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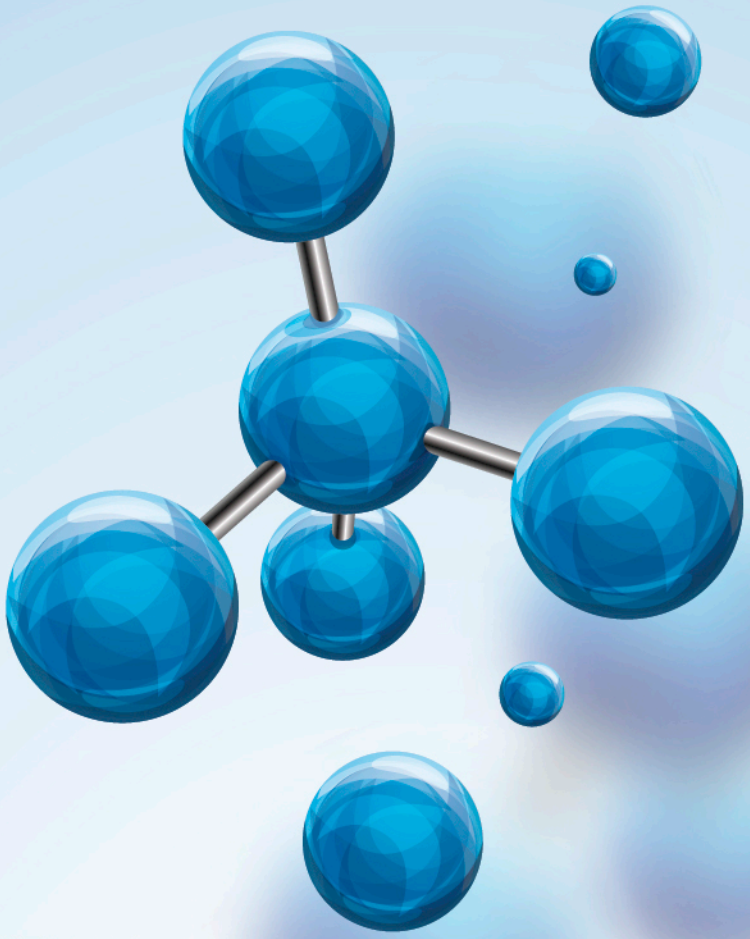

CHEMISTRY AT ULISBOA

& 2018 SUMMER SCHOOL

3rd MEETING OF THE CQUL (3ECQUL)

Book of Abstracts

27-29 JUNE 2018

Reitoria da Universidade de Lisboa

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It is a great pleasure and an honor to extend to you a warm invitation to attend the 3rd Meeting of the College of Chemistry of the University of Lisbon (3ECQUL) entitled *"Chemistry @ULisboa & 2018 Summer School"*, to be held on June 27-29, 2018. The College of Chemistry is now in cruise speed, and the 3ECQUL will show the excellence of the Chemistry developed at ULisboa and its impact on Society. The programme of this meeting comprises oral, flash and panel presentations, as well as invited presentations by renowned national and international speakers in topics of current significance in Chemistry and other sciences in which the former play an important role. In addition, this 2018 edition also includes the Summer School that hosts invited speakers and provides exceptional networking opportunities for PhD students.

We thank the Rector, Prof. António Cruz Serra, for his continuous support to the College of Chemistry and to this Conference. A special welcome word is addressed to all the participants who will be the players in this Conference, hoping that they will benefit from a very fruitful and pleasant scientific event, in a relaxed environment.

Rui Moreira and Luísa Martins
Chairs of the Organizing Committees

Armando Pombeiro
President of the Colégio de Química da Universidade de Lisboa

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PROGRAMME

Chemistry at ULisboa

June 27th	
08h30	Check-in
09h00-09h15	Opening Session **Rui Moreira (President of the Organizing Committee)** **Luísa Martins (Chair of the 2018 Summer School)**
Technology & Industry	
09h15-10h00	Plenary Lecture **Luis Oro (University of Zaragoza)**
10h00-10h20	Invited Oral Communication 1 (Academia) **Maria de Fátima Montemor (CQE-IST)**
10h20-10h50	Poster Session + *Coffee Break*
10h50-11h10	Invited Oral Communication 2 (Industry) **Rudi Oliveira (Hovione)**
11h10-12h10	Oral (15 min) & Flash (5 min) Presentations **[O] Jaime Coelho (Univ. California & iMed.ULisboa-FFUL)** **[O] Dmytro Nesterov (CQE-IST)** **[O] Ali Sen (CEF-ISA)** **[F] Elisabete Alegria (CQE-IST & ISEL)** **[F] Elisabete Silva (CQB-FCUL & CERENA-IST)** **[F] Filipa Siopa (IPCM-Sorbonne & iMed.ULisboa-FFUL)**
12h10-12h30	Invited Oral Communication 3 (Academia) **João Moura Bordado (CERENA-IST)**
Lunch	
Materials	
14h00-14h45	Plenary Lecture **Matthias Epple (University of Duisburg-Essen)**
14h45-15h05	Invited Oral Communication 1 (Academia) **Manuel Minas da Piedade (CQB-FCUL)**
15h05-16h05	Oral (15 min) & Flash (5 min) Presentations **[O] Peter Eaton (iMM-FMUL & LAQV/REQUIMTE-FCUP)** **[O] Ana C. P. Fernandes (CICECO-UAveiro & CQB-FCUL)** **[O] Kamran Mahmudov (CQE-IST)** **[F] Nuno Bandeira (ICIQ-BIST, BioISI-FCUL & CQE-IST)** **[F] Ricardo Simões (CQB/CQE-FCUL)**
16h05-16h35	Poster Session + *Coffee Break*
16h35-16h55	Invited Oral Communication 2 (Industry) **Cristina Freire (Innovcat)**
16h55-17h15	Invited Oral Communication 3 (Academia) **Carlos Henriques (CQE-IST)**

June 28th	
08h45	Check-in
Energy & Environment	
09h15-10h00	Plenary Lecture **Anna Trzeciak (University of Wrocław)**
10h00-10h20	Invited Oral Communication 1 (Academia) **Ana Viana (CQB-FCUL)**
10h20-10h50	Poster Session + *Coffee Break*
10h50-11h10	Invited Oral Communication 2 (Industry) **Eugénia Cardoso (Águas de Portugal)**
11h10-12h10	Oral (15 min) & Flash (5 min) Presentations **[O] Ana C. S. Fernandes (CQE-IST)** **[O] Virgínia Ferreira (CQE/CQB-FCUL)** **[O] Olinda Monteiro (CQE/CQB-FCUL)** **[F] Luís Frija (CQE-IST)** **[F] Luís Moreira (ISEC & CQB-FCUL)**
12h10-12h30	Invited Oral Communication 3 (Academia) **Carlos Afonso (iMed.ULisboa-FFUL)**
Lunch	
Life & Health	
14h00-14h45	Plenary Lecture **Edward Tate (Imperial College London)**
14h45-15h05	Invited Oral Communication 1 (Academia) **Maria de Jesus Perry (iMed.ULisboa-FFUL)**
15h05-16h05	Oral (15 min) & Flash (5 min) Presentations **[O] Ivo Martins (iMM-FMUL)** **[O] Hélio Faustino (iMed.ULisboa-FFUL)** **[O] Ana Melo (Univ. Pennsylvania & CQFM-IN/IBB-IST)** **[F] Ana Paula Francisco (iMed.ULisboa-FFUL)** **[F] Elisa Palma (C2TN-IST & CQE-IST)** **[F] Rita Gonçalves-Pereira (CQB/CQE-FCUL)**
16h05-16h35	Poster Session + *Coffee Break*
16h35-16h55	Invited Oral Communication 2 (Industry) **Sofia Corte-Real (TechnoPhage)**
16h55-17h15	Invited Oral Communication 3 (Academia) **Gonçalo Bernardes (University of Cambridge & iMM-FMUL)**
17h15-17h30	Closing Session **Rui Moreira (President of the Organizing Committee)** **Presidents of the Divisions of the College of Chemistry**

2018 Summer School

June 29th	
08h30	Check-in
09h00-09h15	Opening Session **Armando Pombeiro (President of the College of Chemistry)**
09h15-10h00	Lesson 1 (Entrepreneurship) **Pedro Vilarinho (HiSeedTech)**
10h00-10h30	*Coffee Break*
10h30-11h30	Lesson 2 **Lifeng Liu (International Iberian Nanotechnology Laboratory)**
11h30-12h30	Lesson 3 **Maria-Magdalena Titirici (Queen Mary University of London)**
Lunch	
14h00-14h30	Lesson 4 (Technological Tools I – Nuclear Magnetic Ressonance) **Konstantin Luzyanin (University of Liverpool)**
14h30-15h00	Lesson 5 (Technological Tools II – Mass Spectrometry) **Maria da Conceição Oliveira (CQE-IST)**
15h00-15h30	Lesson 6 (Technological Tools III – Electron Microscopy) **Isabel Nogueira (IST)**
15h30-16h00	*Coffee Break*
16h00-16h30	Lesson 7 (Technological Tools IV - BioImaging) **José Rino (iMM-FMUL)**
16h30-17h00	Lesson 8 (Technological Tools V – Computational Methods) **Rita Guedes (iMed.ULisboa-FFUL)**
17h00-17h10	Closing Session **Luísa Martins (Chair of the 2018 Summer School)**
Chill-Out	

Technology

&

Industry

T&I.PL

Mechanistic Studies on Rhodium N-Heterocyclic Carbene Catalysts

Luis A. Oro

Departamento de Química Inorgánica, Instituto de Síntesis Química y Catálisis Homogénea, Universidad de Zaragoza-CSIC, Spain

Precise determination of the mechanism of a catalytic process is essential in order to control the selectivity outcome. The catalytic activity of a set of rhodium complexes with N-heterocyclic carbene (NHC) ligands in two specific homogeneous reactions, vinyl selective H/D exchange and alkyne hydrothiolation will be presented. The high steric hindrance and powerful electron-donor capacity of the bulky NHC´s used, along with ancillary N-donor ligands, seems to be determinant to get selective transformations and to facilitate valuable information about the mechanism of the mentioned reactions[1-2].

Rhodium(III)-NHC complexes containing quinolinato or acetonitrile ligands are active and selective catalysts for the H/D exchange of aromatic α-olefins, using CD_3OD as deuterium source. Most of these complexes resulted to be selective in the vinylic-H/D exchange of styrene without the concomitant deuteration of the aromatic region, being able to deuterate the vinylic β-positions with very high selectivity. The proposed mechanism implies an initial H/D exchange, a 1,2 or 2,1 insertion of the coordinated olefin on the Rh-D bond, to give linear or branched alkyl products, followed by rotation and β-elimination. Interestingly, the steric constraints exerted by the bulky IPr NHC ligand (IPr = 1,3-bis(2,6-diisopropyl-phenyl)imidazol-2-carbene) control the rotation of the alkyl intermediate, which in turn determines the selectivity towards H/D exchange at the β-position of aromatic α-olefins.

Rhodium(I) compounds of formula $[Rh(\mu\text{-}X)(IPr)(\eta^2\text{-olefin})]_2$ (X = Cl, OH), $RhCl(IPr)(py)(\eta^2\text{-olefin})$ and $Rh(oq)(IPr)(\eta^2\text{-olefin})$ (py = pyridine, oq = quinolinolate) are very active catalysts for alkyne hydrothiolation under mild conditions, presenting high selectivity towards α-vinyl sulphides. Several intermediates relevant for the catalytic process have been detected. Most of the studied rhodium carbene catalysts have in common a mechanism that proceed via oxidative addition of the S-H bond to rhodium(I) intermediates and successive alkyne insertion into the Rh-S, or Rh-H, bond followed by reductive elimination steps.

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Luis A. Oro obtained his PhD from the University of Zaragoza in 1970. His post-doctoral studies were undertaken at Cambridge University. He has served on the faculties of the Universities of Zaragoza, Madrid Complutense and Santander. He became Full Professor of Inorganic Chemistry in Zaragoza in 1982. He has (co)authored well over 600 scientific papers and several reviews on synthesis, reaction mechanisms and homogeneous catalysis of platinum group metal complexes. He is Series Editor of "Topics in Organometallic Chemistry". He has received numerous awards and honours, and is member of several international scientific academies. He has been President of the European Association for Chemistry and Molecular Sciences (EuCheMS) (2008-11).

T&I.IOC1

Redox active metal compounds for aqueous assymetric supercapacitors

M. F. Montemor

CQE, DEQ, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049-001 Lisboa, Portugal

Supercapacitors are currently emerging as promising technologies for electrical energy storage, particularly for high power applications. Although conventional electrochemical double layer supercapacitors provide high power density and long-term stability, these devices lack energy density. Thus, new strategies for improving their energy density need to be addressed.

New functional materials tailored for enhanced energy density and new device assemblies, combining assymetric redox-active electrodes are crucial steps for implementing the next generation of redox-based supercapacitors working in aqueous environments and meeting the demands of low CO_2-based technologies.

This talk overviews the latest trends on the development of a novel generation of assymetric redox supercapacitors for energy storage applications, and highlights recent work that has been developed at CQE – Técnico/University of Lisbon.

Acknowledgments

Fundação para a Ciência e Tecnologia (FCT) for the funding under the contract UID/QUI/00100/2013 and under the contract M-ERA.NET/0004/2014.

M.F. Montemor thanks all co-workes that have contributed to this work: Tuyen Nguyen, Sónia Eugénio, M. João Carmezim, T.M. Silva, Alberto Mas, Katarzyna Siwek, Kush K. Upadhyay, Maryna Taryba, Ana Mafalda and Rodrigo Nocce.

M. F. Montemor obtained her PhD from the Technical University of Lisbon in 1995. She is Full Professor at the Department of Chemical Engineering, researcher at CQE and Vice President of Instituto Superior Técnico. M. F. Montemor is co-author of more than 200 scientific papers published in international journals and more than 300 works presented in international and national congresses. Actually her h index is 52. She is Editor of the Elsevier Journal “Applied Surface Science”. Scientific interests include the development of functional surface coatings for multipurpose applications in different fields such as biomedical, transportation and energy storage.

T&I.IOC2

Flow Chemistry – Pursuing New Opportunities

Rudi Oliveira

Hovione FarmaCiencia SA, Sete Casas, 2674-506, Loures, Portugal

Pharmaceutical manufacturing is based on three main pillars: safety, product quality and performance. Safety comes first in order to produce products with the best quality to be administered to patients in need. Performance comprises environmental considerations, productivity and adequate management of costs. To continuously improve in integrating these pillars, Hovione keeps looking for new technologies and approaches to incorporate in its DNA. Flow chemistry and continuous manufacturing is a technology and an approach that touches each of the mentioned pillars.

Miniaturization of the manufacturing allows improved and continuous control over process parameters and adds to an increased safety when working with hazardous processes. These features enable scientists to explore process conditions that are not effective or even advisable to use in batch manufacturing.

This presentation frames the application of flow chemistry in the manufacturing of pharmaceutical products, showcasing some of the opportunities that derived from the application of this technology.

Rudi Oliveira holds a degree in Pharmaceutical Sciences and a PhD in Medicinal Chemistry, with a strong component on organic chemistry. He worked as a PostDoc in Chemical Biology before joining Hovione in 2015 as a chemist in the Continuous Manufacturing group. Here he was responsible for gathering knowledge on flow chemistry and conduce process development work of continuous processes with view to industrialization. Later in the Process Chemistry Development group he contributed to the combination of traditional batch manufacturing with continuous processing. More recently, he enrolled in the R&D Products team looking for opportunities to improve and increase Hovione's product portfolio of pharmaceutical products.

T&I.IOC3

New Primary Raw Materials for the Chemical Industry

J. C. M. Bordado, R. Galhano
CERENA, Instituto Superior Técnico, Universidade de Lisboa, Lisboa, Portugal

The predicted Crude shortage after 2040 imposes a serious effort to develop new Chemical processes for the production of the Basic Chemicals and important intermediates. The industrial and technological advances achieved over the years, regarding well-being and economic stability of modern societies, depends on secure and affordable energy and commodities. A new paradigm and economic models, involving greener processes and raw materials, are vital to assure the liveability of the planet for the generations to come. Concepts such as biorefineries, circular economy, and neutral emission cycles play a vital and crucial role in the conversion of waste into valuable resources. Such processes will assist to achieve the targeted low-carbon economy, aimed by the European Commission. Presently, biomass is faced as a viable option to contribute to the development of alternative renewable resources. Wastes arising from end-of-life products and those generated by the industrial sector should also be considered. This "new" feedstock includes products containing, e.g., oils, carbohydrates, crops residues, algae, lignocellulosic feedstock/residues along with others without any value. Livestock sector can also be considered a source of raw material. Up to now, the preference has fallen mainly on lignocellulosic biomass due to its abundance. In this scenario, underpinned by a transition to renewable energy sources and materials, the development of a Technological Platform for the Production of Energy and chemicals, by upgrading wastes and biomass, is envisaged. Such platform should integrate the circular economy concept along with sustainable and regenerative processes, in opposition to the pernicious impact of petrol exploitation. In a nutshell, a platform that integrates some unit operations to upgrade different biomasses and wastes, heading the attainment of eco-sustainable products is aimed (figure 1). The central and critical process involved is the Thermochemical Liquefaction. Such process was already scaled-up allowing the development of a pilot plant (figure 2). The liquefaction of lignocellulosic materials has already been applied to several residues allowing the production of polyols, foams, sugars, fuels, antioxidants and intermediates for adhesives and polyesters (PHAs).

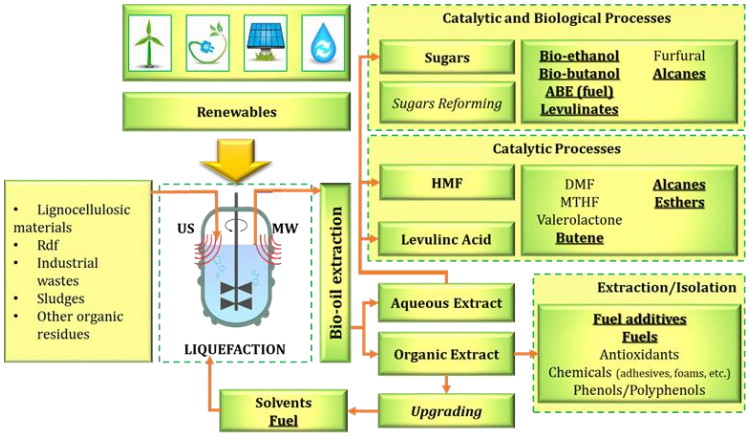

Figure 1. Schematic representation of a Technological Processes Platform for the Production of Alternative Energy Carriers

Figure 2. Pilot Plant for Lignocellulosic biomass liquefaction and subsequent valorisation of fractions constructed under the scope of a Portugal 2020. Project leaded by SECIL.

J. C. M. Bordado is Full Professor of Chemical Engineering at IST since 2004. He possesses an extensive experience in the Industry sector: Technology transfer of the basic know how and contract licensing for construction of a new plant (unsat. polyester) (1978-79); Process design and detailed engineering of one unsat. polyester plant at Barreiro and follow up of the erection of the new plant (78-81); Erection of a very versatile pilot plant for the development of new unsat. polyesters for different applications (81-82); Director of R&D for UP and polyurethanes, at Quimigal, and development of several new reactive polymers (82-86); Revamping of a Zinebe plant to produce potassium amyl xantate and startup of the plant (83-84); Director for R&D at Hoechst in Portugal and development of new resins at Resiquímica pilot plant (87-99); President and CEO of Hoechst Ambiente (1995-99); R&D on reactive polymers at IBB (1999-2004). He is author of more than 40 Patents and 200 Papers and was President of *Sociedade Portuguesa de Materiais* (2009-2011).

T&I.O1

Parameterization of Noncovalent Interactions for Transition State Interrogation: Catalytic Asymmetric Fluorination of Allylic Alcohols

Jaime A. S. Coelho[1,2], Manuel Orlandi[3], Margaret J. Hilton[3], Matthew S. Sigman[3], F. Dean Toste[1]

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Development of methods to form carbon-fluorine bonds enantioselectively is a very active area of chemical research.[1] An attractive strategy to address this goal is the use of chiral anion phase transfer (CAPT) catalysis in combination with an electrophilic source of fluorine to form a chiral ion pair for enantioselective delivery to a prochiral nucleophile.[2] An emerging characteristic of this approach is the importance of non-covalent interactions (NCIs) to guide effective asymmetric induction. This prerequisite often includes the use of a directing group, either preinstalled or formed *in situ*.[3] Multivariate linear regression analysis has emerged as a tool in asymmetric catalysis to quantitatively correlate the structure of a chiral catalyst or substrates to selectivity, resulting in predictive equations that can improve the stereoselectivity of a reaction.[4] Herein, a new class of parameters is presented for postulating NCIs in multivariate correlations. The validation of this new parameters was achieved by directly connecting non-covalent interactions defined through empirical data set analyses to the computationally derived transition states for diverse catalytic systems, including our recent developed enantioselective fluorination of allylic alcohols.[5] Furthermore, this protocol can be generalized and applied to the expansion of the scope of catalytic reactions in which NCIs govern the selectivity, as demonstrated by our recent advances towards the enantioselective fluorination of homoallylic alcohols.[6]

Acknowledgements

J.A.S. Coelho thanks Fundação para a Ciência e a Tecnologia (SFRH/BPD/100433/2014) for a postdoctoral fellowship.

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T&I.O2

Catalytic behaviour of Co^{III}, $Co^{III}Cd^{II}$ and $Co^{III}Zn^{II}$ Schiff Base Complexes in the Stereospecific sp^3 C–H Oxidation with *m*-CPBA

Dmytro S. Nesterov[a], Oksana V. Nesterova[a], Olga Yu. Vassilyeva[b], Elena A. Buvaylo[b], Brian W. Skelton[c] and Armando J. L. Pombeiro[a]

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Complexes of transition metals are efficient catalysts for a broad range of organic reactions, including direct C–H functionalization[1]. Herein we explored the catalytic behaviour of the three related Co^{III}-based complexes, $[CoL_3]\cdot DMF$ (**1**), $[CoCdL_3Cl_2]\cdot 0.5H_2O$ (**2**) and $[CoZnL_3Cl_2]\cdot CH_3OH$ (**3**) with the Schiff base ligand L (HL = 2-methoxy-6-[(methylimino)methyl]phenol; DMF = N,N-dimethylformamide) in the stereoselective oxidation of *cis*-1,2-dimethylcyclohexane (*cis*-1,2-DMCH) with *m*-chloroperbenzoic acid (*m*-CPBA) using promoters of different acidity, under mild conditions[2]. All the complexes reveal notable activity with the yields of products up to 17% and 61% based on *cis*-1,2-DMCH and *m*-CPBA, respectively, and retention of stereoconfiguration of alkane substrates up to 99%. The heterometallic $Co^{III}Cd^{II}$ (**2**) and $Co^{III}Zn^{II}$ (**3**) complexes are considerably more active than the mononuclear Co^{III} complex (**1**), exhibiting higher products yields and a higher stereoselectivity. This finding can be understood in terms of the *synergistic catalytic effect of different metals*, where the probable role of the cadmium or zinc centres is in influencing the coordination geometry and redox properties of the cobalt atom, facilitating, *e.g.*, its interaction with *m*-CPBA.

The acidity of the promoter was shown to influence catalytic parameters so that the better parameters are achieved with the acid possessing lower pK_a values (a stronger acid). From the pronounced stereo- and bond selectivities, high kinetic isotope effects in the C_6H_{12}/C_6D_{12} mixture oxidation (5.7 and 6.2 for **1** and **2**, respectively) and ^{18}O labelling studies, the overall reaction mechanism was proposed to proceed without the participation of free alkyl radicals.

Acknowledgements

This work was supported by the Foundation for Science and Technology (FCT), Portugal (projects PTDC/QEQ-QIN/3967/2014 and UID/QUI/00100/2013; fellowship SFRH/BPD/99533/2014).

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T&I.O3

Effect of isothermal heat treatments on low-grade cork

Ali Sen[1], Isabel Miranda[1], Helena Pereira[1]

[1]*Forest Research Centre* (CEF), *Instituto Superior de Agronomia, Universidade de Lisboa, Tapada da Ajuda, 1349-017 Lisboa, Portugal*

The effects of isothermal heat treatments on structural and chemical characteristics of *Quercus cerris* cork were examined. Granulated cork samples (2-4 mm) were subjected to isothermal air heating treatments between 150 °C and 400 °C and analyzed for mass loss, cell structure and chemical composition.

The mass loss pattern of *Q. cerris* cork is similar to that of *Q. suber* cork. Cork is thermally stable below 200 °C and the overall mass loss depends on final temperature and heating time: increased mass loss is observed at higher final temperatures and longer heat treatment times, i.e. 3% at 200 °C 10 min and 46% at 350 °C 60 min. At heat treatments over 200 °C, cork cells are expanded, cell wall thickness is reduced and cell corrugations are lost.

Cork extractives are degraded at lower temperatures than cork macromolecules. Between the extractive compounds, aliphatic extractives are shown to be more stable. Suberin from *Q. cerris* is more heat resistant than that of *Q. suber*, while lignin showed similar resistance in both species.

These results suggest that low-grade corks such as *Q. cerris* cork, can be valorized as expanded cork agglomerates for insulation purposes by application of isothermal heating treatments over 200 °C.

Acknowledgements

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T&I.F1

Simple solvent-free preparation of dispersed composites and their application as catalysts in oxidation and hydrocarboxylation of cyclohexane

Elisabete C. B. A. Alegria[1,2,*], Ana P. C. Ribeiro[1*], Maximilian N. Kopylovich[1], Ana M. Ferraria[3*], Ana M. Botelho do Rego[3], Armando J. L. Pombeiro[1*]

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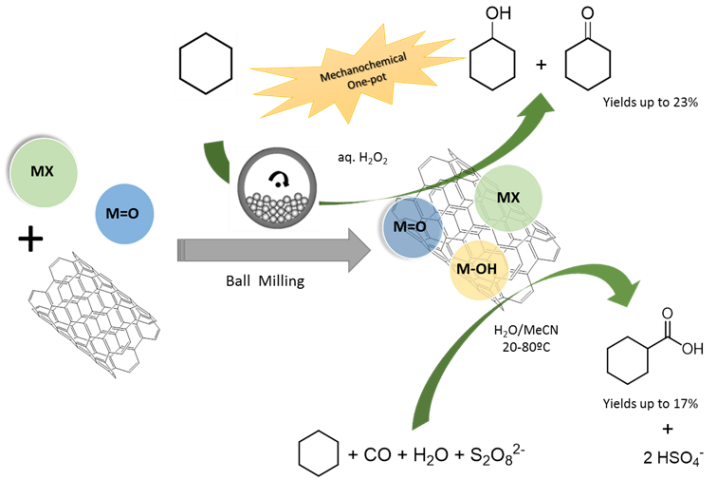
A simple and clean mechanochemical synthesis at room temperature was employed to prepare *3d* metal based dispersed composites with different ratios of components using simple metal salts/oxides The thus prepared composite materials were tested as catalysts for peroxidative oxidation or hydrocarboxylation of cyclohexane and show remarkable efficiency in the oxidation of cyclohexane. The hydrocarboxylation of cyclohexane to produce cyclohexanecarboxylic acid bearing one more carbon atom, is also achieved.



Acknowledgements

Financial support from the Fundação para a Ciência e a Tecnologia, Portugal (fellowships SFRH/BPD/90883/2012 and SFRH/BPD/108338/2015 to A.P.C. Ribeiro and A.M. Ferraria, respectively, and the "Investigador 2013" contract to M.N. Kopylovich with respective IF/01270/2013/CP1163/CT0007 project, the UID/QUI/00100/2013, PTDC/QEQ-QIN/3967/2014 and UID/NAN/50024/2013 projects).

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T&I.F2

Antimicrobial monolithic filters for water bio-decontamination

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Waterborne bio-contamination is a global concern which calls for urgent preventive measurements, particularly in the water treatment sector. One of the most important causes of this problem is the unwanted spontaneous colonization of aquatic organisms on submerged surfaces, forming the so-called biofouling. This biofouling formation on water circuits can easily be detached from external stresses such as the water flow itself, hence promoting microorganisms release. These may be pathogens, which enter the water, and thus become a vector of serious health risks[1]. This bio-contamination is conventionally treated with strategies based on the controlled release of toxic agents into the contaminated water or surface. But the intrinsic ecotoxicity of those agents is also causing significant environmental and economic penalties, also demanding environmental friendly alternatives. In this work a new non-toxic strategy able to prevent biofouling through a non-biocide-release method was developed[2]. This approach comprises the covalent immobilization of isocyanate functional agents (e. g. NCO-Econea) in polymeric coatings for filters surfaces protection. The isocyanate functionality of the modified biocidal agents was confirmed through Fourier Transform Infrared spectroscopy (FTIR) and Nuclear Magnetic Resonance (NMR) spectra analysis. A bioactivity study of the biocides and their functional counterparts evidenced antimicrobial activity with similar Minimum Inhibitory Concentration (MIC), particularly against *S. aureus* (SA) bacteria. This behavior suggests that the biocide main structure was not significantly affected by the functionalization process. Antimicrobial polymeric coatings systems were further developed and used to coat monolithic filters. The obtained bioactive monoliths were evaluated in terms of antimicrobial activity against SA bacteria, evidencing auspicious effects[3]. A complete growth inhibition and a bacteriostatic behavior were confirmed on a coated monolith with a silicone based coating containing Econea biocide in a content as low as 0.5 wt.%.

Acknowledgements

Support for this work was provided by FCT through UID/MULTI/00612/2013, PEst-OE/QUI/UI0612/2013 and UID/DTP/4567/2016. The authors also acknowledge Hempel A/S for paints supply. O. Ferreira is also grateful for the PhD Grant PD/BD/128370/2017 under the CATSUS Programme, provided by Fundação para a Ciência e a Tecnologia (FCT). E.R. Silva also acknowledges the FCT support through the Post-Doc fellowship SFRH/BPD/88135/2012.

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T&I.F3

Imine Furfurals for Ruthenium-Catalyzed Direct C3-H Arylations and Alkenylations

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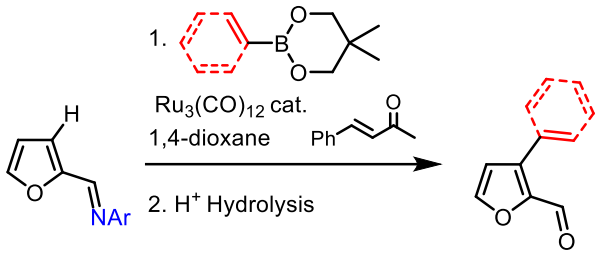
Implementation of catalytic C-H transformations[1] on renewable feedstock is becoming an attractive strategy for green transformations. In particular, lignocellulosic biomass valorization has received significant attention as an alternative to the limited petroleum resources.[2] Furfural and 5-(hydroxymethyl)furfural (HMF) are among the most important unsaturated large-volume chemicals that can be directly prepared from biomass.[3] Although some transition metal catalyzed direct C-H functionalizations of furfural have been reported,[4] only very few address the selective C3-H functionalization.[5]

Herein, we describe the Ru(0)-catalyzed[6] C3-H arylation and alkenylation of furfural imines with boronated erivatives, followed by mild acid hydrolysis, to access the arylated- or cinnamylated-furfural derivatives (Scheme 1).[7]



Scheme 1. Direct C3-H arylation and alkenylation of furfural derivatives.

Acknowledgements

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T&I.P1

Synthesis and application of multiple catalyst species for solvent-free oxidation of 1-phenylethanol

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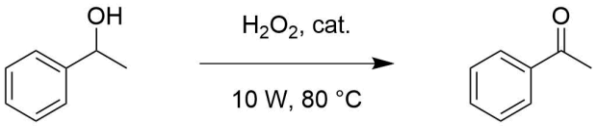
The alcohol oxidation is a very common and important type of reaction as it is needed to obtain pharmaceuticals[1], agro-chemicals and fragrances[2]. New catalysts for alcohol oxidation which work under mild conditions are always in demand of the industry to do reactions greener and safer[3]. Therefore, the inorganic iron compounds $FeCl_3 \cdot 6H_2O$ and $[FeBr_2(depe)_2]$ as well as the organic heterostructure dimethyl pyridine-2,5-dicarboxylate were used as catalysts for the oxidation of 1-phenylethanol to acetophenone by means of microwave irradiation. Additionally, the combination of inorganic $FeCl_3 \cdot 6H_2O$, $[VO(acac)_2]$ and Fe_3O_4-NPs with the organic heterostructure in two different ratios were synthesized and applied for the oxidation of 1-phenylethanol. The NPs were investigated with Fourier Transform infrared (FT-IR) spectroscopy. The yield of acetophenone was analyzed with Gas Chromatography-Flame Ionization Detector (GC-FID).



The synthesis and their application for the oxidation of 1-phenylethanol will be discussed. The optimization of the catalytic parameters (reaction time, amount of catalyst) will be presented.

Acknowledgements

Funding from FCT (Fundação para a Ciência e a Tecnologia, Portugal) for the UID/QUI/00100/2013 and PTDC/QEQ-ERQ/1648/2014 projects and for K. Acar fellowship from IAESTE is gratefully acknowledged. M.H.G. Prechtl acknowledges the Heisenberg-program (DFG) for funding.

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T&I.P2

Novel Copper Isatin Schiff Base Complexes as Functional Alcohol Oxidase Mimetics

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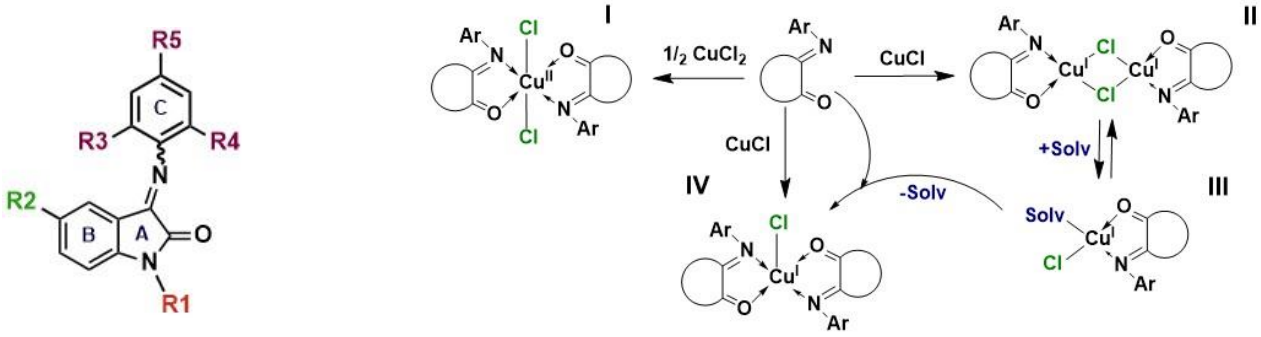
Copper complexes with organic ligands are widely used in organic synthesis as catalysts *e.g.,* in selective oxidation reactions[1]. Isatin Schiff base derivatives (ISBDs, Figure 1a) are widely studied as bioactive probes whereas their coordination chemistry remains scarce.

Herein we report novel ISBDs copper(II) and copper(I) complexes. Two types of products were formed depending on the ligand structure and copper oxidation state: charged mononuclear $[Cu(L)_2]Hal_x$ and neutral binuclear halo-bridged $[Cu_2(\mu\text{-}Hal)_2(L)_2]$ species (Figure 1b).



(a) **(b)**

Figure 1. (a) Isatin Schiff bases used in the current study; (b) Reaction products between copper ions and ISBDs.

The obtained complexes showed ability to catalize the oxidation of benzyl alcohol to corresponding aldehyde – functionally mimicing alcohol oxidase, thus these data present proof of concept that ISBD ligands can behave as non-innocent ligands in combination with copper ions and catalize oxidation of alcohol substrates.

Acknowledgements

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T&I.P3

Novel phenoxazine and phenothiazine derivatives for OLED applications

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Luminescent materials for organic light-emitting diodes (OLEDs) have been an important subject of both academic and industrial research in recent years[1]. Although OLEDs that employed fluorescent materials have been progressively replaced by metal-based phosphorescent materials, the latter exhibit certain disadvantages, such as cost and the need to use heavy metals. Recently, organic emitters displaying thermally-activated delayed fluorescence (TADF) have become relevant in this field, leading to remarkable results[2,3].

In this communication are presented four novel phenoxazine and phenothiazine luminescent derivatives, which were designed having in mind their ability to display TADF, in order to explore their potential application in OLEDs.

Acknowledgements

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T&I.P4

Current Methodologies Used in Process Development of Active Pharmaceutical Ingredients and Intermediates

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The aim of pharmaceutical development is to provide a manufacturing process that is able to consistently deliver a pharmaceutical product with its intended performance. The information and knowledge gained from the pharmaceutical development stage and manufacturing experience provide scientific understanding that supports the establishment of a design space, specifications, instrumentation and controls.[1,2]

According to the ICH-Q8 guideline, a Quality by Design (QbD) approach in pharmaceutical development results in the establishment of a design space from multivariate experiments understanding the critical quality attributes of the product and critical process parameters, recurring often to process analytical technology (PAT) tools to monitor and build control strategies.[1,2]

Statistical design of experiments (DoE) is an established and proven methodology for optimizing processes that identify robust operating regions and critical process parameters that yield a product with the desired quality. It establishes an empirical relationship between those variables and specific responses of the system using a minimum number of experiments.[3]

Mechanistic modeling combines physicochemical events as mass and heat transfers with reaction kinetics, flows, pH effects, scenarios (e.g. equipment used) taking into account physical and chemical equations translating data into fundamental knowledge.[4]

Other methods such as one-factor-at-a-time (OFAT) approaches can also provide valuable information but struggle to characterize systems with interacting variables and might need a larger number of experiments to reach the same conclusion.[5]

This presentation shows a case study where the use of design of experiment coupled with mechanistic modeling greatly increases the understanding of an API manufacturing process while reducing the number of experiments required describing each system.

Acknowledgements

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T&I.P5

Carbon dots as catalysts for industrially sustainable oxidative processes

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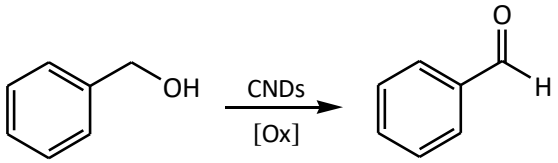
The selective oxidation of alcohols to aldehydes or ketones is playing a fundamental role in organic synthesis. These products are highly used as intermediates in pharmaceutical, perfumery, dyestuff and agrochemical industries. Due to these valuable products, there have been a large interest in the development of sustainable, selective and efficient catalytic systems to obtain these compounds, that can be used in the industries in conjunction with benign oxidants species.[1,2] Recently, stoichiometric oxidants have been replaced by heterogeneous catalysts owing to their high catalytic activities. However, these catalysts are not only relatively expensive but may also generate a lot of environmental problems.[2,3]

Carbon nanodots (CNDs) produced from various carbon sources, including industrial wastes, can be conceptually designed to improve catalytic processes for the oxidation of alcohols either by photocatalysis or by chemical oxidation. These CNDs offer unique physicochemical properties and have the advantage of to be environmentally acceptable and economically useful.[3]

Herein we report our studies regarding the synthesis and characterization of CNDs as well as the evaluation of their ability to behave as catalysts in oxidation processes.



Scheme 1. Oxidation of benzyl alcohol to benzaldehyde catalysed by CNDs.

Benzyl alcohol (Scheme 1) was selected as a model substrate. Following chemical and photochemical procedures, a series of reaction parameters (*e.g.* reaction time, amount and source of CNDs and oxidant type) were surveyed.

Acknowledgements

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T&I.P6

Biomass processing and Conversion by a Green Chemistry approach

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For the protection of the environment, and because of the limited amount of fossil fuels available, renewable resources such as biomass (from waste, marine litter, etc.) are receiving increased attention as important sources of raw materials for the production of a wide range of high-value products.

With this study we intend to understand the influence of raw materials (waste from fruits) and to transform them in supports for catalysis. The different synthesis methods will be discussed.

Acknowledgements

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T&I.P7

A More Sustainable Process for the Preparation of the Muscarinic Acetylcholine Antagonist Umeclidinium Bromide

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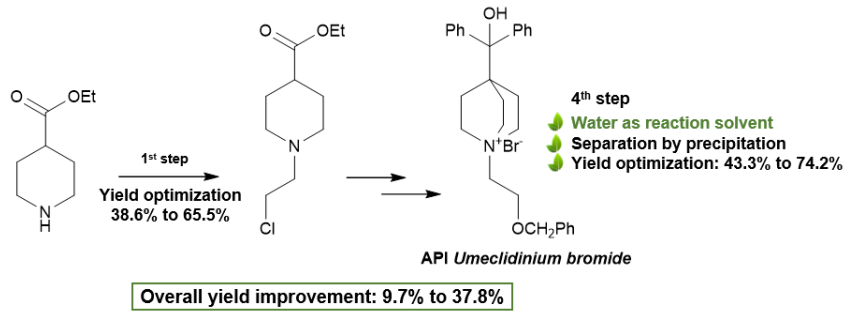
Chronic obstructive pulmonary disease (COPD) is responsible for millions of deaths each year. Umeclidinium bromide, a long-acting muscarinic acetylcholine antagonist, is one of the drugs used for the treatment of COPD, approved by the US FDA in 2013.[1] In 2005, GlaxoSmithKline disclosed the first synthetic method to obtain the API in four steps (overall yield of 9.7%). The first step comprises a nucleophilic addition of ethyl isonipecotate to 1-bromo-2-chloroethane, in the presence of potassium carbonate in acetone, to obtain the intermediate **3** in low yield (38.6%). The fourth synthetic step has also a negative impact in the overall yield of the process (umeclidinium bromide is obtained in 43.3% yield). Moreover, the solvents used in the last step (acetonitrile and chloroform) are not favourable for industrial application due to environmental and safety reasons.[2] Herein, we describe a more sustainable synthetic process to obtain umeclidinium bromide in a more efficient way. Relative to the first synthetic step, potassium carbonate was replaced by triethylamine, improving the yield from 38.6% to 65.6%. Also, in this step we disclosed, for the first time, the chemical structure of the by-product formed during the reaction in 14% yield. In order to optimize the synthetic process of umeclidinium bromide we also focused our attention in the fourth step. Other solvents were tested as toluene, acetone, THF, ethanol and water, improving the yield to 53-83%. The most positive result was when water was used as solvent, obtaining the API directly from the reaction medium by precipitation, in 74.2% yield. Therefore, the proposed optimized process (Scheme 1) represents a clear advantage for the large scale synthesis of umeclidinium bromide by the pharmaceutical industry.[3]



Scheme 1. Synthetic route optimization of the API umeclidinium bromide.

Acknowledgements

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T&I.P8

New Ni(II) redox active complexes as catalysts for the microwave-assisted oxidation of cyclohexane

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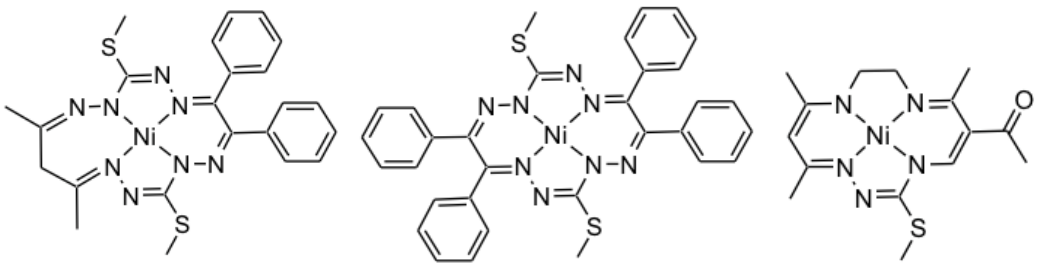
Currently, industrial catalytic oxidations are one of the most important processes to produce useful value-added chemical compounds from petroleum-based materials. However, several are energy-intensive low efficiency processes and the search for efficient, selective, environmentally benign, and economic catalytic oxidation methods towards the sustainable development of chemical processes is urgent.

An exemplary large-scale building block industrial production is the oxidation of cyclohexane which presents significant weaknesses. Herein we report the synthesis and characterization of new Ni(II) complexes (Figure 1) as well as their redox behaviour.



Moreover, the catalytic activity of the above Ni(II) complexes in the microwave-assisted selective transformation of cyclohexane to cyclohexanol and cyclohexanone in environmentally friendly reaction conditions is also discussed.

Acknowledgements

Support for this work was provided by Fundação para a Ciência e Tecnologia through UID/QUI/00100/2013 and PTDC/QEQ-ERQ/1648/2014 projects.

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T&I.P9

Production of structured lipids by enzymatic catalysis using crude olive pomace oil

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Structured lipids (SL) are novel lipids with functional properties obtained by chemical modification of a triacylglycerol (TAG) or oil, namely by the addition of new fatty acids to the glycerol backbone or the rearrangement of the original fatty acids[1]. SL containing long chain fatty acids (LCFAs) at the *sn*-2 position of TAG and medium chain fatty acids (C6:0-C12:0, MCFA) at the *sn*-1,3 positions (MLM) have gained attention for their nutritional applications. These compounds have been shown to be a quick source of energy due to a rapid absorption of MCFAs at *sn*-1,3 position during digestion, resulting in less adipose tissue storage, and a more efficient absorption of LCFAs at *sn*-2 position, in form of 2-monoacylglycerol after lipolysis[1,2].

In this study, MLMs were produced by acidolysis of crude olive pomace oil with caprylic (C8:0) or capric (C10:0) acids, in solvent-free medium, catalyzed by commercial immobilized lipases. The lipase from *Candida antarctica* immobilized in acrylic resin (Novozym 435) and the *sn*-1,3-regioselective lipase from *Rhizomucor miehei* immobilized on macroporous anion exchange resins (Lipozyme RM IM) were tested as biocatalysts. Acidolysis was carried in batch reactions for 48 h at 50 °C, using a substrate molar ratio (FFA:TAG) of 2:1. Crude olive pomace oil is a low-cost raw-material with a fatty acid composition similar to that of olive oil (oleic acid as major fatty acid) obtained from olive pomace by solvent extraction, after olive oil extraction. High acidic crude olive pomace oil (20.3% of free fatty acids) with high contents of oxidation products (K_{232}=6.982 and K_{270}=2.222) and pigments (chlorophylls a and b) was used (oil A). Also, this oil was submitted to a sequential adsorption process with 4% activated earths at different time/temperature combinations (65 °C/60 min; 90 °C/45 min; 110 °C/30 min). The obtained oil (oil B) showed a decrease of 77.8% in chlorophyll content but an increase of 21.2% in final oxidation products, promoted by the high adsorption temperatures used. This oil was also used in acidolysis reactions.

Conversion of C8:0 varied from 52.4% with Novozym 435, to 56.2%, catalyzed by Lipozyme RM IM, both with oil B after 48 h reaction; conversion of C10:0 varied from 46% with Lipozyme RM IM, after 24-h acidolysis of oil A, to 53.2% with Novozym 435 after 48-h acidolysis of oil B. No significant differences were obtained between oils, showing that the pigments did not affect lipase activity.

Acknowledgements

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T&I.P10

Immobilization of scorpionates complexes on carbon materials for the oxidation of cyclohexane

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Catalytic reactions are preferred in environmentally friendly green chemistry due to the reduced amount of waste generated. A convenient strategy to overcome the limitation of homogeneous catalysts is the immobilization of the catalyst on a solid support in order to combine the advantages of homogeneous and heterogeneous catalysis[1]. This can be achieved by anchoring the catalyst on carbon materials to produce active, selective and recyclable catalysts for the oxidation of cyclohexane. The current industrial process uses homogeneous cobalt catalysts and dioxygen as oxidant, with considerably high temperature (150 °C) and low yield of product (5%) to achieve a good selectivity (around 85%)[2], hence the need to search for more active systems that would work under milder conditions.

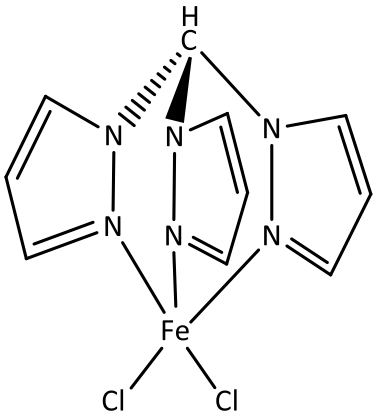

Figure 1. Schematic structure of the complex [$FeCl_2$(Tpm)].

In the present study the C-scorpionate iron(II) complex [$FeCl_2$Tpm] [Tpm = k^3-HC($C_3H_3N_2$)$_3$) (previously synthetized)], was immobilized on different carbon materials: a commercial oxidized carbon (GL-50 oxi) and an ordered mesoporous carbon (CMK-3). The catalytic behaviour of the immobilized catalysts for the oxidation of cyclohexane is being studied and the optimization of the operating conditions regarding the effect of temperature, time, oxidant and catalyst amount is on-going. Recycling studies of the catalysts will also be performed. The products of the reaction, cyclohexanol and cyclohexanone, were analysed by Gas Chromatography using nitromethane as an internal standard.

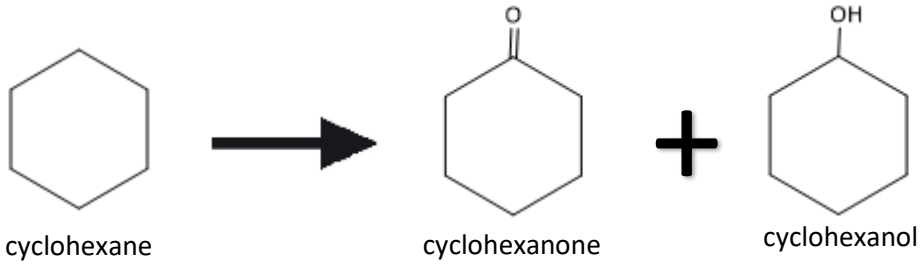

Figure 2. Reaction of cyclohexane oxidation.

Acknowledgements

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T&I.P11

Alkane and alcohol oxidation catalyzed by Cu(II) and V(V) complexes bearing arylhydrazones or carbohydrazones

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A series of first-row-transition metal complexes have been synthesized and fully characterized: *i*) copper(II), $[Cu(1\kappa N,O^2{:}2\kappa O\text{-}HL^1)(S)]_2$ [S = CH_3OH (**1**), $(CH_3)_2NCHO$ (**2**)] and $[Cu(\kappa N\text{-}HL^1)(en)_2]\cdot CH_3OH\cdot H_2O$ (**3**), where H_3L^1 = (*E/Z*)-4-(2-(1-cyano-2-ethoxy-2-oxoethylidene)hydrazinyl)-3-hydroxybenzoic acid;[1] *ii*) dinuclear vanadium(V), $NH_4[(VO_2)_2(^{H}LH)]$ (NH_4[**4**]), $NH_4[(VO_2)_2(^{t\text{-}Bu}LH)]$ (NH_4[**5**]), $NH_4[(VO_2)_2(^{Cl}LH)]$ (NH_4[**6**]), $[(VO_2)(VO)(^{H}LH)(CH_3O)]$ (**7**), $[(VO_2)(VO)(^{t\text{-}Bu}LH)(C_2H_5O)]$ (**8**) and $[(VO_2)(VO)(^{Cl}LH)(CH_3O)(CH_3OH/H_2O)]$ (**9**), where $^{H}LH_4$ = 1,5-bis(2-hydroxybenzaldehyde)-carbohydrazone, $^{t\text{-}Bu}LH_4$ = 1,5-bis(3,5-*tert*-butyl-2-hydroxybenzaldehyde)carbohydrazone and $^{Cl}LH_4$ = 1,5-bis(3,5-dichloro-2-hydroxybenzaldehyde)carbohydrazone.[2] Complexes **1**–**4** are efficient catalyst precursors for the solvent-free microwave(MW)-assisted selective oxidation of primary or secondary alcohols and diols to the corresponding aldehydes, ketones and diketones, respectively. Compounds **4**–**9** were applied as alternative selective homogeneous catalysts for the industrially significant oxidation of cyclohexane to cyclohexanol and cyclohexanone. The peroxidative (with *tert*-butyl hydroperoxide) oxidation of cyclohexane was performed under solvent-free and additive-free conditions and under low-power MW irradiation. Reaction parameters such as temperature, time and also oxidant nature, chemoselectivity, organic radical and acid influence were studied.

Acknowledgements

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T&I.P12

Catalytic performance of ionanofluids in Sonogashira C-C coupling reaction

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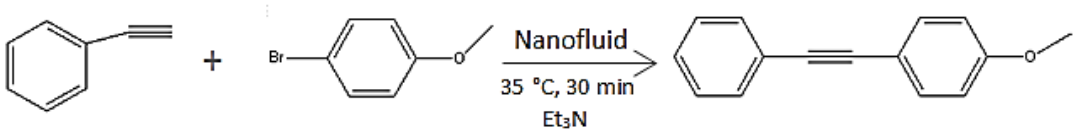
Sonogashira C-C coupling reaction under unconventional conditions, namely in a ionanofluid where the base fluid is an ionic liquid (IL), is still understudied.[1,2]

In this work we present the coupling between phenylacetylene and 4-bromoanisole to afford 1-methoxy-4-(phenylethynyl)benzene (Scheme 1), using $Pd(OAc)_2$, $PdCl_2$ or Pd/C (5% w/w) as nanocatalysts in several ionic liquids such as 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide, 1-hexyl-3-methylimidazolium bis(trifluoromethanesulfonyl)-imide or 1-octyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide, by two different heating methods (conventional heating and microwave irradiation).



Scheme 1. Sonogashira C-C coupling reaction.

The characterization (*e.g.,* by TEM, EDS and SEM) of the used nanofluids is reported and the catalytic results obtained by the two different heating methods are discussed.

Higher conversions for the Sonogashira C-C coupling reaction and easier separation and recycling of the nanocatalyst are obtained in ionanofluids.

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T&I.P13

One step further in the rationalization of solvent effects as addressed by Grunwald-Winstein and TAKA model equations

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Over the years, both Grunwald-Winstein (G-W) plots[1] and the TAKA model equation[2] have been independently used to rationalize solvent effects in solvolysis reactions. Our previous work[3] has shown good correlations between G-W scales (N_T, N_{OTs}, Y_{Cl} and Y_{Br}) and TAKA parameters (π^*, α and β) thus suggesting that: i) the former are indeed a "mixture" of different solvent effects instead of pure solvent parameters; and ii) both approaches reveal unsuspected similarities. However, a systematic deviation was observed for fluorinated alcohols. This has been previously reported[4] and was one of the reasons for the introduction of an extra solvent parameter, *C*, in the TAKA equation. This term, which accounts for solvent–solvent interactions, is called the cohesive energy density and corresponds to the square of the Hildebrand parameter, δ_H, being related to the standard molar enthalpy of vaporization, $\Delta_{vap}H_m^0$, through the following expression:

$$C = \delta_H^2 = \frac{\Delta_{vap}H_m^0 - RT}{V_m} \quad \text{(eq. 1)}$$

where, *R* is the gas constant, *T* the absolute temperature and V_m the molar volume.

As the number of independent variables increases in the correlation analysis, the number of possible combinations among them increase considerably. As such, it rapidly becomes infeasible to do all calculations, outliers' check and removal "manually". Hence, a visual basic macro was developed within MS Excel which automates the iterative process of calculating the regressions, checking for outliers, and redoing the calculations until no outliers are found. This macro first computes the different combinations of independent variables and then for each dependent variable it iteratively calculates the regressions for each combination and organizes the results, as well as relevant statistical parameters, in a results table for easy comparison.

In this work, we have experimentally determined the standard molar enthalpies of vaporization, at 298.15 K, for 38 G-W mixtures and 5 pure solvents by Calvet calorimetry. Using the developed macro, each Grunwald-Winstein parameter was expressed as a linear combination of 1 to 4 TAKA parameters (π^*, α, β and *C*) and the correlations were globally re-evaluated and interpreted, leading to new insights on the solvent effects for these processes.

Acknowledgements

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T&I.P14

Oxidation of Olefins with Hydrogen Peroxide Catalyzed by Bismuth Salts: A Combined Experimental and Theoretical (DFT) Study

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The oxidation of olefins with the Bi/H_2O_2 system was investigated with reaction time up to 32 h. Typical conditions used: substrate (0.25 M), catalyst ($1x10^{-3}$ M), H_2O_2 (1.2 M), at T = 60 °C in MeCN. The total reaction volume was 10 mL. Experimental studies of the cyclohexene, cyclooctene and 1-octene oxidation with the systems $Bi(NO_3)_3/H_2O_2/CH_3CN+H_2O$ and $BiCl_3/H_2O_2/CH_3CN+H_2O$ lead to the formation of both enol and epoxide/diol products. The maximum yields obtained with $Bi(NO_3)_3$ were 24%, 16% and 6% using cyclooctene, cyclohexene and 1-octene, respectively, as substrate. No significative difference was observed when $Bi(NO_3)_3$ was substituted by $BiCl_3$ in the peroxidative oxidation of cyclohexene.[1]

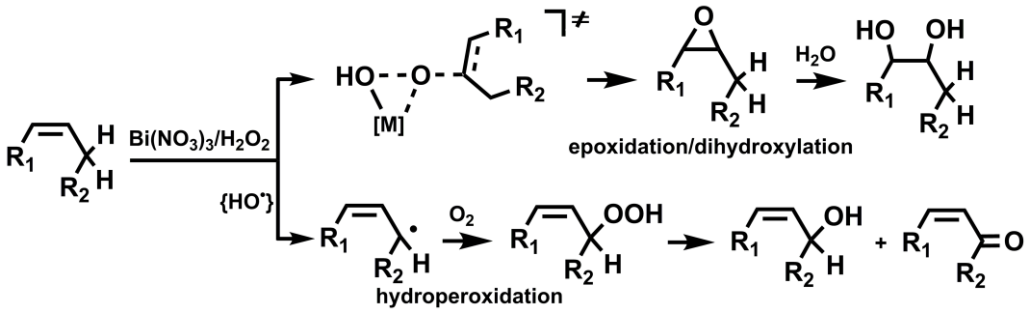

Figure 1. Oxidation of a generic olefin with the system $Bi(NO_3)_3/H_2O_2$

The selectivity observed was studied by theoretical (DFT) calculations which indicated that the reaction occurs via two competitive channels. The first one is non-radical epoxidation of the C=C double bond with possible subsequent hydrolysis of the epoxides to produce *trans*-diols. The second one is the radical hydroperoxidation of the allylic C atom(s) to give alkenylhydroperoxides – with involvement of the $HO^{\bullet}$ radicals which abstract a hydrogen atom from the substrate molecule – leading to enol and enone products (Figure 1).

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T&I.P15

Improved cyclohexane oxidation catalyzed by a heterogenised iron(II) complex on hierarchical Y zeolite

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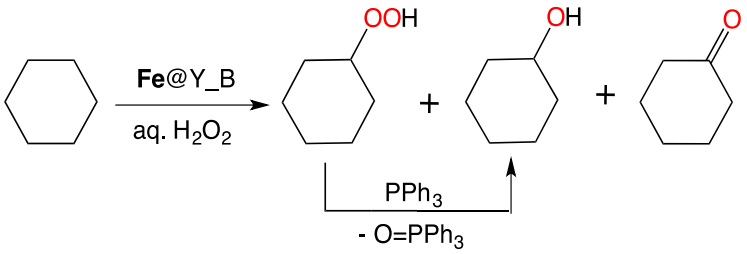
Efficient catalytic oxidation of alkanes into high value functionalized products under sustainable conditions remains challenging. An exemplary large-scale building block industrial production is the oxidation of cyclohexane which presents significant weaknesses. Therefore, there is an urgent need to develop a selective and energy efficient cyclohexane oxidation that could lead to environmental and economically superior catalytic processes and allow natural resources to be used more efficiently as feed-stocks for chemicals.

Herein we report the development of hierarchical Y zeolites to act as an efficient support for the immobilization of a C-scorpionate iron(II) complex, [$FeCl_2(HCpz_3)$] (pz = pyrazolyl)[1], to be used as heterogeneous catalysts in the transformation of cyclohexane to cyclohexanol and cyclohexanone in environmentally friendly reaction conditions (Scheme 1).



Scheme 1. Oxidation of cyclohexane to cyclohexanol and cyclohexanone catalyzed by **Fe**@Y_B (B = NH_4OH, NaOH or TPAOH).

The hierarchical supports were prepared using NaOH, TPAOH or NH_4OH as alkaline agents in the presence of CTAB surfactant, under autogenous pressure. The complex was immobilized in the supports by the incipient wetness impregnation method using water as solvent. Hierarchical zeolites behave as more efficient supports, when compared with parent Y zeolite, with a higher possibility of reusing without significant decrease of product yield.

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T&I.P16

Magnetic rhodium nanoparticles used as catalysts for hydrogenation

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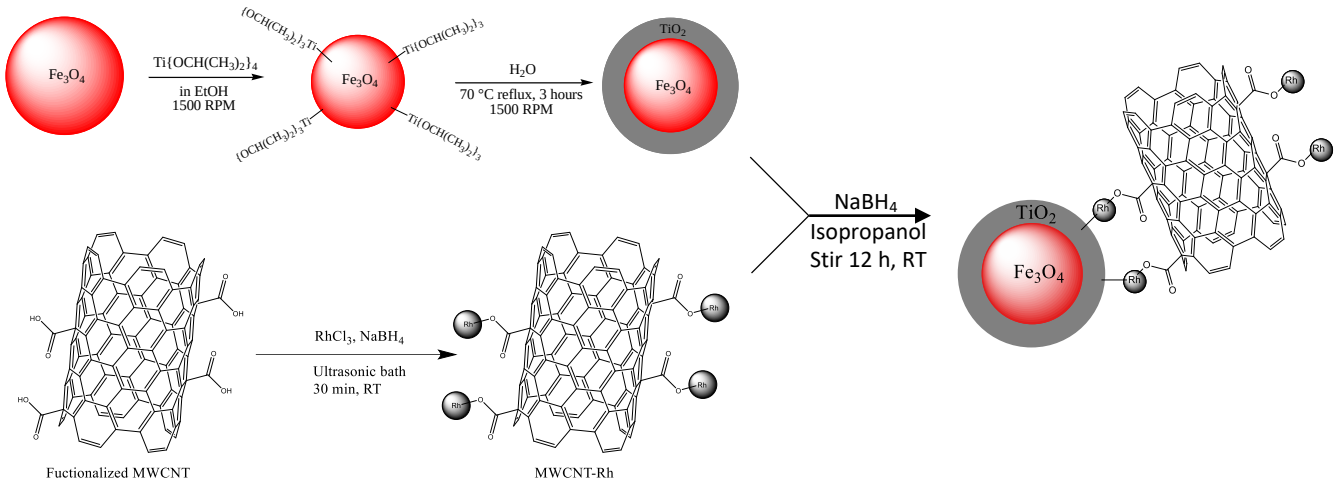
Rhodium has many catalytic applications, particularly in hydrogenation reactions due to its specific properties[1]. Moreover, rhodium nanoparticles have a high surface area with an increased catalytic activity and can be easily separated and recycled without loss of activity compared to their bulk counterparts[2]. Nevertheless, the use of rhodium as a nanocatalyst is still under studied.

Regarding our work, rhodium nanoparticles were supported on multiwalled carbon nanotubes (MWCNTs) and bound to the magnetic core-shell system Fe_3O_4@TiO_2.[3] The synthetic pathway is shown in Scheme 1.



Scheme 1. Synthesis of magnetic rhodium nanoparticles.

The composite Fe_3O_4@TiO_2-Rh-MWCNT and the intermediates were characterized by SEM, EDS, BET, FTIR and TEM. Their catalytic activity was studied using: i) the hydrogenation transfer of nitroarenes and cyclohexene in the presence of hydrazine hydrate; ii) the reduction of 2-nitrophenol with $NaBH_4$; and iii) the decoloration of pigments in the presence of hydrogen peroxide. The reaction results were monitored by gas chromatography (i) or UV-visible spectrophotometry (ii and iii).

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T&I.P17

ZnO-catalyzed transesterification of methyl-benzoates to ethyl-benzoates

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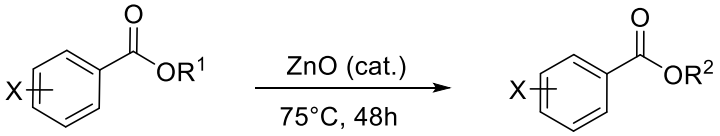
Transesterification reactions show a crucial importance towards organic synthesis for chemical industries,[1,2] specially for polyesters and biodiesel.[1,3] Improving the transesterification reaction to a mild and economic procedure is still a major challenge, as many homogeneous catalysts require high temperature and acidic conditions.[1,2]

For this purpose, the catalytic activity of Zn(II)-oxides towards transesterification reactions on methyl-benzoates to ethyl-benzoates was performed using several Zn(II)-oxides. To study the catalytic activity of the ZnO-catalyst, the reaction parameters like reaction time, amount of catalyst and starting material were varied.



X = NO_2, NH_2, OH, OMe,

The successful catalytic conversion of the methyl-benzoates to ethyl-benzoates as well as the reaction progress were analysed via ^{1}H-NMR at 300 MHz by calculation of the yield.

Acknowledgements

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Materials

Mat.PL

Synthesis, microstructure, and properties of metallic and bimetallic nanoparticles

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Metallic nanoparticles have been used in nanomedicine since decades, due to their easy preparation and the possibility for selective surface functionalization. In particular, noble metals found applications as they are typically biologically inert in the body, i.e. they do not dissolve, and they do not have harmful side-effects. Silver is an exception because its antibacterial effect is due to the release of silver ions. Alloyed nanoparticles give a combination of the properties of the single metals, e.g. antibacterial effects and surface plasmon resonance (SPR). Synthetic concepts for preparation and characterization of such nanoparticles are presented. Bimetallic nanoparticles with different elemental distribution (core-shell or alloy or graded alloy) were analysed by high-resolution transmission electron microscopy, including elemental distribution inside a nanoparticle. Besides such larger nanoparticles (size about 10 nm), recent developments on ultrasmall gold nanoparticles are highlighted. They are smaller than proteins, and they can be selectively functionalized to address specific surface epitopes of proteins.

Acknowledgements

To the Deutsche Forschungsgemeinschaft (DFG) for funding. M. Epple also thanks all contributors as given in the references for their contributions.

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Matthias Epple is Full Professor of Inorganic Chemistry at the Faculty of Chemistry, University of Duisburg-Essen (Germany). He graduated in Chemistry (1989) at the Technical University of Braunschweig where he also obtained is PhD in 1992. He was post-doctoral scientist at the University of Washington (Seattle, USA), at the Royal Institution (London, UK), and at the University of Hamburg (Germany). In 1997, he obtained his Habilitation at the University of Hamburg and was appointed Associate Professor at the Ruhr-University of Bochum in 2000. In 2003 he moved to his current position at the University of Duisburg-Essen. His research interests comprise solid-state reactions, biomaterials, biomineralisation, and the synthesis and biomedical application of nanoparticles. He was President of the German Society for Biomaterials and is currently Vice-President of the German-Ukrainian Academic Society. He has graduated 57 PhD students and authored about 425 papers in refereed journals.

Mat.IOC1

Polymorphism and Function of Organic Materials

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Since the middle of last century, it has been widely recognized that many organic compounds can be obtained in more than one crystal form, a property known as polymorphism. It also became clear that the adopted crystal structure often exerts a significant effect in the solid-state properties of the compound, so that each polymorph corresponds, in fact, to a different material. Controlling polymorphism is, therefore, essential to ensure the manufacture of products with highly reproducible properties. It also provides a means to tune the properties of a product in view of an application, without changing the molecule involved. Problems and benefits related with polymorphism in molecular organic solids will be illustrated through a few examples covering dyes, active pharmaceutical ingredients, and non-linear optical materials.

Acknowledgements

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His research interests are mainly focused on the energetics of molecules (e.g. fullerenes, PAHs, ionic liquids), crystals (nucleation, polymorphism, crystal engineering), and, very recently, also of cell metabolism and adaptation. He currently serves as a member of the "RSC Advances" Editorial Board and of "The Journal of Chemical Thermodynamics" Advisory Board.

Mat.IOC2

From CATALVALOR project to INNOVCAT Spin-off UP

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CATALVALOR project – a catalyst for change – is a sustainable solution to solve the problems of biodiesel offering a disruptive technology based on a renewable, eco-friendly and reusable solid catalyst (X-CAT) combined with a simplified process to transform multiple feedstocks (low-grade, low-cost fats/oils) into biodiesel reducing simultaneously OPEX and CAPEX, turning the biodiesel market more competitive (Figure 1). CATALVALOR project was selected to participate in Cohitec program (www.actbycotec.com), a technology commercialization program to turn research projects into business ideas. CATALVALOR project was the winner, in the most important national entrepreneurship competition in Portugal, category Industry – *Acredita Portugal* – and finalist in two awards: *Brisa Mobilidade* and iUP25k (2015).

INNOVCAT Company (www.innovcat.pt) was created in 2015 to provide the continuity of the CATALVALOR project. It is a spin-off of University of Porto focus on R&D, production and commercialization of solid catalysts and functional materials, scaling-up and development of new industrial catalytic processes in the context of biomass valorization.

Figure 1. CATALVALOR project. The IP protection of CATALVALOR invention (Portuguese patent application-2017 and PCT) is co-financed by PT2020 funding. "*Catalisadores heterogéneos, processo de preparação e sua aplicação no processo de produção de ésteres alquílicos de ácidos gordos*" Portuguese Patent application nº2017100002065; "Heterogeneous catalysts, preparation process and application thereof in fatty acid alkyl esters production process", International PCT application: PCT/IB2018/052027.

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Mat.IOC3

CO_2 methanation over Ni-zeolite catalysts

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This work concerns the use of Ni-supported USY zeolite as catalyst for CO_2 methanation (Sabatier) reaction. Different parameters were optimized in order to maximize CO_2 conversion, CH_4 selectivity and catalysts stability, under relevant experimental conditions (GHSV; reactants concentration, temperature range).
Considering the well-known zeolite features and the possibility to finely modulate its properties, inducing relevant changes on the adsorbed metal species and in the CO_2 activation ability of the catalyst, potentially interesting catalytic properties were generated also towards this transformation.
Correlations between the characteristics of these materials, found as relevant for CO_2 methanation, and the catalytic properties are suggested and discussed, in a structure-reactivity approach.
IR spectroscopy *operando* results allow us to suggest a heterogeneous reaction mechanism.

Acknowledgements

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Carlos Manuel Faria de Barros Henriques is Associated Professor of the Chemical Engineering Department (DEQ) and Research Group Leader of the Centro de Química Estrutural (CQE) at Instituto Superior Técnico (IST), University of Lisbon. His main scientific activity is centred in the area of the heterogeneous catalysis with zeolites and is developed in the laboratories of the CATHPRO (CQE/IST): (i) Catalysis for Energy: production of Synthetic Natural Gas from CO_2 with Ni-zeolite based catalysts; (ii) Environmental Catalysis: NOx and COV's abatement with multifunctional catalysts; (iii) DBD plasma-assisted heterogeneous catalysis applications: the study of CO_2 valorisation; (iv) Synthesis of nano-structured materials containing transition metals; (v) Bifunctional catalysis by zeolites; (vi) Development of spectroscopic techniques for in situ characterisation and operando/mechanistic studies of heterogeneous catalytic systems.
He is author and co-author of eight book-chapters; author and co-author of more than 50 papers in international peer-reviewed scientific journals; author and co-author of over 40 publications in scientific conference proceedings. Moreover, has participated in 18 research projects and recently has coordinated (IST part) three international projects: (i) ERANATMED SOL-CARE: Solar Assisted Catalytic Reforming: an Hybrid Process to Transform Municipal Waste into Energy (2016-2019); (ii) CEOPS–CO2: Loop for Energy storage and conversion to Organic chemistry Processes through advanced catalytic Systems" – FP7-NMP-2012-SMALL-6 (2013-2016); (iii) METANOX: Modified metal-zeolite catalysts for Selective Catalytic Reduction of NOx with methane: Improved catalytic performances and study of catalysts stabilisation", funded by GDF-SUEZ/ENGIE (2012-2016).
He has been in charge of the direction and co-direction of 6 post-doctoral internships, and 8 PhD thesis, in the fields of NOx abatement, hydrotreating and hydrocracking of heavy oil fractions, microwave field induced heterogeneous catalysis and CO_2 methanation with Ni/zeolite catalysts. Moreover, he is co-author of three patents concerning CH_4-SCR DeNOx and CO_2 methanation catalytic systems.

Mat.O1

Methods to Measure Dimensions of Synthetic Nanoparticles

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The unique properties of nanoparticles are due to their small size when compared to bulk materials. The dimensions of synthetic nanoparticles must be determined with sub-nanometre accuracy in order to understand their preparation and structure-property relationship.

In this work, four characterization methods commonly used to characterize the dimensions (and often also the shape) of nanoparticles, either in solution or dried from solution, are critically compared. These were transmission electron microscopy (TEM), scanning electron microscopy (SEM), atomic force microscopy (AFM), and dynamic light scattering (DLS). The accuracy and precision of the four methods applied to synthetic nanoparticles of different sizes composed of three different core materials – gold, silica, and polystyrene – were determined. Additionally, the suitability of the techniques to discriminate two different populations, with sizes within the same order of magnitude, of these nanoparticles in mixtures was also studied.

The results indicate that in general, scanning electron microscopy is suitable for larger nanoparticles (Ø > 50 nm), while AFM and TEM can also give accurate results with smaller nanoparticles. DLS gives details about the particles' solution dynamics but is inappropriate for the mixtures of differently sized samples. SEM was also found to be more suitable to metallic particles, compared to oxide-based and polymeric nanoparticles. The conclusions drawn from this data can help researchers choose the most appropriate technique to characterize the dimensions of nanoparticle samples.

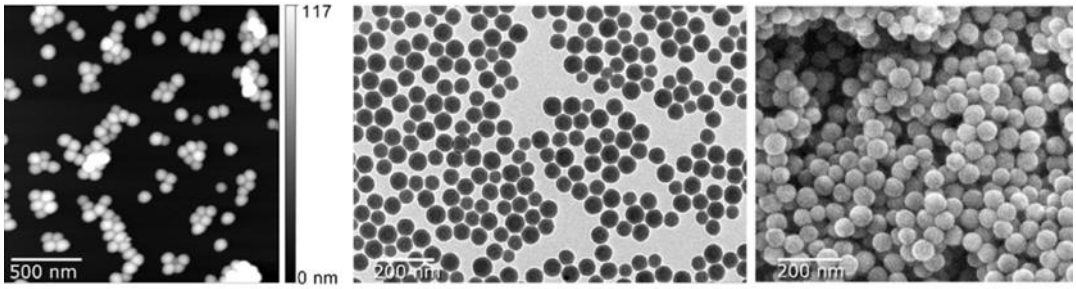

Figure 1. Silica nanoparticles micrographs from AFM (left), TEM (centre), and SEM (right).

Acknowledgements

Scanning electron microscopy was performed at Centro de Materiais da Universidade do Porto, CEMUP. Transmission electron microscopy was performed at the Electron Microscopy Laboratory (Microlab) of the Instituto Superior Técnico, Universidade de Lisboa. The authors are grateful to Fundação para a Ciência e a Tecnologia (MCTES funds) and European Union (European Social Fund and European Regional Development Fund), for financial support through projects PTDC/CTM-NAN/109877/2009 and UID/QUI/50006/2013–POCI-01-0145-FEDER-007265 (LAQV-REQUIMTE), in the context of the COMPETE program from QREN, project NORTE-01-0145-FEDER-000011, in the context of the NORTE 2020 program, and fellowships SFRH/BPD/84018/2012 (P. Quaresma), SFRH/BD/61137/2009 (C.S. Neves) and SFRH/BD/95983/2013 (M.P. de Almeida), in the context of the POCH program, both from Portugal 2020 partnership agreement.

Mat.O2

Functionalized SBA-15 for the storage and therapeutical release of H_2S

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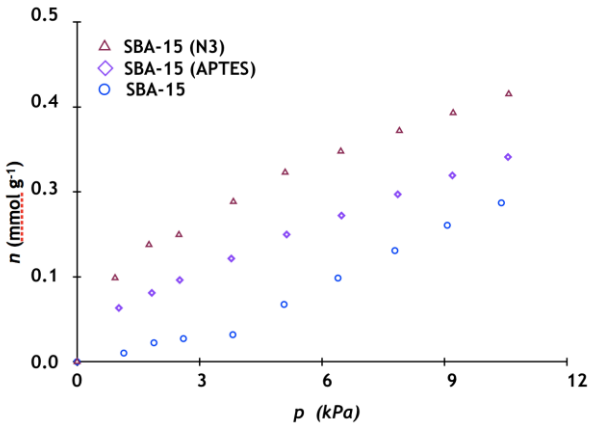
In the present work, SBA-15 before and after functionalization with 3-aminopropyl-triethoxysilane(APTES) and n-3-(trimethoxysilyl)propyl-ethylenediamine(N3) are being studied on the adsorption and therapeutical release of hydrogen sulfide (H_2S). Results of H_2S isotherms adsorption in the materials are presented in the figure below.



H_2S used to be considered as a toxic molecule[1] but, in 2005, a paper in Science drew attention to the its beneficial physiological effects, showing that H_2S can induce a state of hibernation in rats[2]. Recently, the anti-inflammatory properties of H_2S have also been highlighted[3]. H_2S exogenous donor systems are still at the experimental stage and mainly involve NaHS. Given its high toxicity, H_2S concentration has to be maintained in a very narrow concentration range[4]. To date, there are only a few studies addressed the subject of H_2S storage in porous materials for therapeutic purposes[5,6], so, much work remains to be done.

To be used in drug delivery, a material must be biocompatible. Because biocompatibility is an essential feature of any drug-delivery material, the cytotoxicity of these materials was also evaluated.

Acknowledgements

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Mat.O3

Noncovalent interactions in diazene dyes

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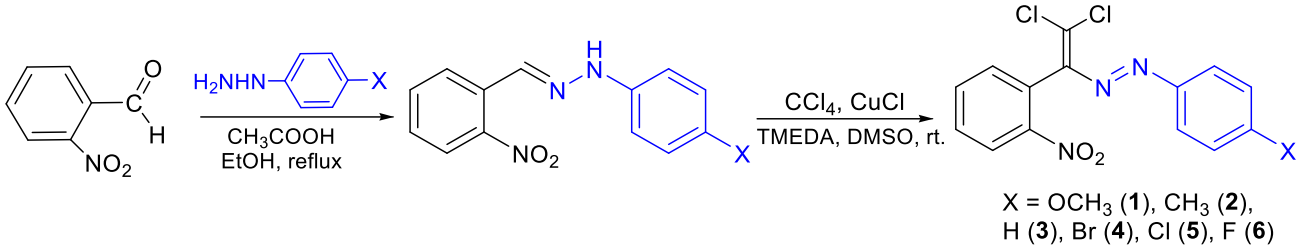
In the last decade halogen, chalcogen, pnicogen and tetrel bonds, noncovalent interactions formed between positive regions in the electrostatic potential on group VII, VI, V and IV atoms, often referred to as σ-holes, and electron rich sites, have gained a lot of interest[1-7]. As ''old'' hydrogen bonding[8,9], these ''young'' noncovalent interactions can also be used in the synthesis, catalysis and design of materials. Herein, we found an important role of intramolecular N···Cl pnicogen bonding, as well as intermolecular Cl···O and F···π types of halogen bonding, hydrogen bonding and π···π interactions in the synthesis and design of diazene dyes (Scheme).



X = OCH_3 (**1**), CH_3 (**2**), H (**3**), Br (**4**), Cl (**5**), F (**6**)

Scheme. Synthesis of **1**–**6**.

Acknowledgements

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Mat.F1

The effect of bipyridine as a redox active ligand in uranium complexes

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Recently the tetra-bipyridine complex with uranium [U(bpy)$_4$] has been synthesised and characterised by Fortier and others[1]. Since bipyridine is the quintessential redox active ligand the question naturally arises as to whether the complex could be aptly characterised as being formally U(0) or whether some radical character is present. Two years prior to this report another complex namely [U(TpMe$_2$)$_2$(bpy)] was identified in the literature[2] also bearing a radical anion bipy ligand.

In this presentation we present the detailed electronic structures of these interesting complexes resorting to multi-configurational calculations and provide an analysis of the lower region of the energy spectrum and the magnetic processes at play.

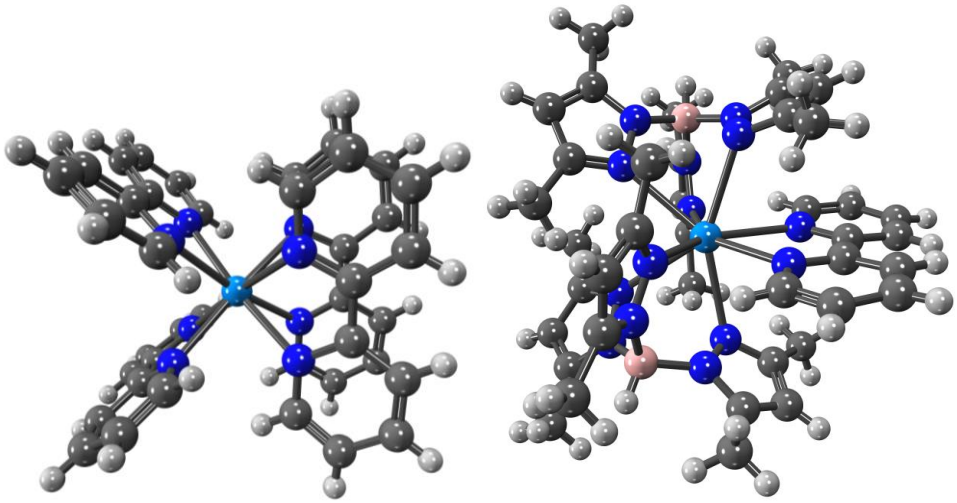

Figure 1. The [U(bpy)$_4$] (left) and [U(TpMe$_2$)$_2$(bipy)] (right) complexes.

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Mat.F2

Packing Energetics in 4-HOC_6H_4COR Compounds: The Influence of the Side Chain

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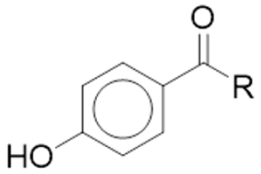
Assessing how systematic changes in molecular structure influence the packing of a crystalline solid, and its physical properties, is a fundamental issue for the understanding of crystallization phenomena. Such studies can offer insights into the design and synthesis of molecular solid-state structures, with specific properties, through the control of their intermolecular interactions. This is of considerable technological interest, as different packing architectures can strongly affect the manufacture and processing of a product and its end use characteristics (e.g., the color of dyes, the conductivity organic conductors, or the bioavailability of drugs).

Compounds with the 4-HOC_6H_4COR backbone, containing H-bond donor (−OH) and acceptor (−C(O)R) substituents separated by a phenyl ring, are well suited for this type of studies since they have been shown to be susceptible to polymorphism, as found, for example, in the cases of HBA, HAP, and HVP (Figure 1),[1-3] and can provide information on how the length of the R side chain impacts the observed crystallization patterns and crystal structures.

In this work the thermodynamic properties (e.g. enthalpies of fusion and sublimation) of different 4-HOC_6H_4COR compounds (Figure 1), and their dependence on the packing architectures, were analyzed as a function of the length of the side chain.



HBA	R = H
HAP	R = CH_3
HPP	R = CH_2CH_3
HBP	R = $CH_2CH_2CH_3$
HVP	R = $CH_2CH_2CH_2CH_3$
HHxP	R = $CH_2CH_2CH_2CH_2CH_3$
HHP	R = $CH_2CH_2CH_2CH_2CH_3CH_3$

Figure 1. 4-HOC_6H_4COR compounds studied in this work

Acknowledgements

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Mat.P1

Sensors based on donor/acceptor ligands

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Hofmann clathrates are bimetallic three-dimensional (3D) and two-dimensional (2D) coordination frameworks constituted by Fe(II) ions that are coordinated with cyanometallic anions $[M(CN)_x]^{y-}$ (where M = Ni, Pd, Pt, Cu, Ag, Au, Nb) and N-donor heterocyclic ligands.[1] These pillared structures are appealing for potential chemical sensing applications since they can adjust their porosity.[2]

Spin crossover (SCO) complexes show magnetic responses to subtle external stimuli, e.g., temperature, light, pressure and guest molecules, involving simultaneously changes in colour, dielectric constant or electrical resistance.[3] These characteristics make them potential candidates for the detection of different organic and inorganic compounds. Hofmann clathrates, a class of metal-organic frameworks (MOFs), and their analogues are among the most known and well-studied for practical applications as SCO compounds. Our strategy on Hofmann clathrates consisted in inserting a photoactive unit (Figure 1) that has both acceptor and donor capabilities promoting the electronic and optic properties of the 3D structure envisaging a material with applications in photocatalysis, solar cells, LEDs and OFETs. Here we present the synthesis and characterization of Hofmann clathrates with thiazole-derived spacers and the magnetic and optical properties are also discussed.

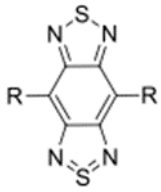

Figure 1. Thiadiazole spacer.

Acknowledgments

The authors thank Fundação para a Ciência e Tecnologia for financial support UID/MULTI/00612/2013 and PTDC/QEQ-QIN/3414/2014.

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Mat.P2

Gold Nanoclusters incorporated into Polymer Nanoparticles

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Gold Nanoclusters (AuNCs) have unique properties, including low toxicity, biocompatibility, catalytic activity, fluorescence emission and very high photostability, and have promising applications in different fields.[1]

Although they have potential for different applications, they still have an important drawback: stability. To overcome it, our group successfully developed an encapsulation strategy of AuNCs into polymer nanoparticles by miniemulsion polymerization[2]. Polymer particles of different monomers with 50 nm to 100 nm diameter were obtained, which maintain the optical properties of the AuNCs. It was also shown that after incorporation, the AuNCs were more tolerant to environmental changes, such as pH and temperature.

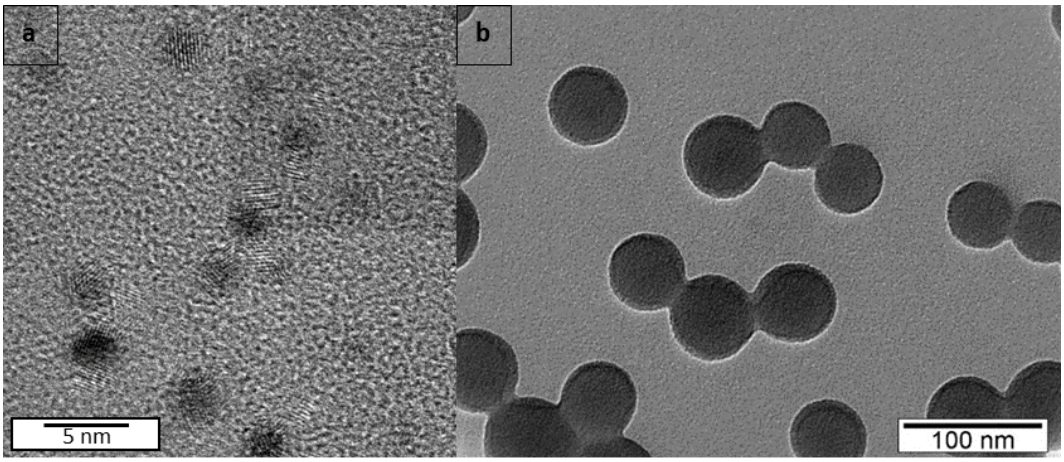

Figure 1. a) HR TEM of $Au_{25}(MHA)_{18}$. b) TEM of polymer nanoparticles produced by miniemulsion polymerization.

Acknowledgements

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Mat.P3

Ethylene polymerization with Aluminum modified dendrimeric silica (DSAl) supported metallocene catalysts: The influence of texture and acidity

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Typical industrial olefin polymerization requires solid catalysts due to their ability to control polymer morphology and prevent reactor fowling to a certain extent. Silica is a widely used, versatile and easily processable support. Diverse types of porous silicas have been recently tested, such as MCM-41 and SBA-15 nanosilicas[1]. Dendrimeric silica is a recently reported and novel type of silica consisting of fibrous nanospheres that result in an unorthodox porosity[2]. The modification of the silica surface with heteroatoms, such as aluminum, introduces surface acidity which increases the reactivity of the support and influence the catalytic performance. The nature and the strength of the acidic sites affects the interaction of the metallocene complex with the support originating different types of surface species with different degrees of polarization and more or less prone to be converted in active species[3].

This work aims to investigate the effect that both the textural and the acidic properties of an aluminum containing silica support with a dendrimeric morphology may play on the activation of a metallocene catalyst and their subsequent performance in polymerization. Various DSAl materials were synthesized via one and two-step direct synthesis methods, as well as a post-synthetic incipient wetness impregnation method. The supports were characterized regarding morphology, chemical composition, textural and surface acidic properties. Zirconocene dichloride (Cp_2ZrCl_2) was afterwards immobilized onto the DSAl materials via direct impregnation, producing the DSAl-supported metallocene catalysts. These systems were then applied in ethylene homopolymerization. The direct synthesis methods lead to stronger acidity and higher textural parameters than the post-synthesis modification procedure. Additionally, the importance of acidity on the activation of the zirconocene is verified. It is found that weak Brønsted acidity inhibits catalytic performance, while Lewis acidity appears to present an optimum range.

Acknowledgements

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Mat.P4

Optical properties of bottom-up carbon nanodots

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Over the past decades, two-photon absorption (TPA) probes have attracted much attention due to their applications in biomedical imaging and biosensing. The application of TPA probes in multiphoton microscopy affords low background signal, deep tissue penetration depth, reduced photobleaching and low phototoxicity. However, to facilitate the use of two-photon excitation in biomedical research, there is a strong need for development of efficient, application-specific, two-photon responsive materials. Carbon nanodots (Cdot) are promising next generation TPA materials due to their unique properties, such as fluorescence emission, water solubility, high cell permeability and good biocompatibility.[1,2] However, exploration of C-Dot for two-photon imaging and sensing is hindered by the lack of fundamental understanding of their structure-optical properties relationship.

In this poster we discuss the optical properties of nitrogen-doped Cdots. The Cdots were produced by pyrolysis of citric acid in the presence of different amides. The final product is always an heterogeneous mixture of Cdots with excitation wavelength dependent emission upon one-photon excitation.[3] The emission spectrum is essentially dominated by two different emitting sites, with emission centred in the blue (440 nm) or in the green (520 nm). The most interesting observation of this study is illustrated in figure 1, where it is shown that for the same total excitation energy, the emission spectrum depends dramatically on the excitation mode. Excitation with one-photon is unspecific resulting in emission by the two emitting sites, while excitation by two-photon results in selective excitation of the green emitting site. The C-dots have TPA cross-section ranging from 200 to 1000 GM (Figure 1).

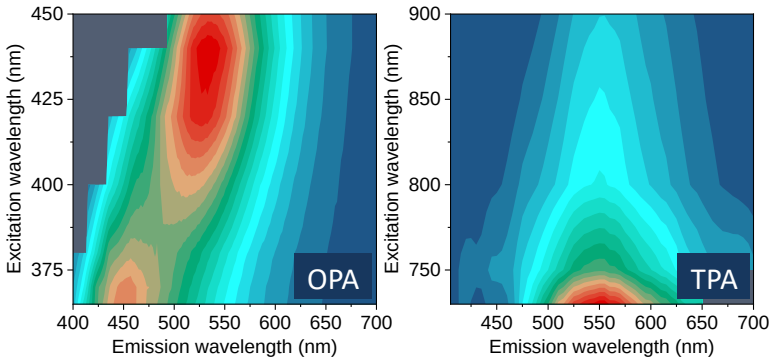

Figure 1. Excitation-wavelength dependence of the emission spectra of Cdots upon one-photon (OPEx) and two-photon excitation (TPEx).

Acknowledgements

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Mat.P5

Chemical composition of cork, phloem and xylem of *Quercus suber* trees from different provenances

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The chemical composition of cork, phloem and xylem of the cork oak (*Quercus suber* L.) from young trees of three provenances was determined using three trees per provenance. The objective was to investigate if the provenance of the seeds influences the chemical composition of the different tissues i.e. if there is a provenance effect on the chemical composition of cork, phloem or xylem.

The trees (with six years) were collected from a provenance trial located on Herdade do Monte da Fava (Santiago do Cacém), Southern Portugal. The trial was established in March 1988 with 35 provenances from Europe (France, Italy, Portugal and Spain) and North Africa (Algeria, Morocco and Tunisia) representing the cork oak natural distribution[1]. The provenances chosen for this study were from Portugal: Provenance 14 from Alcácer do Sal, Provenance 15 from Azeitão and Provenance 19 from Santiago do Cacém.

The chemical composition of cork ranged from 0.63 to 0.69% in ash, 10.4 to 12.6% in extractives, 41.0 to 43.3% in suberin, 23.4 to 24.9% in lignin and 15.5 to 16.8% in polysaccharides. Overall, these values are in the range of those reported for cork chemical analysis[2,3].

In phloem, the chemical composition ranged from 2.7 to 3.1% in ash, 3.9 to 4.6% in extractives, 37.9 to 38.4% in lignin and 47.9 to 52.1% in polysaccharides.

In xylem, the chemical composition was 1.1% in ash, and ranged from 5.0 to 5.9% in extractives, 22.6 to 24.5% in lignin and 63.8 to 67.4% in polysaccharides. Literature is scarce regarding chemical analysis of cork oak phloem and xylem; Lourenço *et al.*[3] reported values similar to those reported here.

Statistical analysis showed that there are no differences in the chemical composition of each tissue of the studied provenances.

Acknowledgements

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Mat.P6

Lignin monomeric variation during pulping and bleaching of eucalypt stumps

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Stumps are the basal part of the tree that remains in the soil after tree harvesting. In the eucalypt plantations targeted for pulping in Portugal, the eucalypt trees are harvested after 9 to 12 years and the plantations are managed as coppice systems with 2 or 3 growth cycles after which the stumps are removed before a new plantation is established. The resulting stumps are usually used for energy, but now are under consideration as feedstock for the pulp & paper industry, driven by the limited supply of raw material for pulping.

Compared with stemwood, stumps have similar content of lignin (24.8%) and holocellulose (67.0%) although a higher content of extractives (15.1%) which presence is negative for pulping since they consume liquor and bleaching reagents [1,2]. According to Gominho *et al.*[2] stumps can be delignified to produce pulps with low residual lignin and acceptable yield of 42%.

The objective of this work was to evaluate the variation of the lignin monomeric composition along the kraft pulping and bleaching of stumps. For stemwood it is known that the lignin composition is dominated by S and G units (S/G around 4)[3], and that stemwood delignification produces pulps rich in G and H units (S/G ≈ 0.5)[4], but no information exists about stumps. Therefore, kraft pulps were produced with different H-factors (400, 500, 600) and bleached with a $D_0E_0D_1E_1D_2$ sequence. The lignin monomeric composition of the initial stumps, and the residual lignin present in the three pulps (before and after bleaching) were determined by Py-GC/MS.

Stumps kraft pulps were obtained with yields between 47.4% and 48.6%, with a high residual lignin (kappa number 35-40), that increased chemicals consumption during bleaching. The S/G ratio varied from 2.5 in stumps, decreasing in the unbleachead pulps (ranging from 1.1 to 1.6), and reaching lower values in the bleached pulps (1.0 to 1.1). This work confirms the potential use of stumps for pulping and confirms the lignin reactive behavior with a preferential depolymerization of the S units under the kraft delignification conditions and further continued with bleaching.

Acknowledgements

The authors thank Altri for the stumps chips, under project “Stumps4Pulp” funded by PT2020-33/SI/2015. Support for this work was also provided by Fundação para a Ciência e a Tecnologia (FCT) through funding of the Forest Research Center (UID/AGR/00239/2013). A. Lourenço acknowledges funding from FCT through her post-doctoral grant (SFRH/BPD/95385/2013) and D.M. Neiva a doctoral grant (PD/BD/52697/2014).

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Mat.P7

Effect of Chlorhexidine Loading on the Surface Free Energy of Acrylic Reline Resins

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In order to evaluate the effect of chlorhexidine loading on surface free energy of three acrylic reline resins and compare this surface property between the resins under study, the following acrylic reline resins were evaluated: Kooliner, Ufi Gel Hard and Probase Cold. The experimental specimens were incorporated with chlorhexidine at a proportion of 1%, 2.5%, 5%, 7.5% or 10% of the acrylic resin's powder weight (w/w). The control specimens were left without drug. For surface free energy test, the mixture was placed in metal molds that, after polymerization, allowed to obtain rectangular specimens with 24×18×1 mm dimensions (n=5) for each group. Surface free energy was calculated by determining the contact angle and estimated by the Wilhelmy plaque technique. Data were analyzed using Kruskal–Wallis and Mann–Whitney tests with Bonferroni correction (α=0.05).

Statistical differences were found between groups of different percentages of chlorhexidine in total surface free energy values from Kooliner, Ufi Gel Hard and Probase Cold ($p<0.05$). However, in dispersive and polar components, only Kooliner showed differences ($p<0.05$). Statistical differences were observed among acrylic reline resins in total surface free energy values, with Ufi Gel Hard demonstrating total surface free energy values significantly higher than the other reline resins ($p<0.001$), supported by the increased values of the dispersive component.

Therefore, we concluded that the chlorhexidine loading has influence on surface free energy of 3 acrylic reline resins and the type of acrylic resin used affects the values of this property.

Acknowledgements

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Mat.P8

Development of a new protocol for the analysis of vegetable tanning materials in leathers: The study of Portuguese historic leathers

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This communication aims to report a PhD interdisciplinary work between Arts, Chemistry and Conservation of Heritage. This study is a project between Faculty of Fine Arts and Faculty of Sciences, from University of Lisbon, and it is focused in the material characterization of post-medieval historic leathers from Portuguese museum collections.

The most common European heritage leathers are vegetable tanned leathers, i.e. leathers produced with plant materials rich in tannins. These leathers have been adapted to very diverse functional, decorative or artistic need, such as footwear, saddles, book-bindings, upholstery, wall-hangings or painting support, and therefore are commonly found in art, archival, archaeological, decorative or ethnographic museum collections.

Tannins, extracted from barks, leaves, wood or galls, are polyphenolic plant secondary metabolites which have been employed for many thousands of years to convert animal skins into leather. The properties that tannins confer to the leather are as varied as the different sources from which they are extracted and, consequently, these compounds have impact in leathers stability, durability and its chemical deterioration.

Characterization of tannins in heritage leathers it is therefore of a paramount importance to comprehend leather technology, degradation susceptibility and condition. Our communication presents a new protocol, combining the evaluation of data collected from colorimetric/chemical tests, UV-Vis and FTIR spectroscopic techniques in the characterization of historic vegetable tanned leathers[1-4].

Acknowledgements

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Mat.P9

Ni^{II} and Cu^{II} *arylhydrazone complexes as catalysts in nitroaldol reaction*

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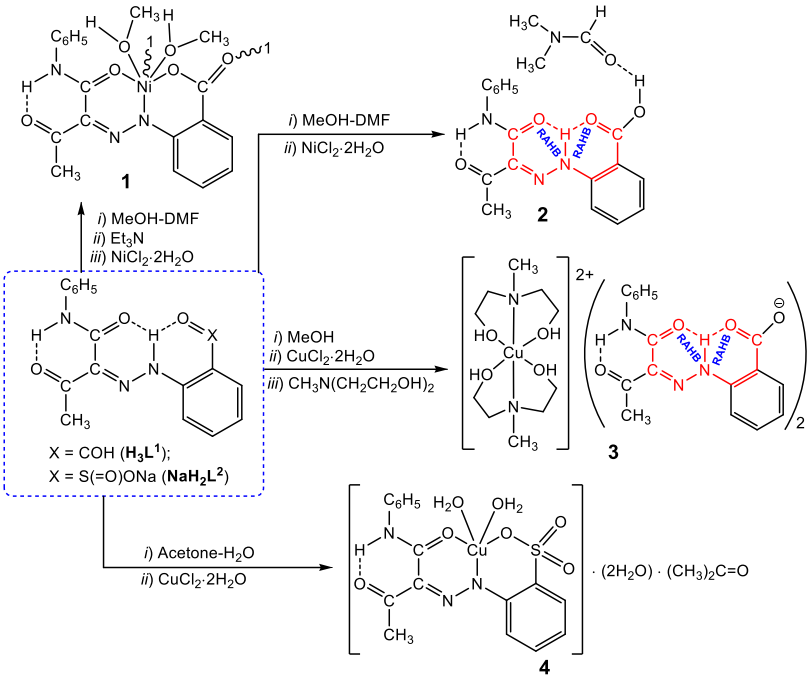
The new nickel coordination polymer $[Ni(HL^1)(CH_3OH)_2]_n$ (**1**) and co-crystal H_3L^1·DMF (**2**) were obtained by reaction of $NiCl_2·2H_2O$ with 2-(2-(1,3-dioxo-1-(phenylamino)butan-2-ylidene) hydrazineyl)benzoic acid (H_3L^1) in the presence and absence of triethylamine, respectively, in a mixture of methanol and dimethylformamide (DMF). Reaction of $CuCl_2·2H_2O$ with H_3L^1 in the presence of 2,2'-(methylazanediyl)*bis*(ethan-1-ol) (HR) in methanol yields $[Cu(HR)_2(H_2L^1)_2]$ (**3**), whereas treatment of this copper salt with sodium 2-(2-(1,3-dioxo-1-(phenylamino)butan-2-ylidene)hydrazineyl)benzenesulfonate (NaH_2L^2) in a mixture of acetone and water produces $[Cu(HL^2)(H_2O)_2]·2H_2O·\{(CH_3)_2C=O\}$ (**4**). Compounds **1**–**4** were characterized by IR and ESI-MS spectroscopies, elemental and X-ray crystal structural analyses, and tested as catalyst for the Henry reaction of aliphatic and aromatic aldehydes with nitroethane in different solvents such as acetonitrile, methanol or water. Good yields (up to 87%) and diasteroselectivities (*syn/anti* 77:23) were observed in the reactions catalyzed by **3** in water.



Scheme. Synthesis of **1**–**4**.

Acknowledgements

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Mat.P10

Synthesis, Structure and Catalytic Properties of Iron and Manganese Complexes with 4-substituted-2,2':6',2''-terpyridine and Bis{4'-(2,2':6',2"-terpyridine)}-benzene Ligands

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A series of Fe and Mn complexes with 4-substituted-2,2':6',2''-terpyridine, bearing phenyl (**L^1**), methoxyphenyl (**L^2**), nitrophenyl (**L^3**), furyl (**L^4**), 1-naphthalene (**L^5**), or 2-naphthalene (**L^6**) groups, and 1,4-bis{4'-(2,2':6',2"-terpyridine)}-benzene, 1,3-bis{4'-(2,2':6',2"-terpyridine)}-benzene have been prepared starting from the respective metal chlorides and nitrates, then characterized by IR, elemental analysis and single crystal X-ray diffraction. The compounds of iron show preferable coordination of two ligand molecules to the metal centre, as illustrated by the complex $[Fe^{II}(L^2)_2][Fe^{III}_2OCl_6]$ (**1**) (Figure 1a). In contrast, the complexes of manganese reveal the coordination of one ligand molecule to the metal centre, as illustrated by the complex $[Mn^{II}(L^3)Cl_2]$(**2**) (Figure 1b). The complexes with terpyridine ligands have great catalytic potential in highly selective oxidation of inert C–H bonds with dioxygen and peroxides as terminal oxidants.[1] The catalytic studies disclosed pronounced activity of $[Fe(L^2)_2][Fe_2OCl_6]$ and $[Fe(L^4)_2][Fe_2OCl_6]$ in the catalytic oxidation of alkanes with H_2O_2. Oxidation of cyclohexane afforded cyclohexanol and cyclohexanone as the main reaction products. The product of the C_6 ring cleavage, hexanedial, was detected in amount comparable to that for the main products when using the acetic acid promoter.

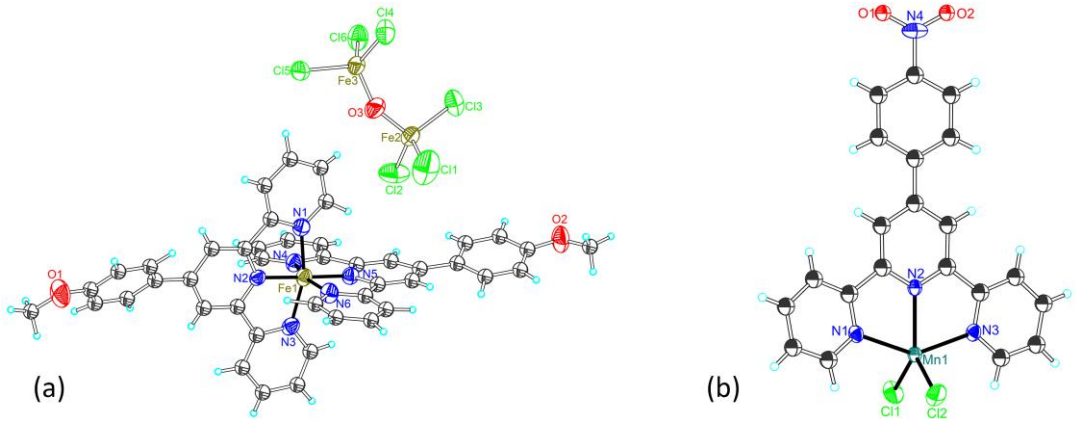

Figure 1. The molecular structures of the **(a)** complex **1** and **(b)** the complex **2**.

Acknowledgements

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Mat.P11

Solvent Impact on Polymorphism in Sulfonamide Compounds

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Polymorphism, the ability of a compound to crystallize in more than one solid form, has a significant impact on the properties of that compound (e.g. melting point, solubility, colour, morphology). Thus, although consisting of the same molecular unit, different polymorphs should be regarded as different materials. The control of polymorphism requires a good understanding of the crystallization conditions (e.g. solvent, solution concentration, cooling or evaporation profiles) and pathways favouring the formation of specific crystal forms. Very little fundamental knowledge still exists, however, on the mechanisms involved in the formation of crystals from solution, in particularly at early stages. For this reason, trial and error approaches still play a significant role in the set-up of crystallization processes.

In this work, a sulfonamide family of compounds was used as model (Figure 1) to study the solvent effect on their crystallization from solution. This was the first family discovered with antibacterial properties. These compounds were selected because they are prone to polymorphism, the reproducible preparation of specific crystal forms was never achieved, and conflicting results regarding their crystallization are often found in the literature.[1-3]

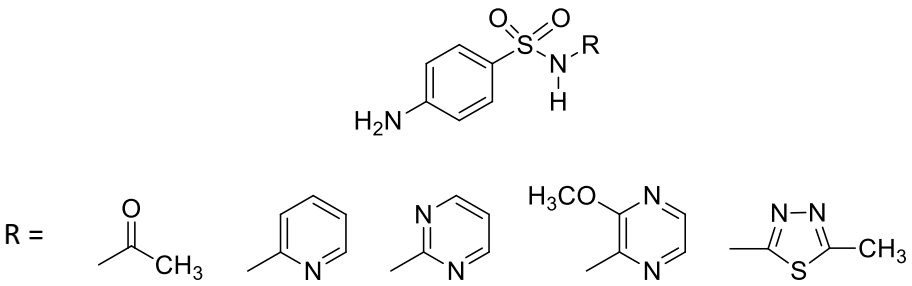

Figure 2. Molecular structure of the sulfonamides studied in this work.

Acknowledgements

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Mat.P12

Hydrosoluble Copper Complexes for Catalytic Multi-component Azide-Alkyne Cycloaddition in Homogeneous Aqueous Medium Leading to 1,2,3-Triazoles

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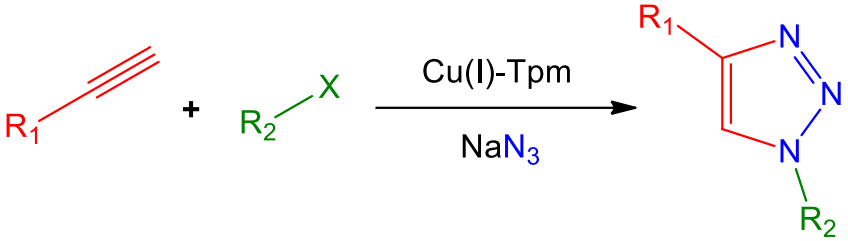
The Huisgen 1,3-dipolar cycloaddition[1] of alkynes and azides, to produce the corresponding 1,2,3-triazoles, is classified among the top reactions fulfilling the click criteria. Copper catalyzed azide–alkyne 1,3-dipolar cycloaddition (CuAAC), first reported in 2002 (Scheme 1)[2,3] became one of the most useful click reactions, as it represents an excellent synthetic tool for 1,4-disubstituted 1,2,3-triazoles and enables a large variety of applications in molecular biology, medicinal chemistry, polymers and materials science.[4]



Scheme 1.

As part of our interest on new hydrosoluble complexes, a set of copper (I & II) complexes were prepared using the water soluble ligands 3,7-diacetyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane (DAPTA), 3-(2-sulfonic phenylhydrazo) acetoacetamide (SPA) and tris(pyrazolyl)methanesulfonate (Tpms). The catalytic activity of the complexes was investigated for the one-pot multicomponent Huisgen cycloaddition reaction in aqueous media under microwave irradiation to produce the corresponding 1,4- or 2,4-disubstituted-1,2,3-triazoles.

Acknowledgements

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Mat.P13

Spectroscopic and Magnetic investigation of symmetric and asymmetric binuclear hydrazide metal complexes

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In the last few years, the need to produce smaller information devices increased and has attracted a large number of research groups from across Europe to tackle this need. Their effort led to the production of materials that store information at the molecular level with increased capacity. A promising phenomenon for information storage is spin crossover (SCO). SCO candidate compounds can be found among a limited group of $3d^4$–$3d^7$ transition metal ions, the most common being Fe(II), Fe(III) and Co(II). Fe(III), with its advantageous redox stability, is a good candidate for fabrication of SCO materials, an area towards which research has been moving.[1]

Among the ligands known to have the right ligand field strength to promote SCO, hydrazide derivatives are a class of versatile candidates. These compounds are easy to synthesise and have the option of ligand derivatization, thus allowing to fine-tune the SCO properties.

Here we report the synthesis and characterization of both symmetric and asymmetric hydrazides ligands with different halogen substituents on the phenolate ring. These ligands were reacted with Fe(III) and Co(II) to form binuclear complexes with different aromatic environments. The magnetic profiles of the new compounds were determined by SQUID magnetometry and the ligand effect studied.

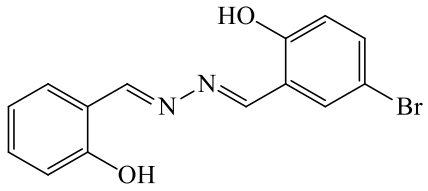

Figure 1. Molecular structure for symmetric ligands.

Acknowledgments

The authors thank Fundação para a Ciência e Tecnologia for financial support through UID/MULTI/00612/2013 and PTDC/QEQ-QIN/3414/2014.

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Mat.P14

Particle size effect on the magnetic behaviour of Fe(III) Schiff-base complexes

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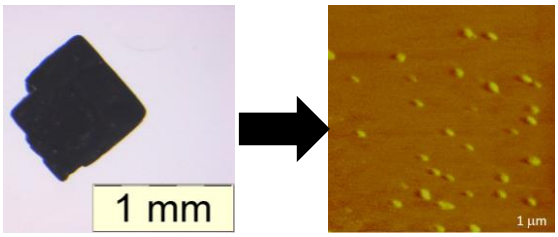
Technological advances have been pushing the limits of chemistry for the last years towards more efficient and multifunctional molecules and materials. A phenomenon that shows great promise in molecular electronics is spin crossover (SCO). This switching can be harnessed to develop materials with a wide range of possible applications such as memory storage or sensing nano-devices.[1] Halogen derivatised SCO molecules are of great interest as they can interact with neighbouring molecules through either halogen or hydrogen bonds and additionally they can be modified through substitution or coupling reactions conferring additional properties and high versatility to the SCO molecules.[2] The synthesis of new materials using SCO complexes allows their application on spintronics with the particle size affecting their magnetic behaviour.[3]

Here we report the synthesis and characterisation of magnetic micro- and nano-particles with an Fe(III) metallic centre coordinated to tridentate (N_2O) halogen derivatised Schiff-base ligands, through a micellar method. Several studies such as AFM and SQUID magnetometry were performed to investigate the size effect between the reported bulk crystals[4] and the new particles with reduced size.



Acknowledgements

The authors thank Fundação para a Ciência e Tecnologia for financial support through UID/MULTI/00612/2013, PTDC/QEQ-QIN/3414/2014 and COST Actions CM1305 and CA15128. P.N. Martinho thanks FCT for financial support (SFRH/BPD/73345/2010).

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Mat.P15

Silica-polymer nanoparticles for coating application

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Hybrid nanoparticles have been studied for many applications, including coating applications, due to the low-cost materials and well-controlled excellent properties.[1] Here we described some of our work developed towards the fabrication of hybrid silica-polymer nanoparticles containing a silica and a polybutyl methacrylate shell. Encompassing in a single vehicle the properties of the nanofillers (silica nanoparticles) and of the polymer shell, these hybrid materials shall provide the mechanical strength from monodisperse silica nanoparticles and flexibility, transparency and hydrophobicity from the polymer shell.[2] The polymer chain will be later decorated with groups that react reversibly in aqueous dispersions of the nanoparticles (dynamic covalent chemistry), allowing error-correction during self-assembling, but crosslink the nanoparticles in the dried film.

The silica nanoparticles were prepared by adaptation of the Stober method[3] and characterized by dynamic light scattering (DLS) and scanning electron microscopy (SEM), confirming diameters of ≈150 nm with a low size dispersity. The polymer shell was obtained by emulsion polymerization of butyl methacrylate that grew from previously surface-modified silica nanoparticles.[4] The surface was modified with methacrylate-alkoxysilane quantified by ^{1}H NMR and the shell presence was confirmed by the increased size observed by DLS and SEM. The water dispersion was applied onto glass substrates and a very uniform film was obtained, which might be used for coating applications.

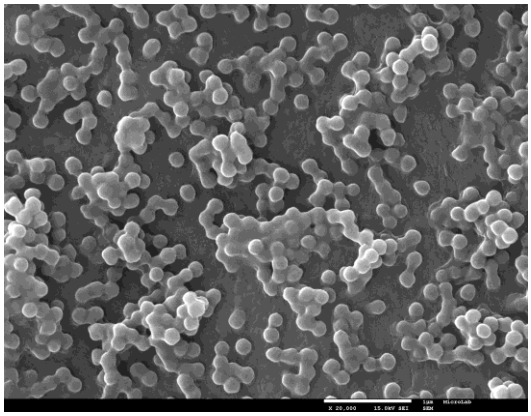

Figure. SEM of silica-polymer hybrid nanoparticles.

Acknowledgements

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Mat.P16

Synthesis, Crystal Structures and Catalytic Properties of Homo- and Heterometallic Diethanolamine-based Complexes

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Synthesis of coordination compounds with close-packed molecular cores and sophisticated crystal structures is an important topic since such complexes have recognized applications as magnetic and catalytic materials[1]. Following our interest in the preparation of homo- and heterometallic complexes with N,O-donor ligands[1,2] we have explored the synthetic systems containing N-*tert*-butyldiethanolamine (H_2*t*BuDea) and N-butyldiethanolamine (H_2*n*BuDea) ligands.

The interactions of zerovalent metal and/or metal salt with H_2*t*BuDea (for **1**, **3** and **4**) or H_2*n*BuDea (for **2**) and pivalic acid (HPiv) (for **3** and **4**) in non-aqueous solutions lead to the formation of the novel homometallic complexes $[Cu_2(HtBuDea)_2(OAc)_2]$ (**1**) and $[Cu_2(H^nBuDea)_2Cl_2]\cdot 0.5H_2O$ (**2**), as well as the heterometallic compounds $[Cu^{II}_4Mn^{III}_2(OH)(Piv)_4(tBuDea)_4Cl]$ (**3**) and $[Cu^{II}_4Fe^{III}_2(OH)(Piv)_4(tBuDea)_4Cl]\cdot 0.5CH_3CN$ (**4**). X-ray analysis shows that **1** and **2** are based on the same binuclear $\{Cu_2(\mu\text{-}O)_2\}$ core. In **1** the molecules are joined together forming H-bonded 1D chains (Figure 1), while in **2** the neighboring pairs of molecules are linked into tetranuclear supramolecular aggregates. The crystal structures of **3** and **4** are based on the hexanuclear $\{Cu^{II}_4M^{III}_2(\mu\text{-}O)_7(\mu_3\text{-}O)_2\}$ core (M = Mn, Fe), which can be seen as combination of two $Cu^{II}_2M^{III}$ $(\mu\text{-}O)_2(\mu_3\text{-}O)$ fragments linked by three bridging oxygen atoms. The obtained compounds were tested as catalysts in the reaction of amidation of cyclohexane with benzamide in benzene medium.

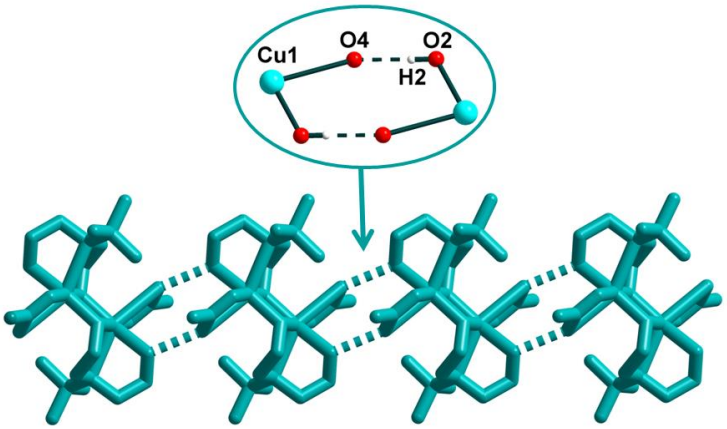

Figure 1. The representation of the supramolecular chain in **1** with the enlarged fragment showing H-bonding interactions between bimetallic units.

Acknowledgements

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Mat.P17

Micronization of Calcium Acetate from a Food Residue Using Supercritical Antisolvent Precipitation

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The food industry generates annually thousands of tons of egg shells around the globe. This important source of calcium carbonate has called the attention of the chemists for many applications in different areas[1]. In the catalysis perspective this raw material can be a source of calcium oxide, which can be used as a heterogeneous catalyst to produce, for example, biodiesel. On the other hand, one of the crucial points for the improvement of the catalysts is the nanoarchitecture of the particles. A way to achieve this objective is the use of processes with supercritical fluids.

The supercritical antisolvent process (SAS) has been used to produce micro or nanoparticles of different compounds for a wide range of applications[2]. The study of the SAS experimental conditions (temperature, pressure, concentration and flow rate ratio) is important to optimize the size and morphology of the obtained particles. The aim of this work is to produce nanoparticles of calcium oxide from egg shells using the SAS micronization process. In order to attain this purpose, the calcium carbonate of the egg shells was derived into calcium acetate, which was then successfully micronized by the SAS process. The micronized calcium acetate and the calcium oxide, obtained by the calcination of the former, were evaluated in terms of morphology and particle size by scanning electron microscopy analysis.

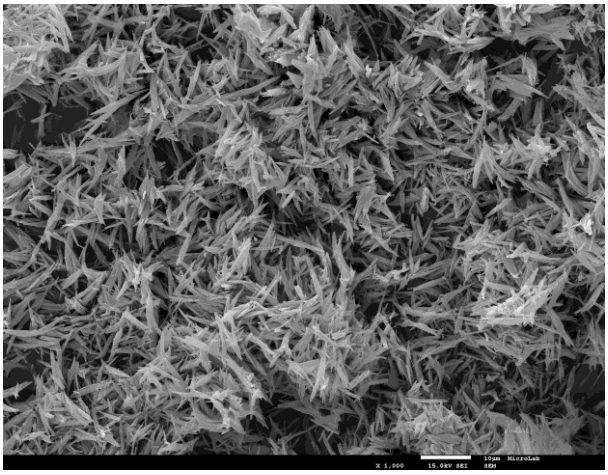

Figure 3. Calcium Acetate micronized from egg shells, at T = 313 K and P = 100 bar.

Acknowledgements

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Mat.P18

Sensors Based on 1D and 3D Iron(II) Coordination Polymers

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Spin crossover (SCO) complexes show magnetic responses to subtle external stimuli, e.g., temperature, light, pressure and guest molecules, involving simultaneously changes in colour, dielectric constant or electrical resistance. These characteristics make them potential candidates for the detection of different organic and inorganic compounds, working as sensors. Iron(II) coordination polymers and their analogues are among the most known and well-studied for practical applications as SCO compounds.[1,2]

Due to the importance of chirality in biological processes there was an increase in the development of chiral zeolites and related porous solids over the past few decades. There are numerous examples of porous metal-organic coordination networks reported in recent years, but chiral coordination polymers synthesized from chiral components are much less explored. Herein we present the synthesis and characterization of some asymmetrical ligands using different chiral amines (Figure 1).

The study of the magnetic properties of these materials using SQUID is also explored. Using different ligands with distinct characteristics such as polarity, size and chirality we can compare the properties of the structures formed and debate about their application in the fields of pharmaceuticals, biology, chemistry and engineering.

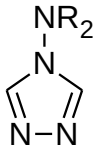

Figure 1. General structure of the ligands (R=chiral groups).

Acknowledgements

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Mat.P19

Nitric oxide-releasing porous materials and their potential biological effects

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Nitric oxide (NO) plays a wide range of physiological and pathophysiological functions (i.e. cardiovascular homeostasis, immune response to infection, wound repair, tumor biology and pathology) and the use of NO-carrying and release matrices for therapeutic benefit has been proved an excellent alternative to conventional drugs[1]. Nevertheless, due to NO short half-life, rapid diffusion and its high reactivity, it is challenging to establish suitable methods for delivering NO gas in a controllable manner. The design of new NO donors is thus required and, in recent years, a novel approach using nanoporous materials has been demonstrating its superiority regarding the existing donors due to its high NO storage capacity, safe storage and a controlled delivery of pure NO[2]. However, studies concerning fundamental issues such as toxicity and stability of the delivering materials, as well as their effectiveness to regulate biological processes with the delivery of NO are still very limited. In this work, titanosilicates (ETS-4 type and ETS-10 type) and clay-based materials were evaluated in terms of toxicity (using primary cells), stability and NO release under biological conditions. Moreover, it was investigated for the first time the potential of these new NO donors in the regulation of two relevant biological functions: (1) mitochondrial respiration and (2) cell migration.

ETS-4 demonstrated to be the most promising material, combining good biocompatibility, stability and slow NO release. ETS-10 and ETAS-10 showed the best biocompatibility and, in the case of clay-based materials, CoOs is the less toxic and the one that releases higher NO. Moreover, the NO released by ETS-4 actively regulate the cells O_2 consumption by varying the material concentration and promote the cell migration of more 8% than the controls after 6 h, being this last effect a promising indication for the potential use of these new donors in wound healing therapy.

Acknowledgements

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Mat.P20

Ligand and spin state effects in Mn(III) and Mn(IV) Complexes

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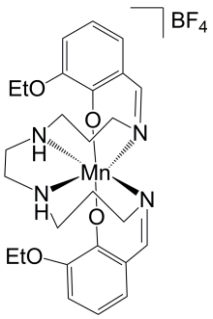
Mn(III) Schiff-base complexes have been widely developed because of their promising applications. These compounds have been reported as displaying single molecule magnet behaviour or spin-crossover phenomena, which can be used in storage devices and quantum computing.[1]

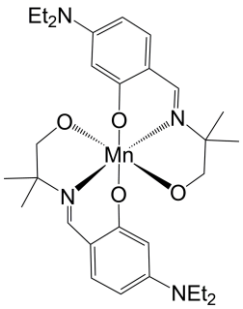
When displaying single molecule magnet behaviour, the most important properties are both the magnetization relaxation (τ_0) and barrier (Ueff). The former should be as lower as possible and the latter as higher as possible to avoid the loss of information. This magnetization barrier can be enhanced if there is an axial distortion (D<0) on the dz^2 orbitals providing a zero-field splitting that can be observed in Mn(III) high spin state (S=2) due to the permanent Jahn-Teller effect.

When displaying spin-crossover behaviour a switch between the d-electrons on the Mn(III) orbitals can occur and this can be promoted by temperature changes, light induction, etc.[2]

We report a series of Mn(III) and Mn(IV) complexes with N_4O_2 and N_2O_4 donor atoms and study their magnetic behaviour. The ligands were obtained by reacting three different amines with four different aldehydes to form both hexadentate and tridentate Schiff-base ligands.

The Mn(III) and Mn(IV) complexes were formed reacting $MnCl_2{\cdot}4H_2O$, NH_4BF_4 and the different ligands in air. All compounds were characterized by FTIR, UV-vis, NMR, cyclic voltammetry, elemental analysis and X-ray crystallography. Magnetic measurements on all compounds were also performed by SQUID magnetometry.





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Mat.P21

Steam activation of hazelnut and almond shells chars

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Even though the number of experimental procedures described in the literature to prepare activated carbons is quite high, for industrial purposes steam activation is by far the most used process. The same can be said regarding the biomass precursors, since wood and coconut shell have the highest industrial importance, in contraste with an enormous set of biomass considered in academic studies. The selection of the percursor is determined by several parameters, among which the quantity available is one of the most important. In this context, in the present study we consider hazelnut (HN) and almond nut (AN) shells as carbon percursor since their world annualy production reached 743 and 3200 kton in 2016, respectively[1]. The materials were obtained by a two-step procedure carbonization+steam activation, with 55% (HN) and 35% (AN) burn-off on the latter process. The properties of the lab-made samples were compared with those of two carbons commercialized for water treatment purpose. The N_2 adsorption results (Figure 1) show that both lab-made samples are microporous carbons, being the characteristics of the AN derived sample close to those of carbon CP.

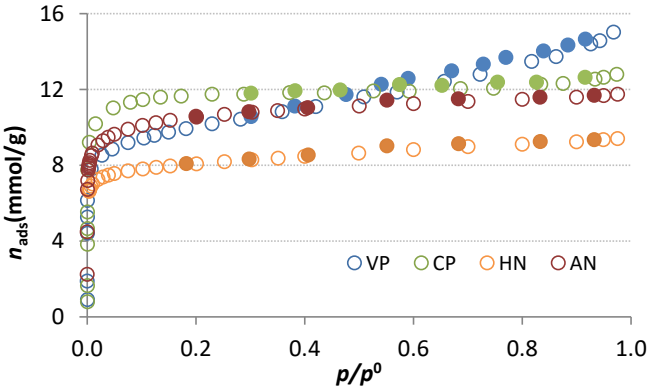

Figure 1. N_2 adsorption isotherms on hazelnut (HN) and almond nut (AN) shells chars derived carbons and commercial samples (CP and VP).

To have a first indication about the ability of the lab-made carbons as adsorbents of organic compounds in aqueous media, they are being applied for caffeine adsorption from an aqueous inorganic matrix that simulates the inorganic composition of a real wastewater effluent.

Acknowledgements

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Mat.P22

Solvent Mediated Control of 5-Hydroxynicotinic Acid Molecular Conformation in the Crystalline State

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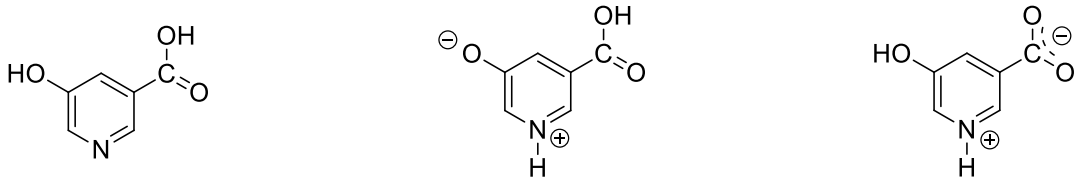
Crystallization from solution is the most widely used method to obtain and purify compounds. Nevertheless, despite being used by man for millennia, there is still little understanding on how molecules associate in solution to form crystalline materials. A particular unexplored aspect within this scope is how tautomeric equilibria in solution can influence the crystallization of molecules in a particular conformation. The hydroxyl derivatives of nicotinic acid (which have biological importance and ample applications, including the manufacture of pharmaceuticals, herbicides and insecticides), are very convenient models for these studies, since they exhibit competing tautomeric forms.[1]

In this work the crystallization of 5-hydroxynicotinic acid (5HNA; Figure 1) from a protic (water) and an aprotic (DMSO) solvent, was used as a model to investigate possible relationships between the dominant molecular conformation in solution and in the corresponding crystallized material. Single crystal X-ray diffraction analysis showed that crystallization of 5HNA from water and DMSO led to a hydrate and a solvate, respectively, of 1:1 stoichiometry. Furthermore, the conformation adopted by the molecule in the hydrate is zwitterionic (Zwitterion 2 in Figure 1) and in the DMSO solvate is hydroxylic (Hydroxy in Figure 1) which, according to NMR evidence, correspond to the predominant tautomers found in the corresponding mother solutions. This work, therefore, suggests that the formation of hydrates and solvates, where the memory of solution is not completely lost, may provide a mean to control the molecular conformation in crystalline materials.



Hydroxy Zwitterion 1 Zwitterion 2

Figure 1. Tautomeric forms of 5-hydroxinicotinic acid.

Acknowledgements

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Mat.P23

Experimental and Theoretical Study of Low Temperature Solid-Solid Phase Transition in 4'-Hydroxyacetophenone Polymorphs

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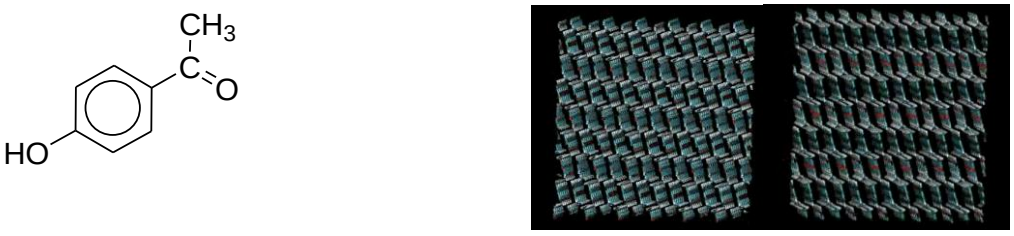
Polymorphism, the ability of a substance to crystallize in more than one lattice arrangement, is currently a major concern for the manufacture of organic products, since each crystal form can exhibit significant differences in physicochemical properties (e.g. fusion temperature, solubility/dissolution rate). For this reason, each polymorph corresponds, in fact, to a different material. To control polymorphism it is extremely important to understand the stability relationships between different polymorphs under specific pressure-temperature conditions, so that transitions to unwanted phases can be prevented during production and storage of polymorphic materials.

4'-Hydroxyacetophenone (HAP; Figure 1a) is a compound with significant commercial applications and additional potential end uses. Two polymorphs of HAP have been reported up to now, which are related by an enantiotropic solid-solid phase transition that occurs at ~303 K.[1,2] Recent adiabatic calorimetry and neutron diffraction studies revealed a new phase transition in both polymorphs at ~79 K, which, according to the structural results, does not involve a modification in the crystal packing of the two polymorphs.[3] In this work, molecular dynamics simulations were used to investigate the nature of this transition. The obtained results suggest that the observed changes are related with an order-disorder transition, and the existence of a modulation effect below 79 K (Figure 1b).



(a) (b)

Figure 1. (a) 4'-Hydroxyacetophenone (HAP); (b) Molecular dynamic snapshots, showing a modulation effect on the crystal structure of HAP form I at 10 K.

Acknowledgements

This work was supported by projects FCT UID/MULTI/00612/2013 and LISBOA-01-0145-FEDER-028401, and by a Post-Doctoral grant (SFRH/BPD/101505/2014) awarded to C.E.S. Bernardes. We also acknowledge COST Action CM1402.

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Mat.P24

Electrochemical properties of Fe(III) catalysts for alcohols oxidation

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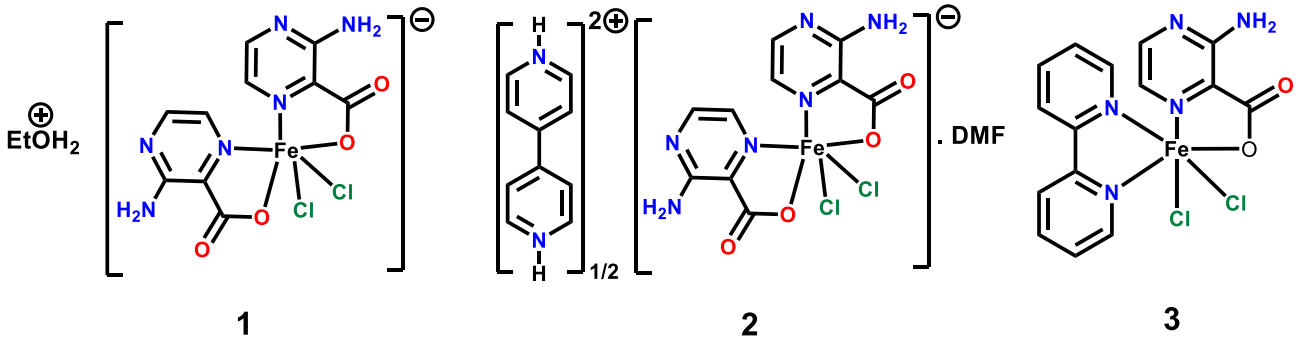
The electrochemical behaviours of complexes **1**-**3** (Figure 1) as well as of 3-amino-2-pyrazine-carboxylic acid, doubly protonated 4,4'-bipyridine [$(H_2bipy)Cl_2$] and 2,2'-bipyridine, were investigated by cyclic voltammetry (CV) and controlled potential electrolysis (CPE), at a platinum working electrode at room temperature in a 0.2 M [$^nBu_4N$][BF_4]/NCMe solution.



1 **2** **3**

Figure 1.

Complexes **1**-**3** exhibit a first single-electron (as measured by CPE) reversible cathodic wave at *ca*. 0.06 V *vs*. SCE, assigned to the Fe(III) to Fe(II) reduction. A second irreversible cathodic wave in the -0.62 to -1.12 V *vs*. SCE range is also observed, which involves the L^- ligand.

The electrochemical study provided a valuable tool to establish the structures of complexes **1** and **2**. Moreover, the very similar catalytic activities found for the MW-assisted oxidation of 1-phenylethanol to acetophenone catalyzed by **1**–**3** are in accordance with their very similar reduction potentials as detected by cyclic voltammetry.

Acknowledgements

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Energy

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E&E.PL

Structure and catalytic activity of rhodium complexes in hydroformylation reaction

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The exceptionally high catalytic activity of rhodium complexes in the hydroformylation of unsaturated compounds is well known. Today, despite of high price, rhodium is a metal of choice in industrial installations, producing millions tons of C_4 aldehydes from propylene. For economic reasons, not only high productivity but also high selectivity towards linear aldehydes is expected in these systems. Many parameters, such as pressure, temperature or kind of solvent should be optimized to get the desired aldehydes in high yield. However the fundamental role is played by phosphine ligands which coordinate to rhodium and influence on the structure of the catalytically active hydrido-complexes. In most cases, π-acceptor phosphine ligands favor formation of linear aldehydes (l) over branched (b) isomers, promoting achievement of high l/b values.

N-pyrrolylphosphines, $P(NC_4H_4)_3$, $PPh(NC_4H_4)_2$ and $PPh_2(NC_4H_4)$, present a good example of π-acceptor ligands very efficient in hydroformylation when used with $Rh(acac)(CO)_2$ precursor. Thus, in hydroformylation of 1-hexene, C_7 aldehydes were obtained with high yield and l/b ratio over 25. Similarly, excellent selectivity in hydroformylation of propene and 1-butene was noted.

The studies of the reaction mixture resulted in identification of hydrido-rhodium complexes of the type $HRh(CO)L_3$, which were synthesized and characterized. These complexes used without any additional ligands very efficiently catalyze hydroformylation of different unsaturated substrates, such as alcohols, dienes or esters. However, at the presence of chiral BINAP phosphine, hydrido-rhodium complexes form active systems for asymmetric hydroformylation. In these mixed systems N-pyrrolylphosphine facilitated significantly the reaction rate, while chiral phosphine influenced on the high enantioselectivity.

Interestingly, catalytic activity of rhodium complexes with N-pyrrolylphosphines increased at the presence of water, despite of the fact that phosphines are hydrophobic. Most probably, intermolecular interactions, such as hydrogen bondings, are responsible for the observed selectivity increase to the normal aldehyde.

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E&E.IOC1

Enzymatic and affinity biosensors for environmental applications

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Electrochemical biosensors have a tremendous potential to become cheap, fast and reliable analytic tools in clinical, industrial and environmental analysis, eliminating the need of expensive equipment, highly trained personnel and time-consuming steps[1]. Effective bio-functionalization strategies and biocompatible materials are thus required to ensure the maintenance of the biological performance, under appropriate operational conditions[2]. Such goals may be achieved by mimicking the natural environment of biomolecules, to avoid denaturation and get high selectivity of detection.

In this work, we explore distinct surface chemistry strategies to build biosensing interfaces with optical or electrochemical transduction. First, the construction of universal affinity sensors targeting the detection of small pollutant molecules (e.g. toxins), is presented. To this end, immobilization of antibodies or more stable and cheap DNA aptamers was carried out on gold surfaces, using alkanethiol self-assembled monolayers or *in-situ* formation of dithiocarbamates[3]. Secondly, we propose the use of biomimetic polymers on carbon surfaces to prepare Laccase biosensors for the sensitive electrochemical detection of phenolic compounds. Polydopamine (PDA) films[4] rely on aminocatechol moieties to mimic the high adhesion of mussels to wet surfaces, and their properties (e.g. thickness, wettability, electroactivity) can be tuned by changing the polymerization method (chemical, electrochemical). The incorporation of metal or metal oxide nanoparticles on the modified gold/carbon surfaces was also explored as a mean to enhance the sensitivity of the optical[5] and electrochemical detection signals[6]. The information provided from several surface sensitive techniques, namely atomic force microscopy, ellipsometry, surface plasmon resonance and electrochemical methods is determinant to correlate morphology, thickness, biomolecule surface density to the analytical performance of the modified surfaces.

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E&E.IOC2

Role of a WWTP as a reducing system of specific pollutants in the aquatic environment: A short overview

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The role of wastewater treatment plants (WWTP) in the environmental quality of water receiving bodies is significant and critical. Municipal wastewaters are considered an important source of organic and inorganic contaminants to the aquatic environment. The majority of industrial effluents are sent to municipal WWTP for treatment along with the domestic sewage. The majority of WWTP are designed primarily to treat domestic wastewater and activated sludge plants employ the biological treatment processes to facilitate nitrification, rather than to deal with the range of substances likely to be present in industrial waste[1]. On the other hand, urban wastewater may contain several compounds, coming from anthropogenic activities, resulting not only from point source contamination, but also from diffuse origins that can have potential critical impacts in the aquatic environment. The composition of municipal wastewaters is very complex containing a large number of regulated and non-regulated contaminants, among them endocrine disrupting compounds, for instance, pharmaceuticals compounds, and also metabolites of compounds related with illegal drugs. Pharmaceutical compounds are well characterized in the point of view of their clinical effects, but in what concerns their behaviour in the different environmental compartments, including the role played by the WWTP in their removal from waste water[2], specific knowledge are only in the beginning. WWTP can also play a role in epidemiological studies concerning illicit performing studies of sewage epidemiology that covers information concerning drugs consumption, studies the occurrence and fate of illicit substances in sewer systems, and estimates the community drug use, drug metabolism[3-4]. Wastewater treatments can eliminate or remove a substantial amount of these products, but there may still be significant concentrations of them in effluents discharged into surface water bodies. Different removal rates can be observed for various substances undergoing the same treatment. Therefore, a wastewater management has a crucial role in sustainable development, and, for this reason, an integrated management of wastewater treatment plants (WWTP) is important. Reducing concentrations of trace organic chemicals with the potential to induce ecological effects is one of the target of the future treatments technologies in WWTP. The next step can be advanced treatments, controlling the continuous release of pollutants and the associated chronic effects in the environment, but those options must be integrated in a holistic approach taking in account technical feasibility, social impact and economic sustainability.

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E&E.IOC3

Synthesis and Toxicity of Furan Based Biorenewable Resources

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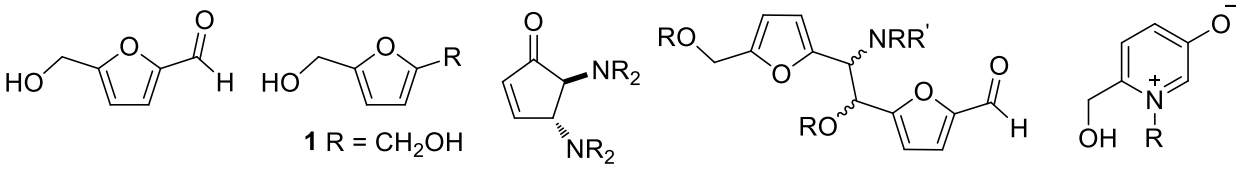
Due to the reduction of fossil resources for energy consumption and platform chemicals for different purposes, several building blocks derived from renewable resources such as ethanol, glycerol, lactic acid, furfural, succinic acid, levulinic acid, are already in use or considered with potential importance in the near future.[1] Among them, 5-hydroxymethyl-furfural (HMF) has been considered a very promising intermediate building block due to its potential rich chemistry that allows different transformations such as to biofuels, polymer monomers, levulinic acid, adipic acid, caprolactam and caprolactone and many other more specific molecules.[2] In line with our interest in the valorization of natural resources, will be described recent achievements from this laboratory on the transformation of HMF and furfural to several building blocks such as via Cannizzaro reaction **1,2,** amine condensation-rearrangement-cyclization **3,** homo Mannich reaction of trienamine/iminium-ion pair **4**, *N*-alkyl-pyridinium salts **5**, oxidation and Friedel-Crafts reaction by taking advantage of the reactivity of the furan core.[3] In addition, will be presented some biological activity of the synthesized heterocycles and selection guidelines for human and environmental exposure of furfural-related compounds.[4]



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E&E.O1

One-pot synthesis of nitrogen and phosphorus compounds from biomass resources

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Conversion of biomass resources into value-added products provides a sustainable alternative to the current chemical industry that is predominantly dependent on fossil fuels. However, these processes typically afford chemicals containing only C, H, and O. There is growing interest in the production of renewable chemicals that contain other heteroatoms, such as N and P atoms, but its availability in the biomass resources can limit the productivity of these compounds. For these reason, development of alternative strategies including the conversion of renewable O-containing chemicals into their nitrogen- and phosphorus-analogues can offer viable pathways for a more sustainable chemical and pharmaceutical industries.

This communication describes the first methodology for the one-pot conversion of mono- and polysaccharides into furfurylamines and α-aminophosphonates catalyzed by $HReO_4$.[1,2] These *one-pot three*-reaction and four-*reaction processes* allow the conversion of xylose and xylan, respectively, into a large variety of secondary and tertiary amines and also into α-aminophosphonates with good overall yields and chemoselectivity (Figure 1).

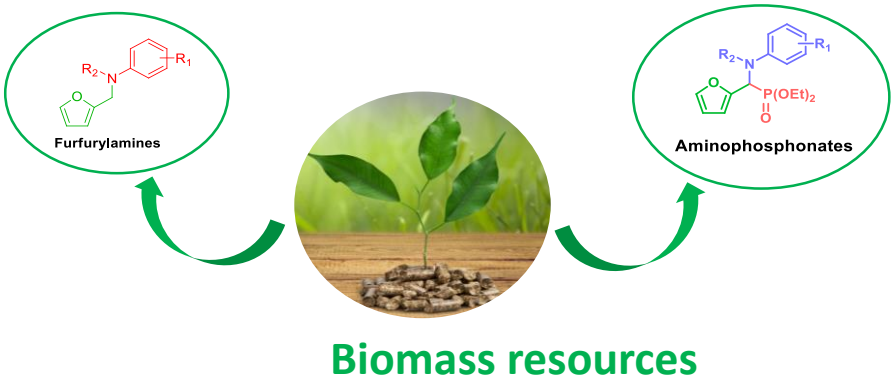

Figure 1. One-pot synthesis of nitrogen and phosphorus compounds from biomass resources.

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E&E.O2

Photocatalytic removal of industrial dyes using semiconducting nanoparticles supported on textile fibers

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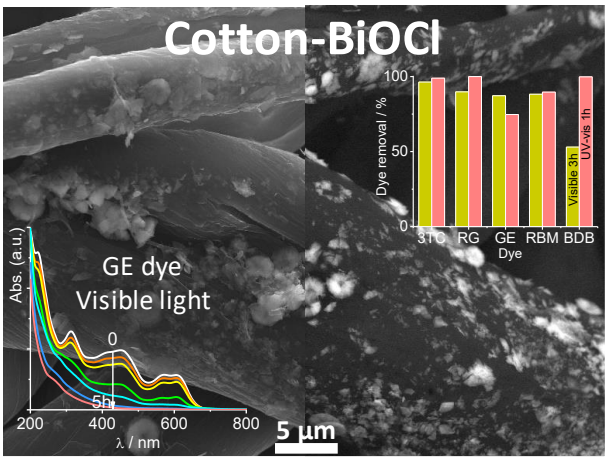
The decontamination of wastewater by advanced oxidation processes (AOPs) has been in the scope of recently published literature. The photocatalytic degradation of pollutants is one of such processes which is initiated by photolysis using UV-vis or visible light irradiation[1-3]. Among the nanocatalysts used for this purpose, TiO_2 nanoparticles are the most widely studied, however its wide bandgap and recombination rate limits its applicability[1]. Therefore, novel catalysts, composites and hybrid materials displaying small bandgap, low recombination rate and activity under visible light are highly desirable. To do so, several approaches have been used, including combination of catalysts, sensitisation and doping[2]. The use of powder catalysts has disadvantages, such as catalyst loss and release to the environment and pressure decrease in flow systems[1,3].



In this work, the synthesis of the semiconductor catalysts, bismuthoxychloride (BiOCl) and/or bismuth sulphide (Bi_2S_3), and its attachment to textile fibers surface was successfully performed *in situ*, which was confirmed by XRD, DRS, EDS and SEM analysis. The spontaneous sensitisation of the BiOCl by light irradiation decreases its bandgap energy (from 3.4 to 0.9 eV) and extends its absorption to the visible range. Bi_2S_3 being a naturally low bandgap semiconductor (1.3 eV) absorbs in the whole visible and UV range. Both nanomaterials show high ability to remove a range of collagen dyes by adsorption (Bi_2S_3) and photodegradation (BiOCl). Moreover, the BiOCl sensitisation allows the use of the BiOCl-modified cotton fibers under visible light irradiation, broadening the application environment and decreasing operation costs. The nanocatalysts were swiftly recovered when attached to the fibers surface. Therefore, the use of supported semiconductor catalysts proved to be a promising and suitable approach for future wastewater treatment technologies to be applied for pollutants removal by combined adsorption/photodegradation methodologies with advantage on catalyst recovery.

Acknowledgements

The authors gratefully acknowledge the financial support from Fundação para a Ciência e a Tecnologia (FCT) [SFRH/BPD/77404/2011, PEst-OE/QUI/UI0612/2013 and UID/MULTI/00612/2013].

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E&E.O3

Novel C-dots/titanate nanotubes composite materials for pollutants photocatalytic degradation

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Aiming to develop advanced materials with enhanced optical and photocatalytic properties for the photodegradation of emergent pollutants, in particular pharmaceuticals and personal care products (PPCPs), titanate nanotubes (TNTs) modified by carbon dots (C-dots) were successfully prepared by a swift synthesis method developed by our group[1,2] and using cork industry wastewaters as carbon source[3]. The influence of several experimental parameters, like TNT/C-dots ratio, on the final material properties was carefully analysed.

The structural, microstructural, morphological, and optical properties of the new hybrid nanomaterials were studied by XRD, TEM, FTIR, PL and UV-Vis diffuse reflectance spectroscopy. Specific surface areas were obtained by the B.E.T. method. In particular, an increase on the visible light absorption was observed for the C-dots/TNT mesoporous nanocomposites in comparison to the TNTs' light absorption.

The catalytic ability of C-dots/TNT samples for pollutant photodegradation was investigated using caffeine as a pollutant model. The results show that the photocatalytic performance is depending on the amount of C-dots present in the nanocomposite. Studies concerning the active role of several photo-active oxidant radicals in the caffeine degradation process were carried out. Based on the obtained results, a mechanism for the charge-transfer processes in the hybrid nanoparticles, after being activated by the light, is proposed.

Acknowledgements

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E&E.F1

Synthesis of novel tetrazolyl-benzisothiazole derivatives and their application as catalysts on the oxidation of alcohols

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The building blocks tetrazoles and isothiazoles, themselves, have relevant applications in major areas such as medicine, agriculture and food chemistry. These heterocyclic compounds are important units in organic synthesis and are widely used in coordination chemistry as ligands. Furthermore, there are several tetrazolyl derivatives with a successful track record as organocatalysts. The most remarkable example is (*S*)-5-(pyrrolidin-2-yl)-*1H*-tetrazole (proline isoster) which has emerged as a 'privileged' organocatalyst to mediate a wide range of useful asymmetric reactions, including aldol, Michael, Mannich, α-amination reactions and so forth.[1,2]

New catalytic systems for the anaerobic oxidation of benzyl and secondary alcohols, using a tetrazole-amino-saccharin organocatalyst or Cu(II) and Co(II) tetrazole-saccharinate complexes, have been established by us and will be presented in this communication.[3,4]

Acknowledgements

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E&E.F2

Design of an excel spreadsheet to estimate kinetic and efficiency parameters associated with the removal of pollutants from real waste samples from the printing industry

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The Graphic Industry produces and handles toxic products that can cause serious health and environmental problems. One strategy to deal with this topic involves the extraction of the pollutants from the resulting wastes. Solid-Phase Extraction (SPE) combined with UV-Vis spectroscopy are powerful methods to follow the adsorption kinetics of the extracted compounds.

In previous works, we have successfully used C_{18} polymeric discs to extract BXTE (benzene, xylene, toluene and ethylbenzene) compounds from laboratory simulated wastewater samples.[1] Recently, we have used the same methodology to remove pollutants (containing BXTE) from real wastewater solutions from a printing industry.[2]

The attained results indicate that C_{18} polymeric disks show a low (yet effective) extraction efficiency for these pollutants from this type of wastes. The treatment of results also shows the need to: i) compute a new set of adjustable parameters that can be more easily understood by industry professionals; and ii) design a dedicated excel spreadsheet to enable a prompt calculation of the kinetic and efficiency parameters and associated errors.

In the present work we show and discuss: i) the mathematical treatment inherent to the determination of the alternative set of kinetic and efficiency parameters and respective associated errors; ii) the design philosophy which was followed to establish the layout of the spreadsheet; and iii) the used Microsoft Excel functionalities that allow a better visualization of the results and a user-friendly environment to facilitate or to hasten the calculations.

We hope that the tools provided in this spreadsheet, as in others we presented before,[3] will allow the users to perform rigorous mathematical determinations with a considerable economy of time and effort.

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E&E.P1

Photocatalytic CO_2 conversion with binuclear metal complexes

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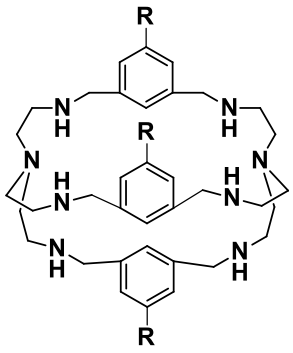
Host-guest structures have proved to be useful for the recognition and activation of small molecules[1]. Cascade complexes with polyaza ligands have demonstrated ability to bind different small molecules by adapting their binding sites towards these molecules. Nelson's cryptands[2] are an example of a dynamic structure with useful applications, which demonstrated the ability to capture and convert CO_2 to carbonate and methyl carbonate following its coordination to encapsulated metal ions. Photochemical reduction of carbon dioxide is used to produce carbon monoxide, formic acid, methane, among others through type I photocatalysis. The mechanism is composed by a molecular light absorber and a transition metal catalyst working together to promote the conversion of small molecules[3].

Here we explore the fixation chemistry of small molecules by derivatised dinuclear Cu(II), Ni(II) and Co(II) cryptands (Figure 1) where the phenyl ring was modified towards engineering these metal-organic structures into supramolecular assemblies. Attaching electron withdrawing or electron donating groups to the phenyl ring proved to affect their ability to capture CO_2. The photocatalytic conversion of CO_2 is also explored, and the reduction products were analysed by GC-TCD and IC.



R = H, Br, NO_2, C≡CH

Figure 1. Derivatised cryptands.

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E&E.P2

Synthesis and application of novel titanate nanotubes modified with diethylenetriamine for emergent pollutants photodegradation

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Pharmaceuticals and personal care products (PPCPs) disposal has become very problematic nowadays. These emergent pollutants are resistant to conventional treatments and even at very low concentrations, they may impose toxicity at all biological hierarchy levels. Several treatments have been proposed but new solutions with improved effectiveness are mandatory. Photocatalysis has attractive potential applications in many areas such as conversion of solar energy into chemical energy as well as an emergent advanced oxidation technique to remove pollutants from wastewater and/or air[1]. Many nanocrystalline semiconductors have been explored and examined in detail for their use possibilities in this area.

In this work, new hybrid nanomaterials, were obtained through sensitization of titanate nanotubes (TNT) and titanium dioxide nanoparticles (TiO_2) with diethylenetriamine (DETA) to produce DETA-TNT and DETA-TiO_2 materials, respectively. The materials were prepared using a hydrothermal approach[2,3], and were structural, morphological and optical characterized by XRD, DRIFT, DRS and B.E.T. surface area. The results show that no modifications on the structure were detected after DETA incorporation but an increase on the visible light absorption was observed. The application of these new hybrid nanomaterials on photocatalytic applications was investigated. The photocatalytic ability of the sensitized materials for the diclofenac degradation was evaluated. All the secondary products were identified and quantified using LC-HR-ESI/MS. Additional study of reusability of the samples were evaluated in four successive degradation assays using visible light. The sensitized samples demonstrated excellent catalytic reusability ability, without loss of chemical stability and photocatalytic performance. The results show that, within 60 min under UV and visible radiation, the DETA-TNT and DETA-TiO_2 samples were the best catalysts for the degradation processes. Based on the obtained results, a mechanism for the charge-transfer processes in the hybrid nanoparticles, after being activated by the light, is proposed and discussed[3,4].

Acknowledgements

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E&E.P3

Adsorption performance of a commercial activated carbon for the removal of caffeine and iopamidol from synthetic inorganic water matrix

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Modern lifestyles rely on the use of a large range of synthetic compounds – pharmaceutical compounds (PhCs), personal care products, pesticides, etc. – which after performing their function end up in water streams usually at trace amounts. To face these environmental and human treat treatment barriers onto wastewater treatment plants need to be improved and activated carbon materials are one of the best available technologies to do it[1].

The present work aims to evaluate the performance of an activated carbon (Norit SAE Super) commercialized by Cabot-Norit for wastewater treatment on the removal of two PhCs – caffeine and iopamidol – in synthetic water matrix resembling the inorganic content of a wastewater effluent from a wastewater treatment plant in the Lisbon region. Since most adsorption studies are focused on evaluating the adsorption of PhCs onto activated carbons using deionized water these data will allow a step forward to understand the PhCs adsorption mechanisms in a system closer to the real scenario, i.e. synthetic organic-free wastewater. The kinetic data (Figure 1) reveal that the caffeine adsorption onto the activated carbon is faster than that of iopamidol. However, at 24h of contact time the removal of iopamidol is close to 80 % while for caffeine is 60 %.

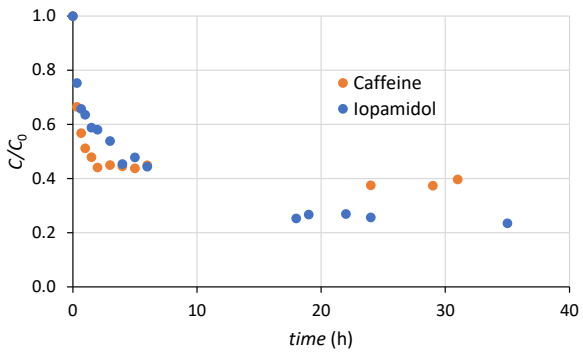

Figure 1. Kinetic results of caffeine and iopamidol adsorption at 30 °C (2.5 mg activated carbon/250 cm^3 of PhC solution with 2.7 $mg.dm^{-3}$).

Equilibrium adsorption studies are ongoing and the liquid phase adsorption data will be correlated with the properties of the activated carbon and PhCs under study.

Acknowledgements

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E&E.P4

CO_2 hydrogenation over supported bimetallic nickel – lanthanide oxides

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The development of competitive processes to decrease the emissions of greenhouse gases through the elimination and valorization of gaseous pollutant (e.g. CO_2, CH_4 and N_2O) is one of the most important research goals all over the world[1]. Two main routes continue to be developed, namely: mitigation of CO_2 via capture and storage[2] and conversion of CO_2 into value-added products, e.g. hydrocarbons and alcohols[3,4]. In our group, the second route and various materials containing nickel or copper and f block elements were synthesized and studied aiming the development of competitive and stable catalysts working at low temperatures and atmospheric pressure[5]. The purpose of this work was to study carbon dioxide hydrogenation over bimetallic nickel-*4f* element block oxides (Ni:Ln, 5:1 molar ratio) supported on silica and prepared by different methodologies: classic impregnation and electrospinning. The catalysts were characterized by different techniques (XRD, SEM/EDS, H_2-TPR). Figure 1 shows the obtained image by SEM that illustrate the spherical shape of the catalysts particles and the supported nickel-lanthanide bimetallic oxides (see insert). The best results obtained for the CO_2 hydrogenation were those got over the bimetallic nickel-dysprosium oxide catalyst over which the activity is equivalent to that of a commercial supported rhodium catalyst on alumina (5 wt.% Rh/Al_2O_3) used as reference and tested in the same conditions (Figure 2). Moreover, all catalysts are more active than a monometallic nickel oxide supported on silica, which stresses the influence of the *4f* element block on the activity of the bimetallic nickel – lanthanide oxide catalysts.

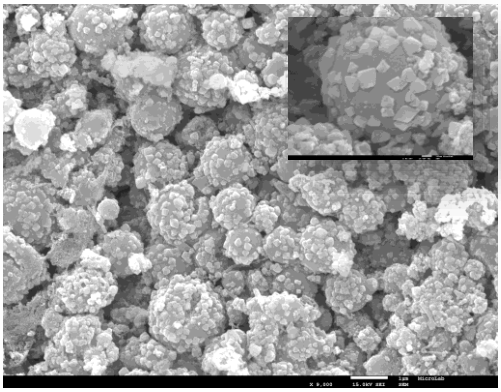

Figure 4. SEM image of the nickel-cerium bimetallic oxide supported on the silica.

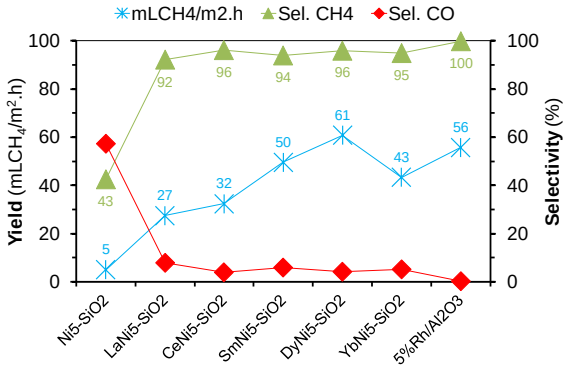

Figure 2. Methanation of carbon dioxide: results obtained at 350 °C using a GHSV=15000 mL/g.h.

Acknowledgements

C^2TN/IST authors gratefully acknowledge also the FCT support through the UID/Multi/04349/2013 project.

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E&E.P5

Chemical characterization of young and mature invasive *Acacia melanoxylon* biomass residues

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Acacia melanoxylon is a fast-growing tree native from Australia. Due to it invasiveness character in Mediterranean areas, control its negative impact in ecosystems services should focus on the sustainable and cost-effective management. Obtaining benefits of woody residues from control measures may alleviate eradication plans costs. To visualize new biomass uses, it is essential to investigate their chemical constitution. This study aimed to evaluate the chemical composition of wood and bark residues (Figure 1) from *Acacia melanoxylon* young (less than 6 years) and mature (around 25 years) tree stands. Barks had higher total extractives content (soxhlet solvent sequence Dichloromethane-Ethanol-Water) than woods, young bark (30.0%), followed by mature bark (21.5%) and both woods (less 9.0%), where ethanol was the solvent with greater yields. The opposite was verified for hollocellulose, similar content in young (58.9%) and mature (57.7%) woods, and lower in young bark (48.2%) and mature bark (27.1%). Lignin content of both woods (24-26%) was in regular range compared to other temperate hardwoods, while barks presented greater values, and mature bark, after suberin extraction (4.4%), showed a total lignin content about 37%. After extraction with NaOH (1% w/w), mature bark maintained a high total lignin (31.2%) that suggest its potential for further research applications.

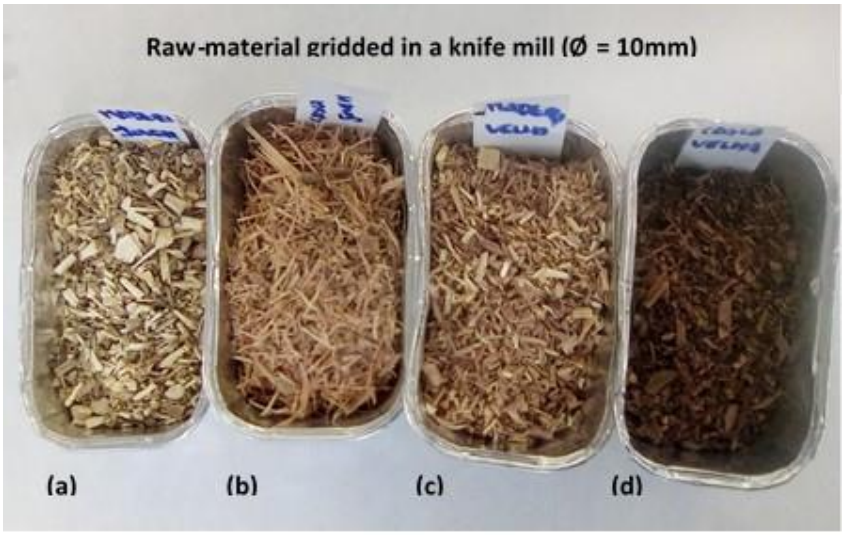

Figure 5. Residues of *Acacia melanoxylon* biomass before chemical characterization: **(a)** young wood, **(b)** young bark, **(c)** mature wood, and **(d)** mature bark.

Acknowledgements

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E&E.P6

Exposure to particulate matter and inhaled dose during commuting in Lisbon

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Commuters are inevitably exposed to large concentrations of air pollutants namely particulate matter (PM)[1,2]. In fact, exposure to PM is particularly high in the transport microenvironment due to the proximity of travelers to mobile sources[3]. Even though people spend a limited amount of time in this microenvironment, the high concentrations of PM lead to a significant contribution to the overall daily exposure[3]. This exposure is extremely important since it can lead to short and long term effects on human health. These include, for example, non-accidental mortality and morbidity due to respiratory or cardiovascular diseases, among others[4].

This study aims to assess commuters' exposure and inhaled dose of particulate matter, namely ultrafine particles (UFP), PM_{10}, $PM_{2.5}$ and black carbon (BC) in some transportation modes in Lisbon (car, bus, bicycle and subway). For this purpose, a system composed by continuous measuring portable monitors has been developed to quantify the mass concentrations of $PM_{2.5}$ and BC and the number concentrations of UFP in real-time and to collect PM_{10} and $PM_{2.5}$ with a Personal Environmental Monitor (PEM). The number of studies evaluating air quality during commutes in Lisbon is relatively scarce. Therefore, this study will provide new information on the daily exposure of commuters, in order to establish the actions towards an effective reduction of PM levels, by identifying and encouraging the adoption of practical and focused air pollution mitigation strategies.

This work is part of the European project LIFE Index-Air (www.lifeindexair.net) whose objective is to create a tool to support policy makers through the identification of effective measures to improve air quality, well-being and health of the population.

Acknowledgements

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E&E.P7

Children exposure assessment to particulate matter in urban environment

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Air pollution, particularly in urban areas, has adverse impacts on the human health, ranging from respiratory and cardiovascular diseases to premature mortality[1]. The particulate matter (PM) is considered one of the most harmful air pollutants[1]. In Portugal, 3710 people die per year prematurely due to the high concentrations of fine particles (PM2.5) [1]. Children are considered a susceptible group to the harmful effects of air pollution, since they breathe higher volumes of air relative to their body weights and their tissue and organs are growing[2]. Furthermore, most of the children's time is spent indoors[3]. Therefore, the assessment of personal exposure of vulnerable groups to air pollutants is essential to develop mitigation strategies in various microenvironments, ensuring the protection of public health.

The main objective of this study is to quantify the children's daily exposure to airborne particles considering different size fractions. Ten children aged 7-10 living and studying in the city of Lisbon were selected to carry personal monitors during all their daily activities along three days. Each child carried a trolley with equipment: a GPS that registered the coordinates of the routes, a SKC Leland Legacy pump connected to a personal cascade impactor (PCIS) to collect the particles in different size ranges below 2.5µm and also two portable monitors to quantify the real-time measurements of PM2.5 and black carbon (BC) concentrations. Additionally, the children filled out a time-activity diary to record all the information about their time-activity patterns. This study assesses the daily exposure to PM by children and the respective inhaled dose, identifying the pollution sources and main activities carried out indoors and outdoors. The results showed that the exposure depends on the different microenvironments where children spend time and respective activities. Furthermore, the highest concentrations of BC on a daily basis were reached when commuting.

This study is part of the European project LIFE Index-Air (www.lifeindexair.net), which aims to develop an innovative and versatile decision support tool for policy makers that will help them identify measures to improve air quality. Moreover, this tool will be used to quantitatively evaluate the impacts of policies on air quality, health and well-being of the population.

Acknowledgements

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E&E.P8

Polyoxometalates as tools for phosphate decontamination

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Polyoxometalates (POMs) belong to a family of metal oxide molecular clusters with a rich variety of structures exhibiting remarkable properties and high impact on many fields such as catalysis, biology, medicine and materials science.[1] The first POM, $[PMo_{12}O_{40}]^{3-}$, was reported by Berzelius[2] in 1826, but only in 1934 the first structure was solved by J. F. Keggin[3], using X-ray diffraction. This family of compounds have a general formula of $[XM_{12}O_{40}]^{n-}$ (named Keggin ions) where X is a heteroatom (P, Si, S, Ge, As, Co, Fe). Based on the clathrate model[4] the Keggin ion can be viewed as a $M_{12}O_{36}$ cage encapsulating a charged $[XO_4]^{n-}$ anion.

It is now reported a $[PMo_{12}O_{40}]^{n-}$ synthesized in aqueous media under room temperature, in contrast with previous methodologies[5]. Structural characterization, by X-ray diffraction analysis, show that a phosphate ion is encapsulated in the molybdenum polyoxometalate structure (Figure 1). Additionally, this structure has an unusual type of counter-ion. The optimization of the synthesis of related tungsten polyoxometalates, using mild experimental conditions is under progress, the process being followed by ^{31}P NMR to achieve the best conditions for crystallisation. Future work should be focused on cationic cages[6], also known as reverse Keggin, to lead to phosphate accumulation outside of the cage cleaning water contaminated with phosphates. Metal cations will be incorporated into cages for this achievement.

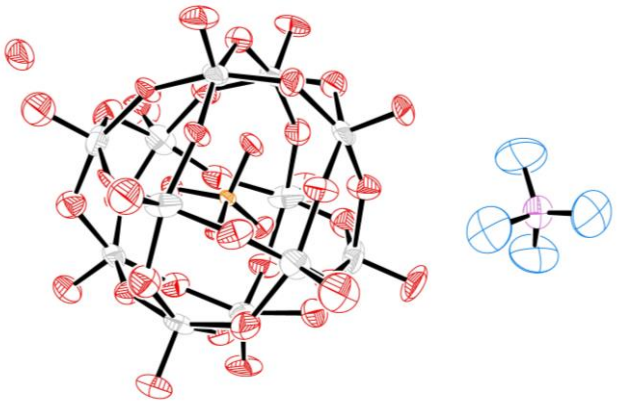

Figure 6. Keggin crystal structure generated by Ortep $[PMo_{12}O_{40}]$ with tetramethyl ammonium; Red-Oxygen; Grey-Molybdenum; Orange-Phosphorus; Purple-Nitrogen; Blue-Carbon

Acknowledgements
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E&E.P9

Sodium Dithionite Stabilization of 5-Hydroxymethylfurfural

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5-Hydroxymethylfurfural (5-HMF) is obtained from the acidic dehydration of fructose and was included by US Department of Energy in the previous "Top 10" list of bio-based chemicals.[1]
However the lack of thermal and storage stability and occurrence of side reactions during the processing of 5-hydroxymethylfurfural (5-HMF) limits its potential as biorenewable platform molecule.[2] In this work we show the addition of small amounts of readily available sodium dithionite promotes remarkable effect over the 5-HMF stability and the inhibition of side reactions thus allowing to circumvent those limitations[3].

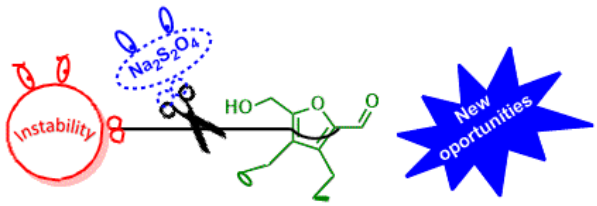

Figure 1. Sodium dithionite breaking the instability chains of 5-HMF.

Acknowledgements

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E&E.P10

Cobalt catalyst electro-regeneration for H_2 on-demand in $NaBH_4$ systems

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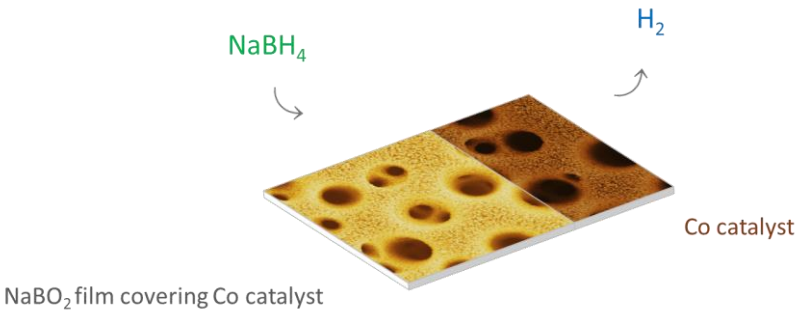
Cobalt-based catalysts are the most studied for the hydrolysis of $NaBH_4$, which allows producing H_2 for on-board applications, such as fuel cells[1]. $NaBH_4$ is a non-fossil and non-flammable fuel, has long-term stability with the joint benefit of storing and generating clean H_2.[2] Theoretically, gravimetric hydrogen storage capacity (GHSC) of the $NaBH_4$ aqueous system is 10.8 wt.%.[2] However, after several catalytic hydrolysis of $NaBH_4$, the $NaBO_2$ by-product leads to catalyst deactivation lowering the GHSC and H_2 generation rates. Hence, despite the acknowledged high activity of the Co catalysts, the deactivation and regeneration over successive catalytic cycles remains a challenge[1]. Methods for Co catalysts regeneration such as acid wash and thermal treatments have been explored, however they are mainly *ex-situ*, time consuming procedures[3,4], thus not recommended for on-board H_2 generation $NaBH_4$ systems. This work aims at studying the regeneration of cobalt-based catalysts via electrochemical methods. This approach consists of a fast, one-step *in-situ* catalyst regeneration adequate for development of H_2-$NaBH_4$ systems with a recycled catalyst.



Acknowledgements

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E&E.P11

Pyrolysis of forestry waste for Energy Recovery

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In recently years, there is a substantial increase in the energy production from biomass. Portugal has a very large potential for the use of biomass as an energy source. The exploitation of biomass can contribute to forest management, minimizing the risk of forest fires.[1] One of the major difficulties in biomass utilization for energy recovery is the collection of the biomass and its transportation to a processing site, since biomass has a relatively low bulk density. One way to overcome this problem is to process the biomass by mild thermal treatment, i.e., torrefaction, at 200-300 ^{o}C in an inert atmosphere. This process has already been used for millennia where raw biomass is converted into charcoal[2,3]. Charcoal has an important advantage over the original biomass of being much denser, in terms of energy density, implying that charcoal can have high energy densities compared to coal.

For this propose, *Cistus ladanifer* branches, a common shrub in Portuguese forest, were collected and analysed by thermoanalytical methods, in particular using Differential Scanning Calorimetry (DSC/TG) technique. Two sets of experiments were carried out: torrefaction followed by combustion and complete combustion. The preliminary results showed that using torrefaction at 250 ^{o}C as a pre-treatment step before combustion leads to 71% char content, which has higher heating value than raw biomass.

This work is an active collaboration between Instituto Superior Técnico and Instituto Superior de Agronomia.

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E&E.P12

Evaluation of matrix effects

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The measurement of trace levels of analytes in complex matrices, such as heavy metals in sediments or pesticide residues in foodstuffs, is frequently affected by matrix effects that vary with the analysed item. In some cases, the determination of the analyte in items of the same class, such as sediments with equivalent organic matter contents or the same fruit, are affected by different matrix effects due to the type of organic matter of the sediment or the maturation of the fruit.

During the development and validation of the measurement procedure, it is necessary to take the variability of matrix effects into account and it can be extremely useful to quantify these effects separately in order to know if it is necessary to improve the robustness of the procedure to matrix effects to increase measurement quality (i.e. to reduce measurement uncertainty).

The standard addition method is the most popular tool used to eliminate matrix effects that vary with the analysed item. However, since its use involves additional analytical work, it should only be used whenever strictly necessary.

This work, presents a methodology to separately quantify the variability of matrix effects in complex measurements in order to decide about the need to improve measurements robustness to these effects. This methodology is based on the comparison of the mean recovery estimated from the analysis of various reference materials[1] and was applied to measurements of heavy metals in sediments by atomic spectrometry where measurements trueness was assessed from the participation in proficiency tests.

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E&E.P13

Lipase-Catalyzed production of glycerol-free biodiesel from crude olive pomace oil

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The European Union obliges all member states to start changing from fossil fuels to renewable energies within the frame of the European Directive 2009/28/E.C, 2009. In this context, biodiesel is one of the options for biofuels. Biodiesel (FAME, fatty acid methyl esters) is obtained by transesterification of oils and fats with an alcohol molecule (methanol in EU). This reaction is currently catalyzed by chemical catalysts (e.g. sodium methoxide) with environmental problems, among others, related with purification process of FAME and glycerol.

In this study, FAME were produced from crude olive pomace oil by lipase-catalyzed reactions (esterification and transesterification) using an immobilized *sn*-1,3 regioselective lipase from *Rhizomucor miehei* (Lipozyme RM IM) as catalyst. This enzyme acts only at positions *sn*-1,3 of triacylglycerol (TAG) molecules. Thus, by transesterification of one molecule of TAG, two molecules of FAME and one of *sn*-2 Monoacylglycerol (*sn*-2 MAG) are produced. MAG are added-value compounds with emulsifying properties. Crude olive pomace oil is a low-cost raw-material obtained from olive pomace by solvent extraction. Its fatty acid composition is similar to that of olive oil (oleic acid as major fatty acid).

High acidic crude olive pomace oil (20.3% of free fatty acids) with high contents of oxidation products (K_{232}=6.982 and K_{270}=2.222) and pigments (chlorophylls a and b) was used (oil A). This oil was submitted to a sequential adsorption process with 4% activated earths at different time/temperature combinations (65 °C/60 min; 90 °C/45 min; 110 °C/30 min). The obtained oil (oil B) showed a decrease of 77.8% in chlorophyll content but an increase of 21.2% in final oxidation products, promoted by the high adsorption temperatures used. This oil was also used for biodiesel production. Reactions were carried in batch reactors at 50 °C, for 24 h, in solvent-free media, using a molar ratio methanol/oil of 3:1 and a biocatalyst load of 5% (in relation to oil amount). Stepwise methanol addition was carried out (seven additions of equal volumes every 30 min during the first 3 h) to avoid lipase inactivation. After 5 h reaction, a quasi-equilibrium was attained with both oils. FAME production was 47.1% with oil A and 10% with oil B. The lower productions observed with oil B may be ascribed to the presence of higher amounts of oxidation products in the reaction medium, which has been related with lipase inactivation. The removal of pigments showed not to have a positive effect on lipase activity. These are promising results since using a crude acidic oil without any treatment, it is possible to obtain high yields of FAME (71% of the maximum FAME obtained with *sn*-1,3 regioselective lipases of 66%) in short reaction times.

Acknowledgements

The support for this work was provided by FCT through the research unit LEAF (UID/AGR/04129/2013) and developed under the scope of the cooperation FCT/India 2017/2019 (*Developing magnetic nanoparticle immobilized enzyme catalysts for biofuel applications).* The olive pomace oil samples were kindly donated by UCASUL União de Cooperativas UCRL (Alvito, Portugal).

E&E.P14

Optimization of soybean oil ethanolysis by response surface methodology

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In the next decades, the worldwide energy demand will continue to increase. Fossil fuels continue to supply most of the energy consumed in the transportation sector although their availability is limited. Hence, it becomes increasingly important to maximize the use of renewable sources, replacing fossil fuel with more sustainable energies like biodiesel.

Biodiesel is a mixture of fatty acids alkyl esters, mainly produced by catalyzed transesterification of vegetable oils and animal fats with short chain alcohols, such as methanol or ethanol. The mild reaction conditions needed, the fast reaction time and the easy phase separation combined with its low-cost and industrial availability make the methanol the most used alcohol in biodiesel production[1,2]. However, the use of this alcohol has some drawbacks. Methanol is more toxic than ethanol and due to be majorly obtained from a fossil source, natural gas reforming, the biofuel produced is not a fully renewable biodiesel. On the other hand, ethanol is made from agricultural products such as potatoes, grain, and corn, allowing the production of a renewable fuel. Ethanol has a higher oil dissolving capacity compared with methanol. Due to the extra carbon atom, fatty acid ethyl ester (FAEE) cloud and pour point are lower than that of fatty acid methyl esters (FAME)[3]. In addition, the combustion heat and the cetane number are higher for FAEE than for FAME. The storage properties of FAEE fuel are also improved[1]. The main drawbacks of ethanolysis in biodiesel production are its lower reactivity, compared with methanol, as well as the more difficult separation of biodiesel from the coproduced glycerin[4].

In order to improve the process, the ethanolysis reaction of soybean oil was carried out over Ca heterogeneous catalyst obtained by calcination of calcium rich alimentary wastes. A response surface methodology (RSM) was applied to determine the influence of reaction variables such as ethanol to oil molar ratio, catalyst loading and time reaction on the FAAE yield. The optimization of the reaction conditions was also done in order to maximize the biodiesel yield.

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E&E.P15

Biodiesel Production using CaO nanocatalysts

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Considering heterogeneous catalysts for transesterification reaction, calcium oxide (CaO) is a widely-used catalyst due to being cheap, non-corrosive, economically benign, easy to handle and having a high basicity compared to homogeneous base catalysts.[1] It can be obtained from natural sources through the calcination of waste egg and oyster shells (~95% $CaCO_3$) at 850 °C for 3 hours, exhibiting high activity for the transesterification of soybean oil due to its superior basic strength.[2,3] However, heterogeneous catalysts are, currently, somewhat time consuming, need more reaction time to achieve high FAME (Fatty Acids Methyl Esters) yields and present some mass transfer limitations.

Using CaO nanocatalysts, it is possible to overcome some of these issues, as they present higher surface area and catalytic activity, thus allowing to achieve a significant improvement on transesterification efficiency, resulting into faster reactions i.e., shorter reaction times, low reaction temperatures and lower catalyst concentration.

In the present work, CaO from natural sources was micronized using the SAS (Supercritical Anti-Solvent) technique with supercritical CO_2. The obtained nanocatalysts were then analysed by SEM and DLS, to study their structure and particle size.

The transesterification of sunflower oil into biodiesel (FAME) using these catalysts was tested at 60 °C with methanol reflux. Reaction conditions such as reaction time, methanol/oil molar ratio and catalyst loading amount were studied and so was their effect on the triglyceride conversion into FAME yield.

Acknowledgements

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E&E.P16

Polyphenols from olive oil industry residues: extraction, identification and their antioxidant properties

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Extracted olive pomace (EOP) and olive stones (OS) are abundant residues generated by the olive oil industry. However, these materials have been only used as fuel in cogeneration plants to produce energy or as organic fertilizer after a composting process. These raw-materials are rich in bioactive molecules, such as sugars, tannins, polyalcohols, pectins, lipids, and phenols, which have not been used. Thus, they are a low cost and renewable source of high value-added compounds[1].

One line of research of our group involves the valorization of residual and waste cellulosic materials to produce added-value compounds, under the Biorefinery concept. In this study, the EOP and OS were chemically analyzed regarding their composition and antioxidant properties of polar extractives, aiming at the valorization of these raw materials. Plant polyphenols present a wide range of chemical, physical and biological activities[2]. Polyphenols in the ethanol and water extracts of EOP and of OS were quantified as total phenols, flavonoids and tannins, and tested for the antioxidant activity.

The ethanol and water extracts from EOP and OS have a high content in phenolic compounds: total phenols ranged from 120.3 to 136.7 and 145.8 to 160.5 mg gallic acid equivalents/g extract, for EOP and OS, respectively; flavonoid content ranged from 44.1 to 102 and 46.4 to 93.0 mg catechin equivalents/g extract, for EOP and OS, respectively, and tannins from 13.4 to 27.7 and 19.1 to 28.8 mg catechin equivalents/g extract, for EOP and OS, respectively. These extracts showed a low efficiency as free radical scavenger, with an IC_{50} value of 58.8 and 57.8 µg/mL, for EOP and OS extracts, respectively.

Acknowledgements

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E&E.P17

Using titanate nanostructures to remove Cr(III) and Cr(VI) and their posterior use for pollutants photocatalytic degradation

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Pharmaceuticals and personal care products (PPCPs), which include pharmaceutical drugs, cosmetics, food supplements and other personal care products, have become essential for human life. Unfortunately, their disposal after use has become very problematic as they are extremely resistant to conventional treatments and, even at very low concentrations, they may impose toxicity at all biological hierarchy levels.

Nanocrystalline semiconductors, mainly TiO_2, have been studied as photocatalysts to removal organic pollutants from wastewater. However, TiO_2 has a major drawback in processes associated with solar photocatalysis due to its wide bandgap (3.2 eV) and high recombination rate of photo-generated carriers. Therefore, the synthesis of TiO_2-based materials, *e.g.* titanate nanowires (TNW) which hold a broader range of light absorption and a lower charge recombination rate, makes them successful photoactive materials.

Chromium (Cr) is a highly toxic water contaminant that commonly occurs in industrial effluent from electroplating, tanning, mining, etc. Hexavalent (Cr(VI)) and trivalent (Cr(III)) chromium are the two main forms of chromium found in the aqueous environment.

The present work focuses on the synthesis and photocatalytic application of novel nanocrystalline TNW-based materials modified by Cr(III) and Cr(VI) ions. The materials were prepared by using ion-exchange (TNW/Cr) and doping (Cr-TNW) methodologies. To study the influence of the Cr position in the TNW structure and optical properties, the powders were characterized by XRD, DRS, XPS, TEM and B.E.T. The photocatalytic activity of the modified Cr-titanate nanowires was investigated using methylparaben (a preservative mainly used in food and cosmetics) as a contaminant model to evaluate the photocatalytic activity of the TNW-based samples under UV-vis irradiation.

The results show that Cr incorporation possess significant influence on the structural and optical properties of the pristine material, and the modified materials were found to exhibit a higher photocatalytic activity for the methylparaben photodegradation. Therefore, TNW materials show that they are excellent candidates not only for the removal of Cr ions from water, but also for photocatalytic degradation of PPCPs.

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E&E.P18

Strontium-modified Ca-based catalysts for biodiesel production

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Nowadays, society faces a challenge related to its energy habits. The main energy sources are all of fossil origin, with problems such as the depletion of their reserves and the CO_2 emissions, the latter contributing to global warming. Thus it is necessary to search for renewable and sustainable energy sources. Biodiesel, a mixture of fatty acid alkyl esters, turns up as a feasible biofuel to replace the fossil diesel in the transport sector[1].

The industrial production of biodiesel is currently attained through the transesterification of fat feedstock with an alcohol, usually methanol. Sodium or potassium hydroxide are used as catalyst precursors[2]. This homogeneous catalytic route has several disadvantages. On one hand, the removal of the catalyst from the reaction medium requires large amounts of water, decreasing the sustainability and environmental benefits of biodiesel. On the other hand, the removed catalyst cannot be reused or regenerated, increasing the already high production cost[1].

Aiming to overcome the drawbacks associated with homogeneous catalysts, heterogeneous ones, such as calcium oxide (CaO), have been studied in the last decades. Although they present a high performance towards the transesterification, CaO catalysts can still be improved when modified with strontium oxide (SrO), since the latter has higher basicity, which have been proved to improve the transesterification efficiency. Furthermore, SrO is not toxic and it cannot be dissolved neither in methanol, vegetable oil, nor biodiesel[3].

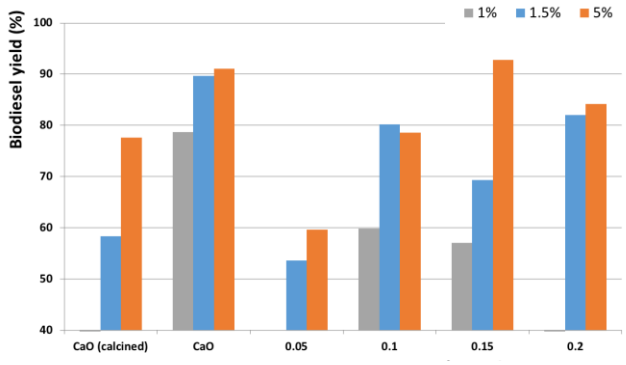

Figure 7. FAME yield for the different amounts of catalyst and Sr/Ca molar ratio tested.

In this work, strontium-modified CaO catalysts were prepared by a sol-gel method. The obtained powder was calcined at 800 °C for 3 h under air flow. The methanolysis tests were carried using a methanol:soybean oil ratio of 12:1 with different amounts of the catalyst. The reactions were performed for 1.5 h at methanol reflux temperature.

From the results presented in Figure 1, it can be seen that the higher FAME yield (93%) was achieved for 5 wt.% (oil basis) of catalyst with Sr/Ca molar ratio of 0.15.

Acknowledgements

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Life

&

Health

L&H.PL

Proteins, lipids and drug discovery: from malaria to the common cold

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Department of Chemistry, Imperial College London, United Kingdom

My group develops chemical biology approaches to identify and validate potential drug targets, particularly in the field of protein post-translational modification[1-10]. In this talk I will discuss our recent work in the field of protein lipidation (acylation, cholesterylation and prenylation), where we have contributed to validation of protein targets in infectious diseases caused by parasites (malaria, leishmaniasis, trypanosomiasis), bacteria and viruses, and in cancer. I will also illustrate how we have used chemical tagging technologies in an analytical platform for quantification and identification of protein lipidation in live cells and animals, providing the first insights into how lipidation changes in response to drug treatment at the whole proteome level. This research has enriched our understanding of these traditionally challenging classes of protein modification, and delivered novel small molecules into pre-clinical development.

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L&H.IOC1

Challenging strategies for targeted therapies

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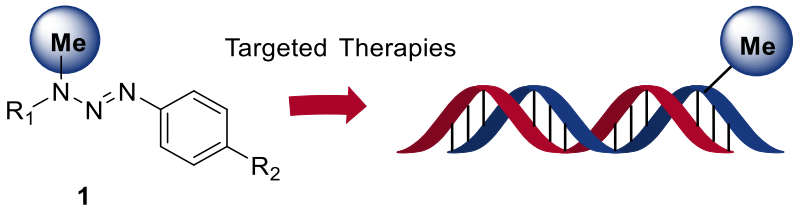
One of the major limitations in the efficacy of antitumor drugs is the occurrence of undesirable or secondary effects, resulting from the interaction of these drugs with targets other than the tumor cell. Thus, two premises play an important role in the development of antitumor drugs: (i) drug targeting and (ii) spatio-temporal control on drug release.[1] These two conditions have pulled by the imagination of chemists and biologists, in order to achieve greater efficiency and selectivity in anti-tumor therapy, particularly when it comes to DNA alkylating agents.

In the anticancer approved armamentarium, dacarbazine and temozolomide represent the class of triazenes used in the treatment of metastatic melanoma and brain tumors respectively, acting as DNA alkylating agents. Unfortunately, the therapeutic efficacy of this class is conditioned by the occurrence of resistance phenomena and by the limited pharmacokinetic properties of these drugs.[2] Our research group has developed a comprehensive engineering of aryltriazenes (1), in order to improve target specificity. We will emphasize the design of triazene prodrugs for different applications, including antibody directed-enzyme prodrug therapy (ADEPT), tyrosinase targeted melanoma therapy, as well as hybrid or multi-target drug strategies for the treatment glioblastoma. The advances and setbacks of these approaches will be discussed.[3-5]



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Maria de Jesus A. R. Perry da C. S. Rocha graduated in 1987 and obtained her PhD in 2003 in Pharmaceutical Sciences by the Faculty of Pharmacy - University of Lisbon. In 2017 she obtained a post-graduation in Science Communication by the Nova School of Social Sciences and Humanities (FCSH-UNL). She is an Assistant Professor of the Department of Pharmaceutical Chemistry and Therapeutics of the FFUL (2003-present). Member of iMed.ULisboa, Drug Design Program Area-Medicinal Chemistry Research Group, her research areas of active interest include organic synthesis and identification of biologically active small molecules, prodrug development, targeted drug delivery, drug metabolism and drug stability. In the recent years has been involved in the development of hybrid drugs for resistant malignancies namely cancer and malaria.

L&H.IOC2

Old New Molecules – Drug Repositioning

Sofia Côrte-Real

Technophage, SA, Lisboa, Portugal

Sofia Côrte-Real developed her professional career in the area of Health Sciences, performing different functions, from conducting scientific research and doing a PhD in the area of antibodies and virology, to functions related with the preclinical development of drugs, as well as support to technology and strategy development at TechnoPhage, SA. Her main know-how and interest has been in regulatory strategy, devising and implementing all non clinical studies, manufacturing and process development studies, interacting with regulatory bodies such as FDA, EMA and Infarmed on a regular basis. Over the years she has gained an interest in intellectual property (IP), having drafted diverse patents, analyzing FTO as well as revising all IP strategy in various therapeutic areas and with different classes of molecules (bacteriophages, antibodies, small molecules). Her biggest professional challenge has been to direct the R&D Department of a Biopharmaceutical company which includes scientific support of three different technology platforms as well as development of the products in pipeline, in collaboration with China, US and Europe. This has given her competencies in developing full-scale project plans and communicating project expectations to team members and Board stakeholders in a timely and clear fashion.

L&H.IOC3

Chemical Physiology of Antibody Conjugates and Natural Products

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Our research uses chemistry principles to address questions of importance in life sciences and molecular medicine. This lecture will cover recent examples of emerging areas in our group in:

(i) methods developed for site-selective chemical modification of proteins at cysteine, disulfide and lysine and their use to build stable and functional protein conjugates for in vivo applications[1,2,3];

(ii) bioorthogonal cleavage reactions for intracellular drug activation[4];

(iii) harnessing the power of natural product architectures in cancer chemical biology. By identifying on- and off-targets for anti-cancer entities and unveiling the underlying molecular mechanisms of target recognition, we explore the use of natural products as cancer modulators and ligands for the selective delivery of cytotoxic payloads[5].

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Gonçalo Bernardes is a Tenured Lecturer at the Department of Chemistry, University of Cambridge, U.K.. He is also the Director of the Chemical Biology and Pharmaceutical Biotechnology Unit at the Instituto de Medicina Molecular, Portugal. After completing his D.Phil. degree in 2008 at the University of Oxford, U.K., he undertook postdoctoral work at the Max-Planck Institute of Colloids and Interfaces, Germany, and the ETH Zürich, Switzerland, and worked as a Group Leader at Alfama Lda in Portugal. He started his independent research career in 2013, and his research group interests focus on the use of chemistry principles to tackle challenging biological problems for understanding and fight cancer. He is a Royal Society University Research Fellow and the awardee of a Starting Grant from the European Research Council (TagIt). He has received a number of accolades including the Royal Society of Chemistry Harrison-Meldola prize and the ChemSocRev Emerging Investigator Lectureship, both in 2016. Just recently he co-founded and spun-out Targ.Tex that uses proprietary artificial intelligence models to deconvolute complex phenotypic read outs of clinically relevant natural products.

L&H.O1

N,O-Iminoboronates: Useful Scaffolds for the Construction of Reversible Linkers

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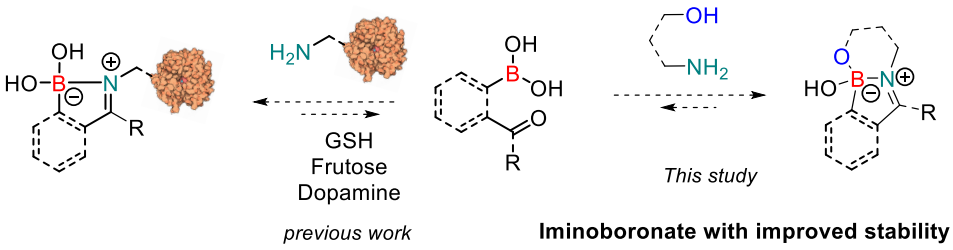
Iminoboronates are a class of reversible-covalent based compounds in which an imine is stabilized by the coordination with an adjacent boronic acid. Our group used this strategy to perform the reversible functionalization of the ε-amino group of lysine residues exposed on the surface of proteins.[1] One of the most important attributes of iminoboronates is their inherent reversibility, which can be accelerated by endogenous molecules like glutathione (GSH), fructose or dopamine. However, recent studies showed that iminoboronates also hydrolyse under physiological conditions.[2] Based on this issue, we set-out to improve the stability of iminoboronates aiming at their use in the preparation of reversible linkers for targeting conjugates.

We envisioned that a strategy to improve these construct's stability would be to design a *N,O*-bidentate ligand that enables the formation of the iminoboronate with an additional B-O bond.

Herein we demonstrate that this molecular arrangement contributes to improve the construct stability in biocompatible conditions, while the iminoboronate can still be reversible in more acidic environments. 2-Acetylbenzene boronic acid was also reacted with a fluorescent amino-coumarin to yield a stable and non-fluorescent *N,O*-iminoboronate. This mechanism was further used to assemble a folate receptor targeting conjugate that selectively delivered the fluorescent amino-coumarin to MDA-MB-231 human breast cancer cells.



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L&H.O2

Using minimal physiological pH changes to probe solvent accessibility and the structural arrangement of disordered regions of proteins via NMR

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Understanding protein structure and dynamics, which govern key cellular processes, is crucial for basic and applied research. Intrinsically disordered protein (IDP) regions display multifunctionality via alternative transient conformations, being key players in disease mechanisms. IDP regions are abundant, namely in small viruses, allowing a large number of functions out of a small proteome, by means of the transient structural arrangements that their IDP regions provide. Each IDP conformer can play different roles within the cell. However, IDPs are hard and time-consuming to study via classical techniques, originally designed and optimized for globular proteins with well-defined conformations. Thus, new methods are required to study these key protein regions. Here, employing dengue virus capsid protein, with which we worked before, we describe a straightforward and fast NMR method to differentiate the solvent accessibility of single amino acid N-H groups in structured and IDP regions. We also gain insights into DENV C biological activity, especially concerning the function of the flexible fold region. The method, based on minimal pH changes uses the well-established 1H-15N HSQC pulse sequence to report on protein dynamics and secondary structure, being easily implementable in current protein NMR routines. The data generated are simple to interpret, with this rapid approach being of general use by serving as a first-choice method for IDPs structural and dynamics characterization.

Acknowledgements

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L&H.O3

Exploring the conformational plasticity of tau by single-molecule FRET: Insights into its biological function and dysfunction

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Tau is an intrinsically disordered protein (IDP) found primarily in the axons of neurons. Its aggregation and deposition as neurofibrillary tangles is linked to several tauopathies, including Alzheimer's disease. Additionally, the loss of native interactions between tau and microtubules (MTs) is thought to contribute to pathology. Here, we explored the largely overlooked first step of microtubule assembly, namely the interaction of tau with soluble tubulin heterodimers. Using single-molecule Förster Resonance Energy Transfer (smFRET), we determine the topological features of tau in complex with tubulin[1,2]. Tau adopts an overall extended conformation upon tubulin binding, in which the long-range of contacts between both termini and the microtubule binding region (MTBR) that characterize its compact solution structure are diminished. Surprisingly, the individual repeats within MTBR that directly interface with tubulin undergo an expansion in order to accommodate tubulin binding without changing the overall MTBR dimensions. Notably, it suggests the formation of such a "fuzzy complex", in which tau displays significant flexibility to allow for local changes in conformation while preserving global features. Moreover, our results contrast differences in tau isoforms and a conformational ensemble of tubulin-bound state distinct from its aggregation-prone structure. This work provides insights into the molecular mechanism of tau-mediated tubulin polymerization into MTs and also draws attention to the importance of the role of tau's conformational plasticity in function[1].

Acknowledgements

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L&H.F1

Toward triazene-hybrid molecules with improved melanocytotoxic activity

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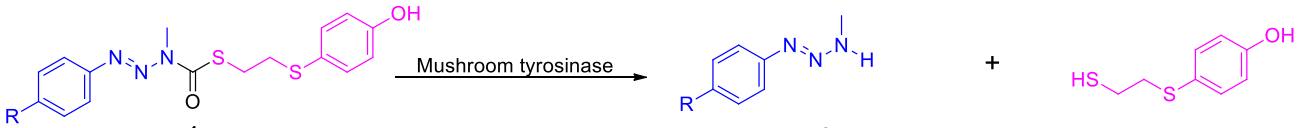
Through a rational drug design approach a new series of triazene-hybrid molecules **1** were synthesized. Our goal in designing these molecules was to discover new molecules able to interact with multiple targets for malignant melanoma chemotherapy. Triazene-hybrid molecules **1** involve the conjugation of two pharmacophores: a triazene **2** (blue moiety) and a sulfur analogue of tyrosine **3** (pink moiety)[1,2]. These two distinct moieties covalently joined, act through different mechanisms of action, triazenes are DNA alkylators. The sulfur tyrosine analogue is capable of inducing a specific apoptosis mechanism in melanoma cells while being a very good tyrosinase substrate, an enzyme overexpressed in melanotic tumour cells[3]. The oxidation of the hybrid compounds by tyrosinase in tumour sites will allow the simultaneous release of both pharmacophores, potentiating the targeting properties of the compounds **1**. Stability studies of hybrids **1,** showed that they are very stable in PBS ($t_{½}$ >15d) and also in human plasma (98<$t_{½}$ <145h). *In vitro* cytotoxic evaluation of the synthesized hybrids **1** showed IC_{50} values in the micromolar range in murine (B16F10, CT-26) and human (MNT-1, HCT-116) melanoma and colon cancer cell lines, respectively. Moreover, a keratinocyte human cell line, HaCat, was also tested as control and IC_{50} values were higher than those obtained for cancer cell lines demonstrating the specificity of the synthesized compounds towards tumour cells. Hybrids **1** are very good tyrosinase substrates, the most reactive compound **1a** is activated in 10 sec (10<$t_{½}$<30 sec) and liberates both pharmacophores quantitatively by the action of mushroom tyrosinase. With the already discovered properties hybrids **1** constitute very promising candidates to malignant melanoma chemotherapy.



35<IC_{50}<40 μM in B16F10

1a R=CN; **1b** R= CH_3CO; **1c** R= Br; **1d** R=C_2H_5OCO

Acknowledgements

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L&H.F2

Bis(thiosemicarbazonato)^{64}Cu(II) complexes: Structure-Activity Relationships and Mechanistic studies

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Among the available positron-emitting copper radioisotopes, Cu-64 is the most practical due to its relatively long half-life ($t_{1/2}$ = 12.7 h) which offers a relatively large time window (2-3 days) for PET imaging. It decays by emission of a positron (18%) with low energy that is conducive to high-resolution PET imaging. Also, it emits Auger electrons and beta particles and both of which find use in therapy[1]. Thus, Cu-64 can be used for both diagnostic and therapeutic (theranostic) purpose in nuclear medicine. Aiming to develop Cu-64 based theranostic agents we studied new copper (II) complexes with bis(thiosemicarbazone) (BTSC) ligands, which were obtained based on the structures of Cu(II)ATSM and Cu(II)GTSM as parental complexes. Here we report the synthesis and characterization of Cu(II)BTSC derivatives carrying terminal piperidine and morpholine fragments, as well as the evaluation of their cytotoxicity and mechanisms of cellular uptake in a diversified panel of human tumor cell lines. The presence of the piperidine and morpholine groups affects the mechanism and extent of cellular uptake, increasing in some cases the water-solubility of the complexes without affecting significantly their cytotoxic activity[2].

Acknowledgements

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L&H.F3

Novel Glycosyl Triazoles and Theobromine Isonucleosides as Promising Anti-Alzheimer Agents

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Neurodegenerative diseases are a major public health issue of the twenty-first century. Alzheimer's disease (AD) is the most common neurodegenerative disease for which no cure is available. The current treatment options are symptomatic and target acetylcholinesterase, an enzyme that cleaves the neurotransmitter acetylcholine, whose levels are low in AD patients[1].The currently used drugs are donepezil, galantamine and rivastigmine. Previous reports from our group showed the potential of nucleoside analogs to inhibit cholinesterases, namely glucuronamide-based purine nucleosides and isonucleosides containing triazole and theobromine moieties[2,3]. Therefore, and motivated by our constant interest in the access and exploitation of the biological potential of novel nucleoside and nucleotide analogs, the work that will be presented in this communication was focused on the synthesis of novel furanosyl nucleoside analogs possessing a triazole or a theobromine unit linked to the anomeric position of a glucofuranuronamide unit or connected to xylofuranose templates at C-5, respectively.

Some of the newly synthesized glycosyl triazoles and a theobromine isonucleoside showed selective and potent inhibition of acetylcholinesterase along with low cytotoxity in human fibroblasts and in a neuronal cell line, rendering them promising lead molecules for AD and motivating further studies. The synthetic work and the results of the bioactivity assessment will be revealed and discussed herein.

Acknowledgements

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L&H.P1

New functional ingredients from *Salvia sclareoides* for the prevention of Alzheimer´s disease

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Salvia sclareoides is a plant of spontaneous Portuguese vegetation that has relevant properties, as part of its cholinergic action and in the prevention of the formation of amyloid plaques. Previous studies suggested[1,2] that this species of *Salvia* can be used as a functional food and also in the development of a food supplement in the context of the prevention and treatment of Alzheimer's disease. Salty cookies were developed with the incorporation of different concentrations (2% and 5%) of *S. Sclareoides.* The nutritional composition of the cookies was determined, namely: fatty acid profile[3], moisture content, ash, total protein, total fat[3], dietary fibre and salt[3]. The available carbohydrates and the energetic value were obtained by calculation. Ethanol extracts from the salty cookies were prepared to evaluate the antioxidant (DPPH) and anticholinesterase (Ellman method) activities. Total phenolic content was evaluated by the Folin-Ciocalteu[1] method and the phenolic composition was analysed by high performance liquid chromatography with diode array detection. The ethanol extracts of the cookies with 5% of *S. sclareoides* showed the best acetylcholinesterase inhibition (44.4%), the highest concentration of phenolic compounds (22.78 mg GAE/g dry extract), and antioxidant activity (10.3%). The flavonoids rutin and (7-*O*-glucosyl)luteolin are clearly the major constituents present in the extracts, along with epicatechin, ellagic acid, and (7-*O*-glucosyl) naringenin. The incorporation of this plant in the cookies formulation resulted in a pleasant and nutritionally interesting functional product with potential application in the prevention of neurodegenerative diseases.

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L&H.P2

Small-molecule immune checkpoint blockade: New approach in cancer immunotherapy

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Immunotherapy is currently a powerful strategy in cancer therapy with very exciting outcomes. In particular, modulation of immune checkpoint receptors has gain special attention. These immune regulators limit proliferation and activity of T cells and other immune cells enrolled in these signalling pathways. Under normal conditions, they are essential in modulation of immune responses; however, they are also one of the major mechanisms used by tumors to evade immune system recognition and destruction. To date, several immune checkpoint receptors have been identified and used as therapeutics in oncology, as programmed cell death protein 1 (PD-1). When engaged by one of its ligands (PD ligand 1 (PD-L1) and PD ligand 2) PD-1 limits autoimmunity. PD-1 ligands are upregulated in many human cancers and their blockade could lead to activation of T cells and therefore enforce tumor recognition. In fact, PD-1/PD-L1 pathway is one of the most successful pathways in the context of clinical cancer immunotherapy with several approved drugs. These successful therapies rely on the use of antibodies. However, despite their outstanding success, they still have numerous disadvantages as severe immune-related adverse events.

Recently, small-molecule modulators have emerged as safer therapeutic alternative. However, limited efforts have been directed toward immune checkpoint receptors. Our study is focus on the discovery of small-molecule inhibitors targeting PD-L1 in order to block PD-1/PD-L1 interaction and therefore overcome antibody therapy disadvantages. Limited structural information of PD-L1 led us to a detailed structural characterization based on *in silico* studies (molecular docking). After assessing structural features (e.g. flexibility and binding pocket) and following a computer assisted drug discovery approach we accomplished a structure based virtual screening campaign. Potential PD-L1 inhibitors were selected and their activity have been tested by Homogeneous Time Resolved Fluorescence (HTRF) assay. We were able to identify new small-molecule PD-L1 inhibitors that are currently being tested *in vitro*. Therefore, immune checkpoint blockade using small molecules represent a step forward in cancer immunotherapy.

Acknowledgements

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L&H.P3

Synthesis and anti-proliferative activity evaluation in human cancer cells of cyclopentenone derivatives

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Functionalized cyclopentenones (CP) are an important class of molecules present in several natural products that actuate as intermediates for the synthesis of many biologically active compounds.[1] The reason for this biological activity is mostly due to the electrophilic character of the CP ring. The α,β-unsaturated carbonyl group can function as a Michael acceptor resulting in the alkylation of critical biomacromolecules of the cells that is being a plausible mechanism of cytotoxic activity.[2] Moreover, some cyclopentenones are known to form a highly electrophilic intermediary upon 1,4-addition by glutathione.

Our group have been involved in the preparation of novel CP and in this work we have synthetized a library of CP derivatives with lateral substituents in position 2 and position 4 and evaluated their biologic activity on human cancer cells in an attempt to elucidate the structure activity relationship (SAR) and to gain some insight on the mechanism of action of these structures.[3]

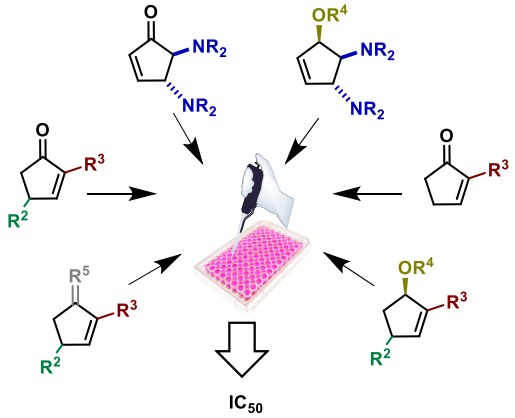

Figure 1. Biological evaluation of cyclopentenones

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L&H.P4

Old diazaborines, new perspectives: A new class of serine protease inhibitors

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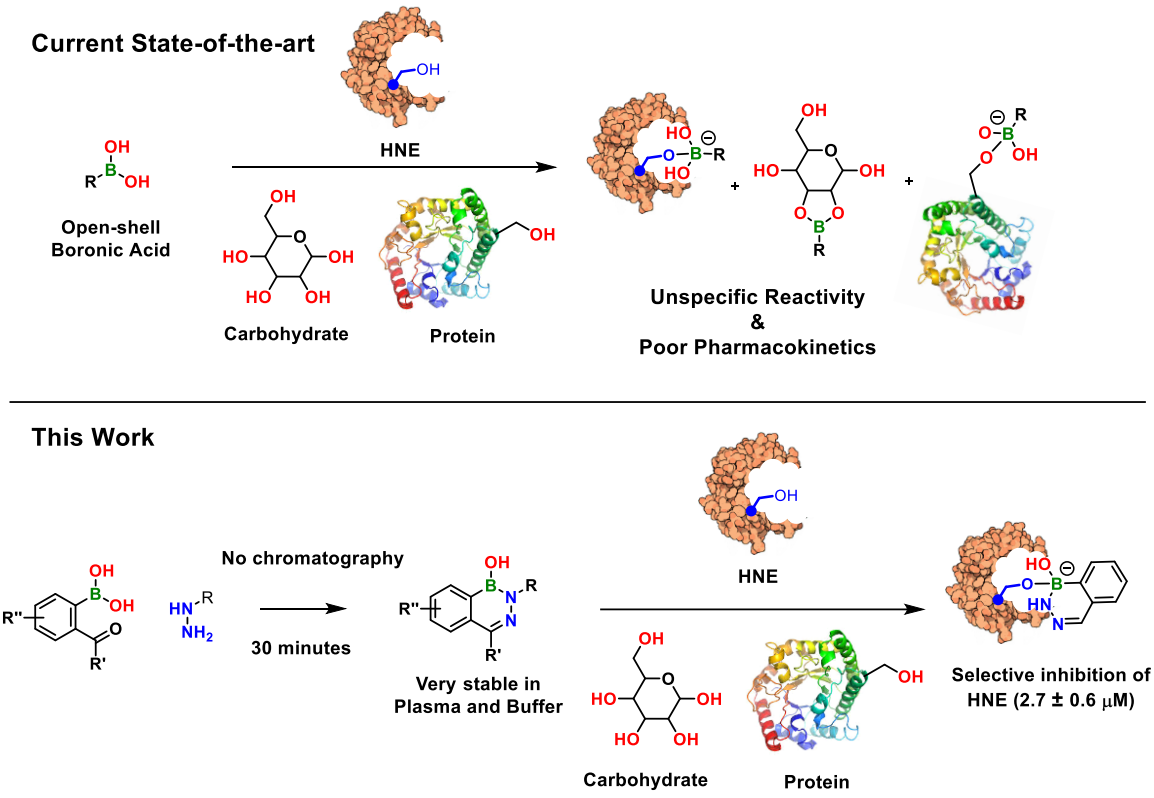
Boronic Acids (BAs) are a preeminent functionality extensively used to design biologically active compounds and functional biomaterials. Due to boron's open shell, this class of inhibitors also exhibits unspecific reactivity with endogenous nucleophiles that often increases their off target toxicity. Here diazaborines are presented as a new class of boron based warheads for serine proteases inhibition, in which the boron functionality is stabilized in the form of an aromatic BN heterocycle. In this study, diazaborines were readily synthesized in a single step in yields up to 96%, without any chromatographic operation and were shown to selectively inhibit HNE serine protease with IC_{50}'s values in the low µM range. Synthetic and theoretical studies performed on this system suggest that, like BAs, the reaction mechanism involves the formation of a reversible covalent bond between the diazaborine boron center and the catalytic serine oxygen. Finally, and differently from BA, diazaborines were shown very stable in different biocompatible conditions like buffer and human plasma.



Acknowledgements

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L&H.P5

Multivalent boronate complexes for drug-conjugates targeting

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Neoplastic state represents the main focus at which medicinal chemistry strategies point nowadays to tackle cancer. Interrupting its evolution involves a variety of biological process be considered, therefore multifunctional constructs that combine the lethality of a cytotoxicity drug with the targeting ability of specific biomolecules, are required. Despite conceptually simple, the assembly of multifunctional construct is often hampered by the complexity of the synthetic steps. In addition, stability and reversible proprieties are necessary to internalize and release cargo into cells. On the basis of our experience[1] we envisioned that a promising strategy to create such compounds, known as Targeting Drug Conjugates (TDC), could take advantage of iminoboronate formation.

Here is presented the development of multifunctional hydrazoneboronate. We addressed the synthesis of different boronic acid salicylidenehydrazone (BASHY) complex. Recently, Gois *et al.* reported that BASHY complexes exhibit a fluorescence nature along with selectivity towards cytoplasmic lipid droplets substructure without any appreciable cytotoxicity.[2] In addition, based on our previous experience regarding the formation of boronate complexes[3] we convinced that the substituent on the imine carbon present in the core structure, would play an important role by affecting its stability. Therefore, hydrazoneboronate complexes featuring different 4-methoxysalicylhydrazone, phenylglyoxylic acid, Bortezomib and SN-38 as cytotoxic agents, were prepared. They were assessed in aqueous media for stability and trough targeted imaging for their potential to deliver cargo into cells.

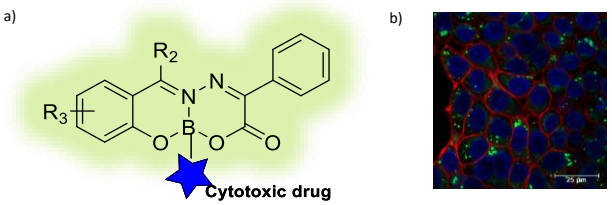

Figure 8. a) Modal boronic acid salicylidenehydrazone complex featuring a cytotoxic drug; b) Confocal images of HT-29 cells incubated with a BASHY complex.

Acknowledgements

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L&H.P6

Aerobic glycolysis: More efficient deviating energy towards cellular division than respiration?

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Several fast-proliferating cells show high glycolytic rates[1] even in the presence of enough oxygen to support respiration (aerobic glycolysis). In cancer cells, this is known as the Warburg Effect, though it also occurs in other cell types such as *Saccharomyces cerevisiae* (*Sc*)[1]. Since respiration generates ATP much more efficiently than glycolysis, the reason why aerobic glycolysis is favored during fast-proliferation is a fundamental biological question. Furthermore, albeit recent evidence suggests that cell metabolism is highly dynamic with the dissipated power per cell changing during growth[2], a steady-state growth process is still commonly assumed.

Microcalorimetry is a very sensitive technique to address questions related to metabolic efficiency[3], since it provides information about the heat dissipated by a given cell culture in real time, usually in the form of power *versus* time (*P*-*t*) curves. The measurement is, however, non-specific and the interpretation of calorimetric profiles greatly benefits if other metabolic indicators are simultaneously recorded. With this in view, our group has developed an apparatus that combines calorimetry with the measurement of cell count by optical density (OD), and CO_2 and ethanol production.

Using this set-up to follow *Sc* growth in synthetic complete medium, we observed that the growth profile obtained by normalizing the corresponding *P*-*t* curves by the number of cells changes drastically, when compared to the typical *P*-*t* curve shape. Most interestingly: (i) the dissipated power per cell continuously changes with time; (ii) it reaches a maximum value during the lag phase where an extensive metabolic reprogramming occurs; (iii) it decreases during the exponential growth, concomitantly with a decrease in the rates of oxygen and glucose consumption, while cell division rate remains constant. This clearly demonstrates that cell metabolism is highly dynamic and not a steady-state process. One major conclusion is that for the same growth rate, cells with higher respiration rates waste larger amounts of energy. We, therefore, propose that aerobic glycolysis is favored because it is more efficient in directing cellular energy towards cellular division.

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L&H.P7

Impact of Ca^{2+}-dependent $PI(4,5)P_2$ clustering on the properties of $PI(4,5)P_2$ binding proteins

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Phosphatidylinositol 4,5-bisphosphate ($PI(4,5)P_2$) is a key modulator of membrane associated signalling events. Although $PI(4,5)P_2$ comprises only around 1% of phospholipid content of the plasma membrane of eukaryotic cells, temporal and spatial regulation of its concentration can achieve localized increases in its concentration which are crucial for activation or recruitment of proteins to the plasma membrane. The recent observation of the dramatic impact of physiological divalent cation concentrations on $PI(4,5)P_2$ clustering, suggests that protein anchoring to the plasma membrane through $PI(4,5)P_2$ is likely not defined solely by a simple (monomeric $PI(4,5)P_2$)/(protein bound $PI(4,5)P_2$) equilibrium, but instead involves protein interactions with $PI(4,5)P_2$ clusters. Nevertheless, the impact of the complex organization of $PI(4,5)P_2$ at the plasma membrane on its biomolecular interactions with $PI(4,5)P_2$ binding proteins is largely unknown.

Using different advanced spectroscopic methodologies (Förster Resonance Energy Transfer, Fluorescence Correlation Spectroscopy and Photon Counting Histogram), we characterized the impact of calcium on the oligomerization of pleckstrin homology (PH) domains tagged with a fluorescent protein (FP). We show that in Giant Unilamellar Vesicles (GUVs) presenting $PI(4,5)P_2$, the membrane diffusion properties of PH-FP are affected by the presence of Ca^{2+}, suggesting interaction of the protein with $PI(4,5)P_2$ clusters. Importantly, PH-FP is found to dimerize in the membrane in the absence of Ca^{2+} and this oligomerization is inhibited in the presence of physiological concentrations of the divalent cation. Furthermore, Ca^{2+} induced clustering of $PI(4,5)P_2$ was shown to enhance protein sequestration of the phosphoinositide, significantly depleting the levels of free $PI(4,5)P_2$.

These results confirm that Ca^{2+}-dependent $PI(4,5)P_2$ clustering has the potential to dramatically influence affinity, oligomerization and organization of $PI(4,5)P_2$ binding proteins in the plasma membrane.

Acknowledgements

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L&H.P8

Self-immolative triazene prodrugs triggered by endogenous up-regulated nitroreductases

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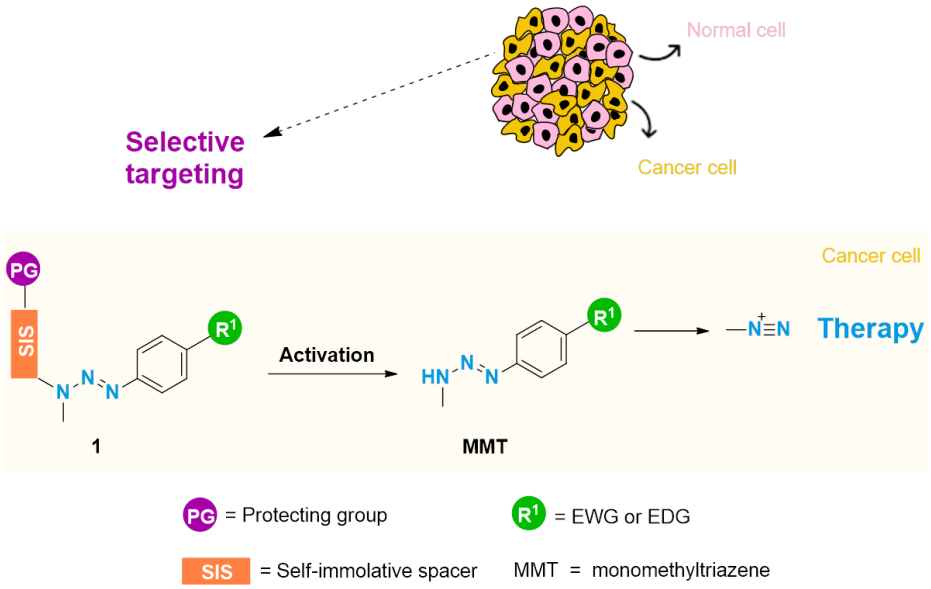
Displaying a broad-spectrum chemistry, triazenes are best known for their cytotoxic properties, as exemplified by dacarbazine and temozolomide, well-known anticancer agents. Triazenes exert their chemotherapeutic activity through a unique mechanism of action that involves formation of a reactive alkyl diazonium intermediate capable of alkylating DNA and promoting cell death.[1] To improve the selectivity towards cancer cells we developed a triazene-based platform that can be selectively activated by specific enzymes. In particular, we focused on up-regulated nitroreductases representative in hypoxic solid tumors[2], as triggers for the activation of triazene prodrugs. Upon specific nitroreductase activation, these prodrugs undergo a dynamic model of self-immolation that culminate with the release of the cytotoxic drug. A series of 4-nitrobenzylcarbamate prodrugs **1** of cytotoxic triazenes were synthesized and enzyme-mediated hydrolytic activation was investigated by liquid chromatography-mass spectrometry (LC-MS). This strategy is expected to lead to selective cytotoxic effect of triazenes, providing novel therapeutic agents in the field of cancer.



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L&H.P9

Heterobimetallic Cu(I)-Fe(II) complexes with NN-, NO-, NS-heteroaromatic ligands for cancer therapy: A combined structural, electrochemical and biological study

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Cancer is the second cause of death in the world. Up to date, Cisplatin and its analogues are the only metallodrugs approved for clinical use. Although they are highly effective for a variety of cancers, they present quite adverse side effects. These limitations stimulated an extensive search for other antitumor inorganic complexes with improved pharmacological properties. Copper complexes have attracted much interest as possible alternative chemotherapeutic drugs.[1]

Over the past few years our group has been committed to the development of new copper(I) complexes, which revealed in most cases higher cytotoxicity than cisplatin against ovarian and breast cancer cell lines[2,3].

This presentation highlights our most recent results in this field. Nine new Cu(I)-Fe(II) complexes of general formula [Cu(dppf)(LL)][BF_4] (dppf=1,1'-bis(diphenylphosphino)ferrocene; LL= NN-, NO-, NS-heteroaromatic ligands) were synthesized (Figure 1). All complexes were fully characterized by NMR, IR, UV-Vis., Elemental Analysis and Cyclic Voltammetry. Their anticancer activity was evaluated *in vitro* against MDAMB231 and MCF7 adenocarcinoma breast human cancer cells.

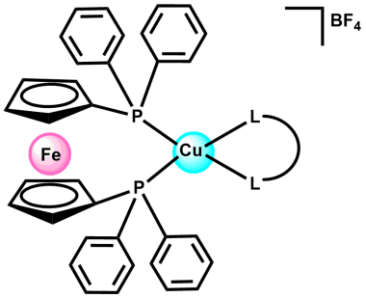

Figure 1. General structure of the coordination compounds [Cu(dppf)(LL)][BF_4] with LL= NN-, NO-, NS-heteroaromatic ligands.

Acknowledgements

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L&H.P10

Discovery and validation of novel inhibitors of necroptosis using phenotypic high-throughput screening of a large compound library

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Necroptosis contributes to the pathogenesis of numerous disorders including inflammation-driven liver and intestinal diseases. It is regulated by receptor-interacting serine/threonine-protein kinase 1 (RIPK1), RIPK3 and mixed lineage kinase domain-like protein (MLKL). Here we aim to discovery novel, selective and potent inhibitors of necroptosis, which might evolve to potential therapeutic strategies. Benefiting from privileged research collaborations on target innovation between academia and pharma industry, we have gained access to a high-quality, large compound pharma collection of over 250,000 compounds. Compounds were screened at 30 µM for ability to block TNF-α-induced necroptosis (30 µM; 8 h) in murine fibrosarcoma L929 cell line, using a bioluminescent cytolysis assay. From the full library screening, valid data was achieved for 251,879 compounds. For hit selection, exclusion criteria included qualitative and quantitative parameters, ZScore and percentage of cell death inhibition. A cut off threshold of > 30% inhibition of cell death by tested compounds and a ZScore < -10, led to 3,353 active hits, corresponding to 1.3% hit rate for the full library. For positive hits, dose-response curves were built using a 10-point concentration range of 0.004-100 µM to quantitatively assess inhibitory potency of selected compounds in murine L929 and human Jurkat T FADD$^{(-/-)}$ cell lines. Further selection comprised exclusion criteria of pEC_{50} < 5 (EC_{50} < 10 µM) in both cell lines, leading to 1,000 actives at 29.8% hit rate. Next, using Jurkat E6.1 cells stimulated with cycloheximide (0.5 µg/mL; 8 h) for apoptosis induction, selected compounds were tested in caspase-3/-7 enzymatic activity assays using a 4-point concentration range of 0.03-30 µM; active hits protecting from apoptosis were excluded. Moreover, 33 and 21 compounds showed RIPK1 and RIPK3 inhibitory kinase activity, respectively, although the vast majority protected from necroptosis through yet undetermined mechanisms of action. Based on chemically clusters and drug like properties, 109 compounds were selected for evaluation of long-term necroptosis inhibition in L929 cells. From those, 27 compounds showed protection from cell death in under 15 µM concentration. These compounds displayed better EC_{50} values, protecting from necroptosis at 24 and 48 h, and no toxicity, at a maximum dose of 100 µM. In addition, compounds decreased p-MLKL/MLKL protein ratio. Finally, selected compounds were tested in HT29 cells undergoing necroptosis induced by TNF-α, BV6 (inhibitor of IAP proteins) and Z-VAD-FMK (caspase inhibitor) at 10 and 1 µM for 24 h. Membrane integrity and metabolic activity were evaluated by enzyme release, and ATP levels, respectively. Eight compounds, plus necrostatin-1 completely prevented cell membrane damage and metabolic viability at both concentrations. Target identification and hit to lead medicinal chemistry is now expected to deliver optimized molecules that will then be evaluated in vivo using disease models.

Acknowledgements

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L&H.P11

Structural optimization of azaaurones as antitubercular agents

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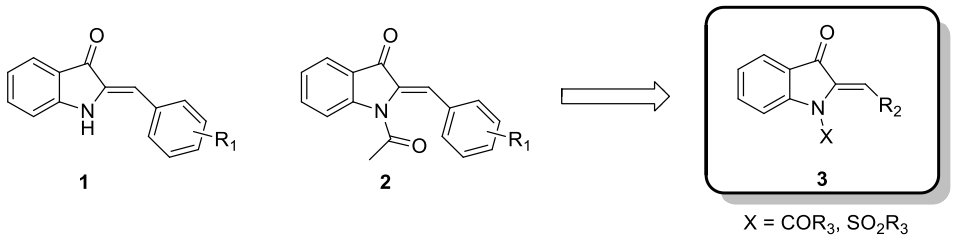
Tuberculosis stands as a major global health issue, with one third of the world population infected by the causative agent, *Mycobacterium tuberculosis*. The emerging resistance along with the low compliance to known drugs are key factors in increasing the disease burden and mycobacteria proliferation.[1] Strains resistant to first line antibiotics represent one fifth of all tuberculosis cases and bacteria resistant to every known treatment are already emerging in both developed and developing countries.[2] It is, therefore, urgent to find new and improved antitubercular drugs that may simplify the treatment and solve the resistance problem.

The azaaurone scaffold, **1**, identified as having antitubercular potential, showed MIC99 values of ca. 1-10 µM against *M. tuberculosis* H37Rv strain. *N*-acylated counterparts, **2**, revealed an increased activity against the bacillus, however the scaffold still displayed poor metabolic stability and low aqueous solubility. We now report the optimization of the azaaurone scaffold with different *N*-protecting groups, **3**, and the preliminary study of their physicochemical properties.



Scheme 1. Optimizing the pharmacokinetic properties of N-protected Azaaurones.

Acknowledgements

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L&H.P12

Liposome encapsulation of a fibrinolytic agent and its effect on clot degradation

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There is increasing evidence for a consistent association of denser fibrin clot structure and higher resistance to degradation (fibrinolysis) with cardiovascular diseases (CVDs). CVDs account for nearly one-third of deaths worldwide and there is an urgent need to overcome this scenario. Fibrin polymerization starts by thrombin-mediated cleavage of fibrinopeptides A and B from the N-terminal of Aα- and Bβ-chains of fibrinogen, respectively. This exposes small residue sequences, knobs A and B, that interact with their respective binding pockets on the C-terminal region of the Aα- and γ-chains of another fibrinogen molecule, leading to the formation and growth of protofibrils, which culminates in fibrin fibres. The aim of the work is to develop an encapsulated fibrinolytic nanoparticle strategy with lower bleeding risk, to be incorporated in the clot structure. We studied the impact of the empty liposome nanoparticle on blood clot formation and lysis and demonstrated that it does not affect haemostasis properties, by recording clot polymerization and lysis kinetics. Using dynamic light scattering and zeta potential assays, we concluded that the nanoparticle is stable over time, without any measurable aggregation or change in its surface charge. Turbidimetry studies showed that the presence of the nanoparticles reflected a non-significant small increase in fibrin fiber radius, protofibril packing and protein content with increasing lipid concentrations. The fibrinolytic agent tissue plasminogen activator (tPA) was added as liposome cargo, using two different methods of encapsulation, with one of them achieving 90% encapsulation efficiency. Ultracentrifugation was used to separate non-encapsulated material without triggering nanoparticle aggregation. Preliminary results demonstrated a controlled release of tPA in a solid emulation of a clot, without activity loss. The work is now focused on optimizing the nanocarrier by surface decoration with a targeting element toward fibrin clots.

Acknowledgements

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L&H.P13

Peptide-conjugate to target brain metastases

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Therapeutic peptides are one of the most promising biopharmaceutical agents. They are attracting more attention owing to their low toxicity, target specificity, potency, broad disease targets, and a small risk of developing drug-drug interactions (DDIs). The evolution of recombinant DNA technology and chemical synthesis, in particular solid-phase peptide synthesis (SPSS), also contributed to their dissemination[1].

Here, we report the therapeutic value of a peptide conjugate, namely PepH3-vCPP2319, produced *via* SPSS using the Fmoc-approach. The conjugate is a combination of an anticancer peptide (vCPP2319) (unpublished data) and a peptide capable of blood-brain barrier (BBB) translocation (PepH3)[2]. The linker used to conjugate two peptides was the aminohexanoic acid. The goal of the therapeutic approach is the translocation of the blood-brain barrier (BBB), and the elimination of brain metastases derived from triple-negative breast cancer (TNBC). The treatment of such disease represents an unmet clinical need since the only therapeutic strategy at this stage is radiation and surgery. The poor efficiency of both methods significantly decreases patients' prognosis[3].

Preliminary data demonstrated that the conjugate has similar properties as its counterparts. It is potent against MDA-MB-231 cells with a low IC_{50}, similar to vCPP2319, and it is capable of BBB cross with a translocation percentage comparable to PepH3. BBB integrity is maintained. The mechanism of action is under evaluation. Biophysical and biological techniques are being applied to elucidate it. The conjugate interacts with the membranes as vCPP2319. However, the effect of the interaction (membrane disruption, pore formation, uptake) is still unknown. Gathering all this information will be important to further validate the applicability of the conjugate in the treatment of brain metastases.

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L&H.P14

Rhamnolipids: Choosing *Burkholderia thailandensis* for antimicrobial glycolipids synthesis

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Infectious diseases are one of the main causes of death and top causes of disability-adjusted life years worldwide. Among these are hospital acquired infections associated to the use of medical devices that are responsible for significant raise of morbidity and mortality. The improvement of medical devices with antimicrobial properties is an approach to be followed and although different options have been suggested there is an emergent need to find new and safe active molecules[1]. Within this scope, rhamnolipids, low toxicity biodegradable biosurfactants with antimicrobial activity, can be a viable alternative, nevertheless they are mostly produced by the pathogenic bacteria *Pseudomonas aeruginosa*.

This study aims the use of *Burkholderia thailandensis,* a non-pathogenic microorganism, to produce active antimicrobial rhamnolipids.

Rhamnolipids were biosynthesised by the non-pathogenic yeast *Burkholderia thailandensis* and different hydrophilic and hydrophobic carbon sources were added to culture media in order to test their influence on microorganism growth and rhamnolipids production. Rhamnolipds production was evaluated through contact angle measurement of culture media, TLC and ESI/LC-MS-MS.

Although rhamnolipids were produced as a mixture, with all the carbon sources supplemented, it was with coconut oil that the production was more evident

In conclusion, coconut oil was the carbon source selected for the biosynthesis of rhamnolipids intended to further experiments on medical devices surface-functionalization.

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L&H.P15

Innovative chemical tools to explore Parkin pathway

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Parkinson's disease (PD) is the second most common progressive neurodegenerative disorder worldwide, affecting approximately 1.5% of the population above 60 years old and 4% of the population at the age of 80.[1]

Although PD is primarily a sporadic disorder of unclear aetiology, it is now clear that genetic factors contribute to the pathogenesis of the disease. For example, mutations in the *parkin* gene, which encodes Parkin protein, are a relatively frequent cause of autosomal recessive early-onset forms of PD[1].

Parkin is a ring-in-between-ring (RBR) E3 ubiquitin ligase, composed by six distinct domains. The catalytic module of Parkin has a multidomain architecture consisting of RING1, IBR and RING2 domains (the latter harbouring the catalytic cysteine), and is responsible for the ubiquitination and consecutive proteasome degradation of a number of protein substrates[2,3].

The ubiquitination-proteasome system is fundamental to several cellular events and its malfunction induces impairment in mitophagy and accumulation of dysfunctional mitochondria, indicating that loss-of-function of Parkin protein may be a key to the neurodegeneration process and to the pathogenesis of PD. Therefore, restoring Parkin function using rationally designed peptides and small molecules has been emerging as a potential therapy for Parkin-linked PD.

However, medicinal chemistry approaches to regulate this pathway have always been hindered by the lack of suitable robust methodologies for screening endeavours[2,3].

To address this challenge, a series of activity-based probes for profiling Parkin activity is being developed. Concurrently, a yeast-based phenotypic assay[4] is being implemented and the biological activity of selected probes evaluated.

These novel chemical tools hold promise as innovative biomarkers for Parkin activation, providing the bases for Parkin high-throughput screening campaigns.

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L&H.P16

Isolation and cytotoxicity study of 7α-Acetoxy-6β-hydroxyroyleanone from *Plectranthus hadiensis*

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Cancer is the second leading cause of death globally, accounting for 1 in 6 of all global deaths (World Health Organization)[1]. Natural Products are a rich source of anti-cancer drugs. The *Plectranthus* spp. plants are the focus of several scientific investigations, due to their ethnopharmacological use by indigenous populations. The *Plectranthus* genus is a known source of bioactive diterpenes with antitumor potential[2]. Abietane diterpenoids display an array of biological activities including cytotoxic and antiproliferative activities against human tumor cells. Abietane compounds such as 7α-acetoxyroyleanone and royleanone compounds have been demonstrated to possess alkylating properties[3].

In this work, we evaluated the general toxicity of acetonic extracts of sixteen *Plectranthus* spp. The extracts of the different *Plectranthus* spp. were obtained by sonication (10% (w/v) of dry plant) and the highest yield obtained was from *P. mutabilis* (30% w/v). The general toxicity was initially screened using the *Artemia salina* (brine shrimp) lethality assay and the LC_{50} determined. *P. swynnertonnii* was the most toxic with *A. salina* model (0.036 µg/mL). The antitumor potential of the most toxic extracts was further explored in different cancer cell lines: colon colorectal carcinoma (HCT116), human breast adenocarcinoma (MCF-7) and lung cancer carcinoma (NCI-H460). The results showed that *P. hadiensis* (Forssk.) Schweinf. ex Sprenger with IC_{50} values of 3.45±0.35, 2.9±0.10 and 3.00±0.10, respectively, was the most cytotoxic. The cytotoxic *P. hadiensis* extract was purified by preparative TLC (silica gel; *n*-hexane/AcOEt; 8:2) to afford 7α-acetoxy-6β-hydroxyroyleanone. The royleanone compound was structural elucidated based in physicochemical data (melting point), spectroscopic data (1D- and 2D-NMR experiments) and comparison with bibliographic data. This compound could be the responsible for the cytotoxicity of the extract, however other compounds or its synergetic effect could account for the extract cytotoxicity. More studies are ongoing to unveil the cytotoxicity of this extract.

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L&H.P17

Antimicrobial peptide PaMAP1.9 has high affinity for cancer cells

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Increased resistance to conventional antibiotics has become a major problem worldwide. Existing antibiotics are progressively becoming ineffective, leading to an increase in the number of deaths associated to infections by antibiotic-resistant strains. Moreover, in immunocompromised patients such as in cancer treatments, the risk for severe infection also increases dramatically. One of the most promising alternatives is the use of antimicrobial peptides (AMPs), which play a key role in the innate immune response of different organisms. Their mechanisms of action are not fully understood, but their physicochemical properties are determinant, namely their amphipathic conformation upon interaction with biomembranes, and their positive net charge, which allows them to interact preferentially with negatively charged biomembranes (as those found in bacteria or cancer cells). Synthetic AMPs have been gaining interest, due to the diverse advantages that they present, namely, the possibility to improve their activity or the shortening of the amino acid sequence length.

Two different AMPs (PaMAP2 and PaMAP1.9) were synthetically designed by using a new mathematical algorithm, focusing on antimicrobial activity. In prior studies, we confirmed this activity toward Gram-negative bacteria, studying the peptide-membrane interactions using biophysical methods. Using the same approach and knowing that cancer cells have an increase in negative charge, we studied the efficiency of both peptides against lipid vesicles and cancer cell lines (HeLa and HCT-116). Peptide-membrane interaction was also studied by fluorescence spectroscopy, using the membranes probes di-8-ANEPPS and Laurdan, and by confocal microscopy. Results show that only PaMAP1.9 may be a good drug candidate for cancer therapy, on the contrary to what could be expected, considering that the other peptide showed to be more aggressive toward bacteria.

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L&H.P18

Unraveling the 20S native human proteasome

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The Ubiquitin Proteasome Pathway (UPP) plays a pivotal role in intracellular protein degradation and turnover in eukaryotic cells[1]. Therefore, modulation of the UPP emerged as a rational therapeutic approach in cancer, neurodegenerative diseases (Alzheimer, Parkinson), inflammatory pathologies (arthritis, psoriasis, asthma, colitis), organ transplant, infective diseases (malaria), among others[2].

During the last two decades academia and pharmaceutical industry made huge efforts to develop natural and synthetic proteasome inhibitors (PI). In 2003 FDA approved the pioneering dipeptidyl boronic acid derivative PI bortezomib for the treatment of refractory multiple myeloma (MM) and subsequently frontline therapy for MM. However, despite the enormous potential of PI, their use is still limited to certain types of blood cancer and shows severe side effects, dose limiting toxicity, peripheral neuropathy, limited activity in solid tumour and innate or acquired drug resistance[3].

In this work, we have used Molecular Dynamics (MD) simulations to perform the first conformational and structural characterization of the human native 20S proteasome structure[4]. We focused our analysis on the three catalytic subunits well known for their proteolytic activity (β1, β2 and β5) and we further extended our study to additional MD simulations of three different point mutations in the β5 catalytic subunit, with recognized importance in PI's resistance: Ala49Thr, Ala50Val and Cys52Phe. Hopefully, our studies will be able to shed the light on the structural key determinants that regulate the observed PI's resistance in the different mutations, and ultimately use the acquired knowledge in the development of new alternative and efficient proteasome inhibitors.

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L&H.P19

Valorization of *Quercus faginea* barks

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Bark is an important protection component of trees against several external agents and the knowledge on the bark complex structure and chemical composition allows a more efficient sampling, fractioning and processing towards specific end-uses[1-3]. In addition to their fuel value, barks are also as potential resource for biorefineries given their chemical complexity and diversity and several studies are increasing the otherwise rather scarce information on barks[4,5]. They can be a source of high-value chemicals with different possible end-uses[6].

To our knowledge, little is known about the bark of *Quercus faginea*, so this study is a full resource approach focused on the chemical composition detailed analysis regarding the summative chemical composition and the composition of suberin, lipophilic and polar extractives. Evaluation of results allowed us to propose *Q. faginea* barks as interesting sources of polar compounds including phenols and polyphenols with possible interesting bioactivities, while the sterols and triterpenes contained in the lipophilic extracts may also be valuable bioactive compounds or chemical intermediates for specific high-value market niches, such as cosmetics, pharmaceuticals and biomedicine.

Acknowledgements

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L&H.P20

Potentials Modelators of necroptosis based on oxazol-5-(4H)-ones

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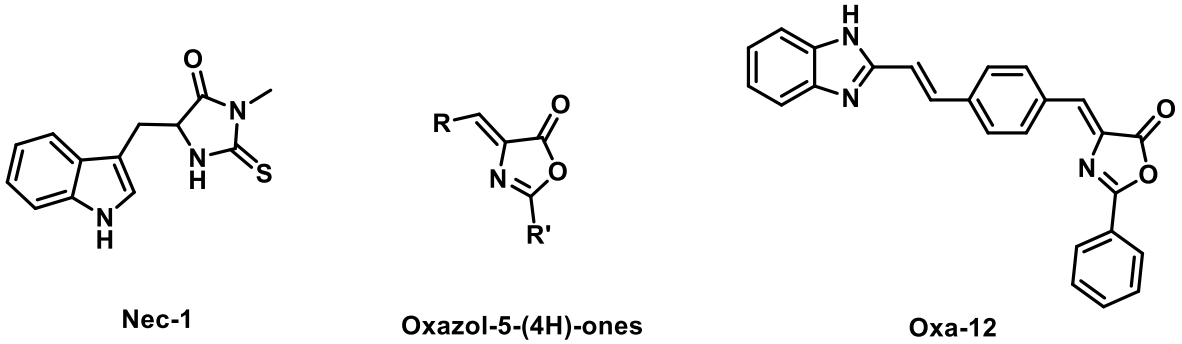
Necroptosis is a caspase-independent regulated form of necrosis that occurs when apoptosis is inhibited. RIPK1 and RIPK3 proteins mediate necrosome formation that activates MLKL and leads to necroptosis. This type of cell death was associated with a variety of pathologies such as stroke, myocardial infarction, septic shock and acute pancreatitis.[1]

Necrostatin-1 (Nec-1) was the first reported necroptosis inhibitor and acts as RIPK1 antagonist. However, it has some associated problems such as off-target effects when used at relevant *in vitro* doses or sub-optimal metabolic stability which results in a short *in vivo* half-life.[1]

From the synthesized oxazolones (OXA)[2] and performing a preliminary screening in cell lines (BV-2 microglia and L929 fibrosarcoma) showed a lead compound, OXA12, with an inhibition activity similar to the know inhibitor Nec-1 (Scheme 1).



Scheme 1. Structures of the Necrostantin-1 (Nec-1), general structure of oxazol-5-(4H)-ones and structure of OXA-12.

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L&H.P21

Development of Torin-based compounds for treating protozoan Neglected Tropical Diseases

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Kinases represent a large proportion of the druggable genome and, as such, have been the focus of drug discovery programs. Comparative analysis on the genomes of the protozoan parasites responsible for some Neglected Tropical Diseases (NTDs) revealed hundreads of protein kinases (PKs) in *Trypanosoma brucei* (176), *Trypanosoma cruzi* (190) and *Leishmania major* (199), most of which are orthologous across these species.[1]

Therefore, the kinase gene family represents a rich source of potential biological targets for pursuing anti-parasitic agents. Repurposing current knowledge about molecular targets that pathogens hold in common with humans is one of the most powerful strategies to bridge the gap between biology and drug discovery for NTDs, using scaffolds that are known as potent inhibitors of the human homologues of essential kinases in the parasites.

Our group has recently disclosed Torin2, an ATP-competitive mTOR kinase inhibitor,[2] as a potent antimalarial with *in vivo* activity against both liver and blood stages and a distinct mode of action compared with currently used antimalarials.[3] These findings inspired us to further explore Torin2 in other protozoan parasites and our results showed that the compound is consistently efficient against *T. brucei* and *T. cruzi* (IC_{50} in the nM range).

Taking into account the gathered knowledge, we have synthetized a highly diversified library of Torin-based analogues in order to establish the key structural features that determine biological activity and those that can contribute to parasite selectivity. In addition, and based on preliminary data from the SAR studies, chemical tools are being developed for *in vivo* imaging of torin-based inhibitors.

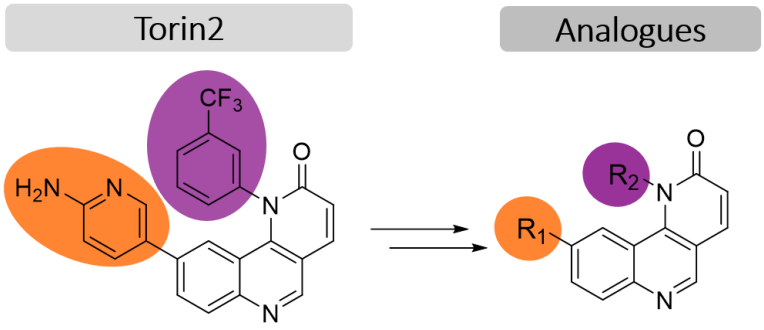

Figure 1. Probing the chemical space around Torin2 scaffold.

Acknowledgements

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L&H.P22

Bioprospecting of Novel Microalgae (*Tetraselmis sp. IMP3*, *Tetraselmis sp. CTP4*, and *Skeletonema sp.*): Lipid Composition and Bioactivity

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Recently isolated microalgae *Tetraselmis sp. IMP3*, *Tetraselmis sp. CTP4*, and *Skeletonema sp*. were studied. Lipid composition and key bioactivities were analysed in order to assess their potential for nutraceutical and other applications. The three novel strains contained relatively high levels of polyunsaturated fatty acids (PUFA) and, among these, n3 PUFA were the most abundant. However, highly unsaturated n3 FA contents were relatively low. In general, eicosapentaenoic acid (EPA, 20:5 n3) contents were low. However, in *Skeletonema* biomass, EPA levels were higher than 10% of the total FA. Conversely, docosahexaenoic acid (DHA, 22:6 n3) never exceeded 3% of total FA. α-Linolenic acid (ALA, 18:3 n3) and 16:3 n4 were the main PUFA in *Tetraselmis* strains and *Skeletonema*, respectively. High contents of myristic (14:0) and palmitoleic (16:1 n7) acids were found in *Skeletonema*, whereas the *Tetraselmis* strains were rich in palmitic (16:0) and oleic (18:1 n9) acids. Linoleic acid (18:2 n6) content was low in *Skeletonema*. This microalga had the highest total polyphenol content, reaching 300-400 mg/100 g dw. The highest antioxidant activity was also displayed by *Skeletonema* with exception of that detected in ethanolic extracts assessed via the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method. Under these conditions, highest antioxidant capacity was observed in *Tetraselmis sp. IMP3* extracts. The Ferric Ion Reducing Antioxidant Power (FRAP) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) methods showed higher antioxidant power for *Skeletonema sp.* extracts, reaching an ABTS reduction of more than 80%. Concerning anti-inflammatory activity, ethanolic extracts of *Skeletonema sp.* exhibited the highest inhibitory capacity of cyclooxygenase-2 (COX-2), 82±2%, which compares to 36±9% in *Tetraselmis sp. CTP4* and 45±5% in *Tetraselmis sp. IMP3*. Aqueous extracts had always a lower anti-inflammatory capacity. Therefore, these microalgae have the potential for multiple applications, ranging from bioactive feedstocks to nutraceutical and pharmaceutical uses.

Acknowledgements

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L&H.P23

Hydrogels as Prebiological Evolutionary Environments

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Water plays an important role in life, suggesting that it was a main solvent for prebiotic syntheses. However, some prebiological reactions, such as phosphorylations, have only been achieved in aqueous solution with low yield[1], due to its hydrolytic activity. Water in hydrogels can have a lower hydrolytic activity than bulk water, allowing phosphorylations within hydrogels. These could have acted as filters for high-energy radiation and as primitive membranes in the primordial Earth, protecting and differentiating important organic compounds (such as nucleosides) from the outside world[2]. Purines derivative hydrogels[3] were studied as potential prebiological media for phosphorylation reactions and the occurrence of phosphorylated species was confirmed by ^{31}P NMR[4] and Mass Spectrometry (including tandem mass spectrometry).

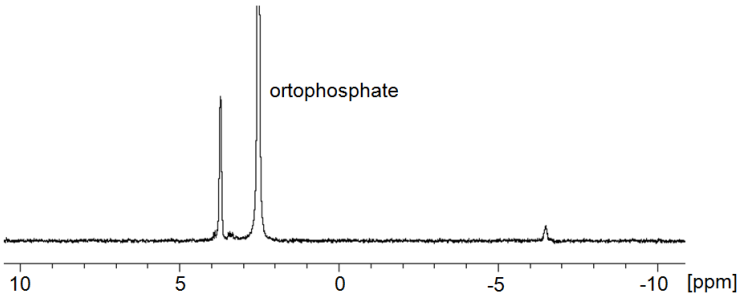

Figure 1. ^{31}P NMR spectrum of purines derivative hydrogel sample.

Acknowledgements

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A. Franco acknowledges financial support from BL-CQE/2017-024 and BL-CQE/2018-012.

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L&H.P24

Synthesis and structural characterisation of a new family of copper(I)-phosphane complexes for cancer therapy

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Despite the intensive efforts continuously taken during the past decades by researchers, cancer is still a leading cause of high morbidity and mortality worldwide. Cisplatin and analogues (e.g. oxaliplatin and carboplatin) are up to date the unique metallodrugs approved for cancer therapy. Even though well-established in the treatment of several varieties of cancer, platinum-based drugs use is keenly limited due to their severe side effects and the increasing drug resistance fully reported. Copper complexes have attracted much interest as potential alternative chemotherapeutics, mainly because are expected to be less toxic and to overcome platinum resistance by acting through different mechanisms[1]. During the recent years our group has been involved in the development of new copper(I)-phosphane derived complexes which cytotoxicity was found, in most of the cases, higher than that of cisplatin against ovarian and breast human cancer cell lines[2,3].

Here we will present a family of copper(I) complexes of general formula [Cu(PP)(LL)][BF_4], where PP represents bi/monodentate phosphanes and LL several N,O- heteroaromatic ligands (Figure 1).

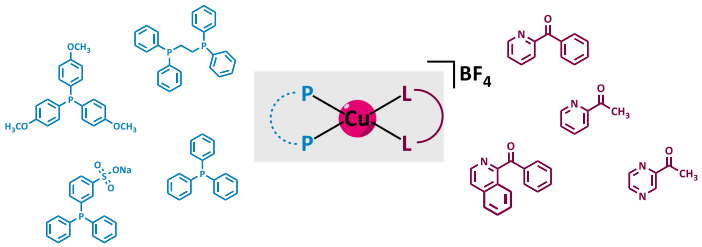

Figure 1. General structure of copper(I) complexes where PP = bi/monodentate phosphanes (blue) and LL = N,O- heteroaromatic ligands (red).

All the compounds were fully characterized by elemental analysis, FT-IR, UV-Vis. and multinuclear NMR spectroscopy techniques and, when single crystals were obtained, X-ray diffraction studies were also performed. The stability of the complexes in organic and aqueous solutions over time was determined to evaluate their suitability for further biological assays, namely test their anticancer activity in different human cell lines with low, medium and high resistance to metallodrugs.

Acknowledgements

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L&H.P25

Structure-based virtual screening for Hexokinase 2 inhibitors aimed at cancer treatment

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Glucose is regarded as the main fuel of cancer cells and the glycolytic pathway has been demonstrated as a potential target to be explored for cancer treatment. Several enzymes involved in glycolysis are overexpressed in different types of cancer cells, namely hexokinase 2 (HK2)[1]. This enzyme is involved in the first and most determinant step of the process, catalysing the phosphorylation of glucose to glucose-6-phosphate, also involved in the pentose phosphate pathway[2,3]. Therefore, the inhibition of the HK2 catalytic centre (Figure 1) is proposed as a strategy to reduce the main source of energy to cancer cells, thus substantially decreasing cancer cell proliferation. As an effort to find hit compounds able to interfere with the HK2 catalytic centre and thereby block its activity, a structure-based drug design strategy was implemented, leading to the virtual screening of several databases such as DrugBank (~2000 molecules), NCI (~265 000 molecules), Chemoteca (~800 molecules) and Enzyme Function Initiative – Phosphate sugars (~100 molecules). The virtual screening was carried out using molecular docking calculations through Gold 5.20 software. Molecules were prepared using Molecular Operating Environment (MOE2016 0802) and then docked into the HK2 catalytic site. Prior validation of the above-mentioned protocol was conducted, by testing different three-dimensional (crystallographic) HK2 structures, the amino acids at the catalytic pocket centre, scoring functions and catalytic pocket radius. Our results have suggested several hit compounds with the potential to act as new HK2 inhibitors that may progress to biological evaluation.

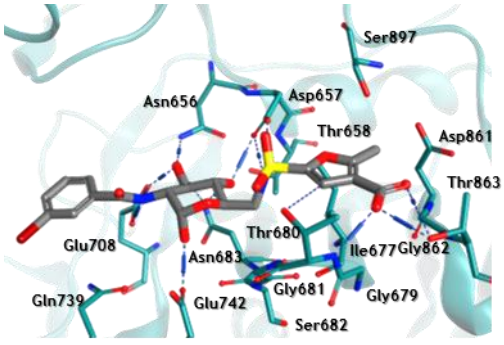

Figure 1: Representation of the HK2 catalytic centre (*C*-terminal domain) in interaction with an inhibitor (grey) (PDBID: 5HEX).

Acknowledgements

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L&H.P26

Diversifying the chemical toolbox to uncover Torin2 molecular targets in Malaria

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Malaria, an infectious disease caused by protozoan parasites of the *Plasmodium* genus, is still endemic in the tropical regions of the globe, where it represents nearly half a million deaths a year, according to the latest data.[1] Parasite resistance is an established concern for most of the available drugs, clearly demonstrating the need for new alternatives that present novel mechanisms of action and can overcome both the resistance cases and fill the void of liver stage active compounds.[2]

Torin2, an ATP-competitive mTOR kinase inhibitor, has been disclosed as a potent antimalarial with *in vivo* activity against both liver and blood stages of malaria through a mechanism of action different to those compounds already in clinic.[3]

To unveil the structural features responsible for antimalarial activity as well as those that induce parasite-host selectivity, we synthetized an extensive library of new Torin2 analogues, which were screened against both liver and blood stage parasites cultures, and we report the structure-activity relationships (SAR) obtained to identify the suitable lead compounds for further development, as well as modifiable positions. Equipped with this knowledge, and through minimally disruptive modifications we prepared a library of Torin-based "turn-on" fluorescent probes and photoaffinity-based probes, providing the chemical tools to further study this class of inhibitors and identify its molecular target(s) (Figure 1).

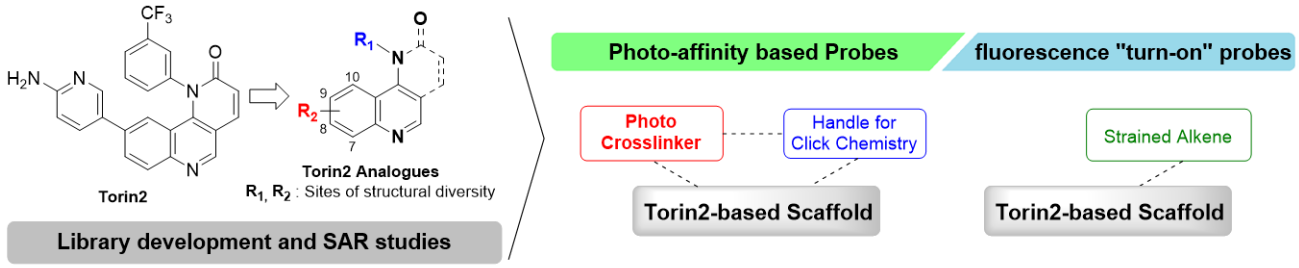

Figure 1 - Development of a Torin2-based chemical library for SAR studies on *Plasmodium* spp. and rationale for the development of chemical probes.

Acknowledgements

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L&H.P27

Fibrinogen-induced erythrocyte-erythrocyte adhesion: A cardiovascular risk factor

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Erythrocyte aggregation is an indicator of cardiovascular risk, which is influenced by plasma fibrinogen concentration. Fibrinogen levels are elevated during cardiovascular diseases. Our main goals were to understand how fibrinogen-erythrocyte binding influences erythrocyte aggregation and how it constitutes a cardiovascular risk factor in essential arterial hypertension (EAH) and chronic heart failure (CHF). Fibrinogen-erythrocyte and erythrocyte-erythrocyte adhesion measurements were conducted by atomic force microscopy (AFM)-based force spectroscopy. Upon increasing fibrinogen concentration, there was an increase in the work and force necessary for cell-cell detachment, both for healthy donors and EAH patients. Nevertheless, higher values were obtained for the EAH patients at each fibrinogen concentration. Fibrinogen-erythrocyte (un)binding forces were higher in EAH and CHF patients, when compared with the control group, despite a lower binding frequency. Ischemic CHF patients showed increased binding forces compared to non-ischemic patients. Erythrocyte deformability (assessed as elongation index) results show that heart failure patients presented higher erythrocyte deformability than the control group at lower shear stresses, and lower deformability at higher shear stresses. This indicates that patients' erythrocytes are more deformable than those from healthy donors in blood vessels with larger internal diameters; however, in smaller-diameter vessels the opposite trend exists. Finally, a 12-month clinical follow-up shows that CHF patients with higher fibrinogen-erythrocyte binding forces, probed by AFM at the beginning of the assessment, had a significantly higher probability of being hospitalized due to cardiovascular complications on the subsequent year. Our results show that AFM can be a promising tool for clinical prognosis, pinpointing those patients with increased risk for cardiovascular diseases.

Acknowledgements

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L&H.P28

New molecules to inhibit the 20S proteasome: Computer-aided drug design methodologies and biological evaluation

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The ubiquitin proteasome system is a nonlysosomal pathway by which cells regulate the controlled degradation of several proteins, not just in cell cycle and apoptotic processes but also in inflammatory and immune responses, carcinogenesis, among other clinical situations. Usually, in protein homeostasis the defective proteins are ubiquitinated and are proteolysed into short peptides by the proteasome. Proteasome substrates include signalling molecules, tumour suppressors, cell cycle regulators, transcription factors, among others. Proteasome inhibition results in an interruption of the degradation of these substrates, leading to activation of apoptotic pathways and, eventually, cell death. Rapidly growing cells, such as cancer cells, are particularly susceptible to proteasome inhibition mechanisms.[1,2]

This work relies on a computational-based drug discovery approach to find alternative new, selective (and more effective) small molecules as reversible proteasome inhibitors that can overcome the severe adverse drug reactions demonstrated by in use drugs. The efforts to discover new anticancer drugs described here combine different computer-aided drug design techniques (i.e. molecular docking and structure-based virtual screening) in order to identify potential hit compounds (Figure 1). The selected molecules were tested in citotoxicity assays (i.e. MTT), being also performed inhibition assays for the chymotrypsin-like, trypsin-like and caspase-like activities of the proteasome using fluorogenic substrates.

Figure 1. Computer-aided drug design workflow.

Acknowledgements

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L&H.P29

In vitro antimicrobial activity of isopimarane-type diterpenoids

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Antibiotic resistance is nowadays an increasingly serious threat to global public health[1]. A growing list of infections related to methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) are becoming more difficult, and sometimes impossible, to treat[2]. An important strategy to overcome this need is the continuous research on natural products and derivatives. Compounds **1** – **6** and **9** were isolated from *Aeollanthus rydingianus* aerial parts[3]. Five new acyl (**7**, **8**) and glycosyl (**10** – **12**) derivatives of these natural isopimaranes were prepared and their structures elucidated by NMR. These new derivatives and the natural ones (Figure 1) were assayed against an enlarged panel of bacteria, which included two MRSA and one VRE strains. Only natural compounds **1** and **6** showed promising results. Compound **1** was the most active, showing MIC values between 1.95 µg mL^{-1} against *S. aureus* (ATCC 43866) and 62.50 µg mL^{-1} against *E. faecalis* (FFHB 427483) and *E. flavescens* (ATCC 49996). In addition, the cytotoxicity of compounds **1** – **3**, **5**, **6**, **8** – **12** was evaluated in the human breast cancer cell line MDA-MB-231. Compound **2** was the only compound showing some cytotoxicity. The IC50 value of compound **2** was 15 µM, suggesting a mild antiproliferative activity against these breast cancer cells.

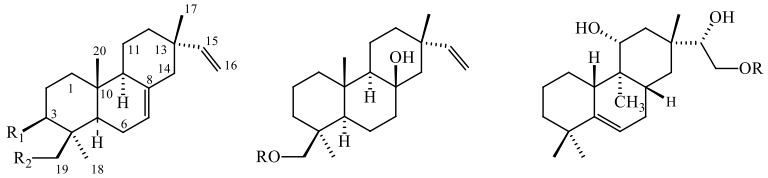

Figure 1. Compounds tested for antimicrobial activity.

Acknowledgements

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L&H.P30

Effects on antioxidant defence mechanisms of lettuce plants exposed to contamination by metformin

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The aim of this work is to understand how lettuce cope with the contamination by metformin, a pharmaceutical product. Metformin is a pharmaceutical product used in therapy of type 2 diabetic patients and is excreted in urine unchanged. Previous studies reported that the uptake of pharmaceuticals by different plants can occur since they can be found in irrigation and wastewaters[1,2].

A hydroponic culture of lettuce was exposed to different concentrations of metformin for 15 days. This contamination was applied after 36 days of growing. During contamination period lettuce plants were harvested three times (days 1, 8 and 15 after contamination).

Different parameters related to oxidative stress were evaluated (H_2O_2, CAT, GPOD, SOD). Generally, it was observed that some enzymatic activities increased for the longer periods of contamination. For instance, catalase and guaiacol peroxidase activity showed significant differences when compared to control plants after 15 days of exposure. In case of H_2O_2 content lettuce plants contaminated with 1 and 5 mg/l of metformin showed an increase in the production of this reactive oxygen species (ROS) on the 1st day of contamination and in parallel SOD activity also increased.

When plants were collected also some physiological parameters where taken into account such as biomass (plant, leaves and roots) and number of leaves but his parameters didn't revealed differences to control plants. The chlorophyll content was also measured as usually photosynthetic activity is one of the most affected parameters when plants are subjected to stress, but no differences were detected in metformin contaminated plants.

Acknowledgements

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L&H.P31

Changes on elasticity and morphology of erythrocytes from amyotrophic lateral sclerosis patients

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Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease. Patients' complications, such as venous thromboembolism (VTE), promote changes in haemodynamic properties and abnormalities in red blood cells (RBC) membrane and on its lipid content. Our main goal was to evaluate changes in the elastic and morphological properties of RBCs in ALS and compare them with the erythrocytes from healthy donors. By atomic force microscopy (AFM), RBC membrane roughness, elasticity and morphological parameters were analysed for both groups. Patients' RBCs are stiffer, have higher penetration depth and are more capable to deform, presenting an increased membrane roughness. Morphological changes on RBCs from ALS patients were also assessed by AFM, showing lower thickness and higher cell area. Zeta-potential analysis showed that the surface of patients' RBCs is less negatively charged, which may be due to a lower density of sialic acid residues. Fluorescence spectroscopy showed that RBC membranes from ALS patients are more fluid. This may be associated with changes on membrane lipid composition and packing. We conclude that ALS disease leads to significant electrostatic and morphologic changes in RBC membranes. These findings may contribute to understand the complex interplay between ALS disease progression rate and RBC lipid profile.

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L&H.P32

Dual p53-MDM2/X interaction inhibitors: A promising approach for cancer treatment

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In all types of human cancers, the p53 tumour suppressor, also known as the guardian of the genome, is inactivated by mutation or gene deletion (50% of the cancers) or by negative regulators (50% of the cancers). When p53 retains its wild-type (wt) conformation, it interacts with negative regulators such as MDM2 and MDMX, which are overexpressed in cancer cells. Currently, the most popular approach to activate the wt p53 is the inhibition of the protein-protein interaction (PPI) of p53 with these two regulators using small molecules. In this way, p53 is released and can act as tumour suppressor.[1]

In this area of research, we have been working in the development of spiropyrazoline oxindoles as p53-MDM2 interaction inhibitors. The first series of compounds showed promising *in vitro* anti-tumour activities in colon and breast cancer cell lines.[2-3] In this communication, we report the synthesis and structure-based computational optimization of this chemical family for the development of dual p53-MDM2/X interaction inhibitors. Our studies will shed lights on the possible binding mode of spirooxindole derivatives to MDM2 and MDMX, and will drive the hit-to-lead optimization strategy.

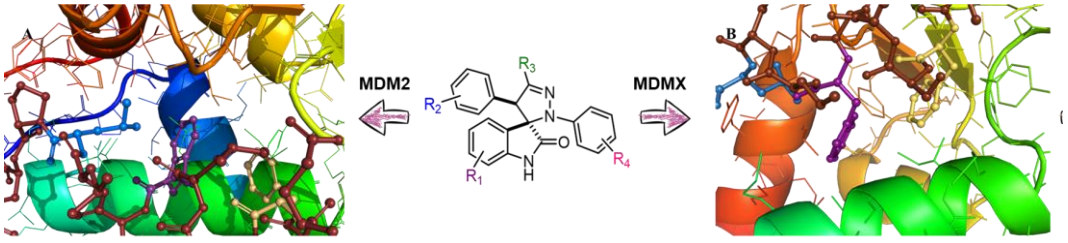

Figure 1. Spiropyrazoline oxindole scaffold (chemical structure) mimics the four critical amino acids of p53 (ball and sticks) to bind to MDM2 (**A**, PDB ID: 1YCR) and MDMX (**B**, PDB ID, 3DAB).

Acknowledgements

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L&H.P33

Reversible N,O-Iminoboronates With Improved Stability For Cancer Cells Targeted Delivery

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Herein we present a new class of iminoboronates[1] obtained from 2-acetylbenzene boronic acids and aminophenols. The N,O-ligand topology enabled the formation of an additional B-O bond that locks the boron centre in a tetrahedral geometry. This molecular arrangement decisively contributes to improve the construct stability in biocompatible conditions, retaining the iminoboronate reversibility in more acidic environments. 2-Acetylbenzene boronic acid was reacted with a fluorescent amino-coumarin to yield a stable and non-fluorescent N,O-iminoboronate. This mechanism was further used to assemble a folate receptor targeting conjugate that selectively delivered the fluorescent amino-coumarin to MDA-MB-231 human breast cancer cells.[2]

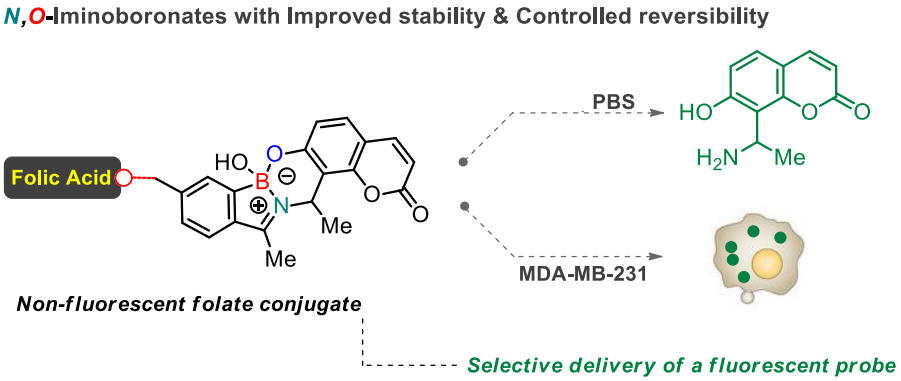

Figure 1. N,O-iminoboronate folate conjugate to selectively deliver the fluorescent amino-coumarin to MDA-MB-231 human breast cancer cells.

Acknowledgements

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L&H.P34

Phytochemical and antibacterial evaluation of two Rutaceae: *Zanthoxylum zanthoxyloides* and *Zanthoxylum leprieurii*

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One of the adaptive mechanisms presented by plants to survive to edaphoclimatic conditions is the biosynthesis of a great diversity of secondary metabolites, including terpene compounds, alkaloids, flavonoids and phenolics. Some of those chemical groups have been a valuable source of natural products, which can help in maintaining human health. In order to a better understanding on the safety and efficacy in the traditional medicinal use of plants, this study focus on the *in vitro* antibacterial activity of different polarity extracts of two Rutaceae species, *Zanthoxylum zanthoxyloides* and *Z. leprieurii.* Plant material was collected in Guinea-Bissau during 2016-2017, species identification was confirmed and vouchers deposited at LISC.

Extracts were obtained by a sequential extraction of the dry plant powder with *n*-hexane, CH_2Cl_2, EtOAc, MeOH and water, filtered, concentrated and stored at -20 °C. Evaluation of the semi quantitative phytochemical profile was carried out thought TLC on silica gel, developed with appropriated mixtures of solvents. Spots were revealed with proper revelators, according to Wagner and Blader[1]. The extracts were tested against six Gram-positive bacteria: *Staphylococcus aureus* (ATCC 6538, 43866, CIP 106706), *S. epidermidis* (ATCC 12228) and *Enterococcus hirae* (CIP 5855), and two Gram-negative: *Pseudomonas aeruginosa* (ATCC 9027) and *Escherichia coli* (ATCC 8739). The minimum inhibitory concentrations (MIC) were determined by the serial broth microdilution method. The MIC values were considered negative when > 100 µg/mL.

Several extracts were able to inhibit the bacteria grow, being *E. hirae* the most sensitive strain. The most active extracts were the apolar ones (CH_2Cl_2 and EtOAc) which were particularly rich on terpenes and flavonoids. The presence of those compounds might be responsible for the antimicrobial activity. These are preliminary results that point to the validation of these species use in traditional medicine and emphasize the worthwhile of additional studies.

Our results of the antimicrobial tests show that these plants can be useful as a new potential source of natural antibacterial agents, providing a possible valorization of the existing biodiversity and resources of Guinea-Bissau flora.

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L&H.P35

Zika virus capsid protein structure and its ability to interact with host lipid systems

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Zika virus (ZIKV), is a mosquito-borne virus from the Flaviviridae family and Flavivirus genus, closely related to other human pathogens, such as dengue virus (DENV) and West-Nile virus (WNV).[1] Although ZIKV was first isolated in 1947,[2] it gathered widespread interest only in 2015, becoming an international public health emergency.[3] This was due to a major outbreak in Brazil and other South American countries, in which a clear causative association with severe congenital microcephaly in new-borns (via placental transmission)[4,5] and with Guillain–Barré syndrome (in adults)[6] was fully documented. Although there is a lack of knowledge on basic aspects of the viral life cycle, much can be inferred from the closely related DENV and WNV. Importantly, DENV capsid (C) protein binding to host lipid droplets is essential for DENV replication.[7] We investigated ZIKV C protein binding to host lipid systems by different experimental approaches. Zeta potential shows that ZIKV C interacts with intracellular lipid droplets (LDs). However, this interaction does not require potassium ions, as previously shown by us for DENV[8] and WNV C. Dynamic light scattering measurements indicate that ZIKV C interacts with human plasma lipoproteins, namely very low-density lipoproteins. ZIKV, WNV and DENV C proteins display similar predicted hydrophobicity, α-helical propensity and tertiary structure, which can thus be targeted via similar approaches. Combining this with our background on DENV C studies and pep14-23 development (an inhibitor of DENV C binding to host lipid systems, designed and patented by us)[8-13], we will use this information in drug development strategies against ZIKV and related flaviviruses.

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L&H.P36

Screening for the best chitosan nanoparticle formulation aiming antibiotic delivery

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Chitosan is a biodegradable polysaccharide that presents analgesic and antimicrobial activity[1]. Minocycline is an antibiotic with positive effects on the bone regeneration and anti-inflammatory activity[2]. In the present work, we tested different formulations aiming the production of chitosan nanoparticles (NPs) loaded with minocycline as a viable alternative of biodegradable local drug delivery system with antimicrobial and anti-inflammatory activity.

NPs were prepared using an ionic gelation technique optimized in our laboratory[3] and modifications regarding pH, chitosan proportion and the presence of surfactant were performed aiming NPs characteristics improvement.

Microstructure and morphological features of NPs were evaluated with a Hitachi H-9000-NA transmission electron microscopy (TEM) operating at 200 kV; the crystal structure of NPs was analyzed by X-ray diffraction using a Bruker D8 ADVANCE Powder Diffractometer; attenuated total reflectance was performed to identify the functional groups of NPs using a Nicolet (Thermo Electron) spectrometer; mean particle size, polydispersity index (PDI) and zeta potential of NPs were assessed by light scattering and electrophoretic mobility respectively, using a Zetasizer Nano-S and Nano-Z, (Malvern Instruments); effects of freeze drying procedure on NPs were also evaluated.

Minocycline release from the NPs was evaluated using a dialysis technique[4] and the antibiotic quantification of the release and the encapsulation efficiency were assessed by spectrophotometry (λ = 350 nm) with a microplate reader (FLUOstar Omega, BMG Labtech).

TEM images showed uniformed shape-rounded morphology; X-ray diffraction showed a pour crystalline structure; attenuated total reflectance confirmed no intermolecular interactions among the antibiotic and the NPs; size distribution was between 250 and 400 nm, with a PDI average of 0.350; zeta potential was higher than +20 mV being a stable colloid; antibiotic controlled release up to 24h was observed.

Thus, chitosan NPs is a viable biomaterial carrier for minocycline and should be further tested as a local delivery system.

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L&H.P37

Synthesis of poly(methyl methacrylate) nanocapsules containing levofloxacin as a drug delivery system for the treatment of osteomyelitis

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In recent years, total bone replacement surgeries are becoming more frequent and problems associated to this procedure such as osteomyelitis are getting more common. Due to the difficulty in the treatment of this disease, a novel drug delivery system with a slow release profile in the bone tissue is necessary. Currently, therapeutical approaches consist on the administration of large doses of antibiotics for a long period of time. This is often ineffective due to the low vascularization of the prosthesis and the formation of bacterial biofilms [1].

The novel drug delivery system we are developing consists of a poly(methyl methacrylate) (PMMA) nanocapsule containing levofloxacin. Levofloxacin was chosen as the antimicrobial agent due to its high efficiency against gram-positive and gram-negative bacteria being highly effective in the treatment of osteomyelitis[2]. A PMMA carrier was chosen due to the known use of this polymer in orthopaedics since it is biocompatible and easy to manipulate[3].

We synthesised PMMA nanocapsules by nanoprecipitation in a water-in-oil miniemulsion by solvent evaporation with the nanoprecipitation occurring at the interface between the water droplets containing the antimicrobial agent and the non-solvent phase creating nanocapsules with an average diameter of 300 nm and 500 nm depending on the PMMA molecular weight.

Due to the structure of these nanocapsules, a slow release profile is expected since, for the drug to be release, it must diffuse through the polymer shell. These nanocapsules are going to be implemented in a bone cement for direct application on the infected bone and slowly maintaining the concentration of antibiotic in that zone constant without causing toxicity on other parts of the body.

Drug release studies as well as the antimicrobial activity of the novel PMMA nanocapsules are planned to evaluate their potential use in the treatment of osteomyelitis.

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L&H.P38

Glycidamide-modified histones as biomarkers of acrylamide carcinogenesis

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The environmental and food pollutant acrylamide is a rodent carcinogen.[1] However, its carcinogenicity potential to humans is still uncertain. Actually it is classified as "possibly carcinogenic to humans" (Group 2B) by the International Agency for Research on Cancer. Nonetheless, taking into consideration the high human exposure to this potential carcinogen, this issue needs urgent clarification.

Acrylamide is metabolized to the highly reactive intermediate epoxide glycidamide, which reacts with DNA to form a variety of DNA adducts and induces a tumor spectrum similar to acrylamide in rodent bioassays.[1,2] Therefore, it is widely believed that the carcinogenicity of acrylamide is due to its metabolism to glycidamide, which reacts with DNA to form DNA adducts that cause mutations in critical genes associated with cancer. Nonetheless, high levels of DNA adducts from acrylamide and glycidamide were found in some tissues (e.g., the liver of mice) and tumors were not formed in these tissues. This implies that DNA adducts are not good biomarkers of acrylamide carcinogenicity

As part of our program, aimed at the evaluation of covalently-modified histones as potential biomarkers of chemically-induced cancer, and with the ultimate goal of investigating the role of glycidamide at the induction of human hepatocarcinomas, we have analysed histones, by mass spectrometry-based bottom-up approach, isolated from the non-tumor hepatocytes cells, THLE2, exposed to glycidamide.

A dose-dependent concentration of a glycidamide-modified peptide at histidine 110 of histone H2BJ and/or H2BK was identified in the THLE2 cells that was accompanied by an increase on the expression of tumoral marker alfa-fetoprotein. These results suggest the role of glycidamide as a promoter of human liver cancer and support the use of acrylamide-modified histones as suitable compound-specific biomarkers of carcinogenesis.

Acknowledgements

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L&H.P39

Estimation of solvation free energies by continuum methods: How to tackle halogenated species?

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The incorporation of halogen atoms into drug candidates has occupied an important role in drug discovery and development processes. While traditionally this design strategy mainly aimed at improving drug-like properties (e.g. biomembrane permeability or pharmacokinetic stability), the pharmaceutical potential of halogenated compounds has been increasingly explored for their ability to modulate protein-ligand binding affinity by establishing halogen bonds (XB)[1]. These are highly directional non-covalent interactions explained by the existence of a positive region on the electrostatic potential (ESP) of heavier halogens (X), called σ–hole, which is available to interact with electron-rich species (i.e. Lewis bases). The development of computational methods that accurately model the charge anisotropy of halogenated compounds is therefore of great importance, in view of their use in computer-aided drug design and virtual screening routines. The simplest approach to describe the ESP anisotropy in halogenated species involves the addition of an off-centre positive extra-point (EP) of charge mimicking the σ–hole[2]. Regarding the prediction of absolute protein-ligand binding free energies, the use of molecular mechanics energies combined with Poisson-Boltzmann surface area (MM-PBSA) continuum solvation is a popular methodology. While EP addition has been shown to improve the molecular mechanical description of halogen-containing systems, its effect on the accuracy of binding free energy as estimated by MM-PBSA is yet to be assessed. This method relies on the estimation of the solvation free energy of the ligand, amongst other terms, for which an empirical assignment of halogen parameters, such as the PB radius, is required. Hence, we conducted a comprehensive study on the effect of varying the X···EP distance, together with the halogen PB radii, on the performance of PBSA-based free energy of hydration calculations for a library of halogenated ligands. The results, highlighting the dramatic impact of varying the two parameters on the computed error, when compared with experimental data, will be disclosed. Implications for computer-aided drug design will also be addressed.

Acknowledgements

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L&H.P40

Synthesis and characterization of new iron cyclopentadienyl complexes with *in vitro* cytotoxicity against cervical cancer cells

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Iron is an essential metal for humans, as it is necessary for the biosynthesis of several proteins required for the correct functioning of the human body. Iron role in human physiology as a co-factor of important biological processes is diverse, including cell replication, metabolism and growth. These features, along with the cytotoxic activity shown by some iron complexes previously developed by our group,[1-2] render iron-based compounds interesting alternatives to be exploited for cancer therapy.

Here we will present our recent studies with a new family of piano stool iron-cyclopentadienyl compounds of the general formula $[Fe(\eta^5\text{-}Cp)(CO)(PR_3)(L)]^{n+}$ where PR_3 = triphenylphosphane, 4-(diphenylphosphino) benzoic acid or tris(4-fluorophenyl)phosphane; when L = I, n = 0; when L = 4-aminobenzonitrile, n = 1 (Figure 1).[3]

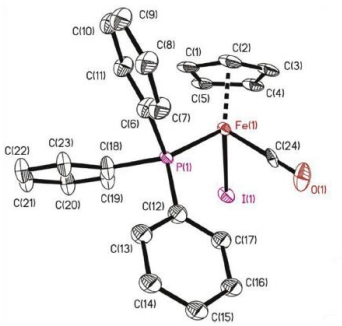

Figure 1. ORTEP plot for the complex $[Fe(\eta^5\text{-}Cp)(CO)(PPh_3)I]$. All the non-hydrogen atoms are presented by their 50% probability ellipsoids. Hydrogen atoms are omitted for clarity.

All the compounds were fully characterized by the usual analytical and spectroscopic techniques. Since all complexes presented adequate stability in aqueous solution they were tested against cervical HeLa human cancer cells. The cationic complexes bearing triphenylphosphane or tris(4-fluorophenyl)phosphane were found to be highly cytotoxic, causing cell death by apoptosis. The Our spectroscopic results point out that the electronic features of the new compounds might be related to their cytotoxic activity.

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L&H.P41

Role of carotenoids in the oxidative response of spinach plants exposed to Cd

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Cadmium is a toxic metal that can be easily taken up by plants from soils or irrigation water due to its high solubility and consequently high bioavailability. Spinach plants are highly tolerant to Cd and can accumulate high amounts of this metal. When plants are expose to Cd, the metabolism can be affected and both enzymatic and non-enzymatic defense mechanisms against oxidative stress can be activated. Carotenoids have an important role protecting the photosynthetic system and detoxifying reactive oxygen species (ROS).

In this work, spinach plants (*Spinacea oleracea*) were grown in nutrient solution with 25 and 50 µM Cd for 14 days and leaf samples were collected during this period for determination of Cd content and carotenoids composition. Cd was determined in acid digested samples by electrothermal atomic absorption spectrophotometry (ETAAS). The carotenoid content was determined by molecular absorption spectrophotometry and high-performance liquid chromatography (HPLC). Comparing the two techniques, the spectrophotometric method is much easier to perform while the chromatographic method has a lower detection limit and allow the quantification of specific carotenoid molecules (like neoxanthin, violoxanthin, anteroxanthin, zeaxanthin, α-carotene and β-carotene).

Spinach plants were able to accumulate in leaves about 100 mg Cd kg^{-1} dry weight without showing visible signs of toxicity. We found that carotenoids levels increased in the presence of Cd. This may indicate that carotenoids (especially of the xanthophyll cycle) are involved in the protection of the photosynthetic system, which is commonly reported to be damaged by exposure to metals at high concentrations. Carotenoids have antioxidative properties and can have a specific role in the sequestration of ROS produced as a consequence of the induced stress.

Acknowledgements

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L&H.P42

Pharmacophore-based drug design applied to EZH2 inhibitors

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Epigenetic pathways are recognized as determinants to cancer development and progression. Polycomb repressive complex 2 (PRC2) is an epigenetic regulator that catalyses the trimethylation of lysine 27 in Histone 3 (H3K27me3), a process that facilitates chromatin compaction and gene silencing.[1] The overexpression of EZH2, the catalytic subunit of PRC2, is implicated in the development and progression of a variety of cancers with the worst prognosis. Thus, the therapeutic targeting of EZH2 emerged as a hot topic and the development of selective small-molecule EZH2 inhibitors is currently a promising research challenge for drug discovery.[2]

We used computer-aided drug design (CADD) methods to identify new starting points for designing EZH2 inhibitors. Specifically, we created 3D-pharmacophore models, using LigandScout Advanced 4.2.1 software[3] to support hits finding. In a first stage, a panel of unique pharmacophore models were generated. The performance of all models was validated against robust databases and the most predictive models were optimized further by systematic modification of the chemical features. The results revealed valuable information about the key interactions and the 3D-geometries associated with of EZH2 inhibition activity. The prioritized models were used for two hit finding campaigns: virtual screening and de novo design. First, using the unique 3D-pharmacophore-based virtual screening method (iscreen) from LigandScout, several databases (e.g., DrugBank, NCI, MuTaLig Chemotheca, and our in-house libraries) were computed and screened. Interesting virtual hit molecules with high inhibition potential were found. In parallel, we started a *de novo* design campaign based on selected pharmacophoric models. Prioritized hits are being tested in biological assays to determine their EZH2 profiles. Those obtained from de novo design are being synthesized to further determine their EZH2 profiles.

Acknowledgements

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L&H.P43

Bifunctional trans-cyclooctenes (BITCO's) for potencial enhancement of spatial and temporal resolution studies in biological systems

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Amongst the bioorthogonal toolbox, inverse electron demand Diels–Alder (IEDDA) reactions stand out from the others by its unmatchable kinetics, excellent orthogonality and biocompatibility for probing and spatial and temporal controlling biomolecule functions in vitro and in living systems.[1] The gold bioorthogonal standard trans-cyclooctene (TCO) is known to react highly efficiently in aqueous solution (2000 $M^{-1}.s^{-1}$).[2] Despite 8-member ring modifications can enhance the kinetics (cis-cyclopropane fusion), increase its stability (dioxolane-fused), or induce a click-to-release mechanism, the scaffold is highly sensitive to modification, prone to degradation and, so far, tolerates only the appendage of a single payload.[3]

We envisioned a double functionalization of the TCO scaffold with minimal impact on reactivity and stability, via diastereoselective cheap silver-catalysed method, to potentially enhance spatial and temporal resolution and double attachment of therapeutic and/or fluorogenic payloads.[4]

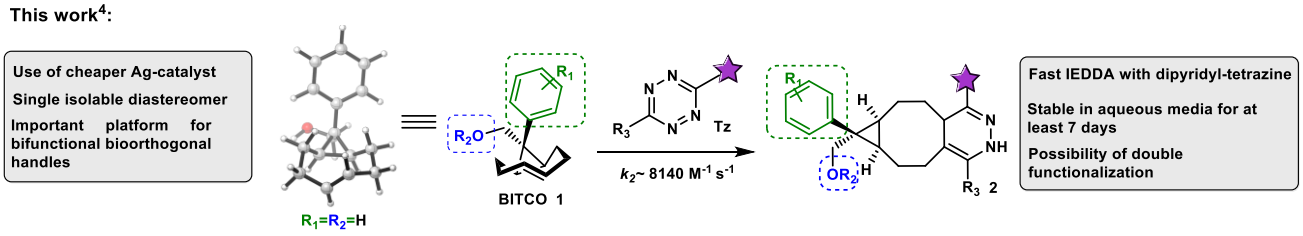

Figure 1. IEDDA between TCO 1 and a generic tetrazine.

Acknowledgments

We thank the Fundação para a Ciência e Tecnologia (UID/DTP/04138/2013, PTDC/QEQ-QOR/3644/2014, and SFRH/BD/120829/2016) and COMPETE Programme (SAICTPAC/0019/2015) and European Research Area Net-work; ERANetLAC (ref. ELAC2014/BEE-0341) for financial support.

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L&H.P44

New selective activator of PKCδ with promising application in colon cancer therapy

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Protein kinase C (PKC) isozymes are widely recognized therapeutic targets in cancer. However, the poor understanding of isozymes-specific functions and the limited availability of selective pharmacological modulators of PKC isozymes have compromised the clinical translation of PKC-targeting agents. In this work, we report the first small molecule PKCδ-selective activator, the 7α-acetoxy-6β-benzoyloxy-12-*O*-benzoylroyleanone (Roy-Bz), which binds to the PKCδ-C1-domain. Roy-Bz, was obtained by semi-synthesis from the natural diterpenoid 7α-acetoxy-6β-hydroxyroyleanone, isolated from a Lamiaceae family plant, as described previously[1]. Roy-Bz potently inhibited the proliferation of colon cancer cells by inducing a PKCδ-dependent mitochondrial apoptotic pathway involving caspase-3 activation. In HCT116 colon cancer cells, the results indicate that Roy-Bz targets drug resistant cancer stem cells, preventing tumor dissemination and recurrence. Moreover, our findings support a tumor suppressive function of PKCδ in colon cancer.

In conclusion, the results reveal a novel encouraging anticancer drug candidate, particularly in colon cancer therapy[2,3].

Acknowledgements

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L&H.P45

3HQ-based pseudopeptidic platforms for boronic acid ligation

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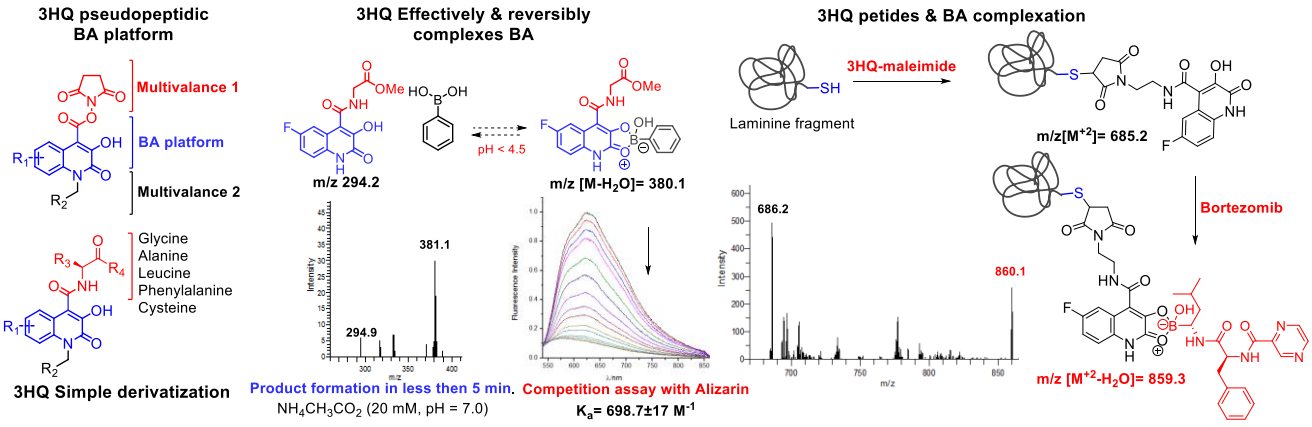
In the field of modern bioconjugation, there is an increasing demand for reactions that are not only bioorthogonal, but also reversible under selected conditions.[1] Boronic acids are excellent candidates for this kind of applications as they are stable under physiological conditions, have good biocompatibility and reversibly bind to diols in aqueous environment.[2, 3]

3-Hydroxy Quinolinones (3HQs) are isosters of Glycine that are also known to chelate various metals[4], and also proved to allow reversible boronic acid conjugation in aqueous medium. The 3HQs derivatives that we synthesized showed remarkable binding capabilities with boronic acids in buffer solution (K_a= 698.7±17 M^{-1}) and were further developed to be inserted in peptidic fragments as pseudopeptidic platforms. The peptides modified with our molecule gained the ability to bind boronic acids in aqueous environment with moderate to good efficiency, allowing us to produce a variety of constructs with cytotoxic drugs and fluorescent probes using this versatile platform.



Preliminary results obtained with the 3HQ technology

Acknowledgements

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L&H.P46

Characterization of Cadmium Accumulation of two tomato plant varieties

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Heavy metal contamination of water, air and soil affects plant productivity, but the most important concern is food chain contamination and food safety.

In this work we evaluated the accumulation and effects of different concentrations of cadmium (Cd) on the growth of two tomato varieties (*Solanum lycopersicum*), *Lusitano* and *Nemabrix* (with normal and high lycopene content, respectively). Tomato is one of the most important crops in Portuguese agriculture, not only for fresh consumption but also for processed products.

Thirty-three days old plants were exposed to Cd contamination (0, 5, 10, 25, 50 and 100 µM) during 17 days. The accumulation of Cd was evaluated in leaves and roots. The impact in growth parameters was evaluated by measuring total plant biomass and chlorophyll content in both old and young leaves, for both varieties.

Cadmium toxicity causes a decrease of biomass that is more evident for longer times of exposition. For 17 days, the biomass decrease was 59% for *Lusitano* variety and 74% for *Nemabrix* variety.

Concerning the chlorophyll content, there is an increase in the control, but for the contaminated plants there is a marked decrease for both varieties, with a reduction of 51% for old leaves and 89% for young leaves in the *Lusitano* variety and 37% for old leaves and 86% for young leaves in the *Nemabrix* variety. This is related to the decrease of chlorophyll synthesis or its degradation in the presence of Cd.

When the plants were exposed to 100 µM Cd for 17 days, the *Lusitano* variety accumulated 1390.3 ± 37.8 mg Cd kg^{-1} DW and 3847.8 ± 410.7 mg Cd kg^{-1} DW respectively in the leaves and roots, and the *Nemabrix* variety accumulated 1345.5 ± 72.9 mg Cd kg^{-1} DW and 3035.6 ± 211.9 mg Cd kg^{-1} DW. The variation of Cd concentration with time in leaves and roots follows a hyperbolic curve.

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L&H.P47

The impact of atypical sphingolipid chemical structure on model and cell membranes biophysical properties

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Sphingolipids (SLs) participate in many cellular events[1]. Their building blocks, long chain sphingoid bases, are formed from the condensation of L-serine and palmitoyl-CoA catalysed by serine-palmitoyltransferase (SPT)[1]. However, SPT can also use alanine and glycine, forming atypical 1-deoxy-sphingoid bases that lack the hydroxyl group at the C1 position[2]. Elevated levels of 1-deoxySLs are associated with the development and progression of HSAN1 and diabetes type II[2,3]. Nevertheless, their biological significance and the molecular mechanisms underlying their pathological role remain elusive.

Using fluorescence-based methodologies we showed that, in contrast to their canonical counterparts, 1-deoxySLs failed to form highly-ordered gel domains in fluid model membranes. Moreover, elevated cellular levels of 1-deoxySLs increased the overall membrane fluidity compared to control cells. To investigate if this was a consequence of impaired H-bond network due to the lack of the C1-OH group, the biophysical properties of 1-methoxy-SLs were studied using model membranes. The ability to form gel domains and decrease membrane fluidity was re-established, although to a less extent compared to their canonical counterparts. These results indicate that C1 headgroup of the SLs determines the formation of tightly packed domains.

In conclusion, canonical and atypical SLs lead to opposite changes in membrane biophysical properties, suggesting a possible mechanism to mediate the distinct biological actions of these species.

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L&H.P48

Blocking viral entry mechanism: Structural elucidation and molecular dynamics study of HIV-2 surface glycoproteins

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The acquired immunodeficiency syndrome (AIDS) is the culmination of the infection by the human immunodeficiency viruses upon destruction of CD4+ lymphocytes of the host.[1] The efficacy of the available antiretroviral drugs is very limited against HIV-2 and, most importantly, none of the current drugs effectively prevents entry into the cells. HIV envelope glycoproteins mediate binding to the receptor CD4 and co-receptors at the surface of the target cell, enabling fusion with the cell membrane and viral entry.[2,3] The discovery of multiple new hit compounds that can be used as useful starting points towards drug candidates for HIV-1 and HIV-2 therapy is the main goal of this work. The gp120 and gp125 are critical to the receptors recognition and internalization of viral material into the cell. The modulation of the glycoproteins activity can lead to the disturbance of the entry mechanism.

Until now, it has been marked by the use of computational techniques to study the viral surface glycoproteins as potential drug targets against HIV infections. A 3D structure of HIV-2ROD gp125 was generated by homology modelling, using MOE2016 and MODELLER 9v19. Additionally, to disclose the importance of the main structural features and compare with experimental results, 3D-models of six V3 mutants were also generated using the C2V3C3 domain. Additionally, molecular dynamics is being performed, using Gromacs 2006.3, in order to better characterize this protein and disclose its the biological dynamic behaviour. The structures to use in molecular dynamic simulations were prepared using MOE 2016.0802 software and further exported as PDB files.

These mutations revealed selectively impact in the behaviour of the protein. Structurally, the mutations studied leads to a loss of aromatic features, very important for the establishment of π-π interactions, which could induce a structural preference by a specific coreceptor.

In the absence of a crystallographic structure of HIV-2 envelope gp125 comprising variable domains, computer aided modulation is crucial to identify structural features in the variable regions that correlate with HIV-2 tropism and susceptibility to neutralization, highly associated with the mutated residues. These new insights into the structure-function relationship will help in the design of better models and into the following of the design of new small molecules.

Acknowledgements

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L&H.P49

Synthesis and characterization of tetraoxanes for cancer therapy

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Metabolism and iron homeostasis are linked through a redox-active labile ferrous iron (Fe(II)) pool[1]. Elevated levels of labile Fe(II) were found in cancer cells, where they represent a unique metabolic signature associated to tumor initiation and development[1]. Nowadays, malaria therapy relies on iron-dependent pharmacology using artemisinins and endoperoxides such as tetraoxanes[2], however, targeting the intracellular labile Fe(II) for tumor-selective drug delivery remains poorly studied. Tetraoxane conjugates were designed to target the parasite through activation by Fe(II) increasing oxidative stress by formation of radical species and releasing a second compound toxic to the parasite[3]. Exploiting iron metabolism offers the potential for selective drug delivery in cancer by designing tumor-activated prodrugs (TAPs) based on endoperoxides[1]. In this project tetraoxane conjugates (Figure 1) incorporating the cytotoxic drug will be synthesized in eight sequential steps, starting from the commercially available 1,3-cyclohexanedione. We now present the synthesis towards anticancer tetraoxanes.

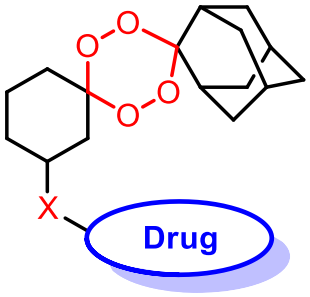

Figure 1. Tetraoxane moiety incorporating the cytotoxic drug payload.

Acknowledgements

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L&H.P50

Thiazolidine cyclisation via iminoboronate intermediates for the functionalization of *N*-terminal amino acids

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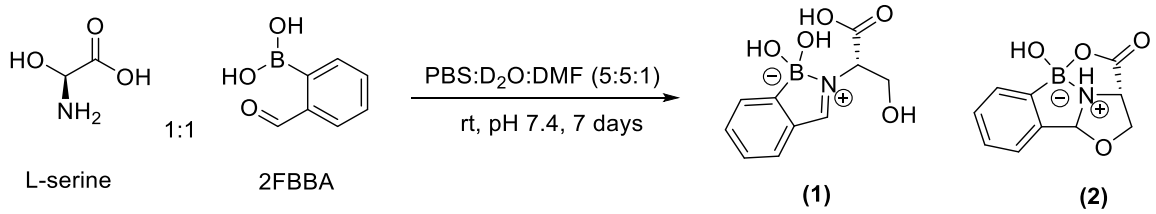
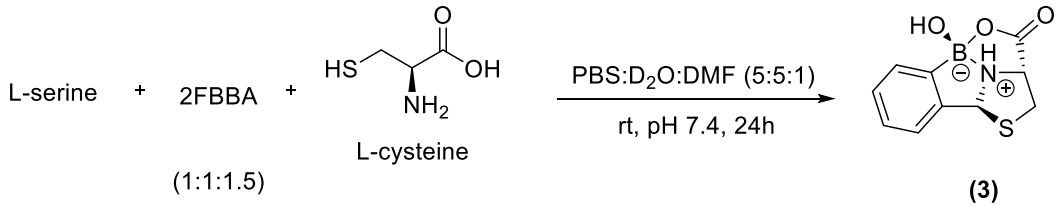
By far the most explored property has been the nucleophilic reactivity of amino acid residues with respect to proteins bioconjugation. In fact, lysine and cysteine have been the election targets especially due their own reactivity since they bear the most reactive nucleophiles in their residue chain.[1] Despite this, there are also other nucleophilic substrates available to react, such as serine hydroxyl.[2] We have shown the high reactivity of formyl benzeno boronic acid (2FBBA) with *N*-terminal cysteines to form a boronated thiazolidine featuring a B–N bond under mild aqueous conditions (pH 7.4, 23 °C).[3] We reasoned that other type of *N*-terminal amino acids such as serine or threonine could participate in similar reactions. In fact, preliminary data shows that when 2FBBA reacts with serine, it generates a mixture of iminoboronate **(1)** and oxazolidine **(2)**, although in low conversion (Scheme 1). Notwithstanding the addition of cysteine shifts the equilibrium to the cyclization of thiazolidine in the competition assay **(3)** (Scheme 1). Herein we will provide some results on the development of this methodology for orthogonal modification of *N*-terminal cysteine in peptides and proteins.

Specificity Assay with 2-Formyl benzene boronic acid



Competition Assay with L-cysteine



Scheme 1. Specificity and Competition Assay adding L-cysteine to the reaction mixture of 2FBBA with L-serine. The reactions' conversion were evaluated by ^{1}H-NMR spectra based on the comparison of the signal of aldehyde (≈ 9.8 ppm), imine (≈ 8.4 – 8.7 ppm), thiazolidine proton (≈ 6.2 ppm) and oxazolidine proton (≈ 6.1 ppm).

Acknowledgements

Support for this work was provided by FCT through PTDC/QEQMED/5512/2014, PTDC/QEQ-QOR/1434/2014, UID/DTP/04138/2013, SAICTPAC/0019/2015.

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L&H.P51

Biophysical characterization of lipid-tagged peptides as fusion inhibitors for respiratory viruses

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Human parainfluenza viruses (HPIV) and respiratory syncytial virus (RSV) are paramyxoviruses and are among the most common respiratory pathogens affecting infants and children worldwide.[1] Nowadays, acute respiratory infections are the leading cause of mortality in children, accounting for nearly 20% of childhood deaths worldwide (nearly 3 million children each year).[2,3] There are no effective treatments available. Consequently, there is an urgent demand for efficient antiviral therapies. Infection of healthy cells by these respiratory viruses requires fusion of the viral membrane with the target cell membrane, a process mediated by a trimeric viral fusion protein, F protein.[4] Inhibitory peptides inhibit viral fusion by binding to F's transient intermediate, preventing it from advancing to the next step in membrane fusion. Here we assessed variants of lipid-tagged F-derived peptides to search for properties that may associate with efficacy and broad-spectrum activity. Fluorescence spectroscopy was used to study the interaction of the peptides with biomembrane model systems, using partition assays. Using acrylamide, a quencher of tryptophan fluorescence, was possible to understand the preferential localization of the peptides in lipid bilayers. The interaction of the peptides with human blood cell-binding was also evaluated using the dipole potential probe, di-8-ANEPPS. Understanding the membrane biophysics processes involved in enveloped viruses entry will enable the development of new inhibition strategies.

Acknowledgements

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L&H.P52

Eco-friendly synthesis of 2-N^5-functionalized 3-aminophenazine derivatives catalysed by CotA-laccase/ABTS system

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Biocatalysis is nowadays considered as a powerful option by organic synthetic chemists, when planning and designing synthetic strategies for the construction of target molecules.[1] In fact, enzymes can be used to replace chemical catalysts imparting a green character to the synthesis and leading to a more sustainable process with a lower overall environmental impact.

CotA-laccase is a bacterial laccase, isolated from the *Bacillus subtilis*, which has already proven to be a robust and efficient enzyme to promote the oxidation of different substituted aromatic amines into higher added value compounds.[2,3] However some substrates, considered potential precursors to obtain important *N*-substituted phenazine heterocyclic nucleus, could not be directed oxidized by the enzyme, due to their high oxidation potentials. Therefore strategies that include the use of laccase mediators, such as 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) could be used extending, that way, the scope of substrates oxidized by laccase.

In this communication we report the synthesis of N^5-substituted phenazine cores using the cocatalytic system CotA-laccase/ABTS, in mild reaction conditions as depicted in Figure 1.

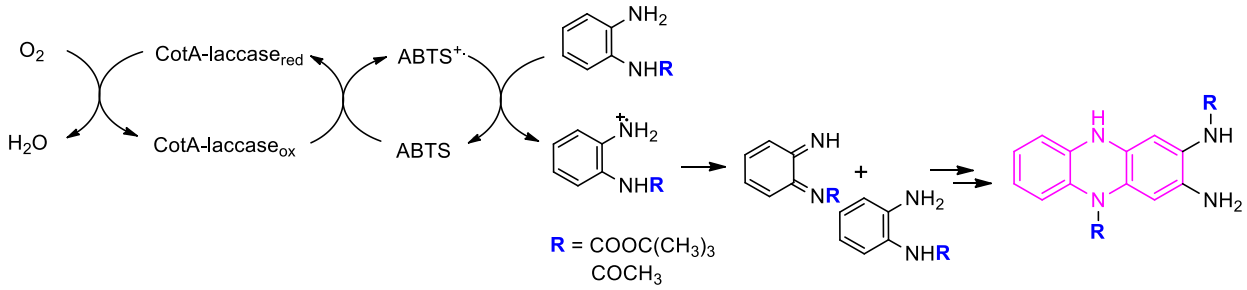

Figure 1. Scheme of catalytic cycle of CotA-laccase/ABTS oxidizing system to obtain N^5-substituted phenazine cores

Acknowledgements

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L&H.P53

Development of hydrochlorothiazide-loaded drug delivery systems: a paediatric formulation

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Hydrochlorothiazide (HCTZ) is one of the most used diuretic drugs in the treatment of paediatric hypertension, being also listed by the WHO [1]. The HCTZ properties namely its low solubility leads to a variable oral availability [2]. In paediatrics, the use of oral solid forms is limited by their rigid dose content and by children ability to swallow, while the preparation of extemporaneous formulations may lead to loss of accuracy of the dosage and formulation errors [3, 4]. The present work describes two strategies to enhance HCTZ solubility thus enabling the formulation of oral liquid dosage forms suitable for paediatric use: a) complexation with cyclodextrins (Cyds); b) encapsulation in lipid nanoparticles. For Cyds complex preparation, the physical mixture (PM) and the co-evaporated product (CoEv) of HCTZ and hydroxypropyl-β-cyclodextrin (HPBCyd) or sulfobutyl-ether-β-cyclodextrin (SBEBCd) were tested. The PM was able to solubilize 48% (6.4% w/w) of the drug while after the coevaporation procedure it increased up to 90% (11.3% w/w). Both solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) were produced using the hot high shear homogenization according a previously published technique [5]. Both SLNs and NLCs present an average size within the range of 44-200 nm, a polydispersion index of 0.21-0.57, and a zeta potential between -12mV and -42 mV, being stable at 4°C for two months. However, low encapsulation efficiency was observed due to very low HCTZ solubility in the lipid matrix [6]. The on-going investigation involves is the incorporation of HCTZ-Cyds complexes into the lipid nanoparticles and the evaluation of drug release profiles under simulated oral conditions.

Acknowledgements

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L&H.P54

Novel Ruthenium(II)-thiosemicarbazone complexes: Synthesis, electrochemistry and antitumoral activity

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As mortality rates related to cancer continue to rise[1], the search for new and more efficient drugs began to be vital. Over the last years, the increasing research on metallodrugs for cancer therapy positioned ruthenium complexes as promising alternatives for conventional platinum-based chemotherapeutics since Ru seems to possess, in general, lower toxicity, different mechanisms of action and the capacity to overcome platinum-resistance[2]. Thiosemicarbazones (TSC) have been described to possess a wide biological activity such as antimicrobial, antifungal and antitumoral properties[3]. In this context, a new panel of complexes bearing a common TSC bidentate ligand and different Ru(II) fragments (Ru-η^5-(methyl)cyclopentadienyl, Ru-polypyridyl, Ru-phosphane), was synthetized and characterized by several techniques. We present herein our first results on some of these systems. This study reveals different coordination modes of the TSC ligand to the metallic center and eventually correlates their chemical structure with their biological properties.

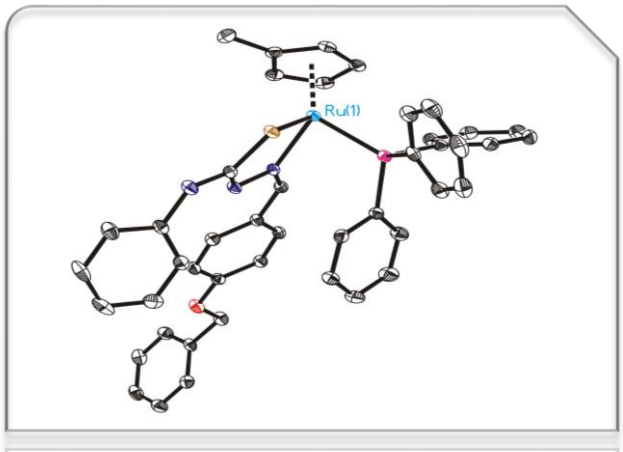

Figure 1. ORTEP view of the molecular structure of complex [Ru(η^5-MeCp)(TSC)(PPh_3)]. MeCp = η^5-methylcyclopentadienyl and TSC = (*E*)-2-(4-(benzyloxy)benzylidene)-*N*-phenyl-hydrazinecarbothioamide.

Acknowledgements

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Summer School

SS.L1

R&D and Entrepreneurship

Pedro Vilarinho

HiseedTech, Lisbon, Portugal

The Lisbon Agenda defined a strategic objective for the European Union to become "the most competitive and dynamic knowledge-based economy in the world capable of sustainable economic growth with more and better jobs and greater social cohesion". For Portugal, as for other EU countries, this objective points out the need for a change in the economic development paradigm, from an economy whose competitiveness is based on low cost of the production factors, to one built up on knowledge, in order for the productivity growth to be sustained on an increase in value creation, that results from the commercialization of products and/or services that incorporate knowledge.

Over the last decades the investment carried out by Portuguese tax payers in research and development (R&D) has increased significantly with a corresponding increase in terms of the indicators related to the R&D output. However, the translation of the knowledge generated by these R&D activities to the market is lagging behind, showing a need for more effective and efficient translation of R&D results to the market.

The figures supporting the above stated claim will be presented, together with a process to support a set of issues identified as key in the translation of R&D results to the market, either through the support of science based start-ups or open innovation. The outcomes of this process will be also be presented together with some case studies of Portuguese science based start-ups.

Pedro Vilarinho is currently the General Manager of HiseedTech – a not-for-profit association aimed at fostering the creation of value from knowledge through technology entrepreneurship and open innovation.

Pedro has over 14 years' experience in supporting researchers in connecting science and technology with the market and, over these years, supported the creation of 13 start-ups that, overall, managed to attract investments over €40 million. He is currently Board Member in three biotech start-ups.

Pedro was previously an Assistant Professor at the Department of Economics, Management and Industrial Engineering of Universidade de Aveiro.

He has an undergraduate degree in Electronics and Telecommunications Engineering from Universidade de Aveiro, a MSc in Computer Science in Industrial Engineering from Universidade de Coimbra and a PhD in Industrial Engineering from Universidade do Porto.

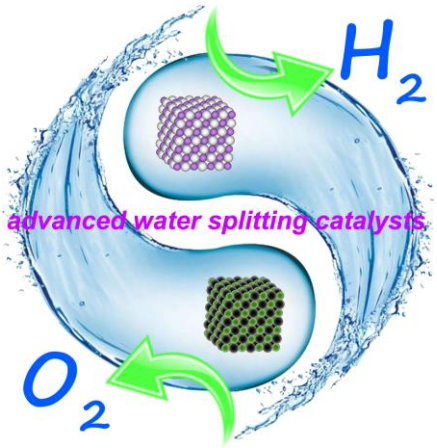
SS.L2

Recent development on noble-metal-free water splitting electrocatalysts

Lifeng Liu

International Iberian Nanotechnology Laboratory (INL), Braga, Portugal

Splitting water into hydrogen and oxygen is an ecofriendly way to produce high-purity hydrogen fuels and has shown substantial promise as a means for renewable energy storage. To enable widespread deployment of water electrolyzers, it is of paramount importance to develop efficient, durable and inexpensive water splitting catalysts so that the electrolyzed hydrogen fuels can become economically competitive and viable. In this tutorial lecture, I will first give a brief overview about the Power-to-X technologies, of which water splitting is an important part. I will then go through the hydrogen evolution reaction (HER) and oxygen evolution reaction (OER), respectively, discussing the reaction pathways, indicators that are widely used to access electrocatalytic performance, recent development on HER and OER catalysts with particular emphasis on transition metal phosphides, and some design strategies/requirements allowing for the improvement of catalytic performance[1-4]. Finally, I will present an outlook about this dynamic research area.



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Lifeng Liu is now a Staff Researcher and Research Group Leader at INL. He obtained his PhD degree in Condensed Matter Physics from Chinese Academy of Sciences in 2007. Afterwards, he joined the Max-Planck Institute of Microstructure Physics in Halle, Germany, first working as a postdoc researcher and then as a staff scientist and Group Head. In 2011, he moved to INL and set up a group where his research primarily focuses on the development of inorganic nanomaterials for use in electrochemical energy storage and conversion.

SS.L3

Going Green with Black: Sustainable Carbon Materials for Energy Storage and Conversion

Magdalena Titirici

Queen Mary University of London, Materials Research Institute, London, United Kingdom

This increasing demand of clean energy will need to be met by a combination of existing as well as new emerging energy sources and technologies. However, this mix of energy sources and new technologies will also affect our environment.

Therefore, when developing novel energy technologies, we always need to also consider the environmental concerns that go hand in hand with modern society's function. This goal cannot be accomplished without developing novel sustainable materials which will be based on clean manufacturing technologies and renewable and abundant resources.

Biomass, in particular waste biomass which is not in competition with the food chain, represents a suitable platform for sustainable materials production to build novel energy storage and conversion technologies.

In this talk, I will present our latest group research advances in the production of electrodes for flexible supercapacitors from lignin, Na-ion batteries electrodes from cellulose and bioinspired porous carbons for Oxygen Electrocatalysis.

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Magdalena Titirici has a PhD from University of Dortmund, a German Habilitation from the Max-Planck Institute of Colloids and Interfaces and is currently a Professor of Sustainable Materials Chemistry at Queen Mary University of London.

She is the author of around highly cited 150 publications (h-index=62) in the field of sustainable materials for energy storage and conversion, several book chapters and one edited book. She is in the Editorial Board of "ChemSusChem" (Wiley) and "ChemPlusChem" (Wiley) and an Associate Editor for "J. Mater. Chem. A" (RSC).

Magdalena has been awarded the Rosenhain Medal and Prize from the Institute of Materials and Mines in London in recognition of distinguished achievements in materials science under the age of 40 in 2016, she is the USERN laureate in physical sciences 2017 as well as the recipient of an honorary PhD from University of Stockholm in 2017, the Chinese Academy of Science President's Fellowship in 2018 as well as the Royal Society of Chemistry Corday Morgan Prize 2018.

SS.L4

Frontiers of NMR Spectroscopy: Chemistry and Beyond

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Over the past decades, Nuclear Magnetic Resonance (NMR) spectroscopy has flourished as the most powerful technique for determining the structure of organic compounds[1]. In addition to the application in organic chemistry, this technique is now widely used in inorganic and organometallic chemistry, catalysis, biochemistry and medicine[2,3]. NMR spectroscopy is a non-destructive technique, and with modern instrumentation quality data may be obtained from samples weighing less than a milligram. In the present report, basics of this technique are discussed alongside recent applications in the field of catalysis[4], inorganic and organometallic chemistry[3-5], and materials research[5].

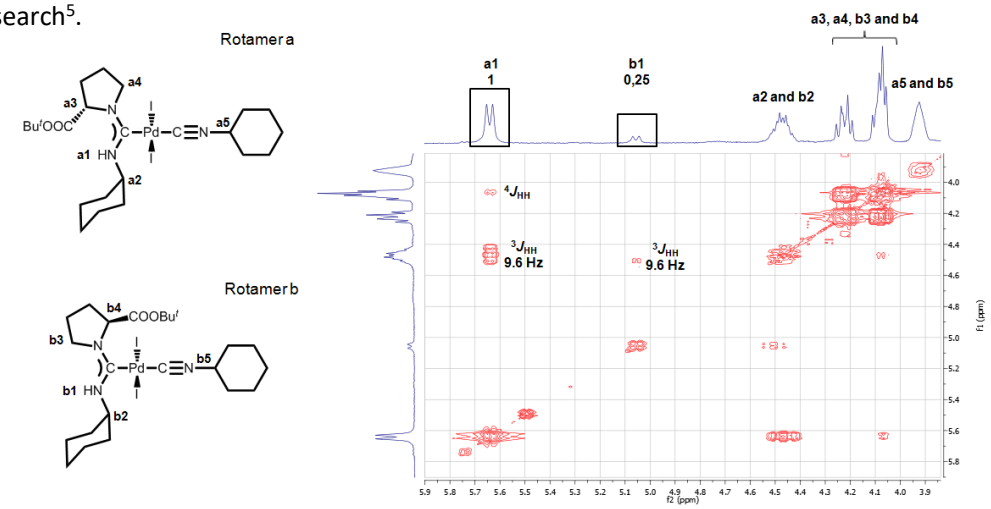

Figure 1. Fragment of the ^{1}H,^{1}H-COSY NMR spectrum allowing to assign the structure of rotamers of chiral aminocarbene complexes[4].

Acknowledgements

K.V. Luzyanin is grateful to the University of Liverpool for support of his research activities.

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Konstantin Luzyanin received his Chemistry degree from Saint Petersburg State University (Russia, 2002) and his PhD in Chemistry from Technical University of Lisbon (joint supervision by Profs. A.J.L. Pombeiro and V.Yu. Kukushkin, 2007). For his PhD thesis, Konstantin was awarded the "António Xavier Prize 2008" from Bruker for applications of the selected NMR spectroscopy techniques in chemistry.

After postdoctoral studies in organometallic chemistry with Prof. A.J.L. Pombeiro (IST-UTL), Konstantin got a position as Senior Research Associate (Ciência-2008 program) at the Centro de Química Estrutural – a research center at the TU Lisbon. In addition, he served as the Manager of IST-UTL Nuclear Magnetic Resonance Center of the Portuguese NMR Network in 2009-2012. In 2013, he was invited to join the group of Cluster Catalysis (Saint Petersburg State University) as a Deputy Head and a Leading Scientist. In 2015, Konstantin joined University of Liverpool as a Scientific Coordinator of the Analytical Services in Department of Chemistry.

Konstantin's current research interests include synthetic transition metals chemistry, in particular of platinum group elements, and development of new methodologies for sustainable/green catalytic processes. He is co-author of ca. 75 publications (65 papers in international peer-reviewed journals, 4 book chapters, and 5 patents), and more than 100 papers in conference proceedings. In the course of last years, he co-supervised several research assistants, MSc and PhD students, and delivered several university courses.

SS.L5

An Introduction to Mass Spectrometry for the Novices

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Mass Spectrometry is an advanced analytical technique that measures the ***m/z*** of ions formed from individual atoms or molecules. The main features of this technique are the unequalled sensitivity, detection limits, speed and diversity of its application.

In analytical chemistry, mass spectrometer methodologies are routinely applied in the identification and quantification of components from reaction mixtures or process monitoring; study of small molecules, commonly known as metabolites, within cells, biofluids, tissues or organisms (Metabolomics); identification and quantification of contaminants (e.g. water quality, food contaminants); pharmacology in the identification/quantification of drug and metabolites; Proteomics, determination of protein structure, function, folding and interactions; clinical testing, as identification of disease biomarkers and forensic analysis; Genomics, sequence of oligonucleotides; Geology for measure petroleum composition and carbon dating, and many others.

A brief description of the basic principles of Mass Spectrometry and some applications will be presented.

Maria da Conceição Oliveira is an Auxiliary Researcher at Centro de Química Estrutural, IST/ULisboa, and Director of the Node IST, Campus Alameda, Portuguese Mass Spectrometry Network (RNEM). Graduation in Chemistry "Physical Chemistry", Faculdade de Ciências da Universidade de Lisboa (1984), and PhD in Chemistry "Physical Chemistry", Universidade de Lisboa, in 1995. Her scientific specialization lies in Physical Chemistry; Gas Phase Ion Chemistry; Mass Spectrometry and Photoelectron-Photoion Coincidence (PEPICO) Spectroscopy. Main scientific areas of research are: Structural Mass Spectrometry; MS-based methodologies for the qualitative and quantitative analysis of (bio)molecules in complex matrices; Metabolomic strategies for the identification and structural characterization of novel metabolites from natural products; Reactional dynamics of ions in the gas-phase: structure, energetic and reactivity.

SS.L6

Electron Microscopy

Isabel Dias Nogueira

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Since the 17th century scientists have developed equipment to magnify what is not visible to the human eye. Optical microscopes use visible light and transparent lenses to see objects separated by about 200nm. Electron microscopes use a beam of electrons and electromagnetic lenses to focus the particles. Due to the electron's characteristics, namely its wavelength (about 100000 times smaller than that of visible light) it became clear that it was possible to achieve much higher resolutions if they were used as a radiation source.

Since Ruska built the first Transmission Electron Microscope (TEM) in 1931, electron microscopes have evolved incredibly, and today are able to reach a resolution of 50pm. Taking advantage of the fact that electrons easily interact with matter, a large number of signals produced when the beam enters the specimen can be detected and used to gather information[2].

From sample topography observable by Scanning Electron Microscopes (SEM) to the inside of very small specimens visible using TEMs, a large range of complementary techniques provide extra information: Energy Dispersive Spectroscopy detects elementary composition, Electron Diffraction allows the identification of crystallographic structures and orientations, High-Resolution TEM lets us look at the positions of atoms[1], among others.

Electron microscopy, as it is understood today, is not just a single technique but a diversity of different ones that offer unique possibilities to gain insights into structure, topology, morphology, and composition of a material. Various imaging and spectroscopic methods represent indispensable tools for the characterization of all kinds of specimens on a smaller and smaller size scale with the ultimate limit of a single atom. Because the observable specimens include inorganic and organic materials, micro and nano structures, minerals, metals as well as biological objects[3], the impact of electron microscopy on all natural sciences can hardly be overestimated.

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Isabel Dias Nogueira holds a degree in Technological Physics Engineering from Instituto Superior Técnico and received her master's degree in Surfaces Science and Engineering in 2004 from the Faculdade de Ciências da Universidade de Lisboa.

In 1997 she took a position at the Microlab-Electron Microscopy Laboratory of Instituto Superior Técnico in Lisbon, where she has been pursuing a career as an electron microscopist up to now. Her work has focused mainly on Scanning Electron Microscopy and Transmission Electron Microscopy, the main analytical techniques at the laboratory.

SS.L7

Optical Microscopy Tools for Research

José Rino

Instituto de Medicina Molecular João Lobo Antunes,
Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal

Optical Microscopy is a key technology in Bioimaging, the imaging of biological samples. More than 400 years after the advent of the compound microscope, light microscopy is still a field of intensive research, with ongoing developments providing biologists with novel tools to explore life processes in cells, tissues and whole organisms. The discovery and development of the Green Fluorescent Protein (GFP) and related fluorescent proteins (FPs) originated an extraordinary revolution in biological research, which was acknowledged with the attribution of the Nobel Prize in Chemistry in 2008. More recently, the achievements of super-resolution microscopy in surpassing the stipulated limit for the maximum resolution of an optical microscope were also acknowledged with the Nobel Prize in Chemistry in 2014. In this lecture, some of the most important microscopy techniques for in vivo imaging of biological processes will be reviewed, as well as recent technological developments that will undoubtedly increase the potential that optical imaging can offer researchers.

José Rino was trained as a physicist in Instituto Superior Técnico, where he graduated in Technological Physics Engineering in 1999. He received is PhD in Biophysics in 2007 from Faculdade de Ciências, Universidade de Lisboa. During his doctoral work at the lab of Prof. Maria Carmo-Fonseca at the Instituto de Medicina Molecular (IMM), he studied the dynamics and interactions of nuclear proteins with confocal photobleaching microscopy approaches. He also participated in an Integrated Project funded by the European Union 6th Framework Programme with the goal of generating and applying novel advanced technology for non-invasive imaging of biomolecular function in living systems. As a post-doctoral researcher, he focused on developing quantitative microscopy techniques to simultaneously visualize the kinetics of transcription and mRNA processing in living cells. In 2009, he was hired under the Ciência 2008 program by the IMM as Head of the Bioimaging Unit, the core microscope facility of the Institute. Between 2013 and 2016 he was also responsible for the Optical Imaging and Microscopy Platform of the Champalimaud Centre for the Unknown, Lisbon. In 2016 he was appointed by the IMM as Head of the Flow Cytometry Facility. He is currently Head of the Bioimaging and Flow Cytometry Facilities at the Instituto de Medicina Molecular João Lobo Antunes.

SS.L8

Computational methods: Virtual Screening Strategies in Drug Discovery some theory… some applications

Rita C. Guedes

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The process to develop new small-molecule drugs is a puzzling multidimensional problem, taking on average 10 to 15 years. Drug discovery had traditionally a basis in trial-and-error. Fortunately, during the last decades this process has been revolutionized and became more rational using approaches focused on the identification of agents. From the identification of potential hits, to hit-to-lead campaigns a long and challenging pathway takes place. In most pharmaceutical companies and also in academia, beyond classical approaches, drug designers are taking advantage of using computational-aided drug design (CADD) to identify and select the best molecules for synthesis that simultaneously are likely to display the desired ADMET (absorption, distribution, metabolism, excretion, and toxicity) properties. The use of computational methodologies, ligand and/or structure-based, have been already proved as a synergic tool to boost the drug discovery process.

Particularly, virtual screening strategies have appeared as a strategic tool to identify hit compounds through being able to screen millions or perhaps billions of molecules in short period of time, by employing knowledge about the protein target or known bioactive ligands and acting as an alternative response to the expensive and time consuming synthesis and high-throughput screening (HTS) paradigm.

An overview of virtual screening methodologies and applications will be presented.

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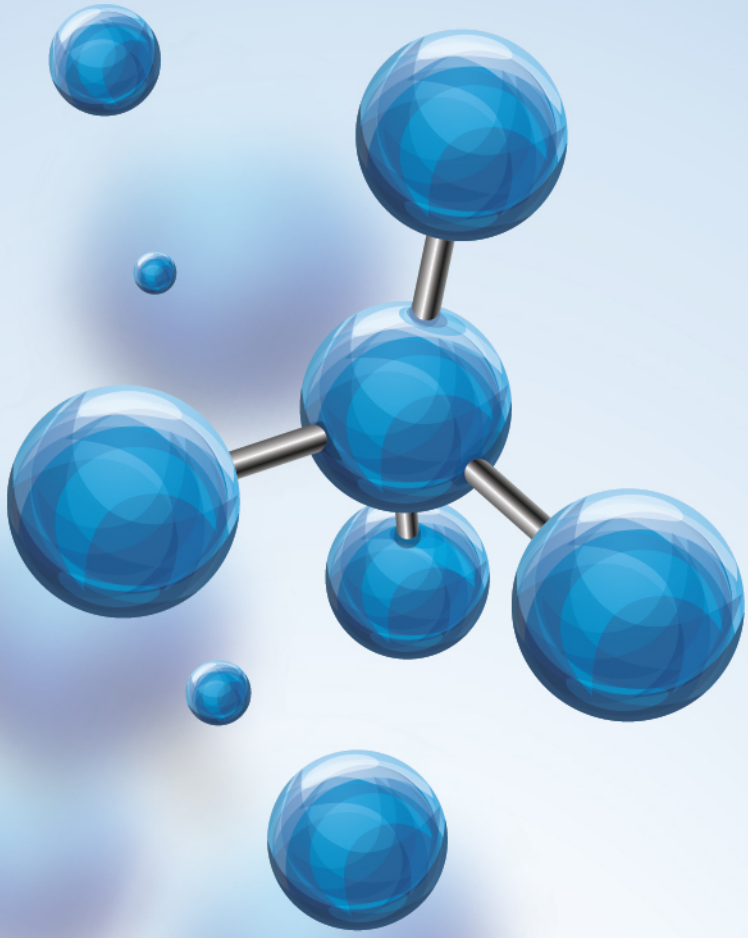
Rita Guedes did her undergraduate studies in chemistry at University of Lisbon, where she also completed her PhD degree in chemistry (Computational/Physical Chemistry) in 2003. After that she moved to Sweden to work with Prof. Leif Eriksson (Uppsala and Örebro Universities). From 2005 she is an Assistant Professor in chemistry/computational chemistry at the department of medicinal chemistry at the University of Lisbon (School of Pharmacy). She is particularly engaged in training and motivation of young European investigators in Medicinal Chemistry and she has been involved in the organization of all YMCS-EFMC symposia. Rita Guedes participate on several funded Doctoral and Master Programs focused on medicinal chemistry (infectious, oncologic, and neurodegenerative diseases) on a national and international level.

Rita Guedes leads the molecular modeling lab at iMed.ULisboa (Universidade de Lisboa) that identifies and optimizes small molecules to target proteins involved in inflammation, cancer and infectious diseases. Her research group uses computational methods like molecular docking, virtual screening, homology modelling, pharmacophore modelling, de novo design, molecular dynamics simulations and quantum mechanics calculations for drug discovery campaigns. She has published >70 papers and supervised several Post-doc, PhD, master and project students (she supervises now 1 Post-doc, 6 PhD's and 3 master students.



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