivity and kinetics have been obtained via deposition of different active elements.



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Acid catalyzed methanolysis of olive leaves crude extract

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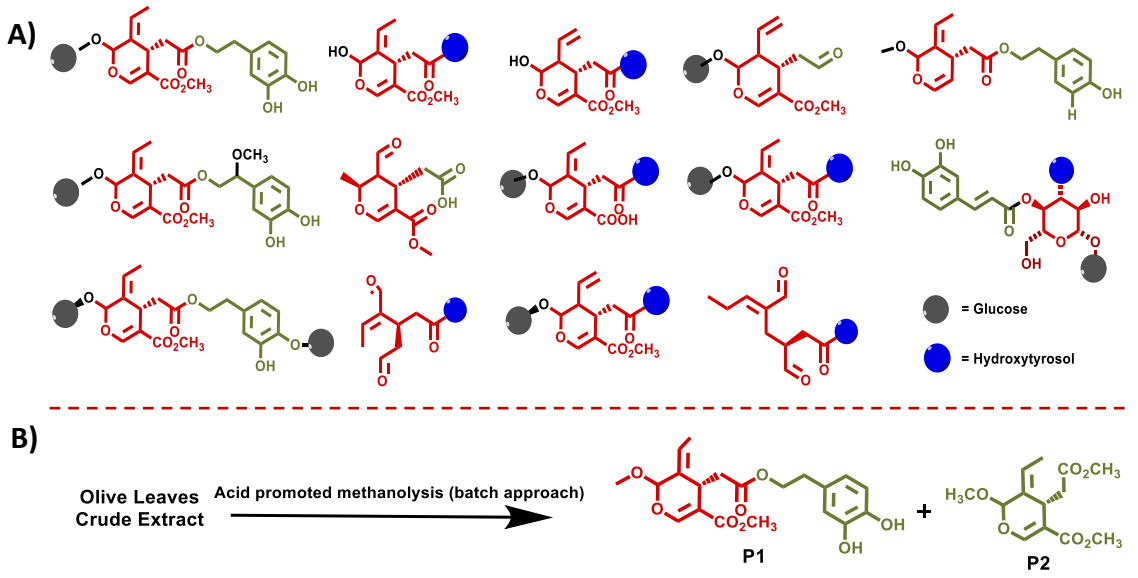
The development of bio renewable chemical building blocks for chemical-based commodities is an important issue. A variety of phenolic compounds exhibit a wide range of bioactivity and can be obtained from olive leaves. Transformations of these structures have yielded important scaffolds with potential pharmacological properties. [1-4]. Aiming at the valorization of olive leaves, we focused on the methanolysis reaction directly from the olive leaves crude extract rich in phenolic compounds, such as oleuropein (Figure 1A).

By exploring different organosilylated and organosulfonated acids (modified catalytic materials known by their eco-friendly characteristics and their low cost), under batch conditions, different temperatures and reaction times, it was possible to fine tune methodologies to synthesize two interesting synthons (P1 and P2) (Figure 1B) by an easy, cheap and scalable method derived from the cleavage of the hydroxytyrosol and glycoside units of secoiridoids present on olive leaves crude extract, opening the possibility to explore the synthetic manipulation of the mono-terpene core of oleuropein and related phenolic compounds.



The authors acknowledge Fundação para a Ciência e Tecnologia (FCT) for financial support (Ref. SFRH/BD/148211/2019, UIDB/04138/2020, UIDP/04138/2020, PTDC/QUI-QOR/32008/2017). The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951996.

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Bifunctional catalysts based on hydrotalcites for Rosaphen one-pot synthesis

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The presented study deals with the preparation of metal-modified bifunctional catalysts based on hydrotalcites and their utilization for the „one-pot“ synthesis of 2-methyl-5-phenylpentanol, also known as Rosaphen. It is a fragrance with the odor of fruit, and roses, similar to green tea, honey, wine, and sweet grapefruit. It is extensively used in the perfumery industry because of its excellent stability and relatively low price.

Hydrotalcites due to their basic properties are considered quite promising heterogeneous catalysts for the synthesis of fine chemicals by aldol condensation. The earliest works [1,2], in which hydrotalcites were used as catalysts, were focused on a model reaction of aldol condensation of benzaldehyde with acetone. The synthesis of Rosaphen starts from cinnamaldehyde and propionaldehyde. Aldol condensation of these compounds using hydrotalcites has not yet been published. Furthermore, hydrotalcites can be modified by precious metals and such prepared bifunctional catalysts can be used subsequently for aldol condensation followed by hydrogenation, the so-called "one-pot” reaction.

In the first step of Rosaphen preparation, aldol condensation, the optimal ratio of Mg/Al in hydrotalcite, the molar ratio of reactants, and temperature were found. The most suitable conditions for the reaction were found as follows - temperature of 35 °C, methanol as a solvent, rehydrated hydrotalcites with the molar ratio of Mg:Al equals 3:1 or 3,5:1, molar ratio of reactants 1:1, the mass ratio of HT to cinnamaldehyde 0,2:1. Under such conditions after 4 hours of the reaction 76% conversion and 85% selectivity to the desired 2-methyl-5-phenylpenta-2,4-dienal were achieved.

In the following, hydrotalcite with molar ratio Mg:Al equals 3,5 was modified with different amounts of Pd. Such catalysts were tested for aldol condensation and then for one-pot synthesis.

During the hydrogenation step, the effect of temperature, hydrogen pressure, the molar ratio of reactants, the amount of palladium, and the catalyst was monitored. The best results were obtained at 115 °C, 7 MPa, 40 wt. % of catalyst modified 0.5 wt.% palladium. The most suitable molar ratio of cinnamaldehyde to propionaldehyde was 1: 1. Under the given conditions, 100% conversion of cinnamaldehyde and selectivity of 91 % to the desired Rosaphen were achieved

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Pyridoxal-catalyzed transamination: molecular evolution and synergistic catalysis in the origins of life

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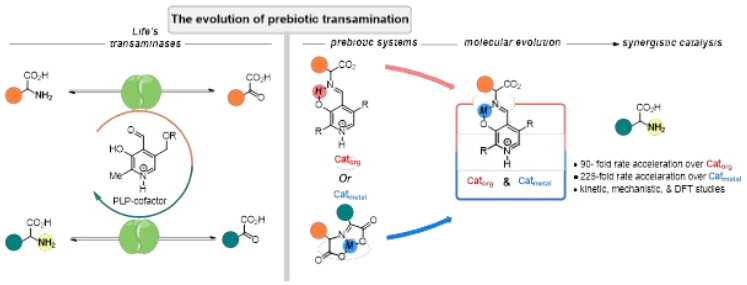
To make amino acids, life relies primarily on the transamination between glutamic acid and various ketoacids – pyruvate in the case of the key amino acid alanine.[1] Enzymes catalyzing the transamination in living cells rely on the cofactor pyridoxal-5'-phoshate (PLP) – a small, non-proteinaceous organic molecule – but enzymes were not present at life's origins. Prebiotic chemistry studies show that transamination can be catalyzed abiotically by simple metals ions (Cu^{2+}, Ni^{2+}),[2] yet this catalytic pattern has not been preserved by biochemistry, even though life does not typically shy away from metal ions as cofactors. Thus, it has long been hypothesized that PLP alone could carry some of the catalytic power before the advent of enzymes. Early reports showed that PLP (or pyridoxal - PL), could catalyze some key steps of transamination. Additionally, when metals were used as co-catalysts some aspects of the catalysis could be improved,[3] while other inhibited.[4] However, still lacking are more holistic approaches to the PLP-mediated transamination in prebiotic settings, to uncover clues for the choice of such a cofactor. Why did life choose to transition from metal catalysis to organocatalysis? To answer this, we performed a comprehensive, systematic study of PLP-catalyzed transamination reactions under prebiotically plausible conditions.

A survey of PLP and PL under plausible prebiotic conditions revealed that PL catalysis was not efficient enough to warrant life's shift from simple metal ions to organocatalysis in transamination. We therefore conducted a systematic evaluation of the 18 most abundant metals as co-catalysts with PL and PLP, under buffered (pH 6), conditions. With an equimolar PL-metal ratio a remarkable picture emerged. The less abundant metals (Cu^{2+}, $V^{3/5+}$, Ni^{2+}) previously shown as catalytically active[2] in the absence of organic cofactor were still effective as co-catalysts with PL (with an increase in activity). However, equally high rates and amino acid production were attained when aluminium and iron were used as co-catalysts. Al^{3+} and Fe^{3+} are the two most common metals on Earth and are not competent transamination catalysts on their own. This synergistic metal-organocatalyst effect was even more pronounced when looking at unbuffered conditions, where rate accelerations of 90- and 225-fold were observed over PL- and metal-only catalysis, respectively – and both metals could be used in a reduced 2:1 loading. In addition, simpler PLP analogs were synthesized and were also found to display a synergistic effect. Therefore, the apparition of PL-like structures would have led to an increase of reaction efficiency by allowing the most abundant metals to take part in transamination catalysis.

This "molecular evolution" pattern is remarkable as transamination catalyzed by metals only and by metal/PL each follows a distinct mechanism. Indeed, metals alone function via a ternary mechanism, whereas PL/metal co-catalysis was presumed to occur via a mechanism similar to today's enzymes: a bi-bi ping-pong cycle. The analysis of kinetic parameters allowed us to demonstrate that enzyme-like kinetics following the ping-pong mechanism were indeed in play. Finally, the robustness of the system was evaluated through the addition of common prebiotic molecules as additives. The modulations of reaction rates observed showed that a synergistic system could have operated in the complex environment of the early Earth.

In conclusion, we have shown through in-depth quantitative, kinetics and DFT studies how the emergence of PL/PLP-like structures from prebiotic chemistry represents a key step in the molecular evolution of transamination reactions, from metal-catalyzed and abiotic towards the present-day complex biochemical machinery.



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CO_2 methanation using MOF(Al)-based / -derived Ni catalysts

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In the last decade, CO_2 methanation has known a revived scientific and technological interest due to its potential advantages from both the energetic and environmental point of view [1]. The main interest is focused on developing efficient catalytic systems in order to operate CO_2 methanation units at low temperatures (exothermic process). Ni supported catalysts are the most investigated ones, due to their promising activity, as well as their lower price, while different metal oxides or even metal-organic frameworks (MOFs) [2] are used as catalytic supports. Due to their excellent properties (in particular their high surface areas, and ordered porous structure), MOFs seem a promising alternative to other supports, since they could enhance both the activation of hydrogen by an improved metal dispersion, or the activation of CO_2, due to their enhanced sorption capacity for different molecules. The aim of this work is to comparatively evaluate the catalytic performance in the methanation of CO_2 of Ni supported catalyst using MOFs as starting materials. For this, three strategies were followed: (1) direct use of MIL-53(Al) as support; (2) immobilization of MIL-53(Al) on alumina to obtain MIL-53(Al)-alumina composites; and (3) derivation of MIL-53(Al) under air to obtain $Al_2O_{3[MIL-53(Al)]}$, which preserves to a large extent the properties of the starting MOF.

Synthesis of MOF(Al)-based catalysts was achieved by impregnation of either MIL-53(Al) or MIL-53(Al)-alumina composites with Ni (10wt.%), followed by reduction with $NaBH_4$. MOF(Al)-derived catalysts were obtained either by derivation of Ni/MIL-53(Al) at 600°C ($Ni@Al_2O_{3[D-Ni@MIL-53(Al)]}$), or deposition of Ni on MIL-53(Al) derived at the same temperature under air ($Ni/Al_2O_{3[D-MIL-53(Al)]}$). Both MOF(Al)-derived catalysts were reduced in H_2 at 750°C, for 3h. Characterization of catalysts was achieved by different techniques: BET, XRD, TGA, SEM/TEM, TPR, H_2-TPD, and CO_2-TPD. Catalytic tests were performed in a stainless-steel tube reactor (i.d. 9 mm), and consisted in either temperature-programmed reactions (TPRea) in the 100–500°C range, or stability tests at 300°C (0.1 g catalyst, 60 mL/min inlet flow, CO_2:H_2=1:4, 8400 h^{-1}). Effluent gases were analyzed by the coupled GC (TCD detector).

The as-prepared catalysts were tested in the methanation of CO_2, and compared to Ni/Al_2O_3 catalyst obtained by impregnation of commercial alumina. Catalytic activity tests show that CO_2 conversion increases with temperature up to 450°C, and then decreases (thermodynamic equilibrium is attained) (Fig. 1). In terms of methane selectivity, all catalysts show values above 85%. It was found that all MOF-based and MOF-derived Ni catalysts show better catalytic activity as compared to $Ni/Al_2O_{3[com]}$, in terms of both CO_2 conversion, and methane selectivity. $Ni@Al_2O_{3[D-Ni@MIL-53(Al)]}$ shows the best catalytic performance over the whole temperature range. Due to the lower thermal stability of the MOF-based catalysts (as revealed by TGA analyses), these samples were tested only up to 400°C. It may be concluded that, at 400°C, the catalytic activity of the investigated catalysts decreases in the series: $Ni@Al_2O_{3[D-Ni@MIL-53(Al)]}$ > $Ni@MIL-53-Al_2O_{3(4-1)}$ > $Ni@MIL-53-Al_2O_{3(2-1)}$ > $Ni/Al_2O_{3[D-MIL-53(Al)]}$ > Ni@MIL-53 > $Ni/Al_2O_{3[com]}$.

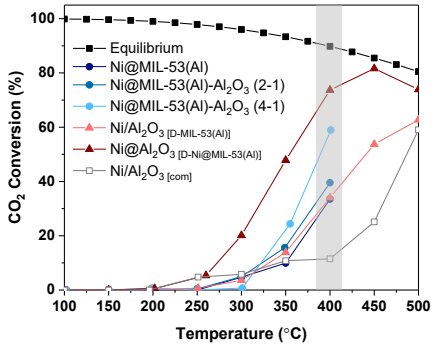

Fig. 1. Comparative CO_2 conversion profiles for the MOF-based / -derived Ni catalysts (CO_2:H_2=1:4, 8400 h^{-1}).

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Design, synthesis and photophysical properties of novel azaindoles

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Azaindole is a bioisoster of the indole scaffold since their biological properties are quite similar. These scaffolds have already been applied as therapeutic agents [1] or in luminescent materials such as organic light-emitting diode (OLED) devices [2].

We have been investigating azaindole derivatives aiming to achieve thermally activated delayed fluorescence (TADF) properties, to be applied in OLED. For this application, these molecules should present a donor-acceptor system, a small singlet-triplet energy splitting, and a small overlap between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) [3]. A wide scope of azaindole derivatives has been designed via computational modeling, to present these properties (Figure 1). Herein, we will present our latest results on the sustainable synthesis of azaindole derivatives, involving a metal-catalysed annulation reaction of new and in situ generated imine intermediates, as well as their photophysical properties.

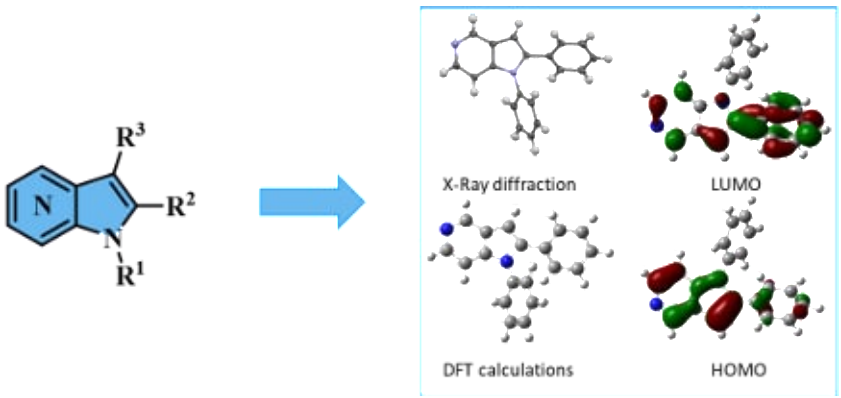

Figure 1: Azaindole derivatives, X-Ray diffraction and DFT calculations.

Thanks are due to University of Aveiro, FCT/MEC, Centro 2020 and Portugal2020, the COMPETE program, and the European Union (FEDER program) via the financial support to the LAQV-REQUIMTE (UIDB/50006/2020 and UIDP/50006/2020), to the CICECO-Aveiro Institute of Materials (UID/CTM/50011/2019, UIDB/50011/2020 & UIDP/50011/2020), financed by national funds through the FCT/MCTES, to the Portuguese NMR Network. SG is supported by national funds (OE), through FCT, I.P., in the scope of the framework contract foreseen in the numbers 4, 5, and 6 of the article 23, of the Decree-Law 57/2016, of August 29, changed by Law 57/2017, of July 19. JRMF thanks FCT and ESF (European Social Fund) through POCH (Programa Operacional Capital Humano) for her PhD grant (UI/BD/151272/2021).

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Highly Enantioselective Anion-Binding Catalyzed N-Arene Dearomatization by Fine-tuned Substrate-Catalyst Halogen-Bonding

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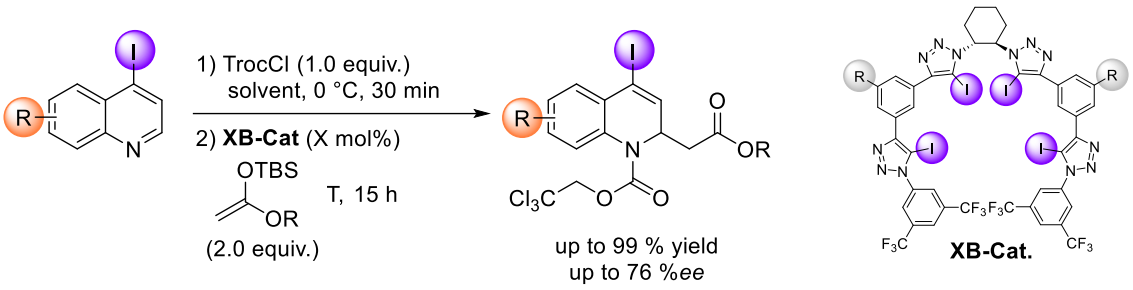
Halogen bonding represents a powerful synthetic tool in the field of noncovalent interactions, which is based on an electrophilic halogen substituent (usually iodine) and a Lewis base.[1] However, applications in enantioselective catalysis are barely explored and so far, resulted only in a moderate enantiomeric excess. [2][3]

Herein, we present the use of various novel mono-, di- and tetradentate halogen bond donor triazole-based catalysts (XB-Cat.) in enantioselective ion-pair organocatalysis. The asymmetric Reissert-type reaction between quinolines and silylketene acetals was chosen to investigate the influence on the enantioselectivity. During initial screening of halogen-containing substrates that might enable additional halogen bonding with the catalyst, the 4-iodoquinoline was selected as the model substrate. As hypothesized, this electrophilic halogen has an important role to form a contact ion-pair with the catalyst and efficiently transfer enantioselectivity to the product. Within the optimized conditions, a boosted enantioselectivity of up to 76% *ee* could be reached by halogen bonding as key interaction.



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Fluorine-containing spirocyclic tin(IV) compounds: Synthesis and characterization of catalysts for the formation of polyurethanes

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Tin-based catalysts are a crucial component of polyurethane synthesis. The most common used representative of these catalysts is dibutyltin dilaurate (**DBTL**). The latter, as an organotin compound, have gotten under some scrutiny. Consequently, intensively searched for are more benign alternatives [1-3]. Hypercoordinated inorganic tin(IV) compounds (Figure 1) lacking any tin-carbon bond are such alternatives. Upon contact with water, they degrade to SnO_2 and the amino alcohol, causing no harm to the environment. Most remarkably, the compounds shown in Figure 1 exhibit also delayed action as a function of temperature.

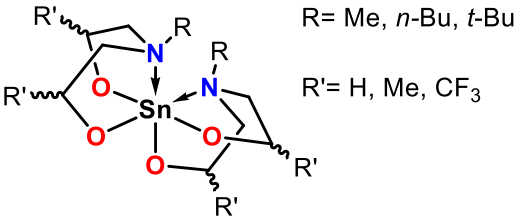

Figure 1. Spirocyclic tin(IV) compounds

The introduction of electron-withdrawing CF_3-substituents in the ligand backbone allows to some extent tuning of the Lewis acidity of the tin center in the compounds shown in Figure 1, which in turn influences the catalytic performance. [4].

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Use of transition-metal based heterogeneous photocatalysts for the hydrogenolysis of lignin model compounds

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Lignin is a complex heterogeneous and robust biopolymer present within lignocellulosic materials, the backbone of all plants. Lignin's structure is based on three phenol-like building blocks (coumaryl alcohol, coniferyl alcohol and sinapyl alcohol) randomly linked through either ether or carbon-carbon bonds (so-called "linkages") [1].

The cost-effective generation of platform chemicals (*i.e.* feedstocks for the chemical and pharmaceutical industries generated from biomass) within biorefineries will be a crucial step for the future of the chemical industry. These compounds are expected to partially replace certain feedstocks currently obtained from petroleum-refining processes (unsustainably) [2].

This project focuses on the heterogeneously catalyzed hydrogenolysis pathway specifically targeting a class of linkage (ether bonds). A commonly used method to simplify such studies is the use of model compounds as substrates [3]. These are small molecules that contain lignin's most common linkages. The use of these eases the analysis of the products but will still allow insights on lignin-related depolymerisation chemistry.

A family of Ni/TiO_2 catalysts (with different metal loadings, 1 %; 5 %; 10 % and 20 %) have been synthetised through a simple hydrothermal method. These have been reduced for 3 h at 500 °C in a 3% H_2/Ar atmosphere. The selected model compounds in this study are 2-phenylethyl phenyl ether (which contains a β-O-4 linkage) and diphenyl ether (which contains a 4-O-5 linkage). The reactions were followed by Gas Chromatography (GC) and GC-Mass Spectroscopy (GC-MS), for quantitative and qualitative purposes, respectively.

The characterization (XRD, TEM, UV-Vis DRS, Photoluminescence spectroscopy and N_2 physisorption) of the synthetized catalysts and catalytic results obtained for the photodriven hydrogenolysis of a range of lignin model compounds are also presented.

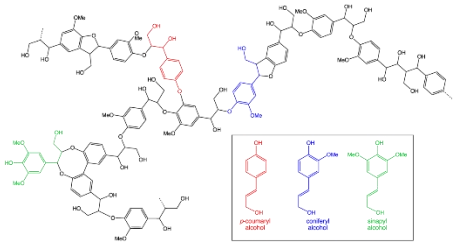

Fig. 1 Representative lignin structure

This research was supported by BiOrbic, Bioeconomy SFI Research Centre, which is funded by Ireland's European Structural and Investment Programmes, Science Foundation Ireland (16/RC/ 3889) and the European Regional Development Fund.

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Microbial pre-treatment of perfluorooctanoic acid prior to photocatalytic degradation

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Per- and polyfluoroalkyl substances (PFAS) which are used as fire retardants, coating materials, and surfactants are commonly known as 'forever chemicals' and are classified as persistent organic pollutants by the Irish Environmental Protection Agency and European Union regulation 2020/784 [1]. The strong C-F bonds in PFAS make them resistant to photolytic, chemical and biological degradation. Hence, prolonged unintentional accumulation of PFAS in humans causes adverse health hazards [1]. Microbial degradation is one of the common strategies which employed in waste-water treatment plants for the decomposition of organic pollutants, but it is time consuming and technologically demanding [2]. The low biodegradability of highly concentrated fluorine-containing compounds such as PFAS impose a challenge for waste-water treatment plants. Furthermore, the possibilities of employing Advanced Oxidation Processes such as photocatalysis where sunlight is used as a renewable energy source for the catalytic degradation of varieties of PFAS have been critically analyzed recently with its existing challenges and limitations [3]. However, pre-treatment of the water prior to photocatalysis can be a viable option for partial degradation of organic molecules, which can then be fed to the photocatalytic reactor for their effective degradation. This study reveals the possibility of using microbial pre-treatment of the model perfluoroalkyl compound perfluorooctanoic acid (PFOA) followed by photocatalytic degradation, using bismuth oxyiodide ($Bi_7O_9I_3$) as a promising visible light-driven photocatalyst.

A tunable band gap, layered structure and good stability in aqueous medium make bismuth oxyhalides attractive for their application in the photocatalytic treatment of PFOA. $Bi_7O_9I_3$ was successfully synthesized following a one-step solvothermal method followed by calcination at 400 °C for 2 h. The catalysts were characterized by UV-Visible Diffuse Reflectance Spectroscopy, X-ray Diffraction (XRD), Thermogravimetric Analysis (TGA) and X-ray Photoelectron Spectroscopy. The morphology of $Bi_7O_9I_3$ was confirmed by XRD. Narrow intense peaks at 2θ = 28.7°, 31.3°, 37.1°, 44.9°, 49.1° and 54.2° correspond to the planes of (102), (110), (103), (200), (114) and (202) of tetragonal phase $Bi_7O_9I_3$. The optical absorption of $Bi_7O_9I_3$ showed a blue shift with an absorption edge at 532 nm compared to 667 nm in tetragonal bismuth oxyiodide which is attributed to the removal of crystal defects through calcination. The band gap of $Bi_7O_9I_3$ was obtained by Tauc plot and was calculated as 2.35 eV. The TGA curve shows the good thermal stability of $Bi_7O_9I_3$ upto 1000 °C. The biological degradation of 100 ppm PFOA was investigated using three strains of *Cunninghamella* fungi (*C. elegans, C. blakesleeana and C. echinulata*), among which *C. elegans* showed the best degradation of PFOA (with a maximum up to 47.1% after 3 days of incubation). The successive photocatalytic treatment of the biodegraded solution resulted in further 14% degradation of PFOA after 2.5 h of photocatalysis using 700 W simulated solar irradiation. Thus, the synergistic effect of the combined process resulted in satisfactory removal of PFOA.

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Influence of the Counteranion on 9-Mesityl-10-methylacridinium salts for the Visible-light mediated Synthesis of Endoperoxides

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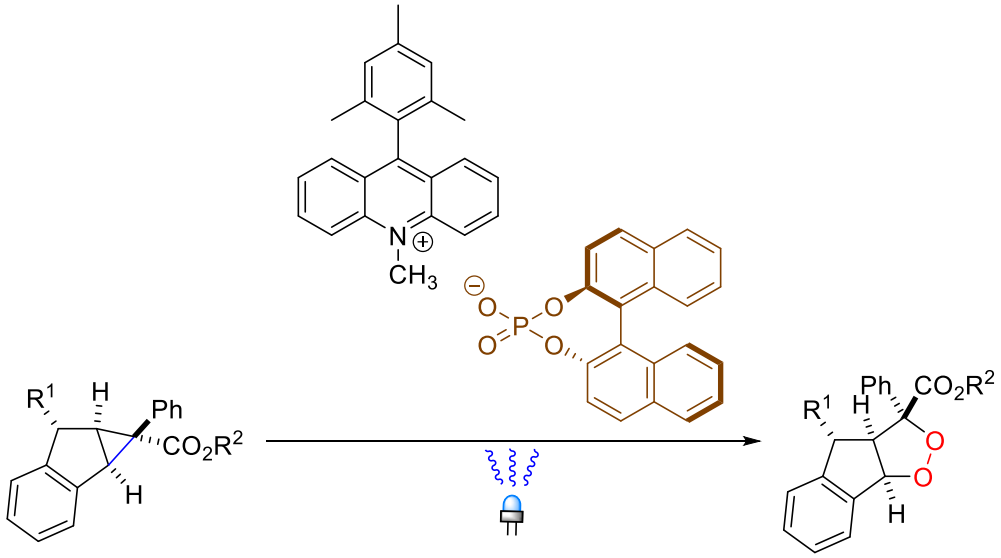
Endoperoxides are prominent structural motifs in drugs with antimalarial activity such as Artemisinin, which can be extracted from the plant *Artemisia annua*. [1] Since the synthesis of Artemisinin is challenging, organic chemists focus on the design of similar compounds, especially *via* photocatalytic pathways. Yoon *et al.* reported in 2014 the photooxygenation of donor-aryl substituted cyclopropanes for the synthesis of monocyclic peroxides using $Ru(bbz)_3$ in excellent yields. [2] A further development applying metal-free conditions was shown by our group, which reported a visible-light mediated synthesis of endoperoxides from anellated cyclopropanes in presence of 9-Mesityl-10-methylacridinium perchlorate. [3]

Inspired by this work and following the trend that antimalarial activities within endoperoxides improve with increasing lipophilicity, the scope of the reaction was further explored by using easily accessible carbocyclic starting materials. Therefore, a variety of alkylated indenes were chosen as suitable precursors for the cyclopropanation *via* traditional Rh-catalyzed conditions. The obtained cyclopropanes were used for the photooxidative ring-expansion to endoperoxides using organic acridinium salt with a chiral phosphoric acid counteranion in the presence of magnesium perchlorate. This new organic photocatalyst was compared to commonly used 9-Mesityl-10-methylacridinium perchlorate and used for the synthesis of novel substituted indene endoperoxides.



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Dual photocatalytic approach: Direct C-H cyanation of arenes mediated by flavin derivative and scandium triflate

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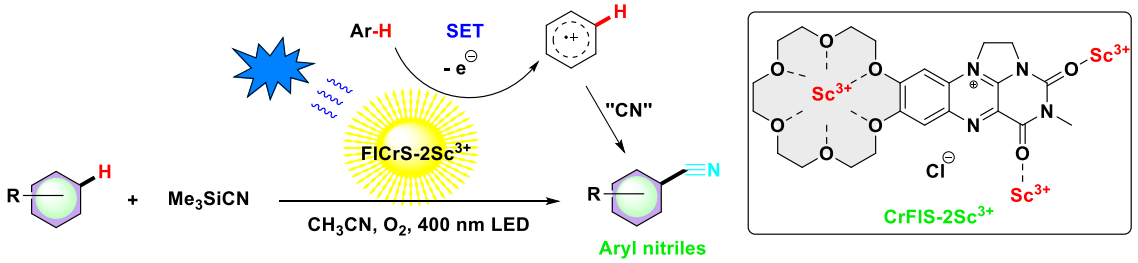
Developing an efficient, non-metal catalyzed, and gentle approach to direct oxidative C-H cyanation of arenes has received much attention because of the considerable importance of aryl nitriles. A great effort and noteworthy progress have been achieved in this field using traditional and transition metal-catalyzed methods; however, they suffer from significant drawbacks: the harsh reaction conditions, the rapid deactivation of the catalyst because of the high affinity of cyanide ion for the transition metal, and the need for the pre-functionalized arenes or assistance by directing groups [1]. Alternatively, mild and direct metal-free C-H cyanation systems, including photocatalytic, would be more attractive for researchers. Because photoredox catalysis facilitates the generation of reactive intermediates such as arene radical cations *via* single electron transfer (SET), the photoinduced-catalyzed cyanation is a synthetically practical strategy [2]. But, previously described photocatalytic cyanating approaches reveal low efficiency [3, 4, 5]. Hence, it is still a need for time to develop an efficient and direct method for C-H cyanation under visible light irradiation of a wide range of arenes considering their electronic structure.

Inspired by the literature reports and the ability of visible light photocatalysis to promote synthetically challenging reactions, we have been interested in establishing a dual photocatalytic system using flavinium salt derivative containing 18-crown-6 and scandium triflate, CrFlS-*2*Sc(OTf)$_3$ to synthesize aryl nitriles under blue light irradiation. The implementation of our strategy was commenced with the cyanation of diphenyl ether using a nucleophilic cyanating agent (Me_3SiCN) and molecular oxygen as a terminal oxidant upon irradiation in CH_3CN as a model reaction. Later on, we successfully applied the developed conditions to various arenes, including electron-rich and electron-poor substrates, and demonstrated good to excellent yield. This research would open a new avenue for arenes' challenging direct C-H cyanation as an efficient and scalable protocol in organic synthesis.



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Design of new flavins for photoredox catalysis

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In recent decades, application of flavins in organic photocatalysis became a subject of a rapid development, due to their availability and possibility of providing reactions in mild conditions by using the visible light sources[1]. However, photocatalysis involving the known flavins (isoalloxazines, alloxazines, deazaflavins)[2] has several problems, such as, insufficient photostability of flavin derivatives or limitations in photoreductions, which do not allow us to expand their application in other areas[3]. In the same time, deazaalloxazines open an unexplored field in flavin photocatalysis that may provide a solution to beforementioned problems. The issue is that the basic skeleton of deazaalloxazines absorbs only in the UV region (around 350 nm)[4], so they have not been tested in photocatalysis yet. Our first results show that they tend to be more stable under irradiation and at the same time have a more suitable redox properties for photoreductions, e.g. very negative redox potential even in ground state (E^0 < - 1.5 V vs SCE).

The aim of this project is a rational design of substituted deazaalloxazines that are able to absorbing above 400 nm with even stronger reducing properties (figure 1). The series of substituted deazaalloxazines have been synthesized via different approaches, such three-component reaction of anilines with aromatic aldehydes and barbituric acid, or through Vilsmeier-Haack closing of anilinouraciles. Suitable deazaalloxazines have been successfully tested in photoreductive dehalogenation of 4-bromoanisole (E_{red} = -2.78 V vs SCE)[5]. Further applications, such as deprotection reactions of various aromatic sulfonamides are under investigation.

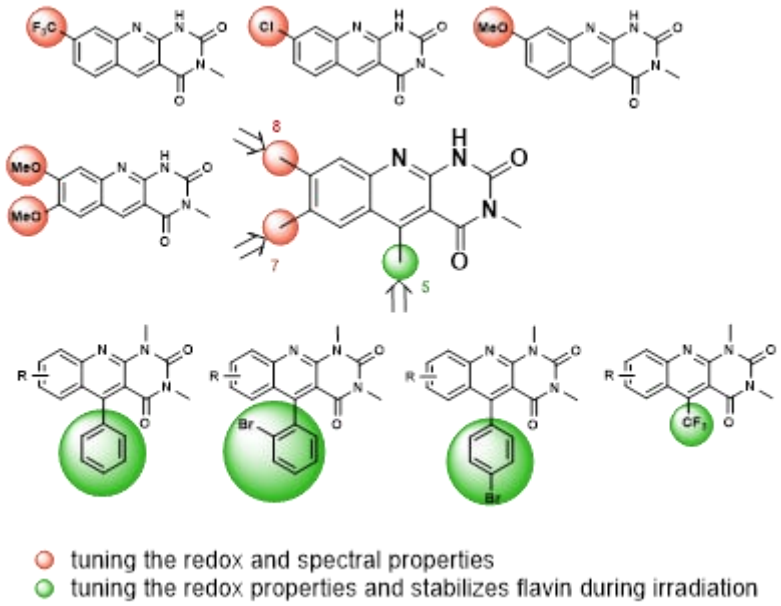

Fig. 1. Structures of substituted deazaalloxazines

This work was supported by Czech Science Foundation (reg. No. 21-14200K) and by grant of Specific university research (reg. No. 110882202).

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1,10-Ethylene-bridged deazaflavinum salts – versatile catalysts for chemoselective photoredox reactions

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In the nature, flavins have special role in biological processes for example in cell respiration. The redox properties of flavin catalysts have been also utilized in various artificial synthetic methodologies, for example, for aerobic photooxidations providing chemoselective transformation of benzylic carbon to aldehydes or ketones and sulfides to sulfoxides. The optimization of structure have led to ethylene-bridged flavinium salts **1**, which belong among the strongest oxidizing organic agents characterized by excited state reduction potential 2.5 V vs SCE.[1]

In the big flavin family exist another analogs – 5-deazaflavins, which participate as cofactors in photolyases or work as an antenna in photoactive systems. In our laboratory, deazaflavins **2**, were shown as very powerful reducing agents participating on photoreductions via conPET mechanism. For example, deazaflavins 2 are able to provide reductive dehalogenation of chlorobenzenes with reduction potential more negative than -2.8 eV (Figure 1).[2]

In this work, we developed general synthetic approach to novel 1,10-ethylene-bridged deazaflavinium salts **3**, which consist from significant moieties from both flavinium salt **1** and deazaflavin **2** (Figure 1)**.** Preliminary results indicate that these species can participate both in photoreductive and photooxidative processes thus allowing design of unique synthetic methodologies.

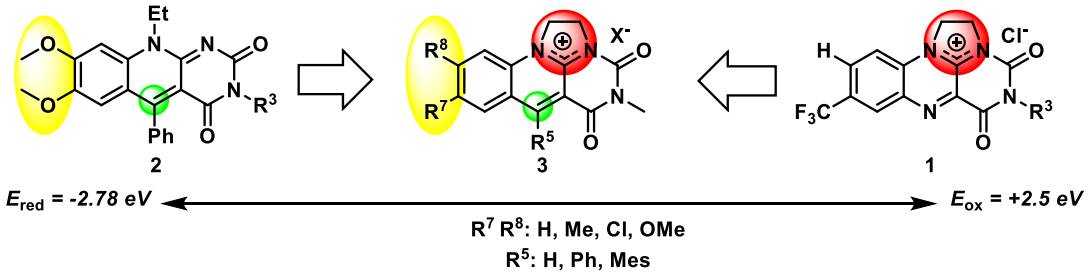

Figure 1.

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The Role of Single-atom Iridium on Haematite Photoanodes for Solar Water Oxidation

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Solar to hydrogen conversion by photoelectrochemical (PEC) water splitting provides a sustainable and cost-effective route to address the energy and environmental crisis [1]. Haematite (α-Fe_2O_3) featuring natural abundance, effective utilization of visible light, and excellent photo and chemical stability, has been targeted as the most promising metal-oxide photoanode for PEC water splitting [2]. However, due to its limited hole diffusion length (only 2 - 4 nm), short carrier lifetime (3 - 10 ps), poor charge carrier mobility (10^{-2} cm^2 V^{-1} s^{-1}), and sluggish surface water oxidation reaction, the solar-to-hydrogen (STH) efficiency of α-Fe_2O_3 is currently far below its corresponding theoretical efficiency.

Integration of hematite photoanodes with suitable cocatalysts has been demonstrated to be one of the most efficient approaches to improve the STH efficiency by lowering reaction obstacles and accelerating water oxidation kinetics [3-6]. Very recently, single-atom catalysts (SACs) have gained significant attention for their advantages of high atomic efficiency, activity, and selectivity in heterogeneous catalysis, which provides an intriguing research direction to overcome the sluggish water oxidation kinetics and boost the STH efficiency of photoanodes [7]. So far, few attempts of SACs assisted α-Fe_2O_3 photoanodes with excellent performance have been reported [8,9]. However, a lack of systematic mechanism study of such system to date, limits our understanding of the role of SACs played on α-Fe_2O_3 photoanodes during water oxidtion *i.e.* whether any enhanced activity results from specific catalytic function effect of the SAC or by retardation of recombination kinetics.

Herein, in this study, by combining in-situ transient absorption spectroscopy (TAS), intensity-modulated photocurrent spectroscopy (IMPS), photoelectron spectroscopy, and density functional (DFT) calculations, we demonstrated that single-atom iridium (sIr) on hematite (α-Fe_2O_3/sIr) photoanodes functions as a true catalyst by trapping holes from hematite followed by serving as water oxidation active sites. In-situ TAS shows a reduced hole amount and shortened hole lifetime in the presence of sIr, especially at second time scale, indicative of fast hole transfer and depletion for water oxidation. IMPS provides consistent evidence of faster hole transfer at the interface of α-Fe_2O_3/sIr photoanode and electrolyte. DFT theoretical calculations reveal a preferable water oxidation pathway on sIr sites with the lowest onset potential as compared to Fe sites. This understanding of the role of single-atom iridium on hematite provides insight into the design principles for efficient photoanodes based on cocoatalysts.

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The effect of nickel doping on the activity and selectivity of Cu-SSZ-13 catalysts in the NH_3-SCR process

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Reducing NOx emissions from combustion engines to the limits set by European standards (Euro VI, 0.06 g km^{-1} - for gasoline engines and 0.08 g km^{-1} - for diesel engines) is a challenge for contemporary environmental catalytic chemistry. The most frequently used technology for the elimination of NOx from exhaust gases is the selective catalytic reduction of NO by ammonia (NH_3-SCR), which is characterized by high efficiency.

This study aimed to evaluate how the introduction of nickel (different amounts of nickel and method of synthesis) into Cu-SSZ-13 can modify its activity (widening of the operating temperature range) and selectivity (reduction of the share of side reactions) in the NH_3-SCR process. The Cu-SSZ-13 catalyst was obtained by introducing Cu at the step of zeolite synthesis *i.e.* one-pot synthesis. Two series of bimetallic Cu-Ni-SSZ-13 catalysts were synthesized by: (*i*) ion exchange carried out in the solutions with various concentrations of Ni ions and (*ii*) impregnation with the aqueous solutions of the $Ni(NO_3)_2$.

Zeolites containing Cu and Ni were characterized in terms of their structure and morphology (XRD, XRF,TEM/EDX) and acid/base properties (NH_3-TPD). The activity tests (NH_3-SCR) were carried out in a fixed-bed reactor in a reaction mixture containing 500 ppm NH_3, 500 ppm NO, 4.5% O_2 with or without H_2O. A strong influence of nickel concentration and the synthesis method of Cu-Ni-SSZ-13 on the activity of catalysts in NH_3-SCR process was demonstrated. Doping the CuSSZ-13 zeolite with nickel allowed to increase the range of the temperature window in which the NO conversion is 100%. The temperature window for Cu-Ni-SSZ IM and Cu-Ni-SSZ-13 IE was from 232 to 550 °C and from 218 to 550 °C, respectively. Whereas for Cu-SSZ-13 the temperature window was from 216 to 496 °C Fig.1a. The introduction of nickel significantly reduced the share of the side reactions - increase in selectivity to N_2 from 80% for Cu-SSZ-13 to 88% and 95% for Cu-Ni-SSZ-13 IM and Cu-Ni-SSZ-13 IE, respectively. The production of NO_2 and N_2O was given Fig. 1b. Additionally, a significant drop in the production of NO_2 by 52% and 74% and N_2O production by 16% and 25% was obtained for Cu-Ni-SSZ-13 IM and Cu-Ni-SSZ-13 IE, respectively.

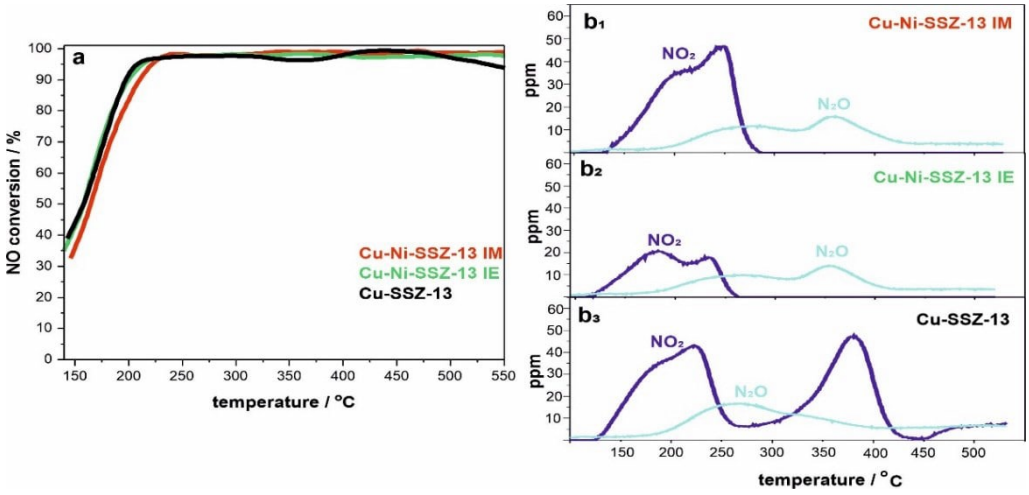

Fig. 1. NO conversion profiles (a) and distribution of the NO_2 and N_2O (b1,b2,b3) of the NH_3-SCR reaction in the presence of Cu-SSZ-13 and Cu-Ni-SSZ-13 catalysts.

The work was carried out within the MOST program for bilateral collaboration between Poland and China, which is financially supported by The National Centre for Research and Development, Poland, grant PNOX no. WPC1/PNOX/2019 and from China side by the Project 2017YFE0131200.

TiO_2/pillared clays synthesized using a nonconventional aluminum source as successful photocatalysts for the catalytic photodegradation of emerging pollutants

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Advanced oxidation processes (AOP) have been studied to remove several organic pollutants from water, including emerging pollutants. Catalytic photodegradation that use a semiconductor photocatalyst (eg. TiO_2) is an example of AOP [1]. Titanium dioxide (TiO_2) can be used by itself or incorporated in a catalytic support. Several solids have been studied as catalytic supports, including clays and pillared clays (PILC) [2]. Titanium dioxide can be incorporated into the clays by a pillaring process (Ti-PILC) or the formation of dispersed oxides by different methodologies (TiO_2-nanocomposites). Both Ti-PILC and TiO_2-clay nanocomposites have been satisfactory used for the removal of pollutants such as dyes [3]. The use of PILC is attractive due to their improved characteristics compared with their raw clays, however, it is an almost unexplored field.

This study focused on the photocatalytic degradation of 2,6-dichlorophenol (2,6-DCP), triclosan (TCS), and bisphenol A (BPA) by both ultraviolet (UV) and visible (VIS) light using TiO_2/catalysts synthesized using a clay (montmorillonite – Mt) and three alumina pillared clays (Al-PILC) as catalytic supports. The three Al-PILC were obtained using various aluminum sources. One of them was synthesized using a commercial aluminum salt as the precursor (Al-$PILC_{CM}$), and the other two using the aluminum in the acidic (Al-PILCAE) or alkaline (Al-PILCBE) extract from a saline slag. Mt was impregnated at different titanium contents (1 - 20 wt.% Ti) and their catalytic performance were compared with those obtained using commercial TiO_2 (anatase). Due to the results, Al-PILC were impregnated at 10 and 20 wt.% Ti to evaluate their photocatalytic performance. Results show that the most photodegraded pollutant was TCS (85.15 ± 0.49%), followed by 2,6-DCP (65.43 ± 0.79%), and BPA (36.15 ± 0.65%). Photodegradation was higher using UV-light and Al-PILC showed higher photodegradation percentages than Mt. Finally, an analysis of the photoproducts in the final solution analyzed by HPLC-MS suggested that the preferred pathway for both TCS and 2,6-DCP photodegradation depends on the type of light used.

Acknowledgments

The authors are grateful for financial support from the Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033) through project PID2020-112656RB-C21. YC thanks the Universidad Pública de Navarra for a pre-doctoral grant (IberusTalent, European Union's H2020 research and innovation program under Marie Sklodowska-Curie grant agreement N° 801586). AG also thanks Banco Santander for funding via the Research Intensification Program.

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Zirconium-catalysed direct substitution of alcohols: enhancing the selectivity by kinetic analysis

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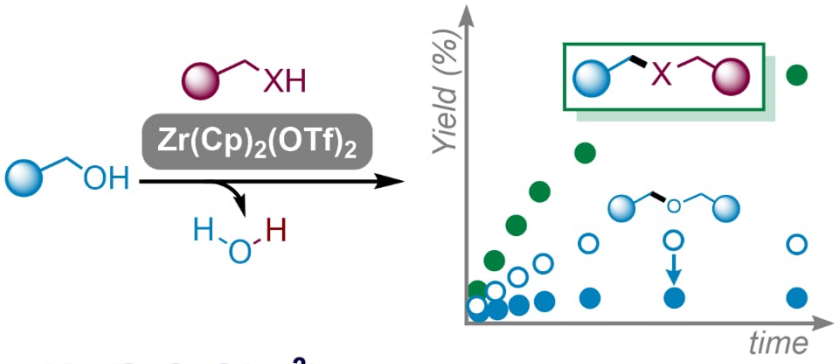
Modern kinetic analysis tools (RPKA and VTNA)[1-4] were used for the rational optimization of a catalytic, direct substitution of alcohols. Unsymmetrical ethers, thioethers, and Friedel–Crafts alkylation products were formed in a selective manner, using a moisture-tolerant and commercially available zirconocene complex (2 to 8 mol%). Operating in air and in the absence of dehydration techniques, the protocol furnished a variety of products in high yields, including glycosylated alcohols and sterically hindered ethers. In addition, the early implemented kinetic studies provided mechanistic insight into the network of parallel transformations that take place in the reaction, and helped to elucidate the nature of the operating catalyst.[5]



- ***X* = *O*, *S*, *C*(sp^2)**
- *Optimization assisted by* ***kinetic analysis***

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Palladium-catalyzed cross-coupling of lithium acetylides with benzyl bromides

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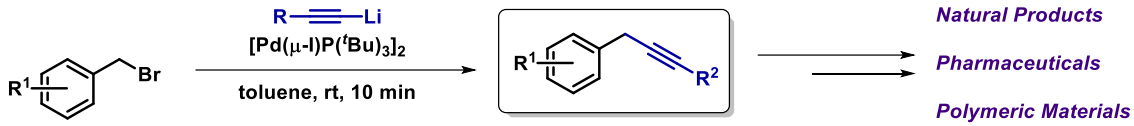
Organolithium-based cross-coupling reactions have emerged as an indispensable method to construct C–C bonds [1]. These transformations have proven particularly useful for the direct and fast coupling of various organolithium reagents (C(sp), C(sp^2), and C(sp^3)) with aromatic (pseudo)halides. Especially the installation of (benzylic) alkynes in organic molecules is a valuable tool for the introduction of versatile handles for further modification. Although the reaction of lithium acetylides with benzyl bromides could be anticipated to be a 'textbook' S_N2-reaction, previous reports have shown the necessity of transition-metal catalysis [2-8] or the use of deaggregation agents [9]. Here we present an efficient method for the cross-coupling of benzyl bromides with lithium acetylides, proceeding within 10 min at room temperature. A remarkable functional group tolerance, including organolithium-sensitive functional groups such as esters, nitriles, amides and boronic esters provides possible opportunities towards late(r)-stage functionalization. Additionally, the versatility of the benzylic alkynes was displayed in the construction of key intermediates applied in the synthesis of pharmaceuticals and natural products.



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Role of electronic and steric effects in deracemization during Suzuki diarylation of binaphthyl

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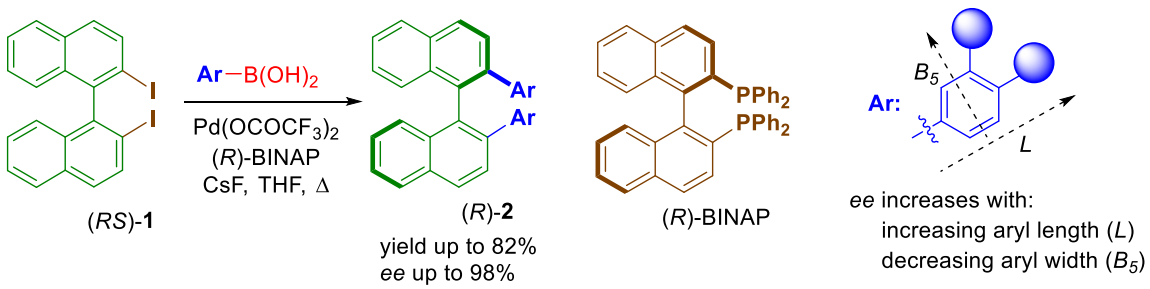
Enantiomerically pure 2,2´-disubstituted binaphthyl scaffold appears nowadays in many biological active natural compounds,[1] as a building block of modern materials[2] or as an useful ligands for asymmetric transformations.[3] Despite of high demand a preparation of enantiopure compounds with 2,2´-disubstituted binaphthyl moiety is still challenging.

Chiral binaphthyl scaffold is usually prepared by enantio-[4] or diastereoselective[5] Suzuki coupling. Here, we present possibility of synthesis enantiomerically enriched 2,2´-diarylated binaphthyls starting from racemic binaphthyl diiodide **1** via deracemization of binaphthyl backbone. Slow transmetalation under control of chiral diphosphane ligand results in double oxidative addition, forming configurationally labile pallada(IV)cyclic intermediate. In this step, stereogenic information is transferred from chiral ligand and finally, enantioenriched 2,2´-diarylated binaphthyl **2** is formed.[6]

We have further optimized the reaction conditions (temperature, palladium source, Pd/L ratio, boronic acid derivative type) to maximize the yield and the stereoselectivity of this reaction. An extensive study of the reaction scope has shown that the product 2 is formed with *meta*- and/or *para*-substituted phenylboronic acids, which have low to medium electronic effect. Multiparametric analysis provided a model explaining the enantioselectivity of this reaction. The analysis showed that the enantioselectivity does not depend on the electronic properties of the arylboronic acid starting materials, but it is strongly dependent on their steric properties, leading to enantiomeric excesses of diarylated products ranging from 0 to 98% *ee*. An interesting phenomenon of self-disproportionation of the enantiomers of diarylbinaphthalenes **2** was observed during separation of the reaction mixtures on silica gel achiral stationary phase.



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Synthesis and catalyst application of Hemicryptophanes in C_1 symmetry

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The use of molecular containers for the design of metalloreceptors is very attractive, as they can act as supramolecular catalysts and can mimic biological entities such as enzymes.[1]

Cyclotriveratrylene (CTV) is a macrocyclic cyclophane presenting a bowl-shaped conformation, it is devoid of stereogenic centers, but is a chiral molecule, usually with a C_3-symmetry.[2] They are often used as building blocks to build cryptophane and hemicryptophane host molecules.[3] These compounds are supramolecular molecules able to recognize guests like crown ethers, calixarens or cyclodexdrines. Hemicryptophanes are composed of three parts: the CTV part, the linkers and another C_3-symmetrical lower unit (**Figure 1**).

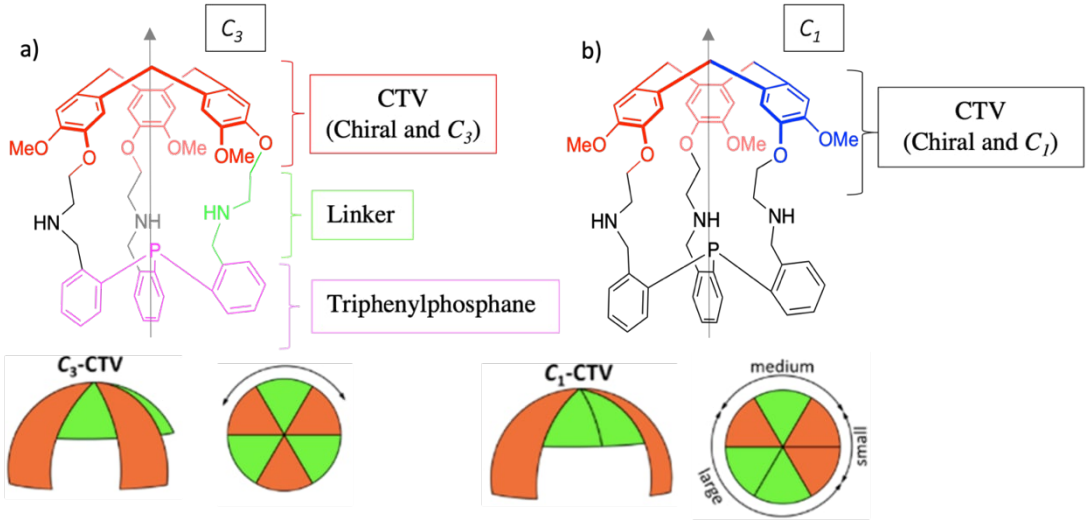

Figure 1 a) Hemicryptophane with a phosphine moiety in C_3 symmetry used for organo and gold catalysis. b) Hemicryptophane with a phosphine moiety in C_1 symmetry used for organo and gold catalysis.

Hemicryptophanes are inherent chiral molecule (induced by CTV), today they are used for their recognition properties, as ligands for transition metals, or in catalysis.[3]

Breaking the symmetry is interesting to increase selectivity for the recognition of complex compounds.[5] One method is the inversion of OMe and OAlkyl groups in the CTV part to obtain a C_1-symmetry compound (regioisomer). Thanks to this modification, the hemicryptophane gets a specific spatial arrangement (windows of different sizes) giving different access to the interior of the cage (**Figure 1**). Different synthetic pathways were tested to get hemicryptophanes with a C_1-symmetry and prevent the CTV racemization. The racemic mixture of each hemicryptophane host could be readily resolved by chiral HPLC, giving an easy access to the enantiopure molecular cages whose absolute configurations have been assigned by ECD spectroscopy.

These new chiral hemicryptophanes C_1 are promising compounds for molecular recognition and catalysis.

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Heterocycles with nitrogen as catalysts in cycloaddition of CO_2

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Cyclic carbonates find the utilization in many fields of chemical industry. The easiest way of their preparation is the reaction of carbon dioxide with epoxides [1]. The most often catalysts described in the industry are ammonium salts, namely tetrabutyl ammonium bromide [2]. Their main disadvantage is the homogeneous arrangement including the complicated removal from the reaction mixture and reuse. The alternative might be the pyridinium salts attached to siliceous supports [3]. We would like to show the alternative homogeneous and especially heterogeneous catalysts based on nitrogen heterocycles efficient in the production of styrene carbonate as a model substance.

In this work, the cycloaddition of CO_2 to styrene oxide leading to the synthesis of styrene carbonate was studied. The reactions were catalyzed by both homogenous and heterogeneous catalysts. The homogenous catalysts were unstable and unsuccessful. The nitrogen salts immobilized on MCM-41 were prepared as heterogenous catalysts, and the effect of used halogen silane and nitrogen compound was studied. The most efficient heterogeneous catalyst was composed of (3-iodopropyl)trimethoxysilane, 1-methylimidazole, and MCM-41 as a support, and its preparation consisted of a modification of MCM-41 followed by a quaternization leading to the synthesis of the salt. The heterogeneous catalysts could be used repeatably without a loss of catalytic activity. It was confirmed that more nucleophilic halogens (I, Br) are better for the cycloaddition of CO_2 to styrene oxide. Conditions 120 °C and 1.2 MPa were chosen as the most suitable, under these conditions 100% selectivity towards styrene carbonate and 88% conversion of styrene oxide was reached after five hours. The prepared materials may be used as a sucesfull catalysts for the cycloaddition reaction of styrene oxide leading styrene carbonate. Moreover, this reaction represents the field of the carbon dioxide utilization.

We acknowledge grant project GACR 21-02183S. We thank to M. Lhotka for the nitrogen physisorption measurements.

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Synthesis of tricyclic fused 2*H*-pyran-2-ones by Rh(III)-catalyzed formal (4+2) cycloaddition of thienopyridine/thienopyrazine carboxylic acids with internal alkynes

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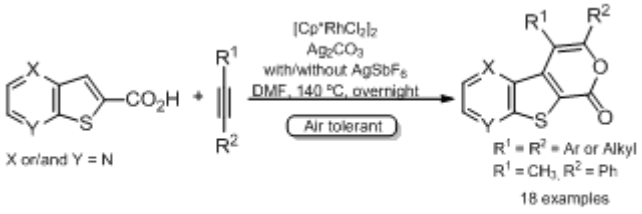
2H-Pyran-2-ones (α-pyrones) represent an important class of naturally occurring δ-lactones and are present in several biological active molecules. 1*H*-2-benzopyran-1-ones (isocoumarins) are their benzo derivatives and have shown a wide range of pharmacological activities but unfortunately, the synthetic processes requires several steps and the use of specifically pre-functionalized precursors. In the last decade, a variety of transition-metal catalyzed annulations relying on the activation and cleavage of C–H bonds have been described. These synthetic strategies are very attractive, among other reasons because they avoid the need of functionalized precursors e.g., halogenated compounds, and favor atom and step economy. Usually, the C–H activation requires the presence of a directing group that assists the metalation step and controls the regioselectivity. Especially attractive are those reactions in which the directing group is also engaged in the bonding process, as this can lead to formal cycloaddition reactions [1].

Herein we report catalytic formal (4+2) cycloadditions of *N*,*S*-heterocycles featuring carboxylic acid substituents, with internal alkynes. The reaction, which works with different aryl or alkyl symmetrical and unsymmetrical alkynes, produces novel tricyclic α-pyrones in a straightforward manner. The optimized conditions established for a model reaction employing thieno[2,3-*b*]pyridine-2-carboxylic acid as substrate, involved the use of Ag_2CO_3/$AgSbF_6$ as additives, and proved to be general for different alkynes. Moreover, analogous cycloadditions using thieno[3,2-*b*]pyridine-2-carboxylic acid and thieno[2,3-*b*]pyrazine-6-carboxylic acid were successfully developed with minor modifications that will be also discussed (**Scheme 1**). Overall, this catalytic technology allows the synthesis, in a single step, of an interesting variety of pharmaceutically relevant tricyclic α-pyrones exhibiting nitrogen and sulfur heterocycles [2].



Scheme 1. Synthesis of tricyclic α-pyrones exhibiting *N*,*S*-heteroatoms.

Thanks to Fundação para a Ciência e Tecnologia (FCT) – Portugal for support to CQUM (UID/QUI/686/2020), also financed by FEDER, and Portugal2020, to PT NMR network and to the PhD grant of J.M.R. (SFRH/BD/115844/2016) also financed by ESF and HCOP. To COST Action CA15106 – C- H Activation in Organic Synthesis (CHAOS). To Spanish grants SAF2016-76689-R, PID2019-108624RBI00, PID2019-110385GB-I00 and FPI fellowship BES-2017-079784 to B.C., the Consellería de Cultura, Educación e Ordenación Universitaria (ED431C 2017/19, 2015-CP082 and Centro Singular de Investigación de Galicia accreditation 2019–2022, ED431G 2019/03, FEDER and the European Research Council (Advanced Grant No. 340055).

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The Visible Light Route to Five Membered Fused Pyrrolidines

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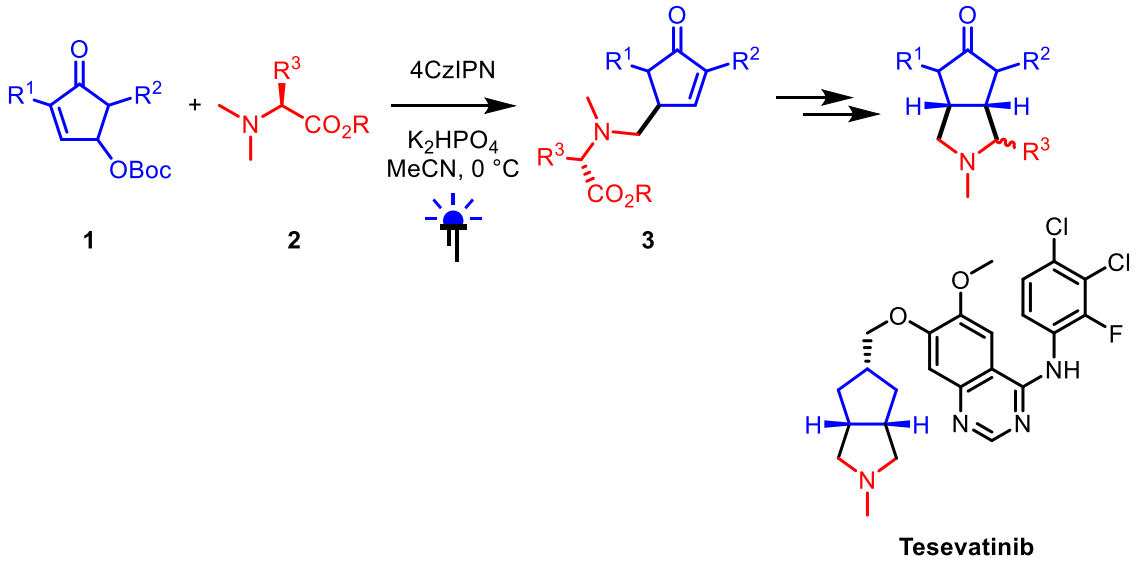
We present a redox-neutral photocatalyzed strategy for the generation of five-membered fused pyrrolidines, coupling *N*-methylated amino acid derivatives **2** and Boc-protected 4-hydroxy-cyclopentenones **1** in two photocatalyzed steps. A radical conjugate addition-elimination cascade[1] initiated from the selectively generated *N*-methylamino radical derived from **2** produces the first intermediate **3**, which is then converted into the desired pyrrolidine through a second decarboxylative radical conjugate addition.



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Systematic studies on transition metal-catalyzed hydrogenation of polybutadiene

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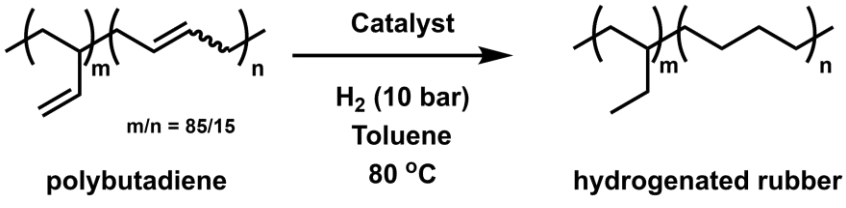
Polymeric materials have become a permanent part of everyday life. Especially important are polyolefins, of which more than about 150 million tons are produced worldwide per year, the majority in transition metal-catalyzed reactions. These materials seem to be excellent starting precursors for further functionalization via post-polymerization stoichiometric or catalytic transformations, taking advantage of their low cost and the presence of high content of easily accessible C=C units [1]. Unfortunately, the presence of the remaining unsaturated carbon-carbon moieties in the polymer chain results in their poor aging behavior, which is caused by their oxidation and leads to deterioration of their properties. Hydrogenation is one of the most effective methods for improving their stability against oxidative, thermal, and radiation-induced degradation of butadiene-based polymers. This process also offers a convenient method to synthesize saturated polymers with required microstructures and unique stereochemistries, that are difficult to achieve by conventional polymerization reactions [2].

Hydrogenation of polybutadiene has been explored in the literature, starting from the reports from Rempel's group [3]. However, it is hard to get the big picture by comparing all the literature reports because they have been carried out with the use of polybutadienes having various molecular weights and microstructures, and under different conditions (temperature, pressure, solvent, catalyst and it's loading). No comprehensible comparison of the activity of metal catalysts has been performed until now.

Here we present the results of systematic studies on the hydrogenation of polybutadiene rubbers in the presence of commonly used transition metal catalysts, including complexes that have not been tested as polybutadiene hydrogenation promoters so far. The application of a wide range of catalysts enabled us to determine the effect of the metal, its loading, and the co-presence of phosphine ligands on hydrogenation efficiency. The systematic studies allowed the selection of the most active catalysts for efficient saturation of synthetic rubbers under mild conditions, regardless of the type of the polymer microstructure. The polymeric products were characterized by FT-IR, NMR spectroscopy, and GPC analysis. The thermal properties of the hydrogenated rubbers were also verified.



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Autonomous Reaction NetworkExploration in Homogeneous and Heterogeneous Catalysis

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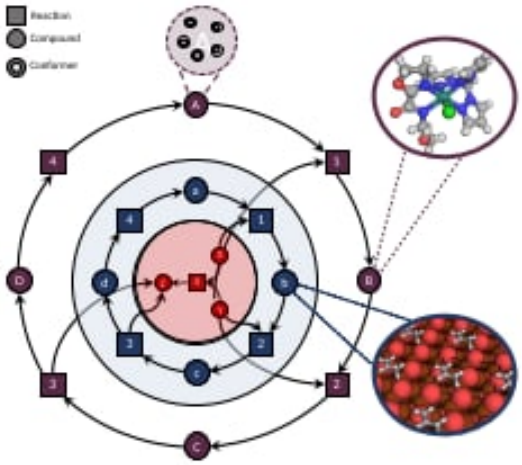
Autonomous computations that rely on automated reaction network exploration algorithms [1,2] facilitate systematic mechanism elucidations of catalytic reactions. They access several orders of magnitude more structures than what would be possible by manual inspection. This provides a high depth in terms of relevant species (including conformer resolution) and competing elementary reaction steps (including side, decomposition, and other deactivation reactions). The high degree of autonomy in automated exploration further reduces the amount of manual human work, processing errors, and human bias, which allows for a high fidelity of the formalization of catalytic processes and for surprising in silico discoveries. Hence, automated explorations offer key advantages for catalysis research. We have carried out automated explorations for both homogeneous [3 , 4] and heterogeneous catalysis [5] and have analyzed the associated resource requirements for such computational campaigns [5]. Here, we present this work and outline how the costs can be reduced by fast electronic structure methods with uncertainty quantification and by allowing the exploration to be steerable with respect to specific regions of an emerging network and with respect to the addition of new reactant species.



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A new Ruthenium (II) hydride complex and its application as a hydrogenation catalyst

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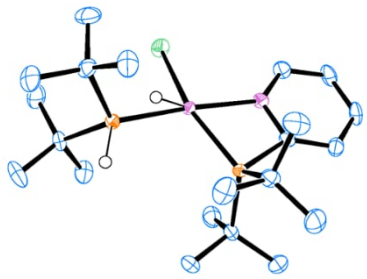
The reaction of 2-di-*tert*-pyridylphosphine (**1**)[1] with [{Ru(COD)Cl_2}$_x$],[2] in the presence of triethylamine and hydrogen led unexpectedly to complex, **2**, by cleavage of a P-C bond and formation of a new P-H bond. The mechanism of this reaction is currently under investigation, through a combination of DFT, NMR and carefully designed experiments. Complex **2** catalyzes the reduction of aldehydes, ketones and olefins under mild conditions. We report here the catalytic results obtained so far as well as our efforts to elucidate the mechanism that led to complex **2**.



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The authors thank FCT for support (projects UIDB/00100/2020 and UIDP/00100/2020 awarded to CQE and LA/P/0056/2020 awarded to IMS). V.C acknowledges FCT for the doctoral fellowship PD/BD/147841/2019 integrated in the PhD Program in NMR applied to chemistry, materials and biosciences (PD/00065/2013). The NMR spectrometers are part of the National NMR Network (PTNMR) and are partially supported by Infrastructure Project No 022161 (co-financed by FEDER through COMPETE 2020, POCI and PORL and FCT through PIDDAC).

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Titanium ketimide complexes: synthesis and reactivity towards isocyanates

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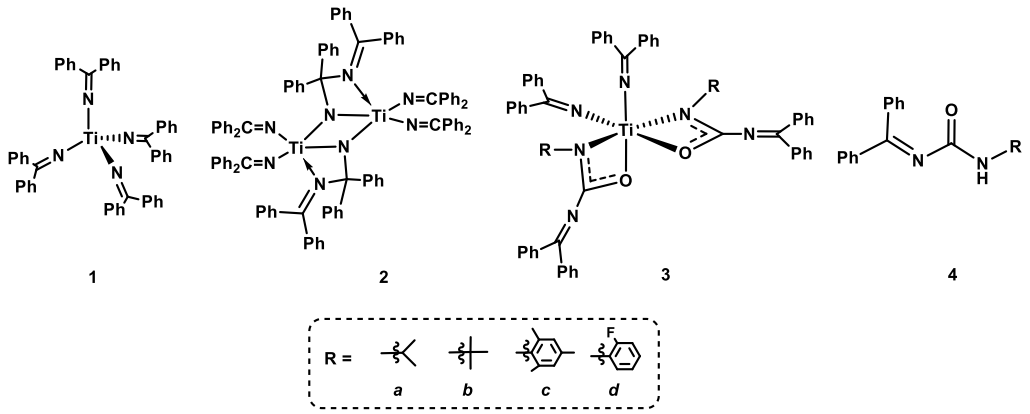
Ketimides are well known support ligands in titanium chemistry.[1] They can also however display non inert behaviour as reported for thorium complexes.[2] Complex **1** reacts with itself to afford **2** and with 2 equiv. of isocyanate to afford complexes **3**. The new ligand formed in **3** can be released with the addition of a proton source to afford compounds **4**. The latter can also be obtained catalytically in the presence of **1**. Compounds of the type **4** are relevant in organic synthesis and pharmacology.[3]



Centro de Química Estrutural (CQE) and Institute of Molecular Sciences (IMS) acknowledge the financial support of Fundação para a Ciência e Tecnologia (Projects UIDB/00100/2020, UIDP/00100/2020, and LA/P/0056/2020, respectively). C.P.R. thanks Fundação para a Ciência e a Tecnologia for a PhD fellowship (PD/BD/152271/2021).

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Core-shell nanocomposites as catalyst for peroxidative oxidation of benzyl alcohol

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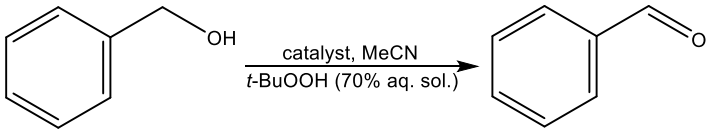
In this study, a Cu-based nanosheet metal–organic framework (MOF), HKUST-1 (also known as MOF-199 or Cu-BTC) was used as a shell for the preparation of the Fe_3O_4@CuMOF and $BaTiO_3$@CuMOF core/shell type nanocomposites, using the layer-by-layer method. Both nanocomposites were applied as heterogeneous catalysts for the ultrasound-assisted peroxidative oxidation of benzyl alcohol with *t*-butyl hydroperoxide (70% aq. solution) as oxidant, to the respective aldehyde, benzaldehyde which is an important starting material in the dyes, perfumes, and pharmaceutical industries.

The metal-based composites were characterized with several analytical techniques including field emission scanning electron microscopy (SEM), X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS) and Fourier-transform infrared (FT-IR) spectroscopy.

The influence of various parameters, such as, reaction time, type and amount of catalyst, temperature, and presence of additives, is also evaluated and discussed. Recycling tests were also performed.



Acknowledgement: This research was funded by Fundação para a Ciência e a Tecnologia (FCT) – projects UIDB/00100/2020 and UIDP/00100/2020 of the Centro de Química Estrutural, the LA/P/0056/2020 of Institute of Molecular Sciences and PTDC/QUI-QIN/29778/2017.

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Fe(III) C-scorpionate complexes as catalysts for the selective peroxidative oxidation of benzyl alcohol

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In the present study, iron(III) complexes bearing the C-scorpionate ligand [1–3], hidro tris(pyrazolyl)methane ($HCpz_3$) were synthesized and their catalytic activity screened for the peroxidative oxidation through conventional heating of benzyl alcohol following the principles of green chemistry. Benzaldehyde, the main product of the toluene oxidation reaction and consequently also the main product from the oxidation of benzyl alcohol (Figure 1) [1,4,5], is an important starting material for the dyes, perfumes, and pharmaceutical industries[4].

The new C-scorpionate iron(III) complexes $[FeCl_3(HCpz_3)]$ **(1)** $[FeSO_4(HCpz_3)]_2SO_4$ **(2)** $[Fe(NO_3)_3(HCpz_3)]$ **(3)** were synthesized using different iron salts ($FeCl_3$, Fe_2SO_4 and $Fe(NO_3)_3$) in order to study the effect of the anionic ligand and his effect on the structure, electrochemistry and catalytic activity of the complex. Therefore, compounds were characterized by elemental analysis, IR, cyclic voltammetry, and single-crystal X-ray crystallography.

The catalytic activity of the iron complexes was then tested for this alcohol oxidation (with tert-butyl hydroperoxide or hydrogen peroxide) under mild conditions (temperature below 80°C, green oxidant, solvent-free or green solvents). The influence of various parameters, such as reaction time, type and amount of catalyst, temperature, and presence of additives, is also evaluated and discussed.

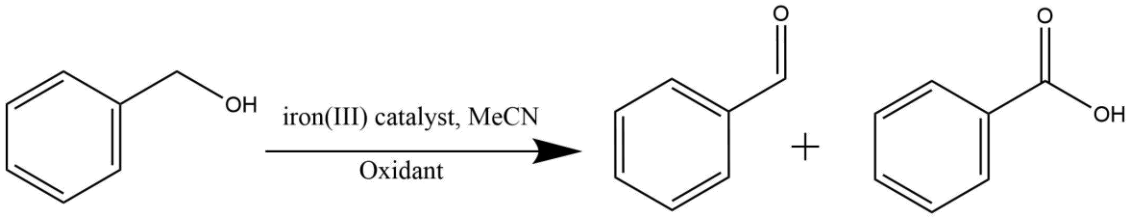

Figure 1 – Peroxidative oxidation of benzyl alcohol in the presence of iron(III) complexes

Thanks to Fundação para a Ciência e a Tecnologia (FCT) for funding this research projects UIDB/00100/2020 and UIDP/00100/2020 of the Centro de Química Estrutural, LA/P/0056/2020 of Institute of Molecular Sciences and PTDC/QUI-QIN/29778/2017.

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One-Pot [3+6+3+6] Macrocyclizations of Diazo Ketones and Cyclic Ethers

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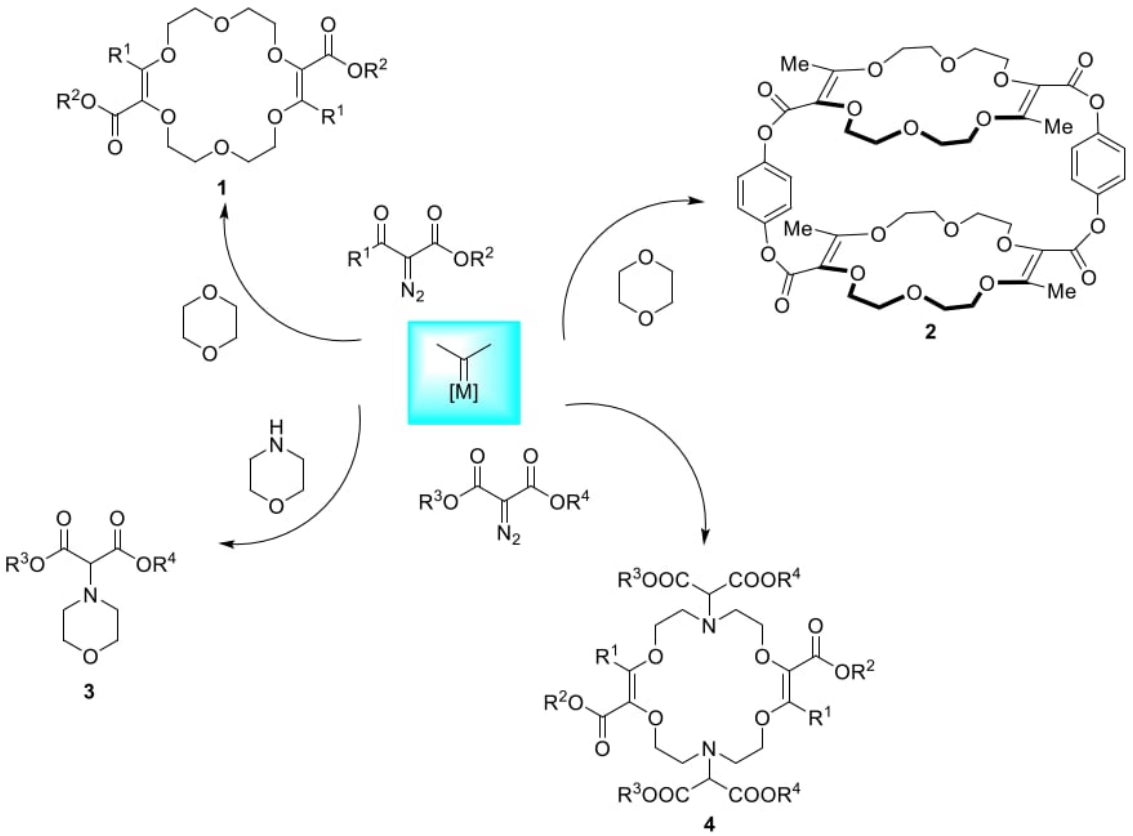
Functionalized macrocycles of type **1** can be prepared in one pot by transition metal-catalyzed decomposition of α-diazo-β-ketoesters in the presence of cyclic ethers. With alkyl ester reagents, under Rh(II)-catalysis, good yields are obtained on multi-gram scale in this formal [3+6+3+6] condensation with 1,4-dioxane. However, with α-diazo-β-keto aryl esters, this procedure is poorly compatible.[1-3] Herein, we present the advantageous use of Pd(II)-catalysis for making to the corresponding macrocycles. Also, with these milder conditions, bis-diazo reagents can be designed to pursue the single-step formation of novel dimeric structures **2** containing two sandwich-like macrocycles. Molecular scaffolds of type **2** entice novel properties that are being currently studied in our group. Finally, considering that polyazamacrocycles are particular favorable in host-guest chemistry, care is taken to use diazo decomposition chemistry to generate morpholine precursors of type **3**, which are then used as substrates for the making of the corresponding aza-macrocycles.[4] Properties of products **4** are currently being explored.



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Unravelling the CO_2 reduction mechanism with a highly active Mn(I)-NHC electrocatalyst

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In this work, we present a mechanistic study of the electrochemical CO_2 reduction catalyzed by a highly active *fac*-[Mn^{I}(CO)$_3$(*bis*-^{Me}NHC)MeCN]$^+$ complex (Mn-MeCN$^+$).[1] By combining *in-situ* IR-SEC, chemical synthesis of intermediates and DFT calculations, we have identified and fully characterized Mn-CO$^+$ (under CO_2) and Mn-H (under Ar) as key intermediates in the CO_2 reduction mechanism. Our observations confirm that, in the presence of low water concentrations, the CO_2 reduction to CO occurs through a protonation-first pathway. However, at higher concentrations of water, Mn-H is formed and easily inserts CO_2 to give the corresponding Mn-O$_2$CH intermediate. The formate release from the latter intermediate is a slow process which explains the decrease of the catalytic activity in the presence of high concentrations of added acid.

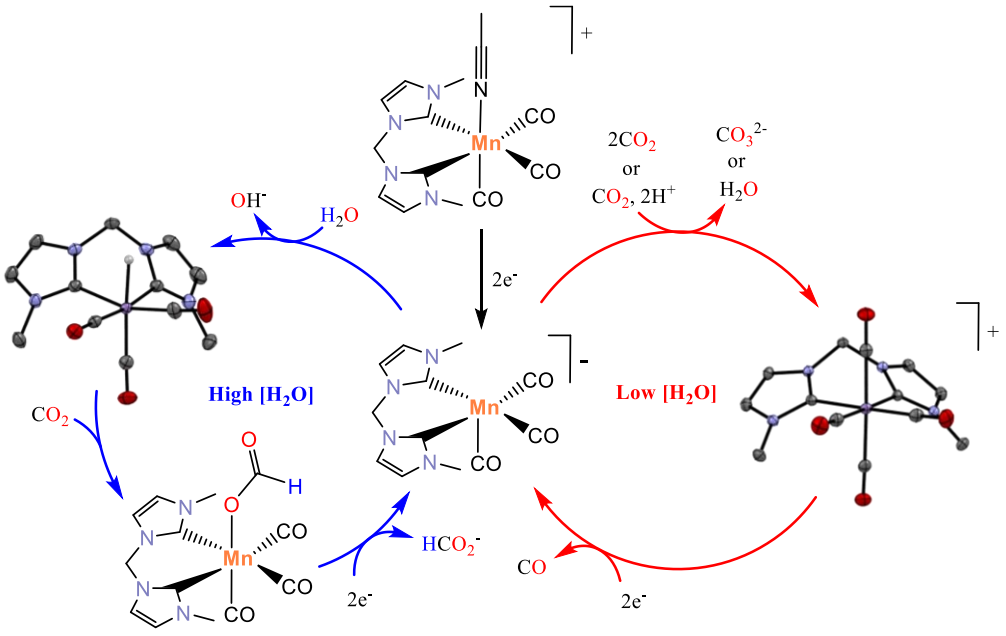

Figure 1. General mechanistic picture of the CO_2 reduction to CO and formic acid with our Mn(I)-NHC catalyts.

The attendance of S.F. to this congress has been funded by the Catalan Chemical Society (SCQ).

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Regioselective synthesis of 8-membered oxadiazocines through selective control of nitrogen vs. oxonium ylide formation and subsequent rearrangements

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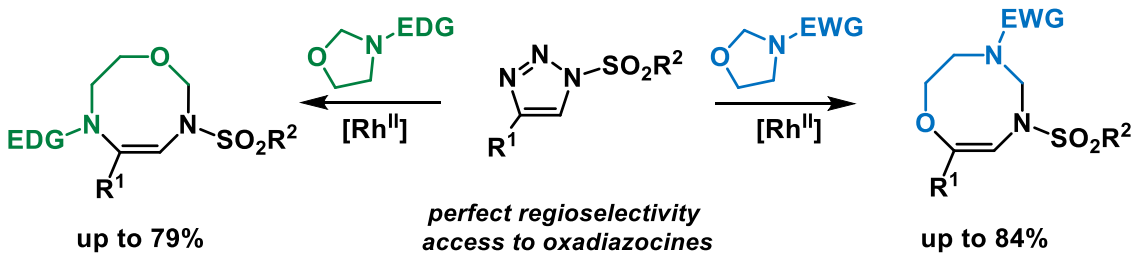
Masked diazo precursors, like *N*-sulfonyl-1,2,3-triazoles have become popular reagents in carbene chemistry over the last decade.**[1]** In fact, α-diazo imine moieties, which result from the ring chain isomerism of triazoles, can react with metal catalysts such as dirhodium complexes to form electrophilic metal carbenes. In presence of *Lewis* bases, ylide formation and subsequent cascade reactions may occur.**[2],[3]**

Herein, in this context and using bifunctional oxazolidines as substrates, selective formation of either nitrogen or oxygen ylides can be achieved. By selecting the nitrogen protecting group with care, full regioselectivity is attained towards the formation of either 8-membered 1,3,6 or 1,4,6-oxadiazocines. In fact, after ylide formation, ring opening and subsequent intramolecular trapping steps form the corresponding medium-sized rings with full regiocontrol and good overall yields (up to 84%).



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Asymmetric Synthesis of Cyclohexenone-Fused Isochromans via Quinidine-Catalyzed Domino Peroxyhemiacetalization/Oxa-Michael Addition/Desymmetrization Sequence

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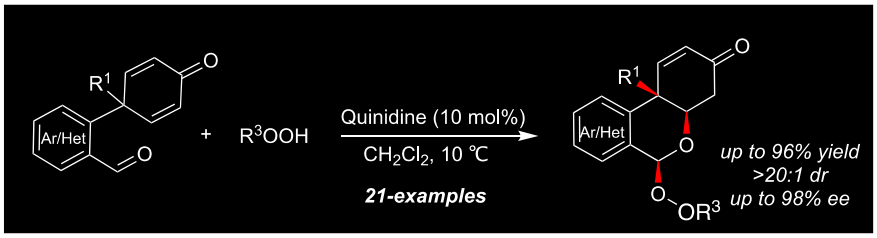
Isochroman, a benzene-fused oxa-heterocyclic framework, is an integral component of various bioactive natural products and essential pharmaceutical compounds exhibiting a broad range of biological properties.[1] Moreover, the isochroman derivatives serve as precursors for synthesizing other oxo-heterocycles. Due to a broad spectrum of biological activities and potential application as drugs and a key intermediate in organic synthesis, the stereoselective synthesis of isochroman scaffolds is highly important.

Recently, ortho-formyl homochalcones were identified as the suitable substrates for the organocatalyzed domino 1,2-addition/oxa-Michael reactions to afford isochromans bearing two stereogenic centers.[2] We have utilized 2,5-cyclohexadienones bearing ortho-formyl aryl system to undergo the organocatalytic nucleophilic 1,2-addition/oxa-Michael addition with a simultaneous desymmetrization of 2,5-cyclohexadienone to generate isochromans bearing three stereogenic centers including a tetra substituted carbon center in good to excellent yields and stereoselectivities under mild reaction condition.[3] To the best of our knowledge, the application of 2,5-cyclohexadienone's desymmetrization for providing isochroman derivatives is not known. Finding of our research work on organocatalyzed domino peroxyhemiacetalization/oxa-Michael addition desymmetrization sequence to synthesize the cyclohexanone fused isochromans will be presented.



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Synthesis and functionalization of silsesquioxanes containing a boron atom in the cage structure

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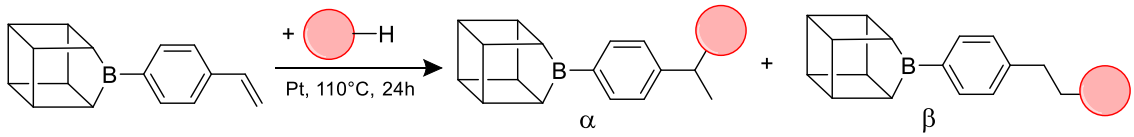
Silsesquioxanes belong to the group of hybrid organosilicon compounds of the general formula $[RSiO_{3}/_{2}]_n$ (where n = 6, 8, 10, 12; R = alkyl, aryl, halogen etc.) [1]. The ongoing research on the chemistry of these compounds and their derivatives has led to the development of a new class of compounds - heterosilsesquioxanes, which possess one or more silicon atoms replaced with another element from the *p* or *d* block in their cage structure. The introduction of boron in the place of silicon atoms results in formation of borasilsesquioxanes [2]. In the earlier studies of our group we researched functionalization of styrylborasilsesquioxanes in a cross-metathesis reaction in the presence of a ruthenium catalyst [3].

In this study we investigated the activity of mono- and distyrylborasilsesquioxane carbon-carbon double bond towards the hydrosilane (Si-H) moiety addition via hydrosilylation reaction. Borasilsesquioxanes were functionalized with organosilicon compounds, i.e. silanes, siloxanes and spherosilicates. A range of new compounds with potential application in materials with special properties (e.g. as flame retardants in polymers) was obtained.



Scheme 1. General scheme for hydrosilylation of vinylborasilsesquioxane with compounds bearing Si-H moiety.

Acknowledgement: The work was supported by grant no. POWR.03.02.00-00-I020/17 co-financed by the European Union through the European Social Fund under the Operational Program Knowledge Education Development.

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Iron(III)-light-induced homolysis: A dual photocatalytic approach for hydroacylation of alkenes using acyl radicals via direct HAT from aldehydes

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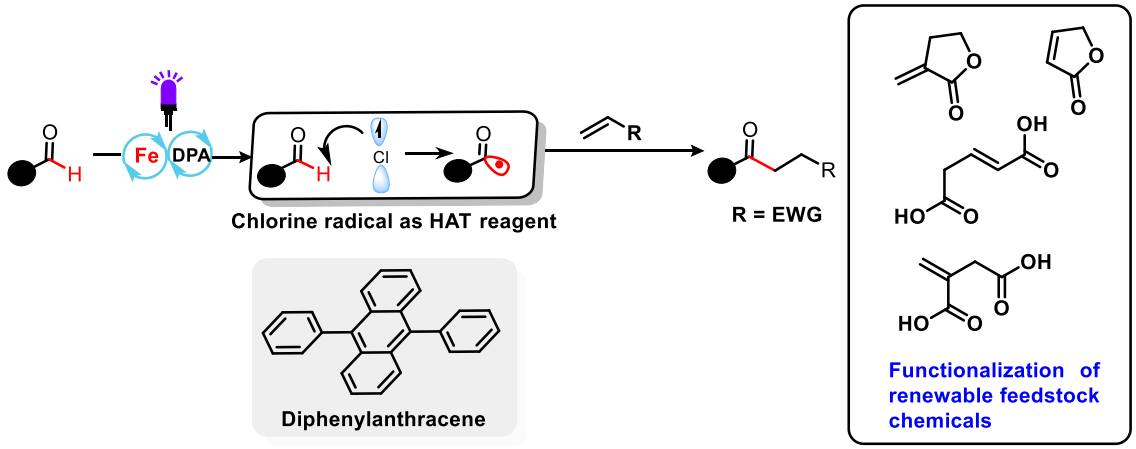
A dual photocatalytic protocol was developed to generate acyl radicals from readily available aldehydes via hydrogen atom transfer. Synergistic cooperation, being supported by DFT studies support, between earth-abundant iron(III)chloride and 9,10-diphenylanthracene (DPA) to activate the aldehyde for a HAT step proved to be an efficient, economic, and green route for the hydroacylation of electron-deficient alkenes with broad functional group compatibility. This methodology can be conveniently scaled-up and applied to produce valuable materials from renewable feedstock chemicals.1



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Design of ZSM-5 zeolite through Gemini surfactants for Friedel-Crafts reactions

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Friedel-Crafts acylation reactions are important routes for the synthesis of intermediates to produce fine and specialty chemicals. As the reactions are usually performed in the presence of hazardous and non-reusable homogeneous catalysts, it is important to find alternative catalysts. Zeolites are inorganic materials with a large set of applications as heterogeneous catalysts. However, the microporous nature of these materials imposes some restrictions in catalytic reactions involving large molecules, especially in the liquid phase, as in the case of Friedel-Crafts acylation reactions. To overcome this limitation several strategies are being explored to produce hierarchical zeolites. Among them, the surfactant-templated method is a particularly appealing strategy since it allows to obtain materials with homogeneous mesopores, that can be modulated according to the type/size of surfactant used [1] (Fig.1).

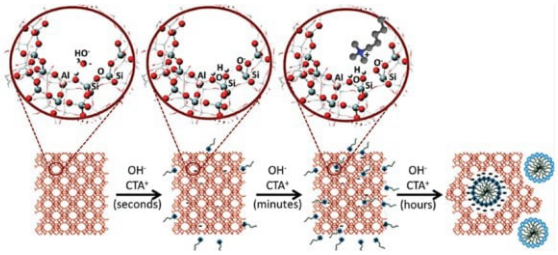

Figure 1. Schematic representation of the steps involved in the surfactant-templating of zeolites using CTAB as surfactant. [1]

In this study, asymmetrical anionic Gemini surfactants of polyoxyethylene laurinol ether sodium sulfoitaconate, Gemini-*n*, with n=4 or 9 were prepared according to ref. 2. The critical micelle concentration was determined by conductimetry and the Gemini surfactants as well as CTAB commercial surfactant were used as templates in a post-synthesis modification at 150 ^{o}C under autogenous pressure during 3-48 h, adapting the procedure described in ref. 3. Parent and modified materials were characterized by X-ray powder diffraction, N_2 adsorption at -196 ^{o}C and scanning electron microscopy. The catalytic tests were conducted using 1 or 2-methoxynaphtalene as substrate and acetic anhydride as acylating agent at 80 ^{o}C, using a ratio acylating agent/substrate=5. The reaction products and unconverted reactants were analysed by GC (Perkin Elmer Auto-System) equipped with a DB-5MS capillary column and FID detector. Preliminary results have shown a promising performance for the Gemini surfactant-templated materials.

Aknowledgment

This research was funded by Fundação para a Ciência e a Tecnologia (FCT) through UIDB/00100/2020, UIDP/00100/2020 and LA/P/0056/2020 and Instituto Politécnico de Lisboa (IPL) through Project IPL/2021/ZeoGemini_ISEL.

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Carbon Dioxide-Catalyzed Transamidation Reactions

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Abstract: We demonstrated that traceless CO_2 can be an effective catalyst for transamidation reactions. Various amines including amino acids showed reactivity in transamidation implying potential applications in polymer degradation (e.g., Nylon-6,6). We found Weinreb amides displayed a unique reactivity in the CO_2-catalyzed transamidation based on our comparative Hammett studies, kinetic analysis and DFT calculations. The positive effect of CO_2 in the transamidation reaction can be explained by the stabilization of tetrahedral intermediates and transition states via covalent binding to the electrophilic CO_2.

Peanut shell as a valuable resource for the development of sustainable catalytic processes for the oxidation of furan-2-carbaldehyde (furfural)

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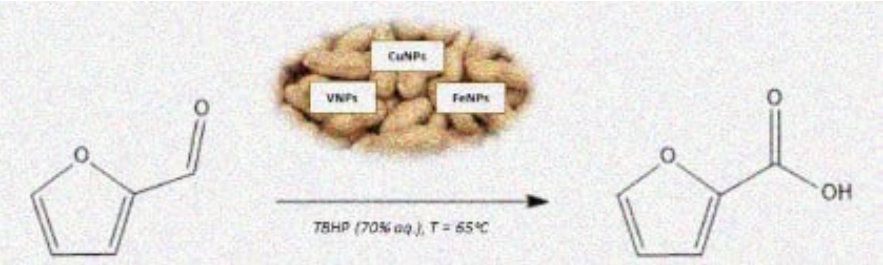
The main goal of this work is the valorisation of peanut shell waste (PSW) in the preparation of new catalysts using alternative and versatile synthetic tools, as well as in the development of new catalytic routes for obtaining biodiesel co-products. Agri-food waste will be used as feedstock for bio-based products encouraging industries to reuse valuable agro-industrial residues in a more efficient way, providing environmental benefits and contributing to the economic sustainability.

The extraction of PSW components was carried out using eco-friendly solvents such as water and ethanol, and using advanced techniques (ball milling, ultrasonic, and microwave irradiation). The PSW extracts were evaluated by UV-Vis for polyphenols and flavonoid detection and by DPPH tests for the antioxidation activity.

PSW biomass residue was applied as support material for zero-valent metal nanoparticles (MNPs) based on Fe, Cu, and V through an easy, fast, and economically feasible route.

The catalytic activity of the supported metal nanoparticles (FeNPs, CuNPs and VNPs) was screened in the oxidation of furan-2-carbaldeheyde operating under mild and environmentally acceptable conditions and using TBHP (70% aqueous solution) as oxidant. The catalytic studies were performed under conventional heating, and, for comparison, other energy inputs were explored. The reaction products were analysed quantitatively and qualitatively employing NMR, GC and GCMS techniques. The results were quite encouraging with conversions up to 75%.

In the final stage, as one of the most important features in heterogeneous catalysis, the recycling/reusability of the applied catalysts will be evaluated.



Financial support from the Fundação para a Ciência e a Tecnologia, Portugal (UIDB/00100/2020 and PTDC/QUI-QIN/29778/2017 projects) and Instituto Politécnico de Lisboa (IPL/2021/WASTE4CAT_ISEL) is acknowledged.

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Evaluation of novel triphenylene-based phosphinite and phosphonite Pd-complexes in Negishi cross-coupling catalysis

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Substituted triphenylene derivatives have been broadly studied in the field of materials science in the last few decades [1]. They have shown not only very good behavior as scaffold in the preparation of liquid crystals but also present other worthy electronic properties [2]. However, while these compounds have been widely investigated as materials, few examples can be found in the literature where they are employed as ligands in a catalytic process [3]. In this context, Negishi cross-coupling catalysis has demonstrated to be a powerful tool in the formation of $C(sp^3)$-$C(sp^2)$ bonds for the synthesis of different target organic compounds. The reaction involves the use of an organozinc reagent, a polar solvent and a precatalyts, usually a phosphine-bound Pd complex [4].

Herein we describe the preparation of novel phosphinite and phosphonite derived from alkoxy-triphenylene and the corresponding allylpalladium complexes, as well as their evaluation as precatalyts in cross-coupling reactions (Figure 1). To the best of our knowledge no precedent of Negishi reaction has been reported using phosphonite and phosphinite as ligands. The solubility of these complexes allows the use of non-common organic solvents in these processes.

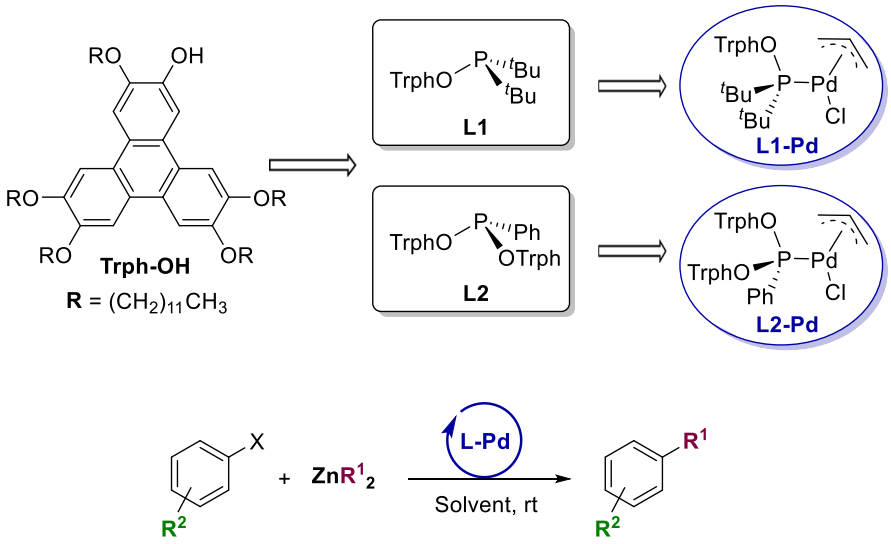

Figure 1. Phosphinite and phosphonite Pd-precatalysts in Negishi cross-coupling.

Thanks to the Junta de Castilla y Leoń-FEDER (grant VA224P20) and to the Spanish MICINN (grants PID2019-111406GB-I00 and PID2020-118547GB-I00) for their financial support.

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Blue Light Catalysed Hydrogenation of 4-nitrophenol with MOF-derived Cu_xO

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Hydrogenation of nitroarenes into anilines is a reaction of great interest as anilines are one of the most important intermediates for the synthesis of pharmaceuticals and dyes. [1] Moreover, nitroarenes - including nitrophenols - are highly toxic pollutants, extensively produced as waste in agricultural and industrial activities. [2] Their transformation into the aforementioned aniline intermediates is highly desirable. $NaBH_4$ is widely used for this reaction, as it effectively hydrogenates a wide range of nitroarenes in aqueous media using metals or metal oxides as catalysts. [3] Among them, Cu and CuO are among the most effective. [4] In recent years, the metal-oxide-assisted photoreduction of nitroarenes, mainly by TiO_2, has yield very promising results. [5] Here, we extend this study to CuO/Cu_2O heterojunctions, as we hypothesized that the hydrogenation of the nictroarenes can be significantly enhanced due to the improved charge separation, as described for other reactions. [6]

Specifically, we present the preparation of Cu_xO by controlled decomposition of Cu(BTC) MOF, with various amounts of Cu_2O/CuO (Figure 1A) and their evaluation as photocatalysts for the hydrogenation of 4-nitrophenol. The presence of Cu_2O in the surface of the nanostructures (Figures 1B & 1C) drastically boosts the performance of the CuO, doubling the rate constant using blue LEDs as light source (Figure 1D). Furthermore, CuO/Cu_2O mixture as catalyst yields excellent performance for the hydrogenation, specially under blue LEDs (Figures 1E & 1F), which can be associated to the effective separation of the photogenerated electron-hole pairs due to the composite nanostructure.

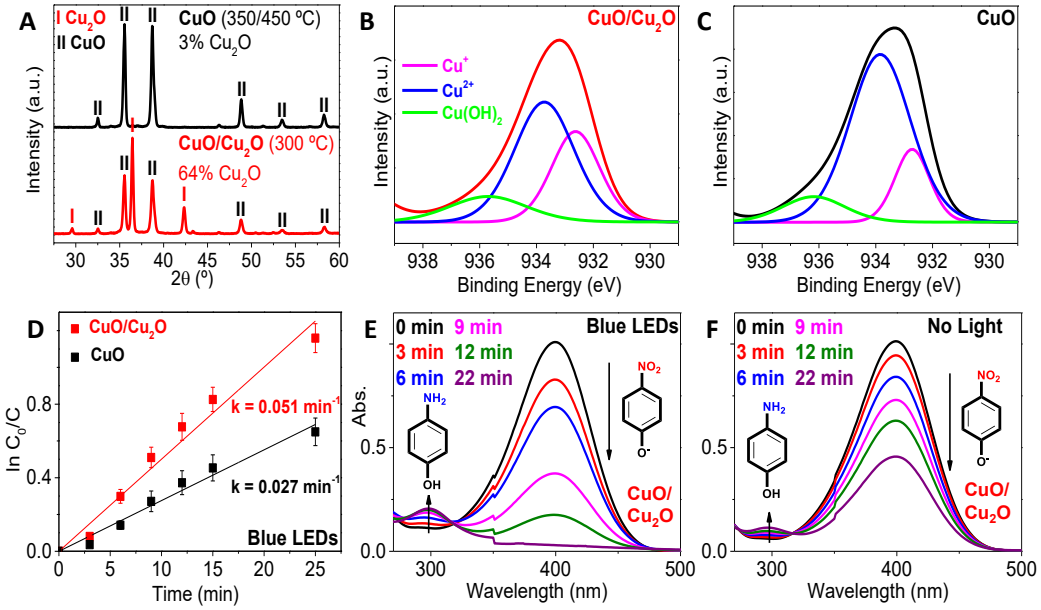

Figure 1. (A) XRD patterns and (B-C) Cu 2p XPS spectra of MOF-derived samples, namely, CuO/Cu_2O (red line) and CuO (black line). (D) Comparative study of the $\ln(C_0/C)$ vs time plot for the same catalysts using $NaBH_4$ and blue LEDs as light source. UV-vis absortion spectra of 4-nitrophenol hydrogenation in the presence of $NaBH_4$ (E) with light and (F) without light using CuO/Cu_2O as catalyst.

We thank Spanish MINECO and AEI/FEDER, UE through the project ref. RTI2018-099504-B-C21. N.L. also acknowledges the UA for funding (ref. UATALENTO17-05).

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Azo cross-metathesis versus olefin-induced degradation — DFT studies

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Recently, the cross metathesis reaction between two functionally different substrates, such as carbonyl-alkene/alkyne[1-2], or N_2-alkyne[3] leading to the formation of C=C but also C=O/N bonds caught increasing attention. Azo cross-metathesis using azo compounds as one of the substrates is in line with this trend[4]. However, in order to fully understand the still unclear mechanism of this transformation, Ru-complex decomposition studies in necessary in order to the effective design catalyst for these new reactions.

In this work, we investigated the possibility of the ethylene-induced inactivation of the ruthenium imido complex formed in the cross-azo metathesis reaction. We egzamined how the impact of structural changes of the catalyst, such as the presence of specific ligands/substituents, will affect the relative degradation rate. The results of the DFT simulation of the van Rensburg degradation[5] of ruthenium catalysts will be presented and compared with the appropriate part of the azo-metathesis catalytic cycle in the presence of selected model complexes.

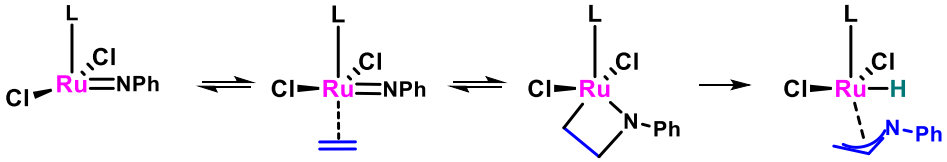

Figure 1: The general idea of degradation of Ru-imido complexes based on van Rensburg mechanism.

Acknowledgements: The Author thanks the National Science Centre for financial support, grant UMO-2019/35/D/ST4/01861.

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Buchwald Hartwig reaction carried out with the use of catalytic systems based on cobalt complexes

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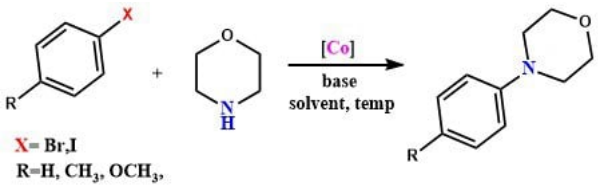
The Buchwald Hartwig reaction is a process of the synthesis of aromatic amines by coupling primary or secondary amines with aryl halides. This reaction, which is a catalytic process, is most often carried out with the use of palladium complexes [1]. Over the years, this process has become an important tool for the synthesis of many natural products and pharmaceuticals, as well as their analogues [2,3]. From medicinal chemistry point of view, it is an extremely important process due to the ubiquitous presence of aromatic amines in biologically active systems [4].

Palladium catalysts of the Buchwald- Hartwig reaction evolved over the years, starting with complexes with ligands such as $P(o\text{-}tol)_3$, which proved to be effective in the case of secondary amines, but failed in the case of primary ones [5]. This problem was solved by the use of POP ligands, e.g. (DPEPhos) and, as in the case of $P(o\text{-}tol)_3$, monophosphines with higher steric hindrance [6,7]. Nevertheless, there is a constant trend in the scientific community to look for solutions to replace palladium with other cheaper and/or less toxic metals while maintaining good process efficiency. One of the candidates for Pd replacement is cobalt. It has found its place among many tested systems and has allowed a number of catalytic reactions to be successfully performed, including hydroarylation, alkenylation, [8] and amination reactions [9]. Economically, cobalt appears to be extremely favorable at the current price of $82,000 per metric ton compared to palladium $67 million (as of 13.05.2022). In addition, cobalt is a metal of lower toxicity and is even a part of vitamin B12, which plays a role in methylation processes in living organisms.

This presentation is going to show our approach to the Buchwald-Hartwig reaction using catalytic systems based on cobalt complexes of predefined structure, characterized by synthetic simplicity and promising results at the initial research stages (scheme 1).



Scheme 1 Model reaction scheme

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New cobalt-based catalytic system for Suzuki-Miyaura cross-coupling reaction

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Today, cross-coupling reactions are a tremendous synthetic tool in the creation of compounds which contain C-C, C-N, and C-O bonds [1]. These reactions are constantly employed in academic and industrial fields to synthesize drugs, agrochemicals, and advanced biologically active materials. Due to high stability of boronic compounds, their high availability and convenient preparation, Suzuki-Miyaura cross-coupling is used more commonly than Stille, Negishi, and Murahashi cross-couplings, whose substrates (organotin, organozinc, and organolithium reagents, respectively) have weak stability in the air. The most common catalytic systems of these transformations are based on precatalysts that contain platinum-group metals (PGM) and often require the addition of ligands [2]. Heck, Negishi, and Suzuki were awarded the Nobel Prize in Chemistry in 2010 for palladium-catalyzed cross-couplings in organic chemistry. Current trends in chemistry have shown that especially the development of catalysis by the first-row transition metals is highly regarded [3]. First-row transition metals, in comparison to PGMs, are essentially cheaper and they are characterized by lower toxicity, which is important in medical purpose. There are many nickel and copper catalysts of the Suzuki-Miyaura cross-coupling, but only a few containing cobalt. Catalytic systems containing cobalt complexes are still explored by scientists.

In our research group, we have discovered that a cobalt complex containing simple N-donor ligands and bromide anions is active in the Suzuki-Miyaura cross-coupling reaction. Aryl iodides and phenylboronic acid were used as the substrates, and the addition of potassium methoxide was necessary to activate the reaction system.

This poster is going to show our work on the Suzuki-Miyaura cross-coupling of phenylboronic acid with aryl iodides catalyzed by simple Co(II) complexes.

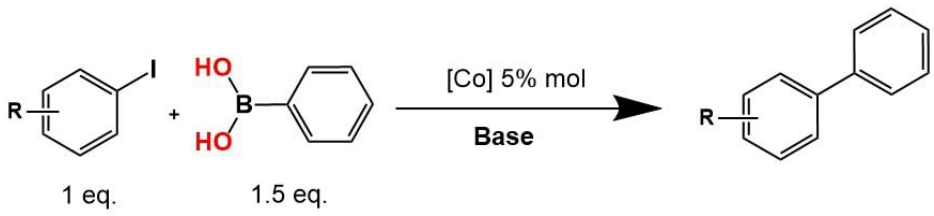

Figure 1 A general scheme of the reported Suzuki-Miyaura cross coupling.

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Thermochemical sulfate reduction by glycerol over Mo-containing catalysts under hydrothermal gasification conditions

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Converting biomass to synthetic natural gas by catalytic hydrothermal gasification (cHTG) is a sustainable and promising route to produce energy and mitigate negative human impact on our mother nature. However, one of the most prominent issues in cHTG is the sulfur-containing compounds in raw biomass which poison the noble metal catalysts (e.g. ruthenium). Therefore, the desulfurization of biomass is of significant importance to the development of catalytic biomass conversion. Although sulfide can be removed by ZnO [1], sulfate and organosulfur compounds can still threaten the catalyst [2]. It is well known in the field of geochemistry that sulfates can be reduced to sulfides at hydrothermal conditions in the presence of organic molecules, which is called thermochemical sulfate reduction (TSR) [3]. Hence, applying TSR to explore the removal of sulfate from biomass is the aim of this project.

Through analyzing different sulfur-containing products by ion chromatography (IC), gas chromatography – sulfur chemiluminescence detection (GC-SCD), ultraviolet-visible spectroscopy (UV-vis) and inductively coupled plasma – optical emission spectrometry (ICP-OES), we examined the impact of temperature (from 290 ℃ to 490 ℃) on sulfate conversion in a model solution that consists of 20 wt% glycerol and 10 mM K2SO4 in a batch reactor without catalyst. Although our results indicated that temperature did not have an obvious impact on sulfate conversion, organosulfur compounds production would be favored at higher temperature (440 ℃ and 490 ℃). To increase the sulfate conversion, another series of batch reactor experiments were carried out with Mo-containing catalysts (NiMo, CoMo, MoO_2 and MoS_2) due to their ability in providing coordinatively unsaturated (active) site for sulfur reduction [4, 5]. Catalysts were characterized by N_2 physisorption, CO chemisorption, X-ray diffraction (XRD), transmission electron microscopy (TEM) and energy-dispersive X-ray spectroscopy (EDX). The results showed that NiMo and CoMo increased the sulfate conversion up to 30 % while MoO_2 and MoS_2 only promoted it by 15 %. However, MoO_2 exhibited the highest turnover frequency implying its active sites for sulfate conversion performed better than that of the other three catalysts. From the perspective of inhibiting the production of organosulfur compounds, MoS_2 presented a slightly superior capability among the examined catalysts. In conclusion, we hypothesize that MoO_2 plays a more important role than MoS_2 in catalytic thermochemical sulfate reduction. To achieve a higher selectivity in removing sulfate and organosulfur compounds at the same time, discovering the optimal sulfidation extent on the catalyst might be the solution.

Thanks to the financial support from the Swiss National Science Foundation. Part of this work was supported by and performed within the Energy System Integration Platform at the Paul Scherrer Institute. The author thanks Prof. Oliver Kröcher, Prof. Frédéric Vogel and Dr. David Baudouin for their supervision and guidance, Pascal Unverricht and Erich De Boni for building up and maintaining of the batch reactor system, Reinhard Kissner for his help on ion chromatography analysis.

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Metallaelectro-Catalyzed Bond Activations

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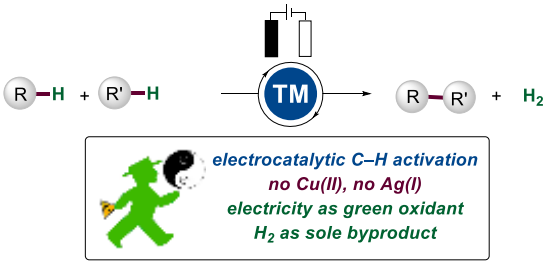
Oxidative C–H activation has emerged as an increasingly powerful tool in molecular syntheses.[1] Despite major progress towards atom and step economy, these transformations largely rely on precious metal catalysts and stoichiometric amounts of toxic metal oxidants, compromising the overall sustainability of the C–H activation strategy. In contrast, employing electrooxidation *in lieu* of reactive chemical oxidants prevents undesired waste formation through oxidant economy and offers efficient use of renewable energies from sustainable sources for chemical bond formation.[2] Inexpensive Earth-abundant 3d metal[3] cobaltaelectrocatalysis set the stage for molecular syntheses at a unique level of resource economy.[4] Our studies towards metallaelectrocatalytic C–H and C–C activation will be discussed, with a topical focus on sustainable base metals.[5]



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Heterodinuclear Catalysts for the Ring-Opening Copolymerization of CO_2 and Propylene Oxide

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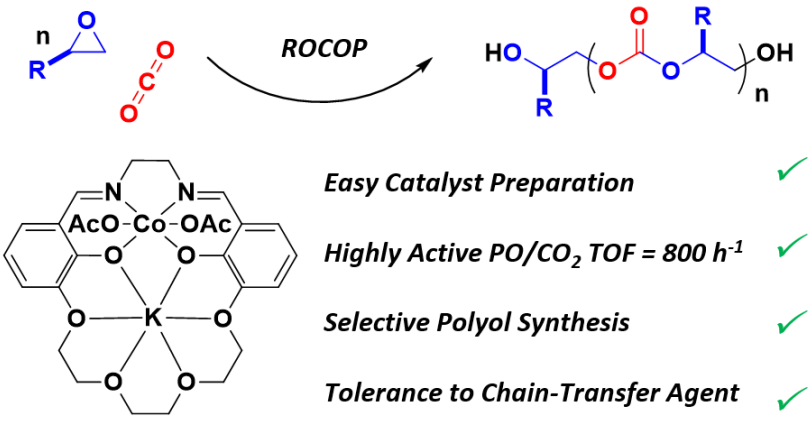
Carbon dioxide utilization is a key challenge of modern chemistry. Although many carbon dioxide reactions are known, very few are true utilizations or viable for larger-scale implementation. This work focuses on the ring-opening copolymerization of carbon dioxide with propylene oxide, producing a commercially viable product poly(propylene carbonate), with properties already shown to allow for replacement of incumbent materials. Further, life cycle assessment has identified a triple win in terms of carbon dioxide (greenhouse gas) emissions – for every molecule of carbon dioxide sequestered into the polymer, two more are saved in avoided petrochemicals. Key challenges remain in the pursuit of improved catalysts: these include high activity, selectivity and tolerance to hydroxyl-chain-transfer agent.

Here, a new heterodinuclear Co(III)/K(I) catalyst is reported displaying outstanding activity (TOF = >800 h^{-1}), polymer selectivity (> 98 %) and tolerance to chain-transfer (up to 250 equiv.). The PPC polyols are determined to be hydroxyl-telechelic with predictable molar masses and narrow dispersities (Đ <1.15). Kinetic analysis was undertaken to derive the rate law which suggests a first order dependence on both catalyst and epoxide concentrations and a zeroth order in CO_2 pressure. The catalyst was found to be highly versatile and displayed excellent activity and selectivity with several other cyclic and acyclic epoxides.



A. C. Deacy, E. Moreby, A. Phanopoulos, C. K. Williams, *J. Am. Chem. Soc.*, **2020** ,142, 19150.

Study of copper, manganese and iron based heteropolysalts in the effeciency of synthesis of 5-ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one

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In this work, we report an efficient and green method for dihydropirimidinone (DHPMs) synthesis according to Biginelli condensation protocol catalyzed for the first time by of Keggin heteropolyacid (HPAs) noted $H_3PMo_{12}O_{40}$ and its ammonium salts $H_{3-2x}M_x PMo_{12}O_{40}$ and $(NH_4)_{3-2x}M_xPMo_{12}O_{40}$ (M: Cu, Mn or Fe) solid catalysts in free solvent conditions.

The POMs catalysts were synthetized by cationic exchange method, then, characterized by FTIR, XRD and TG analysis. The Biginelli cyclocondensation conditions were optimized. The effect of several reaction parameters over DHPMs yield were studied as: temperature and reaction time, reagents report, composition and weight of catalyst, reduction and hydration level of the POM….. Characterized DHPMs were done by FT-IR, ^{1}H and ^{13}C NMR.

The reaction results show that $H_3PMo_{12}O_{40}$ is the best catalyst in our reaction conditions with an excellent yield around 94% which can be explained by significantly higher Brønsted acidity compared to that of traditional mineral catalysts. In the other hand, other excellent yields have been obtained in the presence of $Cu_{0.25}H_{2,50}PMo_{12}O_{40}$ and $(NH_4)_{3,00}Cu_{0,00}PMo_{12}O_{40}$ 76% and 60% respectively.

Very interesting results were obtained in mild and green conditions compared to the conventional method, high DHPMs yield, short reaction time, no solvent and lower energy costs. Then as protocol should be complementary to the existing methods.

KEYWORDS: heteropolysalts, polyoxometallates, Biginelli reaction, green chemistry.

The production of the gasoline with high quality with high octane number by the use of the bifunctional catalyst Pt/Re in the catalytic reforming process

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The original function of the process of platforming is to develop heavy naphtha (HSRN), coming from the atmospheric unit of distillation with a weak octane number (NO = 44), to obtain a mixture of fuels â number octane raised by catalytically supporting specific groups of chemical reactions. The installation is divided into two sections: Section hydrobon. Section platforming.

The rafinat coming from the bottom of column 12C2 to feed the section platforming, is divided into two parts whose flows are controlled and mixed with gas rich in hydrogen.

Bottom of the column, we obtain stabilized reformat which is aspired by there pump to ensure the heating of the column whereas a part is sent towards storage after being cooled by the air cooler and the condenser.

In catalytic catalyst of reforming, there is voluntarily associated a hydrogenating function - dehydrogenating, brought by platinum deposited, with an acid function brought by the alumina support ($Al_2 0_3$). The mechanism of action of this bifunctionnal catalyst depends on the severity of the operation, of the quality of the load and the type of catalyst.

The catalyst used in the catalytic process of reforming is a very elaborate bifunctional catalyst whose performances are constantly improved thanks to the experimental research supported on an increasingly large comprehension of the phenomena.

The American company Universel 0i1 petroleum (UOP) marketed several series of bimetallic catalysts such as R16, R20, R30 and R62 consisted Platinum / Rhenium on an acid support consisted the alumina added with a halogenous compound (chlorine).

Key Words: Platforming, Amelioration, Octane Number, Catalyst.

Mining industrial materials as heterogeneous catalysts for carbon dioxide and epoxides coupling reaction to obtain cyclic carbonates

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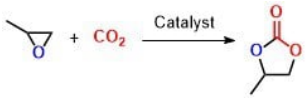
The increasing concentration of CO_2 in the atmosphere contributes to the global warming and it is a cause of the demand for urgent environmental protection. Chemical fixation of CO_2 and its utilization as C1 building block into fine chemicals are among key areas of research to mitigate this greenhouse gas. In fact, a well-known strategy consists on using catalysts (homogeneous and heterogeneous) to form cyclic organic carbonates by coupling reaction between CO_2 and epoxides [1,2]. Cyclic carbonates are very interesting products for industry due to a wide range of applications such as green and non-protic solvents, electrolytes for ion-lithium batteries and as scaffolds for the synthesis of fine chemicals and polymers, among others [3].



The huge potential of MgO material as sustainable heterogeneous catalyst for this reaction has been previously demonstrated [4,5]. Moreover, this material can be readily separated from mixture to be recycled and reused. According to European Commission research, global raw material extraction has grown 14 times, with the sharpest increase in industrial minerals at 45 times. In fact, it is not disputed the necessity of recycling industrial minerals and revalorize byproducts as a solution for the Circular Economy. This research focus on the exploration of some industrial mining raw materials as novel catalysts for the cycloaddition reaction between CO_2 and epoxides. The case of magnesite mining byproducts used as heterogeneous catalyst for the obtention of cyclic carbonates has been studied as a challenge in both zero residue and revalorization of secondary raw materials for industrial solutions. Then, coupling reactions between CO_2 and different aliphatic and aromatic epoxides were performed efficiently by Sulfamag byproduct, showing yields between 71-91% and selectivity of 99% under mild conditions, demonstrating their potential as a renewable raw material solid based heterogeneous catalyst. Furthermore, Sulfamag showed recycling efficiency in a test of four cycles and its deactivation was compared with commercially available MgO. Then, not only the improvement of reaction conditions has been studied, but also the selection of recycled mineral mining raw materials has been offered as a wide range of catalysts in a "green" and sustainable portfolio. Thus, industrial minerals will emerge as the new alternative "mineral source" and become the "new normal" supply chain option for mineral consumers [6].

As a conclusion, we have explored industrial mining raw material byproducts, with potential valorization interest, as a renewable, recyclable, non-toxic, cheap and readily available heterogeneous catalysts for the transformation of CO_2 in high-valuable-products as cyclic carbonates.

This work was performed under collaborative projects between Magnesitas Navarras, S.A and *Asociación de Investigación de materiales plásticos y conexas* (AIMPLAS). AIMPLAS authors thanks to *Instituto Valenciano de Competitividad Empresarial* (IVACE) the founding from the project IMAMCA/2022/4.

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Effect of Si doping on the single-catalyst production of clean and sustainable fuels

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Our current lifestyle is highly dependent on non-renewable energy resources, such as petroleum, natural gas, and coal. Extracting energy from fossil fuels results in releasing unwanted particles and in an abnormal increase of CO_2 in the atmosphere. One potential way to circumvent the use of these resources involves Gas-to-Liquids (GtL) processes for the production of clean and sustainable fuels. Fischer-Tropsch (FT) is seen as a good alternative approach for the production of synthetic fuels since it is a promising clean technology, with the products showing high cetane number (up to 75), higher energy density than gas-phase fuels such as H_2, in addition to being sulfur- and aromatic-free [1].

The objective of this work was to prepare single catalysts containing dual functionalities, *i.e.*, capable of not only growing hydrocarbons from light gas molecules (e.g., syngas), but also inducing cracking of long hydrocarbon chains, especially waxes (C_{20+}), through the incorporation of acidic sites on the support. In order to achieve this, a boehmite-based support doped with different amounts of Si (Siral-x, x = 0, 5, 30 and 40 wt. % and corresponds to the weight fraction of doped Si) was used to deposit Co-Re metals, and its influence over both the catalytic activity and product distribution during the FT reaction was studied.

The reaction conditions used for the catalytic tests were T = 220 °C, P = 20 bar, GHSV = 2.67 $m^3 \cdot kg_{cat}^{-1} \cdot h^{-1}$ and H_2/CO = 2 for a TOS of 28h, and the catalyst was reduced *in situ* prior to the reaction. No major differences in catalytic performance were found for the sample Siral-5, since this did not significantly modify the support's acidic strength. Nonetheless, as the amount of Si increases, the production of organics increases, and that of waxes decreases. Moreover, Si doping reduces cobalt-time yield (CTY), C_{5+} selectivity (Table 1), and olefin production, while increasing C_5-C_{20} selectivity and isomers formation. This occurs due to an increase in concentration of catalytic acid sites, especially Brönsted ones, with the Si/Al ratio; this increase leads to a lower production of waxes and long-chain HCs, while increasing isomers production due to the high activity of these sites to wax hydrocracking and olefin isomerization. These two processes are strongly dependent on catalyst acid sites concentration, which, according to the catalytic results and NH_3 temperature-programmed desorption analysis, reaches a maximum level for the Co-Re/Siral-30 catalyst.

Table 1. CTY, in 10^5 $mol_{CO} \cdot g_{Co}^{-1} \cdot s^{-1}$, α, and CO_2, CH_4, C_2-C_4, and C_{5+} selectivities for a Co-Re/Pural, Co-Re/Siral-5, Co-Re/Siral-30, and Co-Re/Siral-40 catalyst.

Catalyst	Co loading / wt.%	CTY / 10^5 $mol_{CO} \cdot g_{Co}^{-1} \cdot s^{-1}$	Selectivity / %		
			CO_2	CH_4	C_{2+}
Co-Re/Pural	6.5	5.02	0.4	4.6	94.9
Co-Re/Siral-5	6.9	5.66	0.3	4.6	95.1
Co-Re/Siral-30	7.5	3.92	0.2	6.9	92.9
Co-Re/Siral-40	7.0	4.62	0.2	7.7	92.2

This work showed that doping alumina with silica increased the support's acidity, which shifts selectivity towards lighter hydrocarbons while maintaining a chain growth probability sufficiently high due to Co active metal sites, thus allowing for the direct synthesis of syncrude with a controlled product distribution towards the gasoline (C_5-C_{11}) fraction. Besides shifting the product distribution due to hydrocracking, more isomers are produced with increasing acidity due to the hydrogenation of olefins to secondary paraffins.

The authors acknowledge CQE and FCT for funding through project UIDB/00100/2020, funding from NORTE-06-3559-FSE- 000069 – Highly Qualified Human Resources for CoLAB Net4CO2 and project Cat4GtL (POCI-01-0247-FEDER-069953), co-funded by ERDF through COMPETE 2020 under PORTUGAL 2020.

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CO_2 Conversion in Bio-based Aerogels as a Porous Support for Metal Nanoparticle and Ionic Liquid Catalytic Systems

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Carbon dioxide is one of the gases responsible for the greenhouse effect, and therefore climate change. In the last years, the scientific community has been greatly focused on finding new strategies to mitigate CO_2 concentrations in the atmosphere. From CO_2 hydrogenation it's possible to obtain a wide range of chemicals, such as formic acid, formate, methane, lower olefins, higher hydrocarbons, methanol, higher alcohols, and others, most of which can be used as fuels [1]. Imidazolium Ionic liquids are capable to form and stabilize highly active Ru nanoparticles (NPs). This RuNPs/IL system has been successfully applied as a stationary phase in a biphasic hydrogenation reaction of carbon dioxide into methane at relatively mild temperature conditions [2,3]. In order to further increase NPs stabilization and reduce the amount of catalyst required, spheric alginate aerogels were explored in this work, as efficient catalyst supports for CO_2 conversion into methane. Due to aerogel properties as open porous structures, large surface areas, high porosity and low bulk density, they are very attractive for catalytic applications [4]. Besides, it is possible to tune the porous structure of the material in order to diffuse the reactants and products to and from the active sites.

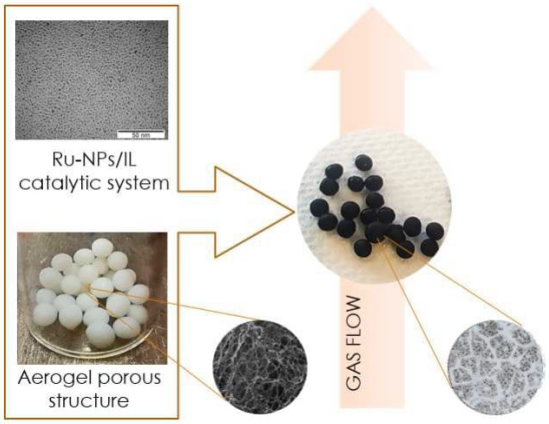

Figure 1. Scheme summarizing alginate aerogels impregnation with Ru-NPs/IL catalytic system.

The obtained aerogel, shown in Figure 1, revealed promising catalytic activity during CO_2 methanation tests. Different methods were used to immobilize the catalyst onto the aerogel surface to improve reaction results. The effect of different ILs, the composition of impregnation solution, time of impregnation in solution and the amount of aerogel impregnated were some of the conditions studied to optimize impregnation technique. To evaluate the influence of studied conditions each sample of aerogel was tested in batch CO_2 hydrogenation reactions. GC analyses were made to calculate the amount of methane produced and reaction yield was compared.

Acknowledgements
This work was supported by Fundação para a Ciência e Tecnologia FCT/MCTES through projects PTDC/EQU-EPQ/31926/2017 and MIT-EXPL/CS/0052/2021, projects UIDB/50006/2020, UIDP/50006/2020 and LA/P/0008/2020 of the Associate Laboratory for Green Chemistry – LAQV, and project UIDB/00100/2020 of the Centro de Química Estrutural – CQE. The NMR spectrometers are part of The National NMR Facility, supported by FCT (ROTEIRO/0031/2013 -PINFRA/22161/2016) (co-financed by FEDER through COMPETE 2020, POCI, and PORL and FCT through PIDDAC).

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Conductometric study of solutions of 1-methyl-3-octylimidazolium chloride ionic liquid in formamide and *N,N*-dimethylformamide at different temperatures

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Molar conductivity [1-3] of diluted solutions of ionic liquid of 1-methyl-3-octylimidazolium chloride (Fig. 1.) in formamide and *N,N*-dimethylformamide, was determined at eight temperatures in the region from 278.15 to 313.15 K, and in the concentration range from ~ 0.0002 to ~ 0.02 mol·dm^{-3}.

The values of limiting molar conductivity (Λ^0), and association constant (K_A) were calculated using the low concentration Chemical Model (lcCM) [4] for investigated systems.

From the limiting molar conductivity dependencies on temperature, the Eyring activation enthalpy values of the charge transfer were determined. Thermodynamic parameters such as Gibbs free energy (ΔG^o), entropy (ΔS^o), and enthalpy (ΔH^o) of ion association were estimated from the values of association constants at various temperatures. All quantities obtained in this work are reported and discussed, together with the Walden product in terms of the ionic size as well as solvent basicity, structure and permittivity.

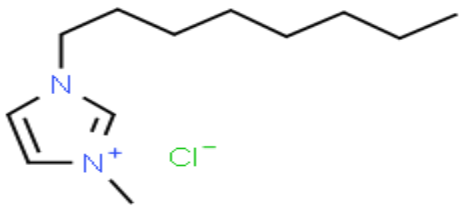

Figure 1. Structure of 1-methyl-3-octylimidazolium chloride.

Acknowledgement

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Enantioselective supercritical fluid chromatography separation of chiral anticoagulant rodenticides

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Supercritical fluid chromatography (SFC) is considered a green separation technique due to the fact that CO_2 is used as the main mobile phase component, together with low consumption of organic solvents that are toxic and harmful to environment. Moreover, SFC has showed great success in analytical science because it allows to obtain good analysis in terms of efficient, robust and fast separations [1]. Different parameters such as temperature, pressure, modifier mixed with CO_2 in the mobile phase and nature/characteristics of the stationary phase are directly involved in selectivity and compound retention. On the other hand, SFC applications have reinforced many different scientific fields.

Rodenticides are widely and specially employed as different emergence treatments in agriculture such us to control rodent infestation and to reduce the associated crop damage [2]. This fact explains the possible occurrence of rodenticide residues in water and soil samples and the importance of having methods for determining them in different samples. Although pure enantiomers of chiral compounds have identical physical-chemical properties, their toxicity, effect and persistence in the environment or in living organisms may be different. Due to these reasons, the role of chirality in environmental chemical pollution cannot be underestimated making necessary to develop new analytical methodologies able to distinguish between the enantiomers of a chiral compound and to determine them individually.

Several analytical techniques have been used to determine levels of rodenticides involving fluorometric, spectrophotometric and chromatography being liquid chromatographic the most commonly utilized [3]. Mass spectrometry (MS), ultraviolet (UV) and fluorescence are the main detectors employed. However, few studies are focusing on enantiomeric separations. The main goal of the present study was to investigate the separation of seven different chiral anticoagulant rodenticides with different chiral centers: one achiral, three with two chiral centers and four with only a chiral center that means a total of nineteen compounds perfectly resolved with SFC coupled to UV-MS. For that purpose, a screening of eight different chiral stationary phases, three different mobile phase and conditions of pressure/temperature were tested in order to achieve the enantiomeric separation of all rodenticides. Finally the proposed method was applied to the determination of the persistence of these residues in water and soil samples.

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A Combined Topological ELF, NCI and QTAIM Study of Mechanism and Hydrogen Bond Controlling the Selectivity of the IMDC Reaction of Nitrone-alkene Obtained from m-allyloxybenzaldehyde

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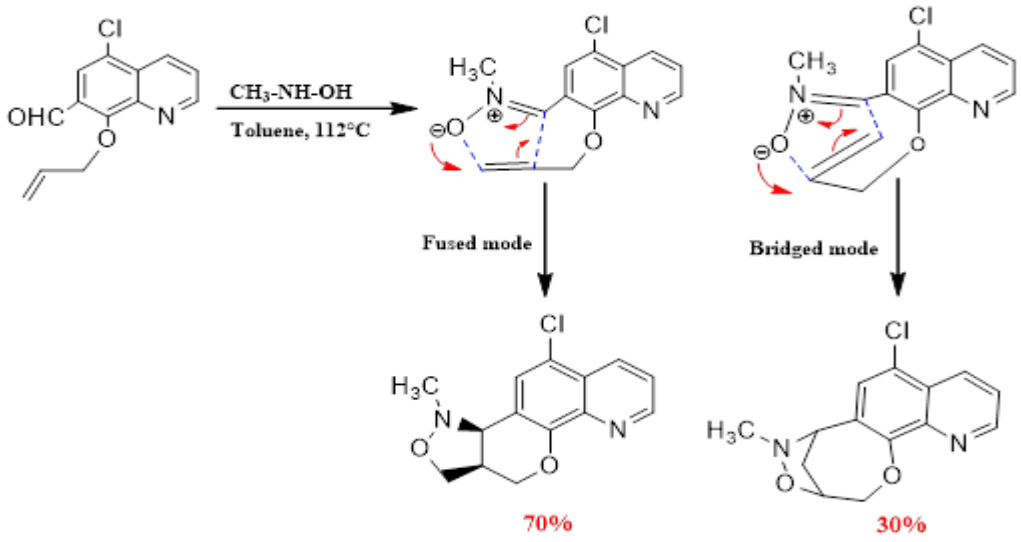
The selectivity and molecular mechanism of the intramolecular [3+2] cycloaddition (IMDC) reaction of nitrone-alkene generated from m-allyloxybenzaldehyde has been studied computationally using B3LYP/6-31G(d) [1] theoretical method. The energy profiles indicate that this IMDC reaction favours kinetically the formation of the fused-endo, as observed experimentally. The solvent has no influence on the mechanism and selectivity, but it increases slightly the activation energy and decreases the exothermic character of this IMDC reaction. The analysis through electron localisation function (ELF) of the favourable fused-endo pathway shows that the formation of the C–O and C–C new bonds occurred via a non-concerted synchronous one-step mechanism. The analysis of noncovalent interaction using Non-covalent interaction (NCI) and QTAIM analyses of the structure of the fused-endo transition state indicates that the hydrogen-bond formed at this approach is the origin for the favouring of the fused-endo pathway.



Scheme: IMDC reaction for the synthesis of tetracyclic isoxazolidines from 8-(allyloxy)-5-chloroquinoline-7-carbaldehyde [2]

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Disentangling the Entropic Changes during Pyridine Adsorption on Au (111) by Deployment of Microcalorimetry

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Up to now, the entropy change(s) during pyridine adsorption on Au (111) have not been thoroughly disentangled. However, this system has been studied in great depth by electrochemical, microscopic and spectroscopic techniques; and has been considered as a model system for molecular switches, as it shows a potential-dependent, structural reorientation upon the adsorption [1-3].

To get direct information on the entropy change upon pyridine adsorption, we measured the Peltier heat for different concentrations of pyridine in aqueous solutions over Au(111), scanning the whole adsorption region, by using our home-build calorimeter [4].

Negative reaction entropy was found for the anodic processes, with a strong decrease of ca. -170 J/(mol*K) observed at about the same potential at which the reorientation occurs. This entropy reduction is in accordance with adsorption of weakly solvated neutral molecules from solution; the entropy from the ion transport, the double-layer polarization and/or solvent reorientation may also contribute.

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Diels Alder cycloaddition reaction between butyl vinyl ether and 3-aroylpyrrolo[1,2-a]quinoxaline-1,2,4(5h)-trione: medt study

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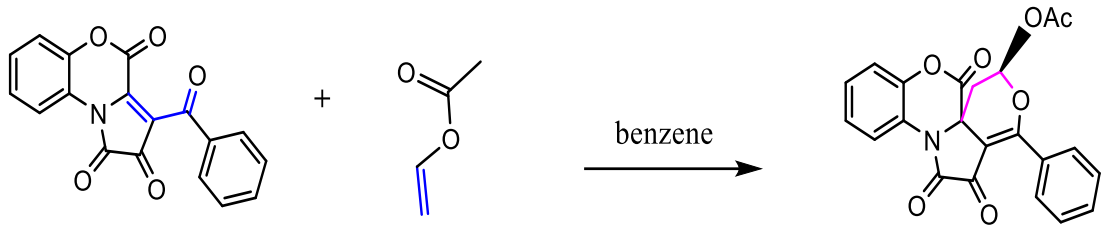
Molecular electron density theory explains the regioselectivity and stereoselectivity between 3-aroylpyrrolo[1,2-α]quinoxaline-1,2,4(5H)-trione and butyl vinyl ether[4 +2] Regioselectivity of cycloaddition reactions. The regioselective mechanisms of these reactions are investigated by evaluating the surface potential calculated for the cycloaddition process and the DFT density-based reactivity index. These methods have been successfully applied to predict the preferred regioisomers for different process alternatives. Reactions are monitored by performing transition state optimizations, calculating intrinsic reaction coordinates and activation energies. The observed regioselectivity was rationalized using DFT-based reactivity descriptors such as the Parr function. The results were compared with experimental data to find good agreement.



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Comparison of Structural and Energetic Properties Between Trioxolane and Tetraoxane Analogues with Established Antiparasitic Activity

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The rise and spread of *Plasmodium falciparum* resistance to artemisinin-based combination therapy in Southeast Asia stimulated the search for novel plasmodial "fast killers," the endoperoxide chemotype offering alternative solutions to artemisinin and its derivatives.[1] Among the synthetic 1,2,4-trioxolanes and 1,2,4,5-tetraoxanes investigated, the candidates **OZ439** (artefenomel)[2] and **E209**[3] proved very promising, showing antimalarial activity similar to or higher than ARTs (Figure 1).

1,2,4-trioxolane **(1)** and 1,2,4,5-tetraoxane **(2)** are the representative building blocks used in the synthesis of the antimalarial candidates **OZ439** and **E209** (Figure 1). Since compounds **1** and **2** differ only in their peroxide pharmacophoric moiety, a detailed analysis of their structure, precisely the relative effect of a trioxolane or a tetraoxane ring on the overall molecule, may aid in a better understanding of the relative reactivity and activity of these classes of endoperoxides.

Over the last few years, tools based on Hirshfeld surfaces have become increasingly popular for molecular crystal structure investigation. In this approach, molecules are viewed as ‘‘organic wholes," so fundamentally altering the discussion of intermolecular interactions by an unbiased identification of all close contacts.[4] Hence, the structures of compounds **1** and **2** were investigated in the condensed phase using X-ray crystallography. A deep analysis of the intermolecular contacts existing in the crystal structure of both compounds was then undertaken by performing a Hirshfeld surface analysis, followed by a calculation of the pairwise interaction energies.

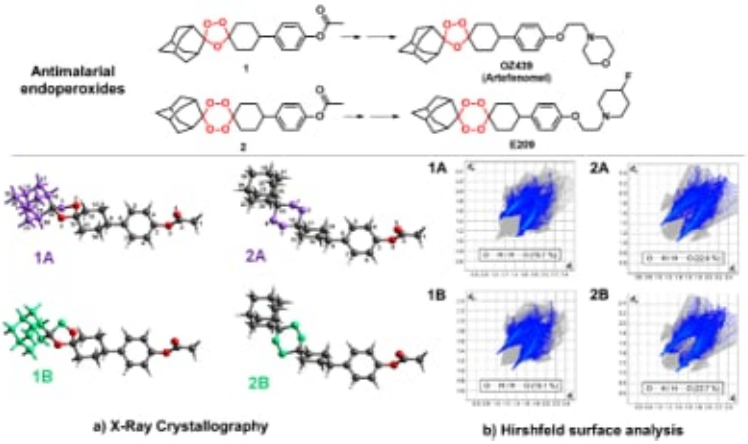

Figure 1. Antimalarial endoperoxides **1**, **2**, **OZ439**, and **E209**. a) Conformations **A** and **B** are adopted by compounds **1** and **2** in the crystal structure. Disordered fragments are highlighted as violet in conformation **A** and green in conformation **B**. b). A section of fingerprint plots calculated for the conformations **A** and **B** of compounds **1** and **2**.

Acknowledgments: We thank Fundação para a Ciência e a Tecnologia (FCT) for projects UID/MULTI/04326/2021 (CCMAR), UI0313B/QUI/2020 (CQC), UIDB/04564/2020 and UIDP/04564/2020. PSMA thanks FCT for Grants SFRH/BD/130407/2017 and COVID/BD/152392/2022.

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Optimization of solid-phase microextraction for polar aqueous extracts regarding GC-MS screening analyses of medical devices

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Serious mistakes in quality control of medical devices often leads to painful experiences in patients. Inferior breast implants or hip prostheses with residues from production, endangered the health of thousands of patients. To protect patients and healthcare workers from any unwanted substance, it is important to know which substances and in which concentration they are released from medical devices. Aqueous extracts in particular play an important role here. The target must be to quantify any released substance to assess the biocompatibility of medical devices according to regulatory standard specifications.

The regulatory requirements of analytical methods are defined in ISO 10993-18. However, there is a gap between the standard ISO 10993-18 and the technical possibilities in terms of sensitivity. To comply with the standards, an analysis of aqueous extracts is required. This in turn requires analytical methods with a very high sensitivity, which can only be achieved by mass spectrometry. Therefore, there is an urgent need in reliable mass spectrometric methods with a suitable sample preparation. The solid-phase microextraction (SPME) is a powerful technique to fulfill this need. A reference standard with 21 common substances from the packaging industry used as additives were utilized for this study. The poster accurately describes the methodological approach to achieve high extraction yields. Important factors such as fiber coating, extraction and desorption conditions as well as stirring speed were optimized. Furthermore, influences of matrix effects on extraction yields, e.g., pH value or ethanol in the aqueous extracts as well as varying salt concentrations were investigated. Subsequently, the enriched analytes were measured in a so-called screening method using gas chromatography coupled to mass spectrometry (GC-MS) to demonstrate the increased measurement sensitivity.

We successfully optimized a method for the qualification and quantification of 21 additives and can recommend to the standards committee of the ISO 10993-18 to implement this analyte enrichment technique. The high enrichment rates of analytes on fiber and good linearity proves that SPME is a very sensitive and robust method. Thus, we comply the normative required sensitivity of 0.1 µg/mL. One aspect of our future work will be to convert the manual SPME method to a fully automated one. This would significantly advance the analysis of aqueous extracts in medical device screening analyses.

Keywords: Solid-phase microextraction (SPME), Gas chromatography-mass-spectrometry (GC-MS), reference standard, aqueous extracts, medical devices

Graph-Based Tools to Handle Chemical Reaction Networks

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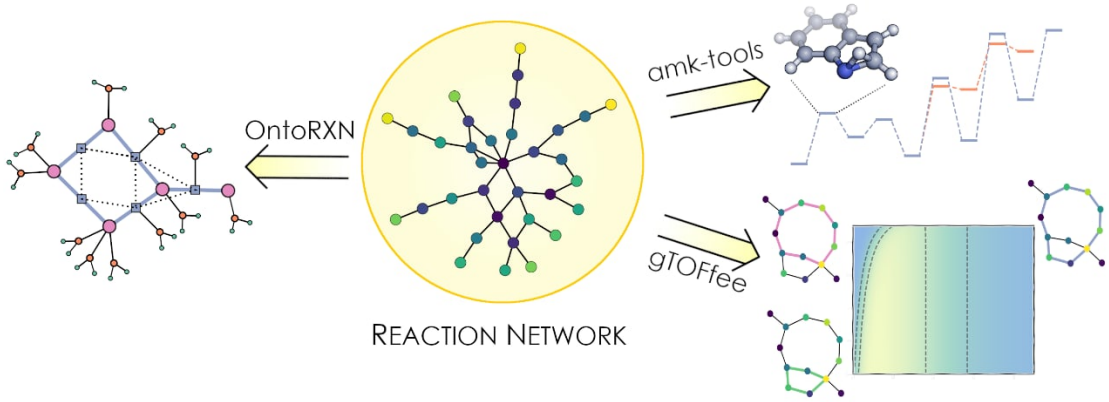
The computational characterization of chemical reactivity and catalysis can produce very detailed reaction mechanisms, whose management and interpretation might get far from trivial. Due to the continuous increase in raw computational power and the simultaneous development of novel theoretical frameworks and automation approaches, the attained level of detail and its consequent complexity is expected to keep on growing. In this context, chemical reaction networks (CRNs) allow to readily depict this kind of complex and highly intertwined mechanisms in a scalable and straightforward manner. Moreover, the immediate connection between chemical networks and mathematical graphs enables the application of sophisticated graph manipulation techniques to chemical information, opening new avenues to process complex data and extract scientifically sound knowledge from it.

In this communication, we will present some of the tools developed by our group to tackle different aspects of reactivity and catalysis under this network-based paradigm: amk-tools [1], gTOFfee [2] and OntoRXN [3]. The first, amk-tools, provides a framework to parse y the likely large CRNs generated by the automated mechanism discovery program AutoMeKin [4] and visualize them interactively, facilitating the chemical interpretation of the obtained results. The second, gTOFfee, is a generalization of the energy span model that can be applied to catalytic cycles of arbitrary complexity, employing concepts of graph theory to detect the unique reactive mechanisms encoded in the input network and compute the corresponding turnover frequencies. Finally, OntoRXN is an ontology that allows to express reaction networks in a semantic manner, transforming the "plain" graphs to highly tagged knowledge graphs (KGs). These KGs collect the complete information about the system in a single entity, from the connectivity of the CRN to the properties associated to the individual calculations in the dataset, and can be directly built from the information stored in the ioChem-BD [5] database. The enforced structure of knowledge graphs allows to readily extract complex information from the dataset using simple queries, streamlining not only the direct analysis of data but also its integration in more complex workflows.



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NIR spectroscopy as a tool to determine the concentration of diesel fuel improvers simultaneously

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Growing concerns about engine emissions over the last decade call for stricter global fuel regulations, in particular significant reduction of sulfur, nitrogen oxides (NOx), carbon monoxides (CO), total hydrocarbons (THC) or particulate matter (PM). These concerns force us to use and improve greener fuels that are more environmentally friendly. However, the reduction of individual substances has a negative effect on the properties of the fuel and its performance. Therefore, fuel additivation in form of improvers is required to maintain high quality fuel properties.

Near-infrared (NIR) spectroscopy in a combination with multivariate statistical analysis was used as a promising tool to determine the concentration of three types of improvers in a diesel matrix simultaneously. Using NIR models, the concentrations ($mg.kg^{-1}$) of additives that improve the cetane number of diesel, the cold-flow properties and the conductivity-lubricating properties of diesel were determined. The root mean square error of calibration (RMSEC), root mean square error of cross-validation (RMSECV), number of factors and correlation coeffiecient was applied as a basic chemometric diagnostic tools to optimize the NIR model predictions. The calibration samples were equally distributed along the line of the NIR models, in addition, a significant correlation close to 1 was observed between the reference values and the predicted values by the NIR model.

These results highlight the potential of NIR spectroscopy as an analytical technique that could provide great accuracy for the simultaneous determination of three types of improvers in the diesel matrix. Moreover, this non-destructive and inexpensive tool could be very promising in refinery/industrial applications, especially for online analysis, which could serve as quality control in production, prevent overdoses with diesel improvers and save not only money but also time.

This work is a result of the project which was carried out within the financial support of the Ministry of Industry and Trade of the Czech Republic with institutional support for long-term conceptual development of research organization. The result was achieved using the infrastructure included in the project Efficient Use of Energy Resources Using Catalytic Processes (LM2018119) which has been financially supported by MEYS within the targeted support of large infrastructures.

Inherent Chirality at Work for Applications in Chiral Electrochemistry, Chiroptics and Spintronics

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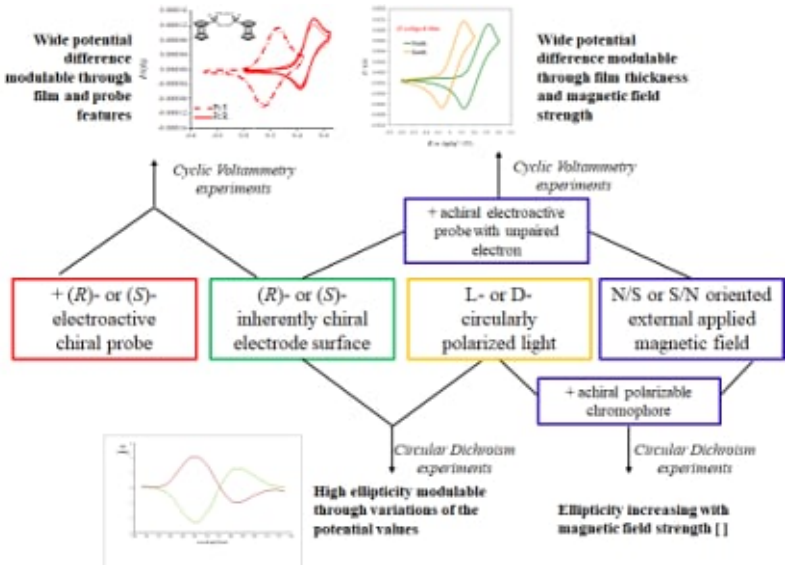
Chiral electroanalysis could be regarded as the highest recognition degree in electrochemical sensing, implying the ability to discriminate between specular images of a given electroactive molecule, in terms of large peak potential differences.

The results presented here are aimed to deeply investigate the innovative field of chiral electrochemistry and electroanalysis, performed at electrochemical interphases with implementation of (inherently) chiral selectors (*i.e.* with the stereogenic element responsible for chirality coinciding with the functional group responsible for the material specific properties) [1,2]. In particular, voltammetric experiments were performed at chiral electrochemical interphases with implementation of inherently chiral or chiral selectors, according to two strategies: *i*) use of electrode surfaces modified with electrodeposited heterocycle-based inherently chiral oligomer films; *ii*) use of enantiopure chiral media of high intrinsic order [3].



A particular focus was on the potentialities of the inherently chiral strategy, not only in the chiral voltammetry field, but also in circular dichroism and magnetoelectrochemistry ones [4], highlighting fascinating symmetries between electronic absorption spectroscopy, dealing with intramolecular electron transitions, voltammetry/potentiodynamic electrochemistry and CV experiments performed under applied magnetic field [5].

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Electronic spectroscopy combined and quantum chemical calculations as a new old approach to assess the oxidation of lipids

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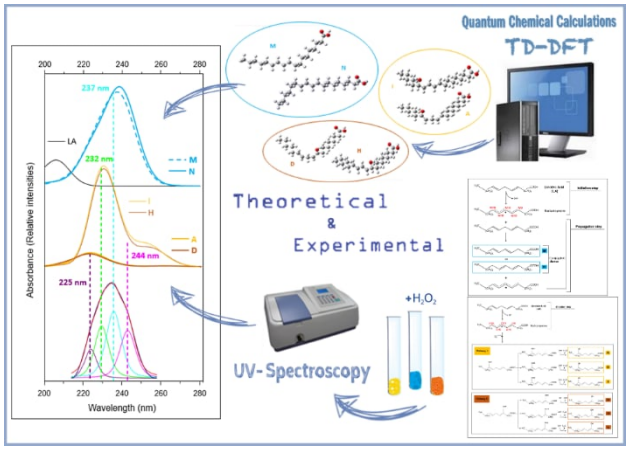
In this study [1], the goal was to set up a UV-based method to assess the peroxidation products of soy lecithin liposomes. The phospholipids are the building blocks of biological membranes in both eukaryotic and prokaryotic cells as well as delivery systems for drugs, nucleic acids and nutraceuticals. Because of the presence of unsaturated fatty acids, lipid membranes are prone to peroxidation reactions (oxidative stress), leading to lipid instability and/or damage. Understanding such processes has a strong impact on physiopathological events as the products resulting from lipid peroxidation are usually associated with cellular aging, mutagenesis and carcinogenesis, among the most important ones. In addition, as lipid membranes are also used as drug delivery systems, peroxidation reactions usually lead to membrane leakage with subsequent degradation of their content, leading to a decrease in the pharmacological action of the encapsulated drugs.

This work employed an experimental-theoretical approach, including computational facilities and deep spectral analysis (*e.g*. peak-fitting) to take advantage of the rich information contained in the experimental UV-spectra. UV spectroscopy is a quick, easy, achievable, and cost-effective technique, available nowadays in most laboratories. The incorporation of the tools employed in this work contributes to revisiting UV-spectroscopy as an invaluable tool to monitor, interpret and quantify lipid peroxidation processes, with applications in different fields of knowledge, including both fundamental and applied sciences. In order to achieve the aim, the UV spectra of liposomes exposed to oxidative stress induced by H_2O_2 were measured and the TD-DFT calculations were used to optimize the molecular structures and assess the UV spectra of all possible oxidation products (minima in the potential energy surface). Based on the quantum chemical calculations, the experimental UV spectra were deconvolved to unravel the molecular mechanisms behind the oxidation of lipids. On the basis of the agreement between the calculated UV spectra (TD-DFT) and observed results, assignments were proposed. The unified experimental and theoretical comparative analysis of UV spectra provided a better understanding of the lipid peroxidation processes.



This work was supported by the Argentinean Agency for the Scientific and Technological Promotion (ANPCyT)(PICT(2016) start-up/4808; PICT(2017)/1344; PICT(2019)/0008). M.M.U., E.E.T. and A.G-Z. are members of the research career from CONICET. J.M.F. is a doctoral fellow from ANPCyT. A.B. acknowledges the financial support of FCT, Portugal, under Strategic Project (UIDB/00102/2020).

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Design and Deployment of Data Science Frameworks for Machine Learning Algorithms to Predict Molar Entropies

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Chemical property prediction studies have been revamped with the recent development of Artificial Intelligence and Data Science into industrial chemistry methodologies [1]. This pivotal step in the study of novel chemical processes gained a new significance with the low-cost generation of descriptors for the green improvement of important industrial routes. But despite promising results, recent studies show how good predictions depend on a trade-off with narrow chemical databases on which the Machine Learning (ML) algorithms can work with, yielding only good results to limited families of molecules [2,3]. The great challenge for Computational Chemistry is to establish new frameworks on which algorithmic can be further tuned and trained using existing published results, capable of making broad spectrum property predictions, avoiding the bias-variation trade-off.

In this communication, we report the development of a ML algorithm based on a Data Science framework (Figure 1) for the prediction of standard molar entropy ($S°$) of a wide range of organic and inorganic molecules. We developed a new database comprised with data from the literature, depicting more than 1000 entries across 14 different families of molecules in which we used to train and test our model. The framework for the generation of the chemical descriptors using the open-source RdKit library is also presented, amassing a total of 107310 input data points. For the property prediction, we used an ML-supervised Random Forest Regression algorithm which was subject to validation studies: first by evaluating overall single prediction of standard molar entropy error and also by calculation error of reaction entropies ($\Delta S_r°$) for several isodesmic reactions. The model yielded good results, displaying a maximum prediction error of 1.11 mol^{-1} K^{-1} and an error bellow 1% for almost all isodesmic reactions tested. This pilot study further stresses the usefulness of Data Science for chemical property prediction, by presenting a sensitive and replicable model framework which can be expanded towards the prediction of thermodynamic properties.

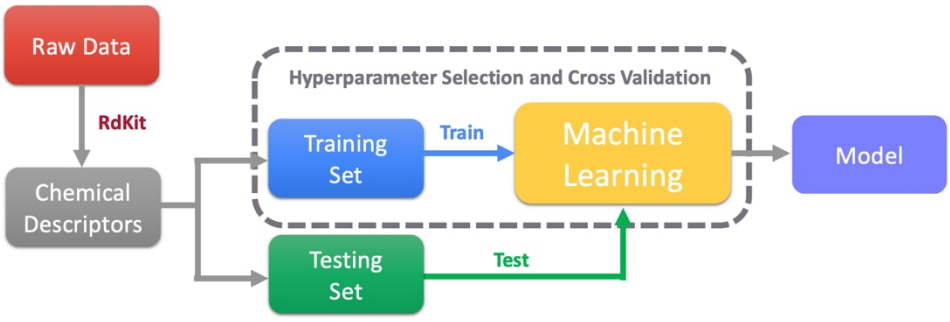

Figure 1. Model framework for property prediction using supervised ML algorithms.

The authors thank Fundação para a Ciência e Tecnologia (FCT, Portugal) for the support of this research [Program fund UIDB/50006/2020 and PTDC/QUI-QIN/30649/2017 awarded to REQUIMTE- LAQV]; José Ferraz-Caetano thanks FCT & MIT Portugal for the support of the PhD Grant (Ref: SFRH/BD/151159/2021).

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Determining the adulteration of paprika powders with Sudan I dye by IR and multivariate classification techniques

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Sweet powder paprika is globally used as a spice for giving taste and colour to meals and it is also very common spice in Serbian cuisine. It is among spices which are often subjected to adulteration mainly using Sudan dyes which are considered suitable for that purpose due to their low-cost and wide availability. Additionally, they are stable compounds which make the appearance of paprika better for longer times since one of the problems of paprika is the degradation of its colour over time [1]. In this study twelve different branded paprika powders were collected from the local market in Serbia. Samples were prepared for analysis using IR spectroscopy with the aim to analyse adulteration of this spice with Sudan I dye. According to obtanied IR data neither of analysed samples were adulterated with Sudan I dye so for further analysis mixtures of this samples with Sudan I dye were prepared and subjected to multivariate analysis. Differente multivariate classifications models were created for discrimination based on adulterant and powder paprika content in sample mixtures. Principal component analysis (PCA), partial least-squares - discriminant analysis (PLS-DA) and PCA-linear discriminant analysis (LDA) were used in the different spectral ranges. All methods were able to differentiate adulterated from non-adulterated samples with models obtained with PLS-DA being the best.

IR spectroscopy results in combination with multivariate analysis have showed that it is possible to discriminate pure paprika powder samples from paprika powder samples adulterated with Sudan I dye.

Acknowledgment

Authors thank the Ministry of Education, Science and Technological Development of the Republic of Serbia for the financial support to the research through institutional funding (Contract number 451-03-68/2022-14/200017).

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Thermally Activated Delayed Fluorescence dyes as electrochemiluminescence emitters with coreactants

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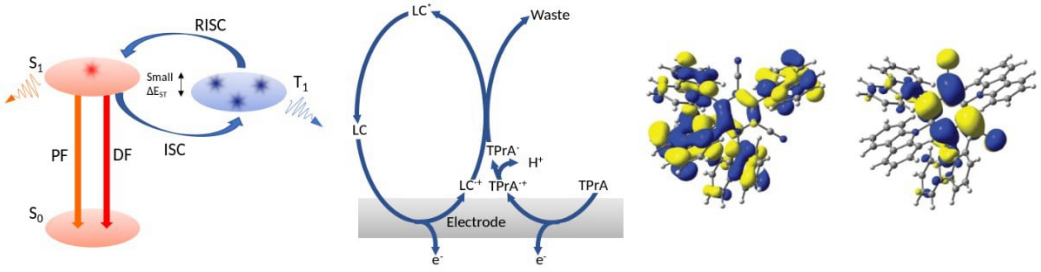
Electrochemiluminescence (ECL) is a process that uses an applied electrical bias to generate reactive species at an electrode surface that undergo subsequent electron-transfer reactions to generate luminescent species [1,2] . This process could be used to amplify signals of analytes, making this technique the most powerful tool for biomedical applications.

However, due to spin statistics only phosphorescent emitters such as metal complexes (e.g. Ru(II) [3] and Ir(III) [4] complexes) could be used efficiently thanks to the spin-orbit coupling which favors intersystem crossing. Recently a new "metal-free" strategy was proposed to harvest triplet excitons to enhance Internal Quantum Efficiencies (IQEs): the Thermally Activated Delayed Fluorescence (TADF) [5], which is a phenomenon shown by molecules that possess a donor-acceptor structure with a tilt angle close to 90° between the two moieties. This geometry gives rise to a spatial separation of HOMO and LUMO, which follows a small energy gap between S_1 and T_1 that makes possible reverse intersystem crossing and enhanced IQEs. The advantages shown by TADF molecules make these molecules intriguing not only for OLED applications[5,6], but also for solution-state ECL [7,8].

However, almost all examples about ECL of TADF molecules are performed in the so-called "annihilation way", where compounds are subsequently oxidized and reduced, while, at the best of our knowledge, there are no examples of electrochemiluminescence of TADF molecules performed with coreactants.

Herein we present the synthesis, and the photophysical, electrochemical and ECL characterization of some already-known and novel TADF molecules.



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The influence of the nitrogen position on the spectroscopic properties of regioisomers based on imidazo[4,5-*b*]pyridine

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Nitrogen-containing heterocycles are, besides their well-known biological features, recognized as an interesting class of organic fluorescent sensors present in a wide range of biological, environmental and chemical processes. Owing to their excellent spectroscopic properties, as well as pronounced and diverse spectral responses, such derivatives offer promising applications in optoelectronics as optical lasers, fluorescence probes, organic luminophores or fluorescent dyes.[1]

This work presents the synthesis and spectroscopic characterization of regioisomers based on imidazo[4,5-*b*]pyridine. Potential application as pH sensors was explored. Due to condensation of 2-cyanomethylimidazo[4,5-*b*]pyridine with 2-chlorobenzoyl chloride, acyclic precursor was prepared. Chloro-substituted tetracyclic precursors were prepared in 2 step procedure including termic cyclization. Amino substituted regioisomers were prepared by uncatalyzed microwave assisted amination.[2]

Structures of newly prepared compounds were confirmed by means of ^{1}H i ^{13}C NMR, as well as MS spectrometry. Structure of regioisomers was determined by 2D NMR spectroscopy. Spectroscopic characterization of regioisomers was performed by using UV/Vis and fluorimetric spectroscopy in 11 organic solvents of varying polarities. Studied regioisomers showed interesting spectroscopic characteristics which are significantly dependant on the used solvent and are different for each regioisomer. pH spectroscopic titrations were performed in order to determine possible application as pH sensors in solutions followed by determination of pK_a values experimentally as well as by computational approaches.

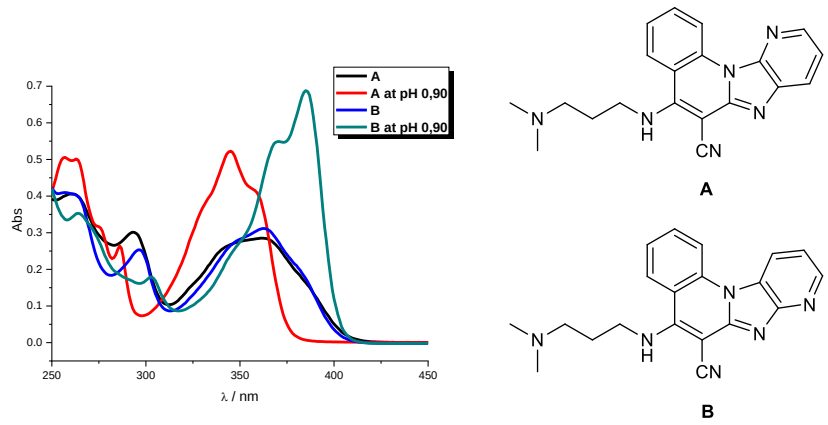

Figure 1. Structures of regioisomers and absorption spectra in acidic medium

Acknowledgments: This work was funded by the Croatian Science Foundation (projects IP-2018-01-4379 and IP-2020-02-8090).

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Novel Types of Electrodes for Vanadium Redox Flow Batteries

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New energy storage devices are needed to balance the fluctuations of renewable energy sources. The Vanadium Redox Flow Battery (VRFB) is a promising candidate as a large-scale energy storage device but still needs to overcome significant lifetime and efficiency challenges. Polarization and pumping losses due to high flow-through resistance of the electrolyte in the electrode account for a large part of the efficiency losses [1,2]. Thus, the electrodes must be optimized concerning the catalytic activity and the flow properties to enhance the battery's efficiency.

This study investigates the influence of the 3D electrode structure of commercial carbon felts, knitted fabric, and bamboo charcoal materials on the flow-through behavior. Therefore, we evaluated these materials using electrochemical techniques, including electrochemical impedance spectroscopy coupled with the distribution of relaxation times analysis [3] and cyclic voltammetry, dynamic vapor sorption, and different visualization methods.



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Molecular symmetry consideration of the vibrational Infrared and RAMAN spectra in the study of polyvinylidene fluoride alkaline reaction mechanism

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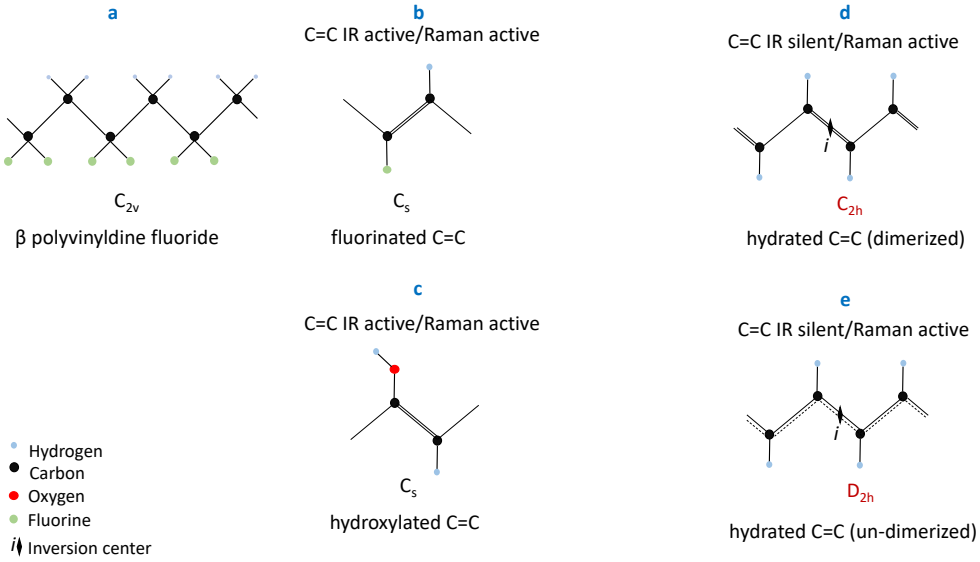
The reaction of polyvinylidene fluoride with a strong base is known to yield a combination of C=C sequences and oxygen functionalities [1][2]. The silence of the double bond signal on FTIR necessitates a focus on symmetry basics in analyzing the spectra which suggests that the rule of mutual exclusion is in effect, whereby all IR active vibrational modes are Raman inactive and vice versa. The consideration of the symmetrical properties leads to a clear structure determination and implies that there is an additional hydrogenation step to the reaction mechanism previously reported. Sodium isopropylalcoholate catalyzes the C_{sp2}—F bond cleavage in a transfer hydrogenation step and results in the formation of the C_{sp2}—H bond, a mechanism supported by the presence of acetone [3].



Point group (a) β-PVDF chain, point groups, and relative C=C IR/Raman activity for a unit cell of (b) fluorine substituted conjugate structure, (c) hydroxyl substituted conjugate structure, (d) dimerized model of the hydrated conjugate structure, and (e) un-dimerized model of the hydrated conjugate structure

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Spectroscopy as a useful tool for identifying changes over time in postmortem liver samples

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The study of postmortem changes in biological tissues is one of the most problematic tasks of forensic analysis. It aims, in particular, at determining the time of committing a crime or the death of the victim, which is the key task of an autopsy [1]. A particular challenge is the large number of internal and external factors influencing postmortem processes, such as the circumstances of death, body position, environmental conditions, and temperature. The conduct of an animal experiment allows complete control of factors relevant to postmortem lesions and is easier to perform than an experiment in human tissues [2]. Today, non-destructive methods are increasingly being used in forensics, including vibrational spectroscopy techniques such as infrared spectroscopy. This technique, in addition to the non-destructive nature of the tests, enables quick and simple measurement of the sample [3].

The study aimed to analyze postmortem changes that occur in rabbit liver tissues, differing in the time of collection after animal sacrifice and the temperature of body storage, using Fourier transform infrared spectroscopy (FTIR). Two FTIR techniques were used: attenuated total reflectance (ATR) and transmission imaging.

Liver samples from animal experiments with New Zealand white rabbits were analyzed. The subjects of the study were samples taken immediately after sacrificing the animals and 12 and 24 hours after storing the corpse at 4 and 20 ° C. For ATR-FTIR measurements, liver samples were homogenized, dried on glass slides, scraped with a scalpel, and transferred to an ATR crystal. For the imaging procedure, tissues, after paraffin fixation, were cut into 7 µm thick slices on a microtome. After the removal of paraffin, the tissues were examined on CaF_2 slides. For the spectra obtained, a chemometric analysis was performed using hierarchical cluster analysis (HCA) and principal component analysis (PCA) methods.

Both FTIR techniques used allowed observations of changes in the intensity and position of the bands, mainly attributed to proteins (amides I and II), but also to sugars and amino acids, which may indicate postmortem changes in the structure and content of these compounds. The imaging results provided additional information on the distribution of components in liver samples and distinguished three classes differing in the proportions of the protein part and the part derived from carbohydrates and nucleic acids as presented in Fig.1. The differences observed for samples taken 12 and 24 h after storage at different temperatures indicate a high potential for the use of FTIR spectroscopy to identify the time of death for cadavers revealed 12/24 h after death.

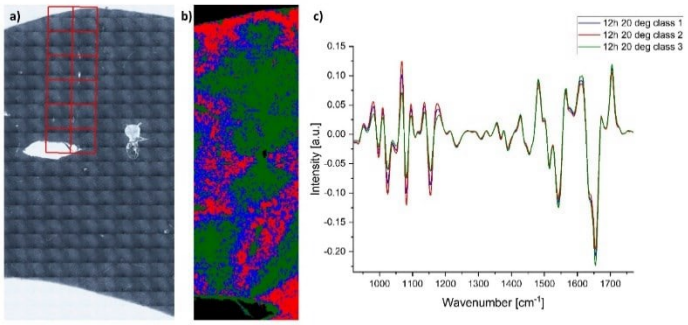

Fig.1. FTIR imaging results obtained for the liver sample stored for 12 hours at 4 ° C a) visible image from the microscope at 15x magnification, b) image obtained as a result of HCA analysis, c) average class spectra from HCA analysis in the range of 920-1770 cm^{-1}

The authors thank the Ministry of Science and Higher Education, National Science Center, Poland, for financial support through the Opus 19 project (R. Wietecha-Posłuszny, A. Wójtowicz, M. Reciak, no. 2020/37/B/ST4/01364).

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Electrochemical *in situ* Raman spectroscopy for the evaluation of furfural/metal interactions

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Due to environmental issues the global society is facing, organic electrosynthesis has received increasing attention as an important research area. It provides a tool to store excess electrical energy from regenerative sources into chemical bonds. The produced compounds can then be utilized as sustainable components in the chemical industry, e.g., in sustainable aviation fuel. Electrochemical processes are often considered greener alternatives to their thermal catalytic counterparts.[1] An example of an electrochemical reaction is the electrochemical hydrogenation of furfural. Electrochemical hydrogenation reactions of furfural have repeatedly been the subject of research efforts. They can produce considerable amounts of furfuryl alcohol and 2-methylfuran on, e.g., a copper electrode in acidic media (Figure 1(A)).[2]

Spectroelectrochemical experiments (Figure 1 (B)) can explain the molecular interactions of the molecules involved in electrochemical reactions.[3] This work focuses on *in situ* Raman spectroscopy and provides insight into processes on the molecular scale of the hydrogenation reaction of furfural. *In situ* Raman spectroscopy enables the investigator to evaluate surface adsorption processes, potential dependent variations, and intermolecular interactions. For a thorough understanding of the influences on furfural/metal surface interactions, the experimental conditions are varied between different electrolyte media and electrode materials.

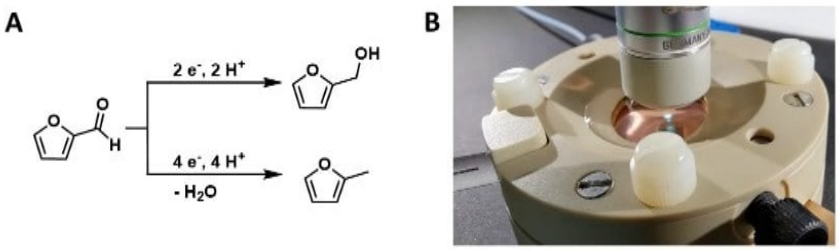

Figure 1: (A) 2-Methylfuran and furfuryl alcohol as an electrochemical hydrogenation product of furfural. (B) Electrochemical *in situ* Raman spectroscopic experiment setup.

Thanks to the funding by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Germany's Excellence Strategy – EXC 2163-1 – Sustainable and Energy Efficient Aviation – Project ID 390881007.

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The extraction procedures for date-rape drugs analysis based on solid-phase microextraction and dried blood spots coupled with microwave-assisted extraction

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Drug-facilitated Sexual Assault (DFSA) has become the main topic of research conducted in the fields of forensic toxicology in recent years. The substances used by the offenders of these crimes are commonly known as Date-rape Drugs (DRD). These substances cause memory loss, sedation, and muscle relaxation in the victim. The number of cases of using stimulants of the central nervous system for intoxication rape victims has also increased recently. The stimulant substances cause euphoria, increasing self-confidence, and libido – which made them perfect DRD substances. The most significant feature of DRD is the quick metabolized process, which makes it impossible to detect them in the human body after a long time. Due to this, the most challenge for analytical chemists is developing sensitive methods for detecting DRD and procedures which enable easy and quick security of the biological samples [1,2].

Effective extraction methods such as microwave-assisted extraction (MAE) or solid-phase microextraction (SPME) coupled with separation methods (e.g. liquid chromatography coupled with the mass detector, LC-MS) seem to be useful tools in the analysis of traces amount of DRD in biological samples. This research presents the use of two analytical methods which seemed to be perfect for use in the purpose of forensic toxicology in DRD determination at low concentrations in human blood samples. The first method, based on Dried Blood Spots (DBS) technique and MAE extraction, was fully optimized and validated for the determination of xenobiotics such as ketamine, flunitrazepam, diazepam, and cocaine [3].

In the process of optimization DBS/MAE/LC-MS method, the parameters of the extraction process were selected. The best results were achieved for extraction with ethyl acetate with a buffer of pH = 9, performed at a temperature of 50°C for 15 min. During the validation, selected parameters were determined: the limits of detection and quantification, inter- and intra-day precision, recovery, and matrix effect. The validation results indicate the possibility of using the developed method in the process of securing and collecting blood samples as well as its qualitative and quantitative analysis. The advantages of the developed method include the small amount of sample taken for analysis, as well as its sensitivity, which enables the detection of the tested substances at the level of even a few ng/mL of whole blood. Based on the validation results of the DBS/MAE/LC-MS method and SPME/LC-MS method it could be assumed that these methods can be used compatibly as needed e.g. depending on the available amount of sample and the predicted concentration of xenobiotic in the blood sample.

Acknowledgments

The work was the result of the research project No. 2019/35/O/ST4/00978 (R. Wietecha-Posłuszny, Preludium Bis 1) financed by the Ministry of Science and Higher Education, National Science Centre, Poland.

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Detection of homemade peroxide-based explosives and their main precursors in water based on spectroscopic methods

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The detection of explosives is of paramount importance in the fields of homeland security and military activities. The production and use of homemade explosives (especially organic peroxides: TATP, MEKP, HMTD) is one of the major issues in the fight against terrorism in Europe. During the synthesis of these explosives in clandestine laboratories, significant quantities of explosives or their precursors can be discharged into wastewater systems. Some of these precursors (especially acetone and hydrogen peroxide) are used for other applications (solvents, bleaching agents, medical and industrial products) and are therefore not specific to the manufacture of explosives. However, they can become tracers of the explosives manufacturing site if an unusual temporal variation can be detected by on-line monitoring of wastewater.

The objective of the study is to develop an alert system based on an on-line analyser (MultiPumping Flow System) for the early detection of traces of peroxide-based explosives and their precursors in public wastewater networks. The on-line analyzer will integrate the whole analytical procedure but also the remote transmission of results and the triggering of alerts according to the type of event detected (level 1 alert for the detection of an unusually high concentration of household chemicals potentially used for the production of homemade explosives, level 2 maximum alert for the detection of traces of explosives or precursors that are not usually found as household chemicals).

Precursor detection is based on derivatization reactions:
- detection of acetone and butanone by Claisen-Schmidt reaction on an aromatic aldehyde;
- hexamine detection by Hantzch reaction [1] ;
- detection of hydrogen peroxide by reaction with titanium oxalate [2].

The detection of precursors will be completed by the detection of explosive residues (TATP, MEKP, HMTD) by photochemical degradation of organic peroxides to hydrogen peroxide [3] which will then be detected following the derivation method cited above. Photodegradation by UV radiation at 254 nm of organic peroxides to hydrogen peroxide must be rapid (less than one minute) to limit the photodegradation of the hydrogen peroxide formed [4].

This poster will discuss the existing analytical methods for the detection of target molecules and present the first results on the detection of H_2O_2 in wastewater.

This work is funded by the French Defense Innovation Agency (AID #2021451) and Aix-Marseille University.

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Thioacetal-Flipper for Membrane Tension Imaging

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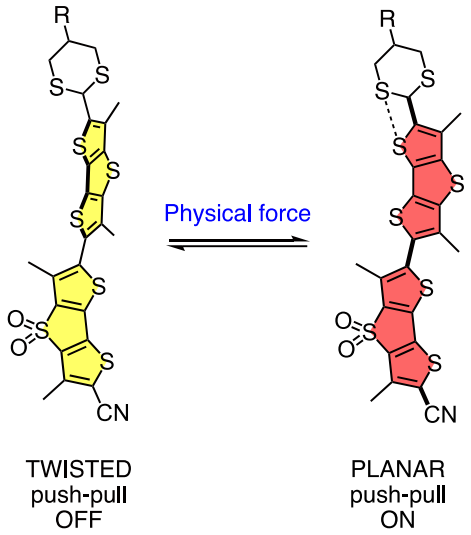
Membrane tension plays a vital role in biological membranes. No matter in cells or elsewhere, physical forces are not easy to be visualized directly but their consequences. However, conventional methods, including micropipette aspiration, optical tweezer, and atomic force microscopy exhibit many drawbacks for membrane tension imaging, such as poor time resolution, low efficiency, and technical challenge. To overcome these problems, our group developed a series of twisted push-pull mechanophores that respond to membrane tension by planarization in the ground state [1]. Such mechanophores are referred to as "fluorescent flippers", which are red-shifted to longer excitation wavelength and fluorescence lifetime in solid-ordered (S_o) and liquid-ordered (L_o) compared to liquid-disordered (L_d) [2][3]. In this paper, we continue to develop a new generation flipper by introducing thioacetal with different R groups into flippers. These flippers have easier synthesis routes and better yields, which is beneficial to optimizing the way how to modify the structure of flippers. In addition, such thioacetal flippers can be ready for membrane tension imaging in biology and open a wide chemical space.



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SPECTROSCOPIC DETECTION OF BIOSIGNATURES IN NATURAL ICE SAMPLES AS A PROXY OF ICY MOONS

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The icy moons of the solar system that have a sub-surface ocean, such as Europa and Enceladus, are the targets of future space missions that search for potential extraterrestrial life forms. The interest is because these locations contain the basic requirements for habitability, i.e., the conditions for life to emerge: presence of liquid water, essential chemical elements (carbon, hydrogen, nitrogen, oxygen, phosphorus, and sulfur – CHNOPS) and a source of energy (tidal heat, solar radiation, radioactive decay, or geochemical) [1] [2] [3].

To understand how biosignatures (i.e., any element, molecule or feature that may be used as evidence for past or present life) can be detected in these icy moons, scientists use planetary field analogues, which are locations on Earth that mimics one or more characteristics of an extra-terrestrial environment, including physical, geological, and/or chemical characteristics [4]. We have recently sampled and performed analysis of the Canadian sub-Arctic region, which is considered to be a planetary field analogue of the icy moons. The compositional analysis was performed with UV-Vis absorption and fluorescence spectroscopies, complementing with IR spectroscopy, and compared with standard solutions of biosignatures (aromatic amino acids, pigments and humic acid) analyzed prior to the field work. A kinetic essay points to a well preservation of the analytes in the moments after the sampling. Current results point to the presence of fulvic and humic acids but further work will be done.

This work shows the possibility of spectrochemical techniques to be implemented on future space missions that will perform *in situ* measurements on icy moons where microorganisms may exist.

The team acknowledges funding from the MIT Portugal Program for project BIOMOON (MIT-EXPL/SOE/0058/2019). Centro de Química Estrutural acknowledges the financial support of FCT- Fundação para a Ciência e Tecnologia (UIDB/00100/2020 and UIDP/00100/2020). Institute of Molecular Sciences acknowledges the financial support of FCT-Fundação para a Ciência e Tecnologia (LA/P/0056/2020). The authors also acknowledge the institutional and logistical support from the Centre d´études nordiques, Université Laval, Canada,
This research is framed within the College on Polar and Extreme Environments (Polar2E) of the University of Lisbon. ZM acknowledges funding from FEDER - Fundo Europeu de Desenvolvimento Regional funds through the COMPETE 2020 - Operational Programme for Competitiveness and Internationalisation (POCI), and by Portuguese funds through FCT - Fundação para a Ciência e Tecnologia in the framework of the project POCI-01-0145-FEDER-029932 (PTDC/FIS-AST/29932/2017). Institute for Bioengineering and Biosciences acknowledges the financial support of FCT - Fundação para a Ciência e Tecnologia (UIDB/04565/2020).

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SERS analysis of selected nitrogen- and sulfur-containing compounds on silver and gold colloidal nanoparticles

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Surface-enhanced Raman spectroscopy (SERS) is a highly sensitive and selective method of detecting molecules located very close to a rough metal surface [1]. By adsorbing the molecule on metal substrate, the scattered radiation is amplified up to a million times, and fluorescence is extinguished, allowing structural investigations of molecules at micromolar concentrations. For more efficient adsorption of analyte and enhancing the scattering, various metal SERS substrates are designed and prepared, mostly in the form of silver and gold nanoparticles, which can be dispersed in suspension or immobilized on a solid support. It is known that gold atoms preferably bind to the sulfur atom of the observed molecule, while silver atoms form a covalent bond with the nitrogen atom, which opens the way to the preparation of a substrate that will preferably bind with a specific part of the observed molecule [2].

In this work, colloidal suspensions of silver and gold nanoparticles were used as substrates for the SERS study of methylene blue and 4-aminotiophenol, in concentration range 1×10^{-7}–1×10^{-4} mol/dm^3. Both molecules contain sulfur and nitrogen atoms in their structure as part of different functional groups, which makes them good candidates for testing the binding path of the observed molecules to different metals in SERS substrates. Three different colloids were used as substrates, which differ in the type of used metal and anions that stabilize the nanoparticles. Silver colloids were prepared by reduction of silver nitrate with trisodium citrate [3] and hydroxylamine hydrochloride [4], respectively, while gold nanoparticles were prepared by citrate reduction of tetrachloroauric(III) acid [5].

When gold colloidal nanoparticles were used as the metal substrate for SERS analysis of methylene blue, a decrease in dye concentration resulted in spectral differences. Few new bands appeared in the spectra and the relative intensity of SERS bands, originated from phenothiazine ring vibrations, changed. Most probably, the dye molecules changed their position on the metal nanoparticles, in a way that sulfur atom of the aromatic system faced the gold surface, hence a stretching vibration of Au–S bond was observed. Using silver colloids as the SERS metal substrate, only small variations in intensity of methylene blue vibrational bands was observed, implying slight changes in position of the dye molecules on the silver surface. In case of 4-aminotiophenol and regardless of using either gold or silver nanoparticles as the metal substrates, concentration-dependent SERS spectra of the compound showed a very similar trend, including only band intensity changes with lowering the dye concentration. It can be assumed that 4-aminotiophenol molecules were very similarly oriented on both metal surfaces.

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SERS spectra of urea disrupted G-quadruplexes on silver and gold nanoparticles

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G-Quadruplexes (G4) are non-canonical nucleic acid structures formed by guanine-rich DNA or RNA sequences. This four-chain spiral structures arise from tetrads of guanine bases which are cyclically linked via Hoogsteen hydrogen bonds and stacked on each other by means of π-stacking interactions. Monovalent cations, such as Na^+ or K^+, located in the center or between G-quartets, reduce repulsion of O6 atoms and stabilize the structure of G-quadruplexes [1]. On the other hand, urea is a well-known denaturing agent which affects the structure of proteins by interrupting the hydrogen bonds. G4 have globular shape and are less charged compared to other nucleic acids, that makes them similar to globular proteins [2]. In order to investigate the effect of urea on the G4 structure, surface-enhanced Raman scattering (SERS) spectroscopy was applied [3].

SERS spectra of human telomeric sequence $d[TTAGGG]_4$ (Tel24) were acquired in the absence and presence of stabilizing Na^+ ions as well as after addition of urea using citrate stabilized silver and gold nanoparticles as the SERS active substrates. Characteristic intensity ratios of marker bands originating from breathing vibrations of adenine and guanine rings indicated unfolded Tel24 structure in the medium without Na^+ ions as well as ordered G-quadruplex upon annealing with Na^+ ions [4]. Addition of urea induced disruption of the folded G4 structure, implied by the SERS spectra that corresponded to the spectra of unfolded Tel24. The SERS spectra obtained on the silver and gold nanoparticles were compared in order to study the effect of the metallic surface on the Raman scattering enhancement.

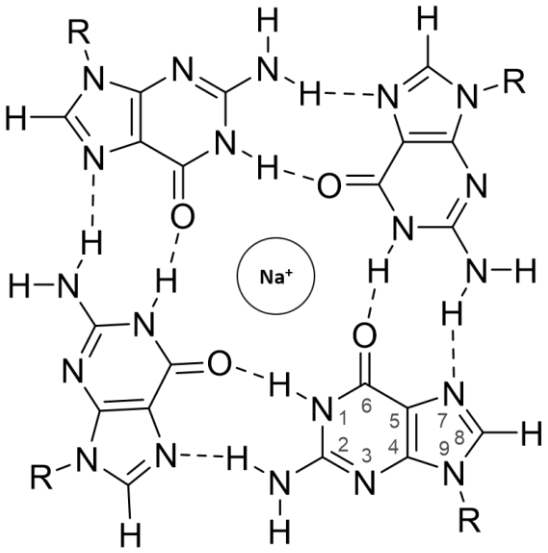

Figure 1. Structure of G-tetrad

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Application of fluorographene chemistry-based biosensor for electrochemical detection of TNBC protein C biomarker

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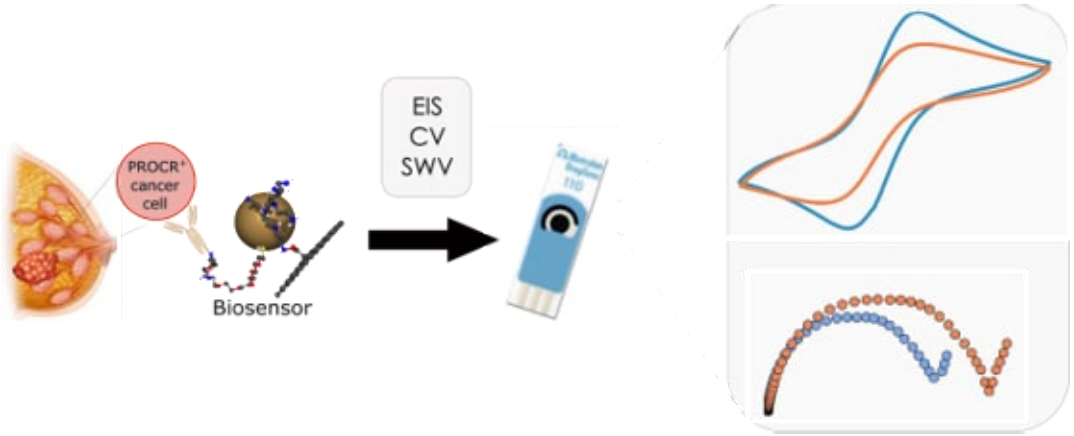
Biosensors have found many applications in various research areas, including biomedicine, food industry,[1] as well as environmental applications[2]. Biosensing devices are often used as sophisticated point-of-care devices for biomarker detection. Since breast cancer is the most prevalent malignancy disease in the world, its easy and early detection is critical.[3]

Triple-negative breast cancer (TNBC) is identified in 15–20 % of all breast cancer cases, mainly in the case of black women. TNBC has a low survival rate and high mortality. Protein C receptor, which is detected in about 50 % of TNBC, can serve as a biomarker analyte in our fluorographene-based biosensor.

Requirements for biosensors include low-cost and rapid and specific determination of analyte with high sensitivity. Electrochemical sensors based on fluorographene derivatives have the potential to fulfil these requirements and can be used as a suitable material for the development of state-of-the-art point-of-care devices. The main advantages of fluorographene-based derivatives are related to enhanced electronic properties and a high specific surface area equipped with a large amount of active functional groups ready to be utilized.

Herein, we present a chemical recognition system based on a fluorographene-derived nanomaterial with target-specific antibodies. Analytical signals were measured and evaluated by means of electrochemical impedance spectroscopy, cyclic voltammetry and square wave voltammetry. Obtained results proved the possibility of detecting the protein C receptor.



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Kinetic sorption study of potassium amyl xanthate and sodium diisobutyl dithiophosphinate on sulphur minerals. Using seawater and drinking water

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Copper flotation is a physicochemical process of concentration and separation of the valuable mineral from the ganga [1][2]. This process uses different reagents, including collectors and large quantities of water, becoming a serious problem for mining because these are developed in areas with low water availability [2]. The aim of this work is to evaluate and compare the use of seawater and drinking water in the sorption kinetics of Potassium Amyl Xanthate (PAX) and Sodium Diisobutyl Dithiophosphinate (DPINa) collectors used for the separation of calcopyrite and pyrite minerals [3]. The minerals were characterized by Scanning Electron Microscopy (SEM-EDS), X-Ray diffraction Spectroscopy (DRX), X-Ray Fluorescence Spectroscopy (XRF) and Cu and Fe content by Atomic Absorption (AAS). Using UV-visible spectroscopy, PAX and DPINa (15 mg/L^{-1}) were characterized at pH 10 (HCl/ $Ca(OH)_2$) and calibration curves were constructed at 227 and 301 nm (PAX) and 236 nm (DPINa). For PAX the highest sensitivity curve was at 301 nm with a linear range of [2.0-20.0 mg/L^{-1}], linear equation: y=0.08026x+0.01231 and (r^2)=0.99899. In DPINa we obtained a linear range of [0.5-5 mg/L^{-1}], linear equation: y=0.25257x-0.0328, (r^2)=0.99899.

The use of seawater was evaluated through kinetic sorption. The experimental data of the kinetics of sorption were adjusted to the model of pseudo second order, and it was concluded that sea water in the presence of PAX with pyrite (pH=8, regulated with $Ca(OH)_2$), causes a decrease in the equilibrium time (3 minutes), with an equilibrium sorption capacity of 1.5 (mg PAX/g Pyrite). Compared with drinking water, presenting an equilibrium time of 8 minutes, with a sorption capacity at equilibrium was 2.9 (mg PAX/g Pyrite).

Thanks to the funding of the Beca de Doctorado Nacional (ANID) 21210131 and the Vicerrectoría de Postgrado from the Universidad de Santiago de Chile for the support granted.

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An electrochemical sensor with surprisingly anti-fouling properties for selective determination of glutathione based on Cu (II)-functionalized magnesium silicate/AgNPs/polyethylene glycol/chitosan nanocomposite

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In this research paper, a novel nanocomposite for the ultrasensitive and selective detection of glutathione (GSH) was proposed. It depends on the combination of chitosan (Chit) and polyethylene glycol (PEG) as anti-fouling nanomaterials; porous magnesium metasilicate (PMMS) as a porous adsorbent that can load large amounts of Cu(II) and AgNPs. Furthermore, silver nanoparticles (AgNPs) not only increase the conductivity and electro-catalytic activity of nanocomposite, but also can adsorb GSH from the solution. With the help of the electro-catalytic ability of Cu(II) released from Cu(II)-PMMS, the as-fabricated electrode could achieve sensitive and selective determination of GSH without the addition of free Cu(II) in the solution. Using square wave voltammetry (SWV) and under the optimal conditions of measurement, a characteristic peak of GSH-Cu(II) was observed at ca. 0.43 V (vs. Ag/AgCl, KCl), which increased linearly with GSH addition. The proposed sensor showed wide linear range for determination of GSH from 0.1 to 125.0 µM with a limit of detection (LOD) of 0.03 µM. The as-fabricated electrode exhibited excellent sensitivity and anti-fouling performance, good selectivity, and sufficient stability. More importantly, the electrode was applied efficiently for the analysis of dietary supplements and human serum samples to quantify GSH with acceptable recoveries % (98.3-104.1 %) and RSDs values not more than 3.2 %. These results prove that the as-fabricated sensor can be used for monitoring of GSH during medical diagnosis.

The authors would like to express their gratitude to the ministry of education and the Deanship of Scientific Research, Najran University, Kingdom of Saudi Arabia for their financial and technical support under code number [NU-RC-MRC-11–2]

Characterization of modified glassy carbon electrodes (GC) with nanohorns carbon (SWCNH) and Nafion (NF) for Cd determination

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Contamination by heavy metals, such as Cd, has harmful effects on ecosystems and humans[1], so international organizations regulate their concentration in food, water and the environment[2]. In this context, it is necessary to develop fast, sensitive, reliable and portable devices to detect at trace and ultra-trace levels this type of species, where electroanalytical techniques based on modified electrodes are an excellent alternative to conventional techniques[3]. Carbon nanomaterials, such as carbon nanohorns, have a large specific area and high conductivity properties that make them attractive for modifying working electrodes. In this work, glassy carbon (GC) electrodes modified with carbon nanohorns (SWCNH) and Nafion (NF) are used for the determination of Cd(II) in aqueous matrices using the drag voltammetry technique.

GC and GC/SWCNH electrodes were characterized by cyclic voltammetry, using the redox couple ferri-ferro-potassium cyanide ($[Fe(CN)_6]^{3/4-}$) 1.0 mmol L^{-1}, Ag/AgCl reference electrode and a platinum auxiliary electrode. From the plot of the current (i) versus the square root of the sweep speed of the potential ($V^{1/2}$) it was determined that the process was diffusion controlled (R^2> 0.99), furthermore the electroactive area was calculated using the Randles-Sevcik equation and the slope of the straight line. An electroactive area of 0.10 cm^2 ± 0.005 was obtained for GC and 0.16cm^2 ± 0.010 for GC/SWCNH.

GC/SWCNH electrode studies for the detection of Cd(II) were performed using formate buffer at pH 4.5, with an accumulation potential of -1.2 V for 90 s, applying preconditioning at +0.2 V for 30 s. The results indicated an unstable signal over time. The results indicated an unstable signal in time; however by incorporating a polymeric resin such as Nafion it is possible to favor the mechanical stability of the modifying agent contributing to improve its preconcentration. Figure 1 shows that GC/SWCNH/NF significantly increases the current for Cd(II) compared to GC and GC/NF (Table 1), evidencing a synergistic effect of NF and SWCNH. Preliminary investigations show that the proposed electrode exhibits properties that make it very tempting for Cd(II) detection.

Table 1. Current intensity obtained by using GC, CG/Nafion, GC/SWCNH/Nafion electrodes at pH 4.5 in 0.1 mol L^{-1} formed buffer for 40ppb Cd detection.

Electrode	Current intensity (µA) ±σ
GC	1.15 ± 0.19
GC/Nafion 0.5%p/p	1.34 ± 0.37
GC/SWCNH/Nafion 0.5%p/p	5.26 ± 0.11

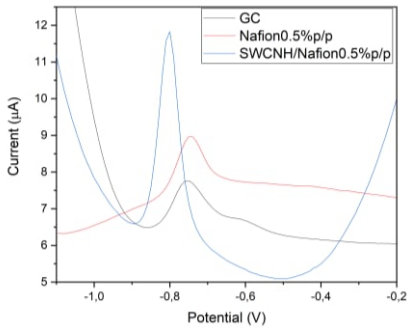

Figure 1. Voltamograms obtained by using GC, CG/Nafion, GC/SWCNH/Nafion electrodes at pH 4.5 in 0.1 mol L^{-1} formed buffer for 40ppb Cd detection.

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TTA-UC emitter based on aggregated Pt(II) Chlorin immobilized with tetraphenylethylene in cellulose acetate films

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Photon upconversion through sensitized triplet–triplet annihilation (TTA-UC) has regained a lot of interest mainly due to its potential for significantly increased solar energy harvesting and applications such as anti-Stokes fluorescence labels for bio-imaging and drug-targeting.[1] In particular the development of TTA-UC emitters is very attractive for the biomedical imaging field because these materials can be excited in the so-called NIR "imaging window" (650-1350 nm) where there is minimal tissue absorbance and autofluorescence and emit light in regions that are easily detected by existing equipment. One of the most important parameters to optimize in bioimaging techniques is the signal-to-noise ratio, which is usually hampered by the problem of autofluorescence of tissues. However, being an anti-Stokes process, TTA-UC overcome this drawback leading to biomedical imaging with high sensitivity. The rarity of anti-Stokes shifts ensures that light at the wavelengths being monitored should only arise from TTA-based processes. Furthermore, the long wavelengths used in excitation have greater penetration into tissue. Moreover, distinct from other upconversion approaches that typically require the use of lasers, TTA-UC can upconvert light from low-power, incoherent excitation sources, making it appealing for practical applications.

The TTA-UC process requires two functional species, a sensitizer and an annihilator. The sensitizer absorbs a photon and transfers the energy to an annihilator through triplet energy transfer. Two annihilator molecules in their triplet excited states undergo triplet–triplet annihilation upon close contact, promoting one molecule to its excited singlet state from where emission of a high energy photon occurs. These materials must rely on triplet exciton diffusion for both triplet-triplet energy transfer (TTET) and triplet-triplet annihilation (TTA), meaning concentrations of sensitizer and acceptor used must be significantly higher than in solution. Although sensitizer aggregation and trap state formation, as well as acceptor self-quenching has been shown to limit material performance. However, we can take advantage of aggregation to achieve more efficient TTA-UC systems by: (i) using the efficient formation of J-aggregates Pt-chlorins to further extent the excitation to the NIR region; (ii) and use aggregation induced emission (AIE) luminogens such as tetraphenylenethylene (TPE) as annihilators, i.e., molecules whose emissions are brightened by aggregate formation and easily screened by common detectors. Indeed, we successfully demonstrated that a Pt(II) complex of 4,5,6,7-tetrahydropyrazolo[1,5-a]pyridine–fused chlorin [2] immobilized with TPE in cellulose acetate films can act as a TTA-UC emitter.

Acknowledgments: The Coimbra Chemistry Centre is supported by the Fundação para a Ciência e a Tecnologia (FCT), Portuguese Agency for Scientific Research, through the projects UIDB/00313/2020 and UIDP/00313/2020.

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Quantification of free Polymers in Polymeric Nanoparticles by GPC and DOSY NMR

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Polymeric nanoparticles (PNPs) have a broad field of application i.e., catalysis or drug-delivery systems where they play an active role as the catalyst itself or a passive role as the carrier for a medically active drug. For both cases it is crucial that the PNP is pure and does not contain any active free polymer chains which are often observed as a residue. Residual free polymer can potentially lead to the deactivation of catalyst in orthogonal tandem catalysis or to hazardous side effects in drug-delivery systems when applied in the human body. In the literature dialysis is known as the method of choice for removing low molecular weight components[1]. However, unwanted higher molecular weight polymers do often remain in solution and are difficult to separate from the nanoparticle. Especially amphiphilic polymers are difficult to remove solely by dialysis due to their tendency to aggregate. Besides the establishment of better purification methods for polymeric nanoparticles, it is also important to quantify the amount of polymeric impurities. We therefore present a combination of two different methods, namely GPC and DOSY-NMR for the quantification of the amount of free polymer in a polymeric nanoparticle.

As a model PNP an amphiphilic poly(2-oxazoline) block copolymer was chosen, as it can be used in both catalysis[2] and medicine[3]. It is synthesized by cationic ring-opening polymerization and is photochemically crosslinked in an emulsion polymerization. It was further characterized by dynamic and static light scattering (DLS and SLS), normal and cryo-transmission electron microscopy (TEM and CryoTEM).

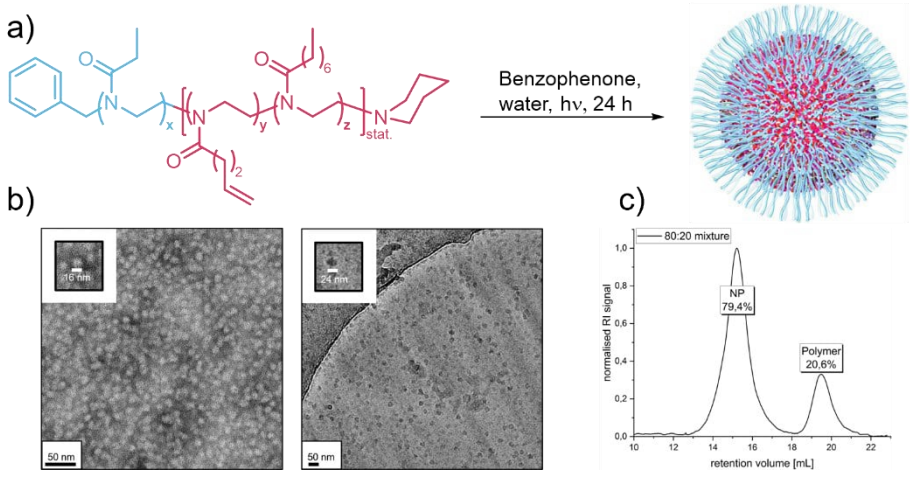

Fig. 1: a) Synthesis of a crosslinked Poly(2-oxazoline) nanoparticle by free radical polymerization in water under UV-light **b)** TEM (left) and Cryo-TEM (right) measurements show swelling of spherical particles in water. **c)** Artificial 80:20 mixture of fractionated NP and its precursor is successfully detected by GPC.

We thank apl. Prof. Dr. Wolf Hiller for the DOSY NMR measurements of the NP mixtures, Volker Brandt of the faculty of Bio- and Chemical Engineering for the TEM measurements and Dr. Oliver Hofnagel of the Max-Planck Institute of Molecular Physiology for the Cryo-TEM measurements.

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Solvatochromic characterization of the ternary mixture Water – Choline Chloride – Ethylene Glycol

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The study of deep eutectic solvents (DES) has increased enormously in recent years. One of the drawbacks for a large number of these deep eutectic mixtures is their high viscosity and several studies use water as co-solvent to decrease viscosity. However, a systematic study of the water influence in these mixtures and of the resulting solvent-solvent interactions is mostly absent.

Within this context, and following previous works [1], we present the solvatochromic study of the ternary mixture water-choline chloride-ethylene glycol, at 298.15 K. The mixtures were characterized by the Kamlet-Taft parameters, α and β (solvent's acidity and basicity by hydrogen bonding, respectively) and π^* (solvent's dipolarity/polarizability), using the characteristic absorption band maximum wavelengths of five solvatochromic probes, namely 4-nitroanisole, 4-nitrophenol, 4-nitroaniline, *N*,*N*-dimethyl-4-nitroaniline and 2,6-diphenyl-4-(2,4,6-triphenylpyridinium-1-yl)-phenolate. The magnitude and the variation of each of these parameters (*e.g.*, figure 1) and their implication on other solvent mixtures' properties will be discussed.

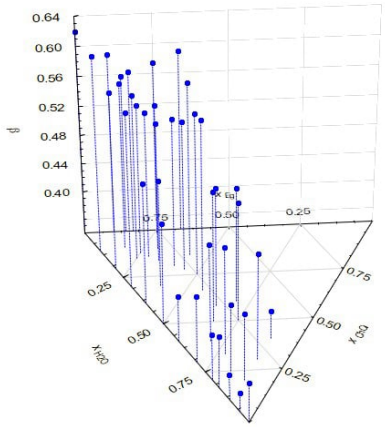

Figure 1. β parameter in the ternary mixture water – choline chloride – ethylene glycol

Thanks are due to Centro de Química Estrutural, a Research Unit funded by Fundação para a Ciência e Tecnologia (FCT), through projects UIDB/00100/2020 and UIDP/00100/2020 and Institute of Molecular Sciences, an Associate Laboratory also funded by FCT, through project LA/P/0056/2020.

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Revisiting gas-phase noble gas ion chemistry by FTICR-MS and *ab initio* computations

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We have been using Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) to examine different aspects of the gas-phase ion chemistry of noble gases (Ng), particularly Kr and Xe, as a prelude to future experiments with highly radioactive and scarcely studied Rn. Several gas-phase studies were reported along the years involving noble gases and fluorinating and oxidizing agents [1]. These studies relied upon the use of different types of mass spectrometers operating at high pressures when compared to FTICR-MS, which operates under very low pressure. The experimental studies have been accompanied by computational studies using MP2 and BCCD(T) methods to evaluate energetics and bonding.

Gas-phase reactions of Kr^+ and Xe^+ with the fluorinating agent SF_6 under our experimental conditions revealed an unprecedented interaction between Kr^+ and neutral SF_6 that gave rise to a new cationic complex of Kr, $[KrSF_5]^+$, although the major reaction channel was dissociative electron transfer to yield SF_5^+ and {Kr,F} (Fig.1, left). The computed energetics indicated that $[KrSF_5]^+$ is marginally stable and that the reaction of Xe^+ with SF_6 is thermodynamically unfavorable, confirming the non-observation of reaction in the MS experiments. An analysis of the bonding in $[KrSF_5]^+$ clearly showed that it is a non-covalently bound species, while in its presumed precursor $[KrSF_6]^+$ a partially covalent Kr-F bond could be present [2]. The lower ionization energy of Rn relative to Xe and Kr points to no reactivity of Rn^+ with SF_6.

Gas-phase reactions of Kr^+ and Xe^+ with oxidants O_3 and N_2O showed, under our experimental conditions, that only O_3 leads to XeO^+ (Fig. 1, right) while N_2O is unreactive; for Kr^+, only electron transfer was observed, indicating that these exergonic reactions (endergonic for Xe^+) dominate. We assessed the energetics of Ng^+–O bonds computationally at the BCCD(T) level that provided a Xe^+–O dissociation energy of 37.7 kcal/mol, in accord with non-observation of reaction between Xe^+ and N_2O; the experimental O-dissociation energies of O_3 and N_2O are 25.5 and 39.9 kcal/mol, respectively [3]. Computed Ng^+–O dissociation energies for Ng = Kr, Xe and Rn show a decreasing trend down Group 18 but indicate that it should still be possible to form RnO^+ from the reaction of Rn^+ with O_3.

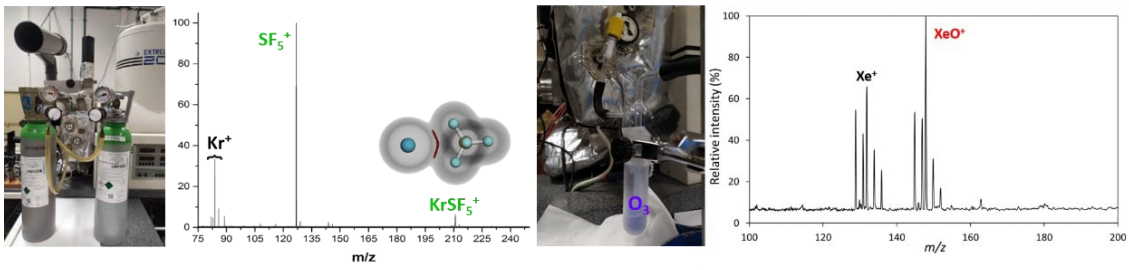

Fig. 1. Mass spectra of a 0.5 s reaction of Kr^+ with SF_6 at a pressure of ca. 5.0 x10-7 Torr (left) and of a 0.2 s reaction of Xe^+ with O_3 at a pressure of ca. 7 $x10^{-8}$ Torr (right).

This work was supported by Fundação para a Ciência e a Tecnologia (FCT) through projects PTDC/QUI-QFI/31896/2017, UIDB/00100/2020 (CQE), LA/P/0056/2020 (IMS) and UIDB/04046/2020 (BioISI), and through RNEM – Portuguese Mass Spectrometry Network, ref. LISBOA-01-0145-FEDER-022125, also supported by Lisboa2020 under the PT2020 Partnership Agreement, via the European Regional Development Fund (ERDF).

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Gas-phase reactivity of gold(I) complexes with noble gases and small molecules

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The study of the interactions of naked and ligated transition metals ions with small molecules in the gas phase is of fundamental interest in coordination chemistry because these systems are good models for understanding the fundamentals of catalytic processes [1,2].

We prepared a gold(I) cationic complex, $[Au(CH_3CN)_2]^+$, in the gas-phase by CID (collision-induced dissociation) of $[Au(CH_3COO)_2(CH_3CN)_4]^+$, a gold(III) complex obtained from CH_3CN solutions of $Au(CH_3COO)_3$ by electrospray ionization quadrupole ion trap mass spectrometry (ESI-QIT-MS). $[Au(CH_3CN)_2]^+$ was highly reactive with different light, inert and noble gases, forming $[Au(CH_3CN)_2(L)]^+$ complexes for L = Xe (Fig. 1, left), N_2, N_2O, NO, H_2O, CO, COS, CS_2, CH_4, C_2H_6 and C_2H_4, but not for L = Kr, O_2 and CO_2. Although not yielding the adduct, H_2 reacted with $[Au(CH_3CN)_2]^+$ to form $(CH_3CN)_2H^+$ and presumably AuH. Remarkably, $[Au(CH_3CN)_2]^+$ was unreactive when produced directly by ESI.

We also used ESI-QIT-MS to produce gold(III) anionic complexes $[Au(qdt)_2]^-$ and $[Au(mnt)_2]^-$ from CH_3CN solutions of (TPP)$[Au(qdt)_2]$ and (TBA)$[Au(mnt)_2]$ (qdt = quinoxaline-2,3-dithiolate; mnt = 1,1-dicyanoethylene-2,2'-dithiolate) [3]. CID of $[Au(qdt)_2]^-$ and $[Au(mnt)_2]^-$ led to the formation of gold(I) complexes $[Au(qdt)]^-$ and $[Au(mnt)]^-$, respectively, that efficiently yielded $[Au(qdt)(L)]^-$ and $[Au(mnt)(L)]^-$ for L = O_2, NO and NO_2 (Fig. 1, right) but not for L = Kr, Xe, N_2 and N_2O. For comparison, we tested the reactivity of gold(I) complex $[AuCl_2]^-$ with the same neutral species but no reactivity was observed.

Additionally, we conducted DFT studies to evaluate the observed reactivity of cationic, $[Au(CH_3CN)_2]^+$, and anionic, $[Au(qdt)]^-$ and $[Au(mnt)]^-$, gold(I) complexes. Computations indicated that formation of $[Au(CH_3CN)_2]^+$ by CID could populate an excited state that enhanced reactivity with neutral species L. The computed energetics for gold(I) anionic complexes were in agreement with experimental observations, highlighting the important role played by non-innocent ligands qdt and mnt.

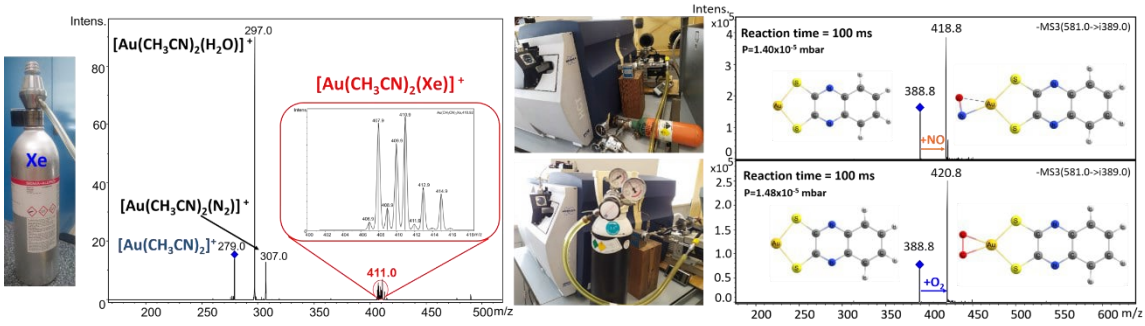

Fig. 1. Mass spectra showing coordination of Xe to $[Au(CH_3CN)_2]^+$ for a reaction time of 100 ms (left) and coordination of NO (top right) and O_2 (bottom right) to $[Au(qdt)]^-$ for a reaction time of 100 ms.

This work was supported by Fundação para a Ciência e a Tecnologia (FCT) through projects PTDC/QUI-QFI/31896/2017, UIDB/00100/2020 (CQE), LA/P/0056/2020 (IMS), UIDB/04046/2020 (BioISI) and UIDB/04349/2020 (C^2TN) and, and through RNEM – Portuguese Mass Spectrometry Network, ref. LISBOA-01-0145-FEDER-022125, also supported by Lisboa2020 under the PT2020 Partnership Agreement, via the European Regional Development Fund (ERDF).

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A novel Zn(II) Schiff base complex as efficient colorimetric and fluorometric probe for sensing copper(II) in drinking water by a transmetalation approach

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Copper is an essential trace element in biology involved in proper functioning of enzymes, neurobiology, and neurodegenerative disorders. An alteration of copper levels in organisms causes diseases.[1] As copper pollution represents an emerging issue for environmental and human health,[2] the World Health Organization (WHO) has recommended a safe limit of 2mg/l for copper(II) in drinking water.[3] A fast, simple, efficient, and direct sensing of copper(II) in water is therefore highly desirable.

Colorimetric and fluorometric techniques allow a direct and rapid detection of analytes. In respect to copper sensing, a great number of probes have been developed, exploiting various sensing mechanisms and approaches,[4] however, transmetalation, or cation displacement, is an approach that has been little exploited for sensing copper.

Zn(II) salen-type complexes are a class of versatile molecular materials that have been investigated for their aggregation and optical sensing properties, mostly related to their Lewis acidic characteristics.[5] Thanks to their versatile optical properties they may find applications as colorimetric and/or fluorometric probes.[6]

Recently, we have studied the transmetalation properties of a *tert*-butyl substituted Zn(salmal) complex (**1**). Acetonitrile solutions of **1** give a naked eyes color change and a fluorescence turn-off when added with aqueous solutions of Cu^{2+} ions. The process is selective with respect to various other cations. From spectrophotometric/spectrofluorometric experiments has been evaluated LOD values, which result to be below the safe limit established by the WHO. Competitive experiments conducted using various cations, namely Na^{+}, Mg^{2+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Cd^{2+}, have been performed to further demonstrate the selectivity of **1** towards Cu^{2+}. Finally, the practical application in quantitation of Cu^{2+} in samples of tap and spring water has been demonstrated to be a simple and fast method that does not require sample pre-treatment. Therefore, **1** behaves as an efficient colorimetric and fluorometric chemosensor for an easy, fast, and effective detection of copper(II) via spectroscopic methods.

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Reduction of substituted nitrobenzimidazoles into radicalanions in relation to the search of novel bioreductive agents

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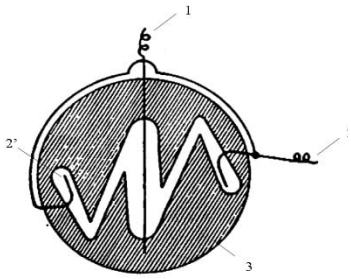
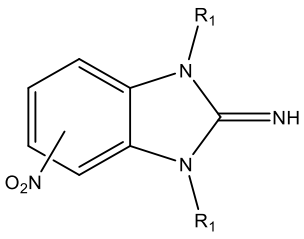
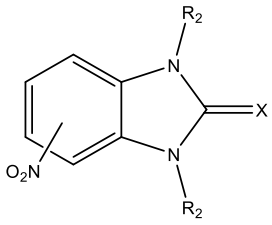
Low supply of cells with oxygen (hypoxia) is one of the main targets in the development of new antitumor drugs. The hypoxide conditions in the cancer cells offer a good opportunity for targeted therapy in which only the cancer cells are selectively killed. Radio- and chemotherapeutics are usually more effective in killing aerobic cells, so anti-cancer drugs activated by bioreduction can be used to enhance their effect. Various bioreducing agents have been developed and the largest groups of them are nitroimidazoles and nitrobezenes. Under the action of enzymes (reductases), the nitro aromatic compounds converts into reduced products, which are the real cytotoxic agents, so they can be regarded as prodrugs or precursors. Benzimidasole heterocycle is an important multifunctional system for medical applications in various therapeutic areas. Given the possibility of activation of the nitrobenzimidazole ring by bioreduction, it was of interest to obtain and study radical products of nitro derivatives from the synthesized groups of compounds. In this aim, the formation of radical anionic products was studied by IR spectroscopy by electrochemical reduction in aprotic solvent DMSO (oxygen-free medium). The changes in structure caused from these transformations were characterized on the basis of the observed IR spectral changes. For this purpose, an experiment was performed in a special IR cuvette equipped with electrodes, in which a solution of the test compound in deuterated dimethyl sulfoxide and tetrabutylammonium bromide as an electrolyte salt was placed. After applying an electric current (1, 3 or 4.5 V) to electrodes, a series of IR measurements is performed at intervals of 10 minutes, thus monitoring the degree of ongoing reduction. After 90 minutes, the polarity of the electrodes was reversed and the experiment continued with a new series of measurements every 10 minutes in order to investigate the possibility of regeneration of the original neutral molecule.







1. Cathode
2. Anode
3. Polyethylene spacer

$R_1 = CH_2COC_6H_5$

X = O, S

$R_2 = (CH_2)_xCOC_6H_5$;

$(CH_2)_xCOC_2H_5$;

Acknowledgements

This work has been financially supported by the National Science Fund of Bulgaria, Contract КП-06-Н39/4. Research equipment of Distributed Research Infrastructure INFRAMAT, part of Bulgarian National Roadmap for Research Infrastructures, supported by Bulgarian Ministry of Education and Science was used in a part of this investigation.

Tyrosine acetylene derivatives as a new group of effective fluorophores

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Fluorescent probes are one the most important and essential tools for using many techniques, which are based on the fluorescence phenomenon. Depending on the spectral and photophysical properties of fluorophores, they are used for various, often complex, research tasks in the field of chemistry, biology, physics and medicine.

Hundreds of new fluorescent probes have been discovered or synthesized over the last years, however, some of them still do not meet the demand, thus fluorophore's catalogues have to be completed. Systems that do not contain a fluorophore or contain a fluorophore that does not have the appropriate properties for the experiment require fluorescent labeling. The internal fluorophore are fluorescent compounds that naturally occur in the analyzed system, such as aromatic amino acids (Tyr, Phe, Trp) in peptide or protein. Their fluorescence is often used to study the conformational changes of proteins, to verify ligand binding by peptides and proteins, or to study other intermolecular interactions. Unfortunately, mentioned above amino acids are characterized by low absorption coefficients, short wavelength of absorption and emission spectra, low quantum yield of fluorescence, short and heterogeneous lifetime of fluorescence, which limits their use in many research aspects. External fluorescent probes, such as the fluorescein and rhodamine groups [1], have other limitations. They can significantly modify the conformational structure of the labeled peptide or protein or drastically reduce the solubility of the analyte.

Non-proteinogenic amino acids seem to be a good direction of searching more sophisticated, selective and sensitive fluorophores, as they have a chance to retain the advantages of internal fluorophores (e.g. easy incorporation into the analyte) and eliminate their disadvantages. Structural modifications of natural amino acids lead to the improvement of their spectroscopic properties, which significantly increases their application potential [2, 3, 4].

The introduction of aromatic substituents symmetrically or asymmetrically to the tyrosine side chain through a triple bond enables to obtain a new effective group of fluorophores. The substitution of phenyl ring at positions 3 and 5 of the tyrosine side chain causes bathochromic shifts of the absorption and emission spectra, an approximate three-fold increase of the value of the molar absorption coefficient, and from 2.4- to 4.5-fold increase in the fluorescence quantum yield. The fluorescence decays are monoexponential in all studied solvents. Moreover, systems of this type show greater sensitivity to changes in the density of the surroundings, which additionally increases the application possibilities of these derivatives.

Initial research on non-proteinogenic amino acids, which structure is enriched with additional aromatic rings connected by an acetylene linker, may constitute a group of new fluorophores with a wide range of applications.

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Evaluation and quantification of electronic conjugation through aromatic spacers

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The existence of conjugation in a molecule is associated with a greater electronic delocalization through π orbitals and substantial energetic stabilization [1]. Besides this stabilizing effect, conjugation can also show structural (e.g., more planar molecules) and optical (e.g., HOMO-LUMO gap) manifestations, among others. Although the concept of conjugation is well known, the true reach of its effects in large aromatic molecules is still poorly described [1, 2]. For instance, theoretical calculations struggle to adequately quantify conjugation and usually underestimate the stabilization energy in such aromatic conjugated systems [2].

Herein, we study a series of aromatic molecules (acenes with phenyl substituents) to evaluate the effect of molecular size and position of substituents on the energetic, structural, and optical properties. The working methodology consists of the following: (i) Synthesis, purification, and characterization of the compounds studied; (ii) Phase behaviour, including melting and sublimation thermodynamics; and (iii) Experimental and theoretical evaluation of molecular energetics, focusing on quantifying the stabilizing effect of conjugation, using a molecular *spacer* approach, and its relationship with molecular structure. This research seeks to answer the following questions: How much is the stabilization energy due to conjugation? How do the molecular size and the position of substituents affect the degree of conjugation? How adequate are computational chemistry methods to describe conjugation?

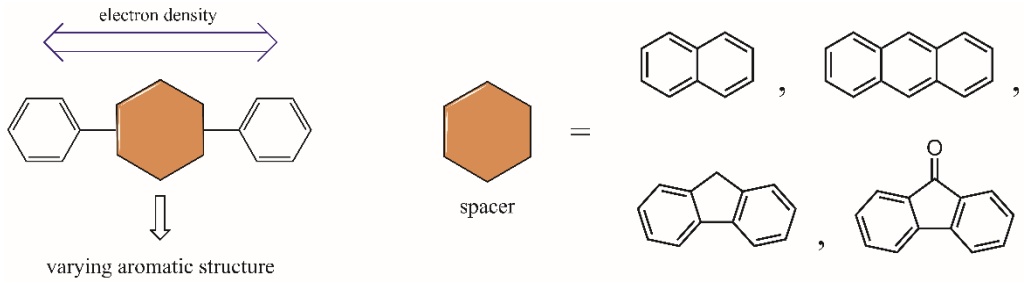

Figure 1. Schematic representation of the conjugated aromatic compounds under study.

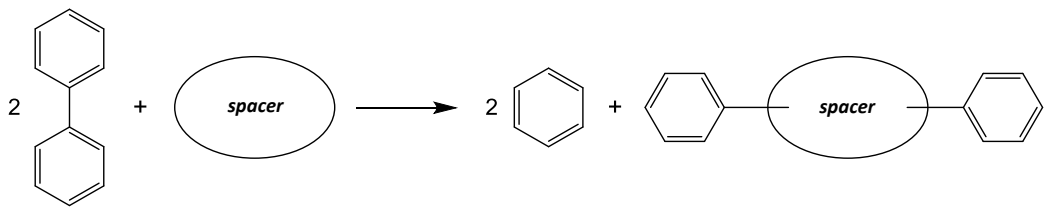

Figure 2. Homodesmotic reaction used to quantify electronic conjugation through aromatic spacers.

This work was supported by the Fundação para a Ciência e Tecnologia (FCT) (funded by national funds through the FCT/MCTES (PIDDAC)) to CIQUP, Faculty of Science, University of Porto (Project UIDB/00081/2020), IMS – Institute of Molecular Sciences (LA/P/0056/2020). CFRACL is also financed by national funds through the FCT-I.P., in the framework of the execution of the contract-program provided in paragraphs 4, 5, and 6 of art. 23 of Law no. 57/2016 of 29 August, as amended by Law no. 57/2017 of 19 July.

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Kinetics and Thermodynamics of Diels-Alder Addition to Fullerenes

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Fullerenes can be functionalized via chemical reactions to obtain derivatives with enhanced physical and chemical properties in order to tune their functionality and applicability.[1-3] In this work, we studied the reactivity of fullerenes C_{60} and C_{70} towards Diels-Alder addition with two conjugated dienes: anthracene and 9,10-dimethylanthracene. The kinetics of the reactions with anthracene and their temperature dependence was studied by UV-Vis. The activation enthalpy ($\Delta H^{\ddagger}$) and entropy ($\Delta S^{\ddagger}$) for the direct and reverse reactions were derived. The reactions with 9,10-dimethylanthracene were found to be much faster, and only the thermodynamic parameters (ΔH_r^0 and ΔS_r^0) were derived from the temperature dependence of the equilibrium.

In order to evaluate the effect of substituents in the C_{60} reactivity, the reaction of ICMA (indene-C_{60} monoadduct) with 9,10-dimethylanthracene was studied using the same methodology.

The addition of dienes to C_{70} was found to be slightly more exothermic than in C_{60}, although this is compensated by a higher decrease in entropy contribution. The higher decrease in entropy contribution for the reactions (in solution) involving C_{60} are in agreement with its higher molecular symmetry. The activation parameters found for the reaction with anthracene were similar for both fullerenes, except for the activation entropy for the reverse reaction, which was found to be more negative for C_{60}.

The reactions of fullerenes (C_{60}, C_{70}, ICMA) with anthracene were also studied using density functional theory. The quantum chemical results indicate similar energetics for the reactions of the three fullerenes. Additionally, the loss of indene in ICMA and in indene-C_{60} bisadduct (ICBA) was studied by Differential Scanning Calorimetry. This process was found to occur at a lower temperature for ICBA when compared to ICMA.

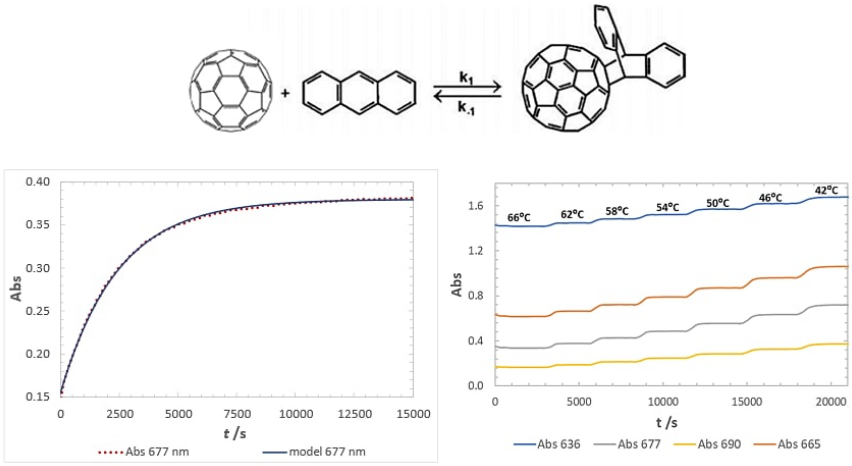

Figure 1. On the left side, the time evolution (of Abs) at λ=677 nm for C_{70} + anthracene solution (T = 82 ˚C); on the right side, temperature dependence of equilibrium (in Abs) for C_{70} + 9,10-dimethylanthracene solution.

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Critical analysis of association constants between calixarenes and nitroaromatic compounds obtained by fluorescence. Implications in explosives sensing

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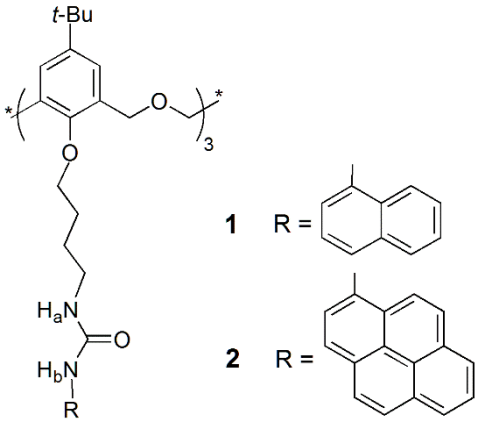
The detection of explosives is a major task in both the fight against terrorism and in homeland security. Nitroaromatic compounds (NACs), such as trinitrotoluene (TNT), dinitrotoluene (DNT) and trinitrophenol (TNP, also known as picric acid), are common explosives used for military purposes and are the principal components of unexploded landmines. They are also considered environmental pollutants.

Although many methods have been used for trace detection of explosives, expensive and complex equipment is often required, causing limitations for their use in real-time applications. Therefore, low-cost detection techniques, with high portability, high sensitivity and selectivity are needed for in-field analyte effective sensing. Luminescence-based methods fulfil these requirements [1].

Lately, a broad range of fluorescence sensors for explosive monitoring in the solid, solution and vapor phases have been developed [2], based on calixarenes [3,4]. Owing to their structural features, these macrocycles have been widely investigated as ion and neutral molecule receptors. They possess a pre-organized cavity available in different sizes and conformations, and can be functionalized at the upper and lower rims, leading to an almost unlimited number of derivatives. Fluorophores like naphthalene, anthracene and pyrene are among the most incorporated in the calixarene framework, leading to potential fluorescent probes for NACs.

In the course of our recent studies on anion binding by fluorescent homooxacalixarenes [5], we have investigated the possible recognition of nitroaromatic compounds by hexahomotrioxacalix[3]arene-based receptors. In this communication we describe the binding behaviour of two ureido-hexahomotrioxa-calix[3]arene derivatives recently obtained and containing naphthyl or pyrenyl residues at the lower rim, towards selected NAC's. Their affinity (or lack of) was determined by UV-Vis absorption, fluorescence and NMR spectroscopy. Conflicting results between the usual approach in fluorescence studies and the other methods prompted us to conduct a broader study. Different computational methods were also performed to bring further insights to the analysis of the complex formation between the calixarenes and the NAC's.



Thanks to Fundação para a Ciência e a Tecnologia, projects UIDB/00100/2020 and UIDB/04565/2020. A. S. Miranda acknowledges PhD grant ref. SFRH/BD/129323/2017 and COVID/BD/152147/2022.

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Optimization of the Ring-Opening Polymerization Reaction of Cyclic Carbonates by Automated Chemical Space Exploration

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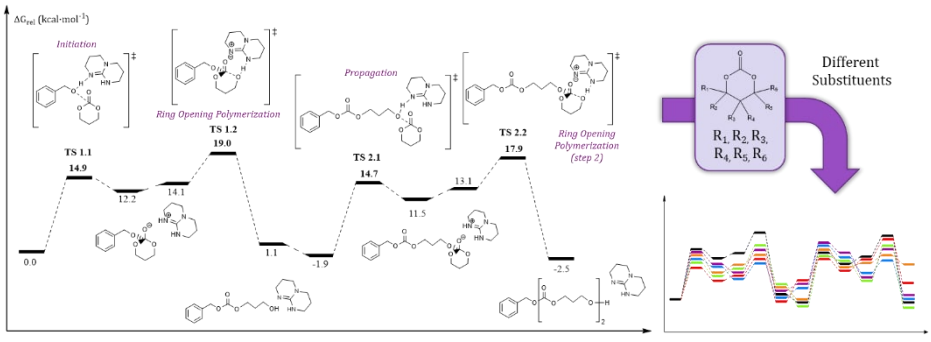
One of the major environmental challenges for today's society is related to waste management, mostly due to the inability to properly recycle materials as ubiquitous as plastics, as these materials are polymers which do not degrade well once used. Another problem comes from the increase in CO_2 emissions, which has had an undeniable impact on global warming and climate change. Luckily, in chemistry it is possible to flip the board synthesizing polymers that are not only degradable, but also use CO_2 as a reactant to generate them, contributing to the reduction of these emissions. Concretely, it is possible to obtain monomers from carbon dioxide, such as cyclic carbonates [1], and use them to produce degradable polymers in a prime example of circular economy. However, neither the synthesis nor the control of the properties (stability, chain length...) of these polymers are easy to rationalize. These properties and the eventual success of the polymerization are mostly dependent on the nature of the monomers, thus requiring assistance in the choice of the ideal starting material. On the one hand, larger rings are more prone to undergo a Ring-Opening Polymerization (ROP) reaction and obtain larger polymer chains, however, on the other hand, larger rings are more difficult to synthesize. [2][3][4]

To guide the monomer selection, DFT calculations were carried out for a wide scope of different molecules to obtain more information about which ones are more likely to be polymerized. Specifically, this work studies the Ring-Opening Polymerization reaction using cyclic carbonates as monomers, with a typical initiator as benzylic alcohol (BnOH) and 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD) as the organocatalyst. [5] The strategy employed to explore this variety of monomers involves the characterization of the initial mechanism on unsubstituted cyclic carbonates, followed by an automated workflow to substitute different positions of the parent structures. The ultimate goal is to employ this computational knowledge to directly optimize the experimental protocol limiting the number of monomers to be tested.



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Modern flow-based systems for advanced Analytical Chemistry

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Flow injection analysis have been proposed for automation of chemical analysis prior to the inception of computers in laboratories. The concept of analytical determinations and sample processing out of equilibrium conditions is still fresh and can nowadays be the basis for innovative methodologies, addressing contemporary challenges [1].

The present communication addresses how flow injection based methods and derived techniques based on computer control, namely sequential injection analysis and bead injection, have contributed to modern analytical chemistry. First, the quantification of nanoparticles using miniaturized optical detection integrated in mesofluidic platforms, like lab-on-valve [2], are presented for the quality control of nanoformulations. Moreover, contributions for sample treatment are discussed, highlighting the advantages of bead injection implementation for solid-phase extraction as sole sample treatment prior to mass spectrometry analysis or prior to chromatographic determination. Using the bead injection mode, a fresh portion of sorbent is automatically packed inside the fluid conduits, rendering a pristine column for each sample in a flow-based format. This feature avoids sorbent fouling and sample carry-over commonly found in online systems. Finally, automated ELISA immunoassays under the bead injection format [3] are critically assessed, showing the possibility of different operation modes (competitive or sequential) through software control. The precise control of operation, regarding incubation time and contact between solid surfaces and solutions, also foster an increased precision when compared to batch operation.

Thanks to financial support from PT national funds (FCT/MCTES, Fundação para a Ciência e a Tecnologia and Ministério da Ciência, Tecnologia e Ensino Superior) through the project UIDB/50006/2020 and project EXPL/QUI-QAN/0360/2021. This work is also supported by AgriFood XXI I&D&I project (NORTE-01-0145-FEDER-000041) cofinanced by European Regional Development Fund (ERDF), through the NORTE 2020 (Programa Operacional Regional do Norte 2014/2020).

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Microwave-assisted synthesis of amino acids derivatives with 1-fluoro-2-nitro-4-(trifluoromethyl)benzene for their HPLC determination

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The quantitation and qualification of total and free amino acids (AAs) are most commonly used in food studies, and provide an excellent way of monitoring these compounds in our diet. Because of this, the scientific interest in evaluating these compounds has resurfaced in recent years and has precipitated the development of a multitude of new analytical techniques. Unfortunately, to determine AAs with a low detection limit, with satisfactory accuracy, reproducibility, and sensitivity, time-consuming derivatization steps are often required. However, most of the described derivatization procedures pointed out some problems, such as a long time of synthesis, low reaction efficiency, interferences from reagents, and instability of obtained products.

According to Meera et al. [1], presently, microwave irradiation is one of the most effective non-conventional activation methods of organic synthesis. The advantages of this technique include substantial reduction of time, greater yield, elimination of side reactions, less chemical waste, higher purity of the formed products, and a fine selection of the parameters of the reaction.

In this work, we proposed microwave-assisted synthesis of amino acids derivatives with 1-fluoro-2-nitro-4-(trifluoromethyl)benzene [Fig.1]. The condition for the synthesis (molar ratio, temperature, and time) in Microwave Synthesizer Discover 2.0 was optimized. The selected conditions were applied for the derivatization of 21 amino acids, followed by flash-chromatography purification of obtained products. Moreover, the obtained derivatives were characterized by spectral methods (^{1}H, ^{13}C, ^{19}F NMR, and IR). Finally, the achieved products were used for HPLC determination. The last stage of this work was to employ the developed method of synthesis, purification, and analysis to the determination of free amino acids contents in food samples.

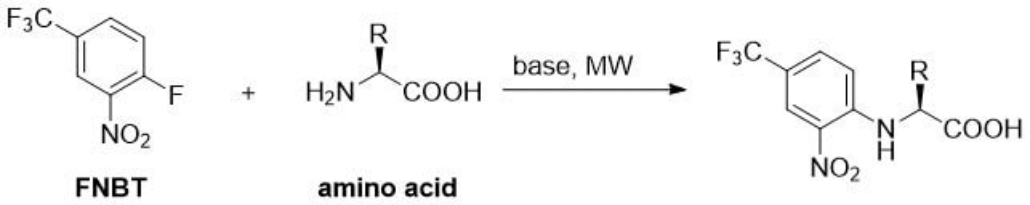

Fig.1. Scheme of amino acids derivatives synthesis

Thanks to National Science Centre, Poland for financial support (project 2020/39/B/NZ9/01694).

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From Blue to Green: Solvent effects on novel emissive molecular probes of dansyl-based dyes

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Five novel dansyl-based compounds (Figure 1) have been synthesized and fully characterized on the pursuit of new fluorescent compounds for the development of stimuli-responsive fluoro-chromic materials. Nowadays, the vanguard chemistry includes the study of materials whose emission were tuned and designed to modulate supramolecular entities to perform various interactions rather in solution or while dispersed in solid matrixes. In recent years, our group has been working with Fluorescent organic and inorganic dyes to create new materials able to exert an applicable response for metal ions, temperature, and solvent studies. [1-5] As a matter of course, their effective photophysical properties provide the key aspects for sensing materials, solar batteries, light-emitting diodes, temperature, and metal sensors, among other notorious applications in biology or biomedicine.

In this communication, compounds L1, L2 alongside their single sulfur bridge derivatives, and L3 have been studied in different solvents with the intention to explore their solvatochromic behaviour in the ground and excited states. Color range for these compounds were shown to be from blue to yellow.

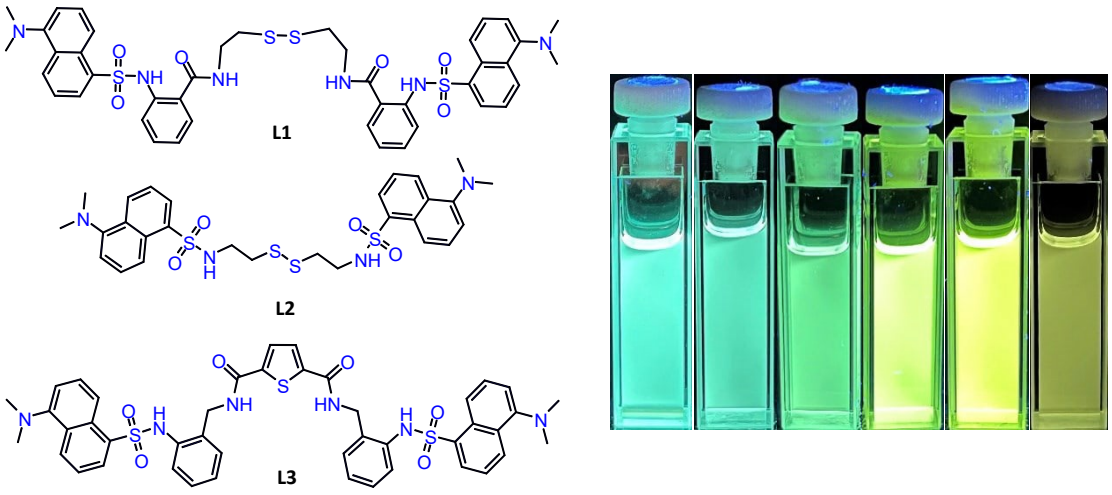

Figure 1: Compounds L1, L2 and L3 studied in this work, and fluorescent emission in toluene, THF, chloroform, ethanol, acetonitrile, DMSO solutions (l_{exc} 365nm, [L] = 1E^{-5}M).

This work was supported by the Associate Laboratory for Green Chemistry – LAQV which is financed by national funds from FCT/MCTES (UIDB/50006/2020 and UIDP/50006/2020) as well as the Scientific Society PROTEOMASS (Portugal) for funding support (General Funding 2022 Grant). F.D. thanks to FCT/MEC (Portugal) for his doctoral grant 2021.05161.BD. E.O. thanks FCT/MEC (Portugal) for the individual contract, CEECIND/00648/2017.

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Visualization of pectin in carrot pomace using FTIR microspectroscopy: feasibility of internal standardization

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Pectins are a group of polysaccharides commonly used in industry as gelling, emulsifying, and stabilizing agents. Traditionally obtained from apple or citrus peel, the increasing global demand for pectin calls for the study of alternative sources [1], [2]. Although currently employed in animal feed, carrot pomace, a by-product obtained after juice production, is considered a good target for pectin extraction [3], [4]. Nevertheless, modifications on the chemical structure during biomass storage have been reported [5], and there is limited knowledge on changes occurring during pectin extraction. Industrial exploitation of carrot pomace requires the development of robust analytical methods to collect information about the variation in composition through the sample.

FTIR microspectroscopy allows the acquisition of spectral and spatial information simultaneously but is not widely implemented in biomass samples due to the inherent limitations of the technique. Uncontrolled physical and chemical phenomena such as changes in sample size, humidity, or instrumental drift are responsible for spectral variance, hindering the potential of this technique for quantitative analysis [6]. Data pre-processing methods can remove the inherent variation in FTIR-spectra but can generate artifacts [7]. Normalization of the spectra based on the signal of an internal standard could overcome this limitation [8]. Nevertheless, internal standardization is not usually employed on biological samples due to the difficulty of finding compounds exhibiting no spectral interference.

This work aims to study the feasibility of internal standardization to develop a spectroscopic method for pectin determination on carrot pomace. In a first step, a calibration model for pectin determination was prepared, enriching carrot pomace residues obtained after pectin extraction with different percentages of pectin and a constant amount of internal standard. Subsequently, the calibration model was tested on samples subjected to internal standardization and analyzed by FTIR microspectroscopy.
Our results show the potential of this approach in FTIR imaging, where internal standardization could provide a method to quantitatively assess the spatial distribution of pectin in complex biomass matrices. The findings open up an attractive prospect of using FTIR microspectroscopy for mapping changes of target compounds at different stages of extraction.

This study is funded by Flanders' Food and VLAIO in the framework of the EffSep project (Grant number HBC.2019.0012)

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Raman imaging methods applied to carbamazepine in pharmaceutical formulations

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Pharmaceutical research and industry require handy analytical and imaging methods to develop new products and formulations. The last decade has assisted an increasing interest in applying confocal Raman microscopy (CRM) methodologies to the development, manufacturing and quality control of pharmaceutical products. The applicability of Raman imaging for pharmaceutics production ranges from the characterization of pharmaceutical formulations, kinetic processes in drug delivery to the rapid detection and identification of polymorphs, co-crystals, impurities/contaminants, amorphous materials and solvates.[1] Our interest in this area led us to explore Raman imaging as a tool to characterize the distribution/aggregation state of specific compounds that are dispersed in composites, which in some cases have great interest for pharmaceutical areas, namely in drug delivery, cancer therapies and bone regeneration.[2,3]

Here, we communicate our research results on the application of CRM as an essential tool to monitor polymorphism transition, hydration processes and degradation/impurity compounds on active pharmaceutical ingredients (API) in commercial tablets. In particular, Raman imaging was explored to identify and monitor the polymorph transition of anhydrous carbamazepine (CBZ III; polymorph III), an anticonvulsant drug commonly used to treat epilepsy, into CBZ I (polymorph I). Also, we explore CRM as a tool to monitor the API degradation into iminostilbene, in function of temperature, [4]; or into the hydrated form (CBZ DH) when exposed to 98% of relative humidity. The spatial distribution of CBZ III/CBZ DH in commercial tablets was also reported using Raman imaging, demonstrating the potential of this approach for quality monitoring purposes.

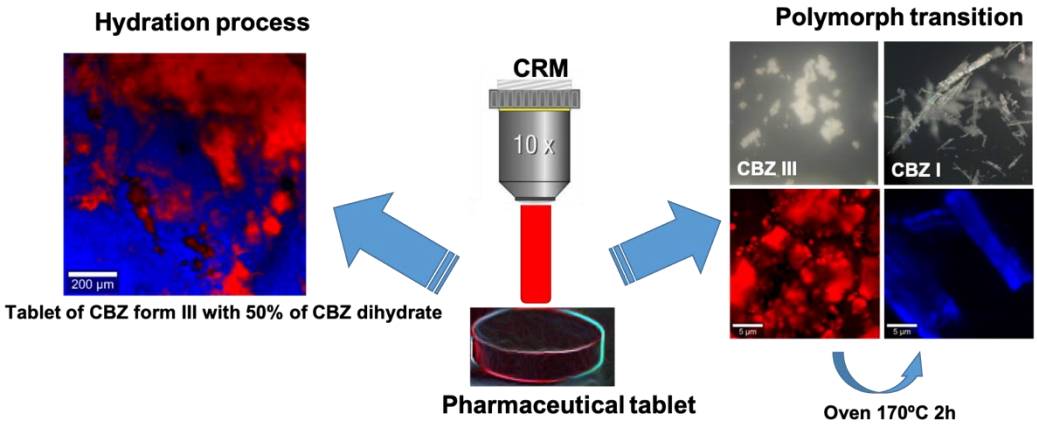

Figure: Raman imaging applied to polymorphism transition and hydration processes on pharmaceutical formulations

Acknowledgements: This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020 & UIDP/50011/2020, financed by national funds through the FCT/MEC and when appropriate cofinanced by FEDER under the PT2020 Partnership Agreement. S. F. thanks FCT for his research contract (REF-069-88-ARH-2018) which is funded by national funds (OE), through FCT-Fundação para a Ciência e aTecnologia, I.P., in the scope of the framework contract foreseen in the numbers 4, 5, and 6 of the article 23, of the Decree-Law 57/2016, of August 29, changed by Law 57/2017, of July 19.

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Development of a Radiolabelled Carborane-based Ligand for Theranostics

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The cannabinoid receptors type 1 (CB1R) and type 2 (CB2R) are part of the endocannabinoid (eCB) system in addition to their endogenous ligands and enzymes responsible for the synthesis and degradation thereof [1]. The CB2R is involved in pathological conditions like inflammation or cancer, and was shown to be overexpressed in neuroinflammatory processes [2]. Since the treatment of these conditions is challenging, the synthesis of suitable drug candidates is of high importance. For the development of a theranostic agent, not only high affinity and selectivity but also factors like metabolic stability, membrane penetration or bioavailability have to be taken into account [1].

Lately, the theranostic approach has gained importance since it offers a fast and easy way to connect the diagnosis of pathological processes with the therapy. An excellent tool to cover the diagnostic aspect is the non-invasive imaging with positron emission tomography (PET). The method is suitable to monitor biochemical features, and the gained information might provide the background for an appropriate treatment [3]. For the PET imaging of neuroreceptors and neuronal changes in pathological conditions, a compound radiolabelled with an appropriate nuclide is needed. To date, no tracer for the imaging of the CB2R with PET in the clinics is available.

In the present study, we evaluate the potential of carboranes as pharmacophoric moieties to improve the biological properties of the available CB2R ligands [4]. For this, lipophilic groups of target molecules, e.g. a cyclohexyl substituent (Figure 1), were replaced with the cluster compounds [1, 5]. Subsequently, the compound with highest affinity towards CB2R was radiolabelled with ^{18}F. The resulting radioligand was further investigated in PET studies. The synthesis, radiofluorination and biological as well as preclinical PET studies will be reported.

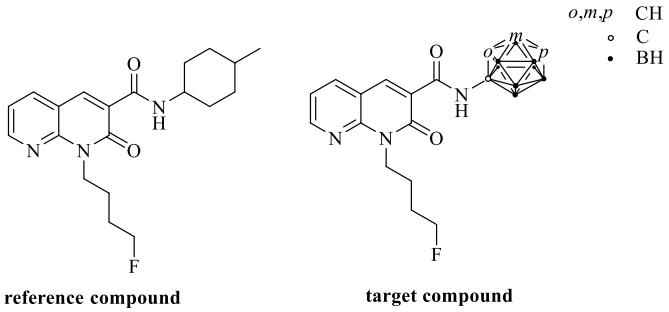

Figure 1: An example of a carborane-based CB2R ligand.

Thanks to the Deutsche Forschungsgemeinschaft (DFG) for funding (grants MO 2677/4-1, HE 1376/38-1 and HE 1376/54-1), Leipzig University, the Graduate School BuildMoNa, the Research Academy Leipzig (RAL) and the GDCh for financial support.

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TURN-ON FLUORESCENT ACIDIC PH PROBE WITH A BIMANE CORE: A BEGINNING OF NIR-BIMANE PROBES

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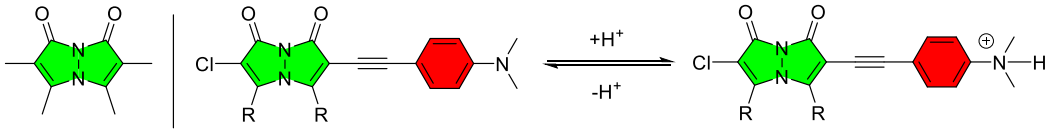
The nature of physiological and pathological processes can be determined by understanding intracellular or extracellular pH variations.[1] Sensing minor reductions in pH in tumor microenvironments has become a significant challenge in the design of anti-tumor therapies since acidic environments are often related to inflammation and tumor malignancy.[2,3] As a result, in the field of life sciences, developing ways to monitor pH changes inside live cells and tissues is a priority. pH indicators and probes based on fluorescence responses have been produced over the last few decades, and various reviews detailing these advances have been published.[4–6] Because of their extreme sensitivity to acid and the exceptionally rapid rates of proton transfer that occur in acid-base equilibrium processes, alkyl, and aromatic amines are often appropriate compounds for use as hydronium ion indicators.[7] As a corollary, amine moieties are commonly used as acid-base reaction sites in fluorescent pH probes.

Alkyl and aromatic amines were involved in rapid acid-base equilibrium reactions. As a result, they were commonly used as part of pH-responsive probe construction procedures. Furthermore, amines are excellent PET quenchers of singlet excited states of fluorophores because of their great electron-donating capabilities. As a result, the free amine form was used in PET processes, but their protonated forms cannot act as electron donor fluorescence quenchers.



1 **2, R = Me, Ph** **2+H+, R = Me, Ph**

Non-protonated Form (Low/No Fluorescence) **Protonated Form (Highly Fluorescence)**

"Bimane" is the familiar name of a class of low molecular weight, heterobicyclic molecules sharing the 1,5-diazabicyclo[3.3.0]octa-2,7-diene-4,6-dione core.[8] Bimanes exist in two isomeric forms: *syn* & *anti*. syn-Bimanes (**1**) are generally accompanied by high quantum yield fluorescence and thus attract considerable interest for applications ranging from biological fluorescent probes to laser dyes. Although bimanes have been known for the last forty years, they have not yet been as extensively examined like other fluorophores such as rhodamine B, BODIPY etc. Currently, bimanes can be readily prepared following our simplified procedures.[9,10] In the present study we focus on the development of first NIR pH responsive molecular switches based on the syn-bimane dyes was applied to the design of unsymmetrical bimanes (**2**).

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Na7[SbW6O24]: A new sensitive and reusable luminescent solid sensor for water detection

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The detection and quantification of water either as trace in organic solvents, or as relative humidity (RH) in air have attracted wide interest over the past years, because of their great significance in industrial process controls, batteries life extension and indoor air quality improvement [1]. In the last five years, photoluminescent (PL) solid sensors for water molecules [2] have been considered as an attractive potential alternative to traditional analytical technics due to their faster response, higher sensitivity and ability of in situ detection. However, new sustainable and reusable sensors are still highly desirable.
Polyoxometalates (POMs) are photoactive molecular oxides of transition metals (W, Mo, V) which are widely investigated as PL sensors of a wide range of analytes,[3] but their ability to detect water have been very scarcely explored.
We have recently designed a new anhydrous sodium salt of the lanthanide-free POMs $[SbW_6O_{24}]^{7-}$ whom the highly intense luminescence at room temperature is reversibly tunable with its degree of hydration (Figure 1). Indeed, combined powder X-ray diffraction (PXRD), thermogravimetric (TGA) and PL analyses revealed that upon exposure to moisture-laden air (100% RH), $Na_7[SbW_6O_{24}]$ is progressively converted to the known hydrated phase $Na_7[SbW_6O_{24}]\cdot 16H_2O$ [4], and the rehydration process is accompanied by a drastic luminescence quenching. Moreover, $Na_7[SbW_6O_{24}]$ particles dispersed into acetonitrile can also detect trace amounts of water (0.008 v%) by rapidly reforming the PL-inactive hydrated salt. Noticeably, the luminescence quenching can be then easily reset by simple thermal dehydration, making $Na_7[SbW_6O_{24}]$ a promising robust and reusable PL solid sensors for water detection.

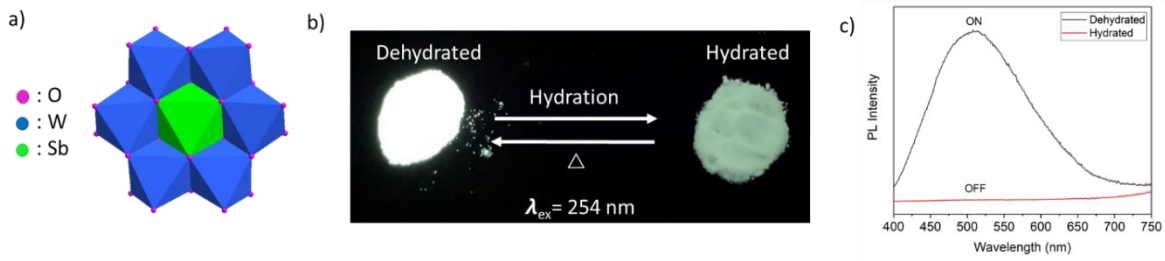

Fig. 1: a) Structure of the $[SbW_6O_{24}]^{7-}$ "Ln-free" POM. b) Photographs and c) photoluminescence (PL) spectra of $Na_7[SbW_6O_{24}]$ (dehydrated) and $Na_7[SbW_6O_{24}]16H_2O$ (hydrated) under UV excitation (λ_{ex} = 254 nm), during a hydration/dehydration cycle.

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Time series analysis of the air pollutions around Ploiesti oil refining complex, one of the most polluted region in Romania

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Refineries and petrochemical industries producing a number chemicals products, negatively influence the air quality by a number of pollutants like Volatile Organic Compounds (VOCs), greenhouse gases and particulate matter during operation. The primary goal of this research was to analyze the time series of $PM_{2.5}$, PM_{10}, As, Cd, Ni, Pb, Benzene, Toluene, Ethylbenzene, o-xylene, m-xylene, p-xylene, CO, NO, NO_2, NO_x, SO_2, and O_3 over a 11-year period (2009-2019) and the connection between air pollution and meteorological parameters (air temperature, precipitation quantity, relative humidity). The studied pollutants except for the SO_2 and O_3 the minimum pollution level during warmer periods, and the maximum concentrations were detected in winter. The meteorological parameters play an important role in the pollutant concentration distribution, due to this fact the highest values of air pollutants concentration in the winter season were 1.25 times higher than in autumn, 1.3 times higher than the annual, 1.57 times higher than in spring, and 1.79 times higher than in summer. Monthly variation of O_3 showed lower concentration during the winter (27.62 µg/m^3), and the higher concentration the summer (46.42 µg/m^3).

Bundle-Type Columnar Cuprous Oxide Photoabsorbers with Vertical Grain Boundaries Fabricated Using Instant Strike-Processed Metallic Seeds and Their Enhanced Photoelectrochemical Efficiency

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The design to control grain boundaries (GBs) causing recombination losses as planar defects in the absorbing layers is an essential strategy for the development of highly efficient photoelectrochemical (PEC) reaction systems. We propose a method to design a progressive bundle-type columnar structure as an alternative to single crystals with the least defects, where the GBs are parallel to the charge transport movement and the electric field direction. An instant strike bias (0.01 s and −1 V vs Ag/AgCl) in the same electrolytes induces the formation of island-shaped metallic Cu nanoparticles in the initial stage. These act as seed crystals for controlling Cu_2O growth evolution, resulting in dramatically high-density Cu_2O nuclei. This is followed by the deposition of bundle-type columnar Cu_2O with longitudinal GBs, contrary to the typical randomly crystallized Cu_2O. Metallic Cu seeds with a stronger electric field than that of the exposed indium tin oxide (ITO) region provide selective crystallization sites for Cu_2O growth along the ⟨111⟩ ionic bonding. Despite the instant strike interval, the p-type Cu_2O photoelectrodes retained an outstanding photocurrent density of 5.2 mA cm^{-2} at 0 V_{RHE} and an onset potential of 0.7 V_{RHE} because of the highly improved charge transport and transfer efficiencies inside Cu_2O induced by effectively suppressing charge scattering in the GBs. The impedance measurements depict the overall decrease in the total resistance, charge-transfer resistance, and the photoabsorber/electrode interface resistance of the PEC systems with the introduction of the instant strike process [1].

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Novel electrode materials for monitoring of biologically active organic compounds of environmental, biological and medical importance

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The main driving force behind the development of new voltammetric/amperometric methods for monitoring of biologically active organic compounds important from environmental, biological and medicinal point of view is the search for novel electrode materials and for new methods of their pre-treatment and modification to improve figure of merits of newly developed methods. This contribution will be devoted to the use of the following novel electrode materials:

1. Solid amalgams [1,2] as a non-toxic and „green" substitute for metallic mercury suitable for monitoring cathodically reducible compounds and for enzymatic biosensors
2. Boron doped diamond films [3,4] with extremely broad potential window, low noise and high resistance to passivation
3. Bismuth [5] and Antimony [6] suitable for cathodic processes
5. Carbon films containing various metallic nanoparticles [7] or carbon particles [8] and suitable e.g. for the evaluation of human macrophage functional state or for electrochemical immunoassay of tick-borne encephalitis,
6. Nanostructured hydrophobic carbon prepared by hydrogenation of carbon formed by pyrolysis of acetylene suitable for monitoring of neurotransmitters
7. Nanostructured metals deposited on various substrates and suitable for monitoring of electrochemically active pesticides, etc.).

Attention will be paid to their pre-treatment, chemical and/or biological modification (enzymatic and or by DNA) and application both in batch arrangement and in flowing systems (FIA, BIA or HPLC with electrochemical detection). Selected examples of using these approaches for monitoring of ecotoxic compounds (e.g. environmental carcinogens and some anticancer drugs as emerging new pollutants), pesticides, various biomarkers etc. will be demonstrated.

Acknowledgement

This research was supported by Czech Science Foundation project No. 20-01589S. Technical, material and intellectual support from Metrohm Czech Republic is gratefully acknowledged.

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Influence of matrix porosity on the heat storage capacity of MOFs based materials–hygroscopic salt composites

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Solar energy is one of the most promising types of renewable energy thanks to its high availability and low cost [1]. Energy storage systems have therefore been developed in order to reduce the discrepancy between demand and supply. In particular, thermochemical heat storage systems using reversible sorption/desorption reactions offer high energy storage density over variable amounts of time with minimal heat losses. Water sorption storage systems using hygroscopic salts such as $CaCl_2$ inside a porous matrix are widely used [2]. These composite materials allow the storage of energy (solar or from any other source) during dehydration (charge) and its release during hydration (discharge). Among porous materials, Metal-Organic-Frameworks (MOFs) have recently been of particular interest because of their high sorption capacity (due to their very high surface area) and tunable properties [3].

This work proposes a study of heat storage/release and water sorption/desorption capacity of composite materials. The materials were subjected to analysis by TG-DSC coupled to a humidity generator during successive hydration/dehydration cycles. A first series of materials based on aluminum fumarate MOF impregnated by different amounts of $CaCl_2$ (25,37 and 58 wt.%) were synthesized (AF-Cax, figure 1). DSC analysis showed that after impregnation, the heat storage/release capacity of MOFs gradually increases with the salt content, reaching 1840 kJ kg^{-1} for sample MOF-Ca_3 (MOF + 58 wt.% of $CaCl_2$). A concomitant increase in water sorption/desorption capacity, as determined by thermogravimetric analysis, is observed (figure 1). The storage properties of MOF-Ca_3 decreases by only 6% after 4 dehydration/hydration cycles, and then remains stable, thus showing the high stability of this material. Moreover, the presence of highly hygroscopic $CaCl_2$ enhances the surface affinity for water and hydrophilicity of the composites, leading to a faster sorption rate.

The storage properties of a second series of materials based on aluminum fumarate membranes on alumina support (AF/Al-Cax, Figure 1) with both micropores/mesopores and a different morphology than aluminum fumarate have also been studied. A comparison of the physico-chemical characteristics of the studied materials sheds light on the impact of host matrix porosity on the properties of the composites. Overall, the remarkable storage capacities of these new materials suggest that they can play a significant role in addressing the problem of renewable energy storage.

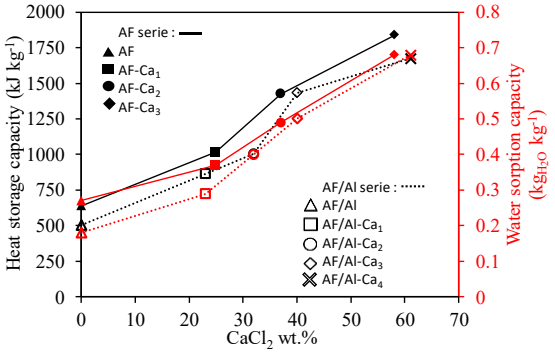

Figure 1: Water sorption and heat storage capacities of composite materials as a function of deposited amount of $CaCl_2$.

Acknowledgments: The authors thank the National Research Agency for the financial support (ANR STOCK-CAR 18-CE-0044).

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Sulfonated MXenes as efficient catalysts for PET depolymerisation

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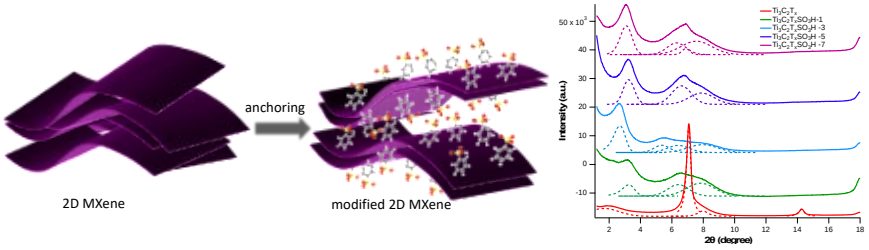
Industrial production of plastics started after the World War II and, today a world without plastics, or synthetic organic polymers, seems unimaginable. Extreme durability of plastics and the sustainability lack of current recycling efforts has rendered the polymers a long-term environmental concern and become a threat to global ecology. Therefore, there is an urgent need to tackle these environmental issues that thrown a shadow over the importance of these materials that play an important role in our economy and daily lives. Heterogeneous catalysis plays a critical role in the chemical processing of waste plastics in terms of promoting targeted reactions, reducing reaction temperature and improving process system efficiency. The most investigated catalysts for plastic pyrolysis are solid acid ones, such ZSM-5, Y-zeolite, USY or MCM-41 [1,2]. To date, none of these have demonstrated outstanding performance and this is why for this process, a viable industrial approach has not yet been developed. Therefore, the ultimate goal of this study is to find new solid acids able to depolymerize PET to the raw materials. Among newly discovered materials, *MXene*, a novel family of two-dimensional (2D) metal carbides, with graphene-like structures is produced by etching of A from of MAX phase [2,3] has drawn our attention. A potentially useful approach to control *MXenes*' catalytic activity is *to manipulate their surface* chemistry [5,6]. Therefore, during this study we intend to extend the *MXene*' acidity by modifying the surface with acidic moiety to have $–SO_3H$ modified MXene (Scheme 1) capable to depolymerize PET by hydrolysis.



Scheme 1. Sulfonation of MXene materials

Modified MXene with sulfonated groups was realized by grafting $–SO_3H$ groups using sulfonated aryl diazonium salt of sulfanilic acid. Different amounts of sulfanilic acid salt were used, in order to establish the influence of the sulfonic group concentration onto the surface, and were denominated $Ti_3C_2Tx–SO_3H$-y, where y=(1, 3, 5, 7). The modified MXenes were investigated by several techniques (XRD, DRIFT, RAMAN, SEM, TEM) and demonstrate that the MXene structure remains lamellar and did not collapse during the modification process. Moreover the distance between sheets increases after modification (see XRD from Scheme1) due to the aryl sulfonate groups anchored between the MXene layers. EDX-from SEM and XPS have confirmed the presence of SO_3H groups on the MXene surface. The use of these materials in PET depolymerization in water showed complete conversion and a yield of 75% terephthalic acid, with terephthalic acid as only product. The influence of reaction parameters: temperature, pressure and amount of catalyst was also studied and indicated that $Ti_3C_2Tx–SO_3H$-y are potential candidates for processing efficiently PET in environmentally friendly conditions.

This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS/CCCDI – UEFISCDI, project number PN-III-P1-1.1-TE-2019-1969, within PNCDI III.

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Regeneration of iron-coated cork granulates contaminated with arsenic: batch and fixed-bed column studies

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Arsenic contamination from waters is a worldwide problem affecting more than 230 million people in 108 countries [1]. Limiting arsenic concentrations in drinking water is one of the best ways to control poisoning and mortality. In terms of advanced water treatment technologies, adsorption is considered the most efficient and inexpensive solution [2] and for arsenic removal, it holds better prospects than other treatment techniques [3]. Desorption and regeneration of the adsorbent play an important role in the adsorption process, in ecological and economical terms [4]. Iron-coated cork granulates (ICG) are modified biosorbents that were developed and successfully applied in batch mode adsorption of As, Sb, and P [5-8] and in a continuous operation lab-scale column for removal of As [9]. In this context, this work investigated the chemical desorption of arsenate from saturated iron-coated cork granulates (ICG) and its regeneration capacity in batch and column modes. Different types of eluents (bases, acids, salts and complexing agents) were tested at different concentrations for their desorbing capacity. Moreover, iron and total organic carbon (TOC) were measured in the eluates to assess the eluent's attack on the adsorbent structure. In terms of desorption efficiency, the basic solution of NaOH 0.1 M achieved the highest arsenic removal rates from saturated media, however, it was aggressive to the adsorbent structure according to high TOC values. The Elovich model ($r^2 >$ 0.98) fitted best the desorption kinetics for sodium hydroxide at different concentrations. The less basic solution of NaOH 0.01M was less aggressive to ICG and allowed media regeneration for at least four adsorption-desorption cycles with a remaining arsenic adsorption capacity of 1 mg g^{-1}, in both batch and continuous modes. ICG´s adsorption capacity was less affected after various cycles than other adsorbents [10, 11] and proved to be potentially applicable on an industrial scale as an alternative green solution for arsenic removal from waters.

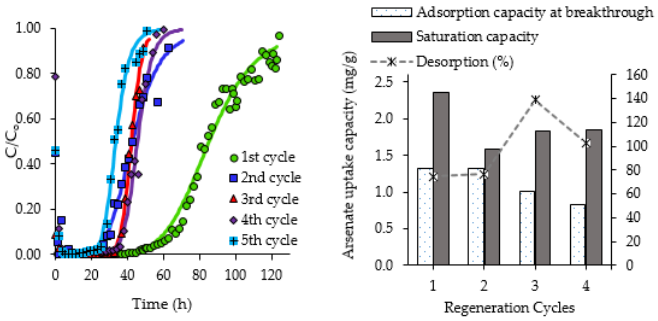

Figure 1. Regeneration of iron-coated cork granulates in five adsorption-desorption cycles using NaOH 0.01M: a) breakthrough curves (left), adsorption and desorption rates in continuous mode (right).

This work was financially supported by LA/P/0045/2020 (ALiCE), UIDB/50020/2020 and UIDP/50020/2020 (LSRE-LCM), funded by national funds through FCT/MCTES (PIDDAC). A. Pintor acknowledges her Junior Researcher contract [CEECIND/01485/2017] by FCT. M. Carneiro acknowledges her Ph.D. scholarship by FCT [2020.07233.BD].

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Phosphorus remediation using a new magnetic system in aqueous samples

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Phosphorus is a natural element that can be found in soils and aquatic ecosystems. Its presence over the recommended concentration, damages the hydrosphere equilibrium, through eutrophication. Consequently, there is a strict environmental regulation that limits the concentration of this element in waste water. Currently, Wastewater Treatment Plants (WWTP) reduce the concentration of phosphorus in water using physical-chemical and biological treatments, which presents several disadvantages. For physical-chemical treatments are the increase of costs and water volume, as well as the disqualification of the water for further agricultural uses; for biological treatments the main disadvantages are the non-stable conversion yields, becoming necessary a combination with physical-chemical treatments. In this work, a wastewater treatment process has been developed to remove phosphorous by adsorption on a patented nanomaterial, M@GO, which combines both excellent adsorption properties of graphene oxide and magnetic nanoparticles and presents a good compromise between adsorbent properties, easy use and low toxicity. M@GO has a high surface area which allows the rapid removal of phosphorus, moreover the material is easily removed and re-used using a magnetic field. The kinetics of the process have been studied, showing a good approximation to the Langmuir's theoretical model. The magnetic adsorption procedure has shown a performance of 50% in 30 min for the elimination of phosphorus, with a dosage of 0.8 g/L of M@GO in a wastewater with an initial concentration of 0.918 mg/L of phosphorus. Once the kinetic parameters and the mathematical expression that relate them have been obtained, the scale has been proposed at a semi-industrial level.

Acknowledgements

The authors thank “Proyecto Prueba de Concepto E30521, Plan Propio, Universidad de Málaga” for financially supporting this study.

Vertical distribution of organic tracer compounds in atmospheric aerosols: Measurement by using meteorological balloons

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Outdoor air pollution constitutes a global threat to ecosystems and human health [1]. The highest human exposure to airborne pollutants is generated by combination of source emissions and adverse atmospheric conditions, such as temperature inversions.

Under temperature inversions, primary emitted atmospheric pollutants are retained in the lowest air layers, which results in strong concentration increases which often involves a need for precautionary health warnings. Moreover, secondary aerosols may be formed under these conditions which involves changes in the qualitative and quantitative composition of aerosols in the upper air layers. Understanding the main changes in composition of these compounds at molecular level will help to define the best strategies to improve air quality and reduce health risks.

The present study aims to analyze the vertical distribution of particle-associated organic pollutants and Black Carbon (BC). The sampling methodology consists in two simultaneous air filtration systems within and above the temperature inversion layer, using captive balloons equipped with particulate matter (PM) samplers and BC monitors.

The organic pollutants are studied under several types of temperature inversions in urban, semiurban and rural environments in different seasons, such as the semiurban area of Osona (Catalonia) where high winter benzo[a]pyrene concentrations and high ozone summer concentrations have been observed [2].

The particle-associated pollutants selected for study involve polycyclic aromatic hydrocarbons (PAHs), anhydrosaccharides, hopanes, phthalates, and other secondary synthesized (SOA) compounds. Some of them are used as molecular tracers to identify the contribution of emission sources and secondary formation to PM [3]. The chemical analysis was performed with a high-resolution Q Exactive GC Orbitrap GC-MS/MS (GC-Orbitrap-MS).



Figure 1. BC and PM sampling with a captive balloon.

Acknowledgement - Technical assistance from R. Chaler is acknowledged. Financial support for this study was provided by the research project from the Plan Nacional de I+D+i of the Spanish Ministry of Science and Innovation INTEMPOL (PGC2018-102288-B-I00) and a Training of University Teachers (FPU) grant from the Ministry of Science and Innovation (Spain). IDAEA-CSIC is a Severo Ochoa Centre of Research Excellence (Spanish Ministry of Science and Innovation, CEX2018-000794-S).

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Long-range visible-light C3N4 photo(electro)catalysts derived from triazol-purpald for benzylamine oxidation and oxygen evolution reactions

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Efficient visible light catalysts are urgently needed to exploit the sun's light. According with the American society for testing and materials (Air Mass 1.5 Spectra)1 the visible range irradiating the Earth's surface is approximately 43% of the total upcoming photons, the most representative region. One of the bottlenecks to ensure significant deliverables in photo(electro)catalysis is available efficient light absorbers.2 In this context, purpald, a triazol derivative3, it is used as platform molecule to rational design functional materials with enhanced visible absorption utility.

The purpald-based materials are synthesize in a single solid-state event comprising two thermal steps, i.e., 250 and 550 °C in presence of melamine. The first step serves to prepare the liquid phase condensation of the two precursors to stimulate the synergic effect. The following step at 550 °C defines the crystallinity degree accompanied by their organizational heptazine units in both in plane and bulk directions. A series of composites varying the purpald and melamine proportions were synthesized. The aim to assess the optimal proportion against benzyl amine oxidation in saturated oxygen and in oxygen evolution reaction (OER) in a standard three-electrode cell system.

The purpald/melamine composites were fully characterized by coupling, X-ray diffraction, X-ray photoelectron, photoluminescence, infrared and UV-vis spectroscopies, thermal gravimetric analysis, SEM and TEM imaging for evaluating their structural, optical, electronical, morphological, compositional, and thermal properties. Photo oxidation and photoelectrochemical measurements were carried out to correlate the structure-activity relationships.

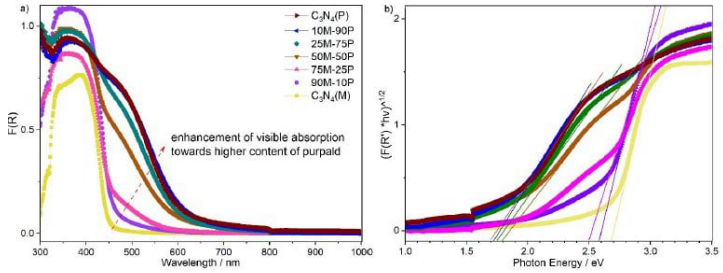

Figure 1. (a) UV-vis spectra via Kubelka-Munk function representation of the purpald/melamine composites and references (b) Tauc plot to determine the apparent band gap of the long-range visible-light semiconductors.

The 50M-50P composite exhibited the highest conversion yield (84±3) of benzylamine to dibenzylimine in the green monochromatic light (535 nm, 20 W LED lamp) after 48h of irradiation. This result is attributed to the co-existence of macro-meso-micropores, the unusual high Sulphur content (1.6wt. %) for a carbonaceous material, enhance large tail in the visible (450-650 nm, Figure 1). Contrarily, the 10M-90P composite exhibited the major photocurrent (0.6 μA cm-2) under full spectrum lamp, presumably for its distinctive strip morphology allowing different access to its surface active sites. Moreover, the lowest Tafel slope was found for the 75M-25P composite. Such result was ascribed to its larger mesopores sizes, enhanced surface area, and farest flat band potential (2.4 V vs RHE) in respect to water oxidation (H2O/O2: 1.23 V vs RHE).

The authors thank Bolortuya Badamdorj for TEM/SEM analyses, Antje Voelkel for TGA, elemental analysis, Jessica Brandt for ICP measurements, Marco Bott for the conception of the electrochemical cell associated accessories. The authors thank the Max Planck Society for its financial support.

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Toxicity of Gadolinium on *Stevia rebaudiana* grown *in vitro*

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Lately, there is growing interest towards the potential toxicity that different nanomaterials or chemicals used more and more extensively in everyday life applications could exert on the environment and on edible plants. Gadolinium (Gd)-based contrast agents are extensively used for diagnostic purposes in magnetic resonance imaging (MRI). Since their approval in 1980's, they have become indispensable for diagnostic imaging, and are currently being used in 33-50% of the MRI investigations [1]. Apart from their tremendous contribution in disease diagnostic, there are several issues related to their use. After administration, the Gd-based contrast agents are excreted unmetabolized and a significant amount is present in hospital effluents and, consequently, in wastewaters [2]. For example, Gd presence in tap water and tap water-based beverages such as Coca-Cola from fast-food franchises in big cities in Germany has been documented [3,4].

In this study, we have assessed the accumulation of Gd on *Stevia rebaudiana* grown *in vitro*, and its impact on plant growth and on plant metabolites such as chlorophylls, carotenoids, ascorbic and dehydroascorbic acids. The plants were exposed to gadobutrol, a macrocyclic compound used as NMR contrast agent, in concentrations up to 3 mM.

The Gd accumulation in the plant tissues was studied by inductively coupled plasma-optical emission spectrometry (ICP-OES) and it was found that accumulation increases in a dose dependent manner. Regarding plant growth and morphology, the results showed that the total plant length and biomass was affected by Gd exposure.

The plant metabolites were quantified using high performance liquid chromatography (HPLC). The concentrations chlorophyll A and B, lutein, zeaxanthin, and beta-carotene showed the same trend upon exposure to increased Gd levels. Their concentrations increased up to 0.1 mM Gd doses, while for the highest exposure level of 1mM and 3 mM, the concentrations of all investigated analytes were significantly decreased compared to controls.

Such pronounced effects of Gd on the levels of antioxidant molecules can be related to a stress response of the plant, aspect which is supported also by plant morphology.

Acknowledgements: This work was supported by a grant of the Ministry of Research and Innovation, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2019-1424.

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Carbon-based monoliths with improved thermal and mechanical properties for methane storage

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Porous materials have been widely applied in the literature for a number of cutting edge processes, from gas adsorption/separation, sensors, drug delivery, etc. [1] The excellent performance of activated carbon materials is based on the presence of a widely developed porous structure and, in some cases, a perfectly tailored surface chemistry. However, bridging the gap from fundamental studies to a potential industrial application of these materials is not straightforward and, indeed, some limitations are still on the ground and require further investigation. One of these limitations concern the densification of these powder samples into pellets, monoliths or any other shape. The conformation of these porous networks is mandatory i) to minimize pressure drops in gas and liquid-phase adsorption processes, ii) to facilitate the manipulation of the material (charging and discharging), iii) to densify the samples and iv) to minimize environmental and health issues due to particulates. [2][3]

A series of activated carbon monoliths have been prepared from petroleum residue using KOH as activating agent. Activated carbon powder have been conformed into monoliths using a small amount of a binder (5 wt.%), either carboxymethyl cellulose (Figure 1a) or polyvinyl alcohol (Figure 1b), with proper mechanical properties. Incorporation of graphite or graphene in the initial formulation does not alter and/or modify the textural properties of the original activated carbon. However, once conformed into monoliths, the presence of graphite or graphene allows to improve i) the packing density of the monolith (up to 0.52 g/cm3), ii) the mechanical properties of the monoliths (compressive strength up tp 12.3 MPa) and iii) their thermal conductivity (up to 0.49 W/mK) without compromising the methane storage capacity (ca. 100 V/V).



Figure 1. Images of a typical carbon monolith synthesized using 5 wt.% of (a) carboxymethyl cellulose or (b) polyvinyl alcohol as a binder.

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Calcium and magnesium modified cork biochars for the removal of phosphate from water

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There is a rising environmental concern with the management of phosphorus. On the one hand, it is an essential nutrient for crop fertilisation, and its reserves as phosphate rock are being depleted, with shortages predicted in a horizon of 50-100 years [1]. On the other hand, its discharge as dissolved phosphate onto water reservoirs leads to eutrophication and loss of aquatic life [2]. Therefore, a technology to minimise phosphorus discharge in wastewaters, while at the same time recovering it in the form of a usable product, is being increasingly sought after.

Adsorption is an easy-to-operate methodology that is adequate for treating low phosphate concentrations [3]. It also concentrates phosphorus on a solid surface, from where it can be recovered. Biochars are low-cost black carbon materials produced from the pyrolysis of biomass. When modified with calcium or magnesium, they have shown high capacities for phosphate adsorption [4].

This work proposes using cork granulates, a byproduct of cork processing, to produce biochars for phosphate removal from water. Cork is a natural, renewable material extracted from the bark of the cork oak (*Quercus suber* L.). Its application as a precursor of adsorbent materials has been widely tested, although rarely for the production of biochars [5].

Design of experiments was used to study several production factors, such as modification element (Ca or Mg), impregnation time, and pyrolysis temperature, heating ramp, duration, and gas (N_2 or CO_2), to optimise biochar production for maximum phosphate uptake from water. A best-performing biochar was selected, also considering the environmental aspects of production, such as energy expenditure and pyrolysis yield. From the obtained results, the modification using magnesium showed substantial advantages compared to calcium.

The novel biochars can be used to recover phosphate from diluted wastewater streams and, due to their characteristics after saturation, are appropriate to be applied as fertilisers in soil [6]. Therefore, the devised solution contributes to the efficient management of the phosphorus cycle while at the same time providing advantages in the valorisation of the cork industry.

This work was financially supported by LA/P/0045/2020 (ALiCE), UIDB/50020/2020 and UIDP/50020/2020 (LSRE-LCM), funded by national funds through FCT/MCTES (PIDDAC). A. Pintor acknowledges her Junior Researcher contract [CEECIND/01485/2017] by FCT.

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EDC-WFD: A project to deliver reliable measurements for better monitoring survey and risks assessments

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Monitoring programs should generate high-quality data on the concentrations of substances and other pollutants in the aquatic environment to enable reliable risk assessment. Furthermore, the need for comparability over space and time is critical for analysis of trends and evaluation of restoration of natural environment. Additionally, research work and exercises at the European level have highlighted that reliable measurements of estrogenic substances at the PNEC level are still challenging to achieve.

The project **EDC-WFD Metrology for monitoring endocrine disrupting compounds under the EU Water Framework Directive** aims to develop traceable analytical methods for determining endocrine disrupting compounds and their effects, with a specific focus on three estrogens of the first watch list (17-beta-estradiol (17βE2), 17-alpha-ethinylestradiol (EE2), and estrone (E1)). Estrogens 17-alpha-estradiol (17αE2) and estriol (E3) will be included to demonstrate the reliability of the developed methods and to support the requirements of Directive 2013/39/EC, Directive 2009/90/EC and Commission Implementation Decision (EU) 2018/840, hence improving the comparability and compatibility of measurement results within Europe. During the EDC-WFD project four selected effect-based methods (EBM) will be deeply investigated in order to improve their rationale use and their support in **water quality assessment**. In particular, the **EBM** sensitivity, **specificity** and **accuracy** on **reference materials** with single or mixture solutions of the **five substances at a concentration of EQS** values will be explored.

This contribution will present the objectives and methods applied within the EDC-WFD project.

From an abundant agrochemical waste to a sensitive and selective sensor of azo dyes

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Olive oil production is quite significant for European agro-industrial economies (68% of the worldwide quota). Two-phase extraction systems are currently the most used to produce olive oil, resulting in a by-product called wet pomace, which reaches around 800 kg/ton of processed olives [1]. We have recently shown that nanostructured carbon-based materials, hereafter called carbon nanodots (CNDs), can be produced from industrial wastewaters from olive oil mills [2]. Furthermore, CNDs were also successfully synthesized from wet pomace [3]. Owing to their excellent luminescence properties (high photostability and fluorescence quantum yield), their use as fluorescence probes for azo dyes was considered.

Herein we report the high sensitivity and selectivity of the CNDs towards two azo dyes in aqueous media: methyl orange (MO, an anionic dye) and methyl red (MR, a neutral dye). Using the Stern-Volmer (SV) formalism, a $K_{SV} = 3.67 \pm 0.16 \times 10^4\ M^{-1}$ was obtained for the most responsive dye, MO. Competitive assays were conducted with a series of organic dyes and transition metal cations, which unambiguously showed a high selectivity to MO (Figure 1). Time-resolved fluorescence measurements have indicated that a predominantly static quenching mechanism was operating ($\tau_0/\tau = 1$). Two possible quenching mechanisms were envisioned, both occurring at very fast rates: a photoinduced electron transfer (PET) or a resonance energy transfer (RET). All the results will be highlighted and discussed in the presentation.

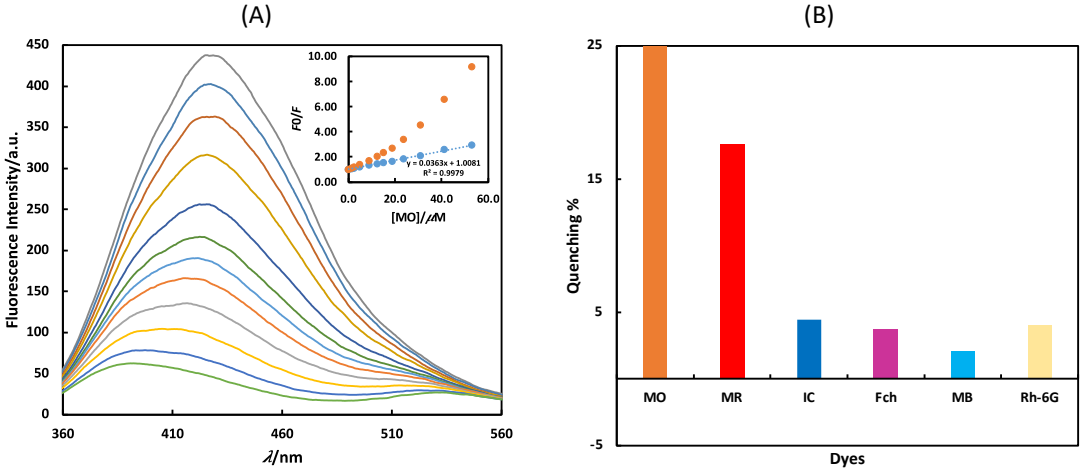

Figure 1 – (A) – Emission spectra of CNDs (0.1 mg/mL) upon titration with MO in phosphate buffer (pH = 7.2) at 25 °C; inset: Stern–Volmer plots obtained from uncorrected fluorescence intensities (orange dots), and after correction for inner filter effects (blue dots). Steady-state data acquired under excitation at 340 nm and 427 nm observation. (B) – Quenching of CNDs fluorescence emission upon contact with MO, MR, Indigo Carmine (IC), Fuchsine (Fch), Methylene Blue (MB) and Rhodamine 6G (Rh-6G) at 10 μM in water.

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Acknowledgments: *We are grateful to Fundação para a Ciência e a Tecnologia/Ministério da Ciência, Tecnologia e Ensino Superior (FCT/MCTES) for financial support (UIDB/00616/2022 and UIDP/00616/2022 and for iBB projects UIDB/04565/2022 and UIDP/04565/2022 and i4HB project LA/P/0140/2020). D. A. S. thanks FCT for the doctoral grant SFRH/BD/143369/2019.*

Decontamination of natural aquatic systems from paralytic shellfish toxins (PST) – a molecular perspective

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Every year, around the world, there are long periods of interdiction to the picking of bivalve molluscs, attributed to the detection of marine biotoxins above the maximum limits legally established, which cause enormous economic and social damages. Paralytic shellfish toxins (PST) represent the highest percentage (46%) [1] of the events associated with seafood toxins and are those causing the most serious health consequences in humans, including death. PST are a large group of toxins, sharing a common core structure (Figure 1). The combination of different functional groups (R1 – R4) defines the subgroup of each analogue (e.g., carbamoyl, *N*-sulfacarbamoyl, decarbamoyl, benzoyl) and influences its mode of action and toxicity level [2]. Some methodologies for decontamination of bivalve molluscs have been disclosed, but most of them imply their death after harvesting, greatly undervaluing the product. Regarding the *in vivo* methodologies, their effectiveness is highly variable, depending on the biotoxin and the species of bivalves tested. In addition, the time required for decontamination far exceeds the recommended depuration time. So, as far as we know, there are currently no methods capable of quickly and efficiently reducing or eliminating marine biotoxins in live bivalve molluscs.

Our group has been working on the development of chemical methodologies to remove PST from natural aquatic systems. Experiments have been conducted using cultures of microalgae that produce these toxins, and in bivalves, following the recommended procedures [3]. For the removal of toxins, a selected adsorbent has been tested over different times. Toxins in natural samples are quantified by HPLC-FLD [4] and the results are promising, revealing different removal kinetics for each toxin subgroup. Therefore, the main objective of this work is to discuss the chemical interaction between each toxin and the adsorbent, focusing on the molecular structure and the contribution that each functional group has to the faster or slower kinetics of adsorption (removal).

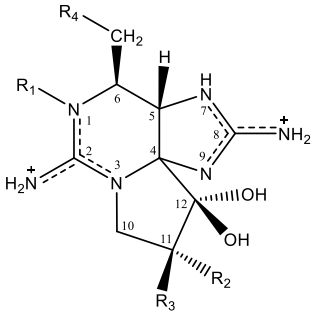

Figure 1 - Representation of the molecular structure of PST, with positive charge fully delocalized.

This study received funds from the project MAR-01.03.01-FEAMP-0049 co-financed by the Operational Program Mar 2020, Portugal 2020 and the European Union (EU), through the European Maritime Affairs and Fisheries Fund (EMFF), and from FCT – Foundation for Science and Technology, through projects UIDB/04326/2020, UIDP/04326/2020 and LA/P/0101/2020 (CCMar). The authors gratefully acknowledge the financial support.

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New environmental friendly disinfectant from bio-based sources: virucidal and bactericidal effects of permaleic acid

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In the last years, research for alternative methods of disinfection is a current and on-going challenge in both Academia and Industry. Microbicides available on the market show toxicity to humans and the environment. The increased attention to environmental issues related to food safety, quality of drinking water and irrigation, as well as the quality of the atmosphere in agricultural and industrial environments, has raised important safety concerns about the application of these chemicals. Peroxycarboxylic acids are excellent oxidizing agents and disinfectants; in particular, peracetic acid is a strong disinfectant with a wide spectrum of antimicrobial activity. However, peracetic acid have some disadvantages associated with the increases of organic content in the effluent, its high cost and its strong odour due to acetic acid. For this reason, we introduced new formulation based on permaleic acid to substitute peracetic acid in, disinfection and inhibition of microorganism growth on surface in hospital sector, food industry and swimming pools. The advantages of permaleic acid for disinfection are the absence of persistent toxic or mutagenic residuals or by-products (permaleic acid degradation produce only CO_2 and H_2O), no quenching requirement (i.e., no dechlorination) and short contact time. In such a case, in addition to having environmental advantages, permaleic acid become cost-competitive with chlorine.

Surveillance is an important issue in public health, linked to the severity of disease and the difficulty associated with eradicating some bacteria and viruses from the water environment. In this work permaleic acid was also tested as an oxidizing agent against three human viruses, such as HSV-1, HCoV-229E and SARS-CoV-2. The inhibition of the viral infectivity was evaluated on different surfaces: plastic, metal, and paper. PMA exhibited a great antiviral effect against all the tested viruses in the range from 3.1 to 50 g/L, and its efficiency resulted better compared to PAA. In addition, SARS-CoV-2 infection was abolished when plastic and metal surfaces were treated with both PMA and PAA, and interesting results were obtained also on the paper surface. The antimicrobial properties were also assessed against Escherichia coli (E. coli) and Staphylococcus aureus (S. aureus) of a new organic peracid, permaleic acid (PMA) compared with the reference peracetic acid (PAA). Disinfectant properties were evaluated by i) disk diffusion agar, ii) broth microdilution, iii) antibiofilm properties. PMA demonstrated a 10- and 5-fold increase in the microbial inhibitory concentration MIC value against E. coli and S. aureus respectively, compared to PAA. Results showed greater efficacy of PMA regarding wastewater WW and treated wastewater TWW disinfection at low concentrations. Based on these promising data, both peroxycarboxylic acids, and especially PMA, could be considered as a valid alternative to the currently used disinfection agents for workplaces and in a variety of other indoor spaces and facilities.

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Potential of synthetic flavonoids as a sustainable alternative for marine biofouling prevention

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One of the major issues for maritime industries is the settlement and accumulation of marine organisms, such as bacteria, diatoms, bryozoans, and mussels, on submerged surfaces, which causes enormous material and economic losses, as well as environmental problems due to the spread of invasive species. To prevent this phenomena, tributyltin (TBT)-based coatings had been used for several decades, however, due to their toxicity against target and non-target organisms, TBT use was banned. Since then, other booster biocides have been incorporated in marine coatings, but these compounds also showed toxicity to the marine environment [1,2].

As an attempt to discover new sustainable and low toxic antifouling compounds and considering the potential of some marine flavonoids as antifoulants [3], our research group has been focused on the synthesis and evaluation of antifouling activity of synthetic flavonoid derivatives [4,5]. Among them, several flavonoids showed promising antifouling activity, namely a prenylated chalcone C1P (Figure 1) [5]. Based on these results, and in an effort to develop more effective antifoulants, a series of chemically related flavonoid analogues was prepared (Figure 1) and evaluated for their antifouling activity in order to perform structure-activity relationship studies. The antifouling activity was investigated using the *in vivo* anti-settlement bioassay with *Mytilus galloprovincialis* larvae and marine biofouling microorganisms. From these studies, flavonoid derivatives with antifouling activity against macro and microfouling species were identified. Complementary assays with *Artemia salina* were also performed to evaluate their toxicity against non-target marine organisms. This study allowed to optimize C1P as well as to infer about the structure-antifouling activity relationship of prenylated flavonoids.

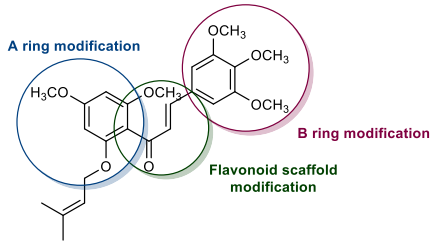

Figure 1. Structure of C1P and synthetic research plan.

Acknowledgements: This research was supported by national funds through FCT (Foundation for Science and Technology) within the scope of UIDB/04423/2020, UIDP/04423/2020, and under the projects PTDC/CTA-AMB/0853/2021 and NASCEM-PTDC/BTA-BTA/31422/2017 (POCI-01-0145-FEDER-031422), co-financed by COMPETE 2020, Portugal 2020 and the European Union through the ERDF and by FCT through national funds. DP acknowledges FCT for the Ph.D. scholarship (grant number SFRH/BD/147207/2019).

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Adsorption processes for the reclamation of R-32 from refrigerant blends and complex waste mixtures

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Fluorinated gases (F-gases) are commonly used in refrigerant systems and for other industrial applications, being used as substitutes for ozone-depleting substances. However, they are powerful greenhouse gases (GHG) with global warming potential (GWP) up to 20 000 times greater than CO_2. In the EU their emissions have increased up to 60% since 1990 and the EU regulation targets to cut their emissions by 2/3 in 2030, compared to the levels of 2014.[1]

Due to the impossibility to reclaim for reuse, resulting from the lack of appropriate technology or from contamination (e.g., all the collected refrigerants in the waste managers facilities are mixed in cylinders for incineration, and very complex mixtures are generated), many refrigerants with market value are being destroyed. The development of technologies for efficient reclamation of F-gases is relevant, not only to reduce GHG emissions to the atmosphere, but also because of their market value. A good example is the EU phase-down of R-410A (one of the most used refrigerants; R-32/R-125, 50/50 wt.%), that is driving the switch from R-410A to R-32 (neat or in blends with lower GWP).

In this work, we use an activated carbon and a zeolite to reclaim R-32 from the commercial blend R-410A and from a complex waste mixture. We studied the equilibrium [2] and kinetics of adsorption of the pure gases and of blends. Several breakthrough experiments were performed to study the dynamic behavior, to validate a mathematical model for process design by simulation, and to develop novel adsorption processes to reclaim high purity R-32 (99.5 wt% - AHRI standard)[3] with increased recovery.

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Functionalized carbon materials as catalysts in the oxidative leaching of copper and zinc sulfides

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The current technologies based on pyrometallurgy treatment for metals recovery from ores implement high energy and generate enormous waste materials. Hydrometallurgy processes have been considered as an alternative to pyrometallurgy due to their advantages including treating low-grade ores and decreasing environmental detriment. Nevertheless, the leaching kinetics of sulfides such as chalcopyrite in traditional acidic mediums tends to be complex and slow [1]. To accelerate it, several materials have been used as catalysts [2]. Among them, carbon materials are of great interest owing to their outstanding physicochemical properties such as developed porous structure, high surface area, high stability that make possible their recovery and recycling, and controlled containing surface functional groups [3-5].

This study aims to utilize six different functionalized carbon materials: commercial activated carbon (CAC), charcoal (C), sulfonic functionalized commercial activated carbon (sCAC), sulfonic functionalized charcoal (sC), biochar obtained from sunflower husk (BC), and magnetic hydrochar obtained from the orange residue (MHC) as catalysts on sulfuric acid copper and zinc leaching from an ore sample (Huelva, Spain).

The functionalized carbon materials were characterized by adsorption-desorption of N_2, elemental analysis, Fourier transform infrared spectroscopy (FTIR), and zeta potential as a function of pH. The recovery of copper and zinc after 24 hours of the leaching experiment was determined by IPC-MS analysis. The addition of six-carbon materials increases the recovery of both metals. Under optimized pH and temperatures, the highest extraction yields of copper (62%, and 75 %) were obtained after the addition of CAC and sCAD, respectively and only 24 hours of leaching. The recovery of zinc achieves 100% in the presence of CAC, sCAC, or BC.

Acknowledgments

This research has been funded by Ministerio de Ciencia, Innovación y Universidades (MCIU), Agencia Estatal de Investigación (AEI) and Fondo Europeo de Desarrollo Regional (FEDER) with grant number RTI2018-096695-B-C31

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Adsorption of copper and zinc using carbonaceous materials obtained from lignocellulosic wastes

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Heavy metal pollution has emerged as one of the most serious environmental challenges facing the world today. The removal of heavy metals from the effluent is of special environmental concern because of their toxicity and persistence in nature. Heavy metals can be accumulated in living tissues, causing various diseases and disorders. Copper and zinc are among the most common heavy metals in wastewater. Adsorption over activated carbons and cheaper carbonaceous materials such as biochar, is a common treatment of wastewater [1,2]. The presence of metals is also common in industrial processes. For example, during hydrometallurgical treatment of minerals or metallic wastes to produce metals, water needs to be re-circulated and concentration of metals need to be optimized. Additionally, during last years, different researches have studied the use of carbonaceous materials as catalysts in the hydrometallurgical treatment of sulfide minerals [3,4]. Some metals can be adsorbed on the carbonaceous materials being necessary their followed desorption for their recovery.

The aim of the present work was to evaluate and compare the use of cheaper carbonaceous materials and commercial activated carbon in the adsorption of Cu (II) and Zn (II) ions from acidic solutions.

Adsorption of copper and zinc was performed employing four different carbonaceous materials: commercial activated carbon (CAC), charcoal (C), biochar obtained from sunflower husk (BCSFH) and magnetic biochar from sunflower husk (MBCSFH). The preparation of BCSFH material was conducted employing pyrolysis (thermochemical treatment in limited oxygen atmosphere). Corresponding magnetic material (MBCSFH) was further obtained by co-precipitation of magnetite nanoparticles into the carbon matrix of BCSFH. Adsorption kinetics was performed using 25 ppm of initial concentration of copper, zinc and mixture of copper and zinc, during 180 minutes of contact time, continues agitation, and room temperature. The influence of initial pH was determined by preparing two aqueous solutions with different pH (pH=3 and pH=5) of copper ($CuSO_4 \cdot 5H_2O$) and zinc ($ZnSO_4 \cdot H_2O$). Moreover, dose of adsorbents material used in batch was 250g in 250mL of solution. In general, four carbonaceous materials used show higher adsorption values of zinc than copper. At pH=5, all carbonaceous materials show values of zinc elimination higher than 90% after 30 minutes. At pH=3, best eliminations were obtain using BCSFH and MBCSFH biochars.

Acknowledgments

This research has been funded by Ministerio de Ciencia, Innovación y Universidades (MCIU), Agencia Estatal de Investigación (AEI) and Fondo Europeo de Desarrollo Regional (FEDER) with grant number RTI2018-096695-B-C31

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Closed and zero-waste strategy for recycling and recovering gold, copper and fiberglass from waste printed circuit boards

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A vast fraction of e-waste generated worldwide is composed by waste printed circuit boards (WPCBs), approximately 6 to 10 % (wt.), which represents 1.61 to 3.22 Mt in 2019 **[1]**. This stream contains a considerable weight of valuable metals (such as gold, copper, silver, etc.), ceramics and polymers. The diversity and the economic value of these materials has made the recycling and recovery of WPCBs an interesting topic of research since the current technologies are not adequate and efficient to address this global issue. In this work, we aim to suggest a novel (a European patent was submitted **[2]**) and more environmentally friendly solution to recover high-value materials (gold plus copper) from the multi-structured layers of WPCBs.

This novel process includes, as shown in **Figure 1,** the following steps **[3]**: (i) the cutting of the connecting terminals of WPCBs containing gold fingers, (ii) the swelling of the cut WPCBs pieces in an appropriate organic solvent inside a low-pressure reactor (with stirring and temperature control), (iii) the recovery of the gold fingers from a mixture of copper foils and fiberglass using a magnetic separation process followed by sieving. Subsequently, microwave-assisted acid leaching with nitric acid was used to leach the base metals from the gold fingers. This process allowed recovering gold, as a solid metal, with high yield (99.9%) and purity grade (74%). Finally, copper was recovered from the acid leachate by alkaline precipitation (pH around 8.8), as a solid salt of copper, with high yield (99.9%) and a purity grade of 87%. Additionally, an economic assessment of the overall process was performed and evidenced to be highly competitive combined with the high sustainability (no generation of dusts and wastewaters) of the recycling process constituting an important step forward to a future implementation in industry.

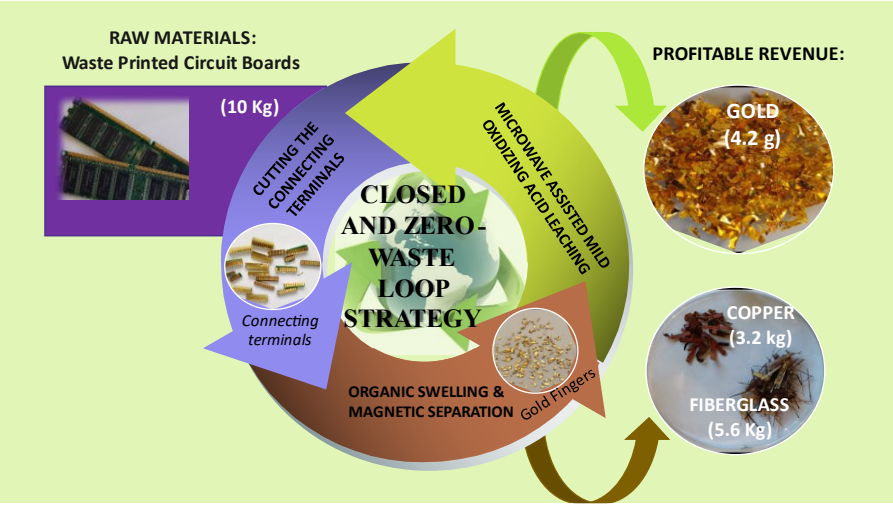

Figure 1: Schematic representation for the proposed solution to recover gold, copper plus fiberglass from WPCBs.

Acknowledgments:
This work was financially supported by: Project PTDC/EAMMIN/31041/2017 - POCI-01–0145-FEDER-031041 - funded by FEDER funds through COMPETE2020 - Programa Operacional Competitividade e Internacionalização (POCI) and with financial support of FCT/MCTES through national funds (PIDDAC).

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Synthesis, biological activity and solvating properties of bio-derived ionic liquids

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Ionic liquids (ILs) have been extensively explored and implemented in different areas of chemistry, medicine, industry, etc. These compounds have been proven to exhibit a wide range of biological activities, including cytotoxic [1], antimicrobial [2] and antiviral activities, as well as being employed as drug delivery systems. A careful selection of suitable ions, synthetic approaches, and accurate study of their biological activity are important steps for their further wide practical application [1]. Synthesis of ILs from bio-compounds such as amino acids, sugars, lignin, cellulose, various natural acids and oils, supposedly, can make ILs more environmentally friendly and biocompatible and find applications in many areas including medicine.

So, new bio-derived ILs on the base of structural frameworks of well-known imidazolium, pyridinium, cholinium ILs in combination with natural amino, salicylic, cinnamic acids and biologically-derived platform chemical (5 HMF) were synthesized, and their biological activity and physicochemical properties were studied [3-6]. Bactericidal activity of some ILs against Gram-negative and Gram-positive bacteria was tested. Depending on the position of the bio-fragment (anion, cation) and the substituents in the cationic core, the biological properties of final ILs varied significantly.

The part of the work was supported by the Russian Science Foundation (RSF Project № 21-73-10262).

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Surface modified porous silica materials as possible candidates for gas storage applications

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Hydrophobic silica materials found their way in many applications (as unique component or in composites), including inks, coatings, paintings, separation media, defoamers, storing materials, plastics, cosmetics etc.

One of the most recent and interesting utilization of hydrophobic silica is related with the storage of methane (CH_4) or carbon dioxide (CO_2). Immediately, one can divide these two domains in energy storage direction (CH_4-like molecules) and carbon capture and storage direction (CCS, CO_2 molecule). Methane or carbon dioxide hydrates are an ice-like substance formed when CH_4 and H_2O or CO_2 and H_2O combine at low temperature and moderate pressure. Under these conditions, the water molecules are forming cage-like structures, in which the CH_4 or CO_2 can be stored. On top of this, it was shown that these types of hydrates are able to form at milder conditions if the ice cages are formed in a confined space, defined by specific porous materials, like silica or carbon-based. In order for the hydrates to form in these well-defined spaces, the surface chemistry of the materials must be very carefully controlled. If the surface is too hydrophilic, the water will adhere too strongly to the walls of the material and the hydrates formation will be inhibited. On the contrary, if the surface is too hydrophobic, the water will not be able to diffuse inside the pores and to form the ice-like cages [1].

In this study, a series of micro/meso-porous silica materials (SiO_2) are modified with different silanes, in order to control the surface properties. In the first step, ordered siliceous materials with mesopores (> 2 nm) and high pore volume are developed, of the type MCM-41 and SBA-15, by templated hydrothermal synthesis. On top of this, by the additional use of swelling agents during the synthesis the pore size can be further enlarged (towards macropore formation), forming foam-like structures (3D-pore network, mesoporous cellular foam MCF). Finally, a KIT-6 SiO_2 material with bi-continuous mesostructured and large ordered domains is modified for its unique combination of micro-meso pores [2][3].

Secondly, the hydrophilization of the silicas is performed in the presence of organosilanes of general formula R_3SiX. Here, besides the type of the modifier molecule, the amount of the molecules on the surface represents a very important parameter for the surface properties. The materials developed are characterized by physisorption (porosity analysis), thermal analysis (thermal stability and crystal phase changes), X-ray diffraction (crystallinity and pore ordering), elemental analysis, SEM/TEM, and FT-IR and spectroscopy. The hydrophobic surface properties of the materials will be assessed by water sorption measurements.

Moreover, the modification degree of porous materials in number of organic groups per nm² (groups/nm²) will be approximated and quantified from thermal and physisorption analyses taking into account the weight loss of the burned carbon group and using the following formula:

$$\left(\frac{groups}{nm^2}\right) = \frac{wt\%(R) * N_A}{MM(R) * S_{BET}}$$

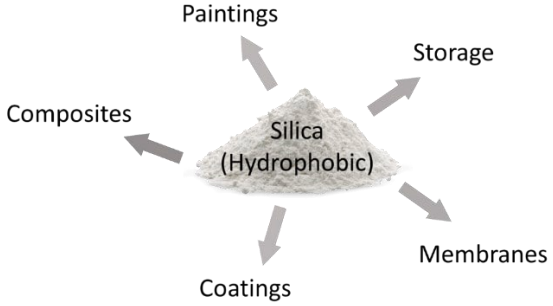

Figure 1. A series of hydrophobic silica utilizations.

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New approaches for the removal of methylene blue and methyl orange using adsorbents based on spent coffee

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Water is becoming a highly valuable resource. Hence, economically viable and efficient methods to produce clean water for the growing world population gain more and more importance. One possible treatment for clean water production is the removal of pollutants via adsorption. Although quite expensive, activated carbon (AC) is commonly used for pollutant adsorption. However, spent coffee (SC) is an abundant and cheap raw material that is daily disposed worldwide in large amounts. It is already known for removal of e.g. heavy metals, dyes or organic acids [1-3].

This work focuses on the preparation of carbon adsorbents for water treatment from SC, aiming for a cheap alternative to commercial activated carbon. On the one hand, we present materials activated with $CaCO_3$ during pyrolysis at different temperatures. On the other hand, a new approach is being presented with the focus on modifying mentioned materials rendering them magnetic. All materials were characterized via IR-spectroscopy, scanning electron microscopy, X-ray diffraction and N_2-sorption. Adsorption capacities are tested on water soluble dyes methylene blue (MB) and methyl orange (MO) vs. the adsorption time and adsorbent mass. Though most materials show no significant surface area despite of treatments, all carbonaceous systems show great adsorption properties in the pilot systems of MB and MO [4]. First experiments show that the magnetic materials are quite efficient in adsorbing the model system dyes MB and MO as well and can be recovered using a simple permanent magnet. In addition to MB and MO adsorption of diclofenac as an unpleasant remnant in waste waters of the pharmaceutical industry is examined on all materials. The created materials show an auspicious talent in the field of pharmaceutical adsorption out of aqueous solutions.

All in all, several materials with high adsorption properties are created which may present another promising alternative to commercially available AC.

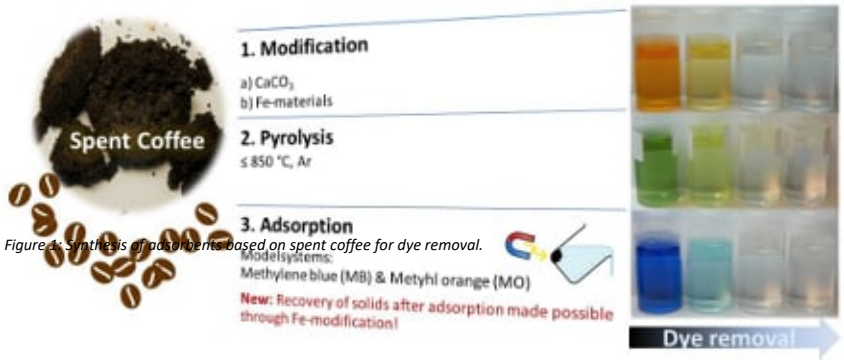

Figure 1: Synthesis of adsorbents based on spent coffee for dye removal.

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Synthesis of SOT-OH and its application as a building block for the synthesis of new dimeric and trimeric Spiro-OMeTAD materials

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Hole transporting materials (HTMs) are an important factor to consider when designing a high performing and time-enduring perovskite solar cell (PSC) or solid-state dye-sensitised solar cell (ss-DSSC). The key criteria that are necessary for an efficient HTM include energy level matching, reversible electrochemistry and light/thermal stability. [1] Spiro-OMeTAD had become the benchmark hole-transporting material for both ss-DSSCs and PSCs due to its superior performance, owing to its ability to achieve the aforementioned properties to an exceptional degree while also possessing desirable visible light transparency. [2,3] However, it has numerous intrinsic drawbacks including its poor long-term stability, low conductivity and hole mobility. [4] As a result, manipulation of its structure has been considered as a means for improving device stability while retaining the desirable properties.

In this work, a mono-demethylated Spiro-OMeTAD derivative, **SOT-OH**, was designed to act as an ideal building block for new Spiro-OMeTAD derivatives. In order to achieve this, two separate synthetic routes were employed: a monodemethylation of Spiro-OMeTAD and a multistep synthesis, to form **SOT-OH** before a dimer (**SOT-D**) and a trimer (**SOT-T**) were fabricated as example derivatives. The optical, redox, thermal and optoelectronic properties of **SOT-D** and **SOT-T** were investigated and revealed that these derivatives retain the redox and optical properties of Spiro-OMeTAD, whilst **SOT-T** exhibits improved thermal and optoelectronic properties. **SOT-D** and **SOT-T** have also been noted to have higher conductivity values compared to the parent Spiro-OMeTAD. Perovskite solar cells fabricated using **SOT-D** as the HTM achieved a power conversion efficiency comparable to those of sublime grade Spiro-OMeTAD.

Manuscript submitted, pending peer-reviewed approval.

We thank the EPSRC for funding (EP/P030106/1, EP/T010568/1). We also thank Dr Logan Mackay of the Scottish Instrumentation and Resource Centre for Advanced Mass Spectrometry (University of Edinburgh; Edinburgh, Scotland, UK), for running some of the HRMS and Dr. Affar Karimullah for measuring the thickness of the films.

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Noble metal-free MXene/TiO_2 as efficient photocatalysts for water splitting reaction

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Humanity is currently facing one of the biggest energy crises ever, overlapping with a major environmental pollution problem. In fact, it is unanimously accepted that the increased pollution due in large part to the burning of fossil fuels has led to an increase in the planet's temperature in recent years, and the future prospects are extremely worrying [1]. Converting solar energy into clean energy, such as hydrogen energy, is admitted as one of the most effective approaches to solve these problems [2], in this regard, photocatalysis being considered as a spearhead of such an approach. Although there are numerous different semiconductors developed so far, only a few of them are suitable as practical photocatalysts. Actually, no single semiconductors fulfill all the requirements for practical semiconductor photocatalysis (i.e., visible light absorption, photostability, low cost, and abundance); thus, a variety of strategies have been developed to enhance the efficiency of semiconductor photocatalysts [3,4]. Among them, the coupling of a proper and powerful photon absorber (the semiconductor photocatalyst) with a material with excellent metallic conductivity (MXene) to perform the reaction at high conversions, is believed to be a good approach for the development of robust, safe, cost-effective and efficient photocatalytic systems for water splitting [5]. Finding the perfect combination is however challenging.

In the view of these aspects, in this study, several MXene/TiO_2 composite materials were successfully prepared via an *in situ* solvothermal procedure. Increase of the stability of the synthesized MXene-based composites was achieved by applying the carbon nanoplating method [6]. The phocatalytic tests were performed in a cylindrical quartz reactor containing either MilliQ water (and no hole scavenger) or a mixture of water and methanol (volumetric ratio of 4:1). As irradiation source, a heatless illumination Xe light lamp setup (MAX-303 from Asahi Spectra Co. Ltd. equipped with a UV-Vis (300-600 nm) mirror module) was used (see Figure 1). The best MXene/TiO_2 photocatalyst generates, under certain experimental conditions, a hydrogen production rate above 500 µmols $g^{-1}h^{-1}$, which is among the highest values obtained on noble metal-free MXene-based photocatalysts. The obtained results open new opportunities in the preparation of very active noble metal-free materials for H_2 production through water splitting.

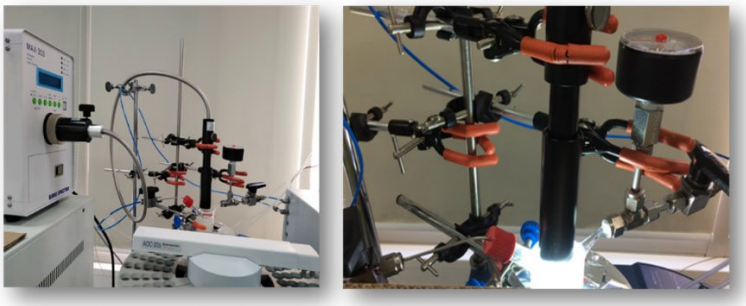

Figure 1. The photocatalytic setup used in this study

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Z-scheme Photocatalytic Systems for Sustainable Artificial Photosynthesis

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Since the industrial revolution fossil fuels have driven economic growth and now**,** approximately 85% of global energy generation comes from combustion of coal, oil, or natural gas. [1]. However, temperature increases due to rising CO_2 concentrations are projected to have many negative impacts, such as rising sea levels and loss of biodiversity, and therefore scientists are looking for methods to tackle this increase in CO_2. In nature, photosynthesis in plants occurs through a z-scheme mechanism that involves a two-step photoexcitation. First, electrons in photosystem (PS) II and PS I are excited to their respective LUMOs following visible light absorption. Next, the electrons in the LUMO of PS II are transferred to the HOMO of PS I through an electron mediator, neutralising the photogenerated holes therein. The remaining photogenerated electrons (used to reduce CO_2) and holes (used to oxidise H_2O) remain in the LUMO of PS I and the HOMO of PS II, respectively [2]. There is much potential to mimic this process artificially. Therefore, artificial photosynthesis (AP) using two distinct light absorbing species is an important area of research as a successful system would mean that waste CO_2 and free solar radiation can create fuels and valuable chemicals.

"Z-scheme" is the term used to explain the observed efficient electron/hole separation mechanism obtained using two co-located semiconductors [3]. These systems consist of a reduction semiconductor photocatalyst that is coupled with an oxidation semiconductor photocatalyst (SC II and SC I in figure 1, respectively). Z-scheme systems carry out photocatalytic reactions using vector electron transfer in which the electrons with relatively low energy in the conduction band of SC I combine with the holes in the valence band of SC II. This leads to retention of strong redox abilities in the two semiconductors, spatial separation of charge carriers, and an extended light harvesting range (albeit with a decreased photon-to-exciton efficiency) [4].

The intent of this work was to investigate a number of heterogeneous direct z-scheme photocatalytic systems synthesised *via* hydrothermal methods, characterise these to determine relevant photo-physical and textural properties and then measure their effectiveness in the AP reaction under batch-reaction conditions under visible light irradiation.

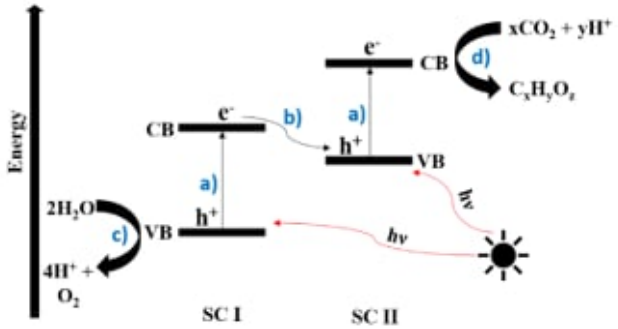

Figure 1: schematic representation of the AP reaction mechanism using z-scheme photocatalysis where a) is photon absorption, b) is neutralisation and charge carrier separation, c) is oxidation, and d) is reduction.

Work to date has involved preparation and characterisation of families of $Cu_2O/BiVO_4$ and Cu_2O/Ag_3PO_4 composite materials and characterising these using a wide range of technique. UV-Visible spectroscopy and CO_2-TPD Experiments demonstrated that both the extent of visible light absorption and levels of CO_2 adsorption increase with the composite materials compared to pure components. These characteristics are potentially beneficial to the AP reaction and, hence, the composites should demonstrate enhanced reactivity compared to that of pure $BiVO_4$, Ag_3PO_4 and Cu_2O.

Acknowledgements: This submission has been supported in part by funding from Science Foundation Ireland (SFI) under grant number 16/RC/3889 and is co-funded under the European Regional Development Fund and by BiOrbic industry partners.

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Crystalline precursors-directed synthesis of phosphorus-nitrogen-carbon materials for high temperature catalysis

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Metal-free polymers have gained considerable attention recently due to their low cost and potential applications, including water splitting, batteries, fuel cells, sensors, photo and electrocatalysis, CO_2 reduction, and more. The introduction of different heteroatoms into carbon matrices is a versatile tool for tuning its chemical and physical properties toward the formation of a large array of materials. For example, inserting phosphorous and nitrogen atoms into carbon materials enables the modification of various properties such as electrical conductivity, photocatalytic performance, and oxidation stability due to the insertion of atoms with different electronegativity and radius size, into the carbon network.[1] The synthesis of these phosphorous nitrogen carbon (PNC) materials is complicated as phosphorus large covalent radius hampers its incorporation into the CN network and achieving its successful inclusion beyond the trace level stands as a current challenge. One classic route to synthesize these materials is via solid-state approach (pyrolysis of pristine solid monomers at high temperatures). Despite the impressive wide range of materials synthesized by this method there are still some drawbacks that limit the progress in this field. The solid-state approach often results in low porosity unordered materials with grain boundaries. Here we show a simple and large scale synthesis to develop PNC materials with tunable properties as well as elemental composition. This approach enables the formation of phosphorus-rich PNC materials by using organic phosphoric acid-melamine crystals as PNC precursors. [2-3] The new synthetic tool allows the fine-tuning of the morphology, chemical, thermal stability, electronic properties, and photocatalytic activity toward the development of a wide variety of materials ranging from polyphosphazenes to phosphorous and nitrogen doped carbon can be synthesized with a wide range of oriented features. The resulted final materials demonstrate remarkable thermal stability, which allows their exploitation as stable substrates in a catalytic reaction at high temperature (200-400 °C), including CO_2 methanation as well as CO_2 hydrogenation to methanol.[4]

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Janus Dione Derivates as High-Performance Organic Cathode Materials

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With the increased application of batteries in powering electric vehicles as well as potential contributions to utility-scale storage, there remains a need to identify and develop efficient and sustainable active materials for use in lithium (Li)- and sodium (Na)-ion batteries. Organic cathode materials provide a desirable alternative to inorganic counterparts, which often come with harmful environmental impact and supply chain uncertainties. Organic materials afford a sustainable route to active electrodes that also enable fine-tuning of electrochemical potentials through structural design.

Here we report the development of Janus Dione derivatives as organic cathode materials for lithium and sodium ion batteries. The Janus Dione core has multiple redox active sites as well as activated CH_2 centres which allow for further functionalisation at either end of the molecule. These materials are prepared through facile and inexpensive syntheses via Knoevenagel type condensation reactions with selected aldehydes to generate fully conjugated redox active systems with high performance in Li- and Na-ion batteries. Each material provides multiple binding sites for Li- and Na-ions, while maintaining low solubility in commercial organic electrolytes. Compounds exhibited high performance in electrochemical Li- cells, and in particular compound **1** demonstrated excellent stability with discharge capacities above 190 mAh g^{-1} after 300 cycles at a 0.1C rate. This material also displayed excellent high-rate performance with a reversible capacity of 142 mAh g^{-1} achieved at a 10C rate. This material affords high power capabilities superior to current state-of-the-art organic cathode materials, with values reaching 5.09 $kWkg^{-1}$. The Na-ion performance of compound **1** was also evaluated, exhibiting reversible capacities of 130 mAh g^{-1} after 90 cycles at a 0.1C rate. This work offers a structural design to encourage versatile, high-power, and long cycle-life electrochemical energy-storage materials.[1]

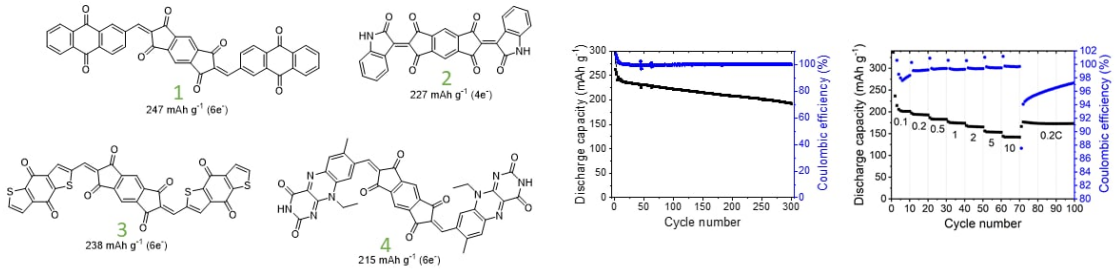

*Figure: Janus dione materials (**1**-**4**) with theoretical capacity, and device performance of compound **1**.*

G.C. and S.C. thank the Supergen hub and EPSRC (EP/P00315X/1) for funding. S.C., M.B., and M.A. gratefully acknowledge the support of the University of Sheffield in our research, as well as grant support from the EPSRC [EP/N001982/2]. G.C. and D.W. thank the EPSRC National Mass Spectrometry Facility (Singleton Park, Swansea, U.K.) for acquiring MS data.

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Leveraging knowledge to improve thermal safety evaluation in API manufacturing

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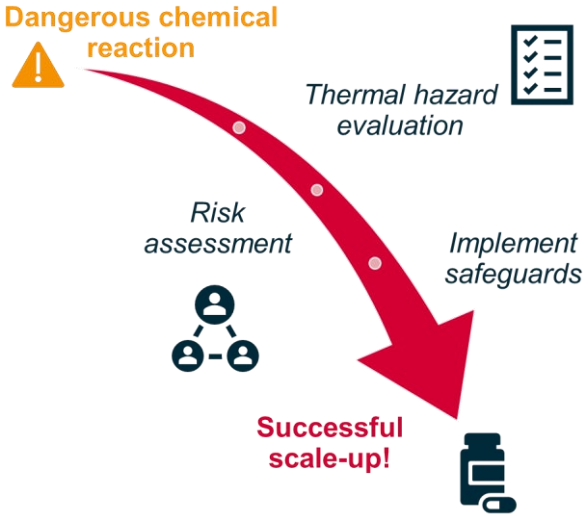
In a world where pharma CDMO's are immersed in an extremely competitive and complex market, success is measured by those who save lives by getting new drugs approved faster. For this reason, safety risk management needs to evolve and adapt to new realities, whilst not leaving its core foundations to fade out. In the specific case of chemical processes thermal safety, one of the most widely employed experimental techniques for hazards screening is Differential Scanning Calorimetry (DSC). Based on a single dynamic measurement with a few milligrams of a sample, the process safety scientist defines a temperature threshold that acts as a safety boundary for an operation. By assuming statistically conservative values for parameters typically unknown, such as the sample-specific heat capacity, decomposition mechanism and the sensitivity of the equipment used in the screening, a semi-empirical safe working temperature (SWT) can be obtained. Unfortunately, and even though these quick-screening strategy advantages are well described [1], it often defines safety intervals that are too conservative and result in inefficiencies, such as lengthy and complex risk assessment meetings, additional experimental testing or process development, and costly and time-draining actions at the plant.

The work described herein leverages several years of thermal hazards analysis done at Hovione Process Safety Laboratory using model-free kinetics with DSC data [2]. We have used information from dozens of materials decompositions, to establish more realistic thermodynamic and kinetic decomposition parameters. This immediately led to more accurate SWT determinations, thus unlocking operating temperatures that were previously seen as too risky, while streamlining the process safety approach by the company's different sites.



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Joule-heating synthesis of free-standing transition metal phosphides-based electrodes as electrocatalysts for CO_2 reduction reaction

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Transition metal phosphides (TMPs) have attracted great interest as high-performance, non-precious heterogeneous (electro)catalysts for energy-related applications.[1] The incorporation of phosphorus into the metal structure imparts exclusive structural, electronic properties, and chemical stability. Although some TMPs can be synthesized through various synthetic pathways, including simple heating of a metal source with red phosphorus (RP) under vacuum conditions or an inert atmosphere using conventional furnaces, the process often consumes time and energy.

Here, we introduce a new strategy to synthesize TMPs *via* electrical Joule-heating and exemplify its advantages for electrochemical CO_2 reduction reaction (CO_2RR). Joule-heating-directed material synthesis technique is an innovative strategy to rationally design and synthesize high-quality materials such as ceramic materials in a facile, rapid, and controllable way.[2, 3] Typically, this method possesses elevated sample temperatures, resulting in fast kinetics and high heating rates. In this work, the Joule-heating-directed route is adopted to easily synthesize TMPs such as copper and nickel phosphides as self-standing electrodes for their utilization in CO_2RR electrochemical systems. To do so, a pressed pellet of precursors is sandwiched between two parallel Joule-heating carbon strips (*e.g.,* carbon cloth) that conformally wrap the pellet and act as radiation heaters with controllable temperatures as a function of the applied input power. This technique enables us to form TMPs-based electrodes that can be utilized directly as stand-alone electrocatalysts for efficient CO_2 reduction towards valuable products (e.g., alcohols and alkenes) with high selectivity and good faradaic efficiencies.

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Alkyl-based 2D perovskites towards stable and efficient perovskite solar cells.

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In the last decade, two-dimensional (2D) halide perovskites (HPs) have been highly appreciated by the scientists. The success of 2D HPs is justified by the attractive properties discovered in such materials. 2D HPs materials are thermally robust, the larger cations prevent internal ionic motion and can provide the needed hygroscopic character to the absorber through suitable organic moieties, which improves the chemical stability compared to the 3D perovskites counterparts [1]. This outstanding property makes the 2D perovskite a strong candidate for perovskite solar cells applications. The purpose of this study was to find potential chemical compositions of 2D perovskites with a general formula of A_2BX_4 as light-absorbing materials to promote the stability of perovskite solar cells. Here, we focused on the design of a large alkali cation in the A-site to prepare 2D layered A_2BX_4 crystals, such as Pentylamine (PA) and Hexylamine (HA) and their combinations with methylammonium (MA) in different proportions. The selected compositions were predicted by DFT simulations to be promising candidates [2]. The structural and optical properties as well as the elemental composition of the obtained crystals were determined by X-ray diffraction (XRD), UV-Vis spectroscopy and X-ray photoelectron spectroscopy (XPS). Diffraction results of $(MA_{0.5}PA_{0.5})_2PbI_4$ and $(HA)_2PbI_4$ crystals show that 2D structure was successfully achieved. Moreover, these compositions demonstrate an interesting band gap for solar cell applications (**Fig. 1**). By decreasing the amount of PA in the perovskite composition, the 2D structure is not predominant and a combination between 2D and 3D is obtained.

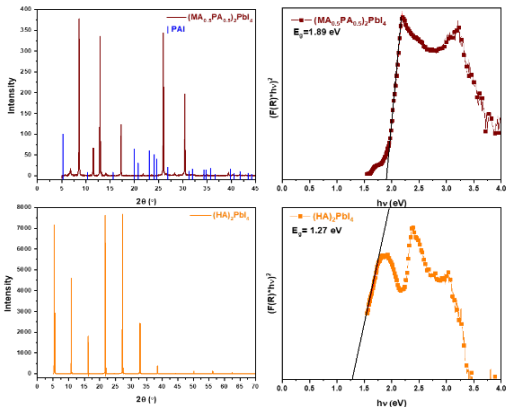

Figure 1. X-ay diffraction patterns and Kubelka Munk results of $(MA_{0.5}PA_{0.5})_2PbI_4$ and $(HA)_2PbI_4$ crystals.

The preliminary data obtained in this work, especially the low electronic bandgap of 1.27 eV in the HA-cation system, indicate that the introduction of PA and HA in the perovskite composition can be used as absorber materials to fabricate thin films and can be implemented in solar devices in order to assess its stability and performance.

This work was supported by a grant of the Romanian Ministry of Research, Innovation and Digitalization, CCCDI - UEFISCDI, project number PN-III-P2-2.1-PED-2019-1567, within PNCDI III and Core Program PN19-03 (contract no. 21 N/08.02.2019).

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Online detection of trace volatile organic sulfur compounds in a complex biogas mixture with Proton-Transfer-Reaction Mass Spectrometry

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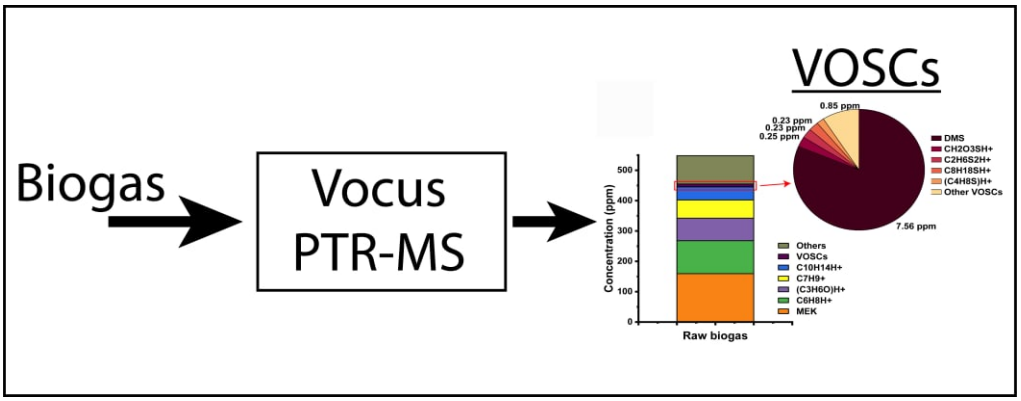
Online monitoring of trace contaminants, especially sulfur-containing compounds, is critical in biogas plants to protect downstream process steps, e.g., fuel cells or catalysts. The high biogas purity requirement for fuel cell applications and the presence of a myriad of unknown contaminants at different concentration levels require untargeted measurement techniques with high sensitivity and high dynamic range. Online measurements are critical to prevent the loss of molecules encountered during offline sampling and to track sudden changes in contaminant concentrations.

Here, we present an online, real-time measurement of trace contaminants in the cleaning stream of a biogas plant with a Vocus proton-transfer-reaction time-of-flight mass spectrometer (Vocus-PTR-TOF-MS). We identified more than 300 Volatile Organic Compounds (VOCs) in the raw biogas in the 30 – 400 m/z range, with total concentrations varying in 54.6 – 548.3 ppm_v on different days. Out of these, more than 30 volatile organic sulfur compounds (VOSCs) were also identified, with a total VOSCs concentration in the range of 0.3 – 9.3 ppm_v during measurement days. Dimethyl sulfide (C_2H_6S, DMS) was found to be the most dominant VOSC in the raw biogas. After cleaning, the total VOSCs in biogas were reduced by ~95% with concentrations below 0.5 ppm_v, which is safe to protect downstream processes.

Furthermore, we showed that VOCUS-PTR-TOF-MS could dynamically measure VOSCs with concentrations varying in several orders of magnitude, in biogas mixtures, with high sensitivity and 1 s time resolution. Typical biogas tracers were also identified in the ambient air around the biogas plant at low ppb_v levels. These results confirm that VOCUS-PTR-TOF-MS can be a rapid, scientific online tool of choice to monitor a biogas facility and, hence, shows excellent ability to characterize biogas production.



Financial support is graciously acknowledged from the ETH Board (Switzerland) via the funds for the program "SynFuels - Synthetic Fuels from Renewable Resources," jointly executed by EMPA (Swiss Federal Institute for Materials Science and Technology) and PSI (Paul Scherrer Institute). Furthermore, the authors would like to thank Tanja Wieseler and Martin Künstle for their support during the measurement and analysis. The authors are incredibly thankful to the SFPI (Swiss Farmer Power Inwil) biogas plant management and operators for hosting the campaign and support during the measurements.

Novel sulfur-containing materials in mercury uptake

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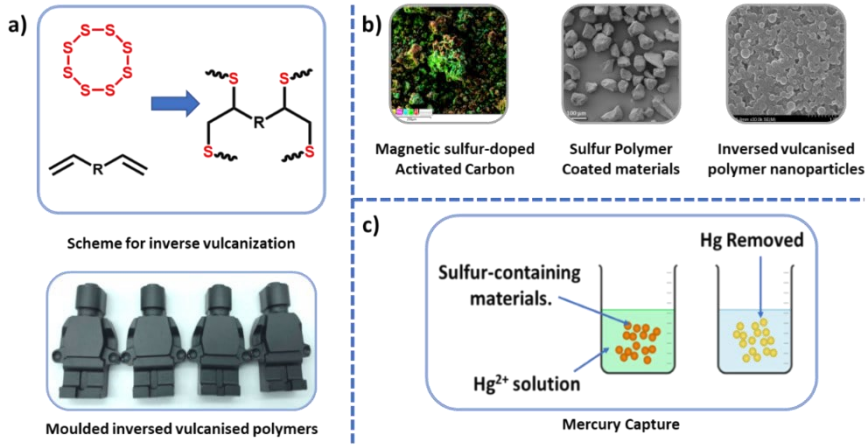
Elemental sulfur is an abundant by-product of the petrochemical industry. Much of this sulfur is stored in open piles and is sold at the cost of shipping. Finding new uses for this unused sulfur would provide an incredibly cheap materials feedstock. Polymers formed from pure sulfur are poor candidates for this as they are not stable and depolymerize to S_8. Inverse vulcanization, a new technique uses vinylic monomers as crosslinkers to stabilize polymers made from elemental sulfur, a process that is facile, atom efficient, and doesn't require solvents [1]. A variety of crosslinkers have been studied to broaden the applications of inverse vulcanised polymers [2,3]. Depending upon the chemical and mechanical properties of these materials, inverse vulcanized polymers were applied in heavy metal uptake, IR transparent lenses, fertilizer release, adhesive application, repairable materials, Li–S batteries, oil–water separation, sustainable and recyclable composites, and antibacterial materials [2,4,5]. Especially, because of the presence of sulfur, which has high affinity for Hg, inversed vulcanised polymers and their derivatives were applied as mercury absorbents, providing a cheap and simple solution to mercury pollution of drinking water [2,6-8].

Herein, we reported different types of inverse vulcanised polymers and their derivatives, including sulfur-doped activated carbons, magnetic sulfur-doped activated carbons, inverse vulcanised polymers coated materials, and inverse vulcanised polymers nanoparticles [2,6-8]. The materials were applied in mercury capture in different conditions and demonstrated high capacity and high selectivity in mercury uptake, showing their potential to be applied in water purification and environmental remediation. More important, these sulfur containing materials were also presented highly promising in industrial scale-up and commercialisation.



(a) Polymeric materials synthesis by inverse vulcanization. (b) Inverse vulcanised polymers derivatives. (c) Novel sulfur-containing materials in the application of mercury uptake.

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Formulation of new composite solid propellants based on metal hydrides

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The aim of this recherche work was the preparation and characterization of new high-performance, low environmental impact propellant formulations. For this purpose, lithium aluminum hydride ($LiAlH_4$) was used as an energetic fuel additive and chlorine scavenger to reduce the hydrochloric acid emission produced by the combustion of composite solid propellants (CSPs) based on ammonium perchlorate (AP), hydroxy terminated polybutadiene (HTPB) and aluminum (Al) [1]. Thus, three CSP formulations, i.e., AP/HTPB/Al, AP/HTPB/$LiAlH_4$, and AP/HTPB/$LiAlH_4$+Al were prepared and characterized using densimetry technique, infrared spectroscopy (FTIR), differential scanning calorimetry (DSC) and thermogravimetry (TG). Then a deep kinetic study of their thermal decomposition was performed by employing four advanced isoconversional approaches [2].

The obtained density values of the different prepared propellants demonstrated an adequate homogenization of the formulations. The FTIR measurements revealed a slight difference in the IR spectra of the manufactured samples, indicating an additional absorption band for $LiAlH_4$-based propellants [3]. TG and DSC analyses exhibited two thermal decomposition stages. DSC curves of $LiAlH_4$-based propellants revealed a shift of the exothermic peak temperatures to low values with an increase in its DSC-heat release compared to the baseline aluminized propellant.

The average activation energy (Ea_{av}) values determined by four integral isoconversional methods demonstrated an excellent catalytic effect of $LiAlH_4$ complex metal hydride on the thermal decomposition of AP/HTPB/Al composite solid propellant, especially for the second decomposition stage. The integral form of the reaction model g(α) that best fits the DSC data, obtained by the employed kinetic models, revealed different decomposition reaction mechanisms for the manufactured propellants. The main thermal decomposition stage of both aluminized propellants (AP/HTPB/Al and AP/HTPB/Al+$LiAlH_4$) involved a diffusion mechanism (three-dimensional diffusion), while the second decomposition step of $LiAlH_4$-based propellant implied a nucleation mechanism (parabolic law).

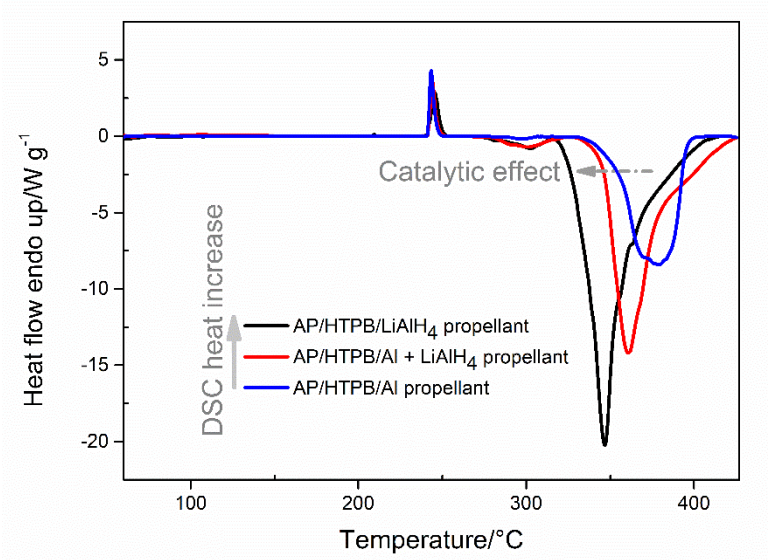

Figure.1. DSC curves superposition of the prepared propellant samples at a heating rate of 15 °C min-1.

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Microwave-assisted phenolation of acid-insoluble Klason lignin and its application to adhesion

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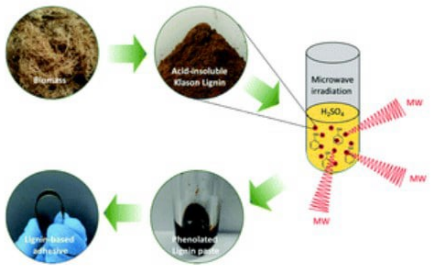
Lignin, a natural heterogeneous polymer made up from three main phenylpropane units, recently was considered to be a renewable and alternative source for petroleum products. The usage of lignin is diverse, such as transformation into bio-oil and bio-fuel, or destructive functionalization to use as polymer, adhesive, and precursor for other applications [1]. However, the usage of lignin in the material field is limited due to its intrinsic complex structure. For example, lignin shows very low solubility in organic solvents, and the reactive sites in lignin structure (ortho and para position of phenyl unit) were occupied by methoxy group [2].

One of the methods that can overcome these limitations is a phenolation that introduces phenyl group into lignin structure, thereby increasing the number of reaction sites [3]. By the phenolation, the lignin becomes more soluble compared with the original lignin. The phenolated lignin has also been proven to be readily reactive in various reactions, such as Mannich reaction, and alkylation reaction with formaldehyde [4].

Klason lignin is insoluble in most types of aqueous and organic solvents. In this research, Klason lignin was phenolated using microwave radiation. It was found that microwave heating significantly decreases the reaction time and reaction temperature compared to conventional thermal heating. Furthermore, the products also exhibit high solubility in widely-used organic solvent such. Experiments and DFT calculations have shown that microwave irradiation induces sulfuric acid overheating thereby increasing local temperature and stabilizing intermediate species during the phenolation [5].



The phenolated lignin was further been applied as adhesive on the surface of glass and polymer material (PAN and PI). Modified lignin showed outstanding binder properties on the surface of polymer material even after 1000 bending cycles, giving a hope to use lignin as a binder for advanced application.

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Sustainable surfactants from Cynara Cardunculus biomass

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Surfactants are used in different industrial sectors, currently non-renewable petrochemical resources are used for their production. The replacement of surfactants from petrochemical origin with surfactants deriving from renewable sources can reduce their environmental impact, thanks to their better biodegradability and lower eco-toxicity.

At this regard, a particularly interesting class of surfactants is represented by alkyl polyglucosides (APGs), which are obtained from vegetable origin's materials, they show an excellent eco-toxicological profile and high biodegradability in aerobic and anaerobic conditions [1]. Alkyl glycosides are synthesized with the Fischer glycosylation process which involves the acetalization of a carbohydrate catalyzed by an acid, in the presence of an alcohol. The starting carbohydrates are provided by the acid hydrolysis of biomass such as: inulin and cellulose. Cellulose is a crystalline polymer characterized by a high stability that makes difficult the controlled hydrolysis process, because of the presence of D-glucopyranoside units linked together by β-1,4 glycosidic bonds.

Inulin, deriveded from Cynara Cardunculus biomass, is a β-D-fructose polysaccharide, its monomers are joined with β-2,1-glycosidic bonds and it is completely transformed into D-fructose thanks to the action of acids or the enzyme inulinase. Among the different methods proposed in the literature [2-3], in this work, the mechanochemical depolymerization will be addressed [3].

The obtained products were used to synthesize different APGs through the reaction with different alcohols. The APGs obtained were subsequently characterized and finally tested to determine their emulsifying and foaming properties.

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Cynara Cardunculus biomass as a resource for a zero-waste biorefinery

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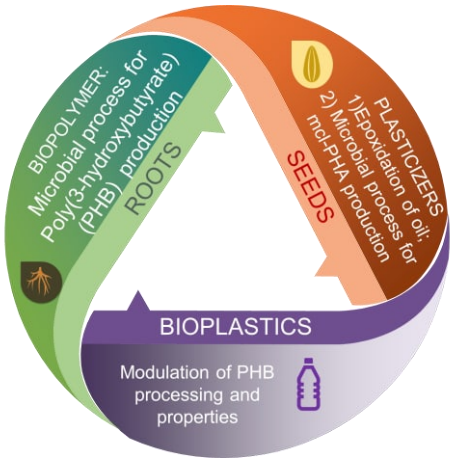
Cardoon, Cynara cardunculus L. from Asteraceae family, represents a challenging, strong, non-food chain competitive crop, able to grow in dry, marginal lands and/or polluted soils of many Mediterranean regions, already exploited for industrial pulp and paper production and domestic heating.

The recently founded national Italian project "CARDIGAN" aims at exploiting a "Cardoon biorefinery model" with a holistic approach. The idea is to valorize all fractions derived by cardoon to obtain high added value products. In this scenario CARDIGAN project aims to design bioplastics from Cardoon, by biological and chemical transformation of its different fractions, such as roots and seeds.

Poly(3-hydroxybutyrate) (PHB) is a homopolymer of 3-hydroxybutyrate, the most significant member of the biodegradable thermoplastic polyhydroxyalkanoates (PHA) family, showing physical properties comparable to those of some petroleum-based polymers. Despite this, PHB use is hampered by its narrow temperature range of processability and by its high crystallinity. The use of plasticizers could solve this issue by reducing brittleness and improving processability [1].

In this work, a Simultaneous Saccharification and Fermentation (SSF) process has been set up to produce PHB from inulin derived from cardoon roots [2]. Furthermore, oil extracted from cardoon seeds has been tested as C-source to produce medium-chain length PHA (mcl-PHA) and has been chemically epoxidized [3] to be used as green and non-toxic biodegradable PHB plasticizers, preserving the eco-sustainability of the whole system. Aimed at widening the industrial applicability of PHB, the synthesized PHB polymer, epoxidized oil and mcl-PHA have been formulated in blends to develop PHB-based films with optimized, chemical-physical, and mechanical properties. The cardoon biomass recovery, separations into different components, and their following recombination in upgraded materials can be framed in a holistic approach of zero waste circular economy.



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Elements chemical forms in Rangárvellir watershed of south Iceland

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In this work we presented results of metals and elements contained in river sediments and soil of the Rangárvellir Rivers in southern Iceland as well as in volcano ash from the Eyjafjallajökull eruption in 2010. The Rangárvellir area is located in southern Iceland in the vicinity of Mt Hekla, Iceland's most active volcano. This study site is ideal to investigate wind and water erosion and sediment transport processes of two main glaciers rivers: the Eystri-Rangá and the Ytri-Rangá. Also, sediments of these rivers consist of volcanoes materials, ash and lava. In all collected samples Al, Fe, Ca, Mg, Si and Na are dominating; up to max. of 5% for Al and about 0.5% for Na. The results reveal that the distributions of Si are the same in all investigated samples of soils, river sediments and volcanic ash pointing to the same geochemical basis. Li and partly B exist in the first phase of volcanic ash and river sediments but no in the mobile phases of soils. In the mobile phase of volcanic ash P was found but it did not exist in the first phase of soil and river sediments. These results suggest that the different chemical fingerprints in the water sediments and surrounding soil could be used to identify erosion processes and watersheds connectivity. Much better correlations among heavy metals and trace elements were found in samples from river sediments indicating a higher connectivity and suggest stronger associations in sediments substrate indicating sediments dynamics and water/sediments physicochemical interactions as key processes. On the other hand correlations among C, N and H were much better in soil indicating their animal origin, most likely from surrounding sheep farms. PCA analyses show that major elements are originating only from one source, both in river sediments and soil while more factors were found among macro, minor and trace elements in river sediments as consequences of the sediments dynamics and water/sediments interactions which connect them according to their physico-chemical properties. Characteristic ratios K/Al, Ca/Fe, P/Al, Fe/Al, Mn/Al, Si/Al and Mg/Al indicate that Fe/Al ratio is significantly higher than those found in African regions, Si/Al are significantly lower and Ca/Al also lower, but Mg/Al and P/Al are in the range found in African regions. The chemical patterns of investigated elements combined with CA statistical method have shown the strong influence of sediments which are transported from the source of the Ytri Rangá to the estuary in the Atlantic Ocean, more than 50 km away. These results suggest that chemical forms of the elements As, B, Cd, P, Sb etc., could be used as tracers for tracking sediment transport. Since each type of the naturally abundant tracer elements analyzed in this study reveals specific characteristic of sediments migration we conclude that our approach of chemical fingerprinting is a suitable method to identify sediment transport patterns and sediment connectivity.

Efficient removal of phosphate ions using Cu-modified zeolite X from fly ash

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Phosphorus (P) is one of the key nutrients crucial for the development of life. However, even its low concentration in water (0.1-0.01 g L^{-1}) can lead to rapid growth of harmful algae and as a consequence cause eutrophication. For this reason, there is a constant need for monitoring of P emissions to the environment and development of its removal methods. In recent years adsorption has gained attention as an efficient method for removal of P from waters, even at low concentrations. Phosphorus in aquatic environment exists in its ionic forms, depending on the pH. Hence, the development of adsorbents, that can operate in a wide pH range to maintain sufficient adsorption capacity toward phosphate ions has become a challenge for the researchers. Among numerous investigated adsorbents, zeolites were found to be promising materials for removal of phosphate ions. To improve their adsorption properties, some modifications are required, *i.e.:* ion exchange or impregnation.

In this study, zeolite NaX obtained from fly ash was modified by ion exchange with copper nitrate at wide range of initial Cu^{2+} concentrations (0.01, 0.05, 0.10, 0.15, and 0.20 M). Zeolite NaX was also impregnated with copper nitrate (3 % w/w) and calcined, to investigate the effect of preparation method on phosphate ions adsorption capacity. It was found, that above copper nitrate concentration of 0.10 M, surface $Cu_2(OH)_3NO_3$ species are formed. As a consequence, further increase in copper nitrate concentration lead to significant drop in the materials specific surface area (S_{BET}) and formation of mesopores. Similarly, after impregnation, the S_{BET} was significantly lower than for parent zeolite NaX. Zeolites were subjected to series of adsorption studies aiming to evaluate the adsorption properties of the modified materials toward removal of phosphate ions. The concentration of 0.05 M Cu^{2+}, was found to be the most efficient and the adsorption capacity was 87.3 mg (PO_4^{3-}) g^{-1}. In comparison with parent zeolite NaX, the adsorption capacity was 20-fold higher. Further increase in copper nitrate concentration used for ion exchange resulted in drop in adsorption properties, probably due to partial blockage of the zeolite pores. Impregnation method allowed to increase the adsorption capacity by 6-fold when compared to parent zeolite NaX. The guiding mechanisms of adsorption were: chemical interaction with Cu species over the zeolite surface, interactions of phosphate ions with oxygen species (M-O, and M-OH), and precipitation as calcium phosphates. The maximum phosphate removal was as high as 32.3% for zeolite dose of 1 g L^{-1} (ion-exchanged zeolite NaX with 0.05 M Cu^{2+}) and further increase in adsorbent dose to 3 g L^{-1} improved the removal of phosphate ions to 65.4%. Adsorption of phosphate ions was also evaluated at both 25 and 40 °C to investigate the effect of adsorption temperature. It was proved that there was no significant change in the adsorption capacities and percentage removal of phosphate ions with an increase in adsorption temperature, implying slight exothermic character of adsorption.

The obtained results indicated high affinity of Cu-modified zeolite X toward removal of phosphate ions. Ion exchange method allowed to obtain materials characterized by greater adsorption properties than material obtained using impregnation method. Further studies can be focused on application of Cu-modified zeolites in agriculture, as non-toxic additive to fertilizers, characterized by slow release of phosphate ions into the soil.

ACKNOWLEDGEMENT: The project "Fly ashes as the precursors of functionalized materials for applications in environmental engineering, civil engineering and agriculture" — is carried out within the TEAM-NET programme of the Foundation for Polish Science POIR.04.04.00–00-14E6/18–00.

Semiconductor nanocrystals as Triplet Sensitizer for Photon Upconversion

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The harvesting and exploitation of solar radiation in PV or photocatalytic devices is severely restricted to frequencies above the active material band gaps; the scientific community therefore is interested on new strategies to overcome this limit. One promising and versatile mechanism, to convert lower-energy photons into higher-energy photons, is the triplet−triplet annihilation-based photon upconversion (TTA-UC) concerning the interaction between two units a sensitizer and an annihilator. [1] The mechanism was first introduced by Parker and Hatchard in the 1960s but remained latent until the early 2000s; then, it had a surge thanks to the availability of the sensitizer/annihilator pairs. [2]

The development of hybrid system using nanocrystals as triplet sensitizer was a turning point in the applications of the UC process since the scarce number of organic sensitizers able to absorb radiation in the near-infrared region. Quite the opposite of organic molecules, the nanocrystal quantum dots have strong and broad-band light absorption that can be tuned through size and composition across ultraviolet to infrared spectral ranges. [3-4] The exploitation of nanocrystals in the UC mechanism requires the presence of organic ligands bound to the nanocrystals surface used to capture and transmit the photoexcited state to the annihilator. The transmitter ligand is crucial to speed up the energy transfer process with the consequence of boosting upconversion quantum yield. [5-6]

In this work we present the synthesis and characterization of inorganic nanocrystals followed by the coupling with an organic annihilator to investigate the upconverted radiation achieving a near-infrared to visible conversion.

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The Application of High-Throughput Computational Screening and Machine Learning Approaches for Investigation of Xylene Isomers Separation by Flexible Metal-Organic Frameworks

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Efficient separation of xylene isomers is a highly challenging problem because of the similarity physio-chemical properties, and moreover demands a lot of energy. Metal-Organic Frameworks (MOFs) are crystalline porous materials with very promising properties for gas storage/separation, catalysis, drug delivery, biomedical imagining and light harvesting. It is believed, that MOFs can be suitable for energy-efficient xylene isomers separation. Nowadays thousands of MOFs were created experimentally and about a million is available in theoretical works. These MOFs are grouped in different databases. Obviously, it is extremely expensive in terms of money, labor and time to perform experimental screening of thousands of MOFs. High-throughput computational screening is the solution for discovering separation properties of MOFs and identifying the most promising structures. In this work, the CoRE MOF database of experimental MOFs was employed for initial screening and revealing MOFs promising for xylene isomers separation. Classical molecular dynamics and Grand Canonical Monte Carlo approaches were used within computational screening process. MOFs were treated as flexible, not rigid structures. The diffusion coefficients for xylene isomers for MOFs structures were revealed and placed in database among the structural and chemical descriptors of MOFs. Having this training database, machine learning (ML) approaches were applied to train the accurate models, and further apply for the other databases for revealing the most promising MOFs for xylene isomers separation. The databases contains totally about one million MOFs, and obviously it is not possible to computationally (with classical molecular dynamics or Grand Canonical Monte Carlo approaches) scan these amount of structures.

Greywater treatment through foam fractionation and photo-Fenton like processes

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Greywater (GW) is defined as domestic wastewater generated in households or office buildings from streams without faecal contamination like dishwasher, bath, hand basin, washing machines and kitchen sink. The separation of grey from black fraction of wastewater can be a safe option for GW treatment and reuse [1].

Generally, to reach an adequate GW quality standard after treatment, a combination of different processes (e.g., biological, physical, and chemical) with a conclusive disinfection step is required [2]. Due to the high concentration of volatile organic compounds and foaming agents (e.g., surface active agents) foam fractionation process could be a good option for GW treatment. This process has been investigated in the past to as valuable technology to remove surfactants and non- surfactant species (e.g., metals, ClO_3^-, etc.) from solutions [3,4]. Advanced oxidation processes (AOPs) have also been investigated in recent years for the treatment of GW (for example Fenton process) [5,6]. Photo-Fenton like process using Fe-IDS (PFI) complex as catalyst has not been tested for GW treatment. This innovative process could overcome some AOPs drawbacks. It allows to perform the treatment at circumneutral pH, assisted by sunlight, reducing the formation of not biodegradable intermediates (Fe-IDS biodegradability = 96% after 28 days) [7]. The aim of this work was to investigate the combination of the physical foam fractionation process and PFI in GW treatment in terms of removal of organic matter, both as COD and BOD_5.

The effect of air flow 1.5 (FF1), 3 (FF2) and 6 (FF3) L/min and treatment time (up to 3 h) were evaluated. A removal of 82.5% and 41.9%, in terms of COD and BOD_5 respectively, for FF3 was achieved after 2 h treatment by foam fractionation. The efficiencies of PFI (i.e., H_2O_2:900 mg/L and Fe^{3+} 2 mg/L) was 63.8% and 33.1% for COD and BOD_5 removals respectively. When the two processes were tested in combination (Figure 1) with the best condition of H_2O_2/Fe-IDS/UV-C a removal of 95.3% and 93.4% of COD and BOD_5 were achieved respectively. By replacing UV-C light source with sunlight the COD removal decreased from 95.3% to 89.5% while BOD_5 from 93.4% to 76%. Both combinations are effective but solar light option is the most sustainable and attractive option for GW treatment also due to the significant lower operation cost (1.99 €/m³ Vs 15.33 €/m³).

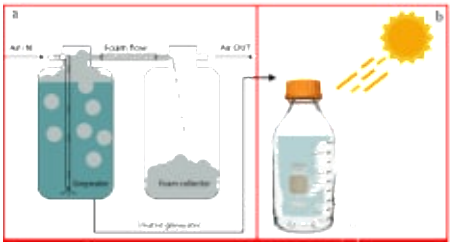

Figure 1 – Experimental set-up of combined process. a) Foam fractionation and b) solar photo-Fenton like process using Fe-IDS as catalyst).

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Synthesis of sustainable polymers from sugars derived from lignocellulosic biomass

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Studies on the liquefaction of eucalyptus wood residues show that eucalyptus sawdust / sawdust comprises 41% cellulose, 31% hemicellulose, 29% acid-insoluble lignin and 5.1% sugars [1]. However, the fraction composed by sugars has not well been studied and they have not been characterized [2], making it important to study and value these sugars aiming at greater process sustainability, as well as the formation of new molecules from these sugars. In this context, the study of the liquefaction process of lignocellulosic biomass is of great relevance because the chemical reactions that occur during this process, as well as the mechanisms that lead to the formation of sugars, have not yet been properly elucidated, constituting an innovation [1]. Lignocellulosic biomass can become an important raw material for the production of polymers containing sugars. Glucose is the best known breakdown product of cellulose. However, the depolymerization of hemicellulose results in the formation of glucose, as well as other hexoses (mannose, galactose, rhamnose) or pentoses (xylose, arabinose) [3]. On the other hand, levulinic acid has been pointed out as a promising molecule with regard to sustainable chemicals, which can be produced from renewable resources such as lignocellulosic biomass [4] The α-angelolactone (AL) can, in turn, be produced from levulinic acid through an intramolecular condensation process followed by dehydration [5], presenting itself as an important raw material for the synthesis of new polymers sustainable [6]. This work has as main objective to investigate the valorization of sugars and their derivatives, present as major components in the aqueous fraction resulting from the liquefaction processes of the wood biomass, aiming at its use in the production of sustainable and biodegradable polymers, which can be applied to processes industrial or agro-industry.

Acknowledgments: Centro de Química Estrutural is a Research Unit funded by Fundação para a Ciência e Tecnologia through projects UIDB/00100/2020 and UIDP/00100/2020. Institute of Molecular Sciences is an Associate Laboratory funded by FCT through project LA/P/0056/2020 This work was carried out under the Project inpactus – innovative products and technologies from eucalyptus, Project N.º 21874 funded by Portugal 2020 through European Regional Development Fund (ERDF) in the frame of COMPETE 2020 nº246/AXIS II/2017.

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Boron oxide modified carbon nano-onions supported platinum nanoparticles for enhanced ammonia electrooxidation in alkaline direct ammonia fuel cells

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Direct ammonia fuel cells (DAFC) have received much attention over other alkaline fuel cells due to the easy handling/transportation of NH3 as a fuel, high power density and low toxicity. [1,2]. Platinum remains the best electrocatalyst for the ammonia oxidation reaction, and carbon supports have widely being used [3]. Herein, we report on the synthesis of well dispersed ultrafine Pt nanoparticles (Pt NPs) supported boron oxide modified carbon nano-onions (B-CNOs) by the ethylene glycol reduction method. Energy dispersive X-ray spectroscopy and X-ray photoelectron spectroscopy confirmed the presence of C, O, B, and Pt on the surface of CNOs with average Pt particle size of 4.4±0.5 nm. Transmission electron microscopy images showed that the incorporation of boron oxide and Pt onto the surface of CNOs did not alter their morphology. The Pt/B-CNOs hybrid nanocatalysts showed enhanced electrocatalytic activity, better stability, and fast charge transfer for ammonia oxidation reactions as compared to Pt loaded on pristine CNOs and the commercial Pt/C hybrids. The improved electrocatalytic activity of the Pt/B-CNO hybrid was attributed to the increase in electronic conductivity of the CNOs by boron oxide and the enhancement of the interaction with water due to the boron on the support, which could contribute to the oxidation of intermediate products from the ammonia electro-oxidation.

This work is based on the research supported in part by the National Research Foundation (NRF) of South Africa, the University of the Witwatersrand (Postgraduate Merit Award, University Research Council) and the NRF-DAAD grant. The authors also acknowledge the efforts and support provided by the University of Johannesburg (Faculty of Science, University Research Council, and Centre for Nanomaterials Science Research).

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Development of a continuous electroorganic production process for sustainable electrofuels

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Latest scientific work regarding electroorganic syntheses often suggests the use of flow reactors, as this reactor type is generally easier to scale up and advantageous for large production quantities in comparison to common batch-type laboratory setups [1]. A number of advantages offsets higher investment cost and increased effort to operate continuous reactors. Ultimately, most work does not provide evidence on how a certain batch reaction benefits from continuous operation beyond the simple improvement of electrode surface to reactor volume ratio. Within this work, we show how easily automatization and process control can be employed at lab scale to exploit the full potential of electrochemical flow reactors. Our experimental results approximate an industrial process and allow more precise statements regarding energy demand, operational parameters and waste volume. At the same time, we prove that electroorganic synthesis in flow reactors offer production pathways that are even more sustainable than in batch.

In order to achieve this, we designed a setup to investigate the Kolbe-coupling of valeric acid toward the potential jet fuel *n*-octane [2]. The products self-separate from the aqueous electrolyte in a given phase distribution equilibrium [3]. We integrated this into a process that allows an energy, material and time efficient conversion and isolation of the bio based product. Productivity and selectivity are enhanced by different ways of stabilizing starting material concentration with full recycling of the electrolyte.

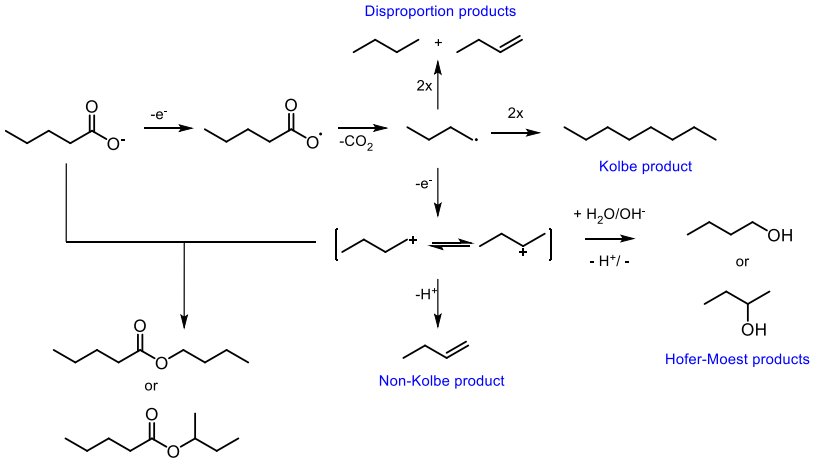

Figure 1: Reaction pathways for the Kolbe-electrolysis of valeric acid, adapted from Holzhäuser et al [4].

Thanks to the funding by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Germany's Excellence Strategy – EXC 2163-1 – Sustainable and Energy Efficient Aviation – Project ID 390881007.

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Useful Analytical Tools for Environmental and Nanomaterial Research Available Within Research Infrastructure NanoEnviCz

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Environmental and nanomaterial research are highly dependent on the availability of specific analytical tools. However, even well-equipped universities and research centers often lack certain equipment and experienced staff to perform all analyses needed. External analyses might be costly and can take a lot of time. Research Infrastructure NanoEnviCz (RI NEC) was founded to address these issues and support cooperation among Czech and foreign researchers. Any student, researcher or company working within environmental and nanomaterial sciences can register and apply for any analysis available at six Czech partner academic institutions for free. Not only does it help students and researchers with their work, but it also enhances cooperation between academia and industry.

In this poster, one can find basic information regarding the RI NEC, its topics and available analytical tools, as well as examples of results. The main topics solved within the RI NEC can be found in Tab. 1.

The RI NEC is funded by the Ministry of Education, Youth and Sport of the Czech Republic.

Code	Topic description
WP3	Creating and designing new multifunctional nanomaterials for environmental protection
WP4	Heterogeneous catalysis for environmental protection
WP5	Novel nanomaterials and technologies for sustainable production
WP5	Novel nanomaterials and technologies for sustainable production
WP6	Nanotechnology for pollutants trapping
WP7	Sensing and monitoring of pollutants
WP8	Toxicity and risks of nanomaterials

Tab.1: The list of the main topics solved within the RI NEC.

Post-modified chemicals for CO_2 capturing and utilization

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The irreversible catastrophic effects of climate change impose a race against time to reduce the impact of greenhouse gas emissions. Significant advances have been achieved in adopting green approaches to implement CO_2 mitigation strategies exploiting post-modified materials for CO_2 capture and utilization.

Herein, we shed light on the work of the Jordanian CO_2-Team (JCO_2T), on applying simple modification procedures to utilize sustainable chemicals for CO_2 activation through C–X bond formation (X: N, O, C & S)[1–3] and to catalyze the CO_2 conversion into carbonates [4–6].

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A comparison of Non-Thermal-Plasma to Promote the Chemical Looping CO_2 + CH_4 reaction over Ni and Fe Containing Oxygen Storage Materials

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Abstract

In 2020 the world's primary energy demand fell by 4.5% and our capacity to generate energy from wind, solar and hydro sources grew by an unprecedented 50%[1]. These figures are heartening news if we are to meet the net zero carbon emissions target, set by the IPCC for 2050[2]. By 2050, electricity will need to supply 50% of the globe's energy (90% of this from renewables), at present this is only 22% (12% from renewables). Generating all our electricity from renewables is possible but storage of excess, for use in times of low power generation, i.e. energy storage is a major obstacle. One solution may lie in thermochemical heat pumps, i.e. using excess electricity to power endothermic chemical processes, the products of which can be easily stored, then back reacted to produce heat when renewable sources are scarce. One such process is the dry reforming of methane (DRM), reacting two ubiquitous greenhouse gases, CH_4 and CO_2, to produce synthesis gas (CO and H_2):

$$CH_4 + CO_2 \rightleftharpoons 2CO + 2H_2$$

Thermally promoted DRM reactions require temperatures greater than 1000 ^oC for any meaningful conversion. The energy required to reach and maintain these temperatures makes the process economically and environmentally unsound. The reaction is equilibrium limited and the most active catalysts require expensive noble metals. Transition metal catalysts have been widely researched. However, these materials suffer severe carbon deposition and subsequent catalyst poisoning. It is possible to mitigate these drawbacks by using a chemical looping process, using inexpensive oxygen storage materials (OSM), driven by a non-thermal plasma (NTP).

The chemical looping DRM process involves switching the feed gases between CH_4 and CO_2, passed over an OSM. This splits the DRM reaction into oxidation and reduction cycles, with the products being CO and H_2O rather than CO and H_2[3]:

$$CH_4 + Fe_3O_4 \rightarrow 3Fe + CO_2 + 2H_2O$$

$$4CO_2 + 3Fe \rightarrow Fe_3O_4 + 4CO$$

$$CH_4 + 3CO_2 \rightarrow 4CO + 2H_2O$$

By using NTP as the promoter, the need for high temperatures is removed. The reaction is instantaneous, as soon as the plasma is ignited, the reaction proceeds. This means when excess electricity becomes available, products can be generated, with no catalyst activation period or maintenance of high temperatures, as is required in the thermal reaction. This makes NTP ideal for driving an energy storage thermochemical heat pump.

In this work, a range of $Ni/MgFe_xAl_{2-x}O_4$ oxygen storage materials were synthesized, then characterized *via* XRD, BET, SEM, EDX mapping, and FTIR and UV-Vis spectroscopies. The redox properties of the materials under CH_4 and CO_2 were investigated, and post-reaction characterization was carried out using XRD, SEM/EDX, DFTIR and TGA/MS. Their activity was tested in the chemical looping dry reforming of methane reaction, using either heat (650 ^oC and 800 ^oC) or non-thermal plasma as the promoter (fig. 1). The results of these tests will be discussed during presentation.

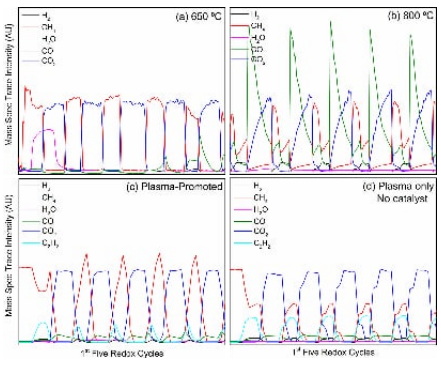

Figure 1. Mass Spec traces for the chemical looping DRM reaction

Acknowledgements: The authors thank and acknowledge the Irish Research Council for funding (grant number GOIPG/2018/2880).

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Oxidation of methane to methyltrifluoroacetate in trifluoroacetic acid solvent using anionic palladium catalyst

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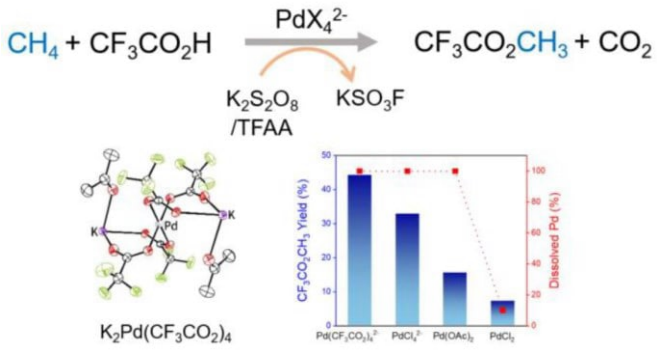
Methane, the major component of natural gas, is one of the most prominent nominees for the chemical industry as an alternative green and cheap carbon feedstock. In the past, the conversion of methane to methanol was carried out through Fischer-Tropsch process by producing syn-gas mixture from methane. However, this two-steps process limits its valorization due to the energy-intensive path-way [1]. Thus, the development of the direct oxidation of methane to methanol at milder reaction conditions to obtain more valuable products is an important issue from both a practical and academic standpoint. However, due to the lower C-H bond-dissociation energy of methanol than methane, the formation of methanol in high yield is almost an infeasible target in this process [2]. Therefore, in order to overcome this issue, one of the best strategy is converting methane to methanol precursors such as methyl bisulfate(MBS) [3] or methyl trifluoroacetate(MeTFA) [4] by carrying out the methane oxidation reaction in oleum or trifluoroacetic acid(HTFA), respectively. In this srudy, various Pd catalysts such as Pd(0), $PdCl_2$, $PdBr_2$, and K_2PdCl_4 were used for the oxidation of mathane to MeTFA in the presence of $K_2S_2O_8$ oxidant and trifluoroacetic acid solvent at low temperature and pressure. A MeTFA yield of 33.0% with a 330 TON was obtained at a catalyst loading of 0.5 mM at 80°C, which proved the highest catalytic activity of $PdCl_4^{2-}$ for this reaction. This high MeTFA yield could be ascribed to the catalysts' high solubility in HTFA and easy dissociation of chloride ligand from $PdCl_4^{2-}$. The mechanism of this reaction was also expected using the DFT calculation.



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Lignite as an ammonia sorbent and stimulator of plant biological activity

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Lignite was formed by the deposition of the dead plants' biomass in the form of peat. Over 11.5 million years, the peat was transformed into the youngest type of lignite, which is still used as a fossil fuel. However, new uses for lignite are being sought. Lignite can be used as a cheap sorption material for ammonia [1] and ammonium salts [2], which are produced during livestock farming. The use of lignite as a litter material should reduce the ammonia load in the environment of farmed animals. Litter enriched with inorganic nitrogen could be used to improve the growth of agricultural crops.

Lignite from the Baňa Čáry mine (Slovakia) was sized, homogenized and structurally characterized. FTIR spectroscopy, organic elemental analysis, thermogravimetric analysis, EPR spectroscopy, 13C CP/MAS NMR spectroscopy, XRD analysis and ICP-OES were used to determine the inorganic and organic fraction, structure and organic functional groups. The specific surface area was determined by BET analyzer. Sorption of ammonia onto lignite was determined by batch tests from ammonia vapor tensions over ammonium hydroxide solutions. The results obtained show that lignite is usable as an ammonia sorbent and the mechanism of ammonia trapping is probably chemisorption on the active centers of lignite.

Crushed lignite was experimentally used as litter in small farms with 60 chickens and then in large farms with 50,000 chickens. The ammonia concentration in the air of the control and experimental boxes/stables (area 9.5 m^2/2,500 m^2) was monitored by ammonia detectors. In the control, commonly used litter was applied and in the experimental, 6.4 Kg of lignite per m^2 of area was applied to the litter. Ammonia concentration was monitored for 40 days. It was found that the litter with lignite was able to reduce the concentration of ammonia in the air by 50 to 77 %.

The stimulating activity of lignite was monitored in seeds of wheat, barley, maize, cucumber, zucchini, pea, lentil and sunflower plants. Hydroponics was used for seed germination and growth. The same nutrient solution was used for control seeds and test seeds; dispersed lignite particles was then added to the test seeds. Root and above-ground plant growths were monitored after 48, 72, 96 and 168 hours of growth in a climate-controlled box. The conditions were set as follows: light for 14 hours at 30 °C and darkness for 10 hours at 20 °C, all under a humidity of 70 % RH. The results confirmed the stimulatory effect of lignite on the growth of the test plants. The increments for the root part ranged from 149 to 300 % and for the aerial part of the plants ranged from 106 to 270 % compared to the control seeds.

The published results were obtained with the support of the MPO TRIO 4 project FV40141 – "Research into the conditions and forms of the application of products lignite as a sorbent of ammonia, and as stimulators of biological activities in vegetable cells".

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Room temperature gas sensing behaviour of capped WS_2 nanoflakes towards ammonia vapours under humid conditions

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Given its application in industries such as agriculture, textiles, rubber, explosives, refrigeration, petroleum, air conditioning and medical diagnostics, it is no surprise that ammonia (NH_3) is receiving a lot of attention [1]. However, NH_3 is a toxic gas whose levels in the immediate environment require monitoring [2]. Current research is now focusing on new low power consumption sensor materials that can be operated near-room temperature [1]. WS_2, a transition metal dichalcogenide (TMDC) is semiconducting with a large surface area and high electrical conductivity making it a potential gas sensor [1]. Most of the WS_2 based sensors for room temperature sensing of NH_3 were prepared by top-down methods and their surfaces are not passivated [2].

Herein, the surface of WS_2 nanoflakes was capped with oleylamine (OLA) during colloidal synthesis. The use of OLA, a capping agent results in the formation of large organic shells which protect the core nanoparticle from oxidation [3]. XRD patterns hinted at slight oxidation of WS_2 to WO_3. Moreover, XPS analysis showed that the most of that oxidation occurred on the protective organic shell. The WS_2 nanoflakes' fast n-type response to NH_3 vapours at room temperature further proved that the oxidation was not to a large extent. It is well known that metal oxide chemiresistive gas sensors operate at higher temperatures (200 – 500 ^oC). However, the sensor showed a somewhat sluggish recovery.

Exposure of the capped WS_2 nanoflakes based sensor to humidity affected the detection of NH_3. The sensitivity towards NH_3 vapours increased significantly under high relative humidity. The adsorbed water molecules increased the electrical conductivity of the WS_2 nanoflakes based sensor due to the increased number of charge carriers on the surface. The sensitivity, recovery time and selectivity of the sensor can be improved by forming composites with other TMDCs, carbon nanomaterials, polymers or doping with a metal atom.

This study received financial support from the National Research Foundation of South Africa. The authors are grateful to the Department of Higher Education, University of the Witwatersrand and the Universidade Federal do Paraná.

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Furfural-derived butenolides: versatile monomers to replace acrylates in paints and coatings

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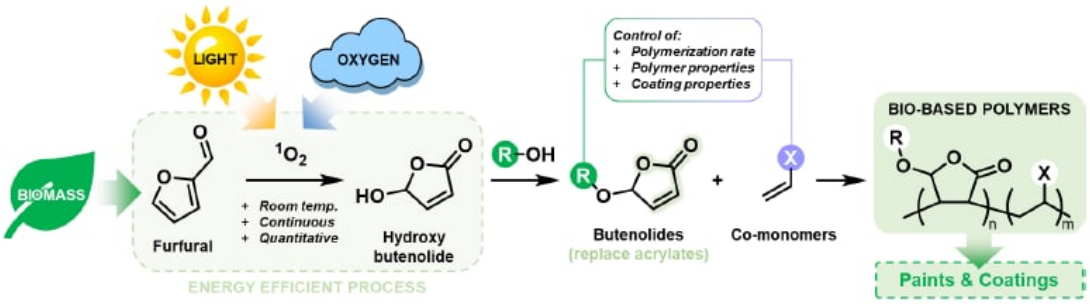
Photo-oxidation of waste biomass-derived furfural with singlet oxygen affords hydroxy butenolide, a singly reduced derivative of maleic anhydride, with minimal waste in matter and energy. This efficient process can be performed both in batch and flow setups. Hydroxy butenolide can be further derivatized through its acetal moiety, for instance by condensation with a variety of (potentially bio-based) alcohols. The resulting butenolides are cyclic acetals which incorporate an acrylate motif and thus constitute a sustainable alternative to acrylate-based polymers used in the coatings industry. The variability in the substituents and in the co-monomers offers a control on both the reactivity during radical polymerization and on the coating properties following cross-linking. The versatility of this new platform holds many promises for bio-based polymers and coatings, and beyond that for functional materials.



Can we turn wastewater in a new source of valuable metals?

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Innovative processes for treating industrial wastewater containing heavy metals had been under study for several years [1]. The main focus of those studies is the removal of heavy metals from industrial wastewater in order to protect environment. Despite the fact that environment protection is a very relevant subject, with the focus on a more circular economy in some literature people start to speak in "harvesting metals form wastewater". Very recently a circular economy approach in the water and wastewater sector model was proposed [2].

In this work, we try to contribute to this area, describing our efforts to develop membranes loaded with ionic liquids that are able to act as a separator/concentrator of metals when placed in aqueous media with very low concentration of the corresponding metals. Due to their strategic value some focus will be placed on rare earths but some other metals will be also addressed.

Several ionic liquids were tested but until now, the ionic liquids that are more efficient in removing metals from the aqueous medium are also those that are more weakly attached to the membranes. Trying to solve this problem, it has been tried to use gamma irradiation on the membranes. The idea is that the loaded membranes with ionic liquid to be irradiated in order to promote crosslinking so that the ionic liquid is less susceptible to exit. Another additional approach is to use crosslinking reagents on the surface of the membrane after it is charged with the ionic liquid and before proceeding with irradiation.

Ongoing work will be presented together with the perspectives to the future.

Acknowledgements: This work was supported by FCT projects UIDB/00100/2020, UIDP/00100/2020 and LA/P/0056/2020..

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Evaluation of produced water pipes mineralogical scaling in a central tunisian oilfield

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In oilfields, every barrel of produced oil is associated with the production of 3 to 5 barrels of water at global level [1]. One of the major flow assurance problems related to this coproduction of water is the inorganic scale deposition in water pipes .

In order to evaluate the scaling mechanism in a central Tunisian oilfield, the chemical compositions of produced water and scale deposits samples have been identified by ICP-OES analysis. All samples have been pre-treated by a microwave assisted acid digestion.

The scale mineralogical characterisation has been realized using XRD and SEM; and hydrocarbons traces have been detected by Rock-Eval pyrolysis.

The physical chemical produced water characterization has been used to calculate the Langlelier Saturation Index values, helping to determine the scaling and corrosive potential and to understand the scale deposition mechanism [2,3].

The future scale inhibition and removal strategies to be implemented in the concerned oilfield are being derived in a large part from the results of the present study.

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Light-Driven Proton Reduction With a Self-Assembled Dye-Sensitized Photocathode

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Consequences of global warming and climate change lead to increasing interest in sustainable alternatives for fossil fuels. Solar fuels, such as hydrogen gas, may be generated in a dye-sensitized photoelectrochemical cell (DSPEC) from water and solar energy. To date, the performance of DSPECs is limited by charge recombination.

We hypothesize that directional design of components in the photocathode can reduce charge recombination (see Figure), leading to the question "***How can organization of the molecular components decrease charge recombination in dye-sensitized photocathodes?***" Via supramolecular organization, using hydrophobic interactions, the catalyst is anchored in close proximity to the photosensitizer, but situated remotely from the NiO surface. This way, electron transfer between the components remains feasible, while charge recombination between the catalyst and NiO is suppressed.

We report the synthesis, construction and characterization of this system, including ultrafast spectroscopy as well as efficiency studies in light-driven hydrogen production.

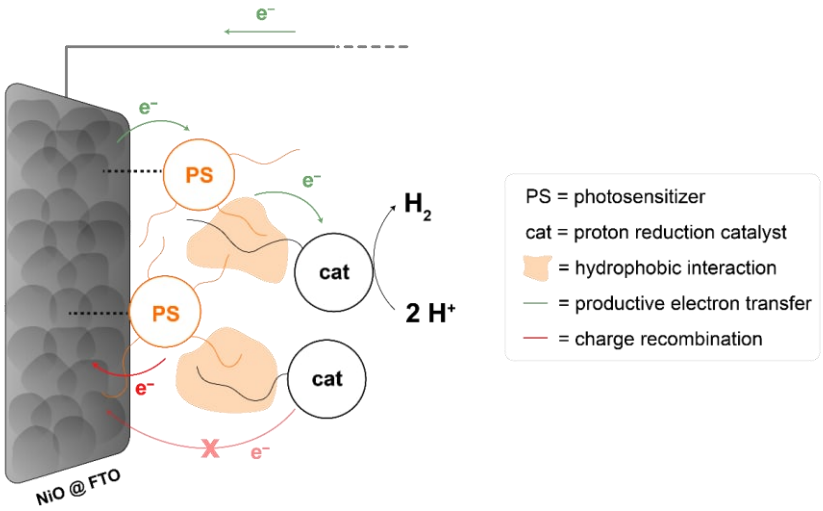

Figure: Self-assembled dye-sensitized photocathode for light-driven proton reduction.

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Biomass valorisation of marula nutshell waste into nitrogen doped activated carbon for high performance supercapacitors

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Electrochemical capacitors (i.e. supercapacitors) are high powered devices that have longlife cycle, fast charging rate, wide operating temperature and high rate compatibility [1]. Carbon materials, including activated carbons (ACs) have been used as active electrodes for energy storage due to their low cost, high surface area, good stability and easy availabily [2]. However, due to to lower conductivity of ACs, nitrogen can be used to improve its conductivity [3]. This study then reports on the valorisation of marula nutshell waste into a valuable electrode material for supercapacitors. Marula nutshell waste, a brown hard residue from marula fruits has been valorised into a nitrogen-doped activated carbon (N-ACs) by KOH treatment and using melamine as a nitrogen source. The microporous and mesoporous nature of N-ACs exhibited a high surface area of 1427 m²/g and pore volume of 0.31 cm3/g. The material was analysed in a two electrode system using 2.5 M KNO3 electrolyte. The high surface area, the efficient presence of micropores and mesopores, defects, and the high content of nitrogen (5.1%) revealed that the material produced an outstanding energy density of 28.4 Wh/kg and a power density of 499 W/kg in 2.5 M KNO3 electrolyte. The conversion of marula nuts waste into N-ACs is thus seen to provide a means of converting biomass waste into a useful energy storage material for supercapacitors.

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Strategy for quantification of vented gas emissions from oil storage tanks

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During production, storage and transportation of crude oil, a portion of the natural gas associated with the oil is vented due to temperature or pressure variations.
These gases are released to the atmosphere without being treated or burned raising hazardous air pollution and greenhouse effect.
Evidently, the gas emission represents a loss of considerable value. But the harmful consequences to the environment are supposed to be of greater importance.
In petroleum production, vented gas begins at the wellhead and occurs at any point of processing until arrival to refinery. This phenomenon covers volatile organic compound emissions (VOC) in separators, storage tanks, pipelines and all facilities.
In this context, we present a review concerning various methods for VOC quantification in crude oil production essentially based on issued emissions from oil storage tank and an application case on onshore Tunisian oilfield.
We quantify three types of emission generated by storage tank: breathing losses, working losses and flash emissions that are estimated by means of several methods. These latter are available for estimating flash emissions from oil and condensate storage tanks [1,2].
On Tunisian fields, it would be interesting to find the adequate way to recover them. This can solve energetic and environmental issue.
As a continuation to this work we suggest to study the possibility of using such emissions as a fuel gas in the same facility or to produce electrical energy using an appropriate generating technique.

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Heat Capacity as a Tool to Explore the Nanostructuration in Ionic Liquids

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It is nowadays well accepted that, when the alkyl chain of an ionic liquid (IL) is long enough, the isotropic liquid phase segregates into two distinct nanodomains: a polar domain, in which the charged parts of the IL are present, and a nonpolar domain, where the terminal moieties of the alkyl chains are located [1]. In this work we report the study of the heat capacity of a series of ILs with a common anion, [$C_nC_1$im][OTf] (with n = 2, 4, 6, 8, 10, 12), which has allowed us to detect the effect of the IL's nanostructuration on this property. The new *i*SenseDSC microcalorimeter system (refurbished and upgraded version of a SETARAM microDSC III), and a high precision drop calorimeter [2] were used to measure the heat capacity of the [$C_nC_1$im][OTf] IL series.

For the high precision heat capacity measurements, sapphire (NBS SRM 720) was used as calibrant. The overall performance of the systems was tested/evaluated with recommended substances, namely: benzoic acid, anthracene and [C_6C_1im][NTf_2]. The attained resolution of 0.3 % and an uncertainty better than 1 % were found to be enough to detect the effect of nanostructuration in the ILs.

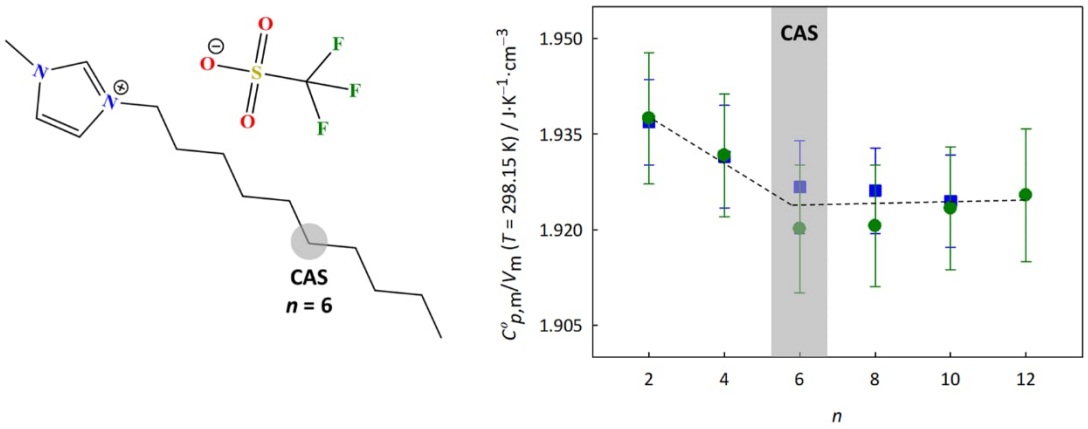

Figure 1. Molecular structure of the [$C_nC_1$im][OTf] ionic liquid, and volumetric heat capacity ($C^o_{p,m}/V_m$), at T = 298.15 K, as a function of the number of carbon atoms (n) in the alkyl side chain of the cation. ●:*i*SenseDSC, ■: drop calorimetry. "CAS" means "critical alkyl size".

Upon plotting the molar, specific and volumetric heat capacities as a function of the number of carbon atoms in the alkyl chain, n, a trendshift at n = 6 (critical alkyl size, **CAS**), was observed. At this alkyl chain length, the volumetric heat capacity reaches a minimum, evidencing the intensification of the nanostructuration in two distinct nanodomains [3,4].

This work was supported by the Fundação para a Ciência e Tecnologia (FCT) (funded by national funds through the FCT/MCTES (PIDDAC)) to CIQUP, Faculty of Science, University of Porto (Project UIDB/00081/2020), IMS-Institute of Molecular Sciences (LA/P/0056/2020). RMAS is grateful to FCT for the award of his PhD grant (Reference: U1/BD/153093/2022). AIMCLF is also financed by national funds through the FCT-I.P., in the framework of the execution of the program contract provided in paragraphs 4, 5 and 6 of art. 23 of Law no. 57/2016 of 29 August, as amended by Law no. 57/2017 of 19 July.

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Resolving the paradox of high donor electrolytes for practical lithium-sulfur batteries

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Lithium-sulfur (Li-S) batteries are considered to be the next-generation power cells, which are lighter, cheaper, and offer higher gravimetric energy density compared to the conventional cells. Despite of these merits, the current operating conditions such as flooded electrolyte conditions (> 20 µL mg_{sulfur}^{-1}) and low sulfur utilization are hampering the attainable volumteric energy density of the Li-S cells [1]. In this direction, decreasing the electrolyte to sulfur (E/S) ratio below 10 µL mg_{sulfur}^{-1}, denoted as a lean electrolyte condition, is one of the ultimate targets in Li-S battery research. Yet, operation under lean electrolyte conditions using conventional ether-based solvents is not possible owing to reduced ionic conductivity resulting from high viscosity and low solubility of lithium polysulfide leading to poor sulfur utilization (Figure 1a). Recently, solvents with high Gutmann donor number (DN) are shown to promote the sulfur redox reactions, increase sulfur utilization and prevent cathode passivation compared to their low DN counterparts [2]. However, with increasing donicity of the solvent, its reactivity towards lithium metal also increases in an uncontrolled manner, resulting in a short cycle life through unstable interface formation (Figure 1c). The electrolytes reported to date can only perform one function, they can either stabilize the Li metal anode surface or increase the solubility of lithium polysulfides, but not both, thus a new electrolyte chemistry enabling this dual function is needed.

To resolve this paradox, we designed, for the first time, the concept of a dual functional high DN electrolyte, which can retain high solubility of polysulfides while simultaneously stabilizing the lithium metal anode surface (Figure 1b), thus enabling stable cycling at high areal sulfur loadings under lean electrolyte conditions even in the absence of $LiNO_3$. Furthermore, the incorporation of the fluorine atom in the solvent passivated lithium metal anode by generating a homogenous LiF-rich SEI layer and therefore mitigating the lithium dendrite growth. These features enabled stable cycling with a specific capacity of 1247.4 mAh g_{sulfur}^{-1} under practical Li-S battery conditions at high sulfur loadings of 2.5 mg_{sulfur} cm^{-2} and lean electrolyte conditions, 7 µL mg_{sulfur}^{-1}. We also observed highly reversible charge-discharge profiles at 0.03C for both 8.0 and 10.0 mg_{sulfur} cm^{-2}, which are unprecedented, with substantial specific capacities of 1322.8 and 1224.8 mAh g_{sulfur}^{-1}. Moreover, these findings surpass all the previously reported high donor electrolytes in Li-S batteries and represent a new benchmark for high DN electrolytes in Li-S batteries [3].

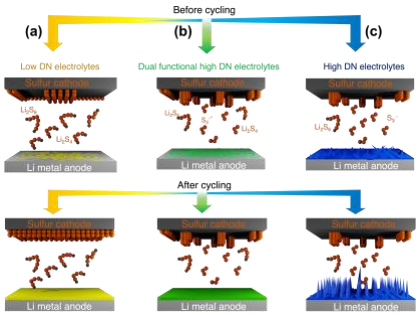

Figure 1. Schematic illustration of operating mechanisms in Li-S cells when the electrolytes with different donicity and functions are used: (a) low DN electrolytes, (b) dual functional high donor electrolytes, (c) high DN electrolytes.

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Synthesis and Characterization of Nitrogen- doped hollow carbon spheres/Cu_2S composites for potential application as counter electrodes in dye sensitized solar cells

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Current solar cells have disadvantages that include weather dependency and high manufacturing costs. Dye-sensitized solar cells (DSSCs) have emerged as possible solutions for these drawbacks. Since it is predicted that the global warming effect will result in the sun emitting less energy. DSSCs have the added advantage of working in low-light conditions, and the ability to harness light energy from other devices. Dye-sensitized solar cells (DSSCs) have emerged as a promising 3rd generation solar cell due to their low cost, ability to work in low-light conditions, and harness energy from other lights [1]. Although DSSCs have low production costs, their low efficiency due to the platinum (Pt) electrocatalyst limits their commercial implementation. DSSCs are made up of many components including dye, and counter electrode (CE). Modifications can be made on these components to improve efficiency and make the DSSC more eco-friendly. For instance, CE research has focused on finding substitute electrocatalysts. In this study copper sulfide (Cu_2S) and hollow carbon spheres (HCSs) have been considered as viable substitutes for Pt since they exhibit good electrocatalytic properties. Carbon materials have corrosion resistance towards iodine, and Cu_2S has superior oxidation resistance. Therefore, they can be used for electrolyte redox reactions at the CE in a DSSC. The properties of HCSs can be enhanced by making the carbon shell porous, increasing the number of carbon shells, or by doping the carbon shell with heteroatoms such as nitrogen (N). These modifications can improve the conductivity, surface area, adsorption, and electronic properties. For this research porous nitrogen doped single-shelled and double-shelled HCSs were synthesized.

The Cu_2S-HCS composites were prepared using OLA as the surfactant, with different percentages of Cu_2S and HCSs. The different composition mixtures were heated to 100 °C and then washed to remove the unreacted elements. The synthesized materials were analyzed using various techniques. TEM showed the spherical morphology of HCSs, the hexagonal morphology of Cu_2S, and the successful formation of the composites. The surface area and porosity of the materials were measured using the BET technique. Graphitization of carbon and the phase composition of Cu_2S was analyzed using PXRD. The successful incorporation of N within the structure of the N-HCSs was confirmed using XPS. The electrocatalytic activities of the composites were investigated using CV,EIS, Tafel polarization, I- V and compared to Pt under similar conditions. The 75 wt% N-HCS: 25 wt% Cu_2S composite had higher current density, lower peak-to-peak separation, and high electrochemical double layer capacitive current, good adhesion to the FTO glass and great photovoltaic performance compared to Pt. This suggests that it was the better performing composite and has the potential to substitute Pt- CE in DSSCs.

We thank the DSI/NRF CoE-SM and the University of the Witwatersrand for financial support.

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Development of bio-based aerogels as efficient cathodes for electrochemical reduction of CO_2

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The possibility of using CO_2 (a by-product of many industrial processes), as an abundant, non-flammable and non-toxic renewable raw material, is promising towards reducing fossil fuels dependence. CO_2 utilization as a renewable carbon source in the electrochemical CO_2 reduction is an attractive field of research due to the potential to close the anthropogenic carbon cycle [1]. Another important advantage of electrochemical CO_2 reduction as a CCU technology (Carbon Capture and Utilization) is the possibility to store energy from renewable sources, such as solar and wind energy, that are seasonal, intermittent and geographical dependent by converting CO_2 into fuels [2,3].

In previous works the development of an electrochemical process to produce syngas ($CO+H_2$) was reported [4,5]. The syngas produced by this green process can be used to synthetize an enormous variety of fuels and chemicals in a sustainable way.

In this work, alginate aerogels were explored as efficient supports for CO_2 conversion to synthesis syngas through electrochemical process. Aerogel properties as open porous structures, large surface areas, high porosity, mesoporous pore size distribution and low bulk density, are very attractive for catalytic applications [6]. The utilization of bio-based materials as catalyst supports is highly interesting in the context of process sustainability. Alginate is a natural biopolymer mainly derived from brown algae, consisting of α-L-guluronic acid and β-D-mannuronic acid residues, linearly linked by 1,4-glycosidic linkage. Due to its biodegradability, low cost, non-toxicity and stability, it is an attractive candidate regarding the greenness of final application.

Acknowledgements

This work was supported by the project "CO2RED – Understanding CO2 Electro-REDuction in Porous Materials" with reference PTDC/EQU-EPQ/2195/2021, funded by FCT – Fundação para a Ciência e Tecnologia. S. Messias is thankful to FCT for the fellowship SFRH/BD/147219/2019.

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Valorization of hydroponic agriculture residues: cellulose and nanocellulose extraction and soil amendment

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Hydroponics is an agriculture innovation where the soil is replaced by a nutrient-rich water. Plants may grow with their roots exposed to the nutritious water, or the roots may be physically supported by an inert substrate.[1] Different types of substrates can be used, such as pine bark, coconut husk fiber and rice husk. The waste produced after cultivation is a valuable resource, due to the properties inherent to its origin, such as being a low-cost, abundant, biodegradable, and renewable material. Such residues are rich in lignocellulosic components that can be extracted and purified to obtain cellulose and nanocellulose.[2]

In this work, we have studied and tested different methods for extracting cellulose and nanocellulose from residues of coconut husk fiber and a mixture of pine bark and coconut husk fiber, used in tomato and strawberry hydroponics, respectively. Residues were grinded, washed and chemically treated to obtain cellulose and nanocellulose. The chemical process consisted in different stages, namely acid and alkaline treatment, and bleaching. The acid hydrolysis followed by ultrasonication is the final stage to obtain nanocellulose. Both materials were characterized by TGA, DSC, and FTIR-ATR, which confirm that they have very low levels of lignin and hemicellulose. The morphological characterization performed by SEM revealed the existence of micro- and nano-crystals in the cellulose and nanocellulose samples, respectively, reinforcing the efficiency of the extraction method used.

Henceforth, the potential of using cellulose and nanocellulose as a soil amendment additive for the immobilization of toxic heavy metals has been evaluated. Contaminated soil samples were treated with cellulose, nanocellulose and substrates after cultivation, and incubated for 30 days under typical environmental conditions. Subsequently, the ability to immobilize the heavy metals Hg, As and Sb is currently under evaluation through single extraction method, using cold vapor (Hg) and hydride generation (As and Sb) atomic absorption spectroscopy.

CIQUP acknowledges financial support from FEDER/COMPETE through grants UID/QUI/0081/2020, NORTE-01-0145-FEDER-000074 (project S4HORT).

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Increasing the efficiency of hydrogen peroxide generation at liquid|liquid interface with Indium tin oxide nanoparticles

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Hydrogen peroxide can be produced in a conventional way using high temeratre and organic reagents, which doesn't play a good role for our environment. This is the reason why generations of chemicals at liquid|liquid interface is an opportunity for sustainable development. In this research we focused on oxygen reduction reduction (ORR):

$$2DMFc_{(NPOE)} + 2H^{+}_{(w)} + O_{2(w,NPOE)} + 2ClO^{-}_{4(w)} \rightarrow 2DMFc^{+}_{(NPOE)} + H_2O_2 + 2ClO^{-}_{4(NPOE)}$$

Instead of using conventional liquid|liquid in bulk solution, the three phase junction with carbon paste electrode (CPE) was checked. [3] Previously, the catalytic effect in ORR was described [4]

In the research carbon paste electrodes were used, which were prepared using graphene powder with addition of indium tin oxide (ITO) nanoparticles mixed with decamethylferrocene solution in viscous 2-nitrophenyloctylether (NPOE). Then the electrode was put in contact with the solution of perchloric acid. When putting the potential to the CPE, the regeneration of electron donor is possible and increase the reaction efficiency. Cyclic voltammetry experiments were performed to check different ratio of ITO/graphite mass and detection of generated hydrogen peroxide by scanning electrochemical microscopy.

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The role of ionic liquids as electrolytes on the efficiency of dye-sensitized solar cells

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Ionic liquids have been extensively used in the composition of both liquid [1], solid [2] and quasi-solid [3] electrolytes for dye-sensitized solar cells (DSSC, **Figure 1**), leading to various improvements in the device's photovoltaic properties. For this purpose, a series of iodide salts containing imidazolium, picolinium, ammonium and guanidinium cations, were prepared and employed as alternative redox mediators in the electrolyte solution of DSSCs. A best overall conversion efficiency (η) of 6.52%, was achieved for the N719 reference dye, when using 1-ethyl-2,3-dimethylimidazollium iodide ([EDMIM]I) and 4-tert-butylpyridine (TBP). In addition to their I-V curves, electrochemical impedance spectroscopy (EIS) was also measured to ascertain the effect of the iodide salts on the photovoltaic parameters.

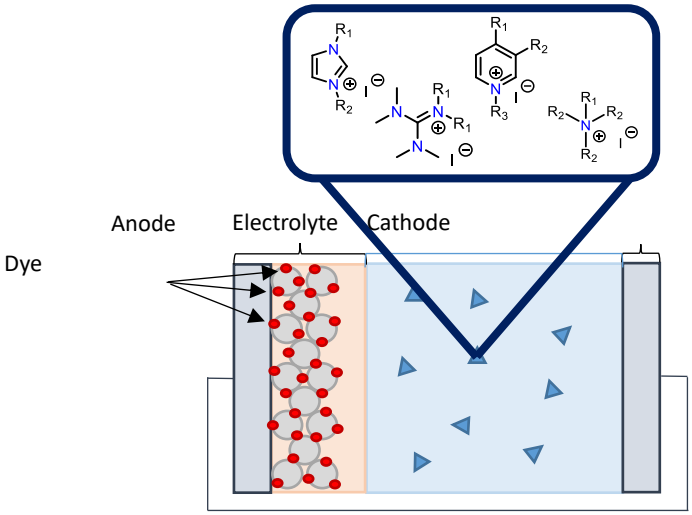

Figure 1. *Schematic representation of a dye-sensitized solar-cell and the iodide structures used as electrolyte additives.*

This work was performed under the projects PTDC/QUI-QOR/7450/2020 "Organic Redox Mediators For Energy Conversion" through FCT – Fundação para a Ciência e a Tecnologia I. P. and POCI-01-0145-FEDER-016387 "SunStorage – Harvesting and storage of solar energy", funded by European Regional Development Fund (ERDF), through COMPETE 2020 – Operational Programme for Competitiveness and Internationalisation (OPCI). This work was also supported by the Associate Laboratory for Green Chemistry - LAQV which is financed by national funds from FCT/MCTES (UIDB/50006/2020 and UIDP/50006/2020). FCT/MCTES is also acknowledged for the National NMR Facility (RECI/BBB-BQB/0230/2012 and RECI/BBB-BEP/0124/2012,) and PhD grants 2020.09047.BD (J.S.), PD/BD/135087/2017 (A.L.P.) and PD/BD/145324/2019/ (G.M.).

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New acenaphthylene-based dyes for DSSC applications

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Dyes containing an acenaphthylene core have remained unexplored for the application on DSSCs when compared with the phenanthrene-based dyes [1]. A new set of novel compounds containing an acenaphthylene backbone was synthesized. These include derivatives of 1,2-diethynylacenaphthylene containing phenyl, thiophene, benzotriazole and thieno-[3,2-b]thiophene rings present in their π-bridge. Their synthesis involved Sonogashira coupling reactions to introduce the ethynyl moiety and the different aromatic rings, formylation reactions, and also Knoevenagel condensations to introduce the cyanoacrylic anchoring groups. The compounds have been applied in DSSCs devices and their performance was evaluated by measuring the current-voltage curves. Photophysical, electrochemical and computational studies were performed to correlate the obtained efficiencies with the different π-bridges present in these dyes.

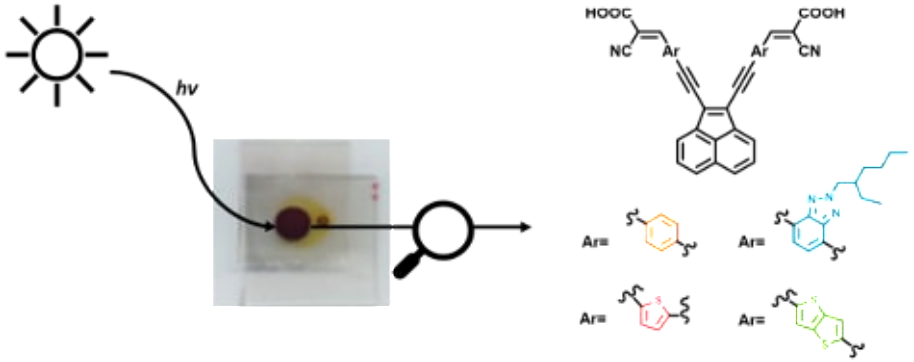

Figure 1: Schematic representation of the synthesized acenaphthylene-based organic dyes.

Thanks to FCT – Fundação para a Ciência e a Tecnologia I. P, this work was performed under the project PTDC/QUI-QOR/7450/2020 "Organic Redox Mediators For Energy Conversion". This work was also supported by the Associate Laboratory for Green Chemistry - LAQV which is financed by national funds from FCT/MCTES (UIDB/50006/2020 and UIDP/50006/2020). FCT/MCTES is also acknowledged for the National NMR Facility Network (ROTEIRO/0031/2013-PINFRA/22161/2016, cofinanced by FEDER through COMPETE 2020, POCI, PORL, and FCT through PIDDAC) and PhD grant PD/BD/145324/2019/ (G.M.).

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Synthesis, Spectroscopic and Photophysical Properties of 7-Substituted Coumarins for DSSCs cells

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Dye-sensitized solar cells (DSSCs have been under extensive research for more than two decades due to their low cost, simple preparation methodology, low toxicity and ease of production. Nonetheless, their low efficiencies are still a disadvantage. 7-Substituted coumarins are one of the most studied coumarin derivatives and have demonstrated antibacterial, anti-inflammatory activity and, monoamine oxidase-B and cholinesterase inhibitor for the treatment of Alzheimer's disease. [1, 2] Coumarin derivatives, especially when extension of the π-conjugated system is carried out at the 3-position have also been reported as relevant chromophores and fluorescent dyes due to their donor-π-acceptor (D-π-A) system. The spectroscopic and photophysical properties they present makes them great candidates as laser dyes and solar chemical concentrators in photovoltaic cells. [3] The organic dye is one of the pieces of this intricate puzzle that constitute the DSSCs but, more than looking only for the dye design, one must consider the process of recombination reactions that play an important role and as such, the electrolyte is also a crucial component in DSSCs. Here we report our initial approach to the synthesis of a new hybrid dye-redox mediator system for DSSCs starting from 7-hydroxycoumarin, having a redox mediator unit based on an ionic liquid (IL) unit covalently linked to the coumarin scaffold via alkyl chains with different lengths. The dyes prepared will have as anchoring site to the TiO_2 layer the cyanoacetic acid or vinylpyrimidine groups (**Figure 1**). The spectroscopic and photophysical properties as also its efficiency as dyes for DSSCs will be presented and correlated to the main structural characteristics.

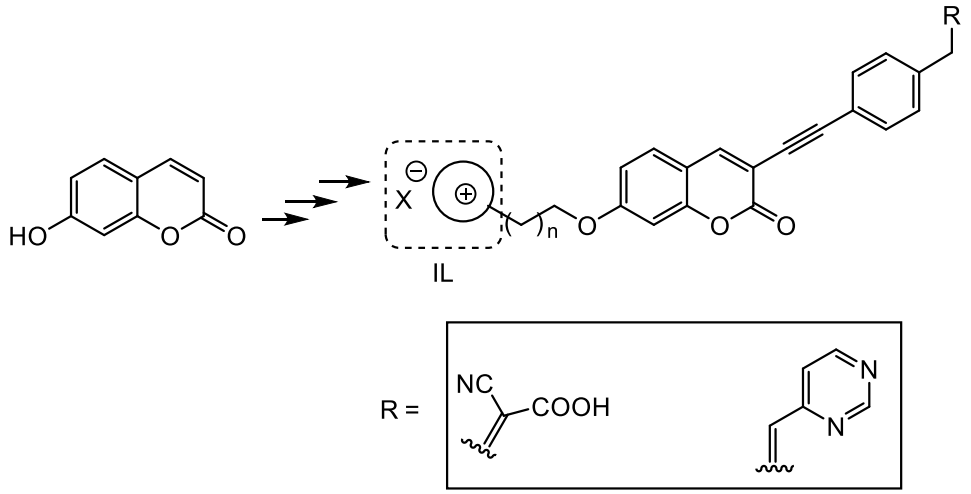

Figure 1. Schematic representation of a new hybrid dye-redox mediator system for DSSCs starting from 7-hydroxycoumarin.

Acknowledgements: This work was performed under the projects PTDC/QUI-QOR/7450/2020 "Organic Redox Mediators For Energy Conversion" through FCT – Fundação para a Ciência e a Tecnologia I. P. This work was also supported by the Associate Laboratory for Green Chemistry - LAQV which is financed by national funds from FCT/MCTES (UIDB/50006/2020 and UIDP/50006/2020). FCT/MCTES is also acknowledged for the National NMR Facility (RECI/BBB-BQB/0230/2012 and RECI/BBB-BEP/0124/2012,) and PhD grants 2020.09047.BD, PTDC/QUI-QOR/7450/2020.

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Phase behavior of the deep eutectic solvent menthol + thymol with supercritical CO_2

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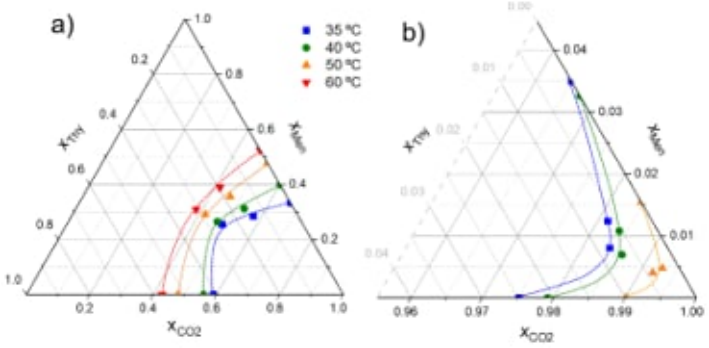
Deep Eutectic Solvents (DES) are a new type of green solvents formed by two solids at room temperature. Upon mixing, the melting point decreases significantly respect the ideal behavior due to strong intermolecular interactions formed. Due to their properties such as low vapor pressure, tunability, low cost and versatility, novel green applications are being proposed for these solvents such as extraction, reactions, gas absorption, materials and drug delivery.

Combination of DES with supercritical carbon dioxide, $scCO_2$, is a promising approach relatively underexplored. Some examples of applications include impregnation, polymer treatment and encapsulation. Moreover, DES have been extensively used for CO_2 absorption. Nevertheless, knowledge of phase behavior of CO_2 + DES is scarce and little is known about the relationship between the intermolecular interactions and mutual solubility with CO_2 or how the addition of CO_2 modifies the composition of the phases. For this, a deep study of a DES + CO_2 system is necessary.

The DES formed by menthol + thymol have potential applications in the pharmaceutical industry as menthol and thymol have antibacterial and anti-inflammatory properties among others. It is also an interesting model mixture as molecular structures are very similar but intermolecular interactions cause strong deviations from ideality.[2] This mixture is considered a DES and present a eutectic composition at molar ratio equal to 1:1. Some of its properties have been previously reported.[1]

In this work we report the phase behavior of the thymol + menthol DES plus CO_2 for two compositions (1:1 and 1:2) at 35, 40, 50 and 60 ºC and pressures up to 220 bar. This includes solubility of the DES in CO_2 and solubility of CO_2 in DES (i.e. mutual solubility). The measurements were carried out using a variable volume view cell. The phase behavior of menthol + CO_2 and thymol + CO_2 were also measured for comparison. The molar ratio menthol:thymol in the vapor phase was also determined by NMR.

From interpolation of the experimental trends, ternary diagrams were built. The results indicate that the mutual solubility of the DES and CO_2 is lower than those of the individual components and this difference is lower as temperature increases and composition approaches the eutectic. Furthermore, the vapor phase is slightly enriched on the most volatile component (menthol) indicating that the composition of the liquid DES mixture is affected by the presence of $scCO_2$. Is was possible to explain the results by considering a deviation of ideality caused by intermolecular interactions menthol – thymol. The CO_2 solubility data were correlated using the Peng-Robinson Equation of State, which is able to reproduce the main features of the ternary mixtures.



a) Solubility of CO_2 in DES at 80 bar. b) solubility of DES in CO_2 at 120 bar

We acknowledge financial support from the Spanish Ministry of Economy and Competitiveness (MICINN), research project RTI2018-097230-B-100.

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Bio-sourced polyamines for the future

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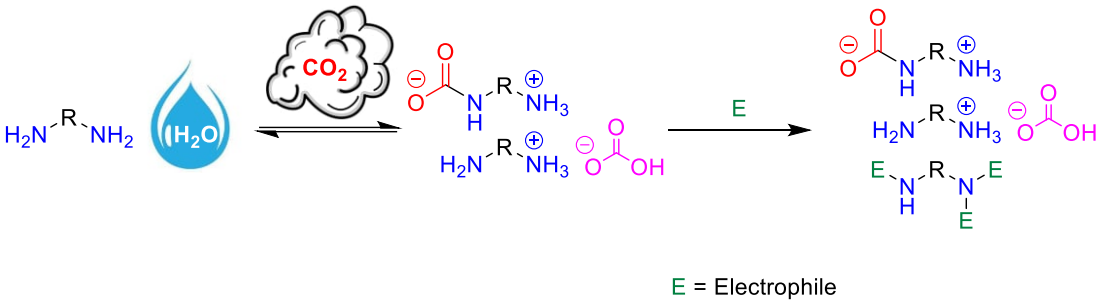
Due to the ever-increasing concentration of CO_2 in the atmosphere, its capture and transformation is an urgent and major challenge for the scientific community to limit its impact on climate change.[1]
In this context, this presentation will show how bio-based polyamines in aqueous media can react with CO_2 molecules to give dynamic combinatorial libraries of carbamate and carbonate species.[2] Given the reversible nature of CO2 capture by polyamines,[2,3] we studied the impact of different stimuli on CO_2 desorption.
In addition, the reactivity of carbonated polyamines with various electrophiles was explored.



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The treatment of the liquid rejects from the petroleum refinery of Arzew-Algeria to the Mediterranean littoral

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During the process of transformation in the refinery of Arzew, some chemical products are brought into the industrial water treatment, which reaches the long term at their effectiveness, are rejected because they are polluted. This pollution is known on the practical level by the deterioration of the quality of the water rejected into the natural environment and to the sea, which bring to a degradation of the environment and with a reduction of oxygene dissolved in aquatic environment. Large quantities of used water , domestic and industrial , are cast each day, without any treatment, directly to the sea, which can be a serious source of pollution according to the degree of harmful effect of products (used oils, solvents, various muds and dangerous waste). The pollution in Algeria, is the origine thus, of the serious medical dangers to the population, and on the littoral, especially on the tourist structures . ALGERIA currently follows a very severe and rigorous environmental policy to fight the pollution.
In all the production factories, it is required to have stations of processing waste and especially to treat the used water. In the refinery of Arzew, which is on the Mediterranean littoral, the waste water coming from the zones of the production, is treated in two stations , where oils are recovered and the solid waste is eliminated, before this water is rejected to the sea . The station contains two basins, first basin PPI (Parallel Plaques Interceptor) to eliminate the bulky solid waste . The second API basin is a separator by gravity, which removes the free compounds of oil and other solids.
In end the water purifyed will be evacuated towards the sea.
The refinery of Arzew works for a protection of the environment, and to protect the littoral against the pollution, by the installation of the stations for the purifying of the used water.

Key Words: Pollution, Environment, Purifying, Waste Water.

The study of the water pollution in the west of Algeria

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One of the objectives of a modern society is the improvement of the living conditions of the Man. If one goes up the course of the centuries, the history teaches us that the water pollution accompanied all civilizations and that it was always a concern for the legislator until the beginning of the century. Nature, thanks to its intrinsic capacities of regeneration managed to overcome the misdeeds of the man. The pollution developed because of the concentration of the population and the development of her industrial activities. Another time, the pollution water was primarily of organic nature biodegradable never not exceeding the purifying capacities car of the rivers, but the industrial evolution contributed to the marketing . Molecules polluting, that micro the organizations cannot always metabolize and of which some constitute a danger to the Man and his environment. An awakening of an alarming situation as regards quality of water dates from the Seventies. All the types of water were concerned, the subsoil waters, until there with the shelter, are also reached and from now on, one does not cease speaking about nitrates, micro mineral and organic pollutants. Vis-a-vis with this very critical situation at the same time for the health of the man and the environment, the resources water; a vast program of prevention and fight launched out to Algeria in the Seventies/80 and which aimed, the construction of several stations of purification in the most important cities, generally of a size higher than 20. 10' living Following an assessment of this effort of investment established in 1989, it appears clearly that ohjectif stations of purification was unfortunately not reached but on the contrary the situations developed well , then it appears very important to us to draw up through this modest work, a point of topicality on the state of the quality of water in our area of West of Algeria, with an analysis of the causes of the pollution and the search for the solutions to decrease by its impact.

Key Words: Water Resources, Pollution Sources, Protection, Purifying,

The pollution of the sea water by the waste from the L.N.G. plant Arzew-Algeria and the waste water purifying system

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Generally, the pollution makes a lot of problems for the environment. The natural gas (N.G.) is a compound of the light hydrocarbons, methane,ethane,propane,butane and other trace elements,like Helium, Nitrogen,Carbon Dioxide and others. After the different zones of the natural gas treatment, a problem of pollution of water is appeared.

In this plant there are eight zones, six units of process, one for the energy production and another for the storage. It exists a system to treat all the effluents contamination coming from these zones.

The treatment of this waste water consists in the separation of the oil and the sludge to satisfy the standard environmental protection.

There are six separators,pools of concrete are connected with a collector for supply which is connected with each separator by three conduits. A diffusion apparatus is put in front of every nozzle of entry in the separator, and this is for a suitable distribution of the liquid in the separator.

In reason of the decrease speed of the liquid when it passes through the separator, the particles carried, deposit in the bottom of the separator. The suspended matters are collected by a chain collector. The float matters up the liquid of the separators, mainly oils, are removed through the creaming tubs.

Key Words: Pollution, waste water, oils, separator.

The study and the development of the renewable energy in the aquatic ecosystem

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The wind, waterfalls, the warmth, the heat of volcanoes, lightning, solar energy captured thanks to solar plates and a lot of qi energy sources are organic and very important, for example the energy of the seas. Ocean energy is renewable energy extracted from the marine environment. The seas and oceans represent 71% of the earth's surface. They could theoretically provide 30,000 SARWG from single solar radiation on the surface which is incredible.
An aquatic ecosystem constantly produces living matter. It is gradually transformed into dead organic matter, which is itself then slowly mineralized, in part or in full.
The engine of the ecosystem is solar energy; Indeed, only holders of plant chlorophyll pigments are able to capture light energy and transform it in the form of chemical potential energy to manufacture, from minerals, molecules carbonaceous substances such microscopic algae and other.
But the ecosystem is a thermodynamically open system, since in fact there are leaks of material therefore energy, following sedimentation and biogeological recycling material, but also due to human samples (fisheries and aquaculture) . Chemical pollutants through the ecosystem and are transferred from one trophic level to the next and are a threat to the ecosystem and ultimately on Hommemais the increase in greenhouse gas emissions are increasing more and this threat affects the habitats and biota and hit the man in fact part.

Key Words: Ecosystem, Renewable Energy, Aquatic.

Assessment of urban environment aged microplastics as potential carriers of micropollutants to soil-plant systems

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Microplastics have been identified as emerging pollutants in soil-plant systems, even if there are still research gaps regarding the behavior and the degree of the effects of microplastics on these systems [1]. The use of treated wastewater and biosolids in agriculture is one of the identified sources of microplastics and other emerging pollutants into soil-plant systems since many of these substances are not efficiently removed during wastewater treatment [2].

Thus, the main goal of this study was to evaluate the potential of microplastics aged by urban environment stressors, such as those of disinfection treatments or exposure to weathering, as carriers of organic micropollutants to soil-plant systems. For that, microplastic particles of three polymers (LDPE – low-density polyethylene, PET – poly(ethylene terephthalate), and uPVC – unplasticized poly(vinyl chloride)) were previously aged by ozone exposure or by rooftop weathering. Then, sorption experiments were carried out to assess the sorption of ten organic micropollutants (OMPs), including pesticides and pharmaceutical substances, on microplastics (virgin or aged). Finally, phytotoxicity tests with the aged and OMP-sorbed microplastics were performed for two species of plants: *Lepidium sativum* and *Sinapis alba*.

The results show increased sorption of several of the selected OMPs on the microplastic particles after the aging treatments, although different affinities were observed between each OMP and polymer. The effectiveness of the aging treatment was previously assessed by characterizing the microplastic particles (i.e., by ATR-FTIR, SEM and XRD) before and after aging [3], allowing to link the modifications between virgin and aged microplastics to the increased sorption capacity of certain OMPs. The phytotoxicity test results showed normal early growth or a very low decrease in the early growth of the plant species selected under the conditions tested. Nevertheless, considering that the hypothesis that microplastics can sorb and, therefore, transport OMPs under certain conditions to ecosystems was confirmed, and that aging can increase their sorption capacities, this study is a further evidence of the pressing need for more research on the toxicity of microplastics with sorbed pollutants on soil-plant systems.

This work was financially supported by: LA/P/0045/2020 (ALiCE), UIDB/50020/2020 and UIDP/50020/2020 (LSRE-LCM), funded by national funds through FCT/MCTES (PIDDAC). M.N.M. acknowledges the PhD research grant from Fundação para a Ciência e a Tecnologia (FCT) (Ref. PD/BD/137730/2018, extended by COVID/BD/152633/2022), funded by national funds and by the European Union (EU) through the European Social Fund (ESF).

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Exploring novel azo compounds as molecular photoswitches

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Molecular switches are bistable chemical systems able to reversibly interconvert under the influence of external physical or chemical triggers, by constitutional, configurational or conformational changes. The systems responsive to light are called photoswitches[1] and they belong to classes such as *N*-acylhydrazones, azobenzenes, diarylethenes or spiropyranes. This field has significantly grown during the past two decades aimed for applications in materials chemistry for construction of smart windows, protective materials against sunlight, solar thermal fuels, data storage[2] or medicinal chemistry, particularly for controlled drug release or photopharmacology.[3]

Heteroayl azoswitches[4] are a new class of photoswitches which have been developed as an alternative to azobenzenes, thanks to their broader structural diversity that result in very different spectral properties, thus solving some of the azobenzenes drawbacks. Although very promising, the field of heteroayl azoswitches is relatively new and there are numerous unanswered questions regarding their structures, properties and mechanisms of actions relationships.

We present herein our work regarding novel azo compounds (Figure 1) involving pyrazole and oxadiazole moieties, from synthesis to study of the main parameters that characterise a photoswitch. In the context of the literature background, our novel 3,5-bis(trifluoromethyl)-4-arylazopyrazole were found to display different behaviour both for N*H* and *N*-protected pyrazole core, exhibiting very long half-lives, excellent fatigue resistance and reasonable photostationary states. At the same time, oxadiazole-decorated azobenzenes were systematically studied for their photoswitching properties, as well as effect on the luminescent property of the oxadiazole core, considering widely recognised ability to emit light of the oxadiazole-based compounds.[5]

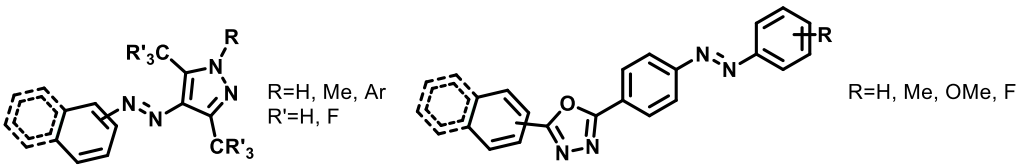

Figure 1 General structure of arylazopyrazoles and oxadiazole-decorate azobenzene synthesized and studied in this work.

Aknowledgments: This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2019-1003, within PNCDI III. The University of Bucharest - UniRem project is also gratefully acknowledged.

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Towards Electron-triggered Coordination-induced Spin State Switching in Viologen-based Metal Complexes

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The control of magnetic properties by external stimuli has attracted much interest over the past few decades and tremendous work has been achieved thereafter.[1] Our contribution to this field is based on the **C**oordination-**i**nduced **S**pin **S**tate **S**witching approach (**CiSSS**)[2] which, as its name implies, aims at changing the spin state of a metal center by modifying its coordination sphere. Therefore, based on our expertise in supramolecular chemistry and with the help of theoretical calculations, a well-suited model system was designed and eventually synthesized. In this presentation, the targeted tweezer-like molecule features a redox-responsive viologen-based hinge tethering a high affinity ligand to a magnetically active metal center. In agreement with the concept depicted below, the electrical stimulation of the hinge is expected to trigger a large amplitude molecular motion driven by the reversible, intramolecular π-dimerization of the electrochemically-generated viologen cation radicals.[3],[4] This fully reversible back and forth self-locking process will enable to control the coordination/dissociation of the ligand to/from the metal center and, consequently, its spin state. The spin-state switching process will be discussed on the grounds of spectroscopic, electrochemical and spectro-electrochemical data supported by quantum calculations.

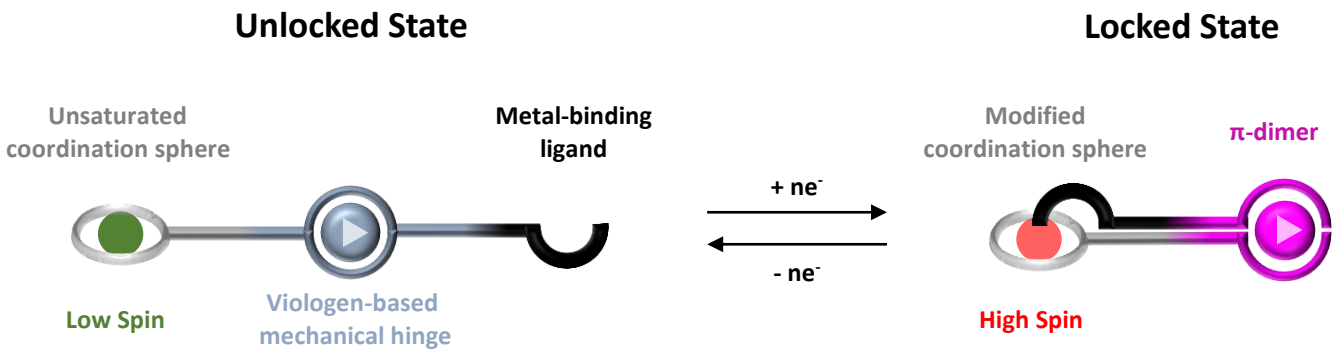

Figure 1: Electron-triggered self-locking behaviour for reversible CiSSS.

We would like to thank the Laboratoire de Chimie of ENS de Lyon for hosting this project and the École Doctorale de Chimie de Lyon (ED206) and the Région Auvergne Rhône-Alpes for financial support.

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From macrocycles into assembled chain-mails!

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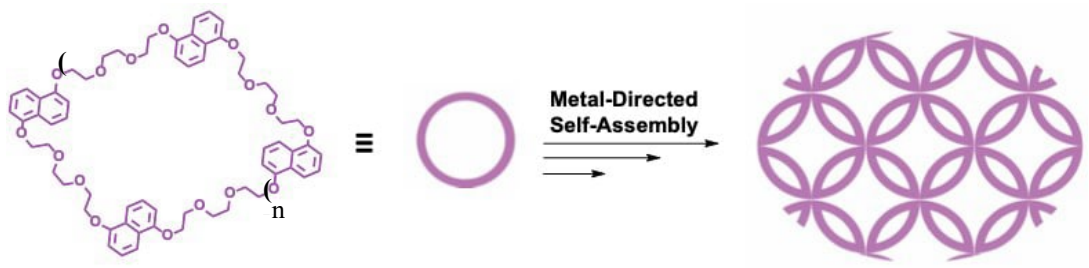
Knots and links, being part of the mechanically interlocked molecular architectures, are related to three-dimensional space. Nevertheless, links are less studied and are not as well classified as knots [1]. Nature shows examples of strong relations between topology and function [2,3]; for instance, complex topological structures such as those present in the chain-mail like bone armour lying under a Komodo dragon's skin are extremely robust [4], as is the non-covalent interlaced protein structure forming the capsid of the virus HK97 [5].

To achieve chain-mail type structures, macrocycles need to interlink with each other. Such complex topologies of links can be analyzed for example by looking at their two-dimensional assemblies at the atomic level. This is achieved by applying imaging techniques, such as AFM and STM.



Scheme 1: New macrocyclic ligands as synthons for interlaced structures

New synthons like a new family of macrocycles with alternating aromatic and polyether chains, have been synthesized and characterized with the aim of obtaining a controlled complex chain-mail structure (scheme 1). Such flexible and robust macrocyclic structures are formed by alternating the mechanical and physical properties resulting from the different building blocks. Their optimal packing arrangement on atomically flat 2D structures have been investigated and compared with the 3D structures obtained from single crystal analyses of the macrocycles and its/their solvates.

The authors thank the synthesis lab of the University of Fribourg as well as Dr. Aurélien Crochet for the X-ray service.

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Substrate Tumbling in Single Diastereomeric Complexes on a Surface

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Time-lapsed STM data for individual chiral amine/α-ketoester diastereomeric complexes on Pt(111) reveal two neighbouring complexation states that are coupled by a tumbling motion. The motion results in prochiral inversion of the α-ketoester. Tumbling between the states requires half-rotation of the entire α-ketoester substrate without branching into either dissociation of the complex or desorption of the substrate. Multi-step tumbling is interpreted as a sequence of transient H-bonded states that are further stabilized by adsorption interactions. The observation of adsorption and H-bond assisted tumbling provides insight on directed molecular motion on surfaces and on stereocontrol in asymmetric heterogeneous catalysis.

DOSY Experiments as an Untapped Tool for Characterizing Interlocked Molecules in Solution

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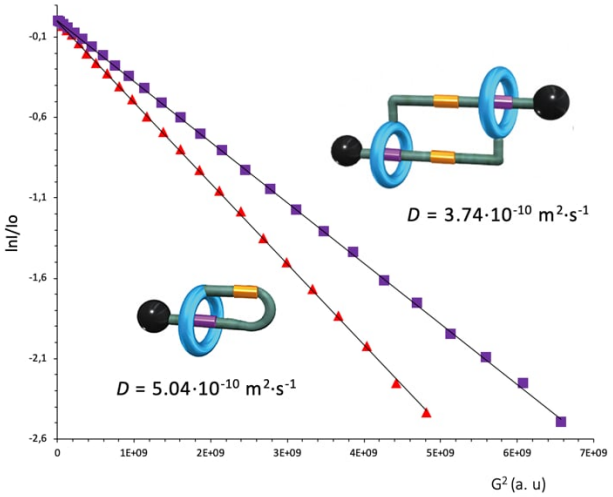
The identification of interlocked molecules, such as rotaxanes, constitutes a big challenge due to several reasons. After the formation of the mechanical bond, the integrity of the interlocked molecule, *i.e.* the entanglement of the components, has to be demonstrated. Moreover, if different interlocked products can be afforded from competitive coupling reactions, the unambiguous characterization of the final product (1+1, 2+2, 3+3,...) can be a difficult task, especially when analogous NMR patterns are expected for the hypothetical products.

DOSY (Diffusion Ordered Spectroscopy)[1] constitutes a major tool for evaluating the size of molecules in solution. Diffusion NMR experiments allow for the measurement of the translational diffusion coefficient (*D*) of a molecular species.[2] The *D* value can be related to the hydrodynamic radius via the Stokes-Einstein equation.[3] Thus, the hydrodynamic size of covalently bonded molecules, which itself it is an invaluable information, can be accurately determined by diffusion NMR experiments. Moreover, the diffusion coefficient can be related with the molecular weight considering a spherical shape.

Herein, we present a structural study of two different interlocked products, a [1]rotaxane and the corresponding dimeric interlocked compound obtained in a competitive coupling reaction from the same starting material.[4] Since both compounds possess similar ^{1}H NMR spectra, diffusion NMR experiments played a key role in the structural elucidation of both structures.



Graphical representation of the intensity changes $ln(I/I_o)$ as a function of G^2 (gradient strength) showing different slopes for the [1]rotaxane and the corresponding dimeric interlocked product.

We acknowledge Prof. Mateo Alajarin for his insightful discussions. This research was supported by the MICINN (PID2020-113686GB-I00/AEI/10.13039/501100011033) and Fundación Seneca-CARM (Project 20811/PI/18). A.S.-S. thanks to the Fundación Seneca-CARM for his contract (20259/FPI/17).

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Single-molecule imaging of dynamic CB[8] crosslinkers in supramolecular hydrogels

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Supramolecular interactions within polymer networks include hydrogen bonding, host–guest molecular recognition or metal–ligand coordination, resulting in physically-crosslinked hydrogels with complex dynamics. For instance, the viscoelastic properties of these hydrogels are dominated by temporal hierarchy of the dissociation and re-association of the supramolecular interactions [1]. Distinct crosslinking kinetics and binding strengths are responsible for emergent properties observed in the supramolecular hydrogels, which are key features for applications such as sensing, biomaterials and smart drug-delivery systems [2]. While some previously papers provide the kinetics of (dis)association events of supramolecular motifs as a method to elucidate the unique viscoelastic properties of hydrogels, most of them rely on independent characterisation of the free supramolecular complexes. However, extracting dissociation binding constants of cucurbit[8]uril (CB[8])-based supramolecular motifs with a range of binding stoichiometries (binary, ternary and quaternary) are not always possible with traditional methods due to limited timescales for these measurements and inappropriate fitting models. In addition, translating the binding kinetics observed for CB[8]-complexes found as free molecules in solution to systems where CB[8] guest molecules are attached to polymer backbones may not be accurate. By employing super-resolution fluorescence microscopy (SRM), we were able to resolve guest-host complexes within hydrogels with high spatial and temporal resolution at a single-molecule level. We synthesized styrylpyridinium (StPy) derivative guest molecules, whose fluorescence intensity is dramatically enhanced upon 2:1 complexation with CB[8] and investigated the lifetime of these complexes (Fig. 1). Due to the significant fluorescence enhancement of StPy-CB[8] complexes compared to StPy, we were able to detect the complexes at a single molecule level by employing real-time imaging. StPy-CB[8] complexes were studied at different concentrations (nM-µM) and we observed that the supramolecular complexes dissociated ten times faster when bound to the poly(acrylamide) backbone compared to free molecule analogues in aqueous media. These results indicated that StPy-CB[8] complexes can be readily detected over a wide range of experimental conditions, and that the dissociation kinetics of backbone-tethered StPy-CB[8] complexes are affected by the polymer chains within the hydrogels. Thus, we demonstrated for the first time a new strategy to directly study supramolecular crosslinks in polymeric hydrogels and their dynamics at a molecular level with high temporal resolution, which will lead to much greater control of the macroscopic properties of hydrogels.

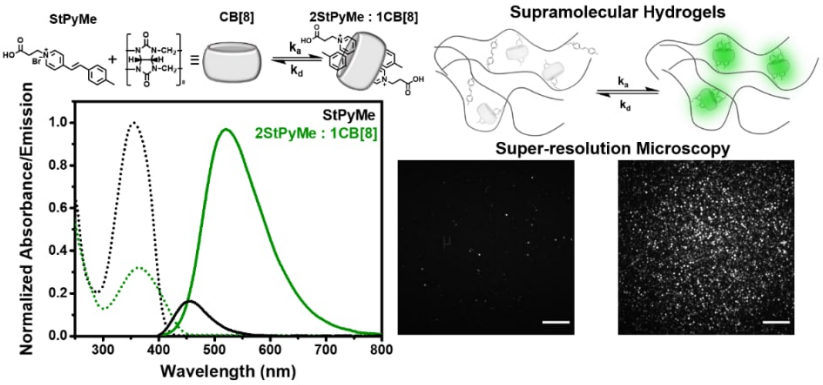

Figure 1. *Supramolecular hydrogels were designed with styrylpyridinium (StPy) derivatives that form 2:1 guest-host complexes with CB[8]. StPy molecules exhibit negligible fluorescence properties in aqueous media, while 2 (StPy):1(CB[8]) supramolecular complexes fluoresce and can be probed by SRM as demonstrated by single-molecule imaging. Scale bar: 5µm*

ERC grant (CAM-RIG, 726470) is acknowledged for financial support.

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Towards single molecule chiral separation using shear flow

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Chiral separation of enantiomers continues to be of significant interest to the scientific community due to their ubiquity in pharmaceuticals, food additives, and agrochemicals. Despite the numerous methods available to carry out chiral chromatographic separation, there are still several limitations. One of the largest being the amount of solvent required to achieve separation. Here we show a new approach, where strong shear flow is used to separate chiral enantiomers at the molecular level with a minimal amount of solvent.

The idea that fluid flow can induce the migration of chiral compounds was originally proposed by Howard et al. in 1971 [1], and, since their report, several other detailed studies have confirmed this theory. [2–4] Although publications have shown that chiral separation cannot be achieved on the molecular scale [3] and Brownian motion complicates the prediction of molecular motion in shear flow [5], they both have limitations, e.g., the authors use buoyancy and gravity as driving forces [3]. Furthermore, accroding to Eq. [5], viscosity has a negative effcet on Brownian motion and a positive effect on seperation. In short, the use of viscous solvents, such as glycerol instead of water can facilitate separation. Based on these findings, we hypothesized that fluid flow can be used to separate enantiomers on the molecular level.

In the current work, we built a new Taylor–Couette cell, with a gap of 100 µm and a height of 30 mm. The shear rate is similar at 6×10^5 s^{-1}, and cooling is circulating in both the inner (stationary) and outer (rotating) cylinder. Figure1 shows a cross-sectional view of the prototype, where we point out the labelled inlets/outlets. Corresponding fractions were then extracted from the different outlets (cf. Figure 1) and analyzed using analytical chiral high-performance liquid chromatography (HPLC).

In this study, we see a mirror image enrichment on concentration for opposite enantiomer BINOL in glycerol. In contrast, we only observed precipitation using samples without the presence of isopropanol or low concentrations of BINOL. In this way, the phenomenon can be explained by chiral crystallization induced by high shear forces.

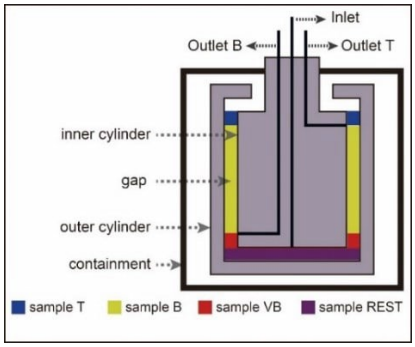

Figure 1. Cross-section of the prototype.

Thanks to my supervisor, Prof. Thomas Hermans for his invaluable advice, support and patience , also the support from Chinese scholarship council for my living expense. I would also thank Dr. Alessandra Tassoni for introducing me to this challenging project of chiral separation, and for guiding me at the beginning.

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Molecular engineering of improved half-life in visible-light responsive Iminothioindoxyl photoswitches

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Recent years have witnessed a surge in the development of light-operated photoswitches. Photoswitches offer the possibility of controlling properties and functions of chemical and biological systems, such as drug delivery systems and photopharmacological agents [1–3]. However, photoswitches are often operated by UV-light, which is harmful to tissues and hampers its applications in biomedical areas, thus highlighting the need for visible light-operable photoswitches. Not only is visible light non-toxic, but it also penetrates tissues more deeply than UV-light [1,4].

Iminothioindoxyl photoswitches (ITIs, fig 1) are a recently reported class of visible light-responsive molecular tools with unprecedented (100 nm) band separation between the absorption bands of the isomers. The *E*-isomer of ITI is thermally unstable and has a half-life of several milliseconds [1,5]. Ideally, for applications in controlling the function of bioactive molecules with light, the thermal half-life of the metastable isomer of a photoswitch should be between 0.1 – 10 seconds, which indicates that ITIs still need improvement in this respect [6].

This poster will present the study on the influence of substituents on four distinct positions of the ITI photoswitch on the half-life of the *E*-isomer. By exploring a library of prepared ITIs, we have discovered that the ortho-positions (R_1 and R_2, figure 1) were critical in this respect, allowing for increasing the half-life to several tens of milliseconds. A second library, centered around the modification at those positions, is currently under preparation. The poster will focus on the synthesis and spectroscopic studies on ITI photoswitches and discuss the best structures for biological applications.

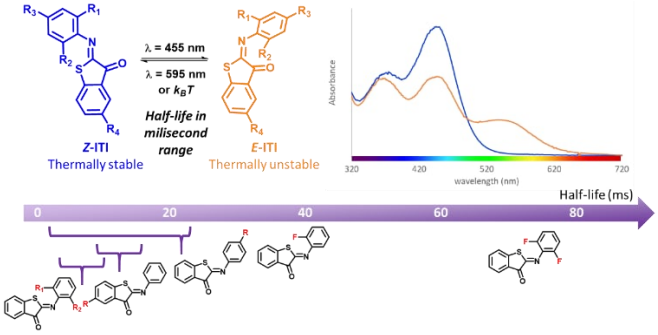

Figure 1: Influence of the substituents of the ITI photoswitch on its half life

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Influence of electronic effects onto performance of novel arylazopyrazole photoswitches

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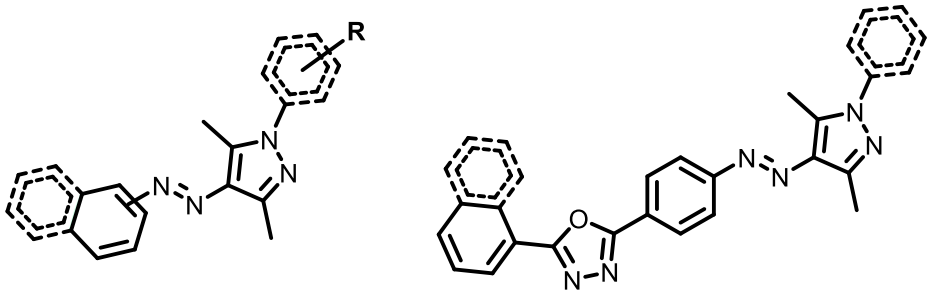
Photoswitches are two-state molecular systems that can interconvert through use of light. This dynamic behaviour attracted a lot of interest in the past years due to numerous applications in molecular or material science that can benefit from the possibility of switching the activity of a function through a safe and easily generable stimulus that is light [1].

Research concerning such molecules has gradually increased, many systems being developed and studied to be further used in applications like catalysis, solar thermal fuels or photopharmacology, involving molecules like, azobenzenes, diarylethenes, spyropyrans or acylhydrazones [1].

One class that has recently outshined is represented by azoheteroarenes, constituting a promissing alternative to azobenzenes given the new horizons it may open, brought by novel and exciting properties with record-breaking photoswitching performance and biological applicability [2,3].

In this context, we report herein synthesis of novel arylzopyrazoles bearing various electron-donor and withdrawing substituents, including compounds that combine two heterocycle moieties (*i.e.* oxadiazole), along with structural characterization and determination of their photoswitching parameters using various techniques, such as UV-Vis, NMR and XRD, with the interest of exploring the influence of electronic effects onto the photoswitching performance.



This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2019-1003, within PNCDI III. The University of Bucharest - UniRem project no. 244 is also gratefully acknowledged.

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Towards the operation of molecular switches in compartmentalized systems

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Rotaxane-based fluorescent molecular switches are systems which combine a fluorescent moiety with the stimuli-responsive behaviour typical of mechanically interlocked molecules (MIM). In 2008, Zhou et al. operated an anthracene-based multilevel molecular switch based upon protonation/deprotonation of a conjugated amine.[1] Recently, Wu et al. reported on a switchable BODIPY-based rotaxane, in which the on/off states were controlled by the mechanical hindrance around the fluorophore.[2]

In this project, we employed an anthracene-based axle endowed with a secondary amine which can complex a crown ether ring upon protonation yielding a (pseudo)rotaxane architecture. The design of the system is schematically illustrated in Fig.1. In the deprotonated state, the axle does not thread through the crown-ether ring and the fluorescence of the anthracene stopper is quenched, while upon protonation, the fluorescence of the anthracene moiety is switched on and the ring slips over the ammonium site. Thereby, in this system, the fluorescence readout can be applied as a direct signal of the threaded or unthreaded state of the axle and ring components. We attempted to operate this molecular switch in a compartmentalized system, in which the molecular switch components (ring and axle), the fuel (an acid), and antifuel (a base) are segregated in different un-mixable liquid phases. By placing the switch in an organic phase whereas leaving the acid and base in aqueous media, we can expect the accumulation of the waste product exclusively in the latter. Furthermore, this approach allows autonomous operation of the switch, which effectively acts as a phase-transfer catalyst for the reaction between fuel and antifuel, with the non-trivial result of converting a simple molecular switch into a full-fledged molecular machine.

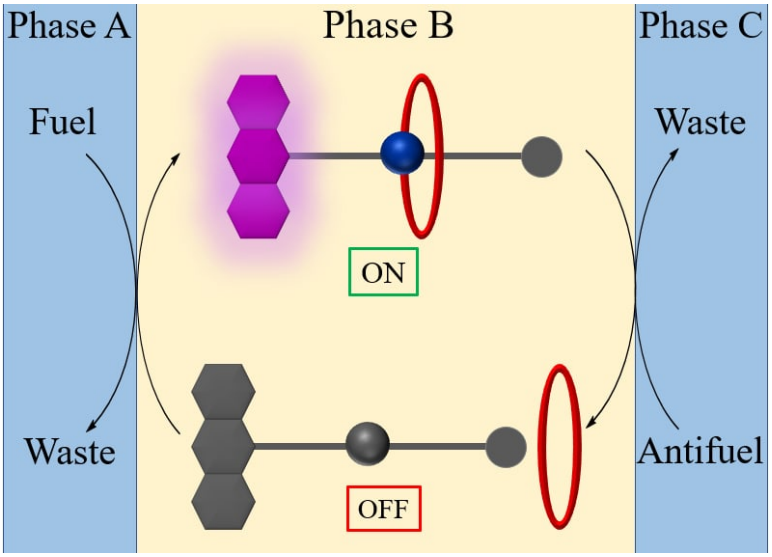

Figure 1. Schematic representation of the system operation.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 860434.

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pH-triggered molecular actuation of a liquid-crystalline [*c*2]daisy chain rotaxane

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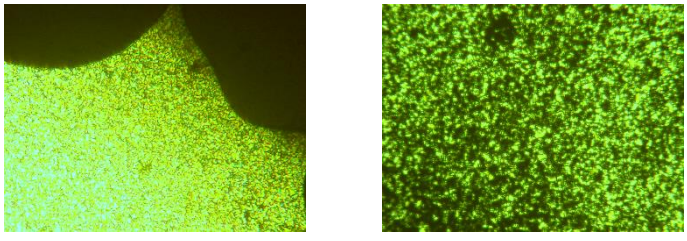
Mechanically interlocked molecules (MIMs) like catenanes and rotaxanes, just to name a few, have raised interest in various fields of research ranging from organic chemistry to materials science owing to their dynamic nature. At the molecular level, inspired by the sliding movement that takes place inside the basic unit of the muscles, the sarcomeres, chemists have designed a MIM named [*c*2]daisy chain rotaxane. This bistable molecular machine is made of two identical units composed by an axle that is covalently attached to a ring and threaded inside each other, leading to a cyclic dimer that can undergo a switching process upon external stimulation (pH changes, redox potential, light) at the nanoscale.[1]

MIMs have also been considered for the next generation of smart materials in the bulk, or in ordered systems with emerging properties. Liquid-crystalline (LC) systems are good candidates to support and translate the oriented molecular motions generated by the actuation of molecular machines. They combine the fluid-like properties of liquids and the anisotropic property of crystals, offering an interesting dynamic environment to MIMs. For instance, Kato's research team in collaboration with Stoddart's group reported for the first time the formation of a redox active [2]rotaxane showing liquid crystalline properties. The [2]rotaxane exhibited a smectic A mesophase in a wide range of temperatures (10 – 150 °C). The corresponding LC films showed a colour change under the application of a redox potential, corresponding to the shuttling of the macrocycle on the axle, while no change of the LC phase was observed upon stimulation.[2]

So far, and to the best of our knowledge, most of examples from the literature are referred to the combination of liquid crystals with (poly-) rotaxanes,[3] however, there are no examples in the literature concerning the use of [*c*2]daisy chain systems in LC phases, nor even a phase transition upon actuation of the mechanical bond. Therefore, we designed, synthesized and characterized a [*c*2]daisy chain rotaxane bearing a mesogen in the structure. The pH change was used as external stimulus to trigger the sliding motion of the macrocycles in the [*c*2]daisy chain rotaxanes, allowing to switch liquid crystalline phases in both extended and contracted states. TGA, DSC and SAXS analyses, as well as POM images (Figure 1) were used to confirm the liquid-crystalline behaviour of this artificial molecular machine.



a) **b)**

Fig. 1. POM images of liquid crystalline phase of: **a)** extended [*c*2]daisy chain rotaxane at 160 °C. **b)** Contracted [*c*2]daisy chain rotaxane at 120 °C.

The authors thank the European Commission's Horizon 2020 Programme as part of the MSCA-ITN project ArtMoMa under Grant No. 860434 and of the FET-Open project MAGNIFY under Grant No. 801378. They also thank the LabEx CSC, the CNRS, and the University of Strasbourg. C.C.C.-V. thanks the icFRC and Solvay Company for an excellence doctoral fellowship.

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Photochemical Study of Oxindole-based Molecular Switches

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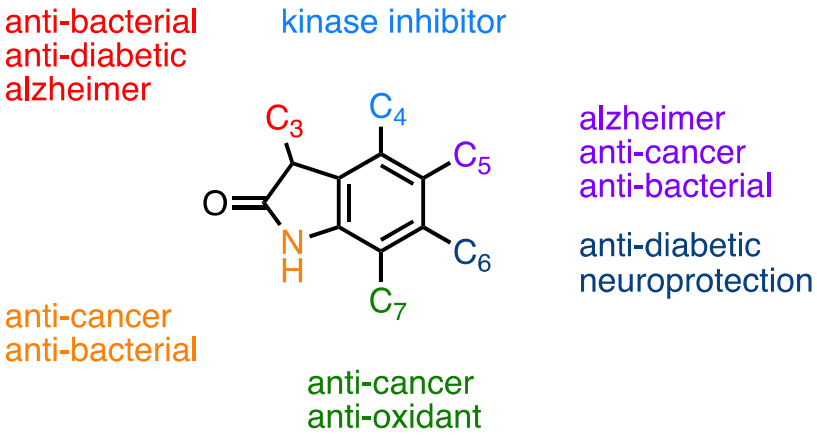
Researchers are inspired by nature's sophisticated molecular machines to mimic their performances in artificial molecular environments. Driving a chemical or biological system out-of-equilibrium through the consumption of e.g. chemical fuels or energy supplied by light, are just some elaborate ways. As a consequence, the field of artificial molecular motors and switches has gained considerable interest throughout the last years.[1,2]

Indoline-2-one-derived molecular structures are important scaffolds in biological and medicinal applications, such as antifungal or inflammatory agents, where the activity of E and Z configurated molecules vary.[3-5]

The aim of this project is to study the influence of various functional groups on the photochemical behavior of oxindole-based molecular switches with the aid of HPLC, HRMS, NMR- and UV-vis spectroscopy. Additionally, the integration of them within biological systems to study their drug release potential is investigated.



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Synthesis and Properties of Photoresponsive Calix[6]Arene-based Oriented Rotaxanes

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During the last years, our group focused its research on exploiting the modular reactivity of the calix[6]arene platform, to synthesize a new generation of calixarene-based devices and prototypes of molecular machines.[1] Recently, to disclose a new strategy for developing novel devices and materials endowed with programmable photoresponsive properties, we explored the complexation in weakly polar solvents of a series of stilbazolium salts by an asymmetric triphenylureido calix[6]arene-based receptor (**TPU**).[2] The studies evidenced **TPU** can bind the stilbazolium guests to yield a mixture of pseudorotaxane orientational isomers. The ratio of these orientational isomers was not fixed, and it could be reversibly tuned by changing the temperature and the solvent. Most importantly, the two orientational isomers experienced spectroscopic properties that depend on the orientation of the fluorophore inside the non-palindromic calix[6]arene wheel.[2] The synthesis and the spectroscopic studies of the synthesized oriented rotaxanes **UP** and **DOWN** (Figure 1) are reported in this communication. Our results show that not only the confinement of a guest but also its orientation inside the host can be employed as tools to tune the spectroscopic properties.

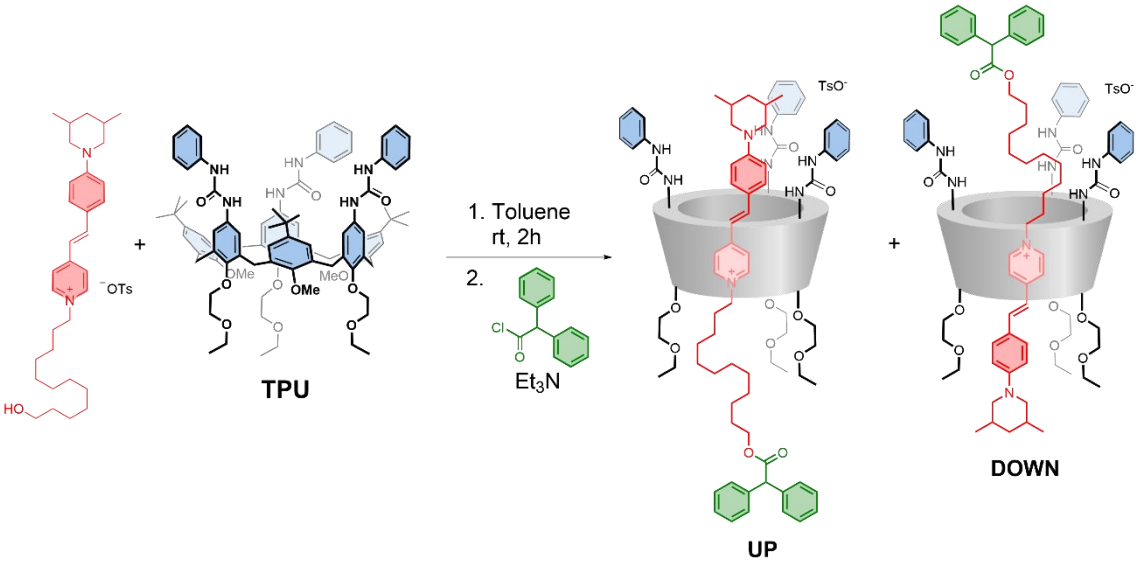

Figure 1. Synthesis of the orientational [2]rotaxane isomers **UP** and **DOWN**. Once isolated, the orientational isomers experience different optical properties because of the different orientation of the encapsulated fluorophore guest with respect to the different rims of the calix[6]arene wheel.

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Photo-triggered complex motion by programmable construction of light-driven molecular motors in liquid crystal networks

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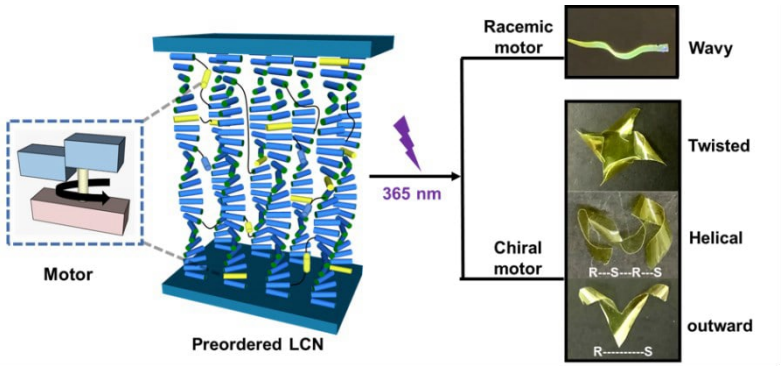
Recent developments towards artificial molecular machines has enabled precisely controlled molecular motion which allows several distinct mechanical operations at the nanoscale. However, harnessing and amplifying molecular motion along multiple length scales to induce macroscopic motion is still a major challenge and an important next step towards future actuators and soft robotics. The key to address this challenge relies on effective integration of synthetic molecular machines in a hierarchically aligned structure so numerous individual molecular motions can be collected in a cooperative way and amplified to higher length scales and eventually lead to macroscopic motion. Here, we reported the complex motion of liquid crystal networks embedded with molecular motors triggered by single wavelength illumination. By design, both racemic and enantiomerically pure molecular motors are programmably integrated in liquid crystal networks with defined orientation. The motors have multiple functions acting as crosslinkers, actuators and chiral dopants inside the network. The collective rotary motion of motors resulted in multiple types of motion of the polymeric film including bending, wavy motion, fast unidirectional movement on surfaces and synchronized helical motion with different handedness, which paves the way to future design of responsive materials with enhanced complex functions.



Syntheses and Properties of Diethylphthalane-Incorporated 10]Cycloparaphenylenes

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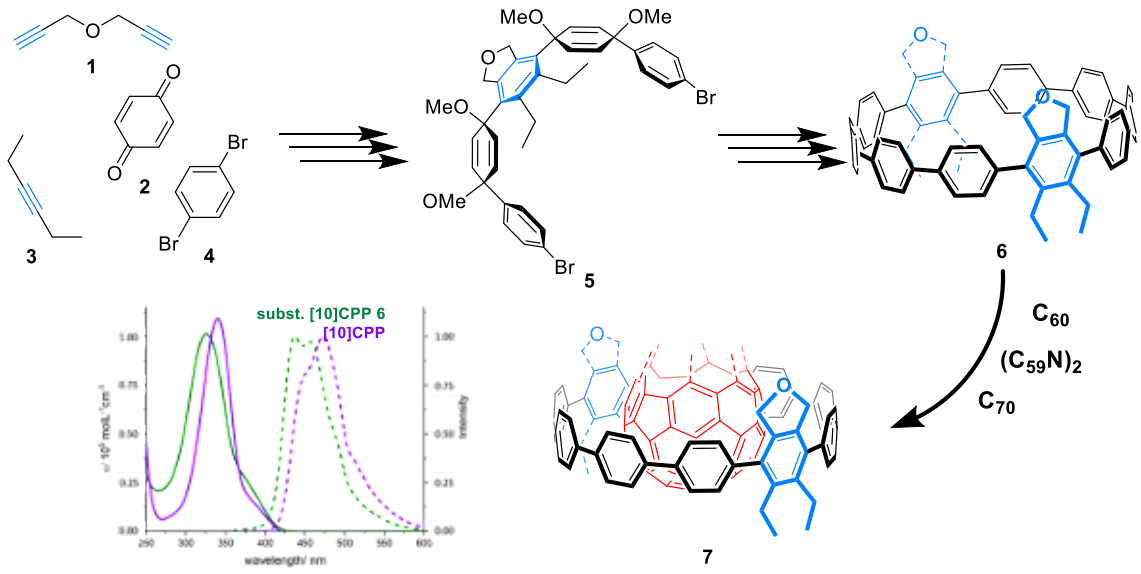
The synthesis and investigation of new macrocyclic aromatic molecules have gained great attraction in the past decade, not only due to their appealing structure, but also for their unique optoelectronic properties and novel host-guest interactions.[1] One class of compounds in this regard are [n]cycloparaphenylenes (CPPs).[2] With their radially oriented π-system and an electron-rich concave side, these nanohoops act as an excellent host for fullerenes, forming orbit-like complexes with intriguing properties, especially in regard to material science and qubit technology.[3,4]

Herein, we present the synthesis and investigation of diethylphthalane incorporated [10]cycloparaphenylenes.[5] The synthesis is based on an symmetric build-up starting with propargyl ether 1. This dialkyne acts as the precursor for the latter rhodium-mediated [2+2+2] cycloaddition with 3-hexyne 3 to form the substituted core unit. With benzoquione 2 and 1,4-dibromobenzene 4 an U-shaped five-membered building block 5 was synthesized as the key intermediate. Macrocyclization with an unsubstituted five-membered building block, followed by a reductive aromatization yielded in the targeted diethylphthalane nanohoop 6 in 8% overall yield. Miyaura borylation of the key intermediate 5 and its subsequent Suzuki coupling can furnish the second nanohoop 6' bearing two diethylphthalane units.

These bivalent substituted CPPs were exposed to thorough Host-Guest studies with monomeric and dimeric fullerene species exhibiting unexpected features within their interactions.



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Mechanochemical preparation of piezoelectric nanomaterials: BN, MoS_2 and WS_2 2D materials and their glycine-cocrystals

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Piezoelectric materials have a unique property that converts mechanical energy into electrical energy or vice versa. Barium titanate is the first piezoelectric ceramic ever discovered, but the ceramic lead zirconate titanate, also known as PZT, is the most used material for piezoelectric harvesting.[1] Different nanomaterials in the dichalcogenides family have been theorised to have piezoelectric behaviour. Some of them have been tested, such as boron nitride and molybdenum disulphide, and confirmed experimentally. Still, the procedures to obtain these nanomaterials, with the right quality to observe the piezoelectric behaviour, are enormously expensive, halting its possible applications.

Here, we show the mechanochemical exfoliation of 2D nanomaterials (FLG, BN, MoS_2 and WS_2) with glycine. We have also successfully synthesised the cocrystals for these nanomaterials,[2] which makes it possible to enhance their piezoelectric responses.

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Optical Pressure Sensing based on Divalent Lanthanide Ions (Sm^{2+}, Eu^{2+}, Tm^{2+}) doped Strontium Borates Phosphors, showing excellent manometry performances

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Pressure shapes universe, stars and planets, continents, oceans and islands, and affects all aspects of our daily life. Pressure, as a crucial and basic physical variable, has giant influences on the physicochemical properties of materials. Compression of materials under high-pressure conditions has been widely utilized for the study of pressure-induced changes of physicochemical characteristics of substances, formations of new phases or materials under extreme conditions, spectroscopic and structural change of the chemical compounds, etc. When mimicking these processes under pressure for scientific and industrial purposes in the laboratory using a high pressure anvil cell, a fast and accurate determination of pressure is of great importance and, due to the transparency of diamonds and other gems in the visible range, optical pressure calibrants are often used.

In the presented research, firstly, several candidates of borate matrices, i.e., SrB_4O_7, SrB_2O_4 and $Sr_3(BO_3)_2$, were synthesized via high-temperature solid-state methods and characterized for stabilization of Ln^{2+} (using Eu^{2+} as an example).[1] The influence of the matrices on the structural, morphological and photoluminescence properties are investigated and analyzed systematically. Subsequently, several strategies of optical pressure sensing was proposed: I) the strategy of luminescent signal enhancement (~ 60 times) of Sm^{2+}: $^5D_0 \rightarrow {}^7F_0$ peak via $Eu^{2+} \rightarrow Sm^{2+}$ ET process in co-doped SrB_4O_7 pressure sensor; The developed sensor also exhibits good pressure shift, excellent temperature independence and wide pressure sensing range.[2] II) The strategy of using the pressure-enhanced (enhancement of 3 times magnitude) 4f-4f emission of Eu^{2+} in SrB_4O_7 for the optical pressure detection toward higher pressure range (~60 GPa). A systematic experimental and computational analysis was performed to reveal the reason of the enhancement, i.e., the electrons transfer from 5d→4f levels and the pressure-driven configurational crossover between $4f^7$ and $4f^65d^1$ states. III) For the first time, the 5d-4f emission of Tm^{2+} in the same matrix were applied as a bifunctional platform for luminescent pressure and temperature sensing, which can realize satisfactory sensing performance in wide pressure/temperature range. [3]

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π-stacking and multicentric bonding of *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine (TMPD) cation radical

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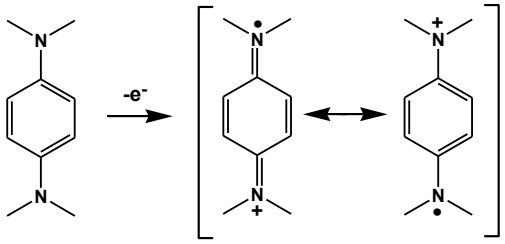
N,*N*,*N*′,*N*′-Tetramethyl-*p*-phenylenediamine (TMPD or Wurster's blue), first prepared in the 19th century [1], is a well-known electron donor. Upon oxidation, it forms a stable radical cation, which has semiquinoid structure (Scheme 1). In combination with electronegative quinones (Scheme 2) it can form charge-transfer systems. Two such co-crystals studied previously [2] comprise mixed π-stacks of alternating quinone and TMPD molecules, and black colour of the crystals indicates a considerable degree of charge transfer.

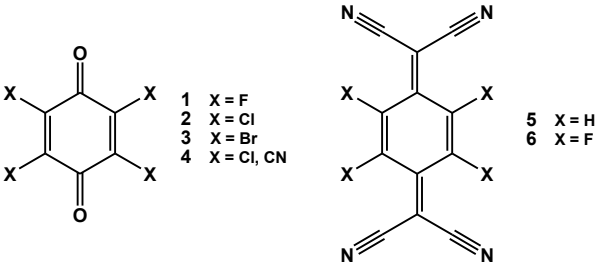
As a part of our systematic study of two-electron multicentric bonding (2e/mc or *pancake bonding*) of organic radicals [3], we have prepared a series of co-crystals of TMPD with differently substituted quinones (Scheme 2). They all involve stacking between TMPD and quinone molecules, but three different types of stacks have been observed: a) equidistant stacks of alternating quinone and TMPD which have already been observed [2] (co-crystals with **2**, **3**, **4** and **5**), b) stacks of *pancake-bonded* mixed quinone-TMPD dimers (co-crystal with **1**; at low temperature also **2** and **3**) and c) 2D arrays of alternating quinones and TMPD molecules (co-crystal with **6**).

Stacking interactions were studied by a combination of variable-temperature crystallography (80 − 400 K) and X-ray charge density [4], which revealed fine details of electron density between the stacked molecules. Temperature-driven phase transitions have been observed in co-crystals with **2** and **3**, which form stacks of type a) at room temperature, but type b) at low temperatures.

Structure and behaviour of TMPD radical cation was studied in its novel chloride salt co-crystal with 2,5-dichlorohydroquinone, which involves *pancake-bonded* dimers of TMPD. This is also the first X-ray charge density study of *pancake-bonding* between radical cations.



Scheme 1



Scheme 2

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Atomic Layer Deposition as a Key Enabler for Halide Perovskites

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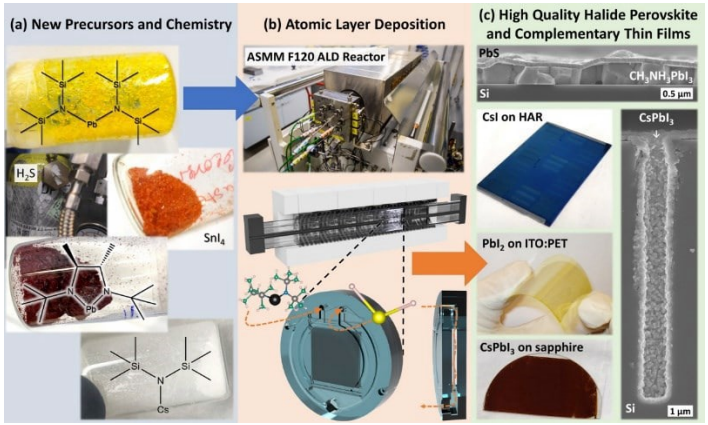
Halide perovskites possess remarkable optoelectronic properties, have attracted a lot of research efforts, and reshaped the photovoltaics research field during the last decade. Halide perovskites (ABX_3) consist of an alkali metal cation or small organic amide (A), lead or tin (B) and a halide (X), typically iodine. Many studies also show the potential of the halide perovskites beyond photovoltaics: in microelectronics components, light emitting diodes (LEDs), X-ray imaging detectors, photodetectors, batteries and other devices.[1]

The challenges of halide perovskites are scalability and stability. Applications of halide perovskites will benefit from methods with which high quality thin films can be deposited on large surface areas and which ensure that these films operate without degradation in ambient conditions. We believe that Atomic Layer Deposition (ALD) can address these challenges.

ALD is an industrially established method whose commercialization was pioneered in Finland. ALD is commercially used in making displays, microelectronics and encapsulation layers. Without ALD there would be no smartphones or computers as we know them today. ALD is inherently scalable to large areas and batches as well as to roll-to-roll processing. ALD delivers uniform and conformal coatings on the most challenging substrates with high aspect ratios which made ALD a method of choice for the microelectronics industry.[2]

At the heart of every ALD process are the precursors and their chemistry that deposit the desired material. ALD process library is vast, over 1400 processes for more than 500 compounds[3], but it has lacked proper precursors and chemistry to deposit halide perovskites and binary metal bromides and iodides, prerequisites to the halide perovskites. We have devoted significant efforts in precursor development and devised efficient chemistry based on volatile and reactive metal amides as metal precursors and metal halides as halide precursors. This chemistry allowed us to develop ALD processes for binary metal halides: PbI_2[4], CsI[5], $PbCl_2$ and $PbBr_2$[6] as well as for the halide perovskites $CH_3NH_3PbI_3$[4] and $CsPbI_3$[5].

Our advances with lead(II) amide precursors led us to develop two new ultra-low temperature ALD processes for PbS.[7] These PbS processes can be used directly on halide perovskite thin films without their degradation whereas the absolute majority of ALD processes are incompatible with halide perovskites because of their too high deposition temperatures. ALD has a proven track record in encapsulating sensitive functional materials and we demonstrated that encapsulation with PbS prevents perovskite degradation in ambient conditions. Unlike alternatives that rely on insulating layers, Al_2O_3 in particular, PbS is a p-type semiconductor and can perform a dual role of being both an encapsulant and a functional layer in a semiconductor device. This dual role allows simplification of existing device designs and completely new ones.



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Gaseous and Volatile Active Compounds: A Missing Piece Toward Successful Application in Active Packaging to Improve Food Safety and Quality

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Food wastes have become a serious issue that needs to be mitigated to achieve the UN's sustainable development goals by 2030. Optimizing the packaging of food products could reduce their waste by 20 – 25%. Gaseous and volatile active compounds are versatile to enhance safety and preserve quality of agri-food products during storage and distribution. However, the use of these compounds is limited by their high vapor pressure and/or chemical instability, especially in active packaging (AP) applications. In recent years, there has been a growing interest in developing controlled release technologies for gases/volatiles compounds to facilitate their uses in AP applications. Stabilization of gases/volatiles is a major requirement to control their release, prevent degradation and evaporation losses, and design controlled release packaging. Various approaches are being explored to stabilize and control the release of gases/volatiles, including encapsulation (e.g., into supramolecular matrices, polymer-based films, electrospun nonwovens) and triggered release systems involving precursor technology. For the encapsulation approach, it is critical to choose the optimal encapsulant for the active compounds, where encapsulants exhibit different physicochemical properties that greatly affect the encapsulation capacity and the release kinetics. Encapsulation of gases/volatiles is challenging due to their evaporation loss during manufacturing. One approach to overcome this challenge is to substitute the gases/volatiles with their chemical precursors with enhanced stability. The release of gases/volatiles from their precursors can be triggered by different mechanisms, including moisture, pH, temperature, light, etc. Although precursors have been developed and applied in cosmetic and perfume industries for many volatile compounds, their uses in AP applications are relatively limited. This session critically discusses the various approaches for the stabilization and controlled the release of active gaseous/volatile compounds, the different criteria for selecting the optimal encapsulant/carrier material for specific active compound, the barriers that hinder the use of gases/volatiles-controlled release systems in the food industry along with approaches for their mitigation, and the existing gap between research and commercialization. Finally, some commercially available and promising controlled releasedelivery systems based on encapsulation and precursor will be presented.

Synthesis of responsive tetra-urea calix[4]arenes and calix[4]pyrroles: a combined experimental and predictive chemical approach

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The design of supramolecular containers incorporating molecular switches is relevant to many areas of chemistry. The switching of such responsive units can be triggered by external stimuli (light, pH, temperature, redox) and may be coupled to significant changes in the thermodynamic stability of their inclusion and encapsulation complexes. For practical applications, the modulation of the container's affinity should induce the quantitative uptake and release of molecular cargo from/to the bulk solution.[1] We recently reported the synthesis of unprecedented tetra-urea derivatives of calix[4]arene and calix[4]pyrrole containing four spiropyran (SP) units at their upper rim and able to self-assemble into capsular homo-dimers.[2] In this work, we investigated the photo- or acid-induced isomerization of the appended SP units to their merocyanine (MC) or protonated merocyanine (MCH+) forms, and its effect on the homo-dimeric tetra-urea derivatives.

Recently, the Retrosynthesis planner in Reaxys was used to evaluate the relevance of our suggested synthetic routes for the tetra-urea derivatives based on calix[4]arene or calix[4]pyrrole scaffolds. The planner helped us compare our approach in the synthesis of the different counterparts of the molecular containers and model compounds with reported procedures. In addition, the new Predictive Retrosynthesis feature added to Reaxys in 2021 helped us identify new possible syntheses suggested by a 3N-MCTS algorithm [3], trained on over 15 M single-step reactions and 500'000 building blocks. We used this information, together with compound-related properties such as commercial availability, physical and spectral data, to assess the novelty and impact of the research project.



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Novel fluoresceine-like emissive 2,6-bis(5-aryl-1,3,4-oxadiazol-2-yl)phenols

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Excited State intramolecular proton transfer (ESIPT) has been studied and exploited for decades mainly for its fundamental importance, exceptional applications and relevance in various fields of chemistry, biology and optoelectronics [1]. Development of ESIPT-based fluorescence probes is particularly attractive due to their unique properties, which include a large Stokes shift, environmental sensitivity and potential for ratiometric sensing. Fluorescence based sensors are important in biology, physiology, pharmacology, and environmental science for selective detection of biologically and/or environmentally important species.

2,5-Disubstituted-1,3,4-oxadiazole derivatives are described in many publications as interesting fluorophores with large Stokes shifts and high luminescence intensities [2]. On the other hand hydroxyphenyl-1,3,4-oxadiazoles were found to display even more interesting features and they were used for example as chemosensors for anions [3].

The synthetic procedures of the 1,3,4-oxadiazole core usually involve oxidative cyclisation of *N*-acylhydrazones. However, in these cases, the difficulty of oxidation arises from the presence of the phenol moiety which suffer from attack by most chemical reagents commonly encountered for synthesis of this compounds.

In this context we report herein synthesis of novel hydroxy-bis-(2,5-disubstituted-1,3,4-oxadiazoles) (*Figure 1*) and their ability to emit green light, through ESIPT mechanism. The synthesis of new compounds starts from *p*-substituted-phenol-dialdehydes and involves a five-step sequence. All compounds were fully characterized by structural analysis and investigated for optical and electronic properties. Study of these properties according to the substituents nature was also performed.

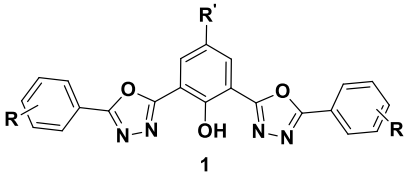

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Figure 1: Structure of the synthesized 2,6-bis(5-aryl-1,3,4-oxadiazol-2-yl)phenols

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Detection of lysozyme in food matrices with a functional antifouling surface on plasmonic aptasensor

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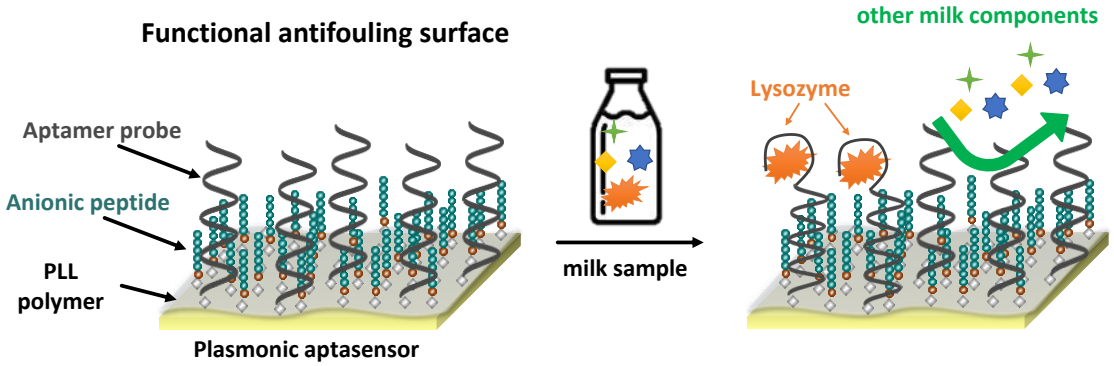
Antifouling coatings are strictly required in optical biosensors for many analytical application fields, from medical diagnostics to foodborne pathogens or antimicrobial agents detection, to prevent the non-specific protein/cell adhesion and select the analytes directly in the complex media [1]. Over the past three decades, the advances in non-fouling plasmonic surfaces have been mainly focused on the detection of ultrasensitive clinical targets in biological samples [1,2], while the development of antifouling coatings for directly analyzing complex sample media for food quality control and safety has been scarcely investigated [3]. Herein, we propose a new low-fouling poly-L-lysine (PLL)-based polymer for the detection of lysozyme, an antimicrobial agent with allergenic properties, directly in food matrices by using Surface Plasmon Resonance technology. The PLL-based polymer contains densely immobilized anionic oligopeptide side-chains to create a charge-balanced layer, able to repel the non-specific adsorption of undesired molecules on the biosensor surface. Also, PLL-based polymer includes sparsely attached aptamer probes with high affinity and specificity for lysozyme capturing directly in milk samples. The sensitivity and affinity of lysozyme's aptamer have been deeply explored by changing the ionic strength, ions, and type of buffer, to obtain a label-free protein detection at the nanomolar level directly in undiluted food samples. The work here described highlights the versatility of the antifouling aptasensor, which can be applied for the sensitive detection of lysozyme in different complex media, such as food or biological matrices, with minimal pre-analytical sample treatments.



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Cu/Zn leaching with commercial activated carbons and waste-biomass biochars

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Metals are essential for production in many industrial sectors; therefore, it is necessary to extract them. However, metals are limited resources, and both their management and extraction must be sustainable [1]. As a consequence, the use of techniques such as hydrometallurgy is proposed to promote the recovery of metals derived from low-grade ores and mining residues [2]. This study covered the implementation of commercial activated carbons and biochars produced by the pyrolysis of residual lignocellulosic biomass (sugarcane bagasse biochar, SCBB) and, additionally, a leaching agent with ferric/ferrous ions and sulfuric acid to extract Cu and Zn from a previously characterized sulfide ore containing Cu and Zn. For the leaching, we used three ratios 1/0.5, 1/0.25 and 1/0.15 of SCGG (obtained by pyrolysis at 550 and 750ºC) and three commercial activated carbons (NORIT, W35, CH12), at 90 ºC and 350 rpm. Every 2, 4, 6, 22 and 24 h, we took aliquots and measured both pH and redox potential. Later on, samples were characterized by ICP-MS and processed. The results showed that the highest extraction percent of Cu and Zn was obtained with W35 at 1/0.25 and CH12 at 1/0.5. Biochars derived from pyrolysis of SCB slightly increased the recovery of Zn and Cu compared to direct leaching without carbon material addition. However, the addition of both biochars in ratio 1/0.25 significantly decreased the leaching of As. Besides matching the previous literature findings, regarding the metal extraction yield at low redox potentials (higher metal recovery percentages are achieved at lower redox potentials) [3, 4], these preliminary results show that carbon-based materials properties such as functional groups and surface area play an important role in their catalytic properties.

Acknowledgments

This research has been funded by Ministerio de Ciencia, Innovación y Universidades (MCIU), Agencia Estatal de Investigación (AEI) and Fondo Europeo de Desarrollo Regional (FEDER) with grant number RTI2018-096695-B-C31

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Selective uptake of fullerene derivatives with macrocycle-based MOFs

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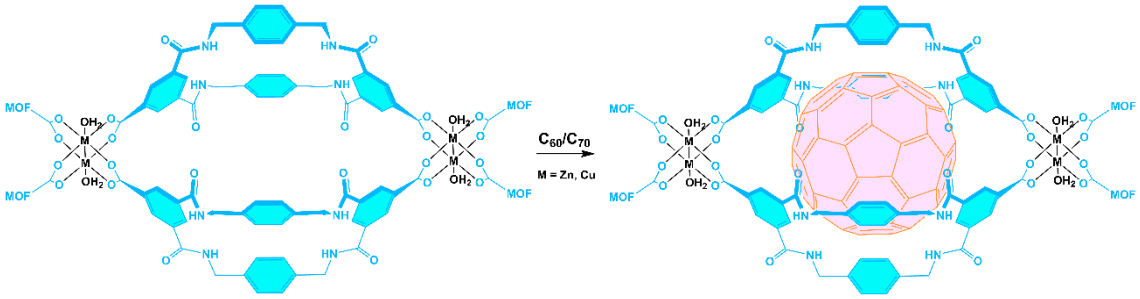
The use of macrocyclic organic linkers in the preparation of metal-organic frameworks (MOFs) provides flexible materials with huge cavities (large pore sizes) in comparison with small and rigid organic ligands [1]. These macrocycle-based MOFs can be employed for the recognition of large molecules, such as fullerene derivatives [2].

Herein, the preparation of flexible metal-organic frameworks using polyamide macrocyclic linkers functionalized with carboxylic acids groups is described [3]. These materials crystallize forming 1D-periodic linear polymers with bent macrocycles coordinated through the carboxylate moieties to dimeric copper(II) clusters. The incorporation of fullerene C_{60} inside the cavities of these MOFs was performed (Figure 1), trapping a remarkable 34% w/w. These metallopolymers show greater selectivity for the smaller fullerene derivative (C_{60}) in comparison with the larger one (C_{70}), allowing the complete elimination of C_{60} from different mixtures of C_{60}:C_{70}.



This research was supported by the MINECO and MICINN (CTQ2017-87231-P, PID2020-113686GB-I00 and RYC-2017- 22700) and Fundacion Seneca-CARM (Project 20811/PI /18). A.S.- S. thanks to the Fundacion Seneca-CARM for his Ph.D. fellowship (20259/FPI /17). The authors also thank the computer resources at Cibeles and the technical support provided by the Centro de Computacion Cientifica-UAM (RES-QSB-2019-3-0012).

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Ionic liquid /cellulose triacetate film: insulation and packaging

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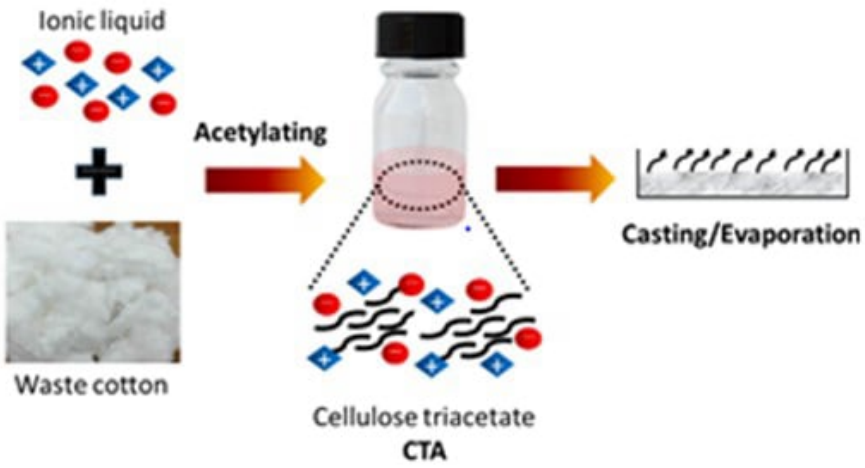
Cellulose triacetate (CTA) is a cellulose ester with high crystallinity, hydrophobicity, chemical, mechanical, and thermal resistance. It is widely used in the electronics industry as a protective film for electronic screens, as well as in the water treatment industry as a metal separation membrane. Their high stiffness and crystallinity, however, limit their use as packaging film. As a result, TAC must be combined with other polymers or additives in order to produce a thermoplastic film with high flexibility. In order to recover industrial textile waste, cellulose triacetate (CTA) has been synthesized from waste cotton fiber. Due to their ionic structure IL possess several advantages over common solvents [1, 2]. For this purpose, a series of ionic liquids were synthesized and used as plasticized CTA film materials. In fact, the films were produced using the solution-casting method, and their physical, mechanical, and thermal properties were examined [3]. Physical results indicate that the prepared films had smooth surface and high transparence. The introduction of ionic liquids, however, reduces their crystallinity. The mechanical and thermal properties depend primarily on the ionic liquid anion. In addition, their water resistance and thermal stability were better. The developed films were self-extinguishing, with a final residue of 97 wt%, allowing CTA films to be used for insulation and packaging.



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Porous composite microparticles containing zein as drug delivery systems

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Porous composite microparticles based on synthetic and natural polymers have received a great attention as carrier matrices in biomedical, environmental and industrial fields due to several possibilities of modification of their chemical and physical properties [1,2]. Among the synthetic polymers, glycidyl methacrylate (GMA) and N-vinylimidazole (NVI) have some attractive properties that can be used in medical and pharmaceutical fields. GMA has low toxicity and lower cost compared with other acrylic and methacrylic monomers and possesses in its structure an epoxy group that can be easily functionalized [3]. N-vinylimidazole is a vinyl monomer that can participate in free radical polymerization reactions leading to the polymeric materials that can exhibit biocompatibility, biodegradability and antimicrobial activity [4]. Due to its biodegradability, biocompatibility and high coating capacity, zein, a corn protein generally recognized as safe by the Food and Drug Administration, is one the few cereal proteins that can be used as carrier for enzymes, drugs and essential oils [5].

The combination between synthetic (GMA, NVI and dimethacrylic monomers) and natural (zein plant protein) polymers or by combination with $CaCO_3$ lead to achievement of the main purpose of our study. The preparation of composite microparticles based on synthetic and natural polymers involves the following steps: (1) synthesis of porous composite microparticles by a slightly modified polymerization technique in order to achieve both crosslinking copolymerization and grafting in one single step; (2) synthesis of porous composite microparticle by grafting approach. The crystallization of $CaCO_3$ takes place from supersaturated solutions of $CaCl_2$ and different carbonate sources and under different preparation conditions (pH, time, and concentration). After purification the porous composite microparticles were structurally and morphologically characterized by: FT-IR spectroscopy, scanning electron microscopy (Figure 1), thermogravimetric analysis, XRD analysis and swelling capacity.

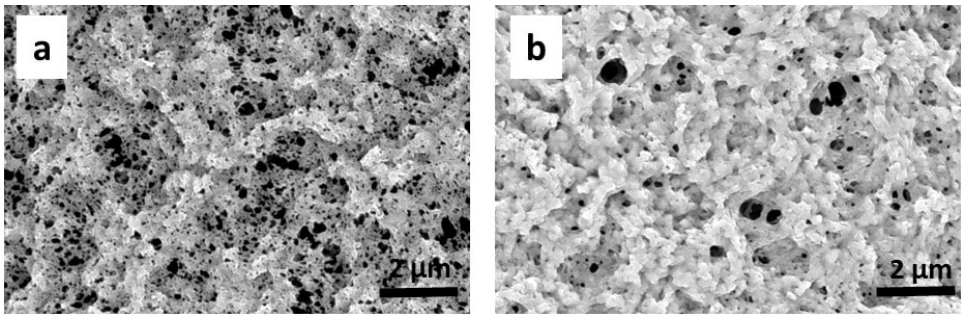

Figure 1. Porous composite microparticles surface morphologies before (a) and after zein grafting (b)

The tetracycline loading into porous composite microparticles was also followed. To elucidate the mechanism of drug release from composite microparticles, several mathematical models were applied. Due to the presence of zein, the antimicrobial activity of porous composite microparticles was studied.

This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS/CCCDI – UEFISCDI, project number PN-III-P4-ID-PCE-2020-1541, within PNCDI III.

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Synthetic engineering of graphene nanoribbons from bottom-up approaches

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Graphene nanoribbons (GNRs) are considered to be quasi one dimensional (1D) polymeric systems. Their properties such as conductivity, charge mobility and magnetism depend greatly on their width, length and edge structure. Edge states in GNRs have undergone intense theoretical scrutiny, because their coherent spin manipulation would be a milestone for spintronic and quantum computing devices. However experimental investigations are hampered by the fact that most nanoribbons do not have the required atomic control of the edges, and that the proposed graphene terminations are chemically unstable. A series of GNRs with different structures, e.g., size and edge configuration, as well as edge doping, have been synthesized, demonstrating the possibility of fine-tuning their optoelectronic, magnetic and supramolecular (self-assembly) properties through the structural modulation from bottom-up approaches.[1-5] Inspired by these spectacular properties, GNR's chemistry and physics has given a tremendous scope for next level development and applications in organic electronics and spintronics.

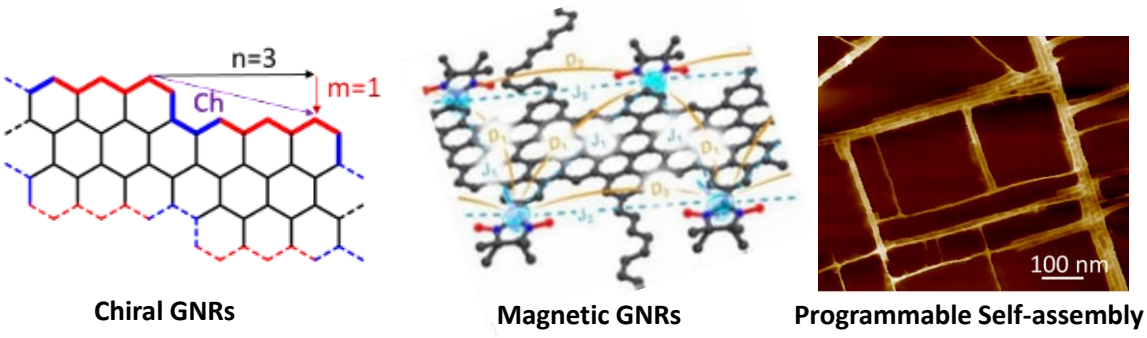

Figure 1 *Schematic representation of various GNRs and AFM image of self-assembly on flat surfaces.*

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A new family of inherently chiral electroactive monomers obtained by chemical resolution

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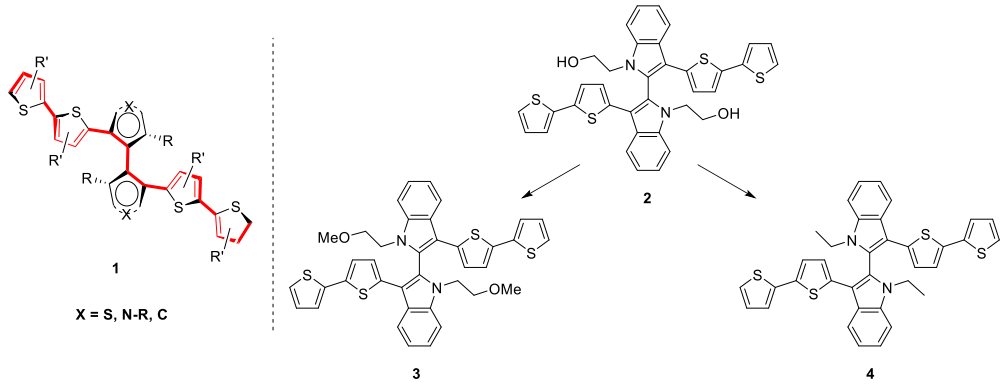
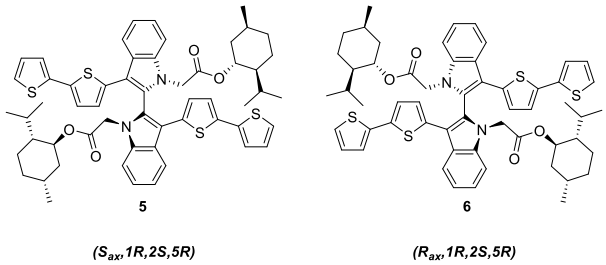
The availability of materials which could couple electroactivity properties and enantiorecognition capability is an ambitious objective of the modern chemical research. In the last years we developed a new class of C_2 symmetric monomers, having the general formula **1** reported below, in which the stereogenic element responsible for chirality and an oligothiophene sequence, responsible for electroactivity properties, coincide (inherently chiral monomers). Dissymmetry results from a tailored torsion produced in the electroconductive backbone by insertion of a conjugated atropisomeric fragment such as 2,2'-biindole[1], 3,3'-bithianaphthene[2] and 1,1'-binaphthalene[3]. Generally these systems were obtained as racemate and the enantiomers were separated through chiral HPLC. The enantiopure films obtained by electrooligomerization of such monomers on a bare electrode showed outstanding enantiodiscrimination ability towards the antipodes of various chiral analytes[4].

Here we report a new family of 2,2-biindole derivatives (**2**-**4**) functionalised at nitrogen atoms with different substituents designed to verify the nature of interactions between the film and the probe on the enantiodiscrimination process.



The reduction of diastereoisomeric esters **5** and **6** gave through a column chromatography the antipodes of compound **2** that was converted into compounds **3** and **4.**



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Development of New Partially Bio-Based Self-Healing Polymeric Materials

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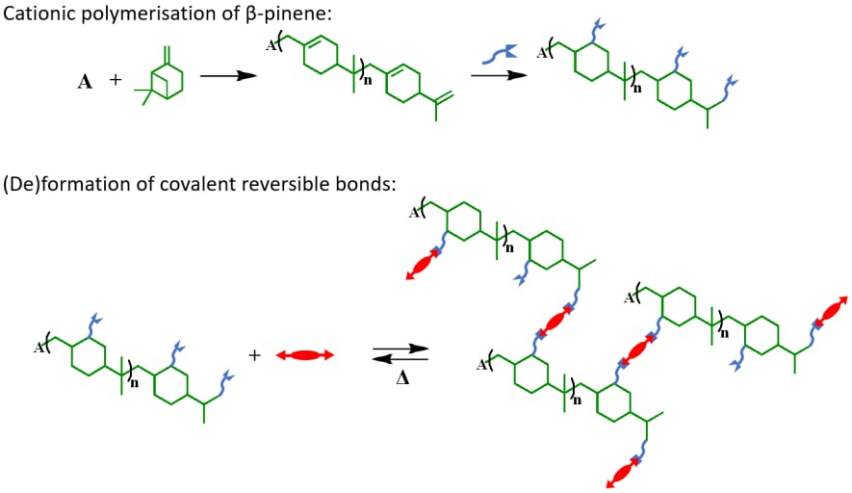
In 2018, approximately 359 million tons of polymers were produced worldwide, among which 97.5% came from fossil resources [1]. The increased concern of climate change in the last few years accelerated the investigation of bio-based materials to replace petroleum-based polymers. In order to be viable, the industrial production of bio-based materials should not impact the feedstock (*e.g.* corn, potatoes), which shifted the focus towards bacterial fermentation production, organic waste recycling or extraction from plants. Among the latter, β-pinene is able to homopolymerise without prior chemical modification *via* cationic polymerisation. Although this technique is usually performed under drastic conditions due to the high sensitivity to water of the most common catalysts, new water tolerant catalysts were developed that allow for the production of oligomers up to a few thousands $g.mol^{-1}$ [2].

In addition, closed-loop manufacturing becomes one of the priorities nowadays, with the production of biodegradable, recyclable or reprocessable materials. However, it is known that thermoset polymers are usually irreversibly cross-linked networks that are thermally and mechanically very stable so difficult to reshape or recycle [3]. To solve this problem, a new class of polymers called vitrimers emerged. Indeed, the introduction of reversible supramolecular (*e.g.* hydrogen bonds, halogen bonds, ionic interactions) or covalent (*e.g.* Diels-Alder cycloaddition, transesterification, hemiacetal esters) bonds allow for the materials to be easily reshaped at temperatures above which the bonds are able to break. This feature also enables self-healing of these materials as the bonds are able to form again when cooling down to room temperature, recovering their original mechanical stength, which increases their lifetime [4].

Following these advances, in this work we first synthesise oligomers of poly(β-pinene) that we further functionalise in order to introduce reversible covalent bonds in the presence of a cross-linker. Then the mechanical, thermal and self-healing properties of the new polymeric networks are studied.



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Functionnalized hybrid mesoporous silica designed for uranium extraction from sulfuric acid medium

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Abstract
Nuclear industry, like all of the other industries, produce wastes. These wastes could be from the normal functioning of nuclear facilities (spent fuel, mining effluents, conversion effluents…) or could be from a specific deteriorated situation (small leaks, contaminated releases, major accident). The producers of these wastes must manage them (storage or recycling) to protect people and environment from contamination. [1]
Sorption of contaminating species into porous solids is an efficient way to extract, concentrate and immobilize undesirable elements into an easily manageable material. Then these elements could be directly stored on their support or could be stripped from it to be recycled. Therefore the benefit of this process is to be compact and reversible. Mesoporous silica are one of the hierarchical material with a high sorption capacity and the ability of their surface to be functionalized make them selective from any competitive species. This selectivity could be tuned by grafting or inserting specific organic extractants on their surfaces. [2]
Silica are acidic resistant [3] so they fit with the medium. These mesoporous silica have been functionalized with amidophosphonate to give hybrids materials, as already proposed and studied [4,5]. The aim of the work was to study the impact of the nature and the structure of the organic layer on the extraction performances. Steric effect was studied by tuning the length of the hydrocarbon chain on the extractant. Various functionalization techniques were studied: (1) grafting of the extractant on the structure with covalent bonds (peptide coupling), (2) sorption of the organic extractant into pre-functionalized silica.
The effects on the uranium extraction efficiency of the functionalization method of three kinds of functionalized silica materials were evaluated in low sulfate (pH = 2) and high sulfate (pH = 1) solutions, with compositions representative of typical effluents from uranium mines and leaching solutions from uranium ore treatment, respectively. The selectivity of the modified silica supports for uranium was determined in the presence of iron and molybdenum as competing cations.
Thanks to material characterization techniques (Nitrogen adsorption-desorption, TGA, IR, NMR) several structural parameters was studied and linked with the uranium batch extraction performances (sorption capacity, U-Fe selectivity, U-Mo selectivity).
Our results show that both incorporation methods yield materials with good extraction efficiency and selectivity in low sulfate solutions. EXAFS data indicate that uranyl species have to be desulfurized prior extraction by the phosphonate ligand. This process appears more energetically favorable for the impregnated ligands than for the grafted ones under high sulfate conditions;likely because the grafted ligands compete less efficiently with the bidentate sulfates coordination in uranyl coordination sphere.



Figure 1: Material study: extracting ligand and immobilization method optimization

Acknowledgments
This work was supported by the French Alternative Energies and Atomic Energy Commission, and the NOPRA Project. The authors also thank Rajae Fakiri for assistance with organic synthesis and on the characterization of organic compounds and Dr Fabio Ziarelli (Spectropole Aix-Marseille University) for performing the CP/MAS NMR experiments. The authors gratefully acknowledge Pier Lorenzo Solari for the experimental support on MARS beamline. Soleil Synchrotron is acknowledged for providing beamtimes.

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Electrical Conductivity Enhancement and Tunable Optical Properties of a New Family of Perylene-based Metal-Organic Framework

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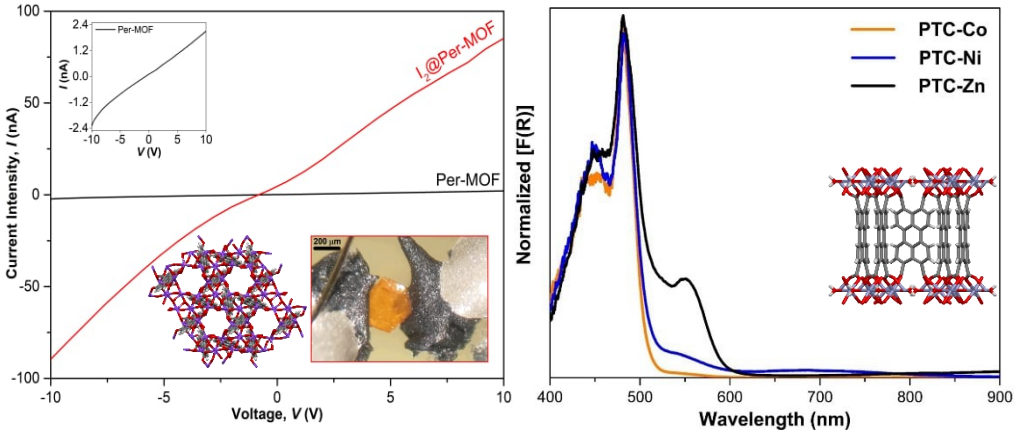
Electrically conductive Metal-Organic Frameworks (MOFs) have emerged in the past few years as promising materials towards applications in (opto)electronics, electrocatalysis or energy storage, among others.[1] Besides their inherent porosity, MOFs may also incorporate tunable electronic properties (electrical and optical) which strongly depend on the selected building blocks, becoming very attractive for their implementation as integral components in electronic devices. One of the most common strategies for the design of conductive MOFs is based on the use of electroactive organic ligands and their partial oxidation/reduction to increase the number of charge carriers.[2] Although perylene salts were reported as the first molecular conductors, they have been scarcely explored as building block for the construction of conductive MOFs.

Herein, we report a detailed study on the electrical conductivity enhancement of a perylene-based MOF upon partial ligand oxidation by iodine doping using two-probe single-crystal devices.[3] This conductivity is ascribed to the partial oxidation of the perylene ligands, as witnessed by EPR and emission spectroscopy, and supported by theoretical calculations. The charge transport is described by means of a through-space hopping mechanism along the herringbone perylene packing, with highest conductivities of the order of 10^{-5} S·cm^{-1}. In addition, we have presented a new synthetic route to prepare a novel family of isostructural MOFs based on PTC and transition metals (TM) exhibiting high crystallinity and stability. These studies on PTC-TM indicate that it is possible to tune the optical properties by switching the TM while the electrochemical properties of perylene are preserved, demonstrates by solid-state cyclic voltammetry of PTC-TM.[4] For these reasons, we highlight the potential of perylene building blocks for the design of electrically conductive and photoresponsive MOFs.



Acknowledgements: This work was developed within the scope of the project CICECO Aveiro Institute of Materials, Grants UIDB/50011 2020 and UIDP/50011 2020 financed by national funds through the FCT/MEC and when appropriate co financed by FEDER under the PT 2020 Partnership Agreement We thank FCT for funding the project PTDC/QUI ELT/ 2593 2021

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Synthesis, characterization and polymerization of aromatic trinitroso compounds

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Aromatic C-nitroso compounds have the ability to dimerize reversibly to *Z*- or *E*-azodioxides. In solid state, they usually appear as azodioxy dimers or polymers, while in solution nitroso monomer-azodioxide equilibrium is established with monomers being the preferred form at ambient conditions. Especially interesting are compounds with multiple aromatic C-nitroso groups which can be employed as starting molecular building blocks for the design of new 1D, 2D and 3D polymeric azodioxides with desired structures and properties. For example, 1,4-dinitrosobenzene polymerizes to remarkably stable 1D long-chain azodioxy polymer which could be possibly used as organic semiconductor [1,2], while polymerization of monomers with tetrahedrally oriented nitroso groups leads to formation of porous 3D diamondoid azodioxy networks [3]. Although the polymerization of suitably designed aromatic C-nitroso compouds undoubtly offers a uniqe pathway to new covalently bonded materials, the main obstacle that must be overcome to reach this goal is that compounds with multiple aromatic C-nitroso groups are not easily prepared.

Herein, we focused on the synthesis and characterization of new aromatic trinitroso compounds and their possible self-polymerization to azodioxy networks. Selected target monomeric compounds differ in central unit (benzene, pyridine, triazine and amine) on which three phenyl rings with nitroso functionalities are attached (Fig. 1). Several synthetic approaches were tested and the obtained products were characterized by using different techniques (IR spectroscopy, solution- and solid-state NMR spectroscopy, powder X-ray diffraction and thermogravimetric analysis). The obtained results suggest formation of poorly soluble *E*-azodioxy oligomers or polymers of relatively good thermal stability. The computational study (binding energies, molecular electrostatic potential values and GCMC simulations) gave further insight into the possible structures of the predicted azodioxy linked porous organic materials and preferred binding modes with N_2 and CO_2.

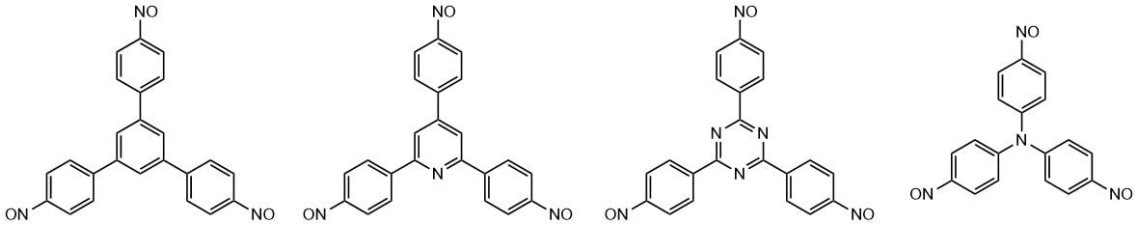

Fig. 1: Selected target aromatic trinitroso compounds for the design of new azodioxy polymers

This work has been fully supported by Croatian Science Foundation under the project IP-2020-02-4467.

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Selective etching of MAX phases to MXenes and different synthesis methods to increase surface acidity

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A family of ternary carbides and nitrides, referred to as MAX phases, unveil compound-specific both ceramic/metallic properties. Their name reveals their chemical formula $M_{n+1}AX_n$, where M is an early transition metal, A is a metal from groups 13–15, X is carbon or nitrogen, and n=1–4 [1], while MXenes are synthesized by selective ethching of A layer from MAX phases [2]. Following the etching process, the new synthesized MXenes will possess various surface terminations that will induce interesting catalytic properties. For instance, the acid–base properties of inorganic solid surfaces are crucial for various catalytic processes, such as isomerization, alkylation, cracking and many others. Therefore, extensive studies are dedicated to tune these properties in order to obtain materials with high catalytic efficiency [3].

In the view of these aspects, the main goal of this study was to functionalize the MXene surface with acid groups. Therefore, we have firstly obtain 2D MXenes ($Ti_3C_2T_x$) from 3D MAX phases (i.e., Ti_3SiC_2 and Ti_3AlC_2) by selective etching process, using HF generated *in situ* from the LiF and HCl reaction. Preliminary results showed that aluminium reacts favourably and was easier to be removed from the system as compared to silicon, the latter being found in high amounts in the obtained material (according to EDX analysis, >14 at.%). The etching optimization was carried out only for the Ti_3AlC_2 material, varying parameters such as concentration, volume and reaction time. During MXenes synthesis, the Al layer is replaced by a mixture of functional groups (−OH, −O and −F).

The strategy to functionalize the MXene surface with acid groups supposed the addition of acid sulfonic groups to the surface of the $Ti_3C_2T_x$, using two different methods: *i)* sulfonation with concentrated sulfuric acid (H_2SO_4, 96–98%) at 160 °C, during 16 hours ($Ti_3C_2T_x$-SO_3H–1) (Figure 1–A) and *ii)* sulfonation with an aryl diazonium salt obtained from sulfanilic acid ($Ti_3C_2T_x$-SO_3H–2) (Figure 1–B). The aryl diazonium salt of sulfanilic acid was prepared *in situ* by reacting sulfanilic acid, sodium nitrite, anhydrous sodium carbonate and a solution of HCl (37%). The mixture was kept at 0–5 °C to avoid decomposition of the aryl diazonium salt. Using the second protocol, other three batches of materials were synthesized with different aryl diazonium salt concentrations in order to synthesise materials with different types and amounts of acid sites. The resulting modified MXenes have been characterized by SEM-EDX, TEM, XRD, Raman, XPS and clearly prove that the 2D layered structure is maintained even after the the addition of sulfonic derived groups. Compared to $Ti_3C_2T_x$, the presence of $-SO_3H$ groups in $Ti_3C_2T_x$–SO_3H determined higher interlayer spacing through the intertwining of functional groups, a hypothesis that is also confirmed by TEM and XRD analyses. NH_3-TPD analyses indicate that the concentration of precursors used in the synthesis led to materials with different types of acidity.

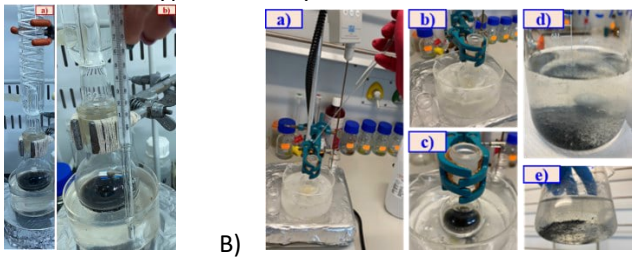

Figure 1. Experimental system of the both methods in order to obtain sulfonated MXenes

This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS/CCCDI – UEFISCDI, project number PN-III-P1-1.1-TE-2019-1969, within PNCDI III.

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Facile Approach to Phosphole-Based Aggregation-Induced Emission Luminogens via Mn^{III}-mediated Oxidative Annulation

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Aggregation-Induced Emission (AIE) describes the phenomenon of molecules that show minimal or no luminescence in solution, but significantly increased light emission in the solid or aggregated state [1]. The interest and importance of this research area has steadily increased and potential applications of AIE range from bioanalytics and materials science to optoelectronic devices [2]. In addition to the well-known AIE luminogens (AIEgens) of tetraphenylethen [1] and phenylpyrazines [3], incorporation of the phosphole motif into π-conjugated molecular frameworks and aryl-rich systems has attracted much interest [4,5]. Due to the low aromaticity of phospholes, chemical modifications are easy to realise and have a great influence on the photophysical properties of the molecule [6]. Here, a facile synthetic strategy to obtain phosphole-based AIEgens via Mn^{III}-mediated oxidative annulation reaction is presented. All synthesized compounds show aggregation-induced emission (AIE) characteristics, strong fluorescence in solid state and substituent-dependency on the photophysical properties. Phosphinated thieno[3,2-*b*]phospholes were found to be powerful solid-state light emitters, which due to their unique structure possess a high degree of restrictions of intramolecular motions.



Figure 1: Solid-state fluorescence of phosphole-based AIEgens of selected crystals under irradiation with UV-light (395 nm).

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Ternary flower-structured nanoferrites with polyvalent cations for potential applications in electrochemical sensors and magnetic hyperthermia

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Nanoferrites have been intensively studied because of the possibility of their use in the fields such as medicine, sensors, environmental, agriculture, weather, battery, etc. Often, they are used as modal systems in fundamental science to study physical and chemical phenomena at the nanoscale. Various pathways were applied for the synthesis of nanoferrites with the same composition were led to different microstructure and structure properties, which further influenced magnetic, electric, catalytic and other properties. Consequently, with a controlled synthesis, it is possible to tune the properties of nanoferrites important for applications. On the other side, properties can be controlled by changing chemical composition. In ternary nanoferrites often deviation of stoichiometry accompanied with cation polyvalence was found [1]. The main idea of our work was the application of the polyol-modified method developed for the synthesis of flower-structured iron oxides nanoparticles in the preparation of ternary $Zn_xMn_yFe_zO_4$ samples to seek a correlation among chemical composition and microstructure with magnetic hyperthermia efficiency and electrochemical properties.

A series of the samples $Zn_xMn_yFe_zO_4$ was prepared by polyol process using a slightly modified procedure described in ref [2]. By elemental analysis performed using the ICP technique, the content of cations in the formula unit was determined as follow: $Zn_{0.640}Fe_{2.360}O_4$, $Zn_{0.394}Mn_{0.138}Fe_{2.468}O_4$, $Zn_{0.309}Mn_{0.240}Fe_{2.451}O_4$, $Zn_{0.182}Mn_{0.344}Fe_{2.474}O_4$, $Zn_{0.098}Mn_{0.447}Fe_{2.455}O_4$, $Mn_{0.624}Fe_{2.376}O_4$. The ICP results pointed to the presence of multivalent cations, Mn^{2+}/Mn^{3+} and Fe^{3+}/Fe^{2+}. Zn has stable valence +2, while the oxidation state of +4 for Mn couldn't be excluded. Different oxidation states of Mn and Fe and possible deviation of stoichiometry, can create physical effects [3] and make $Zn_xMn_yFe_zO_4$ suitable material in practical applications, used for modification of working electrodes in electrochemical sensors. Consequently, we have performed basic electrochemical characterisation of nanoferrites. Cyclic voltammetry of 5 mM $K_3[Fe(CN)]_6/K_4[Fe(CN)]_6$ (1:1) in 0.1 M KCl at bare SPCE and $Zn_xMn_yFe_zO_4$-modified SPCE showed that the highest peak current (I_p) was achieved using a $Zn_{0.098}Mn_{0.447}Fe_{2.455}O_4$/SPCE. The I_p was about 22% higher than the bare electrode.

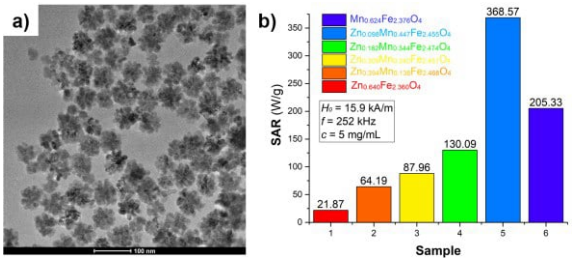

Figure 1: a) TEM micrograph of $Zn_{0.640}Fe_{2.360}O_4$, b) SAR values of $Zn_xMn_yFe_zO_4$.

X-ray diffraction pattern showed the samples were single-phase crystallising in spinel structure type. Morphology and particle size of the samples were analysed from TEM micrographs. Particles (or crystallites) were agglomerated in a flower-like structure (Figure 1). The diameter of the flowers was around 50-60 nm. Superparamagnetic behaviour of the samples was found from magnetization versus field measurements (hysteresis loops). Prepared samples were in the form of stable colloids with hydrodynamic diameter in the range of 50-120 nm. The heating properties of the samples were analysed from the data of specific absorption rate (SAR), Figure 1b. The highest SAR value was found for $Zn_{0.098}Mn_{0.447}Fe_{2.455}O_4$. The best heating efficiency and electrochemical properties had the same sample.

To correlate $Zn_xMn_yFe_zO_4$ different efficiency in magnetic hyperthermia and electrochemical sensor applications with parameters like cation distribution in two non-equivalent spinel crystallographic sites (space group, Fd-3m), local distortion on cationic sites, crystallite size and defects, an integrated study of samples structure and microstructure is in progress.

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Probiotics for increasing iron oxide nanoparticles bioavailability

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One in ten Europeans has iron deficiency. Iron deficiency leads to anemia, tiredness, and reduced productivity. One in Five European women is anemic [1-2]. Vegetarians are 2 times more likely to have iron deficiency. Iron needs to be absorbed from our food, but only 10% of iron is absorbed. Iron supplements cause gastrointestinal cramps and constipation because iron generates free oxygen radicals that cause inflammation and disturb the microbiome [3-6]. Our study aim was to find an iron formulation delivered with better efficacy and fewer side effects. A superior form of bioavailable iron -iron oxide nanoparticles are combined with probiotics that enhance iron absorption and reduce gastrointestinal side effects.

Green synthesis of the iron oxide nanoparticles was used. The obtained nanoparticles were characterized using i) X-ray diffraction (XRD) to determine the crystal structures and lattice parameters of nanoparticles; ii) FT-IR spectroscopy to assign characteristic frequencies to molecular groups and, therefore, the correlation of IR absorption bands with different structural units; iii) Transmission electron microscopy (TEM); iv) BET analysis for the study of surface porosity and particle size; v) XPS techniques will be used to evaluate the actual stoichiometry of the samples. The dependence of the structure, morphology - shape and size of the chemical composition of iron oxide nanoparticles will also be studied. Further probiotic ability to enhance the reduction of Fe^{3+} to Fe^{2+} and enhance transport by the production of lactic acid and p-hydroxyphenylactic acid was evaluated. The evaluation of cellular uptake of the nanoparticles was done using Caco2 cell line model.

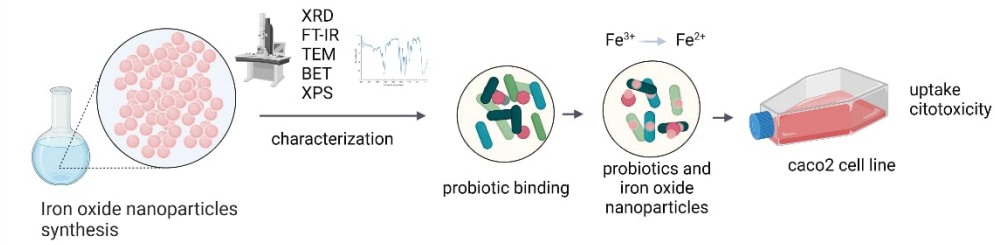

Figure 1. General overiew of the study

This research was funded by UEFISCDI, grant number PN-III-P4-IDPCE-2020-2126

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Synthesis of solely hybrid nanofibers, applications, and future prospective

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Hybrid organic-inorganic nanomaterials made of various types of organosilanes display very promising applications in a variety of fields, including as biocompatible materials. Currently, these types of nanomaterials are notably studied in various forms such as nanoparticles, nanocoatings, nanocomposites and nanofibres which are all often studied in relation to their potential application for various biomedical purposes. In particular, nanofibres (NFs) in the form of scaffolds are under wide investigation, mainly in the field of regenerative medicine, due to their morphological similarity to extracellular matrix [1], with morphological properties in conjunction with chemical structure properties both influencing biological applications. Particularly, hybrid organosilane fibrous nanomaterials are a very interesting class of materials which bring extraordinary properties into the field of biomedicine due to their organic and inorganic parts, which are interconnected via strong covalent bonds between Si and C. These fibrous nanomaterials can be divided into three main groups [2,3]; 1- NFs made from a combination of organic polymers, alkoxides and organo-mono-silylated precursors, 2- NFs which are mainly composed of silica alkoxides together with organo-mono- or bi-silylated precursors, and 3- the very challenging group of NFS comprised purely of organo-bis-silylated precursors. The third group is the focus of this research, whereby formation of NFs comprised of purely the organo-silylated precursor allows for enhanced control on the chemical structure (ie. the organic component) which can then have specific functional groups incorporated for a desired function [4].

The synthetic procedure and successful preparation of pure hybrid organic-inorganic NFs using only the precursor via a one-pot synthesis process utilizing an acid catalysed sol-gel process, without the need of any potentially harmful additives such as co-polymers, surfactants and/ or alkoxides, has been developed. Various organo-bis-silylated precursors have been successfully synthesized with differing organic components, with characterisation and successful electrospinning of NFs following the sol-gel process. Hence, the developed process can control and tune the organic component for development of NFs, without the need for additional potentially harmful incorporations. This process of synthesis has led to the formation of precursors with the organic component incorporating either oxamide, benzene, or pyridine structures with yields reaching 90 % for all synthesised precursors. Organo-bis-silylated precursors were analysed using FT-IR, NMR, TGA, and mass spectrometry for determining structure and stability of the precursors. Following precursor formation, the sol-gel preparation and subsequent electrospinning was undertaken, with NFs formed having a distribution centred around 500 nm with normal gaussian distribution. These fibres were further fully characterised and shown to be thermally stable up to 250 °C, whereby the formed NFs were characterised using FT-IR, solid-state NMR, TGA, and SEM. Subsequently, the formation of these novel fibres using purely the precursor leads to a higher content of the functional organic group, with various other 'linker' organic molecules also in development using a similar technique. This process opens up completely the new possibilities to have a high control on the chemical properties of the fibres and produce materials which have specified purposes such as conductivity, cell adhesion, or even anti-bacterial/anti-virotic properties.

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Use of functionalised thermoresponsive polymers grafted on plasmonic structures for nanoscale surface modification

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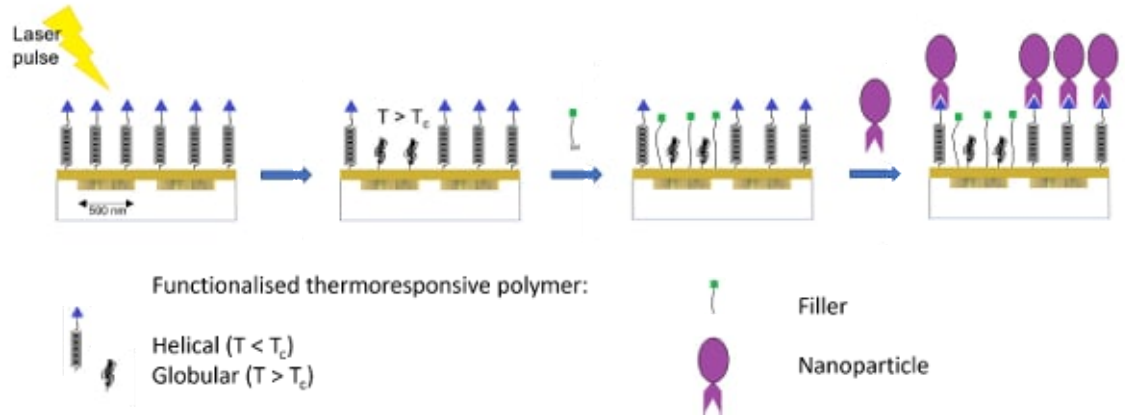
During the last two decades, the continuous push towards technology miniaturization has allowed us to access sub-micron scale surface modification. Tools such as dip-pen lithography[1] and direct laser patterning[2] permit us to control chemical functionalities on nanostructured substrates, and although these are largely established methods, they come with drawbacks, such as low resolution and the requirement of complex alignment. On top of this, they are generally time-consuming processes and therefore not ideal for large area (> cm^2) applications. With this work, we aim to overcome these limitations by using a completely different approach to nano-lithography which promises to significantly increase the write speed by several orders of magnitude.

The selective functionalisation of a specific nanostructure in arrays of multiple structures is achieved by using spatially localised heating of liquid by pulsed laser excitation of nanostructures. Specifically, we employ an engineered plasmonic nanomaterial[3,4,5] onto which a thermo-responsive polymer is grafted. This acts as a temperature-sensitive resist, so that selected areas of the surface can be heated above the critical temperature (T_c) of the polymer, causing it to collapse from its initial helical configuration to a higher density globular state. Thus, hindering the terminal functionalisation and making it unavailable to further react with a recognition group. This work is at the cusp of chemistry, physics and engineering, and promises to revolutionise the field of nano engineering.



We acknowledge financial support from the Engineering and Physical Sciences Research Council (EP/P00086X/1 and EP/M024423/1) and technical support from the James–Watt Nanofabrication Centre (JWNC). M.K. acknowledges the Leverhulme Trust for the award of a Research Fellowship (RF-2019-02).

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Flexible nanoporous activated carbon for adsorption of organics from industrial effluents

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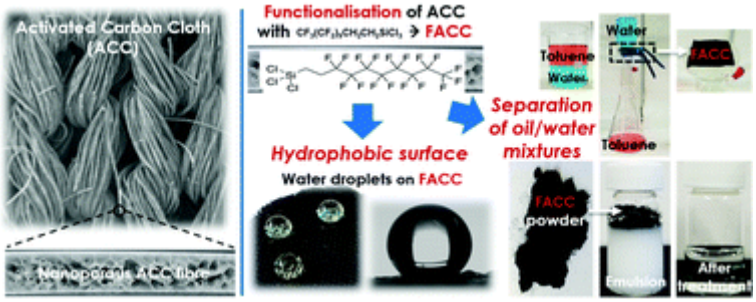
Abstract:

We report the study of the formation of a self-assembled polymeric monolayer on the surface of a high surface area activated carbon to engineer its affinity towards organic contaminants. A nanoporous activated carbon cloth with a surface area of ~1220 $m^2 g^{-1}$ and a pore volume of ~0.42 $cm^3 g^{-1}$ was produced by chemical impregnation, carbonisation and high-temperature CO_2 activation of a commercially available viscose rayon cloth. The subsequent modification with a silane polymer resulted in a nanoscale self-assembled monolayer that made it selective towards organic solvents (contact angle <10°) and repellant towards water (contact angle >145°). The adsorbent showed more than 95% efficiency in the separation of various types of oil/water mixtures under neutral, basic and acidic conditions. Benefiting from inherent nanoscale features, a robust hierarchical structure and a thermally stable monolayer (~300 °C), this nanoporous adsorbent maintained high efficiency for more than 20 cycles and separated surfactant stabilised emulsion with >92% oil removal efficiency. The adsorbent was studied extensively with a series of advanced characterisation techniques to establish the formation mechanism and performance in emulsion separation. Findings from this work provide crucial insights towards large-scale implementation of surface engineered activated carbon-based materials for a wide range of industrial separation applications.



Discotic liquid-crystalline tristriazolotriazines and their tangential-radial Isomerization

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The threefold Huisgen reaction[1]of cyanuric chloride and alkoxyphenyl tetrazoles gives tristriazolotriazines **1a-h**, fluorescent π-conjugated molecules. The phenyl rings are tangentially attached tristriazolotriazine, the torsion angles between triazole and phenyl are 12 – 82°,[2] giving a paddle-wheel structure to these discotic molecules. The melting point of triphenyl-TTT is above 300 °C, but two or three alkoxy chains of medium length result in the formation of broad mesophases, typically with a hexagonal columnar structure[3, 4] and often a complex superstructure.[5] Contrary to earlier reports,[3] these DLCs are not thermostable. A rearrangement of the TTT unit occurs in three successive steps, bringing the phenyl substituents from the tangential positions in **1** to radial positions as in **2**. The new *r*-TTT is nearly planar, dihedral angles are 6° or less. The extension of the molecular diameter and the planarization have a huge impact on the thermotropic properties: higher melting points are typical, complete destruction of mesomorphism, but also the transformation of non-mesomorphous *t*-TTTs to discotic liquid crystals have been observed.

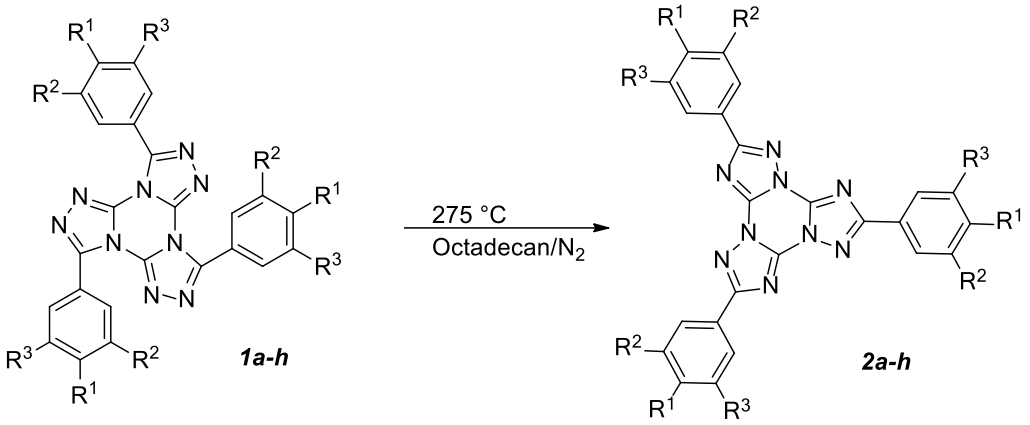

Fig. 1: *Thermal tangential-radial isomerisation of tristriazolotriazines*

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Toward Switching Between TADF and Hyperfluorescence – Tuning by Structural Modifications

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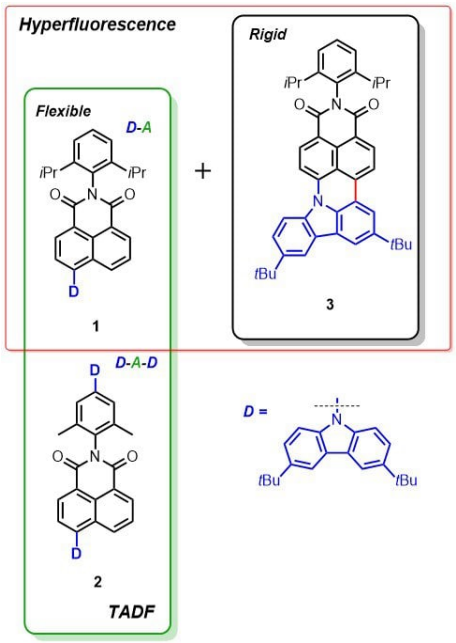
Organic light emitting diods (OLEDs), commonly used as energy-saving, high-yield light source, have been explored for last few decades. Nevertheless, this technology still requires new compounds utilized as emitting layers due to necessity of increasing the device's external quantum efficiency (EQE). Thermally activated delayed fluorescence (TADF) allows to reach this goal[1]. The phenomenon of TADF can be observed for non-planar molecules built with donor-acceptor (D-A) architecture where energy gap between singlet and triplet states is small enough to activate the reverse intersystem crossing (rISC) of excitones. This extraordinary behavior of such molecules places them as very useful in OLEDs 3rd generation.[2]

On the other hand, even for TADF-based devices, the emission wave-lengths were not selective enough. This problem was solved by doping emissive layer with second dopant. Properly set energy levels of both, TADF-active and luminescent molecules, allowed Förster resonance energy transfer (FRET) to be observed. This phenomenon leads to increasing of EQE and also to the strict control of emission wave-length. Generation of emission in such way is called hyperfluorescence.[2,3] The tuning of both dopants' energy levels is crucial for FRET and can be realized by structural modification, where final molecule exhibits lower excited-state energy, e.g. by π-extension.



To show possibility of switching between TADF and hyperfluorescence by a subtle structural change within one molecule we obtained three naphthalimide based molecules with 3,6-di*tert*butylcarbazole as electron donor where degree of rigidity was controlled. While non-planar systems **1** and **2** showed TADF, compound **3** was identified as TADF non-active as it was much more rigid. Extension of π-electron cloud by creating new C-C bond with simultaneous rigidification led to decrease the energy of **3** if compare with **1**, according to the recorded UV-Vis spectra. This two-dopant system was used as emissive layer and showed hyperfluorescence with excellent yield and narrow yellow emission spectrum. Presented strategy definitely confirms that the small structural change can be a key to obtain a pair of TADF-luminescent dopants useful for constructing of 4th generation OLEDs.

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N-doped concave PAHs with fused donor-acceptor structure for high-performance OLEDs and tunable emission mechanisms

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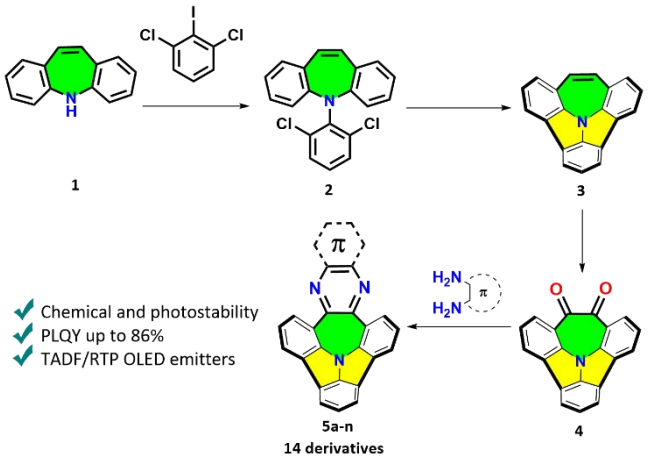
Polycyclic aromatics hydrocarbons (PAHs) have found many applications in recent years including optoelectronics, as organic light-emitting diodes (OLEDs) or organic solar cells. [1] Nitrogen dopant in a polycyclic system, surrounded by 5- or 7-membered rings, results in a negative curvature of the structure and affects the energy of molecular orbitals. [2] Both factors influence the photophysical properties of PAHs. However, the use of N-doped bowl-shaped PAHs in optoelectronics is usually limited by low photoluminescence quantum efficiencies (PLQYs).



Scheme 1. Synthesis plan of bowl-shaped PAHs

Bearing in mind these limitations, here we present the synthesis and characterization of a new class of curved cyclazine-based PAHs with a nitrogen atom surrounded with two pentagons and one heptagon ring. [3] The repetitive and scalable synthetic pathway, demonstrated in Scheme 1, starts from chemoselective Buchwald-Hartwig reaction of commercially available dibenz[*b*,*f*]azepine **1**. This latter one was subjected to Pd-catalyzed, microwave-assisted direct arylation, delivering fully conjugated intermediate **3**. Antiaromatic 7-membered ring of such incorporated dibenzoazepine allows for oxidation to diketone **4**, using benzeneseleninic acid anhydride. Dione **4** has been used for acid-promoted condensation with various 1,2-diamines to yield a series of 14 phenazine derivatives (**5a**-**5n**) with a range of electron-accepting properties and an open way for further functionalization. Wide scope of derivatives gives a possibility to switch the luminescence mechanism between thermally activated delayed fluorescence (TADF) and room temperature phosphorescence (RTP), while the overall PLQY varies from 9% to 86%.

In order to verify the concept, OLED semiconductor devices were constructed. The highest external quantum efficiency was obtained with the -CF_3 group (12%), which is the highest EQE in curved donor-acceptor N-PAHs to date.

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Preparation of Activated Carbon Fibers (ACF) impregnated with silver microparticles from cotton-woven wastes and its performance as an antibacterial agent

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Although activated carbon has been the subject of numerous research applications in water treatment, purification, catalysis, etc., its production is mainly focused on granular and powder presentations due to the commonly used raw materials (e.g., wood, phenolic resin, etc.) [1]. Herein, we report an easily established methodology for preparing activated carbon fibers (ACF) using cotton-woven wastes as raw material under chemical activation with H3PO4. We tested different experimental conditions between the activating agent and the cotton fabrics using a randomized-block experimental design with the specific surface area of the activated fibers as the response variable. A highly microporous structure was obtained with an average specific surface area of 1060 m2/g and pore size of 17 Å [2]. The fibers were later impregnated with silver microparticles using an immersion process in AgNO3 solutions followed by drying and a thermal decomposition to promote the nucleation and precipitation of non-regular shaped microparticles within the fiber's porous. The novel material showed a strong antibacterial effect and complete inhibition of bacterial culture growth at concentrations of silver as low as 0,02 % w/w. However, the presence of silver lowered the specific surface area by approximately 20 % due to the obstruction of the porosities throughout the carbonized structure [3].

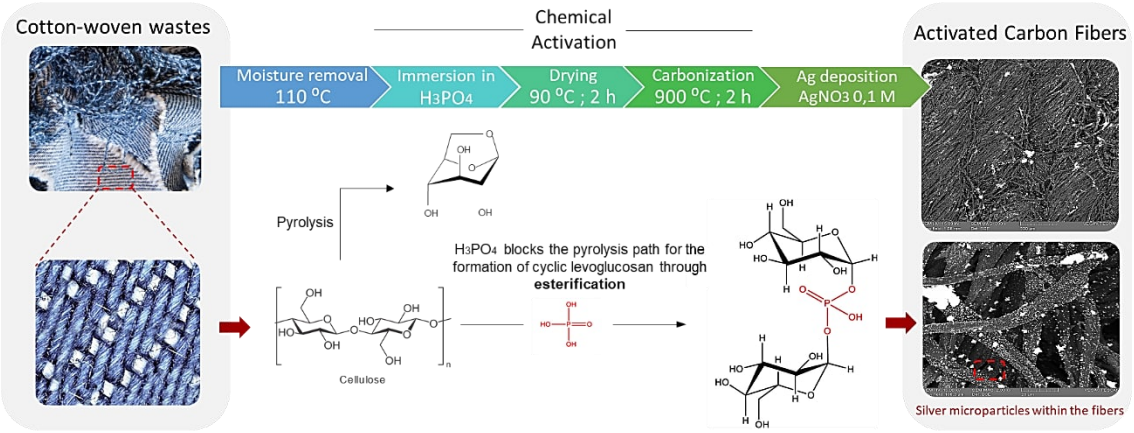

Figure 1. Graphical abstract of the activation and characterization process

The authors address their thanks to the funding project PIS-039-12 and the Escuela Politécnica Nacional for supporting the development of the present research and the Institute of Physical Chemistry of the Polish Academy of Science for its cooperation in the publication the article.

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Polymer-based Nanoparticles for Application in One-Pot Tandem Catalysis

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The combination of incompatible catalytic transformations by nature-inspired site-isolation of catalysts has attracted significant attention in chemistry. The compartmentalization of metal-, organo- or even biocatalysts enables one-pot reactions without the need to isolate or purify intermediates and furthermore creates catalyst-specific microenvironments. [1]
Herein, different mutually inhibiting catalysts are incorporated into polymeric nanoparticles. The polymeric support is based on tailor-made catalyst-functionalized amphiphilic block copolymers obtained by *RAFT*-polymerization. Catalysts are incorporated by direct polymerization of previously synthesized monomers. The amphiphilic properties of these block copolymers allow micelle formation and subsequent nanoparticle formation via crosslinking and carrying out catalysis reactions in aqueous medium. In particular, the immobilized enzyme Candida Antarctica Lipase B (CALB) [2] is used in combination with metal-catalyst functionalized nanoparticles (Cu^{I}/bipyridine) and organocatalyst functionalized nanoparticles (L-proline) in one pot.

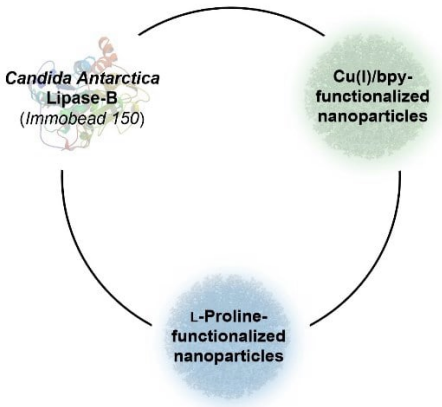

Figure 1 Tandem catalysis using an immobilized enzyme in combination with Cu^{I}/bipyridine and L-Proline functionalized nanoparticles.

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Cyclodextrin Nanosponges Functionalized with Mannose

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Cyclodextrins (CDs) are cyclic oligosaccharides of a natural origin, containing usually 6, 7 or 8 glucopyranose units in the cycle. Cyclodextrins possess the ability to trap hydrophobic molecules in the inner cavity, thus changing the physicochemical properties of the entrapped substances. The benefits of CDs can be further extended by using them in bigger structures, such as polymers, micelles, nanoparticles, and others.

Cyclodextrin nanosponges (NSs) are insoluble polymeric structures consisting of highly crosslinked CDs. Thanks to the number of hydroxyl groups in the structure, NSs can be easily functionalized to meet the requirements of specific applications. Moreover, NSs showed the ability to entrap both hydrophobic and hydrophilic substances in the structure. These abilities make them versatile carriers useful among all in targeted drug delivery.

Glycoconjugation is one of the frequently studied functionalization strategies. In recent studies, glycoconjugates have shown to be promising in targeting specific sites [1]. Among all, mannosylated nanoparticles proved the ability to release entrapped drugs in localities with overexpressed mannose receptors [2].

Mannose-functionalized cyclodextrin nanosponges were prepared as potential carriers for targeted drug delivery. Mannosylation of nanosponges was performed using copper-catalyzed click chemistry, which is a simple, highly selective and efficient method. The material was physically characterized and investigated to prove its suitability for medical applications. Novel mannosylated material may become an efficient tool for providing selective drug delivery to injured or tumorous tissues, which exhibit a high expression of mannose receptors on the cell surface.

Publishing of the results was financially supported by the Ministry of Education, Youth and Sports of the Czech Republic and the European Union (European Structural and Investment Funds - Operational Programme Research, Development and Education) in the frame of the project "International Research Laboratories", Reg. No. CZ.02.2.69/0.0/0.0/18_054/0014685.

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Photosensitized Thermoplastic Nano-Photocatalyst for Potential Applications in Extraterrestrial Facilities

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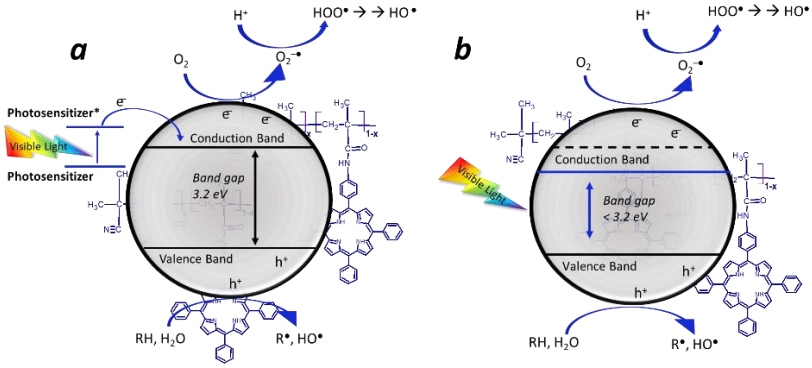
Humankind's ambition for space colonization has led many space agencies to launch different space missions. However, the presence of xenobiotic pollutants in closed environments could represent a health risk for those organisms subjected to long-time exposure, as also happens to astronauts inside the Space Stations. Especially in the case of future space missions that have the intention to settle humans on the Moon and subsequently on Mars, such as NASA's Artemis Program, the lack of primary resources such as air and water and their purification and recycling has determined the need to seek new low-energy depollution methods.

Among different depollution methods, Advanced Oxidation Processes (AOPs) exploit reactive oxygen species to mineralize organic pollutants. Photocatalysis activated by solar light is promising for terrestrial outdoor applications in this field. The most used photocatalyst is titanium dioxide in form of nanoparticles (TiO_2 NPs) [1]. However, the photocatalytic approach cannot be used in underground structures and/or space environments (e.g., extraterrestrial structures), because the indoor lighting system does not generate photons with enough energy to promote the photocatalytic mechanism [2]. Moreover, microgravity makes it difficult the recovery of the photocatalytic slurry from the depolluted solution. To overcome the issues in the use of TiO_2, we synthesized different filmable nanocomposites based on semiconductor nanoparticles supported by photosensitized copolyacrylates. To fine-tune the content of the photosensitizer inside the nanocomposites, an ad-hoc synthesized porphyrinic macromonomer was used together with the methyl methacrylate monomer and TiO_2 NPs, obtaining the nanocomposites via a bulk *in-situ* radical copolymerization. This approach boosts the photocatalytic performance of TiO_2 exploiting the PMMA waveguide effect [3] and ensuring intimate contact between the photocatalyst and the photosensitizer. The photocatalytic activity of the sensitized nanocomposites was studied through photodegradation tests of common probes and recalcitrant xenobiotic pollutants, employing UV-Vis and visible range (λ > 390 nm) light sources. The experimental data showed that the sensitized nanocomposites' photocatalytic performances increased about two times that of the unsensitized nanocomposite, overcoming the issue related to the high band gap value of the TiO_2. This result is due to the photosensitizer which could act as an electron transfer agent and/or a dopant (mechanisms a and b in figure), enhancing the TiO_2 photocatalytic efficiency. Thanks to their intrinsic properties, these photosensitized nanocomposites are suitable to be used in the form of thin films for depollution in indoor environments, such as underground or low Earth orbit laboratories, or, potentially, in lunar shelters [4].



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Benzoxazines modified by inorganic moieties containing silsesquioxane cages

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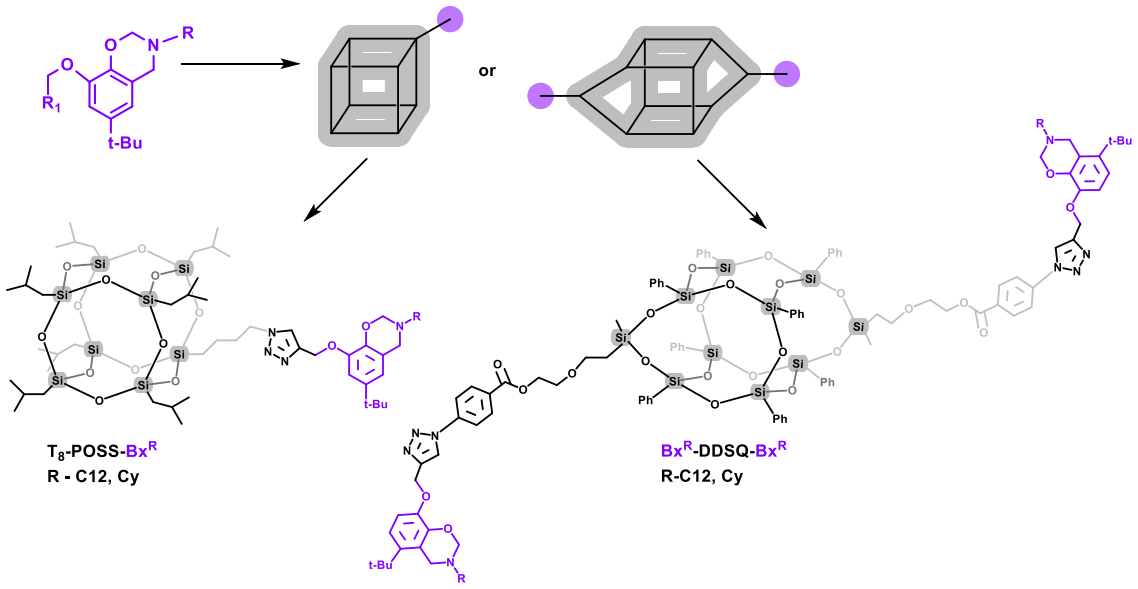
Polybenzoxazines represent the class of dispensable to phenolic resins polymers with unique structure with molecular design flexibility, giving them inherent high heat resistance, good flame retardancy, and excellent properties, including near-zero shrinkage during polymerization, remarkable chemical resistance, low water absorption, and superb electric properties [1].

Polyhedral oligomeric silsesquioxanes (POSSs) have established a position in materials science since cage-like silsesquioxanes, as a unique nanosized additive, effectively enhance polymeric properties such as thermal and mechanical resistance and reduce flammability [2]. Siloxane cages such as POSS or double-decker silsesquioxanes (DDSQs) terminated by benzoxazines could be practical examples of additives to polybenzoxazines that reduce the flammability, improve mechanical properties and allow an opening synthetic way to obtain intrinsically charring polymers. The unique properties of polybenzoxazines are reached through precise functionalization of their monomers – 1,3-benzoxazines that create polymer tailorable properties. That issue is a point of particular interest both in the development of commercial materials and for advanced technologies.

This work aims to synthesize benzoxazine monomers containing POSS and DDSQ moieties with established properties at the molecular level. The cages obtained in this study, especially DDSQ terminated by benzoxazine modules, constitute the first examples of hybrid benzoxazine monomers.



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Application-oriented ZnO QDs derived from self-supporting organometallic approach

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The preparation of semiconducting nanocrystals including ZnO quantum dots (QDs) with specific size and shape as well as desired properties is one of the greatest interdisciplinary challenges for both chemists and materials engineering specialists. Moreover, the unique physicochemical properties of ZnO QDs as functional material offer a wide range of potential applications in many fields, such as electronics, optics, solar cells, anti-counterfeiting etc. The challenge is to obtain a material that is stable, monodisperse and soluble in protic and aprotic solvents, which determines its application.

In this work, we report on the preparation of ZnO QDs using organometallic self-supporting method [1,2]. Our synthetic protocol for the preparation of ZnO QDs involves two steps conducted in a one-pot manner. In the first step, several reactions between Et_2Zn and selected pro-ligands in THF were performed. Then the resulting solutions were exposed to air to initiate transformations leading to ZnO nanostructures with interesting features. The resulting ZnO QDs are highly monodispersed and few nanometers size. Moreover, optical, physical, and chemical properties of resulting ZnO QDs were systematically investigated and were confirmed by many different analytical techniques: HRTEM, DLS, PXRD, UV-VIS, PL, NMR, and IR.
Moreover the colloid of the obtained ZnO QDs using our novel method can be applied as an anti-counterfeiting ink owing to its solubility, colorlessness, and UV-excited luminescence. In a nutshell, the obtained luminescent inks based on ZnO QDs as transparent luminescent labels are stable over time, chemically inert and non-toxic, therefore they can be incorporated into a wide range of consumer products. The results demonstrate that self-supporting organometallic approach is a highly promising method to obtain high-quality ZnO QDs inks for anti-counterfeiting applications or sorting labels.

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UV-induced Photografting of Rhodamine Derivatives on Cotton Fibers for Acidic Gas Detection

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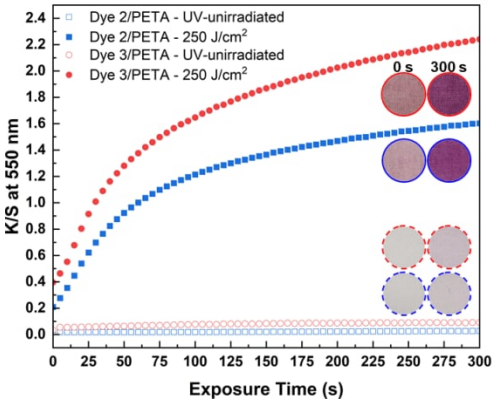
For the immediate detection of strong acids, colorimetric textile sensors based on halochromic dyes have been increasing interest since they allow the detection of gas leaks using the naked eye [1, 2]. However, poor dyeability and washfastness of commercial halochromic dyes on cotton fibers are limiting their applications [3]. In this study, to step over these obstacles, a UV-induced photografting method is introduced to immobilize the dyes on cotton fibers. For this purpose, the radical-sensitive groups were introduced to a rhodamine derivative with a superior pH sensitivity. Thus, two types of graftable rhodamine dyes were synthesized and the textile sensors were fabricated by UV-induced photografting method. The surface morphologies, gas detection performance, washfastness, and reusability of the fabricated textile sensors were investigated. All of the fabricated sensors showed rapid and distinctive color change under acidic condition (100 ppm), in addition to an outstanding washfastness and reusability. From these results, the fabricated textile sensors are expected to serve as promising candidates for practical gas sensing applications.



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Barbiturate derivatives for self-assembly in photovoltaic-effective organic layers

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Organic photovoltaic (OPV) devices represent an interesting clean and renewable energy technology due to involving low-cost fabrication techniques and enabling the manufacturing of semi-transparent, mechanically flexible, and lightweight solar modules. These advantageous characteristics are related with the properties of the organic layer, which combines soluble organic semiconductors with complementary electronic properties (one performing as electron donor and the other as electron acceptor), highly absorbing the solar radiation. Because the OPV device performance greatly depends on the active layer morphology, i.e. the organization of the organic semiconductors, at the nanoscale, the optimization and stabilization of the active layer´s morphology is crucial to produce devices with reproducible high efficiency and long-term stability. One approach to reach high efficiency and morphological stability in OPV's organic layers relies on the formation of supramolecular structures of the donor and the acceptor semiconductors complying with the optimal morphological characteristics, that is, donor/acceptor interfaces should be accessible within ca. 10 nm from the excitons photogenerated either in the donor or in the acceptor. In this communication, we present the synthesis of derivatives of one of the most efficient acceptors used in OPV devices, ITIC (2,2'-[[6,6,12,12-tetrakis(4-hexylphenyl)-6,12-dihydrodithieno[2,3-d:2',3'-d']-s-indaceno[1,2-b:5,6-b']dithiophene-2,8-diyl]bis[methylidyne(3-oxo-1H-indene-2,1(3H)-diylidene)]]bis[propanedinitrile]), containing molecular recognition motives for self-assembling, through hydrogen bonds, and forming both morphologically stable and PV-effective donor-acceptor supramolecular systems. The synthesised compounds contain barbiturate moieties, these being prone to form directional and stable assemblies with (complementary) melamine-containing donors. The barbiturate derivatives, one symmetrical, composed of two barbiturate end-groups, and another one asymmetrical, containing only one modified end-group, were prepared through microwave-assisted condensation reactions of barbituric acid and ITIC precursor compounds. The UV-visible absorption spectra of the new compounds and their electrochemical properties, relevant for applications in OPV devices, are also presented.

Thanks to funding from FCT/MCTES (Portugal) through national funds and when applicable co-funded EU funds under the contracts UIDB/EEA/50008/2020 and PhD Grant to B. Oliveira (2021.04873.BD).

New conducting inks based on poly(3,4-ethylenedioxythiophene):polystyrenesulfonate (PEDOT:PSS) modified with an oxetane reagent

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Printed electronics, making use of organic conducting inks, enables the easy and versatile fabrication of electronic circuits over mechanically flexible and stretchable surfaces. This represents a remarkable benefit for applications in the areas of wearable electronics and biomedical electronics. Poly(3,4-ethylenedioxythiophene):polystyrenesulfonate (PEDOT:PSS) is one of the most interesting conducting polymers due to being commercially available as aqueous dispersion that can be processed, as a conducting ink, by diverse solution deposition techniques, such as spin-coating, spray coating, ink-jet printing, etc. However, PEDOT:PSS still presents low conductivity and structural instability for some applications, for example, for performing as electrode interfacing aqueous/biologic media. In this communication, we present the study of new PEDOT:PSS aqueous formulations, containing an oxetane reagent, 3-oxetanemethanol, which result in printed PEDOT:PSS thin layers with enhanced electrical conductivity and better structural resistance to water. The improved properties were obtained for conducting films deposited by both spin-coating and ink-jet printing methods over glass and on flexible plastic (PET) substrates.

Thanks to funding from the projects at Instituto de Telecomunicações (UIDB/ 50008/2020) and SATRAP project (PTDC/CTM-REF/28108/2017–POCI-01-0145-FEDER-028108) funded by FEDER-POCI and Fundação para a Ciência e Tecnologia – Portugal.

Cellulose meets gecko feet – A biomimetic approach towards surface modification

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The ongoing endeavor towards not only recyclable, but also biosourced functional materials drives research in sustainable materials chemistry. Additionally, biomimetic principles are gaining importance, because nature often provides us well working and environmentally adapted solutions we can learn from.
Here we aim to combine both incentives by manipulation of a biosourced and environmentally benign material towards a biomimetic structure. In our studies, the phenomenon known as "Gecko Effect" is put to use: An array of specifically aligned setae underneath the reptile's foot results in strong adhesion forces, allowing the animal to climb steep inclines or even overhead [1]. While the functionality of artificial nanopillars is a known topic of research, the fabrication of such small structures is very energy-intensive, requires highly specialized equipment and they are made from non-degradable materials [2]. Wood on the other hand is an intrinsically anisotropic material and provides the structural available properties in the form of an uniquely ordered hierarchical cellulose scaffold.

In this work, we present a novel approach to chemical surface modification in order to provide glue-free adhesion of a wooden interface. Free-standing cellulose nanofiber arrays are produced by controlled delignification of the wood to generate a surface similar to the fiber arrays found on the gecko feet [3,4]. In contrast to fragile frameworks of fully delignified wood, the structural integrity of the material is kept intact by only partial and careful delignification, resulting in a functionalized surface of fibrils still anchored in their original wood matrix.
A novel and efficient delignification protocol was established to modify only the desired depth of the wood specimen. Additionally, different wood species were investigated showing unique characteristics that depend on the varying structures of softwoods and hardwoods, respectively.
FTIR measurements verified the delignification progress within the sample, whereas scattering electron microscopy revealed the resulting surface structure, differentiation of the hierarchical cellulose scaffold and thus successful removal of lignin. Tribological measurements are performed to determine the adhesion forces.

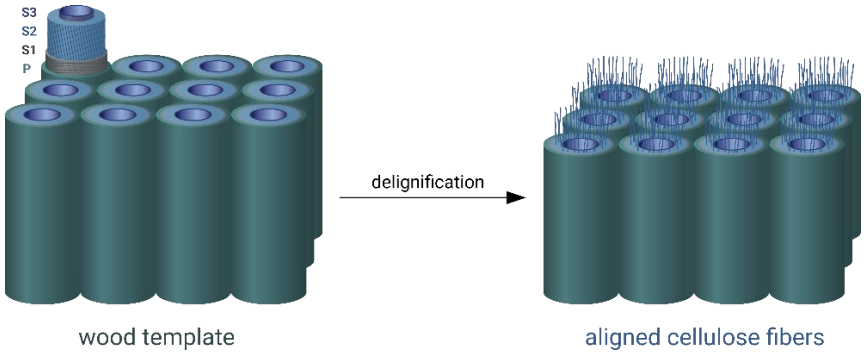

Figure 1. Chemical modification of the wood surface. P: primary wall; S1, S2 and S3: Secondary walls.

This project is funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – DFG Nr. 447247094

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Increasing the electrical conductivity of poly(3,4-ethylenedioxythiophene):polystyrenesulfonate (PEDOT:PSS) for applications as thin film transparent electrodes

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Highly conducting polymer-based thin films performing as electrodes are desirable due to combining the good mechanically flexibility of polymers, therefore enabling applications in flexible and stretchable electronics, with low-cost fabrication methods (i.e. solution deposition techniques, as spin-coating). Among the class of intrinsic conducting polymers, poly(3,4-ethylenedioxythiophene):polystyrenesulfonate (PEDOT:PSS) stands out owing to exhibiting high transmittance in the visible region of the electromagnetic spectrum, in the form of thin films (ca. 100 nm). This foresees applications in a large number of modern optoelectronic devices, performing as transparent electrodes, for which sustainable fabrication with readily available raw materials is needed. In effect, the most widely used transparent electrode in modern devices is a conducting oxide, ITO (indium-tin-oxide), whose availability in the short and medium term is jeopardized due to the scarcity of indium in the earth's crust allied to its increasing demand to the inexorable market of consumer electronics.

In this communication, we present a new method to significantly increase the electrical conductivity of PEDOT:PSS thin films and even improve their optical transparency, which makes use of an oxetane reagent, 3-oxetanol, as an additive to commercial PEDOT:PSS aqueous dispersions. Conductivity values above 1200 S/cm were obtained, this representing an increase by more than three orders of magnitude (analogous films of pristine PEDOT:PSS exhibited conductivity around 1 S/cm). We found that the oxetane reagent reacts in the PEDOT:PSS medium to form a polyether and that the resultant films exhibit higher transmittance, which is beneficial for applications as transparent electrodes. Raman spectroscopy studies indicate conformation modifications of PEDOT segment chains, from benzenoid to quinoid resonant structures, which are expected to promote less coiled chains and favor intermolecular charge transport. Finally, the best performing films were tested in optoelectronic devices, namely in organic photovoltaic cells, replacing the widely used ITO transparent electrode.

Thanks to funding from the projects at Instituto de Telecomunicações (UIDB/ 50008/2020) and SATRAP project (PTDC/CTM-REF/28108/2017–POCI-01-0145-FEDER-028108) funded by FEDER-POCI and Fundação para a Ciência e Tecnologia – Portugal.

Synthesis and photophysical properties of novel *s*-triazine-based TADF emitters

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The reports on highly efficient thermally activated delayed fluorescence (TADF) mechanism in organic compounds and its successful realization in organic light emitting diodes (OLEDs) by Adachi and co-workers [1,2] inspired the design and synthesis of various emissive donor–acceptor organic compounds. Efficient triplet harvesting in TADF compounds leads to internal quantum efficiencies up to 100% and electroluminescence yields exceeding 20% [3,4]. One of the main requirement for efficient TADF is a negligible energy difference between the lowest singlet and triplet states (ΔE_{ST}) which is often achieved in (hetero)aromatic compounds possessing twisted electron donor (D) and acceptor (A) moieties. *s*-Triazine owing to its aromaticity, expressed π-deficiency, strong electron affinity, good optical properties, and easy chemical modification is a desired structural unit in organic structures targeted for numerous applications in organic optoelectronics including development of OLEDS.

Continuing our work aimed to the search of efficient light-emitting materials among the nitrogen heterocycles [5,6] we present herein results on the synthesis and photophysical properties of novel s-triazine-based emitters **TdpPO** and **TflPO** (**Figure 1**).

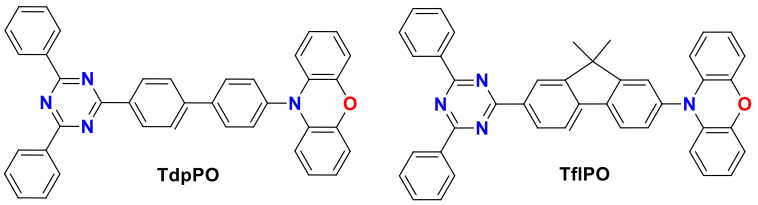

Figure 1. Molecular structures of TADF emitters TdpPO and TflPO.

Synthesis of the target compounds TdpPO and TflPO and some intermediates was accomplished starting with 2-chloro-4,6-diphenyl-*s*-triazine by a combination the Suzuki-Miyaura and Buchwald-Hartwig palladium-catalyzed cross-coupling reactions. Optical properties of the synthesized compounds were assessed by DFT calculations and investigated by absorption, time integrated and time-resolved fluorescence spectroscopies and fluorescence quantum yield and lifetime measurements. Details on the synthetic peculiarities and photophysical properties of the synthesized materials will be presented in the report.

This research has received funding from the Research Council of Lithuania (LMTLT), agreement No S-MIP-22-39.

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AIE-active chiral polyether macrocycle with tunable (chir)optical properties

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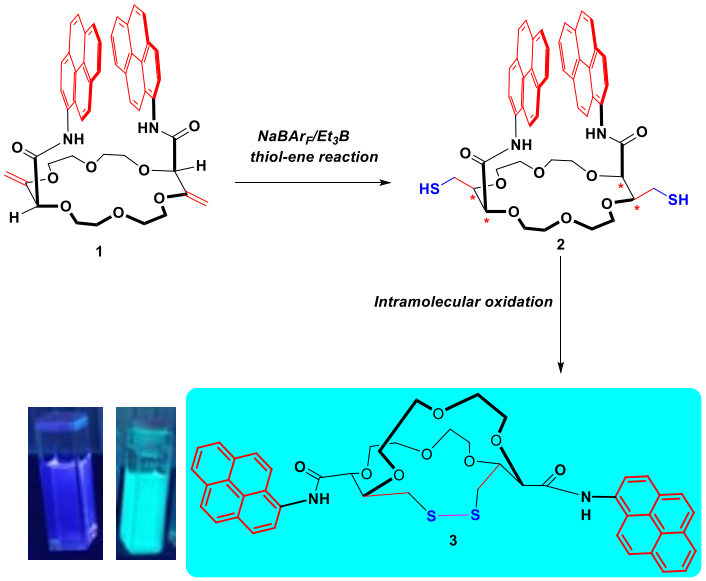
Circularly polarized luminescence (CPL) has received intense research interest due to its broad potential applications in smart sensors, high-resolution three-dimensional (3D) displays, information technologies, etc [1]. Chiral aggregation-induced emission (AIE) luminogens have displayed unique and outstanding advantages in comparison with other asymmetric fluorescent receptors and emitters [2]. Herein, a new type of chiral polyether macrocycle with aggregation induced excimer emission (AIEE) property was designed and synthesized. Double late-stage hydrothiolation of bis enol ether macrocycle **1** (two-step synthesis from 1,4-dioxane only) was achieved in complete regioselectivity and excellent diastereoselectivity, leading to macrocycle **2** containing four defined stereocenters [3]. After intramolecular oxidation, a unique disulfide macrocycle was obtained. In a new development, using aqueous conditions predominantly, chiral disulfide macrocycle **3** exhibits remarkable excimer emission via *intermolecular* arene-arene interactions, unlike precursors of type **1**. Not only high dissymmetry factors (g_{lum}) values are obtained (up to 0.022), but also sign inversion of CPL signals are observed during the aggregation process.



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university of groningen

Mechanochromic Luminescence Based on π-Extended Overcrowded Alkenes

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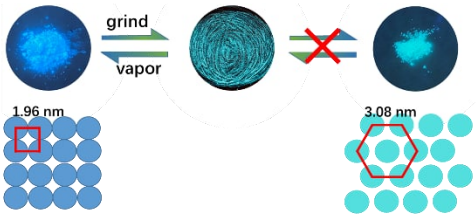
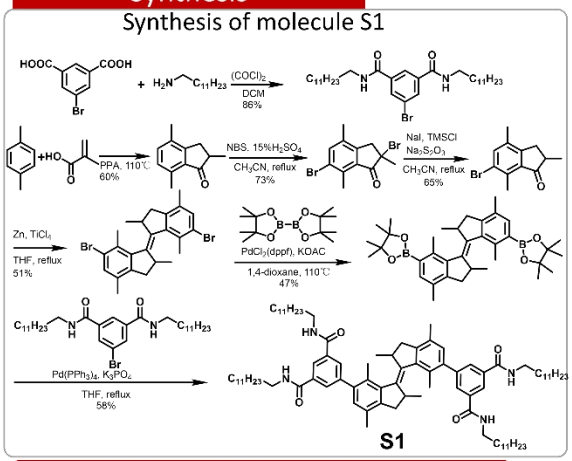
Introduction

Mechanochromic luminescent (MCL) emitters that show reversible color switching upon external stimuli have aroused increasing interest in recent years.[1,2] Tuning the luminescence properties of organic materials is very important for practical applications. The first generation molecular motors have been well established with excellent photo-isomerization, asymmetric catalysis, stereoselectivity properties.[3,4] Whereas, as a π-conjugated luminescent skeletons, the optoelectronic properties has never been reported. Herein, an extended π-conjugated molecule S1 exhibits polymorphism and MCL properties. Different aggregates are observed after precipitation from different solvents. XRD studies indicate that the precipitates from DMF features compact molecular packing, which results in a visible MCL property due to grinding-induced packing change.



Synthesis



MCL property

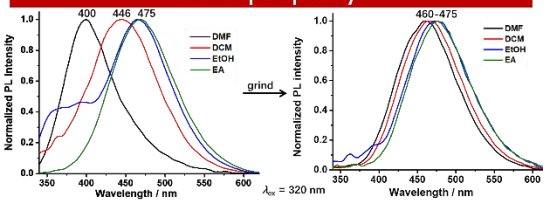
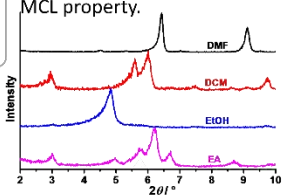


Figure 1. PL spectra of S1 before and after grinding in different aggregation states.

From the PL spectra, the λ_{max} of DMF-precipitate has an obvious red-shift of 60 nm after grinding. The corresponding luminescent changes from blue to green. In comparison, the EA-precipitate almost no change in luminescent. The transformation towards external stimuli indicates the obvious MCL property.



The rectangular columnar phase for DMF-precipitate and hexagonal columnar phase for EA-precipitate could be deduced from XRD which should be the main reason for different MCL property.

Figure 2. XRD analysis of S1 in different solid states.

Conclusions

We have developed a solid-state emitter S1 that exhibits polymorphism, high-contrast MCL properties. Change of molecular packing is responsible for the significantly different MCL behaviors.

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Characteristics of biodegradable spongy materials fused with plant extract with washing properties as prototype wet wipes

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Single-use plastics (SUPs), invented for the busy modern society, are intended to be used only once. It has been proven that SUPs slowly degrade and fragment when exposed to UV radiation, heat, or mechanical stress [1,2]. Nonwovens are the base material of many hygiene products (including wet wipes and sanitary napkins). The composition of the wet wipes material has been identified as white micropolyethylene terephthalate (PET) fibers used in the production of flushable labeled products and other components such as high-density polyethylene (HDPE) and polyethylene/vinyl acetate (PEVA/EVA) [3-5]. Inadequate management of the waste has led to its accumulation in the marine and land environment, also causing sewerage system blockages. Moreover, as a result of the COVID-19 pandemic, there is mounting evidence of an unusual surge in personal protective equipment waste [6,7]. The worldwide nonwovens wipe market is predicted to increase from $19.6 billion in 2020 to $26.1 billion by 2025 [8].

These problems prove a need to design new biodegradable materials that can be alternatives to non-degradable wet wipes. The idea is to prepare sponge-like matrices that are stored in dry form and contain washing agents. It allows for the creation of fully degradable materials, which will not burden the environment.

The objective of my study was to characterize lyophilized materials based on agar and chitosan loaded with *Saponaria officinalis* root extract to provide washing properties. The agar/chitosan matrices were prepared at various weight ratios to evaluate the optimum composition. Aqueous soapwort extract was obtained with a Soxhlet extraction apparatus. The structure and cross-section of 3D materials were examined by scanning electron microscopy (SEM) imaging. The properties of the obtained polymeric matrices were determined by moisture content analysis and mechanical tests.

Biodegradable freeze-dried matrices with washing properties due to the addition of the extract containing natural surfactant have been successfully prepared. The mechanical testing results showed that chitosan matrix exhibited much higher values of Young's modulus and compressive strength compared to agar matrix. The stiffness and strength of 3D matrices made of chitosan and agar mixture increase with greater chitosan content in the materials.

Acknowledgment: Financial support from the National Science Centre (NCN, Krakow, Poland) Grant No 2018/31/N/ST8/02007 is gratefully acknowledged.

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A nanoscale approach for a largescale challenge – POM-ILs as promising candidates to limit iron-gall ink effects on paper supports

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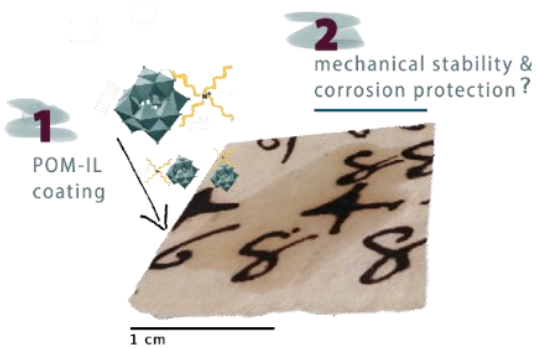
Iron-gall ink (IGI) was the writing medium of choice from the early Middle Ages until the end of the 19th century [1]. Unfortunately, IGI can have tremendous degradation effects on the structural integrity of the documents years after they were written due to its highly acidic nature and the presence of transition metals. Since the late-19th century, various conservation treatments have been used to prevent or attenuate the damaging effects of IGI on paper supports. However, their long-term inefficacy highlights the need for further research. IGI-written heritage requires innovative concepts that could provide effective and long-term mechanical and chemical stabilisation. This study introduces the use of anticorrosive polyoxometalate-ionic liquids (POM-ILs) to prevent and limit severe damage caused by IGI on paper documents. Polyoxometalates (POMs) are a prominent and diverse class of nanoscale molecular metal-oxides [2]. Lacunary Keggin-type POMs feature binding sites that can be used to bind metal ions, such as excess iron from IGIs. Room-temperature ionic liquids (IL) can be formed when POMs are combined with bulky organic cations (e.g. organic ammonium cations) [2]. POM-ILs possess exceptional optical and redox properties and can prevent acid corrosion of metals [3] and natural stone [2].

In this work we are presenting an innovative approach to prevent IGI corrosion degradation by applying dilute and transparent POM-IL solutions on IGI paper mock-ups (unaged and aged) and IGI samples from the 18th century. IGI was produced according to a recipe found in a 17th-century Portuguese manuscript (maniz. cod. 99). To prepare the mock-ups, the IGI formulation was brushed on Whatman® Nº 1 paper samples and artificially aged according to ISO 5630-3 procedure. Further, an antiquarian supplied pieces of manuscripts from the 18th century (of no historical value) with annotated sums written with IGI to be used in the tests. Two room-temperature POM-ILs synthesised from the lacunary Keggin-type polyoxotungstate anion, $[\alpha\text{-}SiW_{11}O_{39}]^{8-}$, were applied by brush on the mock-ups and real samples, forming a transparent coating on the paper matrix. Mock-ups and real samples were characterised before and after using the POM-ILs by visual inspection and photography, pH and colour measurements, SEM/EDS, and FT-IR to follow colour, morphologic and chemical alterations.

This work discusses the applicability and stability of POM-ILs on papers written with IGI opening new possibilities for easier handling and processing for effective conservation of IGI-written heritage.



graphical abstract - POM-ILs used as brush-on coating to limit IGI effects on paper supports

The authors acknowledge the BPE team for providing access to the maniz. cod. 99, FCT for funding (IRONIC project PTDC/ART-HIS/32327/2017, UIDB/04449/2020 and UIDP/04449/2020 HERCULES Laboratory) and the antiquarian who so kindly provided the real samples used. M. Nunes also thanks FCT for a PhD scholarship (SFRH/BD/147528/2019).

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Oxadiazole derivatives obtained via sonogashira and buchwald-hartwig couplings

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Chemistry of the heterocyclic 1,3,4-oxadiazoles has been developed in an effort to achieve more and more complex structures that display improved properties for applications in preparation of optical and electronic devices (*e.g. Organic Light Emitting Diodes - OLEDs*). Cross-coupling reactions essentially contributed to this evolution by allowing new carbon-carbon or carbon-nitrogen bond formation, otherwise very difficult to be performed. [1]

Oxadiazole-substituted phenyl bromides can be considered good candidates as electrophilic partners in palladium catalysed cross-couplings due to a presumptive behavior of the heterocycle core as an electron-deficient group. [2] Convenient and simple synthetic approaches are highly desirable to enhance preparation of such compounds in high yields.

In this context, we describe behaviour of oxadiazole-substituted phenyl bromides in Sonogashira and Buchwald-Hartwig palladium catalysed cross-coupling reactions. Our work firstly involved synthesis of the substrates through oxidative cyclisation of the *N*-acylhydrazones and further optimization of the cross-couplings.

Investigation of the electronic and optical properties of the resulted compounds was next performed, indicating promising behaviour to act as electron-transporting components, useful in the preparation of OLEDs.

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Molecular magnetic actuators based on Fe(III) complexes

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Complexes displaying the spin crossover (SCO) phenomenon demonstrate to have different magnetic behaviour when they are exposed to an external stimulus, such as temperature, pressure, or the application of light. [1] The combination of this property with salient effects can generate molecules that function as molecular magnetic actuators. The thermosalient (TS) effect uses temperature to make work where the crystals are able to jump or change form when exposed to a temperature variation. The photosalient (PS) effect, is triggered by the photochemical covalent/coordination bond formation, such as ring-opening/closing reactions, cycloadditions, etc, using photoirradiation. When the molecule is affected either by the TS or the PS effect, the molecular shape or structure changes by covalent/coordination bond formations resulting in an accumulation of lattice strain in the crystal. The strain is then released in a short time and the crystals of some compounds exhibit a curious behaviour such as crystal jumping, expanding, bending, twisting, or exploding. [2]

Our approach consists in the production of mechanically responsive molecules with magnetic switching properties combining either the TS or the PS effect with the SCO phenomenon in the same material using Fe(III) complexes.

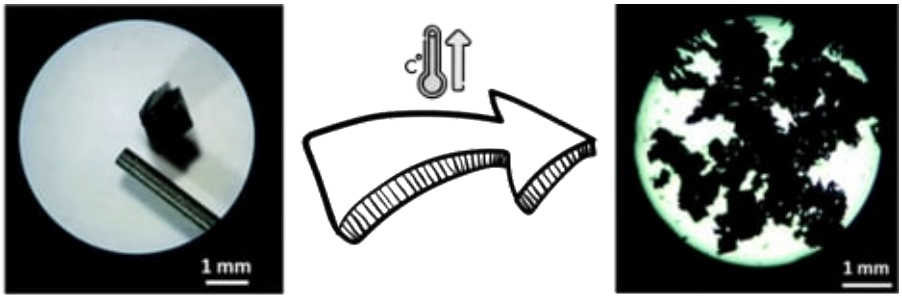

Figure 1: TS effect in the Fe(III) complexes used in this work

We are grateful to Fundação da Ciência e a Tecnologia, FCT, for Project PTDC/QUI-QIN/0252/2021. Centro de Química Estrutural (CQE) and Institute of Molecular Sciences (IMS) acknowledge the financial support of Fundação para a Ciência e Tecnologia (Projects UIDB/00100/2020, UIDP/00100/2020, and LA/P/0056/2020, respectively). The NMR spectrometers are part of the National NMR Network (PTNMR) and are partially supported by Infrastructure Project Nº 022161 (co-financed by FEDER through COMPETE 2020, POCI and PORL and FCT through PIDDAC). P.N.M. acknowledges FTC for financial support (CEECIND/00509/2017).

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Electrochemical fabrication of IRMOF-74 films for uric acid sensing

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Purines play a major role in medical applications since their concentration levels are a useful diagnostic tool for some clinical disorders such as gout, cardiovascular diseases, Lesch–Nyhan syndrome, or type 2 diabetes.[1] Therefore, it became urgent the development of rapid, sensitive, and selective devices for the detection of these compounds, which are converging on the fabrication of thin films and/or membranes based on nanomaterials. Among these, metal-organic frameworks (MOFs) have shown some promising results that can be attributed to their crystallinity, high and permanent porosity, and high surface areas.[2] Electrochemical methods can directly immobilise MOFs on a solid substrate, associated with advantageous shorter synthesis times and milder conditions.[3] MOF-74, constituted by the organic linker H_4DOBDC (Figure 1) is the perfect candidate for molecular sensing. This MOF is constituted by a characteristic crystalline structure: hexagonal channels along the *c*-axis and highly reactive metal sites.[4] In this work, our group reports the synthesis of new ligands, characterised by nuclear magnetic resonance (NMR) and Fourier-transform infrared spectroscopy (FTIR). These will be applied to the cathodic electrochemical fabrication of Fe-MOF-74 and derivatives thereof, characterised by FTIR, atomic force microscopy (AFM), scanning electron microscopy (SEM), particle-induced X-ray emission (PIXE) and Rutherford backscattering spectrometry (RBS). Finally, these devices will be applied for the electrochemical sensing of uric acid.

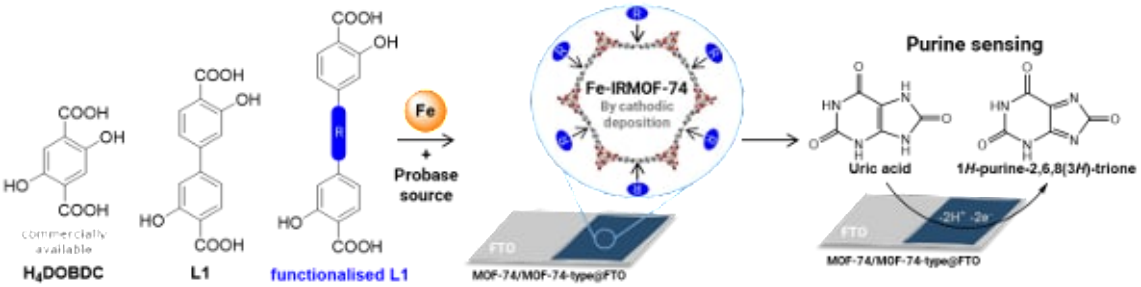

Figure 1: *MOF fabrication process for uric acid detection.*

We are grateful to FCT for Project PTDC/QUI-QIN/0252/2021. The NMR spectrometers are part of the National NMR Network (PTNMR) and are partially supported by Infrastructure Project Nº 022161 (co-financed by FEDER through COMPETE 2020, POCI and PORL and FCT through PIDDAC). PNM and SR acknowledge FTC for financial support (CEECIND/00509/2017 and 2020.02134.CEECIND). CSBG acknowledges the LAQV-REQUIMTE, financed from FCT/MCTES (UIDB/50006/2020, UIDP/50006/2020, and LA/P/0008/2020, respectively). VC and LCA acknowledge FCT for financial support (UIDB/04349/2020).

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Analytical application of newly synthesized polymeric ionic liquid material for separation and determination of inorganic and organic arsenic species in surface waters

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Arsenic is commonly recognized as a hazardous chemical element that occurs in the environment as a result of natural and anthropogenic processes. The toxicity, mobility, and bioavailability of As are highly dependent on its chemical forms (inorganic and organic). Due to the trace concentration of the As species and the influences of coexisting substances in real water samples, development of analytical procedures for reliable and accurate determination and speciation of As is a difficult analytical task. Widely used approaches in routine analytical practice are based on preliminary separation/preconcentration of As species by solid phase extraction with suitable sorbent.

In this study we present new polymeric ionic liquid (PIL) used as a sorbent for separation, preconcentration and speciation of trace inorganic and organic arsenic species in surface waters. PIL was synthesized via chemical modification of polymeric precursor. Initially, poly(glycidyl methacrylate-co-trimethylolpropane trimethacrylate) polymer particles (P(GMA)) were prepared by precipitation copolymerization of glycidyl methacrylate and trimethylolpropane trimethacrylate in the presence of 2,2'-azo-bis-isobutyronitrile as a initiator. Secondly, the P(GMA) particles were modified by chemical binding with 1-methylimidazole (MIA) to obtain PIL material – P(MIA). The composition, structure, morphology and surface properties of the synthesized materials were characterized by using elemental analysis, Fourier transform infrared spectroscopy, scanning electron microscopy, and nitrogen adsorption–desorption measurements. The adsorption properties of P(MIA) toward As(III), As(V), monomethyl arsenic acid (MMA) and dimethyl arsinic acid (DMA) were studied by batch procedure. The different As species were separated on the basis of their selective retention on and elution from P(MIA). MMA, DMA and As(V) were completely retained on P(MIA) particles at pH 8 and sequentially eluted with 1M acetic acid (for MMA and DMA) and 3 M HCl (for As(V)). As(III) was not retained on the sorbent and remained in solution (effluate). The concentration of As species in the eluates and effluate were measured by ICP-OES under optimal instrumental parameters. According to kinetics studies, the adsorption process follows pseudo-second order kinetics model. The adsorption equilibrium data fitted well with the Langmuir isotherm model and the maximum adsorption capacities of the P(MIA) toward As(V), MMA and DMA were 10.5, 7.3 and 4.7 mg/g, which was very close to the experimental values obtained under optimal conditions. Experiments performed for selective determination of As species in surface waters showed that the interfering matrix does not influence the extraction efficiency of P(MIA). The analytical procedure for As(III), As(V), MMA and DMA determination in surface waters was developed and validated through analysis of certified reference materials.

Acknowledgements: The authors gratefully acknowledge the financial support from the Bulgarian National Science Fund (Grant DN19/10 "Smart speciation").

Physicochemical properties of porous bigel-based materials composed of sodium alginate/whey protein isolate hydrogel and sunflower oil oleogel

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Bigel-based materials can be prepared by combining hydrogel and oleogel – aqueous and oily phases gelled with suitable polymers – at a high mixing speed and a specific temperature. Scientists note their numerous advantages, as these systems may have better properties (e.g. mechanical) than emulsion gels [1]. Moreover, they enable the addition of both hydrophilic and lipophilic active substances due to the blending of both phases [2]. Freeze-drying is a dehydration process that involves removing the solvent via sublimation of frozen samples at a reduced temperature and under reduced pressure, which leads to obtaining materials with a three-dimensional structure. Developed sponge-like matrices can form the basis for the formulation of modern, functional materials for dermatological and cosmetic applications. There are few literature reports related to the preparation of bigels, which mainly concern food applications [3]. However, to the best of our knowledge, there are no reports of freeze-dried bigel-based materials. Thus, the idea of using such materials for cosmetic purposes is an innovation in cosmetic chemistry.

This research aimed to optimize the methodology for obtaining materials based on freeze-dried bigels and characterize these materials. The hydrogel was composed of sodium alginate, whey protein isolate (WPI) and glycerol, whereas the oleogel comprised sunflower oil, ethyl cellulose and emulsifier Span 80. They were blended at different hydrogel/oleogel ratios using homogenizator, freezed and freeze-dried. Subsequently, they were characterized by mechanical properties, moisture content, swelling properties, porosity and density.

Modifications in the polymers concentrations and hydrogel/oleogel mixing ratio significantly altered the appearance and structure of matrices, as well as their properties. The materials obtained as a result of this study may be the basis for obtaining a new class of functional materials for dermatological and cosmetic purposes.

The financial support from Grants for Young Scientists awarded by the Dean of the Faculty of Chemistry at Nicolaus Copernicus University in Toruń is gratefully acknowledged.

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Towards the Design Automation of Density-Responsive Chemotactic Nanoparticles

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Nature inspired humans in developing their own new materials for centuries. Recently, a great deal of attention has been received by supramolecular biomaterials, non-covalent assemblies of simple building blocks determining the overall structure and functions of the final construct. In supramolecular chemistry, understanding the nature of the self-assembling sub-units and the structure-property relationship are the key principle driving the bio-inspiration. However, despite the last advances in nanotechnology allowing scientists to control the functionalities of the self-assembly, the design of a supramolecular material starting from its building-blocks reveals a number of challenges and a deeper comprehension of molecular factors controlling nano-bio interface interactions is desirable.

As representative supramolecular architectures, we focused on nanoparticle assemblies. Recent research paved the way to engineering the selective binding of nanoparticles (NPs) on target surfaces[1]. In this process, the investigation of finer molecular models turned out to be essential to rationally design NPs. Compared to experimental analyses, computer simulations offer atomic-level accuracy to observe dynamic changes and predicting structure and behavior of novel supramolecular materials. Furthermore, the most recent machine-learning and optimization algorithms have been accelerating the progress by providing molecular insights unreachable from purely modeling and intuition.

Herein, we combine Coarse-Grained Molecular Dynamics (CGMD) and an optimization process to rationalize the physical and chemical properties of self-assembling monomers allowing the NP to have the desired behavior on target surfaces. As case study, we use NPs composed of amphiphilic self-assembling oligomers which were demonstrated to successfully encapsulate hydrophobic guests. Their modular nature allows to individually change hydrophobic and hydrophilic groups making the assemblies less/more stable and reactive at specific receptor densities. In our recent study[2] we demonstrated that molecular dynamics simulations enable, in principle, not only to design synthetic NPs capable of following chemical gradients on a surface, but also to control their disassembly and where it takes place. Starting from this intriguing perspective, we propose a tool to automatically and effectively explore many possible solutions for designing density-responsive chemotactic NPs which disassemble – and release the encapsulated guest - once they meet a determined receptor density on the target surface. The synergy between CGMD and a discrete optimization algorithm permits to accelerate the materials discovery within a design space that would be hard to evaluate using conventional screening approaches. Specifically, we developed a user-friendly platform requiring: i) the NP starting configuration; ii) the oligomer section (hydrophobic/hydrophilic) to be tuned; iii) the receptor densities where the NP stability/disassembly is desired. The software comes up with several possible beads combinations guaranteeing the user-specified behavior of the NP on the target surfaces.

Ultimately, this work offers chemical routes and guidelines on how altering the hydrophobic/hydrophilic groups and/or changing the moieties in the oligomer units which affect the NP chemotaxis. Notably, such an approach would provide a platform towards the rational design of molecular self-assemblies with controlled chemotactic behavior.

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Bioengineering DNA-based motile life-like nanosystems

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Despite the recent and exciting advances in nanomedicine, only 0.7% of newly developed carriers reach their target locations in vivo, demanding for innovative solutions. One alternative to improve the targeting capacity of nanocarriers is inspired by biological swimmers and machines that abound in nature. The design of "intelligent" artificial systems able to self-propel (swim) in biological fluids and interact with living systems in a controlled way, could pave the way towards new and efficient transport across the biological barriers. Recently, artificial nanomachines that harness chemical energy from enzyme catalysis and convert it into active motion have been developed.[1] These motor-fuel complexes hold a great potential towards nanomedicine thanks to their versatility, bioavailability and full biocompatibility. Although the field is still in its infancy, several milestones have been reached, such as enhanced anti-cancer drug delivery [2] specific targeting and penetration in 3D bladder cancer spheroids [3]. However, when biomedical applications are envisaged, several fundamental questions need to be resolved: what are the optimal design features of enzyme-powered nanomachines? How to integrate multiple and smart functionalities? How to achieve full biocompatibility? Here, we present the use of synthetic DNA as an innovative tool to build programmable DNA-based nanoswimmers. Additionally, we use the unique spatial addressability of DNA to control the number of enzymes bound to the nanomotor chassis for optimal swimming capabilities. For this, we used a hierarchical self-assembly approach for the fabrication of DNA nanoscaffolds, decorated with specific single-stranded (ss) DNA sequences that acted as anchoring strand (Anchor ssDNA). Then, enzymes were conjugated to a ssDNA, which was complementary to the Anchor ssDNA, for their functionalization onto the nanostructure surface. Thanks to the tunability of DNA structures, we were able to control the amount of enzyme binding onto the DNA scaffolds and study the effect of enzyme density on motion behavior. The unique programmability and biocompatibility of DNA could pave the way towards overcoming current challenges on the development of synthetic self-propelled nanomachines by providing new tools to achieve full biocompatibility and design tunability.

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Preparation and characterization of free-standing Cr(III)-imprinted hybrid membranes as a novel nanocomposite sorbent for chromium speciation

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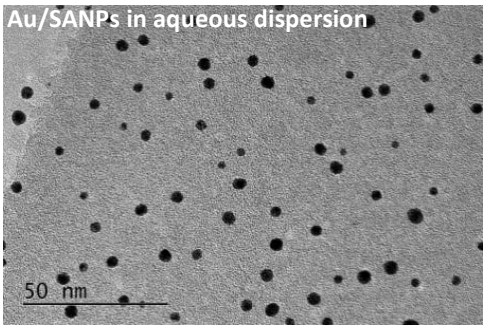
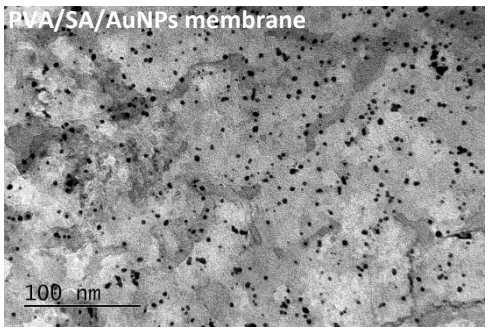
Ion-imprinted membranes (IIMs), combining the membrane separation technique and ion-imprinted technique, are able to achieve selective separation and detection of ions from aqueous solutions via ion-selective recognition. In this work, free-standing Cr(III)-imprinted poly(vinyl alcohol)/sodium alginate/AuNPs hybrid membranes were prepared and characterized, and their application as a novel nanocomposite sorbent for chromium speciation in waters was studied. Equilibrium and kinetic behavior of the hybrid nanocomposite membranes was the focus of this study.

The metal ion imprinted membranes were prepared via solution blending method using blends of poly(vinyl alcohol) (PVA) and sodium alginate (SA) as film-forming materials, PEO as porogen agent, SA stabilized gold nanoparticles (Au/SA NPs) as crosslinking and mechanically stabilizing component, and Cr(III) ions as template species. Cr(III)-IIMs were obtained upon solvent evaporation at 50 °C. Non-imprinted membranes (NIIMs) were also synthesized via solution blending method in the absence of template ions. The physicochemical characteristics of pre-synthesized Au/SA NPs and hybrid nanocomposite Cr(III)-IIMs were studied by UV-vis and FTIR spectroscopy, TEM, SEM, and XRD observations, TG and DSC analysis. The obtained good dispersion of gold particles in a polymer matrix restricts the chain movements and thereby supports mechanical strength of membranes produced.





The adsorption properties of the prepared Cr(III)-IIMs were investigated in terms of adsorption pH, adsorption kinetics and adsorption isotherm. Results obtained indicate that adsorption process attained equilibrium in 16 hours at optimal pH 5. Compared with NIIMs, Cr(III)-IIMs demonstrated higher adsorption capacity for Cr(III) at pH 5. The maximum adsorption capacity of Cr(III)-IIMs was 33.7 µmol/g and the adsorption process was more suitable to be expressed by sigmoidal logistic kinetic and Langmuir models.

A simple and sensitive analytical procedure was developed for separation and speciation of Cr species in aquatic environment using dispersive solid phase extraction of Cr(III) by Cr(III)-IIMs membranes prior to Cr(VI) determination in the supernatants. The determination limit achieved for toxic species Cr(VI) fulfils the requirements for their monitoring in surface water bodies under the demand of Water Frame Directive. In addition, if necessary Cr(III) might be determined in the same sample with even lower determination limit.

Acknowledgements: We acknowledge the Bulgarian Scientific Fund, Project, DN19/10, "Smart speciation".

Development of luminescence films based on graphene/lanthanopolyoxometalates nanomaterials through layer-by-layer assembly for application in the detection of metals in aqueous medium

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The luminescence properties of lanthanides have been explored in a wide range of fields such as optical sensors, luminescence biomarkers, electronic displays, and others. Taking this in account, lanthanopolyoxometalates (LnPOMs) are interesting functional units in materials science due to the excitation paths that involve ligand-to-metal charge-transfer states associated with O-Ln and O-M (M = Mo, W) transitions [1,2]. The incorporation of LnPOMs in graphene materials can explore the unique optical, chemical and electric properties of graphene. However, the preparation of luminescent graphene materials containing this type of LnPOM remains poorly studied.

In this work, a graphene oxide functionalized with an ionic liquid was decorated with LnPOMs to produce a hybrid nanocomposite with luminescent behaviour (rGO-IL-LnPOM). Then, the nanocomposite was attached to a quartz substrate which was previously prepared by a layer-by-layer process, alternating a layer of positively charged polyelectrolyte (poly(allylamine hydrochloride), PAH) and a layer of negatively charged polyelectrolyte (poly(4-styrenesulfonate), PSS) **(Figure 1)**. Due to the presence of negative LnPOM species in the hybrid nanocomposite (rGO-IL-LnPOM), the latter negatively charged species can be attached onto the positive PAH top layer of the quartz substrate. The resulting multilayered structure exhibit photoluminescence behaviour showing that the LnPOMs emission is maintained in the nanohybrid film, with a good potential for application in nanosensors. We have tested these nanohybrid films for the detection of metals ions in aqueous solutions. The nanohybrid film showed a good response for Cr^{3+} in aqueous solution, with selectivity and linearity between 1-10 µM, associated to the luminescence quenching of Cr^{3+}. Our strategy to construct luminescent graphene/lanthanopolyoxometalate nanohybrid films is expected to provide a new methodology to develop economical, fast and sensitive nanosensors for environmental pollutants monitoring.

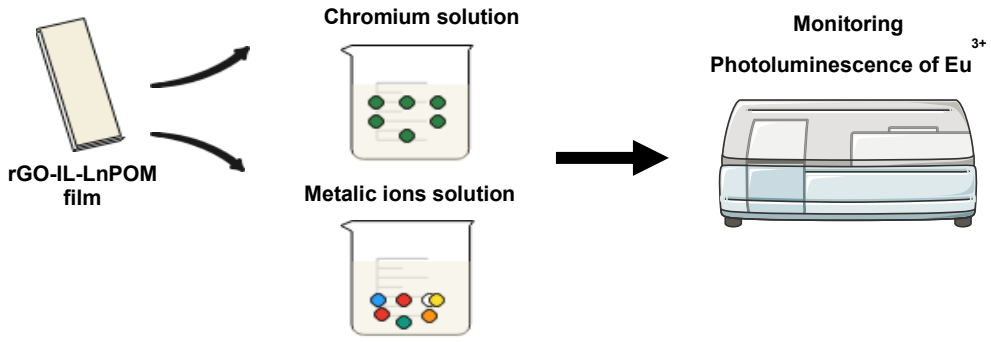

Figure 1. Schematic illustration of the *LbL luminescent graphene/lanthanopolyoxometalates as sensor for detection of heavy metals.*

Acknowledgements

We thank the Fundação para a Ciência e Tecnologia (FCT), FCT/MEC (PIDDAC), European Union, QREN, FEDER, and COMPETE for the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020 & UIDP/50011/2020 & LA/P/0006/2020. Maria Martins thanks FCT for the PhD grant (SFRH/BD/131433/2017 and COVID/BD/151933/2021).

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Langmuir-Blodgett Films of Semiconducting Single-Walled Carbon Nanotubes

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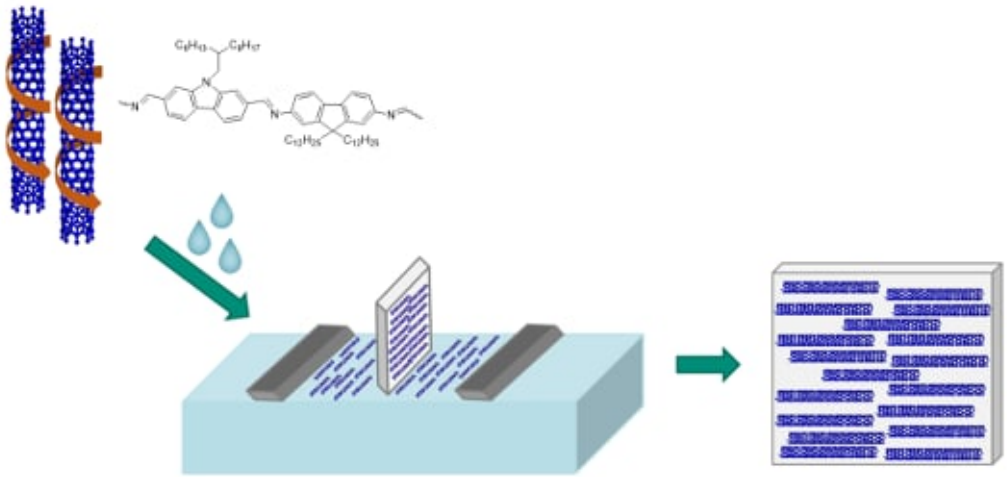
Single-walled carbon nanotubes are typically generated as mixtures of metallic and semiconducting nanotubes which limits their potential use in many advanced applications which require highly pure samples [1]. The alignment of the carbon nanotubes in thin films can provide high mechanical strength and electrical/thermal conductivity producing new structures for a new generation of nanostructured materials and carbon-nanotube electronics devices [2].

In this work we present the preparation of Langmuir-Blodgett thin films using a selective dispersion of semiconducting SWNTs (s-SWCNTs) obtained by the recyclable polymer wrapping separation methodology [3, 4]. The cleavage of the copolymer, due a bridging imine bond in each repeat unit, allow the removal of the polymer after wrapping and the possibility to produce dispersant-free sorted s-SWCNTs thin films.

The ability of the acid cleavable fluorene-carbazole copolymer to form stable monolayers when spread at the air-water interface was studied and also contributed to the formation of a stable film of s-SWNTs dispersion at the interface. The effect of polymer removal on film quality has also been studied. This monolayer was further transferred to a solid support, as a Langmuir-Blodgett (LB) or Langmuir-Schaeffer (LS) film, with a certain alignment degree, as confirmed by surface pressure-area isotherms, UV-Vis-NIR spectroscopy, Raman spectroscopy and Atomic Force Microscopy. Such methodology could lead to well-aligned and density controlled CNT devices.



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Analysis of the photoluminescence for two MOFs based on terephthalato and bispyridyl-like ligands with variable dimensionality and topology

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In recent years, metal-organic frameworks (MOFs) have caught the attention of researchers working in the field of multifunctional materials due to their structural and chemical versatility as a result of the endless combinations of metal centres and organic ligands.[1] This structural tuneability has caused MOFs to become adequate materials in many research fields[2] among which photoluminescence (PL) is to be highlighted.[3] In order to enhance this property, organic ligands with strong light-harvesting capacity are required on the one hand, while metal ions with a closed-shell electronic configuration, which avoid non-radiative quenching associated with the intraionic transitions, are welcome on the other hand.[4]

The present work reports on the synthesis, structural analysis, physicochemical characterization and photoluminescence performance of two ternary compounds based on dicarboxylate and bispyridyl-like ligands and metal ions of group 12, namely $[Zn_2(\mu_4\text{-bdc})(\mu\text{-pbptz})(DMF)_2(NO_3)_2]_n$ (**1-Zn**) and $\{[Cd(\mu_3\text{-bdc})(\mu\text{-pbptz})]\cdot DMF\}_n$ (**2-Cd**) (where bdc = benzene-1,4-dicarboxylate, pbptz = 3,6-bis(4-pyridyl)-1,2,4,5-tetrazine, and DMF = N,N-dimethylformamide). **1-Zn**, consisting of a 2D-layered framework, can be considered as the lower-dimensional analogue of the previously reported $\{[Zn_2(\mu_4\text{-bdc})_2(\mu\text{-pbptz})]\cdot 2DMF\cdot 3H_2O\}_n$ 3D MOF (**1'-Zn**),[5] which is shown to recrystallize into **1-Zn** undergoing a kind of exfoliation. **2-Cd** presents a 3D doubly interpenetrated framework whose porosity is reduced to approximately half of the available solvent-accessible voids contained in the non-interpenetrated homologue reported so far, $\{[Cd(\mu_3\text{-bdc})(\mu\text{-pbptz})]\cdot 3DMF\}_n$ (**2'-Cd**). Structural factors leading to each of the alternative frameworks are detailed by analysing the building units with a perusal of the Cambridge Structural Database and providing a comparative description of the structures. The photoluminescence properties of herein reported compounds (**1-Zn** and **2-Cd**) are also measured and the processes governing the spectra are described using time-dependent density-functional theory (TD-DFT), which allows establishing some structural correspondences by comparing these results with those of the **1'-Zn** and **2'-Cd** analogues.

OPC is grateful to the University of the Basque Country for the predoctoral fellowship. This work is supported by the University of the Basque Country (UPV/EHU) (GIU20/028), Basque Government (IT1005-16, IT1291-19), Junta de Andalucía (FQM-394 and B-FQM-734-UGR20) and the Spanish Ministry of Science, Innovation and Universities (MCIU/AEI/FEDER, UE) (PGC2018-102052-A-C22, PGC2018-102052-B-C21 and PID2019-108028GB-C21).

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Design of Photocatalytic Active Materials for Additive Manufacturing

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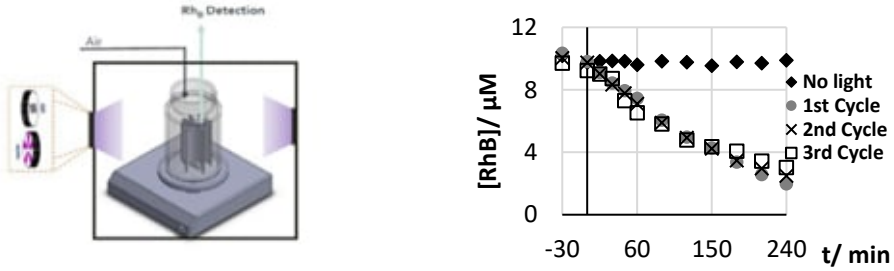
The interest in additive manufacturing (AM) technologies as a tool to develop and build highly tailored reactors increases with the availability of 3D printers and materials at lower costs. In the chemical engineering field, the price/quality ratio of AM technology has been enabling the manufacture of optimized reactor geometries for industrial applications The main application of AM lies in flow chemistry technology, i.e., chemical reactions that are performed in continuous flow processes within narrow channels. These chemical reactions can make use of heterogeneous catalysts and/or can be assisted by light (photocatalytic reactions). Moreover, over the last decade, the range of materials available for 3D printing was considerably amplified, including ceramics, polymers, metals, and carbon-based materials [1]. Some of these materials have been applied as catalyst supports and for reactors manufacturing.

In this work, a commercial resin, Clear V4 (Formlabs) was impregnated with Titanium dioxide (TiO_2) to manufacture 3D structures with photocatalytic activity. The behaviour of the TiO_2-containing resin was evaluated from rheological tests. The printed structure morphology was determined by SEM and EDS analysis. And from the DMA analysis, the mechanical properties of the materials were also studied. For the photocatalytic tests, the 3D printed structure was placed at the center of a cylindrical glass reactor and irradiated from the outside using a UV-LED system (Fig. 1a).



(a) (b)

Figure 1. (a) Experimental setup of photocatalytic degradation of RhB.and (b) Photocatalytic degradation of RhB over 3 consecutive cycles using Clear V4 + 1% TiO_2.

In the absence of light, no RhB degradation was observed. (Fig. 1b) However, when the reactor was irradiated by 370 nm LEDs, an 80% decrease in RhB concentration after 240 min was observed. Moreover, the photo-stability of the 3D structure was confirmed for at least 3 cycles of utilization.

In conclusion, a simple, cost-effective, and fast additive manufacturing (AM) technique, to immobilize catalysts used in photocatalytic applications is proposed and effectively demonstrated.

This work was financially supported by LA/P/0045/2020 (ALiCE), UIDB/50020/2020 and UIDP/50020/2020 (LSRE-LCM), and UIDB/00511/2020 and UIDP/00511/2020 (LEPABE) - funded by national funds through FCT/MCTES (PIDDAC) and project POCI-01-0145-FEDER-031398, funded by European Regional Development Fund (ERDF) through COMPETE2020 – Programa Operacional Competitividade e Internacionalização (POCI) – and by national funds through FCT. I.S.O. Barbosa acknowledges her FCT grant UI/BD/151092/2021.

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Mechanism of oxidations of a chiral biomass-derived substrate namely isosorbide

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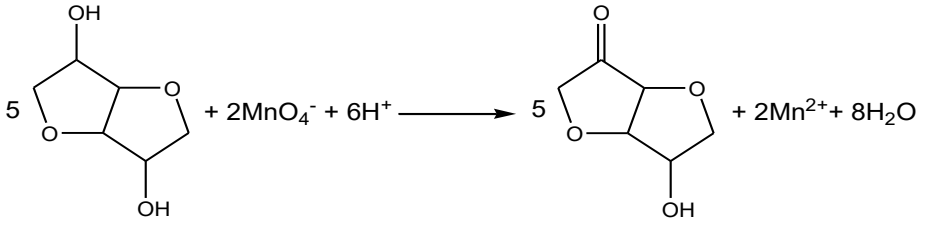
Abstract

Isosorbide is considered to be a versatile biogenic platform compound for the production of chemicals, and has been widely used for the synthesis of elaborate molecules including chiral ionic liquids, phase-transfer catalysts, and ligands (amino alcohols, amines, mono- and diphosphines, etc.). Moreover, isosorbide has been used as a starting material for pharmaceutical applications as well as for organic solvents or fuels, and as a building block for biopolymers. [1-6] Oxidation reactions are very important in organic synthesis. Among the important oxidizing agents, permanganate ion is widely used in the oxidation of various organic compounds in neutral, alkaline and acidic media. The mechanism of oxidation reactions by permanganate ion is governed by pH of the medium. In this work we present the kinetic study of the reactivity of isosorbide towards permanganate ion in different acidic media, in both perchloric and sulfuric acids solutions and we propose the oxidation mechanism of such diol. The final oxidation product of isosorbide was identified by both spectroscopic and chemical tools as the corresponding monoketone derivative, namely (1S,4S,5R)-4-hydroxy-2,6-dioxabicyclo[3.3.0] octan-8-one. [7]



Isosorbide **Monoketone derivative**

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Novel molecularly imprinted impedimetric biosensor based on polypyrrole and decorated graphene oxide for the routine monitoring of Lysozyme

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In this work, a novel molecularly imprinted polymer based on polypyrrole (PPy) and decorated graphene oxide (GO@Fe_3O_4) was developed for the sensitive detection of lysozyme (LYS). The synthesized material (MIPPy/GO@Fe_3O_4) was electrodeposited with LYS as a template on gold microelectrodes. Transmission electron microscopy (TEM) and X-ray photoelectron spectroscopy (XPS) were used to confirm the adequate preparation of GO@Fe_3O_4, and the characterization of the resulting microsensors was carried out with the following analytical techniques: electrochemical impedance spectrometry (EIS), FT-IR analysis and scanning electron microscopy (SEM). An equivalent circuit was suggested to quantitatively analyse each component of the sensor system. EIS was also used for the determination of LYS in a wide linear range from 1 to 1 10^5 pg/mL, presenting good precision (RSD ≈ 10%, n = 5) and low limits of detection and quantification (LOD = 0.009 pg/mL and LOQ = 0.9 pg/mL, respectively). Meanwhile, the microsensor showed a high sensitivity, a good selectivity and reproducibility. The construction process was relatively simple, and provided a rapid and economical method for the routine monitoring of LYS. The microsensor was successfully applied for the detection of this protein in fresh chicken-egg white sample and commercial drug.

Acknowledgements

The Spanish Ministry of Science and Innovation for funding this work with Fellowship FPU18/05371, and the financial support of the EU H2020 WIDESPREAD Program entitled Bionanosens grant agreement # 951887.

Electrochemical oxidation of abietanes

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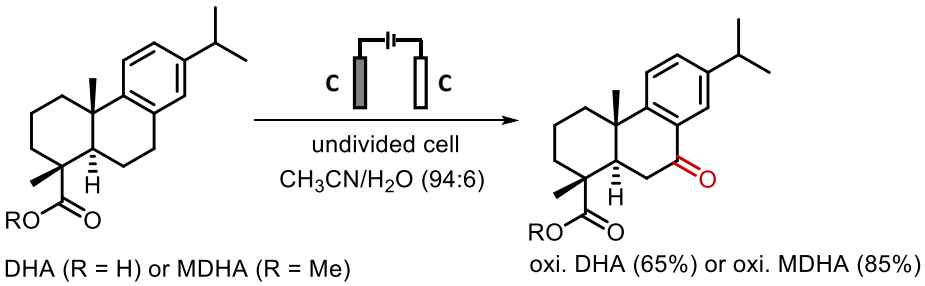
Colophony, a natural resin obtained from coniferous trees, is constituted by a group of diterpenes known as abietanes, which, along with its derivatives, has been found to have a wide variety of interesting biological activities, including the antimicrobial, antiviral, antitumoral, and anti-inflammatory activities. Constituents of this resin have a wide range of industrial applications, including synthetic rubbers, adhesives and fragrances. [1,2]

The benzylic oxidation of dehydroabietic acid, an abietane from colophony, and its methyl ester derivative, has been reported using oxidative protocols, such as using Jones reagent [3], Swern oxidation [4] or either using Chromium trioxide in stoichiometric [5] or catalytic quantities. [6] However, these protocols fail in the context of sustainability for several reasons, such as the use of toxic reagents and stoichiometric amounts.

Herein, we report an electrochemical method for the benzylic oxidation of dehydroabietic acid, an alternative greener protocol for the formation of the benzylic ketone in very good yields using modern electrochemical methods. (Scheme 1). Moreover, this method can be applied to the corresponding methyl ester derivative. [7-9]



Scheme 1: Electrochemical oxidation of dehydroabietic acid (DHA) and its methyl ester derivative (MDHA).

Acknowledgements: The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951996.

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Design, Synthesis and Aggregation Properties of Amino Acid Based Amphicharged Bolaamphiphilic Surfactants

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The noun “bola” relates to the shape of a South American missile weapon.[1] The simplest form of “bola” consists of two balls which are attached to both ends of a cord. The term “bolaform electrolyte” (short form: “bolyte” or “bolion”) was introduced by Fuoss and Edelson in 1951 for a chain of hydrophobic groups connecting two hydrophilic end groups. For less water-soluble analogues, the name “bolaform amphiphiles” (short form: “bolaamphiphiles”) is preferred.[2] The biological and biochemical applications of amino acids and synthetic peptides have evolved over the years, offering an effective means to satisfy the technological demand of modern biomaterials. Design of peptide-based bolaamphiphiles offers a simple and facile means to organize peptide and amino acid motifs with the aid of nonbiological hydrophobic centers, realizing a protein-mimetic configuration at the molecular level. Inspired by these thoughts, we have synthesized a new class of amino acid based bolaamphiphilic surfactants derived from L-Lysine and L-Glutamic acid residues and have studied their applications in different fields. The results of our studies in this direction are presented in the poster.

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The chemical space and some ethical consequences of its uneven growth

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An important aim of chemistry is the discovery of new substances and of methods to procure them. History shows that such a discovery occurs at an exponential rate and that for more than two centuries the driving force for substance discovery has been chemical synthesis. This synthetic activity is strongly tilted towards organic chemistry. If chemistry is about new substances and methods to afford them, to what extent does the historical organic chemistry bias affect the aims of chemistry? If chemists are responsible for chemical synthesis to chemical community, is part of that responsibility to ensure high diversity of substances and of preparative methods? Or is it to achieve deep knowledge on some particular substances and their methods to produce them? I will discuss these and related questions based on recent results on the expansion of the chemical space, as made of substances and reactions reported by chemists over history.

Military Healthcare During Physical Exercises – Monitoring human stress biomarkers in sweat

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Human emotions study through biomarkers is a recent field with high importance to all modern society. It is now recognized that physical and psychological stress are related with physical and mental disorders including post-traumatic stress disorder (PTSD). The control of stress and, naturally, the emotions, is of extreme relevance for military activities (Figure 1).

In the STRESSENSE project, civilian, military and business' association researchers (from FCT-NOVA, CINAMIL/Academia Militar and CITEVE) are united with the common goal to study and early detect stress biomarkers, through non-invasive methodologies (using sweat as target biological fluid), and able to operate in field with real-time monitoring and integrated in wearables. The project has a multidisciplinary team for the biomarker's patterns identification [1,2] and in-situ measurement devices development [3] with extensive expertise in electrochemistry, biochemistry, biomolecules detection, materials and data-processing, together with knowledge associated to individuals' emotional and physical behaviour. The volunteers from Portuguese Army (Academia Militar) take part of a case-of-study that will allow making the proof-of-concept of the new proposed medical methodology. This work is a contribution to the continuous monitoring of stress related parameters and is a societal achievement for wellbeing of military forces.

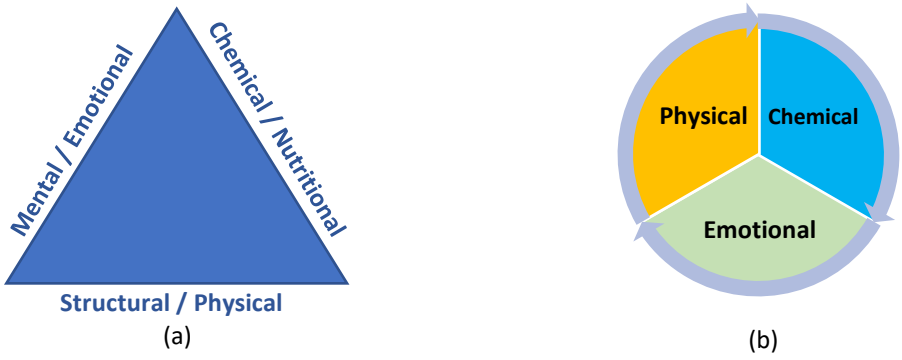

Figure 1. Health Human Factors (a) Triangle of Health and (b) Stress Management.

The authors acknowledge the anonymous Military volunteers and the military team that participated in this work at Academia Militar. The authors acknowledge the Fundação para a Ciência e Tecnologia for financial support through Project PTDC/SAU-SOC/28390/2017 (STRESSSENSE). This work was supported by the Associate Laboratory for Green Chemistry-LAQV, with national funds from FCT/MCTES (UIDB/50006/2020).

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Teaching Responsible Chemistry: A Challenge-Based Learning Framework for the Implementation of RRI Courses in Chemistry Education

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Responsible Research & Innovation (RRI) is a concept of professional attitude and agency in the context of innovation with significant expected societal and environmental impact. In the past decade, it has been framed, theoretically informed, and practically implemented by various disciplines such as the sociology of technology, STS, technology assessment, philosophy and ethics of technology, technoanthropology, and economics,[1] as well as by political organs in the field of science, technology, and innovation governance.[2] By today, the concept is certainly mature enough to be applied in concrete research and innovation practice. Yet, this realisation of RRI's goals faces several methodological and structural difficulties, among them the insufficient implementation of RRI education in STEM majors at higher education institutions, and a lack of normative literacy and discourse skills among researchers, technology developers, and innovators.[3] As a result, design decisions in innovation processes are dominated by scientific-technical and economic thinking (risk assessments, life-cycle assessments, functionality, utility, safety, profitability, economic feasibility, market competitiveness) whereas normative considerations (ELSI, social and environmental integrity, cultural norms, etc.) are underrepresented or not formalised in the innovation procedures.

The proposed course concept aims at filling a gap in the translation of RRI principles into tertiary chemistry education practice. Employing a challenge-based learning (CBL) approach, it draws on a practical framework of RRI as guideline (or orientation) for professional conduct in the context of chemistry (academic research and corporate R&D). This focus is chosen because of the obvious enormous impact of chemical progress on the social and environmental life world, and because of the creative, emerging, and enabling character of most of chemical science and innovation. The highly practical course—with 'lectures' reduced to a minimum—is thematically structured around a fictitious innovation project as it may happen in real-world contexts, potentially in cooperation with local chemical companies and industry. Students form teams, define roles and shared values, identify a challenge of their interest, and are guided through developing and validating a solution. RRI tools such as ethical design thinking, safety-by-design, ethical vision assessment, or normative risk assessment, are brought into the teamwork step-by-step, allowing students to dive deeper into the matters of their interest and needs. The CBL fashion is expected to lead to a high engagement with the course content, a clear realisation of the practical significance and applicability of the acquired skills, and a change in attitude towards normative dimensions of chemical science and innovation activities. The designated course objectives are the formation of normative literacy[3], the shaping of professional integrity and good scientific practice, the strengthening of discourse performance skills, and the ability of interdisciplinary collaboration in multi-stakeholder settings.

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Extraction of uranium using 2-hydroxy-5-nonylacetophenone ketoxime

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2-hydroxy-5-nonylacetophenone ketoxime was utilized to extract uranium from carbonate leach liquor of dolostone sample. The extraction parameters were optimized as 0.36M 2-hydroxy-5-nonylacetophenone ketoxime diluted in benzene at equilibrium pH 4, O/A phase ratio1/1, 10 min. shaking time and at room temperature (25°C). An extraction efficiency of 80.29% was realized under these conditions. The thermodynamic parameters ΔG^o, ΔH^o and ΔS^o were calculated. The negative values of ΔH^o (ΔH^o = - 13.60 kJ mol^{-1}) and ΔG^o (ΔG^o =- 3.48kJ mol^{-1}) indicate that uranium extraction is an exothermic process and spontaneous, respectively.

The uranium content in the organic phase was stripped using 2M Na_2CO_3, A/O phase ratio 1/1 and shaking time 10 min., the stripping efficiency of 95% was achieved.

Chemists' contributions to the global approach for tackling pollution

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On 2 March 2022, the 5th UN Environment Assembly concluded with 14 resolutions to strengthen actions for nature to achieve the Sustainable Development Goals (SDGs). Most of them require contributions from Chemistry community, especially:

- Resolution L13: End Plastic Pollution – by developing a new legally binding instrument
- Resolution L14: Science Policy Panel to support the sound management of chemicals and waste to prevent pollution

This session, which is one of many activities of EuChemS on topics of global concern to which science shall proactively contribute, focuses on the L14 resolution.

Topics to be addressed:

- Setting the scene
- Chemicals Strategy for Sustainability [1]
- How to involve Chemistry community [2]
- L14 (and L13) in relation to SDGs [3]

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Adsorption of malachite green using magnetic carbonaceous materials obtained from lignocellulosic wastes

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Malachite Green (MG) is a cationic triphenylmethane dye commercialized commonly used in aquaculture as an antiprotozoal and antifungal [1]. Due to its high solubility and stability, it can cause effects on the reproductive and immune systems and has genotoxic and carcinogenic properties[2]. This study aims to value lignocellulosic wastes into high-added valued materials that could be applied in water remediation by adsorbing triphenylmethane dye, malachite green (MG), a carcinogenic and mutagenic dye that still has been used worldwide. Adsorption of MG, employing five carbonaceous materials: commercial activated carbon (CAC), charcoal (CC), hydrochar obtained from sunflower husk (HC_{SFH}), hydrochar obtained from orange residues (HC_{OR}), and biochar obtained from sunflower husk (BC_{SFH}) was compared with adsorption by corresponding magnetic carbonaceous materials: activated carbon (MAC), magnetic charcoal (MC), magnetic hydrochar from sunflower husk (MHC_{SFH}), magnetic hydrochar from the orange residue (MHC_{OR}) and magnetic biochar from sunflower husk (MBC_{SFH}). The preparation of carbonaceous materials was conducted employing thermochemical treatments such as pyrolysis and hydrothermal carbonization (HTC). Corresponding magnetic materials were further obtained by co-precipitation of magnetite nanoparticles into the carbon-based matrixes. Adsorption kinetics was performed using 30 ppm of initial concentration of MG, 120 minutes of contact time, horizontal agitation, and room temperature. Besides, kinetic fitting was done using pseudo-first-order, pseudo-second-order, and intraparticle diffusion. Chemical parameters of adsorbate (pKa, Kow) and adsorbent (chemical structure, zeta potential) were considered to study possible mechanisms of adsorption and interactions. Characterization results showed that the feedstocks have a significant carbon percentage that increased when transforming them into biochar and hydrochars. Furthermore, Fourier transform infrared spectroscopy (FTIR) confirms the presence of oxygen-containing functional groups which might be involved in the adsorption mechanisms. Kinetic studies showed that magnetic carbonaceous materials reached percent removal efficiencies ranging from 75-99% within 120 minutes of contact time and adsorption capacities from 10-30 mg g^{-1}.

Acknowledgments

This research was funded by Proyecto de investigación de Grupos de Investigación (PGI Nº 24/ZQ09),UNS.

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Creating Enzymes by Design and Evolution

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Novel enzymes can be created by computational design and directed evolution. Understanding how evolution improves designed enzymes promises invaluable insights into the fundamental principles of catalysis and design rules to create better enzymes in the future[1].

We recently employed directed evolution to improve a computationally designed enzyme catalyzing an elementary proton transfer reaction by four orders of magnitude[2]. Here, we present molecular dynamics simulations[3] revealing that evolution resulted in the closure of solvent-exposed loops and better packing of the active site. The enhanced transition state recognition gave rise to a dynamical network involving large parts of the protein (Fig. 1), which tightens the protein ensemble in the transition state and results in a negative activation heat capacity signaled by a curved activity-temperature profile. Comparable effects are observed in the evolutionary trajectory of a related designer enzyme in which directed evolution introduced a novel oxyanion stabilizing residue for catalysis[4]. Here, evolution gradually altered the protein conformational ensemble on various timescales to populate catalytically superior states[5]. Transition-state stabilization was perfected by evolutionary fine-tuning of extended backbone conformational changes and meticulous organization of the catalytic residues.

Our results have implications for understanding enzyme evolution and the role of allosteric mutations, and suggest that selectively targeting conformational dynamics by design and evolution will expedite the creation of new enzymes.

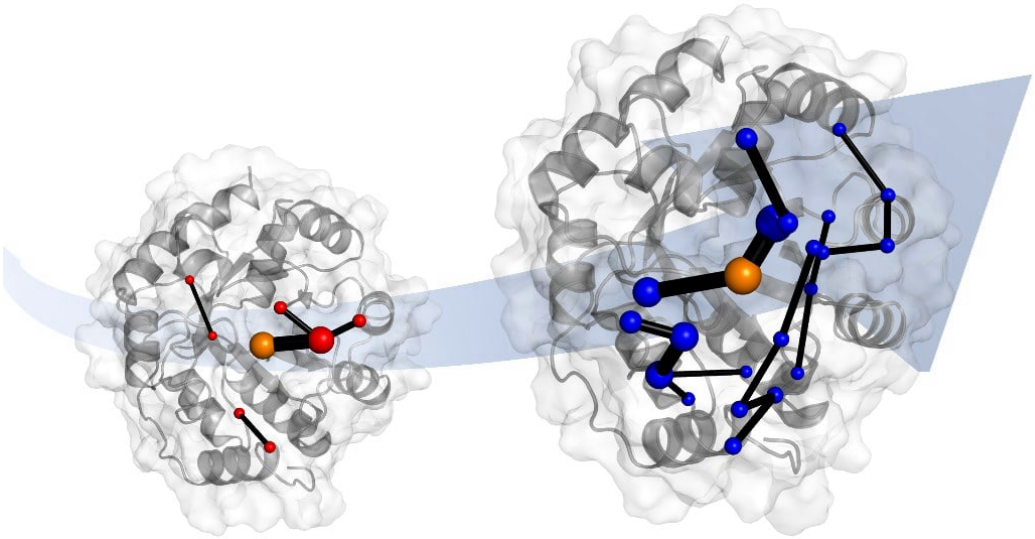

Fig 1: Emergence of dynamical networks during the evolution of a designer enzyme.

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Research Data Management - Time to say goodbye to the analog lab book

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The vision of NFDI4Chem is the digitalization of all key steps in chemical research. NFDI4Chem supports scientists in their efforts to collect, store, process, analyze, disclose and re-use research data. NFDI4Chem provides measures to promote Open Science and research data management in agreement with the FAIR data principles and hereby serves the community with a holistic concept for access to research data. Good research data management (RDM) requires a constant endeavour of the researchers but – first and foremost – user-friendly infrastructure and well accepted standards need to be developed for the researchers. The national research data infrastructure initiative for chemistry in Germany NFDI4Chem sets out to embrace the challenge of creating a general research data management portal and hereby connecting already existing infrastructure as well as to foster the cultural change in chemistry towards digitalization by developing general minimum information standards for all methods used and teaching RDM principles to the community. In order to serve the needs of the chemical community at its best, NFDI4Chem accomplishes regular community surveys. Today's existing data and the upcoming data are too valuable to be preserved on CDs in archives. Only when they are stored in a machine-readable way, can we harness them scientifically. With the FAIR Data Principles, basic requirements were formulated for making data **findable**, **accessible**, **interoperable**, and **re-usable** in the scientific process. **Findable** denotes that data need a globally unique and eternally persistent identifier with rich metadata and that the data are registered in a searchable resource. Logically, **accessible** implies not only that the stored data should be publicly available but, very importantly, also that they should be stored in open, non-proprietary formats where possible. **Interoperable** is a less vivid term, but it is not less important: the (meta)data should use a formal, generally shared, and broadly applicable vocabulary to be understandable. **Re-usable** is key for the next generations of scientists: (meta)data should have a clear data usage license with a transparent provenance and meet domain-relevant community standards. In the initial phase, NFDI4Chem focuses on data related to molecules and reactions including data for their experimental and theoretical characterization. In parallel, the collaboration with scientifically close consortia for other disciplines is sought to obtain a seamless RDM landscape for all scientists. For the first time, GDCh together with other partners within the consortium have resolved to issue a prize for FAIR Data management and practice within chemistry research dubbed FAIR4Chem Award that has been awarded during the 25^{t}th Jubilee celebration of the JungChemikerForum Spring Symposium 2022 in Hannover.

First Synthesis of the Inherently Chiral *Equatorial*$_{face}$ and *Trans*-4' Bisadducts of Azafullerene $C_{59}N$ Utilizing the Tether-Directed Remote Functionalization Approach

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Heterofullerenes are a class of compounds in which carbon atoms of the fullerene cage have been replaced by heteroatoms. Aza[60]fullerene $(C_{59}N)_2$ is a heterofullerene in which one carbon atom of the fullerene cage has been replaced by a nitrogen atom. Aza[60]fullerene is the only stable heterofullerene that can be synthesized in macroscopic quantities and exists in a dimeric form.

In this work, the *equatorial*$_{face}$ [1] and *trans*-4′ [2] bisadducts were prepared, for the first time, by employing *cyclo*-[2]-octylmalonate and *cyclo*-[2]-dodecylmalonate as tethers in a Mannich-type reaction followed by an intramolecular Bingel cyclopropanation. The addition pattern of the newly formed bisadducts was revealed by X-ray crystallography.

Examination of the optical properties of the *equatorial*$_{face}$ bisadduct showed the evolution of new absorption bands, which can be used as signatures for the characterization of *equatorial*$_{face}$ bisadducts of $C_{59}N$. Moreover, redox assays showed that the LUMO level of the *equatorial*$_{face}$ bisadduct was increased compared to that of the parent $(C_{59}N)_2$ [1].

The *trans*-4′ bisadduct was subjected to enantiomeric resolution by chiral HPLC, unveiling two distinct enantiomers. The mirror-image relation of the two enantiomers was probed by circular dichroism spectroscopy and demonstrated the inherently chiral nature of the *trans*-4′ bisadduct. The UV-Vis absorption spectra and the electrochemical data acquired for the *trans*-4′ bisadduct suggest that the addition pattern has a reflection in the light-harvesting and redox properties of the bisadduct, as compared to the *equatorial*$_{face}$ pattern [2].

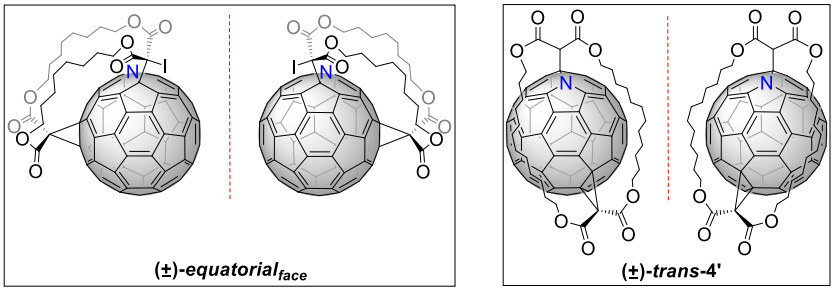

Figure 1: The inherently chiral *equatorial*$_{face}$ and *trans*-4' bisadducts of azafullerene $C_{59}N$ shown as pairs of their enantiomers.

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SYNTHESIS OF TYPE I [3:3] HEXAKIS ADDUCTS OF C_{60} AS BUILDING BLOCKS FOR THE CONSTRUCTION OF A DYNAMIC COVALENT MOLECULAR CUBE

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The design and synthesis of type I [3:3] hexakis adducts of C_{60} targeting the construction of a giant dynamic covalent molecular cubic structure, is presented. More specifically, these fullerene derivatives will be employed as the vertices of the cube while phenyl diboronic acid spacers will represent its edges. Boronic acid esterification will be used to connect the catechol moieties with the boronic acid spacers in order to link the vertices of the cube with its edges by employing Dynamic Covalent Chemistry (DC_vC).

Up to date, only two molecular cubes have been synthesized using DC_vC. The first was prepared by Warmuth and co-workers [1] and was constructed through the imine bond formation reaction between eight equivalents of chiral trialkoxy-triformyl*cyclo*benzylene serving as the cube vertices and twelve equivalents of 1,4-phenylenediamine serving as its edges. The second one was prepared by Beuerle and co-workers [2] and resulted from the dynamic boronic acid esterification reaction between eight equivalents of TBTQ used as the cube vertices and twelve equivalents of 1,4-phenylene diboronic acid used as its edges.

In the present work, type I [3:3] hexakis adducts of C_{60} were prepared consisting of *cyclo*-monomalonate ester addends occupying three consecutive *equatorial* positions of the fullerene core. The remaining three *equatorial* positions are functionalized by a *cyclo*-[3]-octylmalonate ester macrocycle. The monomalonate ester addends are equipped with triple bonds to provide rigidity into their structure and bear catechol moieties as terminal functional groups which will serve as the connection points between the cube vertices and its edges. Similarly, the corresponding *cyclo*-monomalonate ester containing saturated alkyl spacers was synthesized. The reason for synthesizing a less rigid addend molecule is to allow for the correction of any errors occurring during the linkage of the reactants in the reaction connecting the corners of the cube with its edges. 1,4-Phenylene diboronic acid moieties were chosen to serve as the edges of the cube due to their linear geometry, rigidity and their capability of reacting with catechol moieties under DC_vC conditions. All synthetic efforts for the preparation of the aforementioned type I [3:3] hexakis adducts of C_{60} will be presented.

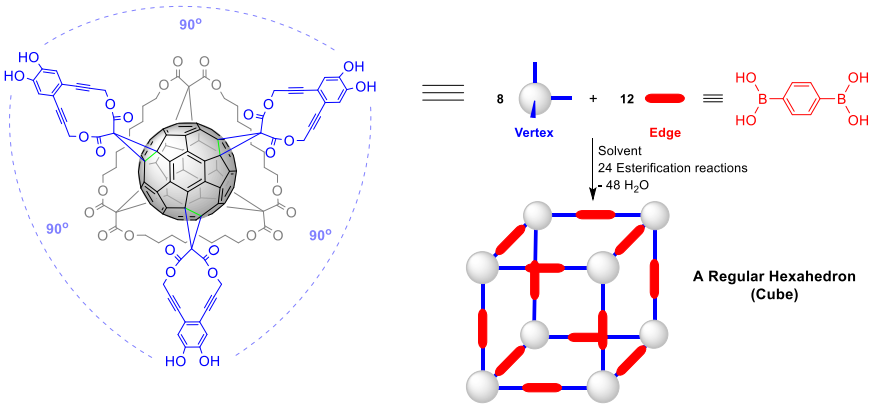

Figure. Construction of a dynamic covalent molecular cube employing type I [3:3] hexakis adducts of C_{60}.

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Trace metal detection in polymers with oxygen bomb combustion and ICP-MS

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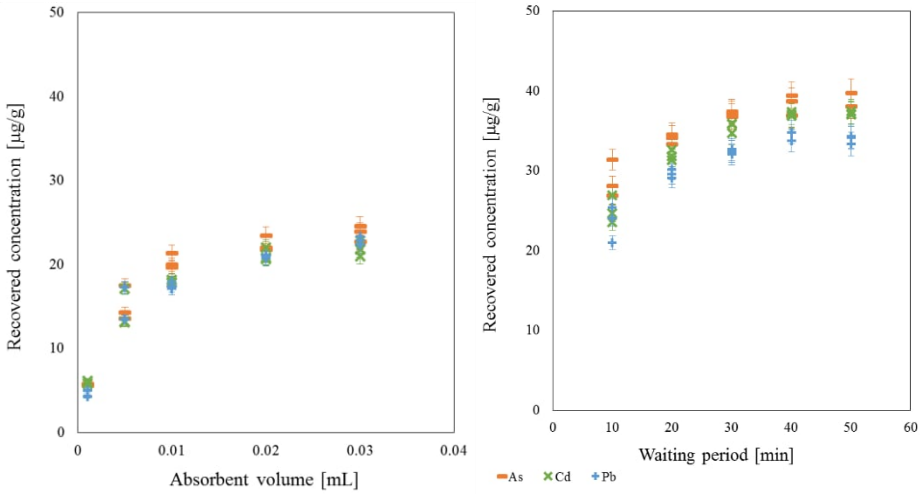
After recommendation in the European and United States Pharmacopoeias, ICP-MS has been frequently applied for detection of inorganic impurities in active pharmaceutical ingredients. In medical devices on the other hand, these impurities have so far been neglected or determined with extraction followed by a non-selective heavy metal limit test. Polymers are a ubiquitous material in medicine technology and are used for a variety of applications from implantable devices to storage containers. Inorganic impurities might be introduced as catalysts or wear metals from machinery. This study is therefore aimed at developing a sample preparation procedure for polymer medical devices and subsequent ICP-MS analysis. An intensified and accelerated exhaustive extraction in accordance with DIN EN ISO 10993-12 followed by ICP-MS performed in this study demonstrated that only a fractional amount of As, Cd and Pb could be extracted from doped polymer matrices. They were additionally not always primarily extracted within the first days of the exhaustive extraction. Consequently, the extraction experiment did not allow for an estimation of total impurity content and pointed towards the possibility of impurity mobilization on prolonged timescales. To avoid false negative findings for extractable impurities during short term extraction experiments, a method for detection of absolute trace metal content is preferable. This might be achieved by in-situ methods like LA-ICP-MS or XRF. These however require certified reference materials in the same matrix and thickness which are not readily available.

As an alternative, this study developed an oxygen bomb combustion method for the decomposition of select polymers and subsequent measurement of inorganic impurities with ICP-MS, namely As, Cd and Pb. Crucial parameters for maximizing recovery of As, Cd and Pb after oxygen bomb combustion were determined during systematic trials using spiked oil samples. The volume of liquid for analyte absorption and the waiting period between combustion under pressure and depressurization of the oxygen bomb were found to have significant influence on the recoveries of As, Cd and Pb. Recoveries of 75 to 86% from the certified polyethylene reference material ERM-EC681m were achieved when conducting the combustion with 2% nitric acid as an absorbent liquid, using between 20 and 30 mL of absorbent and containing the oxygen bomb under pressure for a minimum of 40 minutes after combustion. Te, In and Bi were applied as internals standards for As, Cd and Pb respectively during ICP-MS measurement. In comparison to pXRF as an in-situ method, the oxygen bomb combustion method has 100 to 1000 times smaller detection limits. Unlike pXRF, the oxygen bomb combustion method is not limited by sample size and shape, provided the sample can be cut up into representative pieces of less than 1 g in weight.



Thanks to SAS hagmann GmbH & Co.KG and Geowissenschaftliches Zentrum, Georg – August – Universität, Göttingen for supervision and support.

Is Vibrational Strong Coupling acting by modifying polarity?

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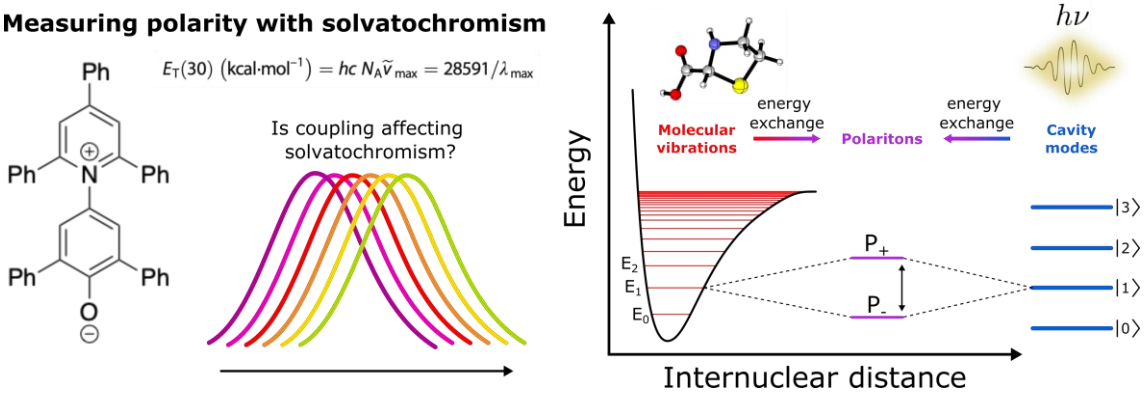
When a molecule is placed inside an optical cavity and resonance conditions are met, vibrational excitation and cavity photons strongly couple to form hybrid light-matter states called polaritons. Vibrational Strong Coupling (VSC) is a new and fast-developing field in the recent years, and its experimental results challenge our understanding of even simple chemical systems. The coupling of reactant or solvent modes have been shown to modify reaction kinetics and even chemo- and stereoselectivity, although the detailed mechanism remains unknown [1,2]. One possible factor that might at least partially contribute to the modified properties is the change of polarity of the reaction medium, as some effects were observed by solely coupling the solvent [3,4]. This study attempts to rationalize the cavity-induced changes in reactivity by comparing the $E_T(30)$ polarity parameter for strongly coupled and uncoupled solvents. Emphasis is put on solvents already used in the published works on VSC. The results may help to reinforce and complement this not yet well understood phenomenon.



Changes in polarity of a medium can be probed and measured using solvatochromic properties of Reichardt's dye (left). If VSC induces polarity and/or solvation changes, the absorption maximum should shift. Those changes can be compared through the $E_T(30)$ parameter for various solvents and between strongly coupled and uncoupled systems.

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The extraction benefits: rice bran *(oryza sativa.)* On human health

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Abstract

Rice is the seed of the monocot plants Oryza sativa (Asian rice) or Oryza glaberrima (African rice). Bran of rice which is referred to as a waste product of rice processing is richer in nutrients than the rice itself. Rice bran is a by-product of the rice milling process. For processing rice as a staple food, the machine/material used could be a sophisticated/modern or a manual/local machine/instrument. The processes followed during the processing of rice as a staple food are Cleaning, hulling, milling, polishing, grading, sorting, and packing. It contains a high level of dietary fibers such as beta-glucan, pectin, gum, and antioxidants that has beneficial effects on human health. A major rice bran fraction contains 12%-13% oil and highly unsaponifiable components (4.3%). This fraction contains tocotrienols (a form of vitamin E), gamma-oryzanol, and beta-sitosterol; all of these constituents contribute to the lowering of the plasma levels of the various parameters of the lipid profile. Rice bran also contains a high level of dietary fibers (beta-glucan, pectin, and gum). Rice bran oil is recommended for use as edible oil other than using those commercially available market vegetable oils whose concentration of saturated fatty acids is high.

Bran of rice itself is recommended for use during the preparation of feed for cattle, and other animal feeds.

My appreciation goes to Mr Oluwatosin Ale, Mr Adeyemi Olugbenga, Mr Adegboyega Dayo, and to all the people who created such a good atmosphere in the Department of Pharmaceutical Chemistry Laboratory, University of Ibadan and who spent countless hours in the laboratory for sacrificing their time in making sure the project was a success. Thank you and best of luck in your future endeavours.

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Quantitative determination of caffeine in supplement herbal product by LC-MS/MS

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Food supplements are a category of products considered safe and therefore commonly used by different types of consumers without any particular attention or precaution.

Coffea Arabica, guarana, green tea are usually used in natural supplements to reduce body weight or as energizing. The principal active compound present in these herbal plants is the caffeine, an active alkaloid with great health benefits, but able to produce episodes of anxiety and blood pressure jumps when high doses are exceeded (400mg/day) [1].

The aim of this work was to develop a LC-MS/MS method able to quantify the caffeine in different supplement herbal products promoting weight-loss, energizing or useful to counteract erectile dysfunction.

Caffeine was detected in positive electrospray ionization (ESI) mode and multiple reaction monitoring (MRM) acquisition. In table 1 the ionization mass parameters are reported.

LC-MS/MS method performance was evaluated taking in account the following parameters: linearity, recovery, repeatability by using negative samples fortified with different levels of caffeine. Subsequently samples purchased online or directly in local supermarkets were analyzed to evaluate the levels of caffeine.

Analyte	MW (g/mol)	Polarity	Q1(m/z) [M + H]+	Q3 (m/z)	DP (V)	EP (V)	CE (V)	CXP (V)
Caffeine	194.19	positive	195.1	138 110.1 83	63	7	26 32 38	13 12 10

Table 1: Multiple Reaction Monitoring (MRM) transitions and optimized MS parameters for caffeine: collision energy (CE), decluster potential (DP), entrance potential (EP), and collision exit potential (CXP)

The HPLC-MS/MS method required minimal sample preparation and good performances were obtained. R2 was 0.999 within the range of 10–300 ppb. Repeatability expressed as relative standard deviation (RSD %) at the three fortification levels (50-100-300 ppb) was lower than 6%. Recovery was estimated from the samples at the three spiked concentrations used for repeatability and ranged between 98 and 101%.

Caffeine was found in 22 out of 91 samples analyzed, at levels ranging from 0.003 to 322.23 mg per 500 mg of supplement. In 5 of these 22 products, caffeine was not declared on the label and it was detected in a range of 0.003-0.500 mg per 500mg of supplement.

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A Strategy for Engineering High Photolysis Efficiency of Photocleavable Protecting Groups Through Cation Stabilization

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Abstract

Photolabile protecting groups (PPGs) enable the precise activation of molecular function with light in many research areas, such as photopharmacology, where remote spatiotemporal control over the release of a molecule is needed. The design and application of PPGs in recent years has particularly focused on the development of molecules with high molar absorptivity at long irradiation wavelengths. However, a crucial parameter, which is pivotal to the efficiency of uncaging and which has until now proven highly challenging to improve, is the photolysis quantum yield (QY). Here, we describe a novel and general approach to greatly increase the photolysis QY of heterolytic PPGs through stabilization of an intermediate chromophore cation. When applied to coumarin PPGs, our strategy resulted in systems possessing an *up to 35-fold increase in QY* and *a convenient fluorescent readout during their uncaging*, all while requiring the same number of synthetic steps for their preparation as the usual coumarin systems. We demonstrate that the same QY-engineering strategy applies to different photolysis payloads and even different classes of PPGs. Furthermore, analysis of the DFT-calculated energy barriers in the first singlet excited state have revealed valuable insights into the important factors that determine photolysis efficiency. The strategy reported herein will enable the development of efficient PPGs tailored for many applications.

Synthesis and characterization of NIR chromophores for plasmonic nanomaterials

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Near infrared (NIR) compounds have gained remarkable importance as active materials in the field of biological application. NIR compounds are suitable candidates for the study of biological phenomena, since they absorb and emit in the biological window (from 700 nm to 1870 nm), where body tissues are transparent, and for this reason they can be applied as fluorescent bio-probes [1]. Polymethine cyanine dyes have been widely used in optical bioimaging. The main problem with these compounds is that they are characterized by a low fluorescence quantum yield, which limits their applicability. In this work, a novel approach based on Plasmon-Enhanced-Fluorescence (PEF) effect was developed. An organic-inorganic hybrid material was created which enhances the fluorescence of these dyes by exploiting the optical properties of the plasmonic nanostructures. From the interaction of the fluorescence of the cyanine dye and the Local Surface Plasmon Resonance (LSPR) of the metal surface, a PEF effect should be observed [2].

The project focuses on the synthesis of cyanine-based dyes designed to be potentially grafted onto the surface of plasmonic nanomaterials. Heptamethine cyanines were functionalized with a terminal disulfide in the central core to covalently anchor the dye to the metal surface. The cyanine derivatives depicted in Figure 1 were synthesized and their optical properties studied by absorbance and fluorescence analysis.

By varying the nature of the heteroatom in the part of the cyanine chain, it is possible to develop dyes with emission and absorbance at different energies. The advantage of using the nitrogen atom as a link between the cyanine and the alkyl chain is to gain large Stokes shift values. However, the limitation is due to the shift of the emission peak from the NIR-I to the UV-VIS region. To obtain an emission at lower energies, nitrogen atom can be acetylated or replaced with a more electronegative atom (Figure 1). Therefore, by inserting a sulphur atom, a shift of the emission in the NIR-I region is observed.

The hybridization of these dyes with nano plasmonic structures (AuNPs and AgNPs) was explored by using a simple covalent approach. The length of the spacer between the fluorophore and the linker was varied to study the efficiency of the PEF effect.

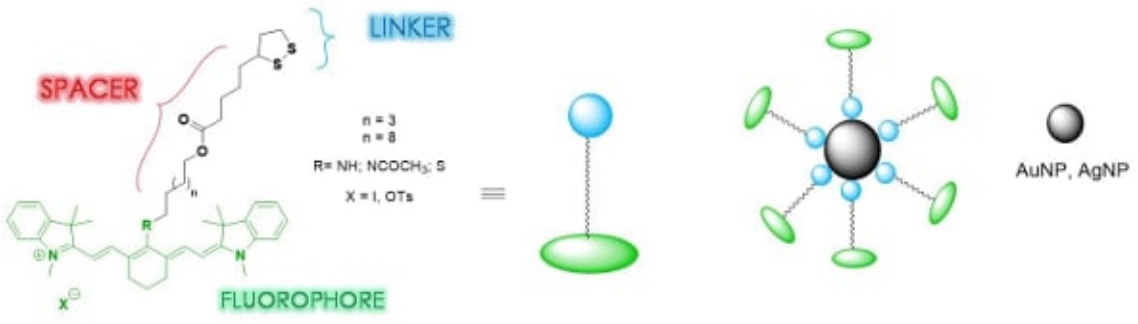

Figure 1: Structure of heptamethine cyanines with different spacers for functionalization of plasmonic nanoparticles.

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Preparation and characterization of a zeaxanthin loading nanoemulsion system for increased bioaccessibility

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Zeaxanthin, together with lutein, are widely known as the macular carotenoids, due to their accumulation in the human retina. Zeaxanthin is an important contributor to eye and brain health and function but its bioaccessibility is low and is influenced by many host or dietary factors. The lipid components in food are essential for the absorption of carotenoids and can modulate their bioaccessibility, depending on the concentration, unsaturation degree and chain length [1, 2]. The aim of our work was to develop nanoemulsions containing zeaxanthin (Zea) and zeaxanthin dipalmitate (ZeaDP) with oils having different composition of fatty acids (ratio between saturated and unsaturated fatty acids, medium or long chain fatty acids) and to examine their effect on the bioaccessibility of carotenoids.

Zea and ZeaDP were obtained at a purity of 95%, from plant material by solvent extraction and purification on column and thin layer chromatography. Five vegetable oils (coconut MCT, olive, sunflower, linseed and palm oils) and one animal fat (cream) were characterized in terms of fatty acids and carotenoid composition by GC-MS and C30-HPLC-PDA. Zea and ZeaDP oil in water (O/W; 1:9 v/v) nanoemulsions doped with carotenoids (0.01 mg/ml in the final emulsion) were obtained by probe ultrasonic emulsification, in the presence of emulsifier at 1 % (Tween 20 and Tween 80). Very good incorporation yield of carotenoids in nanoemulsions were found for liquid vegetal oils (up to 98%). The average hydrodynamic diameter was variable, depending on the type of oil (chain length, unsaturation degree) but lower than 100 nm. The polydispersity index was less than 0.3 and the surface was negatively charged (zeta potential). The emulsions obtained with solid fats (palm oil and cream) had diameters (100-250 nm) and polydispersity indices much higher than those obtained with liquid oils. Nanoemulsions with ZeaDP had a larger diameter than those with free Zea, regardless of the type of fat used. Smaller mean diameters were obtained when Tween 80 was used as an emulsifier, compared to Tween 20. The particles were characterized by Scanning Electron Microscopy. Preliminary test with selected samples (MCT and alive oil), using a standardized protocol [3] showed a significantly higher bioaccessibility of zeaxanthin from nanoemulsions compared with non-emulsified samples.

This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS - UEFISCDI, project number PN-III-P4-ID-PCE-2020-1172, number 243/2021 within PNCDI III.

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Structure and Dynamic Properties of a Glycerol–Betaine Deep Eutectic Solvent: When Does a DES Become an Aqueous Solution?

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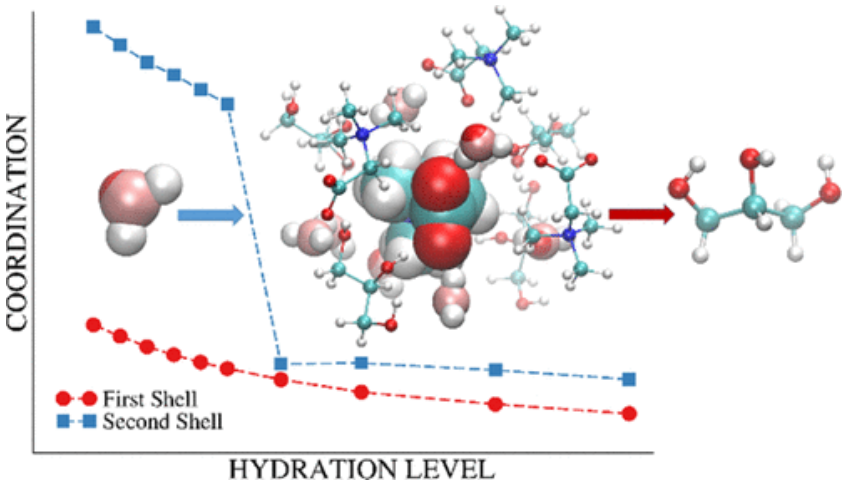
Deep eutectic solvents (DESs) are an emerging class of green solvents with a wide spectrum of potential applications whose properties may be further tailored through the addition of water. We study, through molecular dynamics, the influence of water on the properties of a betaine-glycerol-water (B:G:W) DES (1:2:ζ; ζ = 0 to 100), aiming at getting insight into the structural and dynamic crossover between a DES and an aqueous solution. The density, shear viscosity, and diffusion coefficients are found to exhibit a non-linear dependence of ζ, similar to that observed for the solvation layers' composition. Each Gly and Bet are replaced, respectively, by ∼3 and ∼5 water molecules, with the highest rates of depletion being found for Gly around Bet and Gly around Gly[1]. Above ζ = 7 (70 mol %; 29.5 wt %)[1], a major structural transformation occurs, with the complete disruption of the second Bet-Gly solvation layer and the formation of a new second layer at a shorter distance, accompanied by a sudden change in the rate of increase of the components' diffusion. Nonetheless, opposite to other DES, our results indicate a smooth crossover between a DES and an aqueous solution.



A.P. received financial support from FCT through IF/01146/ 2015. This work has received funding from the ERC-2016- CoG 725034 and was supported by the Associate Laboratory for Green Chemistry (LAQV) financed by national funds from FCT/MCTES (UIDB/50006/2020). N.G. acknowledges financial support from Fundação para a Ciência e a Tecnologia (FCT) of Portugal (CEEC/2018). N.G. acknowledges support from UIDB/04046/2020 and UIDP/04046/2020 centre grants from FCT, Portugal (to BioISI).

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New silver(I) coordination polymers: assembly, structures and volatile iodine uptake

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In recent years, coordination polymers (CPs) and metal-organic frameworks (MOFs) have become an exciting class of coordination compounds due to their unique structural features and remarkable functional properties, including luminescent, catalytic, sensing, conductive, and adsorptive behavior [1,2] In this context, some amorphous polymers have been developed for the uptake of iodine since they usually possess large specific surface areas, however, an irregular pore structure and random distribution of adsorption sites are unfavoured for the fast uptake of iodine [3]. Following our general research line on the assembly of silver(I) coordination polymers, we describe herein the synthesis of new silver-organic networks, namely 2D and 3D coordination polymers derived from 1,3,5-triaza-7-phosphaadamantane (PTA) and dicyanamide (dca) or cyanide ligands. These new compounds were characterized by FTIR, TGA, singe-crystal and powder X-ray diffraction, and elemental analysis. Besides, selected compounds show a potential for fast volatile iodine uptake. The presentation will highlight the synthesis, structural traits, and potential applications of the present series of silver(I) coordination polymers.



We thank the National Science Center (Grant No. 2019/35/D/ST5/01155, Poland) for financial support. AMK acknowledges the FCT (PTDC/QUI-QIN/29697/2017, LA/P/0056/2020, UIDB/00100/2020, Portugal).

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In vitro bioaccessibility of minerals from brewers spent cereals enriched products

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In recent years many studies have focused on proving that brewers spent grain, the major by-product generated by the brewing industry, represents a rich source of bioactive compounds (fiber, proteins, lipids, minerals, vitamins, phenols), which remain unexploited in the brewing processes and needs to be further integrated in the human nutrition [1]. Considering the increasing interest in finding new unconventional sources of functional ingredients, the brewers spent grain flour resulted from four different types of beer were evaluated for their potential to improve the nutritional value of food products. In this sense, the main focus of this research was to evaluate the mineral bioaccessibility in crackers enriched with different spent cereals, using in vitro static systems that simulate digestive processes.

Sample in vitro digestibility was assessed by the standardized static in vitro digestion method suitable for food (COST INFOGEST network) [2]. Four steps were followed: the oral phase, mixing the sample and simulate salivary fluid with amylase at pH 7 for 2 min; the gastric phase, mixing the oral bolus and simulate gastric fluid with pepsin at pH 3 for 2 h; the intestinal phase, mixing the gastric chyme and simulate intestinal fluid with enzymes at pH 7 for 2 h; centrifuging at 4500 rpm for 30 min and filtrating through a 1 µm glass-fiber membrane [3]. Analysis of Fe, Cu, Zn, Ca, Mg, Na and K were performed before and after gastrointestinal digestion using 5300 Optima DV (Perkin–Elmer, Waltham, MA, USA) Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES), while Co, Cr, Mn, Ni, Ba, Sr and Rb with ELAN DRC II (Perkin–Elmer, Waltham, MA, USA) Inductively Coupled Plasma Quadrupole Mass Spectrometer (ICP-MS).

Minerals have various important functions in the human body, from structural to metabolic point of view. Furthermore, due to the existence of some antinutritional factors, responsible for lowering the bioaccessibility of these minerals, it is essential to study their absorption by the human body [3]. According to the obtained results, the replacement of 20% of refined wheat flour with brewing spent cereals was a good alternative to enrich the final products with minerals. Also, compared with the control crackers, the addition different brewers spent cereals flour in the dough allowed a greater accessibility of Na, P, K, Ca, Mg, Fe, Zn and Mn for absorption in the body, highlighting the sustainability of using this by-product as a source of biologically active compounds.

Acknowledgement: This work was supported by a grant of Ministry of Research and Innovation, CNCS - UEFISCDI, project number PN-III-P2-2.1-PED-2019-3622, within PNCDI III.

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Andrographolide Encapsulation in Metal-organic Frameworks (MOFs) as a Drug Delivery System for Cancer applications

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Cancer is one of the main causes of death in the world and its diversity and complexity involves a variety of cell types, physiological distinction, and extracellular matrices that limit therapeutic efficacy. Cancer tissues are marked by an acidic environment concerning the physiological tissues of the body [1]. Although various anticancer drugs are strategically designed, these molecules have a very large particle size, making the metabolism unstable and insoluble which hinders the efficiency to attack cancer cells [2].

Furthermore, most of these agents are highly toxic and their administration leads to serious side effects that could lead to a significant destruction of normal cells along with cancer cells. Therefore, it is of great interest to design a drug delivery system (DDS) that is efficient in achieving effective cancer therapy [3].

Metal-organic frameworks (MOFs), also known as porous coordination polymers (PCPs), are a unique class of hybrid solids based on metals and organic ligands that have attracted a lot of attention due to their physical/chemical properties [4]. These compounds are a large class of crystalline materials, with high porosity, adjustable pore size, and high surface area [5]. These properties are used in a variety of applications including gas storage and separation, heterogeneous catalysis, medical imaging, drug delivery, and light-harvesting, among others.

In this study, two metal-organic frameworks (MOFs), MIL-53(Al) and ZIF-8 were synthesized and used as carriers for Andrographolide (ADG) loading. This encapsulation was carried out by high-pressure (100 bar) contact. This methodology is not only environment-friendly but also energy/time-saving and gives rise to ADG-MOFs with physical features equivalent to those of materials obtained by common liquid phase encapsulation processes. High pressures favor the diffusion of the drug into the material and therefore the use of any solvent is avoided. The MOFs and designed drug delivery systems were then characterized through transmission electron microscope, X-ray diffraction, thermogravimetry analysis, and Fourier transform infrared. The amount of encapsulated ADG was calculated using thermogravimetric analysis. The highest encapsulation value for ADG (20 %) was obtained with MIL-53(Al). The dissolution profile of ADG in MIL-53(Al) in PBS (pH = 7.4) was carried out showing that 96% of the drug was released after 75 h.

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Organic wine – microelements content dependence on the bentonite used

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As a general rule, to make organic wine, the fining agents need to be certified organic, according to Amended EU Regulation No. 848/2018 on authorized oenological practices and treatments in organic winemaking: organic egg whites are one option and bentonite clay or diatomaceous earth are the other option. Separation is a permitted form of processing, but the separation must be entirely physical and mechanical. The most serious problem is that wine treatment with bentonites usually increase concentrations of microelements and this process depends mostly on the type and amount of bentonites used. In the present study as a first step analytical procedure was developed for the determination of very low concentrations of micro elements and U in wine. This procedure includes application of newly synthesized ion imprinted polymer (4-(2-Pyridylazo) resorcinol (PAR, as Na salt as ligand.). The sorbent was synthesized for U determination and template species was complex of UO22- with PAR. Taking into account that PAR forms complexes with different metals ions additional experiments were performed to test extraction efficiency toward other elements. for at least 10 times enrichment factor. Experiments were performed in order to define optimal conditions for quantitative extraction of microelements in the presence of wine matrix containing 10-15% ethanol. Results showed that in addition wine organic compounds strongly influenced the degree of extraction – that is way XAD-2 resin was applied as a preliminary treatment of wine for removal of wine organic matrix. The degree of sorption of most toxic elements such as Cd, Ni, Pb, U and in addition important for wine health elements such as Fe, Cu, and Zn was in the range 85 - 95%. Elution for all studied elements was >99% using 2 mol/L HCl in this way suitable for measurement by ICP-OES. The developed analytical procedure was validated by added found method. Determination limit and relative standard deviation fulfil the requirements for wine analysis for toxic elements defined by OIV.

As a second step systematic study was conducted with various types of bentonites, approved according to the Amended EU Regulation No. 848/2018 with model solutions, based on tartaric acid and with real wine samples, produced according to authorized oenological practices. Different types of wines – white, rose and white were tested. Results obtained undoubtedly showed increased concentrations of micro elements at different concentration levels. The increase depends mstly on the type of bentonite and on the second place on the type of wine. Discussion on the ranges of microelement content will be presented aiming to propose a kind of prognosis for most suitable bentonite and treatment for different element and different wines.

Acknowledgements: The study was funded by Ministry of Education and Science of Bulgaria under the National Research Program 391 "Healthy Foods for a Strong Bioeconomy and Quality of Life", approved by DCM № 392 577/17.08.2018 and by Bulgarian scientific fund, Grant DN19/10 "Smart speciation".

Synthesis of novel aminoadamantane conjugates based on substituted cinnamic acids as potential antioxidants

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Influenza affects millions of people each year, worldwide. Especially, influenza A viruses have the ability to undergo changes by the mechanisms of antigenic drift and shift, and thus to develop a danger of future influenza A pandemics. Currently, the adamantanes (amantadine and rimantadine) representing a class of antivirals (M2 blockers) are used for the treatment of influenza [1]. Various studies [2] confirm the positive synergistic role of administration of antioxidants in combination with approved antiviral drugs against severe influenza-associated complications. Therefore, many efforts are made in a design of new anti-flu agents.

Our aim is focused on obtaining of new amides (using TBTU peptide method) by modifying the amino group of adamantanes with antioxidant molecules such as cinnamic acids. The chemical structures of the synthesized hybrids were confirmed by means of UV, IR, ^{1}H NMR, ^{13}C NMR, and HRMS. The evaluation of their radical scavenging activities against 1,1-diphenyl-2-picrylhydrazyl (DPPH$^{\bullet}$), hydroxyl (OH$^{\bullet}$) and superoxide ($O2^{\bullet-}$) radicals *is in progress*.

Acknowledgements: Supported by Grant KP-06-Russia-7/ 27.09.2019 from the National Science Fund, Bulgaria.

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Chemical and structural characterization of dioxane lignin extract from vine pruning material – a powerful biopolymer

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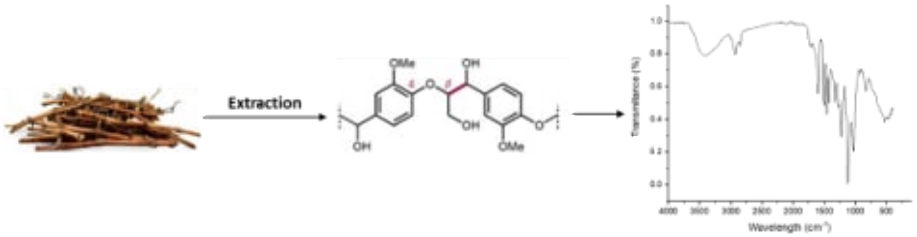
The winemaking sector represents one of the most important food industries in the world. According to the International Organization of Vine and Wine, Portugal appears as the 11th wine producing country and the 9th exporter in the world (1). As a consequence, every year millions of tons of organic wastes are produced, specially vine pruning material. These residues are left in the agriculture field used as domestic fuel due to the calorific power or burned, resulting in greenhouse gas emission and heat to the atmosphere (2). The vine pruning material corresponds to 93% of the residues generated (3), and it is an interesting lignocellulosic biomass containing a lignin content similar to grape stalks around 16-26% (4). This work, proposes the reuse of this material as a feedstock to extract lignin by mild acidolysis to avoid extensive structural lignin changes. Different pre-treatment conditions of plant material and the influence of purification method were tested to understand the impact in the final composition of the obtained lignin. Different lignin fractions were structurally characterized through ^{13}C NMR, Gel permeation chromatography (GPC) and Fourier transform infrared spectroscopy (FTIR). Structural analysis of the different lignin fractions suggests a similar composition regardless of the extraction and the purification methods, with β-*O*-4 structures content around 60 per 100 aryl units and Syringyl/Guaiacyl (S/G) ratio about 1.50. The main difference is the increase of the degree of condensation (DC) ranging from 9 to 21% for pre-treatment with ethanol/toluene and water/toluene, repectively. In the literature, it is described that this feedstock has a significant content in tannins (5). Dioxane lignin extracted with ethanol/toluene showed a higher quantity of condensed tannins around 11%; however, the results indicate that dialysis led to a decrease on the amount of condensed tannins content (around 3% for sample pre-treated with water/ethanol followed by dialysis). SGS-PAGE method allowed to verify the absence of protein in lignin pre-treated with water/ethanol. This extracted lignin can be very promising in different concepts, namely as stabilizers of pigments for biomedical and/or food applications.



Acknowledgements: We thank to FCT from a doctoral grant from (SFRH/BD/146549/2019) and the Associated Laboratory for Sustainable Chemistry, Clean Processes and Technologies LAQV-REQUIMTE through the national funds from UIDB/50006/2020 and UIDP/50006/2020. The authors also thank AgriFood XXI I&D&I project (NORTE-01-0145-FEDER-000041) cofinanced by European Regional Development Fund (ERDF), through the NORTE 2020 (Programa Operacional Regional do Norte 2014/2020).

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Controlling enzyme conformational dynamics: a key aspect in biocatalytic processes

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Initially, enzymes were understood as static (bio)chemical structures capable of accelerating chemical reactions by many orders of magnitude. Notwithstanding, after many years of research, they could be identified as dynamical entities, able to visit different thermally accessible conformations key for their catalytic function.[1] In this regard, recent advances in Molecular Dynamics simulations allowed us to better understand the importance of the conformational diversity of enzymes, harnessing this information to rationally tune them through point-mutations to explore catalytically relevant conformations.

Herein, we present our recent computational studies in two family of enzymes that show different perspectives of conformational dynamics towards their improvement in terms of catalysis. First, a set of laboratory-evolved Monoamine Oxidases (MAO-N) were studied by extensive MD simulations in combination with Markov State Models (MSM). Our simulations showed that the stabilization of closed conformations of a β-hairpin situated at *ca.* 20 Å far from the active site can be related to improved k_{cat} values along the evolutionary pathway. [2,3] In contrast, MD simulations of a number of Imine reductases (IREDs), showed that conformational diversity is key for their catalytic function. MD simulations and diemensionality reduction techniques indicated that the Rossmann fold of IREDs is able to open/close and rotate, being these motions crucial for the different reaction steps.

Overall, our work demonstrates that understanding the role of conformational dynamics is essential for evolving enzymes toward efficient catalysis.

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Designing tryptophan synthases for stand-alone functionality

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Many enzyme complexes are allosterically regulated by a protein partner making them inefficient as a stand-alone catalyst. However, the use of stand-alone protein units is desirable for industrial applications. Tryptophan synthase (TrpS) is a heterodimeric enzyme complex, forming an αββα arrangement. The α-subunit (TrpA) catalyses the IGP-retroaldol cleavage into G3P and indole. In Nature, it already exists a blueprint for a stand-alone TrpA protein named BX1 from Zea Mays (ZmBX1). ZmTrpA and ZmBX1 share the ubiquitously encountered $(\beta\alpha)_8$-barrel fold and show a high sequence identity of 63.3% However, ZmBX1 exhibits high stand-alone activity whereas ZmTrpA is a poor catalyst in the absence of TrpB. Similarly, TrpA from the Last Universal Common Ancestor (LBCA TrpA) depends on LBCA TrpB for enhanced activity (sequence identity with ZmBX1 is about 45.1%). Remarkably, ZmBX1, ZmTrpA and LBCA TrpA have two loop regions that are known to be important for the catalytic activity and the allosteric activation of TrpA: loop6 (residues 174-189 for ZmBX1) and loop2 (residues 56-76). These loop regions interact with β-subunit in the wild-type dimer[1,2]. We recently generated ZmTrpA variants with moderate stand-alone activity by replacing loop6 of ZmTrpA with the corresponding loop of ZmBX1 into[3]. Herein, we use Molecular Dynamics (MD) simulations and correlation-based tools in the apo and IGP-bound states to rationalize the differences between systems and design new variants. Thus, we aim to generate new LBCA TrpA variants with stand-alone functionality and also to elucidate the changes on the allosteric regulation between both subunits through TrpS evolution. This is done by computationally reconstructing the conformational landscapes associated with different key features (i.e. loop6 closure distance, catalytic distance…), and applying the correlation-based tool SPM[4] to design new stand-alone TrpA variants. The most promising TrpA enzymes will be experimentally validated.

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Looking for echoes of the past: reconverting an hydroxynitrile lyase to an arylesterase

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Hevea brasiliensis hydroxynitrile lyase (HbHNL) catalyzes the cleavage of hydroxynitriles, whereas salicylic acid binding protein 2 (SABP2) has esterase activity. They evolved from the same esterase ancestor and share 45% amino acid sequence identity and the same Ser-His-Asp catalytic triad. To understand the differences between both enzymes to catalyze different reactions, Prof. Kauskazlas and coworkers made a set of variants by substituting active site HbHNL amino acids into the corresponding SABP2 residues. Although an increase of esterase activity (EST) and decrease of hydroxynitrile lyase activity (HNL) were expected, pure EST activity was not reached by any HbHNL variant (HbHNL-EST).[1] In this work, we focus on the identification of the missing first and second shell active site amino acids required to convert the most active HbHNL-EST variant to reach a complete esterase activity. To that end, we develop a specific protocol that allows us to locate promising candidates by means of molecular dynamics (MD) with and without the substrate (p-nitrophenyl acetate), and with the tetrahedral intermediate involved in the rate-limiting step of the reaction. For the identification of these positions we use correlation-based tools (e.g. Shortest Path Map) [2]. Our synergy with our experimental collaborators allowed us to identify new variants with a k_{cat} fold increase up to 698 in esterase activity compared to the HbHNL-EST variant of the previous work.

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Computational Exploration and Design of new Halohydrin Dehalogenase variants

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Many enzymes present in Nature could be potentially used to synthesize chemically relevant chiral intermediates for drugs. One example is the enzyme family halohydrin dehalogenases (HHDH)[1], which catalyse the enzymatic conversion of ethyl (S)-4-chloro-3-hydroxybutyrate (ECHB) into the corresponding epoxide. This enzyme in the presence of a chloride ion can also catalyse the epoxide ring opening reaction yielding an ethyl (R)-4-cyano-3-hydroxybutyrate (HN), which is a precursor of Lipitor, a drug used for lowering the levels of cholesterol in blood. Within this enzyme family, different subclasses of HHDH have been identified showing a big spectrum of beneficial properties like thermal and organic solvent stability, activity, enantioselectivity and expanded substrate scope[2].

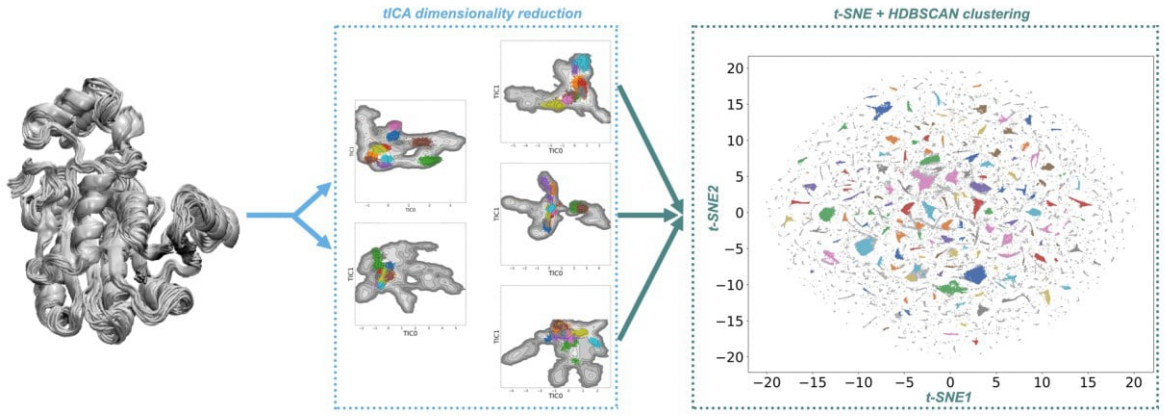

Figure 1. Computational protocol used to reconstruct the conformational landscapes of the different HHDH subclasses.

The computational exploration of the conformational landscape of HHDH can potentially reveal the key residues and conformations that grant these enzymes the properties mentioned. In this talk, Molecular Dynamics (MD) simulations coupled to machine learning and correlation-based tools are used to explore and analyze the conformations of different HHDHs subclasses [3,4]. This is coupled with the analysis of the available active site tunnels for substrate binding on each HHDH conformation, which provides key information of the protein ability to accept bulky substrates, and thus for expanding the HHDH natural substrate and reaction scope. With this knowledge, a rational *in silico* design protocol of some HHDHs was conducted to expand the range of accepted nucleophiles for epoxide ring opening reactions, avoiding non-rational and expensive directed evolution strategies.

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The study of the vacuum distillation and the production of the lubricants in the refinery of Arzew,Algeria

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The line of the vacuum distillation and the production of the basic oils is very complex. It is compounded by one unit of the vacuum distillation and five units of production with a very sensible working.In the refinery of ARZEW, there are two lines for the production of oils.After some years, it was enlarged with other units,and a good working was established,until a rate of production of 90% stable and continuous.
It is very important and it is a necessity to recuperate the used motor oils for the environmental protection and an economic obligation.
The conventional regeneration consists in a treatment with the sulfuric acid followed by a contact with active earths ,but because its capacity is poor and the rate of the acid used is high and for the environmental protection,we use the algerian bentonite,adsorption agent for the purifying of the used oils.

Key Words: Vacuum Distillation, Oils, Regeneration.

Smart natural antimicrobial nanodevice for the enhancement of pathogenic microorganism elimination

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During the last years, the indiscriminate and inappropriate use of drugs and phytosanitary products has often produced the inefficacy of the common antimicrobial treatments. One of the biggest health challenges is to avoid the so call Antimicrobial Resistance (AMR). This challenge could be approached using natural products as antimicrobial agents encapsulated into gated nanodevices. In the present work, a nanodevice consisting of mesoporous silica nanoparticles (MSNs) loaded with an essential oil component (cinnamaldehyde) and functionalised with the Epsilon-poly-L-lysine (EPL), an antimicrobial peptide (AMP), acting as a molecular gate, has been developed. In the presence of the corresponding stimuli (such as exogenous enzymes from the bacteria or fungi with proteolytic activity), the gate is "opened", and the cinnamaldehyde is released, effectively eliminating bacteria or fungi. It has been demonstrated that the new nanodevice presented here can deliver cinnamaldehyde by a bio-controlled uncapping mechanism using exogenous proteolytic enzymes from the pathogenic microorganisms *Escherichia coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*) and *Candida albicans* (*C. albicans*), improving the antimicrobial properties when compared with the free compound. This improvement of the cinnamaldehyde's antimicrobial behaviour can be related to the decrease of its volatility and increase of its local concentration when it is encapsulated inside the porous of the MSNs. In addition, antimicrobial activity evaluation of the nanodevice shows a great antimicrobial activity at low doses against pathogenic bacteria and fungi. The nanodevice presents antibacterial activity against *E. coli* (39.06 □g/mL) and *S. aureus* (9.75 □g/mL) in the treatments for 10^5 cel/mL during 24h. Moreover, results of antifungal activity against *C. albicans* show that nanodevice is capable of eliminating a concentration of 10^7 cel/mL with the dose of 19.5 □g/mL for 24h. The new smart nanodevice exhibits a great antimicrobial activity at a very low dose, with the selective release of the bioactive molecule in the presence of pathogenic microorganisms.

This research was funded by the Ministerio de Ciencia, Innovación y Universidades (Spanish Government) (projects RTI2018-100910-B-C41 and RTI2018-101599-B-C22-AR (MCUI/FEDER, EU)) and the Generalitat Valenciana (project PROMETEO 2018/024). Á.M. thanks the UPV for her PhD grant (DOCEMPR21). A.B. thanks the Ministerio de Universidades (Spanish Government) for her Beatriz Galindo contract BG20/00020.

Application of the Redox-Transmetalation Procedure to Access Divalent Lanthanide and Alkaline-Earth NHC Complexes

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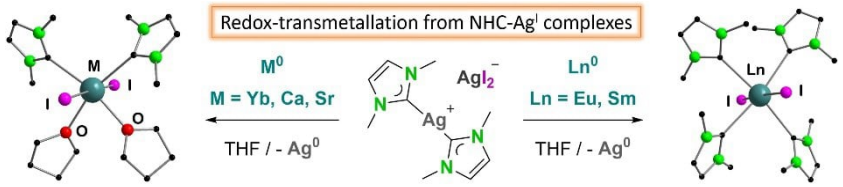
Divalent lanthanide and alkaline-earth complexes supported by N-heterocyclic carbene (NHC) ligands have been accessed by redox-transmetalation between air-stable NHC-AgI complexes and the corresponding metals.[1] By using the small ligand 1,3-dimethylimidazol-2-ylidene (IMe), two series of isostructural complexes were obtained: the tetra-NHC complexes $[LnI_2(IMe)_4]$ (Ln=Eu and Sm) and the bis-NHC complexes $[MI_2(IMe)_2(THF)_2]$ (M=Yb, Ca and Sr).[2] In the former, distortions in the NHC coordination were found to originate from intermolecular repulsions in the solid state. Application of the redox-transmetalation strategy with the bulkier 1,3-dimesitylimidazol-2-ylidene (IMes) ligand yielded $[SrI_2(IMes)(THF)_3]$, while using a similar procedure with Ca metal led to $[CaI_2(THF)_4]$ and uncoordinated IMes. DFT calculations were performed to rationalise the selective formation of the bis-NHC adduct in $[SrI_2(IMe)_2(THF)_2]$ and the tetra-NHC adduct in $[SmI_2(IMe)_4]$. Since the results in the gas phase point towards preferential formation of the tetra-NHC complexes for both metal centres, the differences between both arrangements are a result of solid-state effects such as slightly different packing forces.



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