XXV ENCONTRO NACIONAL

Sociedade Portuguesa de Química

Book of Abstracts

SPQ

Contents

Welcome message

The Portuguese Chemical Society (SPQ) cordially invites you to attend the XXV edition of the SPQ National Meeting (XXVEN-SPQ). The meeting will be held in the beautiful city of Lisbon at the Faculty of Pharmacy of the Lisbon University from 16-19 of July of 2017. This will be a unique event that will bring together the Portuguese Chemical Society (SPQ) and the international scientific community to celebrate the XXV edition of SPQ National Meetings.

Under the general theme of "Chemistry in Action", the XXV-EN will have an exciting scientific program lead by renowned international experts, which will focus on the central role of chemistry in solving fundamental problems of modern societies at the interface of Biology, Material and Environment sciences.

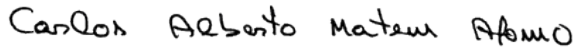
This event will count with 13 plenary lectures, 22 key notes, 13 invited oral communications, 12 oral communications, 13 flash communications and 3 poster session with over 270 posters.

The Portuguese Chemical Society will award 2 scientists with the *Ferreira da Silva – 2016 Award* and *Vicente de Seabra – 2016 Medal* and one poster in each day of the meeting will be also awarded a prize.

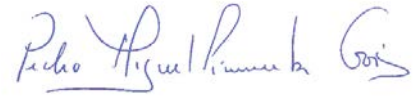
Lisbon is a historical capital full of charm, where more than 800 years of cultural influences blend with modern trends and life styles. It is therefore, the perfect place to receive you all and engage in a fruitful scientific discussion.

Welcome to Lisbon,

Prof. Artur Silva
(President of the SPQ and Chairman of the XXV EN-SPQ)



Prof. Carlos Afonso
(Coordinator of the XXV EN-SPQ)



Prof. Pedro Góis
(Coordinator of the XXV EN-SPQ)

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Armando L. Pombeiro *(UL)*
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Cláudio M. Soares *(ITQB)*
M. Rui Alves *(IPVC)*
Ana Ponces Freire *(UL)*
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Sponsors and acknowledgements

Com o alto Patrocínio de Sua Excelência O Presidente da República

Organization

Sociedade Portuguesa de Química

Institutional support

Faculdade de Farmácia Universidade de Lisboa

iMed.ULisboa Research Institute for Medicines

Universidade de Lisboa

ChemPubSoc Europe

Sponsors

Bial

Bruker

Hovione

XXV Encontro Nacional Sociedade Portuguesa de Química

General information

Meeting venue

The conference venue will be at the Faculty of Pharmacy of the University of Lisbon (FFUL) from 16th till 19th of July, 2017.

Faculty of Pharmacy of UL

Av. Prof. Gama Pinto
1649-003 Lisboa-Portugal
Telefone: +351 217946400
Fax: +351 217946470
http://www.ff.ul.pt/

Registration

The registration should be performed on 16th July from 13:00 to 16:00 at the main hall of FFUL.

How to arrive to venue

By metro: The nearest metro station is ***Cidade Universitária*** (in yellow line), about 3 minutes walk from the venue.

By train: The nearest train station is ***Entrecampos***, about 15 minutes walk from the venue.

By bus: 731, 735, 738, 755, 764, 768 are the main bus services going by ***Cidade Universitária***.

By car: The GPS coordinates of the venue are 38.749599, -9.157169. During the congress is possible to park your car at FFUL park ***(2 €/day)***.

Access to internet

In the faculty library (level 0 floor under the auditorium) the participants can access a computer room. In addition, in the building it is possible to access the wireless network using the following credentials:

Wireless credentials
Guest User Name – fful
Password – fful01
Profile – guest-UL

Language

English is the official language of the congress.

Voltage

In Portugal the line voltage is 220V.

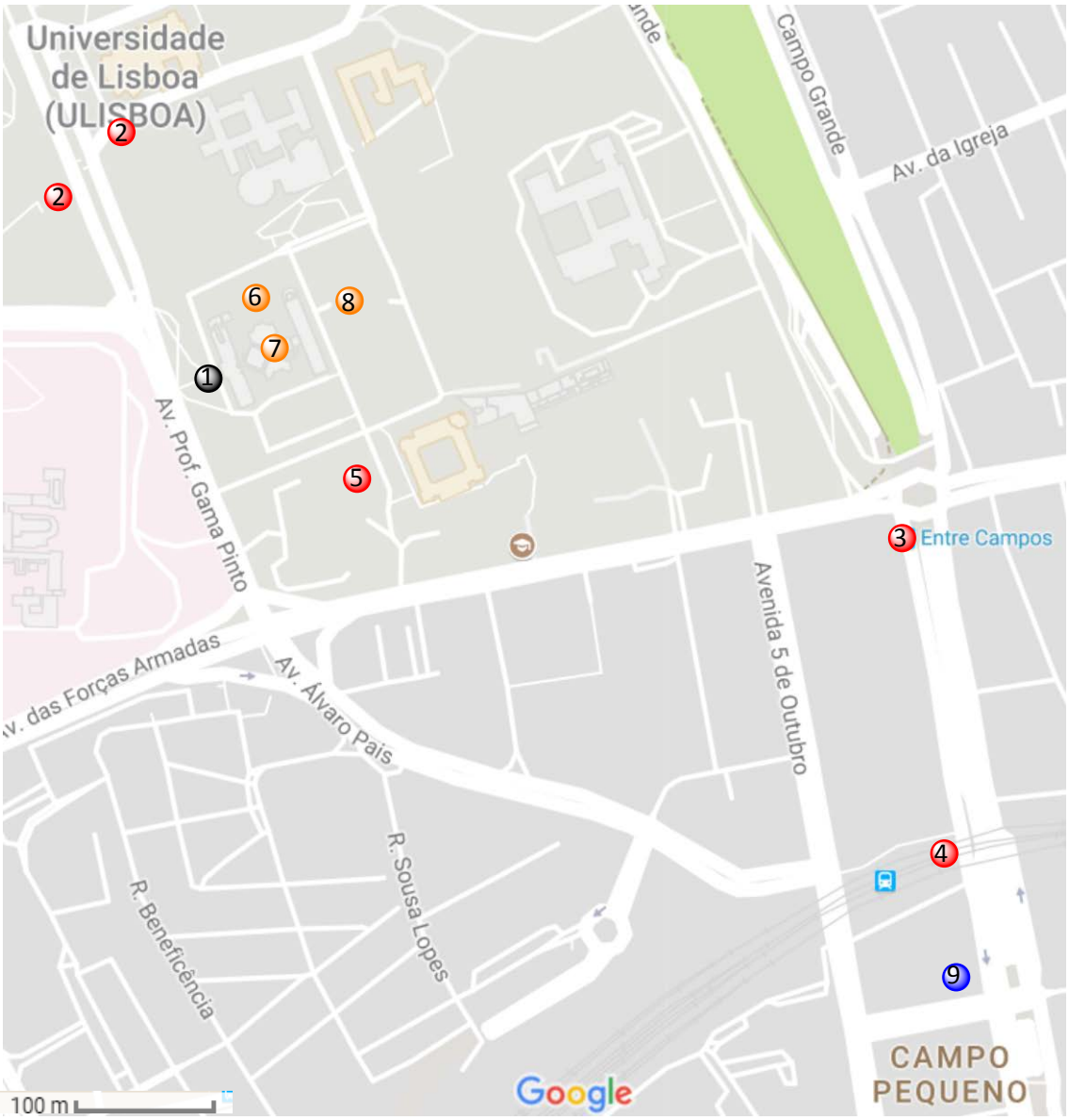
Insurance

Participants are responsible for arranging their own health and accident insurance.

Banking

Several banks and ATMs are located within 5 minutes walk distance from the FFUL.

Points of interest



1. Faculdade de Farmácia da Universidade de Lisboa (FFUL) – registration
2. Cidade Universitária Metro Station
3. Entre Campos Metro Station
4. Entre Campos Train Station
5. FFUL Car Parking
6. Street Food Fest
7. FFUL Bar
8. Faculdade de Medicina Dentária
9. 3K Hotel

Where to eat

Available during the all Congress		*Menu*	*Average Price (€)*
Street Food Fest	***Coal***	Hamburger and *Hambúrguina* *Piadinas* (including vegetarians) Grilled Corncobs Crepes and Waffles	4-6
	Legend Hot Dog	Hot Dogs (including Soy) Hamburgers	4-6
	Kürtös Kalács by Transylvania-Street Food	Kürtös (salmon, chicken and *bifana*) Kürtös Kalács (Nut and almond cakes)	4-6
	Pascoalini Geladaria	Home-made ice creams	2-4
FFUL Bars (3 options)		Soup, Dish of the day and Dessert	4-6
Faculty of Dental Medicine		Soup, Dish of the day and Dessert	5-6

Social Program

Welcome reception

The welcome reception will be held in the venue in the first day of congress (16th July) at 19:00.

Street Food

The Street Food will take place during all the congress days, except in 16th July, in FFUL.

Coal

Legend Hot Dog

Pascoalini

Kürtös Kalács

Street Food & Drinks

To enjoy the hot July nights of Lisbon, on the 17th July we will pep the Street Food Fest zone with music and drinks to relax and socialize.

Sunset Party & Conference Dinner

The conference dinner will take place in the congress day 3 (18th July) in the Mundial Hotel 4* in Praça Martim Moniz in the center of Lisbon. Before dinner we will have a Sunset Party in the Rooftop Bar & Lounge of the Hotel that is considered one of the best Rooftop Bars in Lisbon and with a stunning 360 º view over the historical center of Lisbon and the Tagus River.

The event will cost 35.00 euros and includes the dinner and one drink in the Sunset Party.

MUNDIAL
TIMELESS CITY HOTEL
LISBOA

XXV ENCONTRO NACIONAL
Sociedade Portuguesa de Química

Scientific information

Oral communications

The congress has a large number of oral presentations covering the topics of Health, Material, Environment, Industrial and Teaching Challenges. The oral communications are divided in:

- Plenary sessions (50 minutes);
- Keynotes (30 minutes);
- Invited and selected Oral Communications (20 minutes);
- Flash Communications (10 minutes);

These timings include time for scientific discussion.

To all participants presenting oral communications, it is kindly asked to contact an organization member **24 hours in advance at the reception desk** to deliver your Powerpoint presentation in a flash drive (pen drive).

Poster presentations

Five poster sessions will be held in the congress, giving the opportunity for exchange of ideas and networking between all the congress participants.

- **Poster Session 1 and 2**: **HC1** to **HC116** (10:40-11:40 and 17:00-17:20, **17th July**)
- **Poster Session 3 and 4**: **MC1** to **MC98** (10:40-11:40 and 17:00-17:20, **18th July**)
- **Poster Session 5**: **EC1-45, IC46-57** and **TC58-61** (10:40-11:40 and 17:00-17:20, **19th July**)

The maximum size for the posters is 120x90 cm.

The posters should be placed before 10:00 of the corresponding day and should be removed until 20:00

Awards

During the XXV edition of the SPQ National Meeting (XXVEN-SPQ) two scientists will be awarded with the *Ferreira da Silva – 2016 Award* and *Vicente de Seabra – 2016 Medal*.

***Ferreira da Silva - 2016 Award* – <u>João Rocha</u>**

The *Ferreira da Silva Award* was established by the Portuguese Society of Chemistry in 1981, and is awarded biennially during the SPQ National Meeting. This award is conceded to a Portuguese chemist who, for the scientific work produced in Portugal, has contributed significantly to the advancement of Chemistry in any of its areas.

***Vicente de Seabra – 2016 Medal* – <u>Adrián Silva</u>**

The Vicente de Seabra Medal was established by the Portuguese Society of Chemistry in 2002, and was awarded for the first time in 2004 during the XIX SPQ National Meeting.

The medal is intended to reward the high quality, originality and autonomy of the research work in Chemistry developed by a researcher of age no older than 40 years.

Conference Schedule

	16th of July	17th of July Sponsored by Bial			18th of July Sponsored by Hovione			19th of July Sponsored by Bruker		
9:00		*Health Challenges* Auditorium			*Material Challenges* Auditorium			*Environmental Challenges* Auditorium		9:00
9:50		**PL1** Ben Davis (Uni. Oxford)			**PL6** Stefan Matile (Uni. Genève)			**PL10** David Milstein (Weizmann Institute of Sci.)		9:50
10:40		**PL2** Stephen Caddick (Uni. College London)			**PL7** João Mano (UA)			**PL11** Armando Pombeiro (IST-UL)		10:40
11:40		*Coffee Break & Poster Session*								11:40
12:30		**PL3** Antonello Mai (SAPIENZA-Uni. Roma)			**PL8** Erwin Reisner (Uni. Cambridge)			**PL12** Paul Chirik (Princeton Uni.)		12:30
13:20		**PL4** Rui Moreira (FF-UL)			**PL9** João Rocha – *Prémio Ferreira da Silva 2016* (UA)			**PL13** Antonio Echavarren (ICIQ)		13:20
		Lunch								
		Organic Tools Auditorium	*Analytical Tools* Amphitheatre A	*Fluorescent Tools* Amphitheatre F	*Organic Materials* Auditorium	*Heterogeneous Materials* Amphitheatre A	*Functional Materials* Amphitheatre F	*A Sea of Opportunities* Auditorium	*Teaching Challenges* Amphitheatre A	
15:00	*Registration at FFULisboa*	*Sponsored by TermoUnicam*			*Sponsored by Gravimeta*			*S. by Paralab*	*S. by CPSE*	15:00
15:25		**KN1** Emília Sousa (FF-UP)	**KN3** Eurico Cabrita (FCT-UNL)	**KN5** Jorge Parola (FCT-UNL)	**KN7** Augusto Tomé (UA)	**KN10** Cristina Freire (FCT-UP)	**KN13** Justin Chalker (Flinders Uni.)	**KN19** Anake Kijjoa (CIIMAR-UP)	**KN22** José Gomes (FC-UP)	15:25
15:30									**IOC10** Adelino Galvão (SG-SPQ)	15:30
15:40		**KN2** Teresa Melo (FCT-UC)	**KN4** Paulo Costa (FC-UL)	**KN6** Sérgio Seixas (FCT-UC)	**KN8** Jorge Morgado (IST-UL)	**KN11** Peter Carrott (UE)	**KN14** Mara Freire (UA)	**KN20** Vassilios Roussis (Pharm-UoA)		15:40
15:55									**IOC11** João Paiva (FC-UP)	15:55
16:00									**IOC12** João Paulo André (UM)	16:00
16:10	*Opening Ceremony & Future of Chemistry Session* Auditorium	**IOC1** Alexandra Antunes (IST-UL)	**IOC2** Liana Silva (FF-UL)	**IOC3** Ermelinda Maçôas (IST-UL)	**IOC4** Susana Costa (UM)	**IOC6** Mário Calvete (FCT-UC)	**IOC8** Luisa Neves (FCT-UNL)	**KN21** Deniz Tasdemir (GEOMAR)		16:10
16:20									**IOC13** Vítor Leite (Escola S. Penafiel)	16:20
16:25		**OC1** Maria Manuel Marques (FCT-UNL)	**OC3** Leandro Lourenço (UA)	**OC5** Elisabete Oliveira (FCT-UNL)	**OC7** João Sotomayor (FCT-UNL)	**OC9** Vânia André (IST-UL)	**OC11** Ana Aguiar Ricardo (FCT-UNL)			16:25
16:30	FCT								**IOC14** Desidério Pires (EB 2/3 Frei Estêvão Martins)	16:30
16:40								**IOC9** Susana Gaudêncio (FCT-UNL)		16:40
16:50	Guy Villax (Hovione)	**OC2** Paula Gomes (FC-UP)	**OC4** Rudi Oliveira (Hovione)	**OC6** Ana Lobo (FCT-UC)	**OC8** Igor Reva (FCT-UC)	**OC10** Bruno Medronho (FCT-UALG)	**OC12** Maria Eduarda Pereira (UA)		**FC14** Célia Faustino (FF UL)	16:50
17:00								**FC13** Luís Silva (FC-UP)	**FC15** Marta Corvo (FCT-UNL)	17:00
17:20	Stephen Caddick (Wellcome Trust)	*Coffee Break & Poster Session*						*Awards & Closing Ceremony* Auditorium		17:20
17:40	Kate Lawrence (ChemPubSoc)	*Health Challenges* Auditorium			*Young Chemists* Auditorium	*Young Chemists* Amphitheatre A	*Industry Challenges* Amphitheatre F			17:40
		Sponsored by Izasa			*Sponsored by Soquímica*					
18:00	*SPQ & P. Ferreira da Silva Session*	**PL5** Herbert Waldmann (Max-Planck-Gesellschaft)			**KN9** Fábio Fernandes (IST-UL)	**KN12** Cristina Pereira (ITQB-UNL)	**KN15** Rafael Antunes (Hovione)			18:00
18:10							**KN16** László Kiss (BIAL)			18:10
18:20					**IOC5** Tiago Rodrigues (iMM-UL)	**IOC7** Paula Ferreira (UA)				18:20
18:30							**KN17** Carlos Neto (The Navigator Co.)			18:30
18:40	*Lecture P. Ferreira da Silva 2016* João Rocha (UA)				**FC1** Ângelo Figueiredo (UCL)	**FC6** Ana Paula Paiva (FC-UL)				18:40
18:50		*Medalha Vicente de Seabra 2016* *Adrián Silva* (FE-UP)			**FC2** Alberto Dal Corso (ETH)	**FC7** Andreia Rosatella (FF-UL)	**KN18** Paulo Madeira (SAPEC)			18:50
19:00					**FC3** Hélio Faustino (FF-UL)	**FC8** Luís Cruz (FC-UP)				19:00
19:10	*Reception*				**FC4** Cecília Roque (FCT-UNL)	**FC9** Vera Silva (UA)	**FC11** António Ribeiro (IPB)			19:10
19:20		*SPQ – Meeting* Auditorium			**FC5** Ana C. Santos (IST-UL)	**FC10** Luis Fernandes (FCT-UE)	**FC12** Ricardo Branco (FCT-UNL)			19:20
20:00										20:00
		Street Food & Drinks			*Sunset Party & Conference Dinner*					

PL – Plenary; **KN** – Key Note; **IOC** – Invited Oral Communication; **OC** – Oral Communication; **FC** – Flash Communication

XXV ENCONTRO NACIONAL
Sociedade Portuguesa de Química

Scientific Programme

Sunday, July 16th, 2017

13.00-16.00 Registration

Session 1 | Chairman: Artur Silva, Carlos Afonso, Pedro Gois | Auditorium

16.00	Opening Ceremony & Future of Chemistry Session
16.20	FCT representative
16.40	Guy Villax (Hovione, Portugal)
17.00	Stephen Caddick (Wellcome Trust)
17.20	Kate Lawrence (ChemPubSoc)
17.40	SPQ & Ferreira da Silva Award Session
18.10	Lecture Ferreira da Silva Award | João Rocha (CICECO – UA, Portugal) *The Joy of Science: Personal Account*

19.10-21.00 Reception

Monday, July 17th, 2017

*Session 2 | Chairman: Gonçalo Bernardes (IMM-UL) | Auditorium - Health Challenges - **Sponsored by BIAL***

9.00	PL1 | Ben Davis (Oxford University, UK) *Sugars & proteins: towards a synthetic biology*
9.50	PL2 | Stephen Caddick (University College London, UK) *Chemical modification of proteins and antibodies*

10.40-11.40 Coffee break and poster session 1

*Session 3 | Chairman: Matilde Marques (IST-UL)| Auditorium - Health Challenges - **Sponsored by BIAL***

11.40	PL3 | Antonello Mai (SAPIENZA – University of Roma, Italy) *Sirtuins: To Activate or Not To Activate, That is the Question*
12.30	PL4 | Rui Moreira (FF-UL, Portugal) *Lead discovery for infectious diseases of the developing world: chemistry to unravel a black box*

13.20-15.00 Lunch

*Session 4 | Chairman: Victor Freitas (FC-UP), Fernanda Proença (UM) (Auditorium) | Marcela Segundo (FF-UP), Paula Branco (FCT-UNL) (Amphitheatre A) Maria da Conceição Rangel (ICBAS-UP), Gaspar Martinho (IST-UL) (Amphitheatre F) – **Sponsored by TermoUnicam***

	Auditorium Organic Tools	Amphitheatre A Analytical Tools	Amphitheatre F Fluorescent Tools
15.00	**KN1 | Emilia Sousa (FF-UP, Portugal)** *Old Sources for New Drugs: Challenges and Opportunities*	**KN3 | Eurico Cabrita (FCT-UNL, Portugal)** *NMR and intermolecular interactions: solving health, materials and environmental challenges*	**KN5 | Jorge Parola (FCT-UNL, Portugal)** *Supramolecular multistate multiresponsive systems based ontrans-2-hydroxychalcones*
15.30	**KN2 | Teresa Melo (FCT-UC, Portugal)** *Novel Ring-Fused Chlorins for Cancer Theranostics*	**KN4 | Paulo Costa (FC-UL, Portugal)** *Modeling Halogen Bonds: Relevance in (Bio)Chemical Systems*	**KN6 | Sérgio Seixas (FCT-UC, Portugal)** *Molecules of Colour: Reds, Purples and Blues. From Ancient to Modern Applications*
16.00	**IOC1 | Alexandra Antunes (IST-UL, Portugal)** *Adductomics: a challenge towards the minimization of chemically-induced toxic events and the development of diagnosis/prognosis tools*	**IOC2 | Liana Silva (FF-UL, Portugal)** *Ceramide domains in living cell membranes: from biophysical characterization to biological significance*	**IOC3 | Ermelinda Maçôas (IST-UL, Portugal)** *Carbon Dots in Bioimaging: Myths and Facts*
16.20	**OC1 | Maria M. Marques (FCT-UNL, Portugal)** *Advancing the chemical synthesis of azaindoles: a medicinal relevant scaffold*	**OC3 | Leandro Lourenço (UA, Portugal)** *Combined ammonium and pyridinium zinc(II)phthalocyanines and their photodynamic effect on cell suspensions and biofilms of Escherichia coli*	**OC5 | Elisabete Oliveira (FCT-UNL, Portugal)** *Synthesis of Luminescent Nanoparticles for Drug Delivery and Imaging in Cancer Cells*
16.40	**OC2 | Paula Gomes (FC-UP, Portugal)** *Novel triple-stage antimalarial ionic liquids and their effects on lipid membrane models*	**OC4 | Rudi Oliveira (Hovione, Portugal)** *Process Development in Flow Chemistry using Kinetic Modeling*	**OC6 | Ana Lobo (FCT-UC, Portugal)** *Phthalocyanine Labels for Near-Infrared Fluorescence Imaging of Solid Tumors*

17.00-17.40 Coffee break and poster session 2

*Session 5 | Chairman: Pedro Gois (FF-UL) | Auditorium – Health Challenges – **Sponsored by Izasa***

17.40	**PL5 | Herbert Waldmann (Max-Planck-Gesellschaft, Germany)** *Biologically Relevant Small Molecules for Perturbation of Protein Function: Chemotype – Phenotype - Target*
18.30	**Lecture Medalha Vicente de Seabra 2016 | Adrián Silva (FE-UP, Portugal)** *A catalysis journey: breaking bonds for clean water*
19.10	**SPQ-Meeting**

20.00- Street Food Fest

Tuesday, July 18th, 2017

*Session 6 | Chairman: Maria João Romão (FCT-UNL) | Auditorium – Material Challenges – **Sponsored by Hovione***

09.00 **PL6 | Stefan Matile (University of Genève, Switzerland)**
Functional Supramolecular Chemistry

09.50 **PL7 | João Mano (CICECO-UA, Portugal)**
Nano-multilayered polymeric systems in the development of new biomedical devices

10.40-11.40 Coffee break and poster session 3

*Session 7 | Chairman: Mario Nuno Berberan-Santos (IST-UL) | Auditorium - Material Challenges – **Sponsored by Hovione***

11.40 **PL8 | Erwin Reisner (University Cambridge, UK)**
Semi-artificial Photosynthesis

12.30 **PL9 | João Rocha (CICECO-UA, Portugal) – Ferreira da Silva Award 2016**
'On the Road again, Goin' places that I've never been': a personal account of a journey in Materials Chemistry

13.20-15.00 Lunch

*Session 8 | Chairman: João Brandão (UAlg), Verónica Bermudez (UTAD) (Auditorium) | Costa Lima (FF-UP), Teresa Duarte (IST-UL) (Amphitheatre A) Manuela Carrott (UE), Eduardo Jorge Figueira Marques (UA) (Amphitheatre F) – **Sponsored by Gravimeta***

	Auditorium Organic Materials	Amphitheatre A Heterogeneous Materials	Amphitheatre F Functional Materials
15.00	**KN7 | Augusto Tomé (UA, Portugal)** *Porphyrins and porphyrinoids: functionalization and applications*	**KN10 | Cristina Freire (FCT-UP, Portugal)** *Functional nanomaterials for sustainability*	**KN13 | Justin Chalker (Flinders University, Australia)** *Sulfur polymers for the environment, agriculture and human health*
15.30	**KN8 | Jorge Morgado (IST-UL, Portugal)** *Materials chemistry: from benzene to sustainable energy solutions*	**KN11 | Peter Carrott (UE, Portugal)** *Preparation and Gas-Solid Applications of Activated Carbon Fibres and Cloths*	**KN14 | Mara Freire (UA, Portugal)** *Ionic-Liquid-Based Separation Processes for Bioactive and Value-Added Compounds*
16.00	**IOC4 | Susana Costa (UM, Portugal)** *Phototriggers for light-controlled activation and release applications*	**IOC6 | Mário Calvete (FCT-UC, Portugal)** *Inorganic helping Organic: Tetrapyrrolic Macrocycles Immobilized onto Inorganic Supports and their Applications*	**IOC8 | Luísa Neves (FCT-UNL, Portugal)** *Carbon Dioxide Removal using Mixed Matrix Membranes with Metal-Organic Frameworks Supporting Ionic Liquids*
16.20	**OC7 | João Sotomayor (FCT-UNL, Portugal)** *Eutectic Solvents: Expanding Chemical Profiles*	**OC9 | Vânia André (IST-UL, Portugal)** *BioMOFs targeting antibiotics solubility*	**OC11 | Ana Aguiar-Ricardo (FCT-UNL, Portugal)** *Supercritical-assisted POxylation: Designing new materials for drug delivery and water purification*

16.40	**OC8 | Igor Reva (FCT-UC, Portugal)** *Generation and Stabilization of Triplet 2-Formyl Phenylnitrene in Inert Cryogenic Matrices*	**OC10 | Bruno Medronho (FCT-UAlg, Portugal)** *Controversial Thoughts and Advances in Cellulose Dissolution: From Scattering and Rheology to a New NMR Approach*	**OC12 | Maria Eduarda Pereira (UA, Portugal)** *Metals in Ria the Aveiro (Portugal): Perspectives*

17.00-17.40 Coffee break and poster session 4

*Session 9 \| Chairman: Anthony Burke (UE), Sofia Pauleta (FCT-UNL) (Auditorium) Maria Santos (FF-UL), Richard Gomes (UA) (Amphitheatre A) Artur Silva (UA), Baltazar de Castro (FC-UP) (Amphitheatre F) – **Sponsored by Soquimica***

	Auditorium Young Chemists	Amphitheatre A Young Chemists		Amphitheatre F Industry Challenges
17.40	**KN9 | Fábio Fernades (IST-UL, Portugal)** *Nanoscale Compartmentalization of PI(4,5)P2 in Living Cells and Model Membranes. A Fluorescence Spectroscopy and FRET Imaging study*	**KN12 | Cristina Pereira (ITQB-UNL, Portugal)** *Revisiting the old polymer suberin to develop functional materials*	17.40	**KN15 | Rafael Antunes (Hovione)** *Challenges for Chemists in the 4th Industrial Revolution*
			18.00	**KN16 | Lázló Kiss (BIAL)** *Discovery and Development of Opicapone: A Potent and Peripherally Selective Catechol O-methyltransferase (COMT) Inhibitor for the Adjunctive Treatment of Parkinson's Disease*
18.10	**IOC5 | Tiago Rodrigues (iMM-UL, Portugal)** *Unraveling network pharmacology in natural product space*	**IOC7 | Paula Ferreira (CICECO-UA, Portugal)** *Designing functional porous materials*		
			18.20	**KN17 | Carlos Neto (The Navigator Company)** *The Biorefinery R&D Programme at The Navigator Company*
18.30	**FC1 | Ângelo Figueiredo (UCL)** *A NMR approach to characterise guanidino group of arginine side chains at macromolecular protein interfaces*	**FC6 | Ana Paula Paiva (FC-UL, Portugal)** *Recycling of Valuable Metals from Spent End-of-Life Materials: Research on the Liquid-Liquid Extraction of Palladium*		
18.40	**FC2 | Alberto Dal Corso (ETH)** *Non-internalizing antibody-drug conjugates release potent cytotoxic agents at the tumor site upon proteolytic linker cleavage*	**FC7 | Andreia Rosatella (FF-UL, Portugal)** *Magnetic Ionic Liquids - MILs*	18.40	**KN18 | Paulo Madeira (SAPEC)** *Mass Spectrometry Applications in the Crop Protection Industry*
18.50	**FC3 | Hélio Fastino (FF-UL, Portugal)** *Selective, Rapid and Reversible N-Terminal Cysteine Functionalisation with 2-Formylbenzeneboronic acids (2FBBA)*	**FC8 | Luís Cruz (FC-UP, Portugal)** *Synthesis and physical-chemical characterization of novel anthocyanin-lipophilic bioactives*		

19.00	FC4 | Cecília Roque (FCT-UNL, Portugal) *Affinity materials for medical and biotechnological applications*	FC9 | Vera Lucia (QOPNA-UA, Portugal) *Ohmic Heating Assisted Synthesis of 1,3-Disubstituted-quinolin-4(1H)-ones by C-C Cross Coupling Reactions in Aqueous Media*	19.00	FC11 | António Ribeiro (IPB) *Separation of Nadolol Racemates by Fixed-bed and Continuous Preparative Liquid Chromatography using C18 Columns*
19.10	FC5 | Ana C. Santos (IST-UL, Portugal) *Smart Polymer Fibers for Stem Cell Cultivation*	FC10 | Luís Fernandes (FCT-UE, Portugal) *Alpha-glucosidases and cholinesterases inhibition*	19.10	FC12 | Ricardo Branco (FCT-UNL) *De novo computational design of a protein catalyst for the Beckmann rearrangement reaction*

20.00- Sunset Party & Conference Dinner

Wednesday, July 19th, 2017

*Session 10 | Chairman: Carlos Romão (FCT-UNL)| Auditorium – Environmental Challenges – **Sponsored by Bruker***

9.00	PL10 | David Milstein (Weizmann Institute of Science, Israel) *Design and Applications of Sustainable Catalytic Reactions for Synthesis and Energy*
9.50	PL11 | Armando Pombeiro (IST-UL, Portugal) *Inert Alkanes as Potential Feedstocks for Synthesis?*

10.40-11.40 Coffee break and poster session 5

*Session 11 | Chairman: Beatriz Royo (ITQB-UNL) | Auditorium – Environmental Challenges – **Sponsored by Bruker***

11.40	PL12 | Paul Chirik (Princeton University, USA) *Catalysis with Earth Abundant Transition Metals*
12.30	PL13 | Antonio Echavarren (ICIQ, Spain) *Gold-Catalysis for the Synthesis of Biologically Active Natural Products*

13.20-15.00 Lunch

*Session 12 | Chairman: José Cavaleiro, Carlos Afonso (Auditorium) – **Sponsored by Paralab**; Joaquim Faria, Carla Morais (Amphitheatre A) – **Sponsored by ChemPubSoc Europe***

	Auditorium A Sea of Opportunities		Amphitheatre A Teaching Challenges
15.00	KN19 | Anake Kijoa (CIIMAR-UP, Portugal) *Marine-Derived Fungi: A Promising Source of Bioactive Compounds for Drug Discovery*	15.00	KN22 | José Gomes (FC-UP, Portugal) *A Química no ensino básico e secundário: Um desafio para os alunos?*
		15.25	IOC10 | Adelino Galvão (SG-SPQ, Portugal) *Aprendizagens Essenciais: Os novos desafios transdisciplinares no ensino da Química*

15.30	KN20 | Vassilios Roussis (Pharm-UoA, Greece) *In search of algal metabolites with biomedical-biotechnological potential from the East Mediterranean*	15.40	IOC11 | João Paiva (FC-UP, Portugal) *Manuais escolares em química e desafios futuros: uma experiência e algumas reflexões*
		15.55	IOC12 | João André (UM, Portugal) *A percepção pública da química através do teatro e da ópera*
16.00	KN21 | Deniz Tasdemir (GEOMAR, Germany) *Integrated Strategies to Address Ocean's Microbial and Metabolomic Dark Matters for Marine Natural Product Discovery*	16.10	IOC13 | Vítor Leite (Escola S. Penafiel, Portugal) *Desafios ao ensino da Química*
		16.25	IOC14 | Desidério Pires (Escola Básica 2/3 Frei Estêvão Martins em Alcobaça) *Olimpíadas Regionais de Química: qual a importância em participar e quais os segredos do sucesso dos alunos neste evento*
16.30	IOC9 | Susana Gaudêncio (FCT-UNL, Portugal) *Ocean Treasures: Marine actinomycetes as a source of antimicrobial compounds with biotechnological potential*	16.40	FC14 | Célia Faustino (FF-UL, Portugal) *Development of Chemistry Education Research in Portugal: The Emerging Picture from the Papers Published in the Journal of Chemical Education*
16.50	FC13 | Luís Silva (FC-UP, Portugal) *Characterization of the Chemiexcitation Step of Marine Imidazopyrazinone Chemiluminescence*	16.50	FC15 | Marta Corvo (FCT-UNL, Portugal) *Science outreach activities from early grades to high school*

17:00-18:00 Awards & Closing Cerimony | Auditorium

List of Communications

Plenary Lectures

PL1|*Sugars & proteins: towards a synthetic biology*

Benjamin G. Davis

PL2|*Chemical modification of proteins and antibodies*

Stephen Caddick

PL3|*Sirtuins: To Activate or Not To Activate, That is the Question*

Antonello Mai

PL4|*Lead discovery for infectious diseases of the developing world: chemistry to unravel a black box*

Rui Moreira

PL5|*Biologically Relevant Small Molecules for Perturbation of Protein Function: Chemotype – Phenotype - Target*

Herbert Waldmann

PL6|*Functional Supramolecular Chemistry*

Stefan Matile

PL7|*Nano-multilayered polymeric systems in the development of new biomedical devices*

João F. Mano

PL8|*Semi-artificial Photosynthesis*

Erwin Reisner

PL9|*'On the Road again, Goin' places that I've never been': a personal account of a journey in Materials Chemistry*

João Rocha

PL10|*Design and Applications of Sustainable Catalytic Reactions for Synthesis and Energy*

David Milstein

PL11|*Inert Alkanes as Potential Feedstocks for Synthesis?*

Armando J. L. Pombeiro

PL12|*Catalysis with Earth Abundant Transition Metals*

Paul J. Chirik

PL13|*Gold-Catalysis for the Synthesis of Biologically Active Natural Products*

Antonio M. Echavarren

Key Notes

KN1|*Old Sources for New Drugs: Challenges and Opportunities*

Emília Sousa

KN2|*Novel Ring-Fused Chlorins for Cancer Theranostics*

Teresa M. V. D. Pinho e Melo

KN3|*NMR and intermolecular interactions: solving health, materials and environmental challenges*

Eurico J. Cabrita

KN4|*Modeling Halogen Bonds: Relevance in (Bio)Chemical Systems*

Paulo J. Costa

KN5|*Supramolecular multistate multiresponsive systems based on trans-2-hydroxychalcones*

A. Jorge Parola

KN6|*Molecules of Colour: Reds, Purples and Blues. From Ancient to Modern Applications*

J. Sérgio Seixas de Melo

KN7|*Porphyrins and porphyrinoids: functionalization and applications*

Augusto C. Tomé

KN8|*Materials chemistry: from benzene to sustainable energy solutions*

Jorge Morgado

KN9|*Nanoscale Compartmentalization of PI(4,5)P2 in Living Cells and Model Membranes. A Fluorescence Spectroscopy and FRET Imaging study*

Fábio Fernandes

KN10|*Functional nanomaterials for sustainability*

Cristina Freire

KN11|*Preparation and Gas-Solid Applications of Activated Carbon Fibres and Cloths*

Peter Carrott

KN12|*Revisiting the old polymer suberin to develop functional materials*

Cristina S. Pereira

KN13|*Sulfur polymers for the environment, agriculture and human health*

Justin M. Chalker

KN14|*Ionic-Liquid-Based Separation Processes for Bioactive and Value-Added Compounds*

Mara G. Freire

KN15|*Challenges for Chemists in the 4th Industrial Revolution*

Rafael Antunes

KN16|*Discovery and Development of Opicapone: A Potent and Peripherally Selective Catechol O-methyltransferase (COMT) Inhibitor for the Adjunctive Treatment of Parkinson's Disease*

László E. Kiss

KN17|*The Biorefinery R&D Programme at The Navigator Company*

Carlos P. Neto

KN18|*Mass Spectrometry Applications in the Crop Protection Industry*

Paulo J. A. Madeira

KN19|*Marine-Derived Fungi: A Promising Source of Bioactive Compounds for Drug Discovery*

Anake Kijjoa

KN20|*In search of algal metabolites with biomedical-biotechnological potential from the East Mediterranean*

Vassilios Roussis

KN21|*Integrated Strategies to Address Ocean's Microbial and Metabolomic Dark Matters for Marine Natural Product Discovery*

Deniz Tasdemir

KN22|*A Química no ensino básico e secundário: Um desafio para os alunos?*

José F. Gomes

Invited Oral Communications

IOC1|*Adductomics: a challenge towards the minimization of chemically-induced toxic events and the development of diagnosis/prognosis tools*

Alexandra M. M. Antunes

IOC2|*Ceramide domains in living cell membranes: from biophysical characterization to biological significance*

Liana C. Silva

IOC3|*Carbon Dots in Bioimaging: Myths and Facts*

Ermelinda Maçôas

IOC4|*Phototriggers for light-controlled activation and release applications*

Susana P. G. Costa

IOC5|*Unraveling network pharmacology in natural product space*

Tiago Rodrigues

IOC6|*Inorganic helping Organic: Tetrapyrrolic Macrocycles Immobilized onto Inorganic Supports and their Applications*

Mário J. F. Calvete

IOC7|*Designing functional porous materials*

Paula Ferreira

IOC8|*Carbon Dioxide Removal using Mixed Matrix Membranes with Metal-Organic Frameworks Supporting Ionic Liquids*

Luisa A. Neves

IOC9|*Ocean Treasures: Marine actinomycetes as a source of antimicrobial compounds with biotechnological potential*

Susana P. Gaudêncio

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Adelino M. Galvão

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João P. André

IOC13|*Desafios ao ensino da Química*

Vítor N. Leite

IOC14|*Olimpíadas Regionais de Química: qual a importância em participar e quais os segredos do sucesso dos alunos neste evento*

Desidério Pires

Oral Communications

OC1|*Advancing the chemical synthesis of azaindoles: a medicinal relevant scaffold*

Maria Manuel Martinho Sequeira Barata Marques

OC2|*Novel triple-stage antimalarial ionic liquids and their effects on lipid membrane models*

Paula Alexandra de Carvalho Gomes

OC3|*Combined ammonium and pyridinium zinc(II)phthalocyanines and their photodynamic effect on cell suspensions and biofilms of Escherichia coli*

Leandro Miguel de Oliveira Lourenço

OC4|*Process Development in Flow Chemistry using Kinetic Modeling*

Rudi Micael Santiago de Oliveira

OC5|*Synthesis of Luminescent Nanoparticles for Drug Delivery and Imaging in Cancer Cells*

Elisabete de Jesus Oliveira Marques

OC6|*Phthalocyanine Labels for Near-Infrared Fluorescence Imaging of Solid Tumors*

Ana Catarina Sousa Lobo

OC7|*Digital Optical Memory Devices based on PDLC Films*

João Carlos da Silva Barbosa Sotomayor

OC8|*Generation and Stabilization of Triplet 2-Formyl Phenylnitrene in Inert Cryogenic Matrices*

Igor Reva

OC9|*BioMOFs targeting antibiotics solubility*

Vânia André

OC10|*Controversial Thoughts and Advances in Cellulose Dissolution: From Scattering and Rheology to a New NMR Approach*

Bruno Filipe Figueiras Medronho

OC11|*Supercritical-assisted POxylation: Designing new materials for drug delivery and water purification*

Ana Aguiar Ricardo

OC12|*Metals in Ria the Aveiro (Portugal): Perspectives*

Maria Eduarda da Cunha Pereira

Flash Communications

FC1|*A NMR approach to characterise guanidino group of arginine side chains at macromolecular protein interfaces*

Angelo Miguel M P Figueiredo

FC2|*Non-internalizing antibody-drug conjugates release potent cytotoxic agents at the tumor site upon proteolytic linker cleavage*

Alberto Dal Corso

FC3|*Selective, Rapid and Reversible N-Terminal Cysteine Functionalisation with 2-Formylbenzeneboronic acids (2FBBA)*

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FC4|*Affinity materials for medical and biotechnological applications*

Ana Cecília Afonso Roque

FC5|*Smart Polymer Fibers for Stem Cell Cultivation*

Ana Catarina Santos

FC6|*Recycling of Valuable Metals from Spent End-of-Life Materials: Research on the Liquid-Liquid Extraction of Palladium*

Ana Paula Pereira Paiva

FC7|*Magnetic Ionic Liquids - MILs*

Andreia de Almeida Rosatella

FC8|*Synthesis and physical-chemical characterization of novel anthocyanin-lipophilic bioactives.*

Luis Miguel Neves Ferreira Serra Cruz

FC9|*Ohmic Heating Assisted Synthesis of 1,3-Disubstituted-quinolin-4(1H)-ones by C-C Cross Coupling Reactions in Aqueous Media*

Vera Lúcia Marques da Silva

FC10|*Alpha-glucosidases and cholinesterases inhibition*

Luís António Garrido Nunes Fernandes

FC11|*Separation of Nadolol Racemates by Fixed-bed and Continuous Preparative Liquid Chromatography using C18 Columns*

António Manuel Esteves Ribeiro

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Henrique Daniel Figueiredo Carvalho

FC13|*Characterization of the Chemiexcitation Step of Marine Imidazopyrazinone Chemiluminescence*

Luís Tiago da Costa Pinto da Silva

FC14|*Development of Chemistry Education Research in Portugal: The Emerging Picture from the Papers Published in the Journal of Chemical Education*

Célia Faustino

FC15|*Science outreach activities from early grades to high school*

Marta Corvo

Health Challenges Poster Communications

HC1|*Determination of fluoxetine in hair by high-pressure liquid chromatography with fluorescence detection*

Adriana Patrícia Fernandes Ribeiro

HC2|*A quality-by-design approach for the understanding of the effect of model antigen mannose on PLGA nanoparticles*

Ainhoa Teresa Cardoso Coelho

HC3|*Bioactivation of the anti-HIV drug etravirine to reactive metabolites: in vivo and in vitro approaches*

Ana Lúcia Aguiar Godinho

HC4|*Ionic Liquids as functional ingredients in Lipidic Implants*

Ana Luísa Gomes Júlio

HC5|*Semisynthetic derivatives of monoterpene natural compounds: preparation and evaluation of cytotoxicity*

Ana Maria Branco Alves

HC6|*Mass Spectrometry Methods for Phenolic Compounds Identification*

Ana Patrícia dos Santos Marques

HC7|*Synthesis of new curcumin analogues with potential biological properties*

Ana Patrícia Sequeira Lopes

HC8|*Design and synthesis of novel multi-targeted directed triazene based hybrid molecules as potential anticancer agents*

Ana Paula Gameiro Francisco

HC9|*Structural insights on immune checkpoint blockade: An in silico strategy towards cancer immunotherapy*

Ana Rita de Carvalho Acúrcio

HC10|*Synthesis of asymmetric 1,3-diazetidinediones as inhibitors of HNE to target COPD*

Ana Rita Gomes Félix

HC11|*Nucleoside based N-Heterocyclic Carbenes: Base-Pairing Effects of Carbene Formation*

Ana Rita Guerreiro de Brito Petronilho

HC12|*Cork polyphenols, an alternative strategy against amyloid-beta fibrillization*

Ana Rita Rodrigues Araújo

HC13|*Extracts and new derivatives of anthocyanins as potential cosmetic ingredients – a skin-barrier model optimization using ECIS*

Ana Sofia Marques Mendes Évora

HC14|*Reactivity study and biological activity of royleanones from Plectranthus spp.*

Anastasia Borozan

HC15|*Luz10, a new water-soluble bacteriochlorin photosensitizer: Photochemical, in vitro and in vivo characterization*

André Filipe Sintra Luz

HC16|*Non-enzymatic modifications of human serotransferrin and the dyshomeostasis of systemic iron transport.*

André Moreira Neto da Silva

HC17|*Identification of potential inhibitors against Influenza A virus targeting the RNA-binding domain of NS1*

Andreia Espírito Santo Cunha

HC18|*Synthesis of N-Glycosylsulfonamides from Ribose and 2-Deoxy Glucose: Exo-anomeric Effect and Furanose/Pyranose Isomerization*

Andreia Jesus Lopes Fortuna

HC19|*The Search for New Anti-Cancer Molecules: Catalytic Synthesis of Novel Chiral Oxindole Derivatives*

Anthony Joseph Burke

HC20|*Covalent Functionalization of Nano-Graphene Oxide with Glycol Porphyrins: Synthesis and Effects*

Carla Isabel Madeira dos Santos

HC21|*2-Benzylchromones: Synthesis of novel potential biologically active compounds*

Carlos Fábio Magalhães da Silva

HC22|*Electrophilic derivatives of estrogens from oxidation by Dess-Martin periodinane: evaluation of reactivity toward amino acids*

Catarina Sofia Romão Charneira

HC23|*Exploratory studies on the synthesis of novel spiro-γ-lactams*

Cátia Castanheira Caratão

HC24|*The New Modular Fluorescent BASHY Platform: Stability in Aqueous Media*

Cátia Diana Parente Caldeira Carvalho

HC25|*Chitobiose as starting material to bacterial cell Wall oligosaccharides*

Cátia Vanessa de Almeida Santos

HC26|*Investigating Selective Cytotoxicity of Cancer Cells*

Charlotte Baker

HC27|*Neisseria gonorrhoeae Cytochrome c Peroxidase and the physiological electron donor, the Lipid-modified Azurin*

Cláudia Raquel da Silva Nóbrega

HC28|*The photostability and interaction with Biomolecular Targets of Indirubin*

Daniela Nobre Sarmento dos Santos

HC29|*Novel hybrid drugs approach based on peroxides for Leishmaniasis*

Daniela Sofia Ribeiro Coutinho

HC30|*Synthesis of novel spirooxadiazoline oxindoles and evaluation as anti-cancer agents*

Elizabeth de Abreu Lopes

HC31|*Synthesis of benzopyran-indole dyads with potential cannabinoid activity*

Emanuel Jorge Ferreira Balsa

HC32|*Synthesis of new G-quadruplex ligands*

Enrico Cadoni

HC33|*Modular Construction of Reversible Multivalent Targeting Drug Conjugates*

Fábio Miguel Figueiredo Santos

HC34|*An innovative approach towards bacterial cell Wall oligosaccharides*

Fausto Daniel dos Santos Queda

HC35|*Flow assisted synthesis of bicyclic aziridines via photochemical transformation of pyridinium salts*

Filipa Alexandra Delgado Siopa

HC36|*Pharmacophore modeling of novel EZH2 inhibitors*

Filipa João Fernandes Ramilo Gomes

HC37|*Synthetic optimization process of mesoporous nanoparticles for protein extraction in biological samples*

Gonçalo Alexandre dos Santos Marcelo

HC38|*Indole diversity-oriented synthesis (DOS) based on a promising antimalarial scaffold*

Gustavo Adolfo Lopes Ferreira da Silva

HC39|*Nitromethane conjugate addition to 2-[(1E,3E)-4-arylbuta-1,3-dien-1-yl]-4H-chromen-4-ones*

Helio Miguel Teixeira Albuquerque

HC40|*Dipolar Reorientations in the Amorphous Phase of the API Efavirenz. Some insights from the dielectric TSDC and DRS techniques*

Hermínio Albino Pires Diogo

HC41|*Ionic liquids in the polymorphic control of drugs: Are we solving a pharmaceutical industry problem?*

Inês Catarina Batista Martins

HC42|*Exploring the Chemistry of Nitroso- and Azoalkenes for the Synthesis of Bilanes*

Inês Catarina Ferreira Fonseca

HC43|*Does the antiepileptic drug carbamazepine need bioactivation to react with bionucleophiles?*

Inês Sofia Lança Martins

HC44|*A simple fabrication procedure of ecological screen-printing biosensors for diabetics' monitorization*

Isabel Cristina Ribau Fernandes Coutinho

HC45|*ANTHO4SKIN – Recycling anthocyanins for cosmetic applications*

Iva Luzia Reis Fernandes

HC46|*Synthesis of Smart Biocompatible Nanoparticles for Bio-Applications*

Jessica Ariana Madeira Machado

HC47|*Development of new boron based fluorescent dyes as hydrogen sulphide probes*

Joana Inês Coelho de Pinho Carvalho

HC48|*Functionalization of betulinic acid through Heck reactions*

Joana Lia Cardoso de Sousa

HC49|*Novel neutrophil elastase inhibitor-loaded starch-based nanocapsules with improved pharmaceutical performance: in vitro and in vivo studies*

Joana Marques Marto

HC50|*Synthesis of pyrimidine-based chemical probes to study the biology of liver stage malaria parasites*

Joana Rita Leite Ribeiro

HC51|*Permanent digital maps of the blood serum proteome for diagnostics and prognostics in multiple myeloma and lymphoma*

João Alexandre Martins Forreta Prates

HC52|*Azaindole derivatives in structure based drug design for the discovery of new anti-apoptotic protein inhibitors*

João Carlos Moreno Ramos

HC53|*Micromorphological, phytochemical profile and antibacterial evaluation of two Rutaceae species*

João Carlos Serra e Moura Gomes

HC54|*Investigation of novel sulfonylation methods*

João Cristóvão Santos Silva Macara

HC55|*Incorporation of cimetidine in mesoporous silica nanoparticles*

João Nuno da Luz Teixeira

HC56|*A new reversible clickable linker for protein bioconjugation*

João Pedro Marante António

HC57|*Macrocyclic ligands incorporating a pyridine moiety and their copper(II) and nickel(II) complexes: antifungal activity in Fluconazole-resistant pathogenic yeasts*

Jorge Humberto Correia Pereira

HC58|*Dielectric constants of fluid lipid bilayers measured through the pyrene Ham effect: experimental caveats in fluorescence measurements*

Jorge Manuel Martins

HC59|*Human serum transferrin binding of VIVO2+ complexes - a computational assessment of the transferrin ability to transport drugs*

José Gonçalo Deira Duarte de Campos Justino

HC60|*Development of Torin-based compounds for treating protozoan Neglected Tropical Diseases*

Lara Gião Fidalgo

HC61|*Synthesis of new scaffolds from oleuropein derived building blocks*

Lídia Alexandra Santos Cavaca

HC62|*Synthesis of novel 4-(pyran-3-yl)pyrano[3,4-b]-4H-chromene: role of catalyst and solvent*

LIZA SAHER

HC63|*A Chemoproteomic approach to validate Human Neutrophil Elastase as a Biomarker of Chronic Obstructive Pulmonary Disease*

Luís Miguel Afonso Ramos de Carvalho

HC64|*Synthesis of metabolites from the Benzo Fury's drugs of abuse*

Luísa Maria da Silva Pinto Ferreira

HC65|*Synthesis of benzophenone derivatives by the reaction of nitromethane with (E)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4H-chromen-4-ones*

Lydia SAIDI

HC66|*Site-selective protein chemistry and its therapeutic relevance*

Maksymilian Żegota

HC67|*Validation of cleaning procedures in batch manufacturing of medicines*

Manuel José Matos

HC68|*NMDA receptor antagonists: an alternative approach to treat neurodegenerative disorders*

Margarida Leonor Florindo Espadinha

HC69|*Targeted Mass Spectrometry-Based Metabolomics: From Biomarkers in Biofluids to Mechanistics Studies in Drug Discovery*

Margarida Maria Fernandes Baptista e Silva

HC70|*HPLC-DAD-HRMS characterization of the bioactive phenolic compounds in aqueous extracts of Origanum vulgares L.*

Maria Adilia Januário Charmier

HC71|*Carotenoids content of soups consumed in Portugal*

Maria Celeste de Carvalho N. P. Morais Serra

HC72|*HPLC-DAD-MS characterization of Carpobrotus edulis L. extracts processed by an integrated Green Chemical approach*

Maria da Conceição Monteiro Andre de Oliveira

HC73|*Synthetic strategies in the design of new tetrapyrrolic photosensitizers*

Maria da Graça de Pinho Morgado Silva Neves

HC74|*Evaluation of several phytochemicals as ligands/probes for copper chelation using UV and fluorescence spectroscopy*

Maria Eduarda Machado de Araújo

HC75|*An overview on the biological properties of Ag(I) camphor complexes*

Maria Fernanda do Nascimento Neves de Carvalho

HC76|*Can inhibition of glycolysis increase the selectivity of photodynamic therapy towards cancer cells?*

Maria Inês P. Mendes

HC77|*Platinum Complexes Bearing Guanosine Derived N-Heterocyclic Carbenes*

Maria Inês Paiva da Silva Leitão

HC78|*Orthogonal N-Terminal cysteine modification via thiazolidine cyclization*

Maria José dos Santos Alves da Silva

HC79|*Influence of procyanidin B3 in gliadin digestion under different gastro-intestinal conditions*

maria rosa perez gregorio

HC80|*Flavonols isolated from Hedychium gardnerianum leaves*

Mariana Oliveira

HC81|*Cocrystallization screening of new hydrochlorothiazide cocrystals*

Marisa Abreu Rodrigues

HC82|*Ionic Liquids and Salts of Antibiotic and Antiviral Drugs*

Miguel Maurício Machado dos Santos

HC83|*Synthesis, Characterization and DFT Studies of New 2-Arylidene-Thiazolo[3,2-a]pyrimidines as Prospective Antitumor Scaffolds*

Mohamed Youssef Ahmed Mahgoub

HC84|*New Cu(II) complexes with pyrazolyl Schiff base: synthesis and biological evaluation*

Nádia Raquel Pólvora Ribeiro

HC85|*Determination of fluoride in mineral waters and tea consumed by the portuguese population: is there a risk of fluorosis?*

Nelson Alberto Frade da Silva

HC86|*Synthesis of antibacterial and antitumor alkylaminophenols by Petasis borono Mannich multicomponent reaction*

Nuno Filipe Rafael Candeias

HC87|*Progress towards Neofiscalin A Synthesis, a Potent Antibacterial Agent*

Papichaya Boonpothong

HC88|*Chemical characterization of Pinus pinaster bark and needles lipophilic fractions: a valuable resource of diterpene resinic acids*

Patrícia Alexandra Bogango Ramos

HC89|*Computational approach to structural characterization of Viral Surface glycoproteins in HIV-2*

Patrícia Filipa Alves Serra

HC90|*Triggering a specific immune response against cancer – activation of NK cells with small organic molecules*

Pedro Boto Pereira Franco Pinheiro

HC91|*Understanding Proteasome Inhibition: A Molecular Dynamics study*

Pedro Miguel Pinto Fernandes

HC92|*Chemically Activated Writer – "Click-to-Acetylate" Concept*

Pedro Miguel Saraiva Duarte Cal

HC93|*Synthesis of co-amorphous drugs by freeze-drying of low solubility drugs*

Pedro Ricardo Neves Ferreira Lobão da Cruz

HC94|*Graphene-based magnetic nanocarriers for combined hyperthermia and controlled-responsive drug delivery applications*

Raquel Oliveira Rodrigues

HC95|*Polyphenols in Celiac Disease Prevention: a Multidisciplinary Study*

Ricardo Jorge Correia Dias

HC96|*Optimizing the flavanone core towards a new generation of multiple ABC transporters efflux modulators*

Ricardo José Diogo Grácio Ferreira

HC97|*Therapeutic bioconjugates: Evaluation of iminoboronates as payload delivery system for cancer*

Ricardo Miguel Ribeiro Magalhães Lopes

HC98|*Development of small molecular cores for boronic acid ligation in peptides*

Roberto Russo

HC99|*Targeting the human 20S proteasome: finding new inhibitors through a computational-based drug discovery approach and biological evaluation of the selected compounds*

Romina Paula de Aguiar Guedes

HC100|*In vitro metabolism studies on synthetic cathinones*

Sara Carolina de Carvalho Henriques

HC101|*Tetra-PEGylated bacteriochlorin as potential PDT photosensitizer: Synthesis, characterization and in vitro studies*

Sara Martinho Almeida Pinto

HC102|*Palladium-mediated synthesis of pseudo-C-glycosylxanthone and phenyloxybenzaldehyde derivatives of pharmacological interest*

Sara Mirassol Tomé

HC103|*Compounds with antibacterial activity based on camphor and silver*

Silvestre Amado Santos Leite

HC104|*Synthesis of therapeutically useful multivalent boronate complexes*

Silvia Baldo

HC105|*Bis-(thio)urea-based receptors as potential membrane transporters for anions*

Sílvia Cristina Ferreira de Carvalho

HC106|*A Computational Approach Targeting LRRK2*

Sofia Leonor Afonso Domingos

HC107|*Antitumor Activity of Quinazolinone Alkaloids-Inspired in Marine Products*

Solida Long

HC108|*Peptide Nanofibers as tools for efficient retroviral gene transfer*

Stefanie Sieste

HC109|*Hybrid Silica Nanoparticles to Target the Blood-Brain Barrier for Controlled Drug Release*

Susana Cristina Cristo Cecílio

HC110|*Synthesis and characterization of 3-hydroxy-4-pyridinone functionalized with hydrophilic chains for treatment of iron deficiency chlorosis in plants*

Tânia Alexandra Fernandes de Sousa Moniz

HC111|*Tryptophanol-derived oxazoloisoindolinones: promising small molecules to target cancer*

Valentina Barcherini

HC112|*Development of new NIR dyes by Pd-catalyzed aminocarbonylation*

Vanessa Almeida Tomé

HC113|*Polyurea Dendrimers as Nanocarriers for Ovarian Cancer Therapeutics*

Vasco Daniel Bigas Bonifácio

HC114|*Synthesis of (Triazolyl)methyl Amide-linked Disaccharide Nucleosides as Potential Inhibitors of Glycosyltransferases*

Vítor José Inácio Martins

Material Challenges Poster Communications

MC1|*Hydrosoluble copper complexes for homogeneous catalysis*

Abdallah Gamal Abdallah Mahmoud

MC2|*Fluorescent Conjugated Oligomers Based on Calix[4]arene and -Glucose Units*

Alexandra Isabel Martins Paulo da Costa

MC3|*New promising intermetallic, borates and chalcogenides nanofibers*

Ana Cristina Gomes Ferreira

MC4|*Self-assembled Molecular Conducting Bilayers*

Ana Cristina Teixeira Martins Gonçalves

MC5|*N-Alkylated porphyrin–thiazolothiazole conjugates*

Ana Filipa Reis Cerqueira

MC6|*Acrylic Biomaterials for Targeting Bone Infections: a multidisciplinary approach*

Ana Francisca de Campos Simão Bettencourt

MC7|*A Step Forward In The Control of Monomer/Aggregates Ratio in Hybrid Systems*

Ana Luísa Silva da Costa

MC8|*Porphyrins in 1,3-dipolar cycloadditions. Novel synthetic avenues to annulated chlorins and mixed bisadducts*

Ana Margarida Gomes da Silva

MC9|*Photocatalytic Synthesis of Vanillin Through an Energy-Efficient Process*

Ana Raquel Almeida Fernandes

MC10|*New Trinuclear and Tetranuclear Copper(II) Cores Self-Assembled from Aminoalcohol Ligands*

Ana Sara Oliveira Knittel

MC11|*Metal-free cucurbit[7]uril for the catalytic alcoholysis of epoxides*

Ana Sofia Madureira Bruno

MC12|*Optical and thermal properties of a copper(I)-tin(II) mixture*

André Miguel Lopes Seco

MC13|*Sugar Surfactants Niosomes formed by Ethanol and Methanol Injection Method*

Andreia Alexandra dos Santos Alves

MC14|*Shampoos: new formulations and characterization strategies*

Andreia Alexandra Germano Nunes

MC15|*Ohmic heating approach in the synthesis of pyridyl analogues of rosamines: Synthesis and photophysical behaviour.*

Andreia Daniela Moreira da Cruz Leite

MC16|*Synthesis and characterization of magnetic and luminescent Ionic Liquids*

Andreia Sofia de Almeida Baptista Forte

MC17|*Exploring unconventional fluorinated anions for efficient CO2/N2 separation using supported ionic liquid membrane*

Andreia Sofia Ladeira dos Santos Gouveia

MC18|*Discovery of new intermetallic compounds: the U2Sb case*

António Cândido Lampreia Pereira Gonçalves

MC19|*Phosphine-Gold(I)-Alkynyl-Naphthyridine complexes as luminescent sensors for guanine derivatives*

Artur Jorge Carneiro Moro

MC20|*Difluoroboron complexes of functionalized dehydroacetic acid: Electrochemical and luminescent properties*

Baaziz Samira

MC21|*A thermochromic and a self-organization case studies in an Eu(III) family of Room Temperature Ionic Liquids*

Bernardo Ramos Batista Monteiro

MC22|*Multidisciplinary Approach For Forensic Discrimination Of Latex Gloves*

Bruna Filipa Ramos dos Santos

MC23|*Ligand characterization and functional group conversion in nanostructured silica by 1H-NMR*

Carina Isabel Correia Crucho

MC24|*Enzymatic polymerization of HMF derivatives*

Carlos Manuel Fortes Tavares Monteiro

MC25|*The Molecules of Colour in the Portuguese Postage Stamps (1857-1909)*

Catarina Monteiro Pinto

MC26|*Nonlinear emission in Carbon dots*

Cátia Filipa Oliveira Correia

MC27|*Copper Metalloporphyrins As Catalysts For Microwave-Assisted Oxidation Of Secundary Alcohols*

Daniela Alexandra Gonçalves da Fonte

MC28|*Mono and Di-alkylated Indigo Derivatives: Synthesis and Excited State Characterization*

Daniela Ribeiro Pinheiro

MC29|*Custom poly(ionic liquids) heading microextraction specificity*

David Patinha

MC30|*Bright nanoparticles for an even brighter future: efficient production of luminescent carbon nanodots from olive mill wastewater*

Diogo Alexandre Cartaxo Sousa

MC31|*Cryogenic Nanothermometer Based on the MIL-103(Tb,Eu) Metal Organic Framework*

Duarte Ananias Marques

MC32|*Bio-based polyols for more ecological adhesive formulation*

Dulce Elisabete Bornes Teixeira Pereira Simão

MC33|*Molecular Trends in Surfactant-Assisted Exfoliation and Functionalization of Carbon Nanotubes*

Eduardo Jorge Figueira Marques

MC34|*Light-Driven Hydrogen Generation Using Hybrids of Porphyrins and Graphitic Carbon Nitride*

Eliana Sousa da Silva

MC35|*Multifunctional Lamellar Coordination Polymer*

Filipe Alexandre Almeida Paz

MC36|*Simple and solvent-free synthesis of vanadium oxide composites and their catalytic application towards oxidation of benzoin*

Francesco Ferretti

MC37|*Charge transfer salts of Dissymmetrical TTF donor with Cyano Coordinating Groups*

Gonçalo André Gonçalves Brás Lopes

MC38|*Trypsin goes nano! New nano-sized magnetic trypsin for ultra-high effective protein digestion*

Gonçalo Nuno Gouveia Martins Pinto

MC39|*Strategies for Thin Films of Hybrid Mesoporous Silica Nanoparticles*

Guido Valentini

MC40|*Alcohols as Molecular Probes in the study of Ionic Liquids*

Inês Catarina Moreira Vaz

MC41|*Heptagon-containing Nanographenes as a New Alternative to Graphene Quantum Dots*

Inês de Fátima Afonso Mariz

MC42|*Eutectic Solvents: Expanding Chemical Profiles*

Isabel Maria Delgado Jana Marrucho Ferreira

MC43|*Microencapsulation of Ammodaucus leucotrichus essential oil using chitosan/ TPP/vanillin chemical system*

Isabel Patrícia Martins Fernandes

MC44|*Photocatalytic activity of N,S-doped graphene-based multi-composite for the degradation of organic molecules*

Iwona Kuzniarska-Biernacka

MC45|*Multivariate statistical analysis based on thermal and spectroscopic data for forensic discrimination of plastic bags*

Jessica Ferreira da Silva

MC46|*Photophysics of TADF emitters for bioimaging and sensing applications*

João Miguel Ribeiro Avó

MC47|*How to help find a needle in a haystack*

João Paulo Arriegas Estevão Correia Leal

MC48|*Synthesis of new acylsilanes*

João Rafael Campos do Vale

MC49|*Crystallographic, thermodynamic and spectroscopic characterization of glibenclamide:tromethamine 1:1 cocrystal synthesized by slow evaporation*

Jorge Miguel Gonçalves Sarraguça

MC50|*Direct transformation of fructose to 5,5'(oxy-bis (methylene))bis-2-furfural (OBMF) or diformylfuran (DFF) using Preyssler heteropolyacids*

José Jobanny Martínez Zambrano

MC51|*Mesoporous Silica Nanoparticles with pH-responsive Polymeric Shell for Controlled Drug Release*

José Luís Martins Gonçalves

MC52|*Aiming at cancer: Structural and spectroscopic studies of new metalloporphyrins and metallochlorins*

José Nuno Martins de Almeida

MC53|*Plasmonic office paper as an alternative cost effective platform for trace analyte detection by Surface Enhanced Raman Spectroscopy*

José Ricardo Ramos Franco Tavares

MC54|*Molecular modeling of the intercalation of functional molecules into layered double hydroxidesolecular modeling of the intercalation of functional molecules into layered double hydroxides*

José Richard Baptista Gomes

MC55|*Application of Proteins for organocatalysis*

Karolina Zalewska Patrício

MC56|*Structurally colored photonic pigments by soft lithography droplet microfluidics technology*

Laurinda Rosa Pereira Areias

MC57|*Deep Eutectic Solvents and Functional Ionic Liquids for Material Science*

Luís Alexandre Almeida Fernandes Cobra Branco

MC58|*Oxidative Catalytic Activity of Carbon Nanomaterials from Cork Industry Wastewater*

Luísa Margarida Dias Ribeiro de Sousa Martins

MC59|*Zinc-derived materials for medical applications in orthopaedic implants*

Luísa Maria Leal da Silva Marques

MC60|*Effect of the heating method on the catalytic properties of SAPO-11 materials synthesized with polyethylene glycol*

Luísa Maria Lima Ferreira

MC61|*Photoactive MOFs based in Diphenylanthracene Derivatives and obtained by Mechanochemistry for Energy Applications*

Márcia Almeida Ribeiro

MC62|*Calcium and Phosphorous Incorporation in Silica Nanoparticles for Stem Cell Differentiation in Bone Regeneration*

Márcia Tojeira Tavares

MC63|*Naproxen Incorporation in Organic Silicas as a Strategy to Achieve Guest Amorphization*

Maria da Piedade Oom de Albuquerque d'Orey

MC64|*Strategies to Stabilize High Energetic States of Pharmaceutical Drugs*

Maria Madalena Alves Campos de Sousa Dionísio Andrade

MC65|*Does co-crystallization prevent or enhance polymorphism?*

Maria Susano Pinheiro

MC66|*HPLC-DAD and Chemometric Analysis of the Molecules of Colour in Blue Pen Inks*

Mariana Cardoso de Albuquerque

MC67|*Cellulosic nanostructured materials: an inelastic neutron scattering study*

Mariela Martins Nolasco

MC68|*Novel magnetic scorpionate materials*

Marta Sofia Rosa Domingues Alexandre

MC69|*Biocompatible Heater-Thermometer Nanoplatforms for Hyperthermia*

Mengistie Leweyehu Debasu

MC70|*Preparation of ZnO nanoparticles and their application in transesterification reactions*

Mohamed Soliman

MC71|*New Access to Furanocoumarin Type Structures*

Naouel BOUFROUA

MC72|*Advanced Supported Materials for efficient Lignin Oxidation*

Neide Marisa Costa Gomes

MC73|*Valorization of biomass ash and sludge from pulp and paper industry: characterization of waste materials and new products*

Nuno Miguel Cerqueira Cruz

MC74|*Functional Systems Based on Switchable Host-Guest Complexes*

Nuno Miguel Jesuíno Basílio

MC75|*Halogen bond and luminescence in supramolecular architectures*

Patricia Alexandra Amaro Martins vaz

MC76|*Bis-calix[4]arene-carbazole conjugates for Protein Sensing and Recognition*

Patrícia Alexandra Miranda David Barata

MC77|*Stabilization of Amorphous Cimetidine by Loading in Silica Matrices*

Patrícia Alexandra Timóteo André

MC78|*Inelastic Neutron Scattering study of Reline: shedding light on the hydrogen bonding network of deep eutectic solvents*

Paulo Jorge de Almeida Ribeiro Claro

MC79|*Near-infrared spectroscopy for the assessment of mechanical properties of cork disks used for the manufacturing of sparkling wine stoppers*

Pedro Filipe Couto Madeira

MC80|*The Key Role of Solvent in Ion-Pair Halogen Bonds: Building Efficient Receptors for Halide Recognition in Solution*

Rafael Santana Nunes

MC81|*S-doped carbon nanotubes: a solvent-free methodology*

Raquel Pinto Rocha

MC82|*Revisiting the study of solvent effects: Grunwald-Winstein vs. TAKA approaches*

Ricardo João Granito Rodrigues Nunes

MC83|*Synthesis and characterization of a new copper-phthalocyanine dye*

Roberto Giacomantonio

MC84|*Studies of insertion/desinsertion of K+ and Cs+ in copper hexacianoferrate modified electrodes*

Rui Manuel Marques Antunes

MC85|*Self Assembled Bilayer Molecular Metals (Cnb-Edt-Ttf)4x; Polymorphism And Superconductivity*

Sandra Marisa Baptista Rabaça Rodrigues

MC86|*New BioMOFs based on azelaic acid: Synthesis, Characterization and Stability studies*

Sílvia Andreia Almeida Quaresma

MC87|*Molecular Tuning: Halogen influence on crystal structure and properties*

Sónia Duarte Barroso

MC88|*Hybrid nanoparticles with application in photovoltaic solar cells*

Tânia Raquel Vieira Ribeiro

MC89|*New Water Soluble PDIs for Bioimaging*

Tânia Sofia da Mota Oliveira

MC90|*A Self-Separating Catalysts Based On Molybdenium*

Tatiana Ribau Amarante

MC91|*Mesoporous and biocompatible locust bean gum aerogels for controlled drug delivery*

Teresa Margarida Lopes Martins Cordeiro

MC92|*Design of Bioinspired Copper(II) Aminoalcohol Complexes and Coordination Polymers for Mild Oxidative Functionalization of Alkanes*

Tiago Daniel Adriano Fernandes

MC93|*Synthesis of Monodisperse Hybrid Nanoparticles for Structural Colour*

Tiago Dourado Martins

MC94|*Fluorescent Organoboron Chelates and Their Use in Bioimaging*

Vânia Cristina Fernandes Pais

MC95|*Facile one-step synthesis of POM@MOF(Fe) nanocomposites by using in situ approach*

Víctor Karim Abdelkader Fernández

MC96|*Synthesis of diketopyrrolopyrrole derivatives for dye-sensitized solar cells*

Vitor Alexandre da Silva Almodôvar

MC97|*Ferrocene Modified Bakelite*

Zeljko Petrovski

Environment Challenges Poster Communications

EC1|*Environmental fate and behaviour of (2-hydroxy-4-methoxyphenyl)-(2-hydroxyphenyl)-methanone in aqueous solution*

Albano Joel Moreira Santos

EC2|*Environmental fate and behaviour of caffeine in aqueous solution*

Albertina Alice Ribeiro Mota

EC3|*Theoretical Characterization of Brown Carbon Chromophores Generated by Catechol Heterogeneous Oxidation*

Ana Catarina Oliveira Magalhães

EC4|*Direct conversion of carbohydrates into 5-ethoxymethylfurfural (EMF) and 5-hydroxymethylfurfural (HMF) catalyzed by oxo-molybdenum complexes*

Ana Cristina da Silva Fernandes

EC5|*New insights about Citrus genus revealed by infrared spectroscopy*

Andreia Sofia Domingues Brás Lima

EC6|*Enhancing alkane oxidation using Co-doped SnO2 nanoparticles as catalysts*

Bruno Gonçalo Martins Rocha

EC7|*Fruit peels as low cost sorbents to remove priority pollutants from water*

Bruno Manuel Galinho Henriques

EC8|*Mecanochemistry for the of sustainable synthesis of porphyrins*

Carla Sofia Loureiro Gomes

EC9|*Long Range Theoretical Study On LiH2*

Carolina Maria Apolinario do Rio

EC10|*Camellia japonica cultivars discrimination through FTIR-ATR*

Catarina de Brito Augusto

EC11|*New Green Solvents for Water Purification*

Catarina Isabel Santos Florindo

EC12|*Iridium(I) Catalyzed C(sp2)-H activation and intramolecular addition to alkenes and alkynes*

Catarina Rodrigues

EC13|*The denitrification pathway of Marinobacter hydrocarbonoclasticus*

Cíntia Catarina Souda Carreira

EC14|*Environmental fate and behaviour of paracetamol in aqueous solution*

Cláudia Sofia Gomes Cardoso

EC15|*Assessment of pharmaceuticals in the Lis River (Leiria, Portugal)*

Cristina Maria Fernandes Delerue Alvim Matos

EC16|*Ferromagnetic particles for the removal of arsenic from water*

Daniela Soraia dos Santos Tavares

EC17|*Enantioselective Palladium-Catalyzed [3+2] and [4+3] Cycloaddition Reactions*

Felipe Ignacio Verdugo Leal

EC18|*Magnetic deep eutectic solvents in refinery desulfurization: comparison between liquid-liquid extraction and ultrasound assisted liquid-liquid microextraction*

Filipa Daniela Fernandes Lima

EC19|*Effect of the activated carbons characteristics on phenolic compounds removal from aqueous media*

Isabel Pestana da Paixão Cansado

EC20|*Synergistic gold and enamine catalysis: α-alkylation of aldehydes with allenamides*

Jaime Fernández Casado

EC21|*Metabolic Flexibility Towards Nutrient Availability Allows Desulfovibrio desulfuricans ATCC 27774 Adaptation to Ecological Niches*

Joana Rita Lourenço Sousa

EC22|*Studying the pressure dependance of the termolecular Areaction H + O2 + M→ HO2 + M*

João Carlos Pereira Peres Brandão

EC23|*Bifunctional Cr3+ modified ion exchange resins as efficient reusable catalysts for the production and isolation of 5-hydroxymethylfurfural from glucose*

João Manuel Janeiro Martins Ravasco

EC24|*Methanation of CO2 over bimetallic Ni - 5f block element oxides*

Joaquim Miguel Badalo Branco

EC25|*Adsorption of lipophilic pollutants from biphasic systems by using modified activated carbon materials*

Jose Luis Díaz de Tuesta

EC26|*Gas-Phase Studies of the Relative Affinities of N- and O-Donor Bases toward Ln(III) Ions*

José Manuel da Cunha Oliveira Figueira Carretas

EC27|*Manganese N-Heterocyclic Carbene Complexes in the Reduction of CO2*

Mara Sofia da Fonseca Pinto

EC28|*Simultaneous determination of Pt and Rh at ultra-trace levels: a step towards the current understanding of Pt and Rh cycles and fate in the environment*

Margarida Maria Portela Correia dos Santos

EC29|*Synthesis and anion binding properties of hexahomotrioxacalix[3]arene trinaphthylurea derivative*

Micael Alexandre Santos Miranda

EC30|*Solution enthalpies of 3-methylimidazolium tetrafluoroborates: a QSPR study*

Nelson Guerreiro Cortez Nunes

EC31|*Cationic porphyrin-terpyridine derivatives: Synthesis, characterization and biological evaluation*

Nuno Miguel Malavado Moura

EC32|*Banana peel as a low cost sorbent for cleaning contaminated waters*

Paula Alexandra Macedo Figueira

EC33|*Anion binding by partial cone dihomooxacalix[4]arene-based receptors bearing urea groups at the lower rim*

Paula Maria Jorge Marcos

EC34|*Oxidative β-Functionalization of Secondary Amines with Furan Derivatives: from Biomass to Potentially Active Highly Unsaturated Imines*

Rafael Filipe Teixeira Arbuez Gomes

EC35|*Lupanine removal from lupin beans detoxification wastewater*

Raquel Alexandra Morais Teixeira

EC36|*Microwave-assisted Transfer Hydrogenation using Fe-NHC Based Catalysts in Glycerol*

Rita Isabel Lourenço da Silva Lopes

EC37|*Identification of the transformation products of citalopram, an emerging compound in the environment, by mass spectrometry*

Rodrigo Arimura Osawa

EC38|*Application of a new sensing material for the construction of surfactant potentiometric sensor*

Sanja Petrusic

EC39|*Smart Polymeric Nanoparticles for Boron Scavenging*

Sérgio Paulo do Carmo Alves

EC40|*Manganese N-Heterocyclic Carbenes in Catalytic Reduction Reactions*

Sofia Manuela Pinto Friães

EC41|*Evaluation of the effect of organic matter on the dissolution of Cu from CuO nanoparticles in soils*

Sónia Pereira Lopes

EC42|*Validation of Heavy Metals Determination in Marine Sediments: A comparison of uncertainty evaluation approaches*

Vanessa Moreira Morgado

EC43|*Engineered MAO-N for the enantioselective synthesis of bioactive tetrahydroisoquinolines*

Vasco Figueiredo Batista

EC44|*Rate Constants from elementary reactions may fail for combustion kinetic models*

Wenli Wang

Industrial Challenges Poster Communications

IC45|*Blackberry anthocyanins: Impact of B-cyclodextrin on their stabilization*

Ana Luísa Mosqueira Alves Pires Fernandes

IC46|*Pathway to the synthesis of 1,3-diamines a high value added compound*

Daniela Peixoto

IC47|*Increase of the bioactive compounds in pineapple by-products through postharvest abiotic stresses*

Diana Isa de Oliveira Santos

IC48|*Solvent-free Suzuki–Miyaura reaction by mechanical milling catalyzed by metalla-aminocarbene palladium(II) complexes*

Elisabete Clara Bastos do Amaral Alegria

IC49|*Formaldehyde-Scavenging Nanoparticles for High Performance Resins*

Inês Vareta de Matos Ponce Dentinho

IC50|*An efficient approach for chemical process development using kinetic modeling in batch and continuous mode*

Marianna Katz

IC51|*Influence of ionic liquids on phase diagrams behavior and protein partitioning within the PEG 3350-(NH4)2SO4 aqueous two-phase system*

Mateusz Kamil Marchel

IC52|*In-silico Approach for Process Safety and Scale-Up*

Nuno Alexandre Lousa Pereira

IC53|*Organocatalysis by suported cyclic aminoguanidinines*

Rafael Mestre Mamede

IC54|*Managing protein haze formation in white wines.*

Ricardo Alexandre Ventura das Chagas

IC55|*Ultrasonic metal welding – splice replacer connector*

Sandra Cristina Costa de Matos

Teaching Challenges Poster Communications

TC56|*About the new SI framework and the mole*

Olivier Alain Gérard Pellegrino

TC57|*Detection and Separation of Pigments in Flower Petals: a new and sustainable chromatographic approach*

Paula Alexandra Amaro da Costa

TC58|*Chemistry e-lab online courses in Portugal*

Sérgio Carreira Leal

TC59|*Facing the hard problem of convincing the public and students to appreciate the real importance of chemistry in our world: a personal view*

Sérgio Paulo Jorge Rodrigues

PLENARY LECTURES

Plenary Lecture

Sugars & proteins: towards a synthetic biology

Davis B. G.

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Our work studies the interplay of biomolecules – proteins, sugars and their modifications. Synthetic Biology's development at the start of this century may be compared with Synthetic Organic Chemistry's expansion at the start of the last; after decades of isolation, identification, analysis and functional confirmation the future logical and free-ranging redesign of biomacromolecules offers tantalizing opportunities. This lecture will cover emerging areas in our group in chemical manipulation of biomoleclules with an emphasis on new bond-forming and breaking processes compatible with biology:
(i) New methods: Despite 90-years-worth of non-specific, chemical modification of proteins, precise methods in protein chemistry remain rare. The development of efficient, complete, chemo and regio-selective methods, applied in benign aqueous systems to redesign and reprogramme the structure and function of biomolecule both in vitro and in vivo will be presented.
(ii)'Synthetic Biologics' and their applications: biomimicry; functional recapitulation; effector [drug/agrochemical/gene/radio-dose] delivery; selective protein degradation; inhibitors of pathogen interactions; non-invasive presymptopmatic disease diagnosis; probes and modulators of in vivo function.

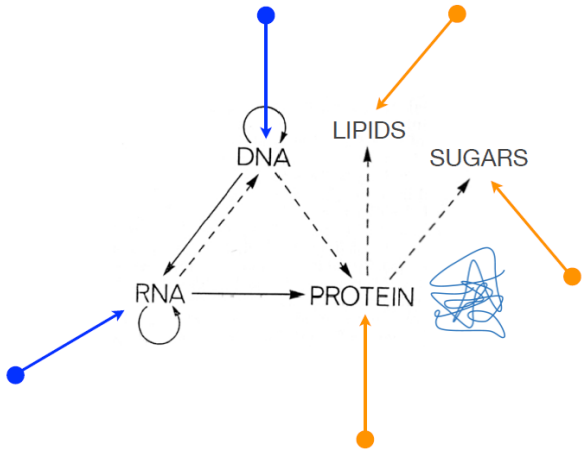

Figure 1: Central Dogma of Molecular Biology[1,2]

Acknowledgements: We thank the RF-2010-2318330, the FP7 Projects BLUEPRINT/282510 and A-PARADDISE/602080for financial supports.

References:

1. Crick F.H.C., *Nature*, **1970**, *227*, 561.
2. Crick F.H.C., *Symp. Soc. Exp. Biol.*, **1958**, *12*, 138.

Plenary Lecture

Chemical modification of proteins and antibodies

Caddick S.

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Synthetic chemistry offers unparalleled opportunities to effect selective modification of biomolecules for biomedical research and applications in medicine. In recent times the emergence of new methods for precise incorporation of natural and non-natural entities provides exciting opportunities to dissect complex biological pathways and to create new classes of therapeutics and diagnostics. This talk will focus on the development of new synthetic methods for bioconjugation - particularly for the development of antibody-drug conjugates.

Sirtuins: To Activate or Not To Activate, That is the Question

Mai A.

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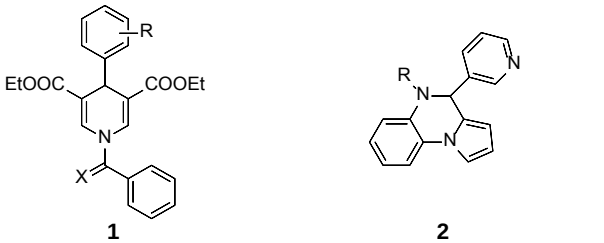
Small molecule inhibitors or activators of sirtuins, the NAD^+-dependent lysine deacetylases (deacylases), are considered promising therapeutic tools for the treatment of cancer, cardiovascular, metabolic, inflammatory, and neurodegenerative diseases. A number of 1,4-dihydropyridines (DHPs) **1** (**Figure 1**) were described by us as SIRT1 activators able to increase nitric oxide levels in human keratynocyte HaCat cells, and to ameliorate skin repair in a mouse model of wound healing. In murine C2C12 myoblasts, two of them improved mitochondrial density and functions. All the effects were reverted by co-administration of compound C, an AMPK inhibitor, or of EX-527, a SIRT1 inhibitor, highlighting the involvement of the SIRT1/AMPK pathway in the action of DHPs. Tested in a panel of human cancer cells, one of our DHPs displayed antiproliferative effects in the range of 8−35 μM and increased H4K16 deacetylation, suggesting a possible role for SIRT1 activators in cancer therapy.[1] By properly decoration of the C4 phenyl ring and/or the N1 substituent of the DHP scaffold, we were able to obtain selective activation by DHPs for SIRT3 or SIRT5, with minimal action on SIRT1. In addition, we identified, synthesized and screened some pyrrolo[1,2-*a*]quinoxalines **2** (**Figure 1**), yielding the first synthetic SIRT6 activators. Biochemical assays show direct, substrate-independent compound binding to the SIRT6 catalytic core and potent activation of SIRT6-dependent deacetylation of peptide substrates and complete nucleosomes. Crystal structures of SIRT6/activator complexes reveal that the compounds bind to a SIRT6-specific acyl channel pocket and identify key interactions. Our results establish potent SIRT6 activation with small molecules and provide a structural basis for further development of SIRT6 activators as tools and therapeutics.[2]



1 general formula of SIRT1 activators

2 general formula of SIRT6 activators

Figure 1: Chemical structures of SIRT activators.

Acknowledgements: We thank the RF-2010-2318330, the FP7 Projects BLUEPRINT/282510 and A-PARADDISE/602080for financial supports.

References:

1. Valente S.; Mellini P.; Spallotta F.; Carafa V.; Nebbioso A.; Polletta L.; Carnevale I.; Saladini S.; Trisciuoglio D.; Gabellini C.; Tardugno M.; Zwergel C.; Cencioni C.; Atlante S.; Moniot S.; Steegborn C.; Budriesi R.; Tafani M.; Del Bufalo D.; Altucci L.; Gaetano C.; Mai A. *J. Med. Chem.* **2016**, *59*, 1471.

2. You W.; Rotili D.; Li TM.; Kambach C.; Meleshin M.; Schutkowski M.; Chua K.F.; Mai A.; Steegborn C. *Angew. Chem. Int. Ed.* **2017**, *56*, 1007.

Plenary Lecture

Lead discovery for infectious diseases of the developing world: chemistry to unravel a black box

Moreira R.

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Parasitic and bacterial infections in the developing world remain a significant medical challenge, and have been largely ignored by the pharmaceutical industry due to the limited economic resources in the most affected countries. Despite widespread prevalence of these diseases, including malaria, leishmaniosis and tuberculosis, the number of new and innovative drugs that have been delivered over the past several decades is still very limited. The emergence of clinical resistance to currently available antiparasitic drugs highlight the need for new therapies acting on underexploited parasite targets in order to delay or overcome the selection of clinical resistance.
Chemistry plays a crucial role in advancing breakthrough discoveries in basic research into new therapies to treat and eliminate parasitic diseases. In this presentation we will discuss medicinal chemistry strategies that have been pursuit to improve selectivity, reduce toxicity and minimize the risk for drug resistance, particularly for malaria. We will address the requirements to develop preclinical candidates and how success is dependent on a strong collaborative platform that brings together expertise in chemistry and biology.

Acknowledgements: We atefully acknowledge the Fundação para a Ciência e Tecnologia (Portugal) for financial support through funding of the research unit iMed.ULisboa (PEst-OE/SAU/UI4013/2014).

Plenary Lecture

Biologically Relevant Small Molecules for Perturbation of Protein Function: Chemotype – Phenotype - Target

Waldmann H.

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The discovery of new bioactive compounds and ultimately drugs is a marathon exercise which combines a multitude of different disciplines including computer science, organic synthesis, cell biology, molecular biology, biophysics and biochemistry. Its success is decisively influenced by the initial choice of the compounds to be synthesized and analyzed in biological formats. In this respect bioactive secondary metabolites ("natural products") have performed exceedingly well. They have been selected in evolution and encode the ability of small molecules to interact with target biomacromolecules.
The lecture will demonstrate that natural products and compound collections based on their core structures – natural product inspired libraries – are rich sources of innovation for both chemical biology and medicinal chemistry research. It will describe the design principles for such libraries, which are rooted in biological evolution, the development of highly stereoselective methods for the efficient synthesis of natural product inspired libraries, their application in cell-based phenotypic assays and the identification of the cellular target proteins of the identified active hits.

Plenary Lecture

Functional Supramolecular Chemistry

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The objective of this lecture will be to entertain you with synthetic supramolecular systems (th)at work. Particular emphasis will be on conceptual innovation and the integration of unorthodox interactions[1] to address important challenges in chemistry, biology and the materials sciences.

The first topic covered will presumably elaborate on catalysis with anion-π interactions[1] and chalcogen bonds[2] as recent examples for the integration of "exotic" interactions into functional systems. Anion-π catalysis, that is the stabilization of anionic reactive intermediates and transition states on π-acidic aromatic surfaces, is very recent and totally new. Realized so far, mostly on the π surface of naphthalenediimides, are asymmetric enolate,[3] enamine, iminium[4] and transamination chemistry, the first anion-π enzyme,[3] and remote control of anion-π catalysis by electric fields. The more delocalized nature of anion-π interactions suggests that the stabilization of long-distance charge displacements in domino reactions that stereoselectively produce one or more carbocycles on π-acidic aromatic surfaces will be particularly rewarding.[4] Complementary to this delocalized nature of anion-π interactions are the advantages of chalcogen bonds in non-covalent catalysis. Substrate activation in the focal point of two σ holes on electron-deficient sulfur or selenium atoms promises access to a directionality that exceeds activation with hydrogen bonds by far. To elaborate on these expectations, dithienothiophenes will be introduced as a privileged motif not only for anion transport but also for catalysis with chalcogen bonds.[2]

A twisted dimer of same dithienothiophenes is at the heart of another topic of current interest with functional supramolecular systems. Fluorescence imaging of forces in biological systems in general is one of those challenges in the life sciences that call for conceptually innovative solutions from organic chemistry. Our approach focuses on mechanosensitive "flipper" probes that change color like lobsters during cooking, that is by a combination of polarization and planarization of the mechanophore in the ground state.[5] They are of interest to, for example, image membrane tension in living cells, so far impossible but considered as most important in biology (unpublished).

A third topic of current interest with conceptually innovative functional systems concerns another most persistent challenge in biology. To find new ways to enter into cells, we have originally focused on counterion-mediated uptake with cell-penetrating peptides, with much emphasis on contributions from repulsion-driven ion pairing and ionpair-π interactions.[6] Currently, attention is gradually shifting toward dynamic covalent disulfide exchange chemistry on cell surfaces, first with hybrid mechanisms in cell-penetrating poly(disulfide)s,then with strain-promoted thiol-mediated uptake with asparagusic acid,[7] and, most recently, epidithiodiketopiperazines (ETPs).[8] With a CSSC dihedral angle near zero, dislfide ring tension in ETPs is at the maximum: The currently emerging ETP-mediated uptake is correspondingly powerful.[8]

Acknowledgements: This research has been financially supported by the University of Geneva, the ERC, the National Centre of Competence in Research (NCCR) Chemical Biology, the NCCR Molecular Systems Engineering and the Swiss NSF.

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Plenary Lecture

Nano-multilayered polymeric systems in the development of new biomedical devices

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Nanostructured multilayered films have been often fabricated using the layer-by-layer (LbL) technology, where consecutive layers of macromolecules are well stabilized typically through electrostatic interactions. Using adequate templates, non-flat coatings can be fabricated with tuned compositions along the build-up assembly. This enables the production of very well controlled multifunctional and structural devices using mild processing conditions that could be useful in biomedicine, including in tissue engineering or in drug delivery. Examples of structures having nano-stratified multilayered organizations as building-blocks are presented, based on the use of natural or biomimetic macromolecules. Functional and bio-instructive multilayers may be produced by introducing special chemical groups or bioactive agents in the assembly, including selective cell attachment, response to external stimuli or adhesiveness. LbL also permits to develop 3-dimensional systems for cell colonisation (e.g. membranes, capsules or porous scaffolds) with tuned structural and geometrical control (including shape-memory ability). Taking the large combination of systems that can be produced using LbL, high-throughput methodologies were implemented to accelerate the tests of individual multilayers.

Plenary Lecture

Semi-artificial Photosynthesis

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In natural photosynthesis, light is used for the production of chemical energy carriers to fuel biological activity and the first protein in the photosynthetic chain is the water oxidation enzyme Photosystem II. This presentation will summarise our progress in the development of protein film photoelectrochemistry as a technique for the light-dependent activity of this enzyme adsorbed onto an electrode surface to be studied.[1] Materials design enabled us to develop 'tailor-made' 3D electrode scaffolds for optimised integration of the 'wired' enzyme and these investigations yielded valuable insights into the performance of Photosystem II and interfacial charge transfer pathways. Examples are the identification of unnatural electron escape routes to the electrode and a recently elucidated O_2 reduction pathway that short-circuits the known water-oxidation process.[2]

The integration of Photosystem II in a photoelectrochemical circuit has also enabled the *in vitro* re-engineering of natural photosynthetic pathways. We succeeded in assembling an efficient enzyme-based full water splitting cell driven by light through the rational wiring of Photosystem II to a [NiFeSe]-hydrogenase (**Figure 1**).[3] This hydrogenase displays unique properties for water splitting applications as it displays good H_2 evolution activity, little product (H_2) inhibition and some tolerance towards O_2.[4] The semi-artificial water splitting cell shows how we can harvest and utilise electrons generated during water oxidation at Photosystem II electrodes for the generation of renewable H_2 with a wired hydrogenase through a direct pathway unavailable to biology.

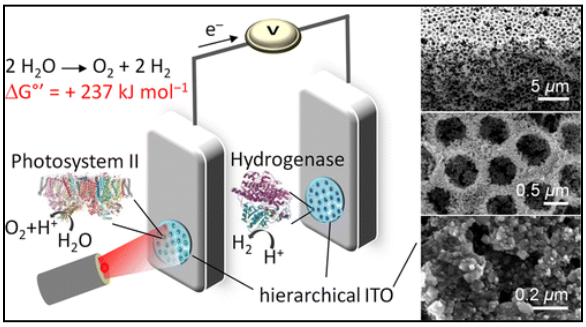

Figure 1: Schematic representation of a semi-artificial water splitting system consisting of immobilised enzyme integrated in a photoelectrochemical cell. Water is photo-oxidized and O_2generated at a Photosystem II-containing photoanode (left), and aqueous protons are reduced at a hydrogenase-based cathode (right). Optimal enzyme-integration was enabled by a hierarchical indium tin oxide architecture (see SEM images on the right).

Acknowledgements: This work is supported by an ERC Consolidator Grant 'MatEnSAP' (682833).

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Plenary Lecture

‘On the Road again, Goin' places that I've never been’: a personal account of a journey in Materials Chemistry

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In my personal scientific quest, I have always travelled with crystallography and nuclear magnetic resonance in the sidecar, faithful friends continuously guiding me on the road. No wonder, one of my visions is to blend together, effectively, NMR, diffraction and modelling into a formidable structural tool.
I have started out on very thin crystals of mineral kaolinite that stacked together forming beautiful ‘libraries’. Later, I became interested in zeolite-type materials, transition metal silicates and phosphates, looking into minerals in nature for inspiration, and seeking applications in catalysis, ion-exchange, and gas sorption and separation (I also confess a fleeting love affair with mesoporous materials). Serendipitously and against all odds, one of these siliceous materials eventually found a real commercial application as a drug. With the turn of the century, I have switched from transition metals to lanthanides to generate ‘light at the end of the tunnel’. Most of the crystallography work up to this point was centred on powder X-ray diffraction. Soon later, the fascinating chemistry and promise for crystal engineering of metal organic frameworks (MOFs) led me to ship-in-the-bottle-chemistry and to the world of single-crystal X-ray diffraction. And in the last decade my interests began switching again, now towards the tinny nanotubes and nanoparticles of oxides and gold. With MOFs and nanoparticles in hand I was able to develop unprecedented nanothermometers and nanoheaters and to revisit the fundamentals of the Brownian motions.

Plenary Lecture

Design and Applications of Sustainable Catalytic Reactions for Synthesis and Energy

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The design of ”green” synthetic methodology and new approaches to sustainable energy are major goals of modern catalysis. Traditionally, catalysis by metal complexes has been based on the reactivity of the metal center, while the ligands bound to it influence its reactivity, but do not interact directly with the substrate. In recent years, complexes based on “cooperating” ligands were developed, in which both the metal and a ligand undergo bond making and breaking in key steps of catalytic cycles, thus providing exciting opportunities for catalytic design.
We have developed a new mode of metal-ligand cooperation, involving ligand aromatization – dearomatization, which provides a new approach to the activation of chemical bonds. Pincer-type complexes of several transition metals exhibit such cooperation, including complexes of Ru, Fe, Co, Rh, Ir, Ni, Pd, Pt, Mn and Re, leading to facile and selective activation of various chemical bonds. This has led to fundamentally new, sustainable catalytic reactions, including several reactions which either produce H_2 or consume it. Synthetic and energy-related applications based on these reactions will be described.

Acknowledgements: We thank the European Research Council, the Israel Science Foundation, and the Minerva Foundation for financial support.

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Plenary Lecture

Inert Alkanes as Potential Feedstocks for Synthesis?

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Alkanes (i.e., saturated hydrocarbons) are abundant and carbon-rich species which are extensively applied as non-renewable fossil fuels, with loss of carbon to the atmosphere and accumulation of carbon dioxide with resulting environmental and economic concerns.
The development of sustainable and selective catalytic processes for alkane functionalization to afford organic compounds with an added value should promote the eventual reorientation of their application towards alternative raw materials for synthesis. Nevertheless, on account of the inert character of alkanes, this possibility remains a challenge to modern chemistry.
Developments obtained in this field by the author´s research group will be discussed, namely concerning the following types of reactions catalyzed by metal complexes:
- Oxidations of alkanes with peroxides to alcohols and ketones, namely in (partially) aqueous media;
- Hydrocarboxylations of alkanes to carboxylic acids in partially aqueous media;
- Alkane carboxylations to carboxylic acids in non-aqueous media.
The use of either transition metal or non-transition metal catalysts with various types of ligands will be addressed, as well as of both homogeneous and supported catalysts.
Some of the systems feature the highest catalytic activities so far reported for alkane functionalizations under mild conditions. Mechanistic proposals and prospects will be evaluated.

Acknowledgements: This work has been partially supported by the Fundação para a Ciência e Tecnologia, namely through the projects PTDC/QEQ-QIN/3967/2014 and UID/QUI/00100/2013. The co-authors cited in the references are gratefully acknowledged.

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Plenary Lecture

Catalysis with Earth Abundant Transition Metals

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Transition metal catalysis has revolutionized modern society by enabling new chemical transformations with unprecedented activity and control over selectivity. Applications range from new silicone materials to transforming hydrocarbons into fuels to building blocks for pharmaceuticals. Our laboratory has been actively engaged in developing catalysts based on earth abundant elements rather than more traditionally deployed precious metals that are some of the least available elements in the Earth's crust. Use of these elements extends beyond potential cost advantages; reduced carbon dioxide production and stability of supply chains are also potential benefits. Ultimately we aim to discover new reactivity that exploits the unique electronic structures off first row transition metals.

My lecture will combine applications developed in combination with industrial collaborators and focus on the multifaceted challenges of transitioning from the academic laboratory to processes used on scale. Earth abundant catalysts for commercial silicone production,1 asymmetric alkene hydrogenation,2 C-H functionalization3 and radiolabeling of pharmaceuticals4 have been developed. More recently we have been focused on the discovery of new catalytic reactions for the valorization of simple alkenes – those that are now overabundant due to the development of vast natural gas reserves. An iron-catalyzed method for the diastereo- and regioselective intermolecular [2+2] cycloaddition of commodity alkenes has been discovered (Figure 1).5 Through continued ligand evolution and understanding of electronic structure, we have discovered base metal catalysts that promote chemistry unknown with established precious metal variants. The mechanisms of the various catalytic transformations, the importance of electronic structure controlled through ligand manipulation and strategies for imparting air stability will be a highlighted throughout.

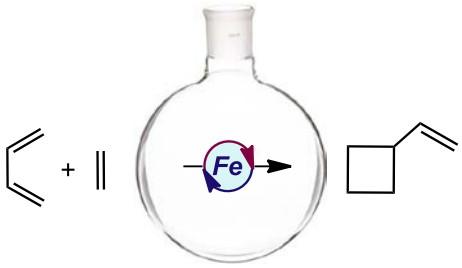

Figure 1: Unique [2+2] cycloadditions of ethylene and butadiene promoted by iron catalysts.

Acknowledgements: We thank the US National Institutes of Health (R01 GM121441) for financial support.

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Plenary Lecture

Gold-Catalysis for the Synthesis of Biologically Active Natural Products

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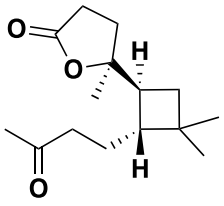
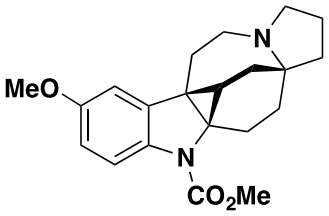
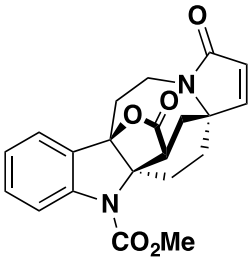
Our group has developed new cyclizations and cascade reactions based on the selective activation of alkynes with cationic gold(I) complexes[1] for the construction of complex polycyclic molecules such as englerin A,[2] schisanwilsonene,[3] and other sesquiterpenoids.[4]
In this lecture, our most recent efforts towards the development of stereoselective cyclizations and cycloadditions for the synthesis of sesquiterpenes such as rumphellaone A[5] and other natural products will be presented.



Rumphellaone A



(–)-Lundurine C



(+)-Grandilodine C

Other work on the development of broad scope cylopropanations of alkenes via gold-catalyzed retro-Buchner reaction as well as on the total synthesis of cyclopropane-containing products of the lundurine family[6] and other related alkaloids such as the grandolodines and the lapidilectines will also be presented.

Acknowledgements: I thank the European Research Council (Advanced Grant No. 321066), MINECO/FEDER, UE (CTQ2016-75960-P), MINECO-Severo Ochoa Excellence Acreditation 2014-2018, SEV-2013-0319), the AGAUR (2014 SGR 818), and CERCA Program / Generalitat de Catalunya for financial support.

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AWARD LECTURES

AL1

Ferreira da Silva Award

The Joy of Science: Personal Account

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Medalha Vicente de Seabra

A catalysis journey: breaking bonds for clean water

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Priority substances (PSs) and contaminants of emerging concern (CECs) have been found in the aquatic environment, often up to μg L^{-1} levels. Directive 2013/39/EU and Decision 2015/495 were launched to update the water framework policy in Europe, emphasizing the need to develop new water treatment technologies to deal with such problem.[1,2] This communication aims to present an overview of the author's experience in the synthesis, characterization and application of active and stable catalysts, including catalytic membranes, for different water treatment technologies.[3,4] Special emphasis will be placed on the use of carbon materials (activated carbons, carbon nanotubes, graphene derivatives, among others) and their respective functionalization.[5,6] Carbon materials with no added metals can be used as active catalysts in some of these processes, or combined with a semiconductor material in the particular case of photocatalysis.[7,8] Hybrid systems are also alternatives, and some of them have not yet been applied in full-scale plants.[4]

Acknowledgements: AMTS acknowledges the FCT Investigator Programme (IF/01501/2013), with financing from the European Social Fund and the Human Potential Operational Programme. Support for this work was also provided by Project POCI-01-0145-FEDER-006984 – Associate Laboratory LSRE-LCM funded by FEDER funds through COMPETE2020 - Programa Operacional Competitividade e Internacionalização (POCI) – and by national funds through FCT - Fundação para a Ciência e a Tecnologia.

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KEY NOTES

Old Sources for New Drugs: Challenges and Opportunities

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The decline or leveling of the output of the R&D programs of the pharmaceutical companies may have begun to turn around when compared to earlier years of the 21st century. Although a responsible for this increase is the immunopharmacology-based treatments, small molecules still play an important role.[1] Medicinal chemistry approach is to find a small molecule lead compound, which shows the desired pharmacological activity, continue to use as sources natural products, synthesis, and existing drugs.

In this communication, we will give examples of antitumor small molecules lead compounds obtained in our research group that arise from both natural and synthetic models. Since other aim in medicinal chemistry is the study of drug metabolites, very recently we engaged a project that intend to understand the influence of metabolites in the cardiotoxicity of an antitumor drug, mitoxantrone (MTX, **Figure 1**). Although the main human MTX metabolites have been identified, their putative cardiotoxicity was not yet assessed.

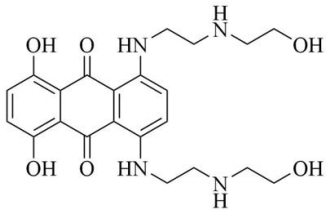

Figure 1: Mitoxantrone (MTX), approved in 1987 as antitumor drug and in 2002 for use in multiple sclerosis.

Herein, we detail the challenges and opportunities in studying drug metabolites as potential sources of new drugs. Initially, the MTX-naphthoquinoxaline metabolite (NAPHT) was synthetized and studies on NAPHT cardiotoxicity revealed that the parent drug, MTX, caused a higher disruption in the energetic pathways in a cardiac model *in vitro*, whereas autophagy is involved in the toxicity of both compounds;[2] therefore, this metabolite should be regarded as a good option for a safer anticancer therapy since it is less cardiotoxic than MTX. Moreover, previous data has shown that NAPHT can have a potential role on MTX anticancer effects.

The case studies presented herein are expected to contribute to a multidisciplinary vision in drug discovery, with the involvement of several sources. To us, small molecules will continue to provide a fruitful solution in drug discovery and development.

Acknowledgements: We thank FCT/MCTES and ERDF through the COMPETE–POFC programme, under the Strategic Funding UID/Multi/04423/2013, the project PTDC/MAR-BIO/4694/2014 (POCI-01-0145-FEDER-016790; 3599-PPCDT) and PTDC/DTP-FTO/1489/2014 (POCI-01-0145-FEDER-016790) in the framework of PT2020,to INNOVMAR (NORTE-01-0145-FEDER-000035, NOVELMAR), supported by NORTE 2020, under PORTUGAL 2020, through ERDF.

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Novel Ring-Fused Chlorins for Cancer Theranostics

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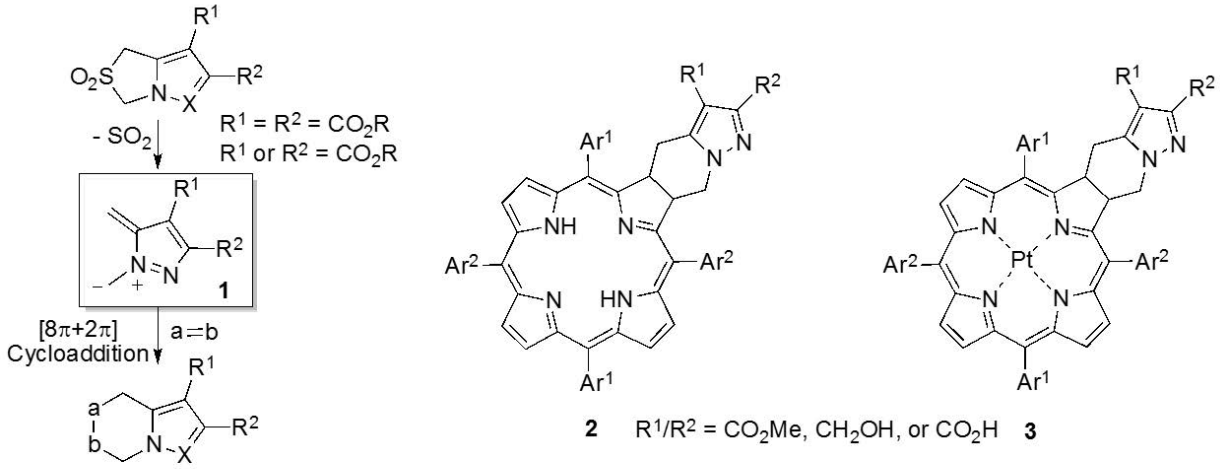
The research team has previously reported the synthesis of a new type of stable 4,5,6,7-tetrahydropyrazolo[1,5-a]pyridine-fused chlorins **2** via an unprecedented [8π+2π] cycloaddition of diazafulveniummethides **1** with porphyrins (**Scheme 1**).[1,2] Preliminary studies on these porphyrin-type macrocycles showed that they are very active photodynamic agents against melanoma cells.[3] Platinum(II) derivatives of 4,5,6,7-tetrahydropyrazolo[1,5-a]pyridine-fused chlorins **3** were also prepared with the aim of developing near-infrared luminescence probes as well as new photosensitizers for PDT.[4] The photocytotoxicity observed against melanoma cells (A375) together with attractive photophysical features, including oxygen-dependent room temperature phosphorescence and potential in ratiometric emission measurements, make them excellent compounds to be used as probes for molecular oxygen, biological imaging and photodynamic therapy. Furthermore, *in vivo* studies demonstrated that they have good selectivity for tumour tissue and adequate biodistribution. In this lecture, further developments of this study will be presented and discussed.



Scheme 1: 4,5,6,7-Tetrahydropyrazolo[1,5-*a*]pyridine-fused chlorins via [8π+2π] cycloaddition.

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NMR and intermolecular interactions: solving health, materials and environmental challenges

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It is perhaps in the study of intermolecular interactions that NMR spectroscopy reveals its full potentiality and great versatility as a technique of structural investigation. In fact, when applied to dynamic processes, NMR allows to characterize, with atomic resolution, phenomena of molecular interaction on a wide variety of time scales both in chemical and biological systems. Here we will present how we have been using NMR to study molecular interactions in ionic liquids in very different contexts, like protein solvation in ionic liquids or CO_2 capture.

In recent years ionic liquids (ILs) have attracted much attention in a wide range of chemical and biochemical applications. ILs physical and chemical properties can be enhanced and modified by both their cationic and anionic moieties and this is the reason for their broad range of applications. But since it is impossible to experimentally investigate even a small fraction of the potential cation-anion combinations, a molecular-based understanding of their properties is crucial.

One potential field of application of ILs is in climate change mitigation efforts, as alternative materials for CO_2 capture. Application of our NMR based methodology allowed us to study the mechanism of CO_2 solvation in ILs and optimize their structure for CO_2 capture (figure 1A).[1,2] Another promising field of application of ILs is as protein structure modulators. We look to understand the molecular mechanisms of ion specific effects on proteins towards protein stabilization and/or destabilization using different protein systems and ILs (figure 1B). [2,3]

Inspired in the high concentrations of organic charged metabolites found in cell milieu and in our previous studies with imidazolium-based ILs we have started to address the importance of ion-pairs and its consequences on protein stability in conditions under artificial crowding conditions mimicking the cell milieu.

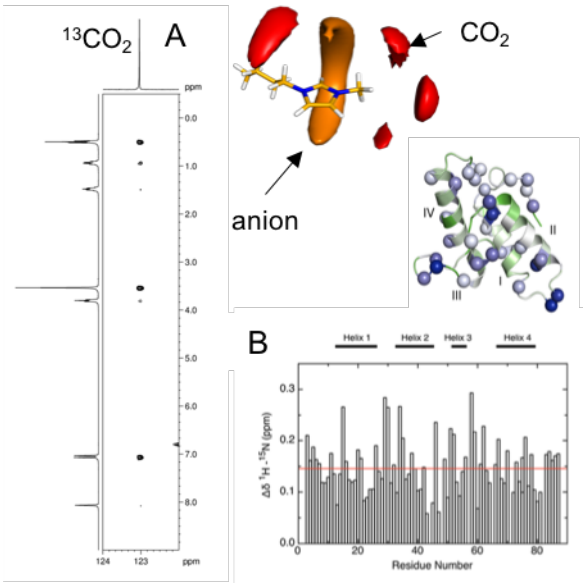

Figure 1: A – Preferential sites for CO_2 localisation in $[C_4MIM]NTf_2$ IL from ^{13}C-HOESY experiments and MD calculation. B – Preferential interaction sites of $[C_4MIM]Cl$ mapped onto Im7 structure from ^{15}N HSQC titrations

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Key Note

Modeling Halogen Bonds: Relevance in (Bio)Chemical Systems

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Halogen bonds (XB) are highly directional, attractive R–X···B (X = Cl, Br or I) interactions involving a halogen atom (X) and a Lewis base (B). They are predominantly explained by the existence of a positive region on the electrostatic potential of X named σ-hole, leading to the main features of halogen atom interactions: side-on with electrophiles, and head-on corresponding to halogen bonds with nucleophiles (**Figure 1**,left). It was soon evident that XBs are present in biological molecules[1] inspiring several (bio)chemical applications ranging from chloride receptors[2] to anion transport across membranes.[3]

In this communication, examples and challenges in computational modeling of XBs will be presented. It will be shown how Quantum Mechanical (QM) calculations can be used to predict and optimize the anion binding affinity in charge-assisted halogen bond-based receptors (**Figure 1**, center) and how the solvent is able to modulate the strength and nature of the interaction[2]. Additionally, the dynamical behavior of different force field implementations that try to emulate the σ-hole will be reported. Typically, the σ-hole is modeled as an extra point (EP) of charge bonded to the halogen atom. The choice of the charges and X-EP distances are crucial. MD simulations on a prototype system consisting of small halogenated molecules (C_6F_5I and C_6H_5I) inside the non-polar cavity of a bacteriophage T4 lysozyme (**Figure 1**, right) will be discussed[4]. The choice of the charges and X-EP distance has also impact on the calculated solvation energies, therefore affecting common approaches for calculating ligand binding affinities based on MD simulations. This illustrates the importance of the correct modeling of these interactions in protein-ligand binding and their relevance in medicinal applications.

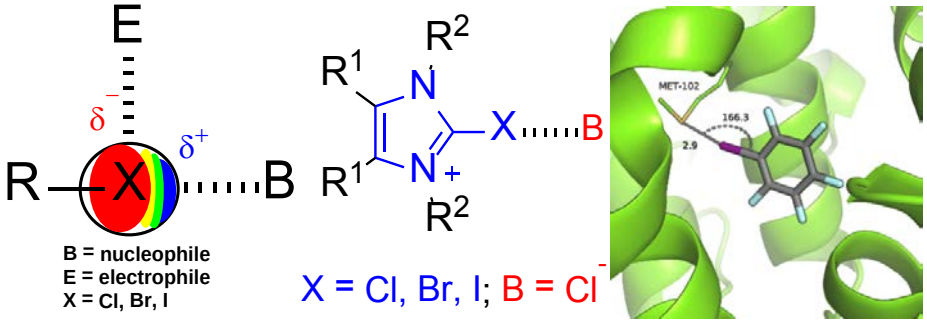

Figure 1: Left: schematic representation of an R−X···B halogen bond showing the anisotropic distribution of charge around the X atom. Center: example of a charge-assisted XB involving a 2-halo-functionalized imidazolium derivative and chloride. Right: halogen bond between C_6F_5I and a methionine in the non-polar cavity of a bacteriophage T4 lysozyme.

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KN5

Key Note

Supramolecular multistate multiresponsive systems based on *trans*-2-hydroxychalcones

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The development of systems able to exist in different states whose interconversion can be controlled by different stimuli (light, ions, electrons) may contribute to the appearance of molecular-level devices and materials with new functionalities. Over the last few years, we have worked in systems mainly based on *trans*-2-hydroxychalcones (Ct).[1]These photoisomerizable compounds originate in aqueous solution intricate pH-dependent chemical reaction networks involving several species. Among these species, flavylium cations are strongly coloured compounds that have been allowing to explore these chemical networks as pH–coupled photochromic systems, responding thus to pH and light.

As aromatic cations, flavyliaare electron poor guests able to intercalate into neutral or negatively charged electron rich cavities such as those of molecular clips[2] and cucurbiturils.[3] This allows the use of supramolecular interactions to further control the conversion between different states of the system. Recent examples of these multistate systems exploitedas photochromic,[4] photorheologic[5] or self-sorting host-guest systems[6] will be shown.

Acknowledgements: This work was supported by the Associated Laboratory for Sustainable Chemistry- Clean Processes and Technologies- LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER – 007265)

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Molecules of Colour: Reds, Purples and Blues. From Ancient to Modern Applications

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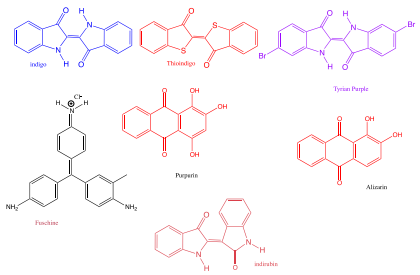
Alizarin, brazilin and brazilein (major colour constituents of Brazilwood), fuschine, indigo, indirubin, mauveine, purpurine, Tyrian Purple and thioindigo, are amongst the molecules that have had a strong impact in our civilization (see **Scheme 1** for some of the structures).[1-4] The majority of these have a natural origin, but man, mimicking and augmenting some of their properties, has produced others. The colour and longevity of these molecules is partially linked to their photostability, which have different origins. In this contribution the photochemistry and photophysics of these and other molecules will be presented, linked with relevant issues such as the photostability (in some cases associated with an excited state proton transfer)[5], photoisomerization[6], mechanisms of photodegradation[7], the origin of the colour, the presence in different environments (in the case of indigo with the clay palygorskite it forms Maya Blue the pigment of the ancient central American civilizations)[8].These (and other) molecules of colour were used in magnificent paintings and in postage stamps.[4]Their presence also provides a way to distinguish authentic from forgeries in valuable works of art. In addition current applications of these molecules include incorporation in solar cell devices and in redox flow batteries[9, 10]. These will also be briefly described.



Scheme 1- Some of the molecules of colour that will be discussed in this communication.

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Porphyrins and porphyrinoids: functionalization and applications

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Porphyrins, corroles, hexaporphyrins, phthalocyanines and other porphyrin-type compounds are currently finding applications in a range of scientific areas namely in medicine (photodynamic therapy of tumors and in the photoinactivation of pathogenic microorganisms).[1] These[2,3] and other pyrrolic macrocycles, namely hexaphyrins, are also being studied as selective anion chemosensors, particularly lethal anions such as cyanide,[4] or metal cations.[5] The work developed by our group in recent years in the functionalization and applications of such macrocycles will be illustrated and discussed.

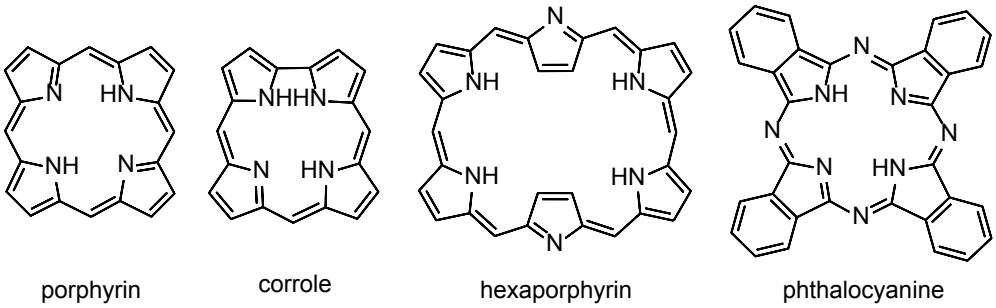

Figure 1: Examples of porphyrin and porphyrinoid macrocycles.

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Materials chemistry: from benzene to sustainable energy solutions

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Energy is considered one of the top ten challenges that the world faces today. Put together with increasing awareness of the environmental impact the human activity is having on Earth, this calls for a critical contribution from materials scientists and chemists in the search for new solutions in multiple areas.
In this communication I will focus on the progress that has been achieved in the last years in the broad area of organic optoelectronics, with a special focus on photovoltaic and hydrogen generation systems that rely on the use of conjugated systems, namely fullerenes, carbon nanotubes and polymers. I will also discuss current materials limitations and prospects to circumvent them.

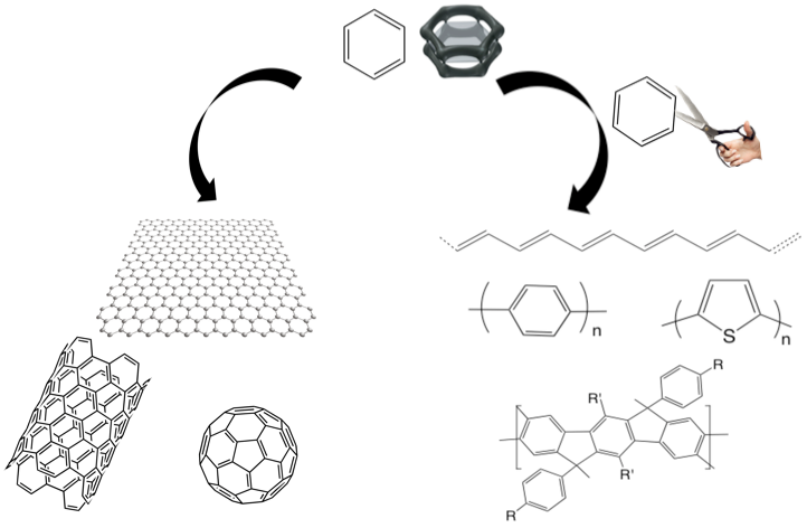

Figure 1: Examples of porphyrin and porphyrinoid macrocycles.

Key Note

Nanoscale Compartmentalization of PI(4,5)P2 in Living Cells and Model Membranes. A Fluorescence Spectroscopy and FRET Imaging study

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PI(4,5)P2 is an essential membrane component involved in a large number of cellular functions, including membrane trafficking and cytoskeleton organization. The variation of its local concentration, in time and space, has been claimed to be responsible for the spatiotemporal recruitment of proteins with diverse functions, such as endocytosis and cytoskeleton adhesion to the membrane. Among other factors, the presence of cholesterol-enriched domains, elevated concentrations of divalent cations and the cytoskeleton itself have been suggested to be involved in determining PI(4,5)P2 organization and clustering. Using a combination of fluorescence spectroscopy and microscopy techniques, we show that both the number and position of phosphorylations in the inositol ring of phosphoinositides are crucial for defining the extent of PIP clustering and relative cluster size. Additionally, we show that formation of the liquid ordered phase strongly promotes formation of PIP clusters in model membranes. Evidence for the formation of PI(4,5)P2 enriched nanodomains in the plasma membrane of living cells was obtained through FRET microscopy of pleckstrin homology (PH) domains tagged with fluorescent proteins. Disruption of the cytoskeleton in HeLa cells decreased significantly the compartmentalization of PI(4,5)P2, proving that distinct pools of compartmentalized PI(4,5)P2 are present, of which one is dependent and other independent of actin cytoskeleton-membrane adhesions. On the other hand, PI(4,5)P2 compartmentalization is shown to be independent of cholesterol concentration.

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Functional nanomaterials for sustainability

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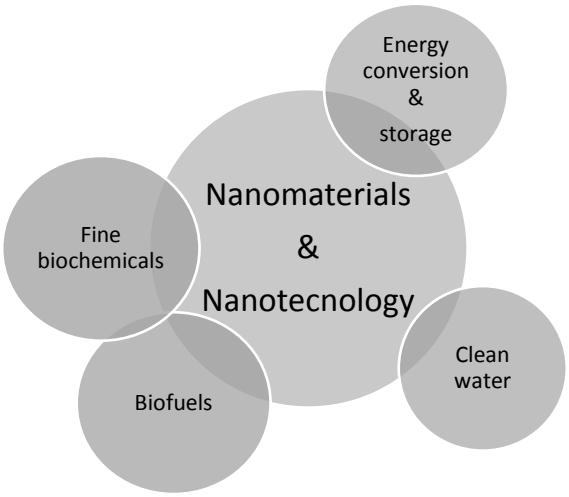
Over the last 30 years, nanomaterials and nanotechnology have transformed the field of Chemistry, in particular the area of Materials Chemistry. The ability to chemically synthesize nanomaterials in a wide range of compositions, sizes, shapes, and morphologies, harness the nanomaterials properties in a way that maximize their integration into key technologies to directly yield societal benefit, in parallel to the contribution for the understanding of their intrinsicproperties, *ca.* high surface reactivity, easy surface functionalization and high surface area to volume ratio. The grand challenge of Materials Chemistry is how to exploit the nanomaterials properties to achieve new functionality and innovative nanotechnologic applications, while minimizing any potential adverse environmental impact associated with synthesis, use, and disposal.

Currently, there are an enormous number of areas in which nanomaterials and nanotechnology have high impact.In this talk it will be provided an overview of our recent breakthroughs in the design of functional hybrid nanomaterials and their nanotechnologic applications in three main areas: Fine Biochemicals& Biofuels, Electrochemical Energy Conversion & Storage and Clean Water. In all the examples to be shown the nanomaterials acted as nanocatalysts for chemical, electrochemical and photochemical catalytic reactions.



Acknowledgements: The work was funded by Fundação para a Ciência e a Tecnologia (FCT)/MEC and FEDER under Program PT2020 project UID/QUI/50006/2013-POCI/01/0145/FEDER/007265, project “UniRCell”, reference POCI-01-0145-FEDER-016422 and project UTAP-ICDT/CTM-NAN/0025/2014 in the framework of UT Austin|Portugal Program

Preparation and Gas-Solid Applications of Activated Carbon Fibres and Cloths

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Activated carbon fibres (ACF) were invented by William Abbott in 1959 by carbonization and steam activation of different types of rayon fibre[1]. In the original patent Abbott also referred to cloths formed by weaving ACF, and also to mats, pads and continuous webs formed by bonding the rayon fibres with urea formaldehyde resins before carbonization. The use of thermoset resinsto make ACF was pioneered in the seminal work of James Economy, initially at the Carborundum Co. and subsequently at the University of Illinois, on phenolic resin (Kynol®) fibres[2]. The first activated carbon cloths (ACC) prepared from woven fabrics were developed in 1969 by Alan Bailey and Fred Maggs, at the Chemical Defence Establishment of the UK Ministry of Defence, who prepared ACC by carbonization and CO_2 activation of viscose rayon cloths[3]. In subsequent years a variety of different precursors have been used as ACF and/or ACC precursors, including PAN, mesophase pitch, Kevlar®, Nomex®, Tencel® and,most recently, lignin.

In comparison with the traditional granular and powder activated carbons, ACF and ACC combine a number of advantages, including high rates of adsorption, easy separation, uniform tailored porosity and purity. They are currently manufactured by a number of companies, including the world's two largest activated carbon manufacturers, Calgon and Osaka Gas Chemicals, and find application in various areas related to health, energy, and environmental control.

Work carried out in Évora has involved, principally, viscose rayon ACC and PAN ACF. The latter[4] was originally carried out using acrylic textile fibres produced by Fisipe in Barreiro. Relatively recently Fisipe / SGL Carbon began commercialization of technical fibres and the ACF we have produced from these show some different properties, including higher micropore volume, which is one of the most fundamental properties of an activated carbon adsorbent material. Recent results obtained with these ACF, in combination with a new method for the determination of micropore size distributions[5], also provide support to a model for the structural changes occurring during carbonization which we had previously proposed on the basis of results obtained with viscose rayon ACC[6].

Areas of application which are studied in Évora include the separation of permanent gases (after conversion of the ACF/ACC to molecular sieve carbons) and the capture of CO_2. Both viscose rayon ACC and PAN ACF, when prepared under appropriate conditions, show good performance. More recently, attention has been turned towards a particular medical application. In addition, a low-cost alternative[7] to the usual CO_2 or steam activation is being evaluated.

Acknowledgements: FISIPE SA (Portugal, Member of SGL Group - The Carbon Company) is thanked for the preparation of the precursor fibres. The work was partially financed by the Fundação para a Ciência e Tecnologia (FCT, Portugal) with National (OE) funds (project UID/QUI/0619/2016).

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KN12

Key Note

Revisiting the old polymer suberin to develop functional materials

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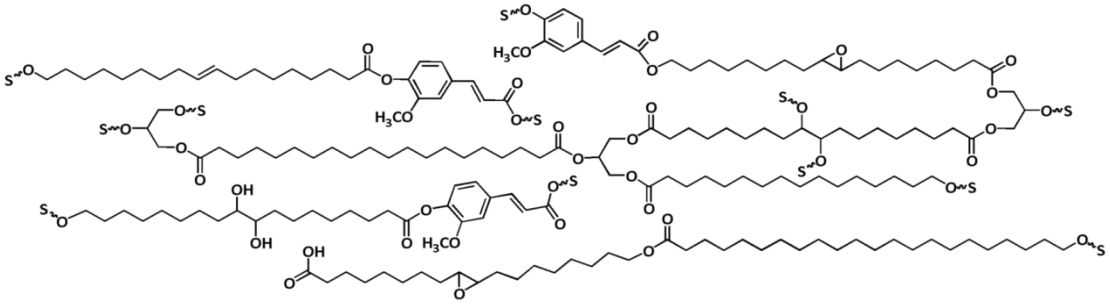
Ionic liquids discovery has just celebrated 100 years. These liquid salts consist solely of ions, one of which is typically organic and asymmetrical. Matchless physical and chemical properties stirred their use as alternative solvents in many chemical processes. Our vision was to explore task-designed ionic liquid, preferentially biocompatible cholinium alkanoates[1], for the hydrolysis of structural polymers in plant cell walls, e.g. suberin (**Figure 1**). We wish to preserve the native properties of the polyesters, particularly their function as barriers to microbial pathogens. In some ways unpredictably, an ionic liquid – cholinium hexanoate – provided us the right means for that. It plays the dual role of solvent and catalyst, promoting the specific cleavage of particular ester bonds in suberin[2]. This ensures the partial preservation of its tridimensional structure, hence the spontaneous formation of materials with potentially broad antimicrobial properties[3]. I will review our major findings and current hypotheses, contextualizing the potential of suberin-based materials to generate functional materials and to provide broad antifungal solutions.



Acknowledgements: We acknowledge funding by the European Commission through the European Research Council through grant ERC-2014-CoG-647928 and the FET-open grant number 713475 and Fundação para a Ciência e Tecnologia through grant UID/Multi/04551/2013 (Research unit GREEN-it "Bioresources for Sustainability"), and the support provided by the COST Action EXIL – Exchange on Ionic Liquids (CM1206).

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KN13

Key Note

Sulfur polymers for the environment, agriculture and human health

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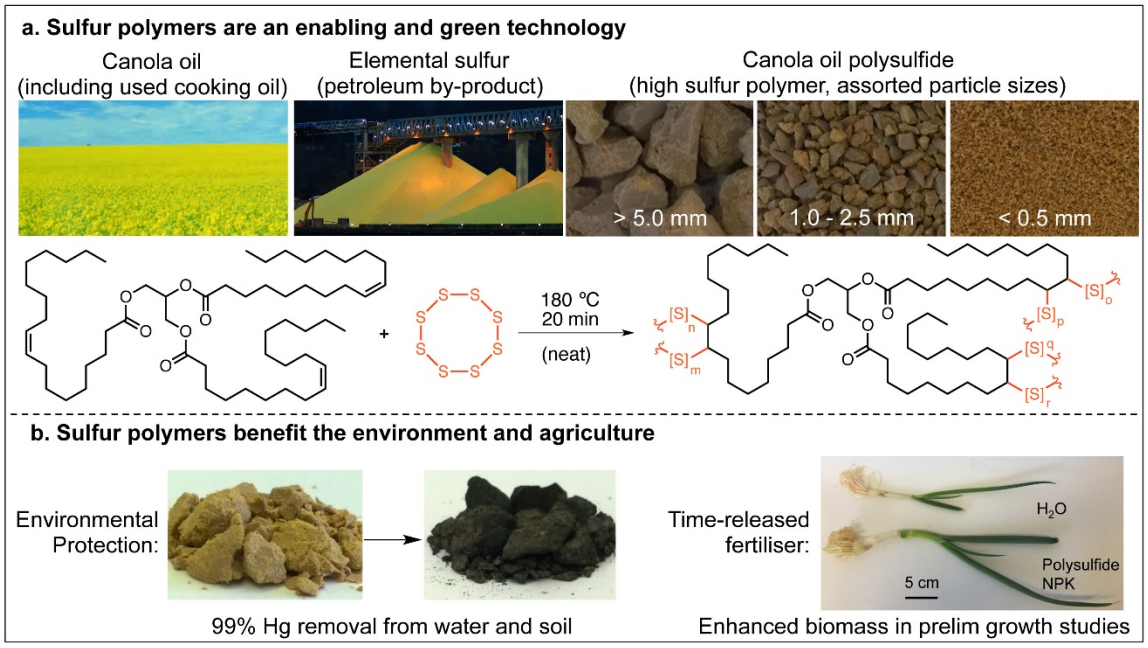
Advances in science that protect the environment and ensure a sustainable supply of food are critical for the future of humanity. This presentation will describe a new class of sulfur polymers[1] made from elemental sulfur and renewable plant oils such as limonene and canola oil.[2] Because sulfur is a by-product of petroleum refining and waste cooking oil is suitable in the synthesis, the polymers are made entirely from re-purposed waste.[3] The high sulfur content (typically 50% by mass or higher) imparts several interesting chemical and thermo-mechanical properties to the material that make it useful in a variety of applications. Several applications of the material will be discussed including using the polymers as inexpensive adsorbents for heavy metal and perfluorocarbon pollution, and also as slow-degrading vehicles for fertilizer.



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KN14

Key Note

Ionic-Liquid-Based Separation Processes for Bioactive and Value-Added Compounds

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Mainly due to their non-volatile nature at ambient conditions, ionic liquids (ILs) have been described as “greener” solvents over conventional volatile organic solvents. Furthermore, the large number of possible ions’ combinations, with highly distinct chemical structures, allows their tuning, and thus, ILs can be designed for a particular application or to present a specific set of properties. Due to these features, ILs have been largely investigated as promising media for the separation (purification) of bioactive compounds from the most diverse origins. ILs have been studied as solvents, co-solvents, co-surfactants, electrolytes, and adjuvants, in liquid-liquid systems, as well as used in the creation of IL-supported materials. In this work, the main results achieved by the use of IL-based processes in the separation/purification of a large range of bioactive compounds (including small organic extractable compounds from biomass, lipids, and other hydrophobic compounds, proteins, amino acids, nucleic acids, and pharmaceuticals) will be overviewed. The key accomplishments and future challenges to the field will be finally highlighted.

Acknowledgements: This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, POCI-01-0145-FEDER-007679 (FCT Ref. UID/CTM /50011/2013), financed by national funds through the FCT/MEC and FEDER under the PT2020 Partnership M.G. Freire acknowledges the European Research Council under the European Union's Seventh Framework Programme (FP7/2007-2013) / ERC grant agreement n° 337753.

Challenges for Chemists in the 4th Industrial Revolution

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The topic of Research, Development and Innovation (RDI) productivity has been one of the main concerns and objectives of both Academy, Industry, Investors and Governments. This is particularly important in areas of intense competition, disruptive innovation and short product life-cycles like advanced materials, information technologies, energy and mobility or pharma.

Looking ahead, we see a world of increased competition for resources and energy in parallel with climate and social changes, market volatility and geopolitical tensions. These factors combined with aging populations, increasing demand for personalized healthcare and evolving life-styles, brings RDI productivity to the top of our priorities.

The societal changes and increased access to information is driving demand to customized products and solutions. Shorter product life-cycles mean shorter time to get return on RDI investments and require recycling to be incorporated in product design. The efficient and sustainable use of raw-materials, water and energy are pillars for those involved in Research, Development, Innovation and Manufacturing.

Portugal and its partners need to develop and nurture the ecosystem for scientific and technological employment and continuous learning, which is fundamental to drive change and growth. RDI policies that reward RDI productivity and value generation, rather than just financing expenditure, and that establish the framework for collaboration and IP sharing between Academy and Industry are also critical success factors.

Chemistry is transversal to many of these challenges and Portuguese chemists must take an active and leading role in the Industry 4.0 Revolution and RDI productivity, upgrading traditional industries and generating new and innovative, knowledge based industries.

Discovery and Development of Opicapone: A Potent and Peripherally Selective Catechol O-methyltransferase (COMT) Inhibitor for the Adjunctive Treatment of Parkinson's Disease

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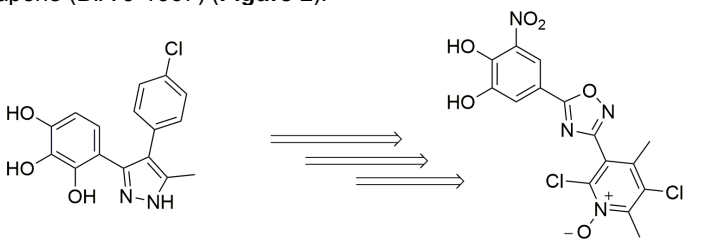
Catechol-O-methyltransferase (COMT) is a magnesium-dependent enzyme, which plays key role in the inactivation of endogenous catechol neurotransmitters and xenobiotics. Inhibition of COMT provides therapeutic benefits in patients afflicted with Parkinson's disease (PD) undergoing treatment with the gold standard drug levodopa. PD is a chronic neurological disorder associated with a reduction in striatal levels of the endogenous neurotransmitter dopamine. Levodopa is a biological precursor of dopamine, which is able to modulate cerebral levels of dopamine by penetrating into the brain. Clinical efficacy of the therapy can dramatically be improved by inhibiting the metabolic degradation of levodopa in peripheral tissues. COMT inhibitors help to sustain the continuous delivery of dopamine to the striatum and thereby motor-related symptoms of PD are diminished.
We have designed and prepared a novel series of COMT inhibitors by modifying screening hit[1]. Structural optimization led to the discovery of opicapone (BIA 9-1067) (**Figure 1**).



1 Opicapone (BIA 9-1067)

Figure 1: Structure of screening hit 1 and opicapone

Efficacy and safety of opicapone was demonstrated in several Phase I-III clinical trials[2, 3]. On the basis of favourable clinical results the marketing authorization was granted in 2016. The milestones of the discovery and development of opicapone will be presented.

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The Biorefinery R&D Programme at The Navigator Company

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Eucalyptus globulus is the raw-material for pulp and paper industry in Portugal. In 2016, the wood consumption was about 8 million m^3 and the pulp production reached 2.5 M ton; more than 40% of this virgin fiber is integrated at mill site for paper production. This industrial activity generates forest biomass as main side stream accounting for more than 1.2 M ton / year (dry basis) divided between bark (30%), leaves (30%) and branches (40%).
The residual biomass potentially available to The Navigator Company, European leader in UWF paper market, accounts for about 700 Ktons, distributed among the main components of the tree. Bark is mainly generated at mill sites from logs debarking, while other forest biomass is generated at plantation; part of this is currently transported to mill site for energy and steam production, benefiting from the logistic chain already settled. Pulp and paper mills generate also other side streams with high fiber content: primary sludge and sawdust generated in chipping process accounting, together, to about 50 K ton. Black liquor accounts for near 9 M ton, containing about 650 K ton of lignin; this side-stream is concentrated and burned at the recovery boiler for energy production and pulping chemicals recovery.
The Navigator Company and RAIZ, the Forest and Paper Research Institute, are completing now two decades of comprehensive and consistent research programme on *Eucalyptus globulus*, pulping, bleaching, papermaking, and biorefinery areas. The new bioeconomy era and a business diversification strategy led The Navigator Company and RAIZ, in strong connection to associated and partner universities, to implement a new comprehensive R&D eucalyptus pulp mill based biorefinery program aiming at upgrading biomass residues and pulp mill streams and by-products into new materials, bioproducts and biofuels, as well as, developing new cellulose-based materials, as summarized in **Figure 1**.

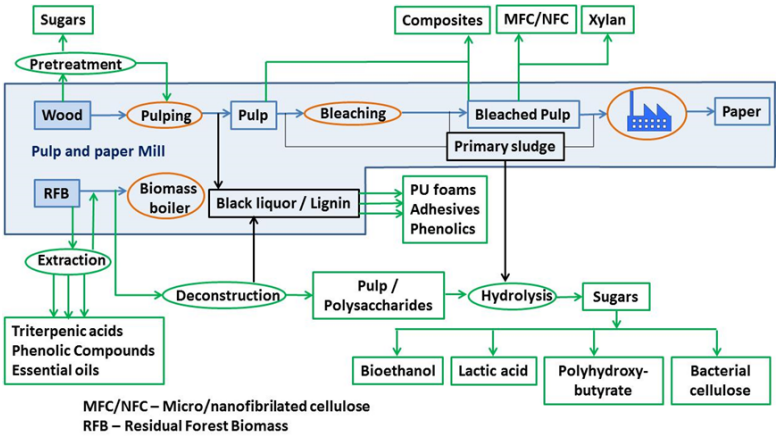

Figure 1.Simplified diagram of pulp and paper production process and research lines in biorefinery processes / products at The Navigator Company / RAIZ.

This paper describes the main R&D routes followed at this research programme as well as the potential market opportunities for thenewmaterials, bioproducts and biofuels issued from the implementation of the biorefinery concept at a pulp and paper mill.

KN18

Key Note

Mass Spectrometry Applications in the Crop Protection Industry

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During this talk, a characterization of Sapec will be given, focusing Research & Development activities performed at the company's Setubal industrial site, mainly using Mass Spectrometry as, both, an analytical and structural characterization technique.
A broad range of application examples will be presented, ranging from the analysis of surfactants in formulated products to the fragmentation patterns of some active substances included in a recently funded and multidisciplinary R&D project will be addressed, as well an interesting gas-phase behavior of cyhalofop-butyl under electrospray ionization mass spectrometry conditions.

Acknowledgements: We acknowledge financial support by *Sistema de Incentivos à Investigação e Desenvolvimento Tecnológico* (SI I&DT), *funded by pelo Fundo Europeu de Desenvolvimento Regional (FEDER)* through *Programa Operacional Regional de Lisboa*, project nº 11130, HYBRID XXI.

Marine-Derived Fungi: A Promising Source of Bioactive Compounds for Drug Discovery

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The marine environment presents different physical and chemical conditions from the land, and can be considered as an extraordinary reservoir of bioactive compounds, many of which possess unique and interesting structural characteristics which are not found in terrestrial counterparts. Recently, researchers have focused much of their attention on marine microorganisms, especially marine-derived fungi since many consider them as one of the still untapped resources for new and biologically relevant chemical entities. Moreover, through established culture methods, they can produce quantity of compounds needed for medicinal chemistry development, clinical trial and even marketing. In the pharmaceutical industries perspective, two major important areas of drug development are anticancer and anti-infective drugs. It is widely recognized that more research is necessary to find new drugs that are more effective and have less side-effects than those currently used in chemotherapy as an alternative and one of these approaches is to search for new chemical entities which can be potential for the development of cancer chemotherapeutic agents from the marine environment. Since natural products from terrestrial environments and their derivatives have traditionally been a major source of new anticancer agents, it is no wonder that marine-derived fungi can be a potential source of anticancer compounds. This hypothesis is supported by the fact that many fungal metabolites exhibit a variety of the *in vitro* anticancer properties such as pro-apoptotic, antiproliferative, anti-angiogenic and anti-migratory effects through different pathways. On the other hand, the infectious diseases are the second major cause of death worldwide and the third leading cause of death in developed countries. It is also recognized that more and more bacterial infections cannot be controlled by a current standard treatment, and more often than not, they are very difficult or even impossible to treat due to the resistance to antibiotics. Therefore, only the continuing discovery and development of new antibiotics can help tackle this problem. From the evolutionary point of view, microorganisms, especially fungi, which successfully produced secondary metabolites as their vital armamentarium in the persistent fight for space and resources against bacterial competitors for millions of years, can be considered as promising target organisms for antibiotic production. However, besides cancer and infectious diseases, many pharmaceutical companies also start to pay attention to obesity, a health problem of a modern society. It was reported that 600 million people worldwide are classified as obese in 2014. Obesity is considered a major risk factor for cardiovascular diseases, diabetes, musculoskeletal disorders and some forms of cancer. In this sense, many compounds from fungi are found to possess interesting properties for the prevention and treatment of obesity and related metabolic complications. Given the importance of bioactive compounds from fungi, recent investigation on the *in vitro* anticancer, antibacterial and anti-obesity activities of the secondary metabolites produced by the cultures of marine-derived fungi of the genera *Aspergillus*, *Neosartorya*, *Talaromyces* and *Eurotium*will be discussed in this presentation.

Acknowledgements: We thank the Foundation for Science and Technology and European Regional Development Fund (ERDF) and COMPETE, under the project PTDC/MAR-BIO/4694/2014, for financial support.

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Key Note

In search of algal metabolites with biomedical-biotechnological potential from the East Mediterranean

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The biodiversity of the Mediterranean ecosystem hosts an immense number of indigenous species, as well as organisms that have migrated from the Atlantic Ocean, the Red and the Black Sea. The Mediterranean basin although it occupies only 0.8% of the world's ocean area, it accounts for 7.5% of all described marine species. Many of these organisms have been proven a prolific source of interesting metabolites with a broad spectrum of bioactivities.
As part of our studies on the chemical composition and biological activity of marine organisms, our group has investigated a significant number of algal species found along the Greek coastline.
In search of a fast and reliable screening tool for the chemical profiling of Laurencia algal extracts and the detection of new secondary metabolites, we have developed a high throughput fingerprinting methodology based on the complementary application of LC-HRMS-DAD and 2D NMR. The preliminary results of this study point out the potential for the direct screening of crude algal extracts in order to detect new compounds, as well as to trace biomarkers and /or monitor the presence of targeted metabolites.
Brominated diterpenes isolated from the red alga Sphaerococcus coronopifolius as well as a panel of synthetic analogues have been evaluated for their settlement inhibitory potential on the cyprids of Balanus amphitrite resulting in the detection of compounds that exhibit high levels activity of without toxic effects on non target organisms. The active compounds were loaded on CuO nano spheres and were incorporated in CNT enriched self healing/self polishing anticorrosive/antifouling marine paints.
Novel fibrous biocomposites comprising ulvan, a sulfated polysaccharide extracted from the green seaweed Ulva rigida, and a number of copolymers were successfully prepared using the electrospinning technique. Such nanofibrous matrices represent potentially useful materials in the biomedical sector as tissue engineering scaffolds, wound dressings, or drug delivery systems.

Integrated Strategies to Address Ocean's Microbial and Metabolomic Dark Matters for Marine Natural Product Discovery

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The oceans represent a very rich but still understudied resource for chemically intriguing and potently active metabolites that have made profound impact on human health, nutrition and life quality. However the relatively young marine drug discovery efforts still face severe issues, including low supply, legal/physical access, insufficient dereplication and the ambiguity of their original (metabolic) source. Marine invertebrates, such as sponges and corals have so far been the most studied sources in the search of new lead compounds, but, many promising marine metabolites have been shown or predicted to have their origin in associated microbes.[1] Nevertheless, only approx. 1% of the estimated microbial diversity are culturable in the laboratory, leading to so-called 'microbial dark matter'. Moreover, many biosynthetic gene clusters (of this 1% portion) largely remain silent or underexpressed due to lack of environmental stimuli, including challenges, cues and competition in the artificial laboratory conditions. Therefore, the discovery rate of new compounds from marine microorganisms is inevitably stagnating. To address all these obstacles, we focus on marine invertebrates from extreme environments (e.g. polar regions) that have remained untapped for marine bioprospecting and often reveal chemically unprecedented compounds. When dealing with microbes, we employ innovative techniques, such as OSMAC and co-culturing, to induce microbial chemical diversity. Proper dereplication of any microbial or invertebrate extracts at the earliest drug discovery stage is crucial, but current untargeted metabolomics studies can only annotate less than 2% of metabolites, representing the major 'chemical darkness'.[2] The recently introduced molecular networking approach, which is based on LC-MS/MS fragment similarity and coupled with the public GNPS database,[3] has opened a new era in metabolome analysis and dereplication of marine extracts. This presentation will deal with our efforts to identify the full chemical inventories of marine organisms by metabolomics approaches and their prioritization for in-depth chemistry in combination with bioactivity data and statistical analyses.

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KN22

Key Note

A Química no ensino básico e secundário: Um desafio para os alunos?

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O ensino da Química acompanha (deve acompanhar!) o percurso do aluno desde o pré-escolar até ao fim do secundário. Tem de estar presente a todos os níveis e para todos os alunos. Os desafios propostos têm de ser ajustados à idade e aos objetivos genéricos dos alunos. Estaremos a cumprir?

A Química é a ciência dos materiais e das suas transformações. A criança constrói progressivamente a sua descoberta do mundo e o objetivo do sistema educativo é moldar essa descoberta individual pelo conhecimento sistemático acumulado pela humanidade e reforçar uma via de construção do conhecimento que foi sendo elaborada, especialmente, a partir do século XVII europeu. A função da escola é acelerar a aprendizagem e incorporar-lhe o conhecimento acumulado. O modelo mais influente da escola da antiguidade clássica é o Liceu e a Academia de Atenas, mas modelos similares existiram em civilizações anteriores. Não se pode esperar que cada geração reconstrua por si todo o percurso anterior da humanidade e o ambiente familiar normal não é capaz de o fazer com a eficiência e a eficácia desejadas. A escola apareceu como complemento dessa experiência familiar e de grupo.

A Química está presente em toda a cultura tecnológica moderna e é indispensável à compreensão do mundo físico. Como podemos compreender a natureza de uma rocha ou as propriedades de um líquido sem falar de átomos, moléculas e das suas propriedades e interações? A imagem pública da Química tem sido injustamente tratada e uma experiência positiva na escola é a melhor forma de a corrigir. Para isso, é necessário que o aluno compreenda bem os desafios que a Química lhe propõe e que encontre respostas satisfatórias para a sua idade e opção de percurso educativo.

Tenho muitas dúvidas de que as propostas dos programas oficiais de Química sejam hoje motivantes, de que não possam ser melhoradas. E teremos de garantir que a busca do encantamento é satisfeita para os mais novos; que o método científico de construção do conhecimento é bem compreendido e vivido (sentido) até aos 15 anos. Depois, há que propor objetivos muito diferenciados conforme o percurso do estudante, mas nenhum deveria ficar por aí na visão química do mundo.

Os desafios da nossa escola não são apenas os da definição de conteúdos e de estratégias de ensino. Todos os países, experimentam sistemas mais eficazes de organização para servirem melhor TODOS os estudantes. Em Portugal insistimos demasiado tempo numa via única. Não parece que tenhamos ainda compreendido que a diversidade dos estudantes exige uma diversidade de propostas, oferecendo a todos um desafio que os leve mais longe no caminho que escolham e vão construindo.

INVITED ORAL COMMUNICATIONS

Invited Oral Communication

Adductomics: a challenge towards the minimization of chemically-induced toxic events and the development of diagnosis/prognosis tools

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Chemical agents of endogenous, drug, dietary, occupational or environmental exposure are a major cause of cancer. Additionally, a great number of the population is currently on chronic therapies, being exposed to high doses of drugs whose long-term toxic effects remain to be accurately elucidated. These constitute the main challenges of chemical toxicology.

The formation of covalent protein adducts with chemicals (or their reactive metabolites) is considered a key event in the onset of a wide range of deleterious health outcomes, including cancer, cardiovascular and autoimmune diseases. The ability of identifying the nature of the covalent conjugate along with its extent and the site of adduction within the protein structure, generically referred as Adductomics, is therefore crucial towards a better understanding of the molecular basis underlying diseases, in general, and chemically-induced toxic events, in particular. This can guide new therapeutic approaches, but also constitutes a huge opportunity for the development of biomarkers that are anticipated to have a profound impact on human lives, as effective tools for diseases diagnosis/prognosis, for the application of personalized medicine approaches and for accurately assessing human exposure to chemical toxicants. This can guide regulatory agencies to make better decisions thereby leading to minimization of these adverse effects.

A multidisciplinary approach, founded mainly on solid synthetic and analytical skills, is used within our research group towards the use of Adductomics as a tool for the development of early compound-specific biomarkers of cancer,[1] the establishment of biomarkers of exposure to drugs used in chronic therapies,[2] and the development of diagnosis tools for diseases more prevalent in women.

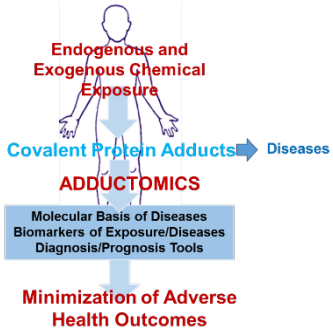

Figure 1: The key role of adductomics towards the minimization of adverse health outcomes.

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Invited Oral Communication

Ceramide domains in living cell membranes: from biophysical characterization to biological significance

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The mechanism of biological action of several bioactive lipids might depend on their effects on membrane structure and biophysical properties. This is particularly relevant for ceramides – the backbone of all complex sphingolipids - which have been implicated in the regulation of several cellular events, through the formation of the so-called ceramide-enriched platforms. However, most of our present knowledge is limited to studies performed in artificial membranes or under non-physiological mimicking conditions, mainly due to the inherent complexity associated to the study of lipid interactions in biological membranes. To overcome this limitation, we developed a bottom-up experimental strategy that enables evaluating the biophysical impact of ceramide in living cell membranes. Using a physiological relevant stress stimulus, we showed that ceramide drives profound changes in membrane properties through the formation of intracellular highly-ordered ceramide-enriched vesicles that colocalize with endocytic markers. Our results link the biophysical changes induced by ceramides to important cell processes and emphasize the existence of vesicles with distinctive biophysical features that might function as intracellular signaling platforms.

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Invited Oral Communication

Carbon Dots in Bioimaging: Myths and Facts

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Fluorescence imaging of biosystems is by far one of the most successful applications of nonlinear fluorophores, and yet commercially available molecular dyes with high emission quantum yield and water solubility have exceedingly low two-photon absorption (TPA) cross-sections. Our work on the optimization of the two photon excited emission of molecular systems has evolved from tailoring small molecules to polymers, water soluble hybrid polymer nanoparticles and more recently to nitrogen-doped graphene quantum dot (N-GQD). In this presentation, emphasis will be laid upon our recent study on the photophysics and nonlinear emission properties of N-GQD as part of a new strategy to improve the nonlinear response of molecular materials. N-GQDs can be described as a 2-4 nm graphene core decorated with various oxygen containing functionalities, such as carbonyl, carboxyl, epoxy and hydroxyl groups on the surface (**Fig. 1A**).[1] The doping with nitrogen introduces additional functional groups such as amides and amines or even pyridinic, pyrrolic and graphitic nitrogen. Despite their ill-defined structure and the largely ignored origin of their emission, their optical properties have been successfully explored in bioimaging, sensors, photocatalysis, optoelectronic devices and nanomedicine.

The fundamental question that we are striving to answer is: what are the critical structural properties of the GQD for an efficient two-photon induced emission? The few existing reports where the TPA cross-section of GQD and carbon dots has been actually quantified seem to converge into a couple of critical factor for observation of an efficient TPA, namely doping with nitrogen and crystallinity. Our conclusion, after production of GQD following many different reported procedures is that none of those factors seem to be sufficient to guarantee a high TPA cross-section. Figure 1 illustrates the typical properties of the crystalline N-GQD we have produced from chemical cutting of GO showing a very modest TPA cross-section (< 1GM), which contrasts with values reported earlier (10^4 GM).

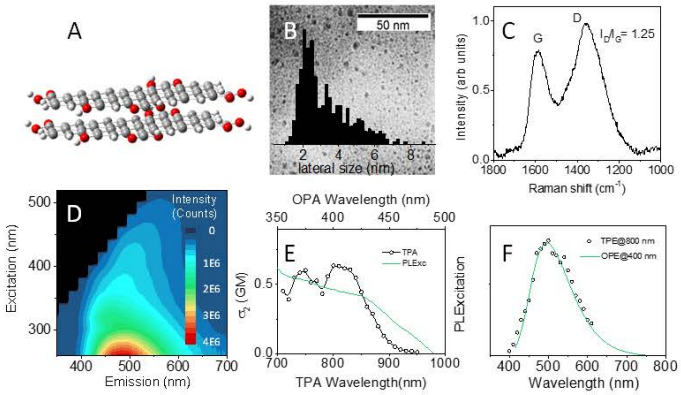

Figure 1: N-GQD (A) with a lateral size distribution peaking at 2 nm (B), with D and G bands in the Raman spectrum indicative of crystallinity, (C), excitation dependent emission (D), two-photon absorption and emission spectra overlapping with the linear excitation and emission spectra (E and F) and an exceedingly low TPA cross-section (< 1GM).

Acknowledgements: Financial support from FCT (SFRH/BPD/75782/2011, SFRH/BPD/105478/2014, IF/00759/2013, IF/00917/2013/CP1162/CT0016 and PD/BD/127805/2016).

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Phototriggers for light-controlled activation and release applications

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Photochemical activation and/or release is an important strategy in areas like chemistry, biology, medicine and materials science, through the use of photosensitive moieties. The release and distribution of the target species, with biological, analytical and biomedical relevance, is controlled in time and space by irradiation with a light pulse. Light has gained increasing significance in recent years as a green and cheap reagent, not only in organic chemistry but also in materials and biomedical applications, such as photocontrolled drug delivery methods from nanocarriers, photoresponsive molecular switches, as well as gated materials for the release of guest molecules from porous supports in response to certain stimuli, for example as photoactivable molecular gates.[1,2]
In the last few years, our research group has been involved in the improvement and tuning of the photosensitivity of heterocyclic phototriggers based on (benzo)coumarins, (benzo)quinolones and fused oxazoles (**Figure 1**) through synthetic tailoring in terms of substituents attached to the heterocyclic skeleton and/or structural adjustments such as ring fusion and expansion of the aromatic system. Such phototriggers have been applied in the caging and uncaging of different bioactive molecules such as amino acids, peptides, neurotransmitters, biogenic amines, and bioactive carboxylic acids such as butyric acid and 5-aminolevulinic acid.[3]

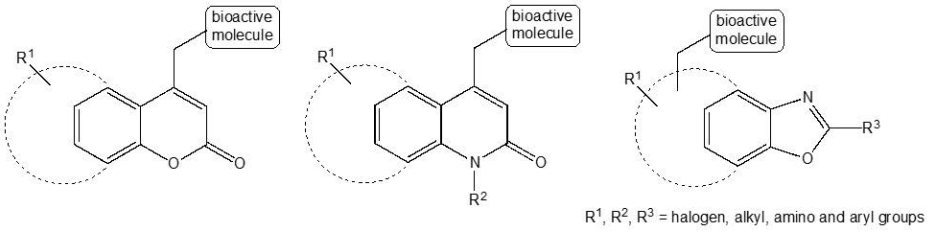

Figure 1: General structure of heterocyclic phototriggers.

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Unraveling network pharmacology in natural product space

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Natural products (NPs) provide excellent starting points for drug development.[1,2] Though, factual knowledge of which targets are modulated remains largely unknown in several cases, hampering the design of NP-inspired chemical matter. Ligand-based machine learning methods have been successfully used to identify both on- and off-targets for NPs, affording opportunities for lead structure development, but also identifying their development liabilities.[2] Herein we provide a brief overview on success stories employing the SPiDER software[3] for de-orphaning intricate macrocyclic[4] and fragment-like NPs.[2,5]

As part of our research program to leverage NPs as anticancer agents we endeavoured to exploit machine learning-enabled pharmacology networks for select examples. We discuss the modulation of $Ca_v1.2$ channels by (-)-englerin A, a known TRPC4/5 agonist,[6] and its selectivity over a panel of voltage-gated calcium channels. We validate target engagement with a range of orthogonal biochemical assays and provide a molecular basis for inhibition of $Ca_v1.2$.[7] Amalgamating analyses of gene-expression profiles with ligand- and receptor-based cheminformatics we also unveil new pharmacology for clinical-stage fragment-like NPs, through engagement of 5-lipoxygenase and TRPV2.[8-10] Modulation of the aforementioned targets correlates with phenotypic outcomes. We discuss the impact of machine learning and related paradigms on future chemical biology and molecular medicine.

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Inorganic helping Organic: Tetrapyrrolic Macrocycles Immobilized onto Inorganic Supports and their Applications

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Metal complexes of pyrrole-based macrocycles, including porphyrins and phthalocyanines are, without any doubt, considered some of the most extensively studied chemical structures for many purposes, of which is putative their applicability in optoelectronics,[1] biomedicine[2] and catalysis.[3] In catalysis, for instance, tetrapyrrolic macrocycles are reputed for their excellence in acting as oxidation catalysts. However, it should be noted that the transformation of their metal complexes as valuable oxidation catalysts for large scale purposes is still a challenging endeavour, mainly due to issues related to stability, cost and reutilization. The envisaged solution relies on the development of efficient procedures for the immobilization of porphyrins into/onto solid supports[4] including mesoporous aluminosilicates and, more recently, magnetic nanoparticles (**Figure 1**).
Herein, a discussion on the synthesis, selective functionalization and covalent linking of the inorganic-organic counterparts to form hybrid materials is presented. Furthermore, their capabilities to act as oxidation catalytic systems in an array of processes is also discussed.

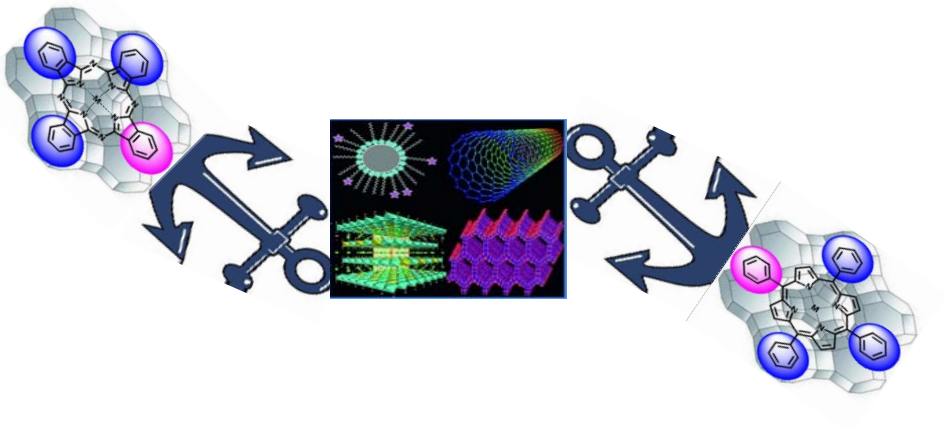

Figure 1: Immobilized tetrapyrrolic macrocycles.

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Designing functional porous materials

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At their early stage, porous materials were mainly though to be applied in catalysis, ion-exchange, adsorption and separation. In the last decades, a strong effort has been made searching other potential areas of application of porous materials based on their attractive high specific surface area, narrow distribution of pore sizes and tunable surface properties. Unique possibilities arise from the ability to develop different functional groups and compositions, and exploit different interaction with guest molecules to design composite materials with unusual properties. Periodically organized porous open an avenue of opportunities in micro-optics and photonic devices, microelectronics, energy harvesting, gases separation, functional and protective coatings, environmental responsive materials, and microfluidics, among others.

In our group we have been involved on the development of porous functional multimetallic oxide materials of ternary and quarternary oxides with perovskiteor spinel structures. These compositions possess extraordinarily useful properties namely to be used as piezoelectrics sensors, as ferroelectric actuators, capacitors and memories, in high-strength dielectrics, for ferromagnetics or even multiferroics. In this presentation, it will be given an overview of several different materials prepared in CICECO in the form of porous thin films (**Figure 1**). It will be discussed the relation between the porosity and properties. Attempts of functionalization of the pores by different strategies will be presented and discussed aiming the preparation of multifunctional composites.[1-4]

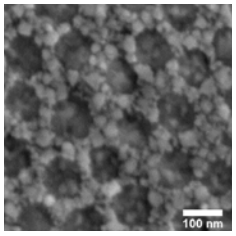

Figure 1. Example of a porous film microstructure observed by top SEM image.

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Invited Oral Communication

Carbon Dioxide Removal using Mixed Matrix Membranes with Metal-Organic Frameworks Supporting Ionic Liquids

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The main objective of this work is the development of a novel methodology for the separation and capture of CO_2 from flue gas in post-combustion processes at high temperatures, using mixed matrix membranes (MMMs) incorporating porous metal-organic frameworks (MOFs) and MOFs with functionalized with task-specific Ionic Liquids (ILs), MMMs-ILs@MOFs. This approach combines the complementary properties of three distinct components in the unprecedented MMMs-ILs@MOF membranes: a hybrid material highly permeable and selective (porous MOF), a CO_2 task-specific IL that will enhance the CO_2 local concentration and will induce high permeability, and the polymeric membranes which are already used at technological and industrial levels.

The MMMs were prepared by dispersing different MOFs in concentrations, between 5 and 30% (w/w), in an organic solution of Matrimid®(polymeric material).The MOFs studied were MIL-101, ZIF-8 and Fe-BTC. Mixed Matrix Membranes with MOFs functionalized with task-specific ILs (MMMs-ILs@MOFs) were also prepared. The MOFs and ILs@MOFs were first characterized in terms of their adsorption properties towards CO_2 and N_2 at different temperatures (between 30 and 80 ºC). The materials that revealed better adsorptive properties for CO_2 were incorporated in an organic solution of Matrimid®. The prepared membranes were then characterized by scanning electron microscopy, thermogravimetry, hydrophobicity by contact angle measurements and mechanical properties. Finally, single gas permeation experiments were carried out for CO_2 and N_2 at 30ºC.

The results obtained showed an improvement on the performance of the new MMMs here developed, in terms of CO_2 permeability and CO_2/N_2 ideal selectivity. Another major advantage of the approach proposed concerns to the use of non-volatile ILs to originate IL@MOF composite materials with exceptional thermal stability. Consequently, the separation and capture of CO_2 may occur at high temperatures, offering the possibility of recovering CO_2 from flue gas without cooling it first, corresponding to a notable reduction in energy costs.

Invited Oral Communication

Ocean Treasures: Marine actinomycetes as a source of antimicrobial compounds with biotechnological potential

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Hospital infections and antibiotic resistance are critical and financially-burdening health problems worldwide and they require urgent efficient solutions. An example of this can be seen with the ability of *Staphylococcus aureus* to acquire resistance to antibiotics, as well as its high number of virulence factors, making it responsible for most nosocomial infections. Bacterial biofilms contribute to antibiotic resistance and wound healing impairment. To date, there are no strategies to address biofilm-associated infections or toxicity/trauma-free solutions for treating wound infections. Currently, band-aids containing silver or iodine and using a secondary dressing for attachment are the only marketed options for bacterial wound infections. These show several disadvantages, such as limited periods of use due to its toxicity and the requirement to remove the dressing, which may result in injury/trauma to the wound.
Four hundred actinomycete strains were isolated from ocean sediments collected from the Madeira Archipelago within the scope of the FCT-funded project "Ocean Treasures"-PTDC/QUI-QUI/119116/2010.[1] Six streptomycete strains belonged to the MAR4 lineage and revealed antimicrobial activity against methicillin-resistant *S. aureus* (MRSA). The MAR4 lineage forms a group of mostly marine *Streptomyces* that is phylogenetically distant to other known *Streptomyces* and whose members have shown a high potential for production of biologically active hybrid-isoprenoids.[2]Followinganantimicrobialbioassay-directed fractionation approach, their bioactive marine natural products (MNPs) were identified through advanced MS/MS networking and MNPs' structures were elucidated using high resolution MS and NMR techniques. These MNPs were incorporated into biocompatible and biodegradable polymeric matrices to evaluate their biotechnological potential.[3]Our bioprospecting-focused MNP discovery strategy paves the way for the development of a novel generation of marine-derived biodegradable, biocompatible, water-soluble band-aids for the treatment/prophylaxis of wound infections.

Acknowledgements: FCT and FEDER through grants PTDC/QUI-QUI/119116/2010, IF/00700/2014, UID/QUI/50006/2013 and UID/Multi/04378/2013 under PT2020 (POCI-01-0145-FEDER-007265). The EU FP7/2007-2013 grants PCOFUND-GA-2009-246542.The NMR spectrometers are part of The National NMR Facility, supported by FCT (RECI/BBB-BQB/0230/2012).

Dedication: Dedicated to the memory of Professor Ilda Santos-Sanches.

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Aprendizagens Essenciais: Os novos desafios transdisciplinares no ensino da Química

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A escola do século XXI tem de se vocacionar, em articulação com a comunidade em que se insere, para fornecer aos alunos competências para a sociedade do conhecimento e para o exercício de uma cidadania ativa e democrática. Neste contexto o Ministério da Educação desenvolveu uma estratégia baseada na definição de um "perfil de competências após 12 anos de escolaridade", que serve de documento orientador para os restantes pilares do projeto: um programa de educação para a cidadania, um programa para a promoção da inclusão e um Currículo para o Século XXI. Este último pilar do projeto baseia-se na definição, para cada disciplina, das Aprendizagens Essenciais e da sua articulação vertical, ao longo da escolaridade obrigatória, bem como horizontal com as restantes unidades curriculares. Na presente comunicação será dado a conhecer o trabalho realizado pela equipa conjunta da DGE/SPQ/SPF na definição das aprendizagens essenciais das disciplinas de ciências físico-químicas (3º ciclo do ensino básico), física e química A, física 12 e química 12 (ensino secundário).

As ciências experimentais são a base da literacia científica e proporcionam, pela sua própria natureza, um entrelaçar natural entre conhecimentos, capacidades e atitudes, para dotar o aluno de competências que lhe permitam a flexibilidade necessária para uma aprendizagem constante ao longo da vida e uma adaptabilidade à volatilidade e evolução dos conhecimentos científicos e técnicos. Por outro lado, a centralidade da química torna-a um veículo importante para a desenvolvimento de uma cidadania ativa e responsável. A química verde, a reciclagem, a promoção de águas limpas e potáveis, a utilização sustentável e responsável de recursos não renováveis, o comprometimento com atitudes positivas em relação às alterações climáticas, a utilização para fins pacíficos do conhecimento e tecnologia são só alguns exemplos de como as disciplinas da área da química podem contribuir para uma cidadania interveniente dos alunos. No entanto, um dos maiores desafios no ensino da química e que resulta de ser uma ciência central, reside nas suas inúmeras interfaces com quase todas as restantes áreas do conhecimento. A inovação tecnológica raramente acontece num estrito domínio científico ocorrendo, quase sempre, na interface entre várias áreas do saber. Assim, o ensino da química, ao aluno do Século XXI, tem de ser um ensino em T: com profundidade nos conteúdos tradicionais da área, mas com largura para incorporar e relacionar esses conhecimentos com as restantes áreas do saber, incluindo as das áreas humanísticas e sociais. As capacidades de comunicação, gestão de projetos, planeamento, gestão do tempo, liderança, trabalho de equipa têm de ser também desenvolvidas nas unidades curriculares da área da química.

Manuais escolares em química e desafios futuros: uma experiência e algumas reflexões

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Contextualiza-se a problemática associada aos manuais escolares, na sua complexa teia científica, pedagógica, social, política e comercial. Mais do que uma reflexão teórica, partilha-se a própria experiência pessoal de quase vinte anos no universo editorial escolar. Partindo desse passado e de um presente indefinido, traçam-se algumas linhas de ação que poderão moldar o futuro dos manuais escolares em química.

A percepção pública da química através do teatro e da ópera

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Nos últimos anos foram várias as peças de teatro de cariz científico que acolheram simultaneamente os aplausos do público e da crítica. *Copenhaga* (1998) de Michael Frayn, *Oxigénio* (2001) de Carl Djerassi e Roald Hoffmann, ou *Photograph 51* (2015) de Anna Ziegler são disso bons exemplos. Em última análise, poder-se-á dizer que as raízes mais profundas destas peças se encontram em obras como *Doutor Fausto* (1592?) de Christopher Marlowe e *O Alquimista* (1614) de Ben Jonson.

Se, por um lado, a ciência tem procurado nos últimos tempos uma maior e mais profunda interacção com a sociedade, reconhecendo no teatro um canal de comunicação eficaz para esse efeito (dramatização de acontecimentos científicos, ideias ou personagens); por outro, os dramaturgos encontraram na ciência um terreno susceptível de reflexões éticas que encontram eco num público cada vez mais sensibilizado para temáticas desta natureza[1].

A ópera, género dramático-musical, também não deixou de ilustrar o interesse do Homem comum pela ciência, sendo disso exemplos obras como *Der Apotheker* (1768) de Joseph Haydn, que abriu o palco operático ao mundo da farmácia, ou a recente *Madame Curie* (2011) de Elżbieta Sikora[2,3].

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Desafios ao ensino da Química

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O ensino da Química tem desafios que dependem de vários fatores, externos e internos à Escola, que interferem diretamente no seu sucesso, na motivação para a aprendizagem e na cultura científica dos alunos; designadamente o currículo, a cultura de Escola, os exames externos, as condições da Escola, os professores e a Direção da Escola. A Escola Secundária de Penafiel tem muitos Alunos em Química e obtido bom resultado, trabalhando com os diversos fatores.

O currículo nacional atual, tanto na carga horária como em conteúdos, é dos mais favoráveis das últimas décadas, com a vantagem de o 12º ano não estar sujeito a avaliação externa, o que permite uma aprendizagem da "verdadeira "Química, ou seja, bastante diferente dos dois anos anteriores (10º e 11º) onde é preponderante a preparação para exame, nem sempre conciliável com os objetivos da disciplina. As informações conhecidas recentemente para as alterações curriculares indiciam um retrocesso, com a promessa de aumento da carga horária curricular de algumas disciplinas, sem o aumento total, portanto com detrimento de outras.

Na Escola Secundária de Penafiel existem dois fatores essenciais que têm contribuído para o elevado número de alunos a escolherem a disciplina de Química no 12º ano. O primeiro, a opção institucional em privilegiar currículos coerentes; o envolvimento dos alunos em atividades que promovem o desenvolvimento do espírito científico. No curso de Ciências e Tecnologias, a Escola tomou a decisão de garantir o equilíbrio entre a componente científica e a da formação geral. Por outro lado, há o envolvimento dos alunos numa cultura científica, em projetos para além das atividades escolares, nomeadamente com o 1º ciclo de outras escolas e concursos nacionais e internacionais. Como retorno há indícios claros de sentimento de sucesso e orgulho em serem alunos das disciplinas de ciências.

Os exames que permitem regular o processo de ensino da Química, além de seriar os alunos no acesso ao ensino superior, revelam-se simultaneamente como um obstáculo, no sentido de que é necessário concentrarem-se esforços na preparação para esses momentos de avaliação, perdendo-se grande parte da criatividade e do verdadeiro sentido e importância da Química na sociedade. É um desafio dar resposta às duas solicitações. É necessário envolver muito os alunos na disciplina.

Não é possível uma aprendizagem completa da Química sem recorrer a uma forte componente experimental. Para dar resposta a essa necessidade é necessário ter bons laboratórios e equipamento adequado. Hoje temos mecanismos financeiros que nos permitem equipar as Escolas,para que estas possuam boas condições. Tão importante como a aquisição é fundamental ter mecanismos de funcionamento eficazes, boa organização, capaz de manter as condições obtidas.

O facto de existirem muitos alunos em ciências e tecnologias depende muito de condições externas à Escola, já no que concerne a existirem muitos alunos a escolherem Química como disciplina de opção no 12º ano, depende essencialmente dos Professores do 11º ano e do 12º ano da disciplina. A escolha da disciplina depende do trabalho e afinidade com o Professor no 11º ano, do seu grau de envolvimento e perceção da importância da disciplina e do conhecimento do trabalho realizado pelos Professores do 12º ano. **O resultado das classificações obtidas pelos alunos no 12º ano em Química é determinante no número de alunos que escolhe a disciplina.**

O Diretor da Escola contribui na organização e orientação das diferentes variáveis inerentes aos múltiplos aspetos que conduzem ao sucesso dos alunos, no âmbito de funcionamento geral da Escola. Concretamente, no que diz respeito à opção dos alunos por uma disciplina, o que se revela crucial é **a distribuição de serviço docente para o 11º e 12º anos**. É também significativa a importância dada às atividades desenvolvidas.

Invited Oral Communication

Olimpíadas Regionais de Química: qual a importância em participar e quais os segredos do sucesso dos alunos neste evento

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Ao longo destes 14 anos, tenho constatado as inúmeras vantagens em levar alunos à participação nas olimpíadas de Física e Química Júnior (5 de Física e 9 de Química). Se há alunos que perdem motivação numa disciplina se nela sentirem muitas dificuldades de aprendizagem, no campo oposto, também há alunos, com conhecimentos acima da média, que podem perder motivação se não lhes forem proporcionados projetos desafiadores.
A vertente competitiva de uma qualquer olimpíada educativa, pode ter uma conotação negativa, mas o desafio e a perspetiva de ganhar, traz inegáveis benefícios para o aumento de conhecimento e competência dos alunos, benefícios esses que se estendem à escola, à comunidade que a envolve e último caso ao país que terá potencialmente cidadãos mais competentes.
Neste evento irei referir os benefícios que tenho notado da participação dos alunos nas olimpíadas bem como alguns segredos que levaram à obtenção de 3 vitórias nacionais, 7 Regionais e 2 segundos lugares no conjunto das olimpíadas de Física e Química.

ORAL COMMUNICATIONS

Advancing the chemical synthesis of azaindoles: a medicinal relevant scaffold

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Azaindoles are an important class of heterocyclic compounds, and are bioisosteres of the indole nucleus, a privileged structure, which have enticed the interest of the scientific community for their physicochemical and pharmacological properties.[1] Bioactive azaindoles have been described, including the synthetic analogues of the natural variolins, possessing cyclin-dependent kinase inhibitory activity, cyclooxygenase (COXs) inhibitory activity, among others (**Figure 1**).[1]

Common synthetic strategies to prepare azaindoles rely on the use of aminopyridines, followed by building up the pyrrole ring. The strategy parallels the indole synthesis starting from anilines. However, the electron-deficient nature of the pyridine ring alters the electronic properties of the conjugated system in such a way that many classic indole synthetic methods are not as efficient or simply do not work,[2] making azaindoles challenging scaffolds.

Despite great progress on azaindoles assembly, there are still drawbacks such as poor regioselectivity, restriction to isomers and limited substrate scope. Additionally N-arylation of azaindoles, in particular 2-substituted azaindoles is difficult.

In 2016, we have developed a practical palladium-catalyzed cascade C – N cross-coupling/Heck reaction of alkenyl bromides with amino-*ortho*-bromopyridines for a straightforward synthesis of substituted 4-, 5-, 6-, and 7-azaindoles using a $Pd_2(dba)_3$/XPhos/t-BuONa system. This procedure consists of the first cascade C − N cross-coupling/Heck approach toward all four azaindole isomers from available aminopyridines. The scope of the reaction was investigated and several alkenyl bromides were used, allowing access to diff erent substituted azaindoles. This protocol was further explored for N-substituted amino-o-bromopyridines.[3]

Due to the interest in 1,2-diaryl azaindoles, we have been working in alternative routes to access these compounds from amino-*ortho*-bromopyridines. In this presentation all our synthetic efforts and achievements on the synthesis of indole bioisosteres will be presented.

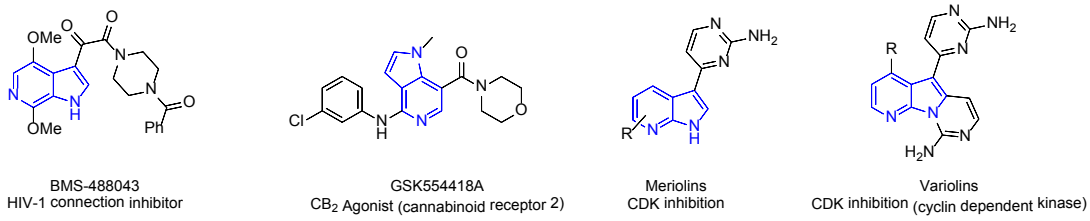

Figure 1: Examples of biologically relevant azaindole-containing compounds

Acknowledgements: We thank to the Fundação para a Ciência eTecnologia for the fellowship SFRH/BD/89518/2012. This work was supported by the Associated Laboratory for Sustainable Chemistry- Clean Processes and Technologies-LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007265). The NMR spectrometers are part of The National NMR Facility, supported by Fundação para a Ciência e Tecnologia (RECI/BBB-BQB/0230/2012).

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Novel triple-stage antimalarial ionic liquids and their effects on lipid membrane models

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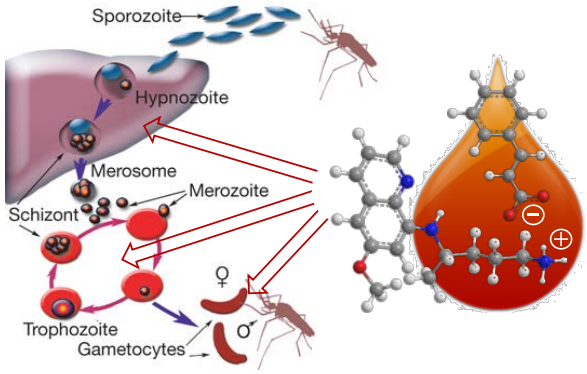
Primaquine-based ionic liquids (IL), obtained by acid-base reaction between parent primaquine and cinnamic acids, were recently found as triple-stage antimalarial hits (**Scheme 1**). These IL displayed significant activity against both liver- and blood-stage *Plasmodium* parasites, as well as against stage V *P. falciparum* gametocytes. Remarkably, blood-stage activity of the ionic liquids against both chloroquine-sensitive (3D7) and resistant (Dd2) *P. falciparum* strains was clearly superior to those of the respective covalent (amide) analogues and of parent primaquine.[1]
Having hypothesized that such behaviour might be ascribed to an enhanced ability of the ionic compounds to permeate into Plasmodium-infected erythrocytes, we have carried out a differential scanning calorimetry-based study of the interactions between the ionic liquids and membrane models. Results provide evidence, at the molecular level, that the primaquine-derived ionic liquids may contribute to na increased permeation of the parent drug into malaria-infected erythrocytes, which has relevant implications towards novel antimalarial approaches based on IL.



Scheme 1. Primaquine-based IL as triple-stage antimalarials hits.

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Combined ammonium and pyridinium zinc(II)phthalocyanines and their photodynamic effect on cell suspensions and biofilms of *Escherichia coli*

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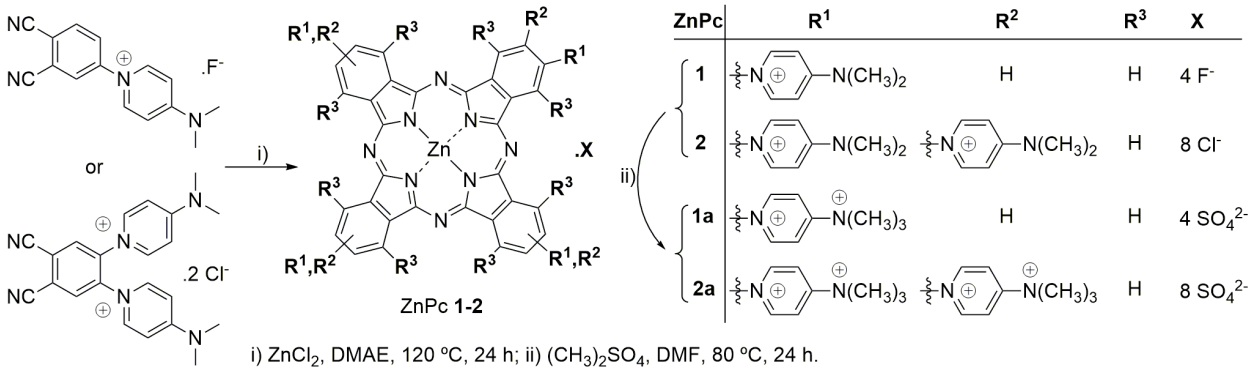
Phthalocyanines (Pcs) are photoactive molecules that can absorb and emit light in a wide range of the UV-Vis spectrum with recognized potential for public health applications.[1] Several Pc molecules have been used as photosensitizers (PSs) in photodynamic inactivation (PDI) of microorganisms.[2] Novel water soluble amphiphilic Zn(II)phthalocyanines (ZnPcs) peripherally substituted with 4-dimethylaminopyridine (DMAP) units (ZnPc **1** and **2**), and the corresponding quaternized derivatives (ZnPc **1a** and **2a**) were synthesized (**Scheme 1**) and characterized. The presence of multi-positive charges on ZnPc derivatives prevent their aggregation and enhance the solubility in aqueous medium. ZnPc **1a** and **2a** exhibited promising singlet oxygen ($^1O_2$) generation and good photostability. The biological assessment toward bioluminescent *E. coli* strain of the amphiphilic ZnPc **1** and **2** and quaternized ZnPc **1a** and **2a** will be discussed.



i) $ZnCl_2$, DMAE, 120 ºC, 24 h; ii) $(CH_3)_2SO_4$, DMF, 80 ºC, 24 h.

Scheme 1

Acknowledgements: Thanks are due to FCT/MEC for the financial support to QOPNA (FCT UID/QUI/00062/2013), CESAM (FCT UID/MAR/LA0017/2013), CICECO (FCT UID/CTM/50011/2013) and CQE (FCT UID/QUI/0100/2013) research units, through national founds and where applicable co-financed by the FEDER, within the PT2020 Partnership Agreement, and also to the Portuguese NMR Network. D.M.G.C.R. (PTDC/QEQ-SUP/5355/2014), C.I.V.R. (SFRH/BPD/85902/2012), N.V.R. (SFRH/BPD/79000/2011) and M.C.G. (SFRH/BD/88334/2012) thanks to FCT for financing their grants. Leandro M. O. Lourenço thanks for the founding support obtained in the FCT Project (PTDC/QEQ-SUP/5355/2014).

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Process Development in Flow Chemistry using Kinetic Modeling

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Process development using flow chemistry takes advantage of the low amount of material required to perform several experiments. The use of kinetic modeling approach is a valuable way to gather deep process understanding while mustering useful information for scale-up at the same time. Kinetics is independent on equipment and manufacturing mode, meaning the data generated previously in batch experiments can be used to build a model that can guide the flow chemistry experiments in the laboratory. Furthermore, kinetic models can be used along the process lifecycle to assist risk evaluation and process troubleshoot.

This batch-to-flow approach was used to convert the manufacturing process of a highly exothermic reaction, not advisable to perform at a large scale in a batch reactor. Data was used to characterize the process, model the reaction and simulate effect of critical parameters.

The success of this approach is currently being applied to other processes that are enabled by the added safety and improved control achieved while working in a continuous setup.

Synthesis of Luminescent Nanoparticles for Drug Delivery and Imaging in Cancer Cells

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Cancer nanomedicines approved so far minimize toxicity, but their efficacy is often limited by physiological barriers posed by tumour environment[1]. Despite the significant advances made until now in the development of advanced nanoscale systems for drug delivery, several key challenges still remain. Luminescent inorganic nanoparticles emerged as a new generation of multifunctional systems with a broad range of applications in drug and gene delivery[2], biomedical imaging[3], photodynamic therapy[4], and photonic crystals. Because of their luminescence these nanocarriers can be easily tracked in biological systems.

Based on such properties, herein we present the synthesis several luminescent inorganic nanomaterials (silver, silica, quantum dots)[5] and their further application and *imaging* in cancer cells, as well as, as drug delivery nanosystems (see figure 1).

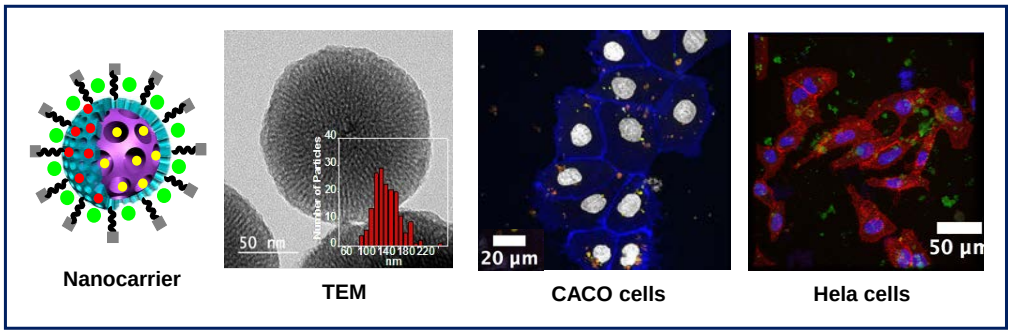

Figure 1: Schematic representation and TEM of a nanocarrier; Imaging of luminescent nanoparticles in CACO and HELA cancer cells.

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Phthalocyanine Labels for Near-Infrared Fluorescence Imaging of Solid Tumors

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Prevention and treatment of cancer are limited by the non-invasive detection capacity of the diseased tissue. Optical imaging has high sensitivity, high contrast and good spatial resolution but imaging for deep tissues remains a challenge due to light scattering and strong attenuation in these tissues. The induced fluorescence endoscopy (IFE) has a higher sensibility than conventional endoscopy to identify precancerous and cancerous lesions of the larynx but insufficient specificity.[1]

Diamagnetic metal complexes of phthalocyanines with n-butoxyl groups in all the α-benzo positions of the macrocycle skeleton, $MPc(OBu)_8$, have strong near-infrared absorptions and intense fluorescences that are Stokes shifted by more than 15 nm, what matches the ideal features for optical probes.[2] Compound $Si(OH)_2Pc(OBu)_8$ has an intrinsic ability to accumulate in the tumor, adequate spectroscopic properties and excellent stability to function as a NIR fluorescent label in the early detection of tumors.[3] Using this phthalocyanine it was possible to detect the fluorescence from a 1 mm 4T1 mouse breast tumor, barely palpable and invisible to the naked eye, located in the mammary fat pad of a mouse **(Figure 1)**.

We are now interested in improving this dye in terms of biocompatibility and tumor specificity through modifications in the periphery of the macrocycle that may improve the biocompatibility and specificity of this family of compounds.

These modifications include polar groups to improve solubility and ligands to improve targeting. This way we may improve the signal-to-noise ratios and open new opportunities for fluorescence imaging of tumors.

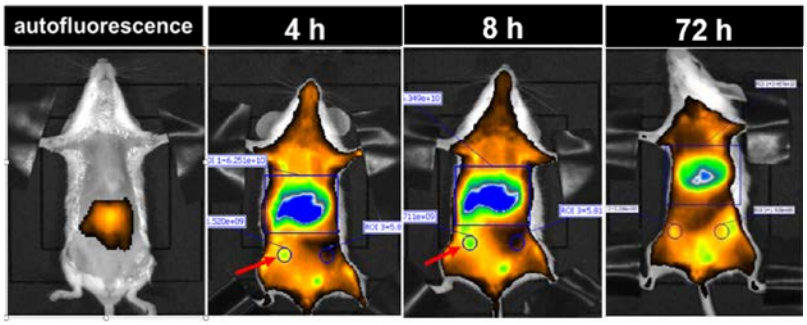

Figure 1: Whole-body fluorescence imaging of BALB/c mice bearing a tumor in the right abdominal fat pad, collected before and after the i.v. administration of 0.2 mg/kg of $Si(OH)_2Pc(OBu)_8$ with excitation at 745 nm and fluorescence emission at 810−875 nm. The times after the administration are presented in the plots.

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Digital Optical Memory Devices based on PDLC Films

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Devices made of PDLCs with permanent memory effect, in addition to be more energetically favorable, can be potential candidates for digital optical memory devices based on write-read-erase cycles. In a multiplexed addressed pixel array, optical elements are formed by PDLC units where voltage can be applied to each unit independently. A robust representation of an optical data storage in a PDLC pixels array is shown in figure 1.[1] In these devices showing bistability, liquid crystal molecules alignment is maintained after the electric field is switched off and each pixel originally opaque can keep its transparency, forming a digital language of zeros (0) and ones (1).[2]

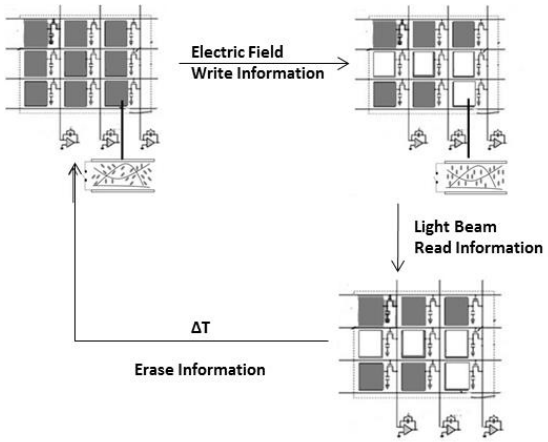

Figure 1: Schematic description of optical data storage using 9 PDLC units with permanent memory effect.

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Generation and Stabilization of Triplet 2-Formyl Phenylnitrene in Inert Cryogenic Matrices

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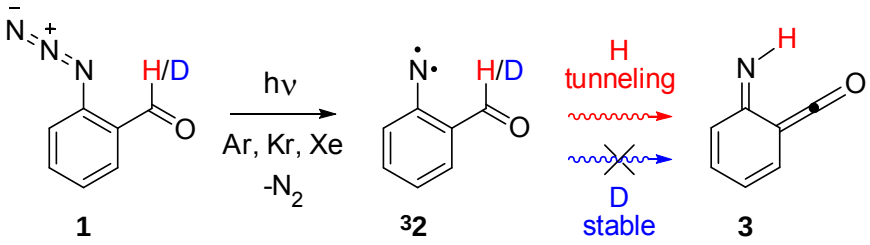
Two isotopologues of triplet 2-formyl phenylnitrene (^{3}**2**, **Scheme 1**), the formyl-protium (red) and its formyl-deuterated (blue) analogue, were generated in cryogenic inert matrices (argon, krypton, xenon) by photolysis of 2-formyl-*h* and 2-formyl-*d* phenylazide (**1**), respectively. The resulting phenylnitrene (^{3}**2**) was characterized by IR, UV-vis, and EPR spectroscopies.[1]



Scheme 1: Photochemical generation of triplet 2-formyl phenylnitrene ^{3}**2** in inert matrices. The protium-substituted ^{3}**2** decays spontaneously. The deuterium-substituted ^{3}**2** is stable.

We found that protium-substituted triplet ^{3}**2** spontaneously rearranges to singlet 6-imino-2,4-cyclohexadien-1-ketene (**3**) in dark, at 10 K (Scheme 1) on the time scale of hours. The observed reaction involves an intramolecular [1,4] H-atom shift. The deuterium-substituted triplet ^{3}**2** was found to be stable under similar conditions. The distinctive behavior of the two isotopologues indicates that it occurs by the tunneling mechanism. The tunneling lifetimes for the H- and D- analogues of ^{3}**2** were estimated theoretically to be tens of minutes and 150000 years, respectively.[1]
Besides the fact that this is the first experimental observation of tunneling in the chemistry of nitrenes, our results also indicate that the aromatic nitrenes are stabilized by introducing heavy-atom substituents at the α-position and could be used as building blocks for preparing new materials. As an example, the photochemical rearrangements of ^{3}**2** and **3** induced by UV and visible light will be discussed.

Acknowledgements:
This investigation has been performed within the Project PTDC/QEQ-QFI/3284/2014 – POCI-01-0145-FEDER-016617, funded by the Portuguese *"Fundação para a Ciência e a Tecnologia"* (FCT) and FEDER/ COMPETE 2020-EU. The Coimbra Chemistry Centre (CQC) is supported by FCT, through the project UI0313/QUI/2013, also co-funded by FEDER/COMPETE 2020-EU. C.M.N. and I.R. acknowledge FCT for Postdoctoral Grant No. SFRH/BPD/86021/2012 and "*Investigador FCT*" grant, respectively.

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BioMOFs targeting antibiotics solubility

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The interest on metalorganic frameworks towards pharmacological applications (BioMOFs) has been increasing, especially for controlled drug delivery and release. However, the coordination of metals can also be an alternative way to induce significant changes in previously known drugs, changing important properties such as solubility and bioavailability, with the further advantage that synergetic effects of the metal can be explored enhancing its performance.[1]

Bactericidal agents, including antibiotics, drastically reduced the number of deaths caused by infections over the last 70 years. However due to their misuse and abuse, many microorganism, specially gram-negative, developed resistance mechanisms and the antibiotics have become less effective. The proliferation of these multiresistant microorganisms is nowadays a major concern and BioMOFs can be useful in this quest.

Nalidixic acid is an antibiotic of broad spectrum of biological applications effective against gram-negative infections, but its oral bioavailability is low due to its poor solubility and slow dissolution. Thus, the development of new forms of this drug that can fill this drawback is of upmost importance. We disclosed new BioMOFs of nalidixic acid with magnesium and manganese and their characterization. These compounds were prepared by mechanochemistry, an efficient and environment-friendly technique.[2] Both BioMOFs have higher solubility than nalidixic itself, with increases over 200% (for the Mn) and 900% (for the Mg). Toxicity tests indicate that these forms are not toxic and that they maintain antibacterial activity. So we demonstrated that BioMOFs can be employed to improve poor aqueous solubility of drug compounds, quite important for drugs whose bioavailability is limited by solubility.

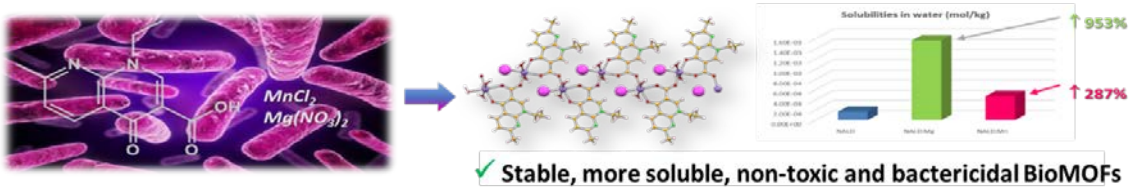

Figure 1: Schematic representation showing evidencing the crystal structures and the solubility increase.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (PEst-OE/QUI/UI0100/2013 and SFRH/BPD/78854/2011)

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Oral Communication

Controversial Thoughts and Advances in Cellulose Dissolution: From Scattering and Rheology to a New NMR Approach

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As the major carbohydrate produced by plant biosynthesis, cellulose occupies a prominent place as a 'green' polymer for the production of innovative and sustainable materials. Unlike other polymers, cellulose is not meltable and therefore most of it applications rely on an efficient dissolution step followed by shaping processes where the properties of the regenerated material are strongly dependent on how well cellulose is dissolved and organized in solution. Cellulose is insoluble in water but can be dissolved in acidic or alkaline conditions, given the proper conditions. However, work in developing new solvents for cellulose has been following a ''trial and error'' empirical character. It is clear that a better understanding of the dissolution of cellulose has deep implications, not least for industrial developments. In the first part of this talk some basic fundamentals will be reviewed together with current perspectives. We will see that hydrogen bonding mechanism alone cannot explain the low aqueous solubility. Our recent work rather emphasizes the role of cellulose charge and the concomitant ion entropy effects, as well as hydrophobic interactions [1-6]. On the second part, a new NMR methodology - Polarization Transfer Solid State NMR (PT ssNMR) – is introduced as a promising technique regarding an efficient and robust characterization of the solution state of cellulose. With this method it is possible to identify the liquid and solid fractions of cellulose, the degradation products, cellulose polymorphs, etc [7, 8]. Finally, combining static light and small angle X-ray scattering we will also probe the effect of cellulose aggregation on solution rheology [9].

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Supercritical-assisted POxylation: Designing new materials for drug delivery and water purification

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Oligo- or poly(2-oxazoline)s (OOxs or POxs, respectively) have been described as biocompatible alternatives to polyethylene glycol, particularly, for drug conjugation and hydrophilization of surfaces. Commonly, oxazoline-based polymers are prepared by a living cationic ring-opening polymerization (CROP) in conventional solvents or using a microwave-assisted synthesis. The possibility to terminate the living oxazolinium species with different nucleophiles enables the construction of OOxs and POxs libraries having specially designed end-cappings. Recently, our group has been investigating the supercritical CO_2 ($scCO_2$) synthetic route for oxazoline-based polymers and their grafting from surfaces. The reported studies demonstrated that OOxs synthesized in $scCO_2$ possess particular features.
This presentation intends to present an up-to-date review of the role of scCO2 on three main applications:
i) development of POxylated systems with enhanced properties for drug delivery and bioconjugation[1];
ii) eco-friendly strategies to assemble surfaces with living OOxs or graft matrices with OOxs;
iii) development of antimicrobial agents[2].
Special emphasis will be put on assembling active devices for the controlled release of drugs or biopharmaceuticals with the ultimate desired properties for drug delivery and also on the development of antimicrobial active devices for water purification (**Scheme 1**). The underlined examples are analyzed highlighting the pros and cons of the $scCO_2$-assisted technologies.

Scheme 1: Synthesis of oligo(2-o apping by conjugation with dendrimers or surface grafting.

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Metals in Ria the Aveiro (Portugal): Perspectives

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Ria de Aveiro is a shallow coastal lagoon, located along the NW of Portugal, with a complex network of inner channels into which industrial and domestic effluents have been discharged during several years. Since several industries were installed around the northern area of Ria de Aveiro the assessment of the contamination by trace-metals was always a matter of concern. Since 1950 the basin has been impacted by the discharge of a mercury-rich industrial effluent coming from a chlor-alkali plant. During several years studies have been performed in the most contaminated areas of the lagoon, to investigate the long term history of mercury inputs to the region, to characterize the dynamics of mercury in the most contaminated areas of the aquatic systems and to evaluate the influence of mercury contamination on the aquatic food chain. However, the assessment of historical contamination in coastal ecosystems like Ria still is an important issue due to less environmental concern at the time that many industries were installed. The main stressors for water quality is the release of industrial wastewaters, containing contaminants such arsenic, lead, mercury and cadmium, which present toxicity even at low levels, have a persistent character in the environment and are classified as priority hazardous substances by the US Agency for Toxic Substances and Disease Registry[1] and by the European Water Framework.

Recently, surveys involving the collection of water, suspended particulate matter, sediments and fishes have been carried out in several sampling places of the entire area of the Ria, monthly and during a one year period of time. Potential toxic elements were measured in all these environmental compartments. Concentrations were generally low, most of the times lower than the quantification limit of the analytical techniques and showed no geographic pattern.

These measurements of metals made in the entire main lagoon, were useful to develop a clear picture of actual level of contamination. Even thought concerns still exists about the future environmental health of the Ria de Aveiro it is clear that the management framework applied in the last years allowed for the recovery of the ecosystem.

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FLASH COMMUNICATIONS

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A NMR approach to characterise guanidino group of arginine side chains at macromolecular protein interfaces

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Arginine (Arg) side chains are important for protein function because the terminal guanidino group is generally positively charged in proteins due to its high pKa moreover it contains five possible hydrogen bond formation sites (**Figure 1**). Such features drive the formation of bidentate salt bridges with carboxylates and phosphates[1], cation-π interactions with aromatic rings[2] and hydrogen bonding networks with side-chain groups as well as with backbone carbonyl oxygens[3]. Thus, Arg residues can serve two main functions: structural and functional. Structural Arg residues contribute significantly to the maintenance of protein's native structure supported by their higher prevalence in thermostable proteins. Functional Arg residues act at active sites or at interaction interfaces[4]. For example, in DNA- and RNA-binding proteins[5,6], phosphate binding modules (SH2 domain[5]), receptors[6], and in many enzymatic active sites to bind and orient substrates or cofactors[7]. Arg residues that form interactions of any kind via their guanidino group experience a restriction rotational motion around the N_ε-C_ζ bond. Such feature can be used to measure the strength of the interaction network. Thus, a method to quantify the N_ε-C_ζ rotational dynamics of Arg side chains will allow greater insights into the range of processes that Arg side chains are involved in. Taking that, we develop a new NMR methodology to quantifiy the N_ε-C_ζ rotational dynamics allowing though the exploration of the interactions of the guanidino group amines under physiological conditions. The method relies on ^{13}C-detection and either D-evolution or longitudinal exchange and it is suitable for the Arg amine groups whose protons exchange rapidly with the solvent. Free Arg and 2D longitudinal exchange experiments were used to cross-validate the new D-evolution method and showed that accurate exchange rates can be obtained (**Figure 1**). Our method gives good results for exchange processes that take place in the slow intermediate to fast intermediate scale (ms range), while the longitudinal exchange experiment is applicable when the exchange is between 0.5-40 s^{-1}. An application to the T4L99A protein and the agreement of the measured exchange rates with observed Arg interaction networks in the crystal structure of T4L99A further demonstrates the direct applicability of this method to monitor Arg interactions (**Figure 1**). A comparison of the chemical exchange of Arg residues in the unbound and bound form of a protein in question could shed light on the extent of participation and free energy contributions of individual Arg residues to the interaction. It is envisaged that the new method would be a valuable tool to characterise active sites in enzymes, protein-protein or protein-nucleic acid interactions, where arginine residues are expected to play a crucial role.

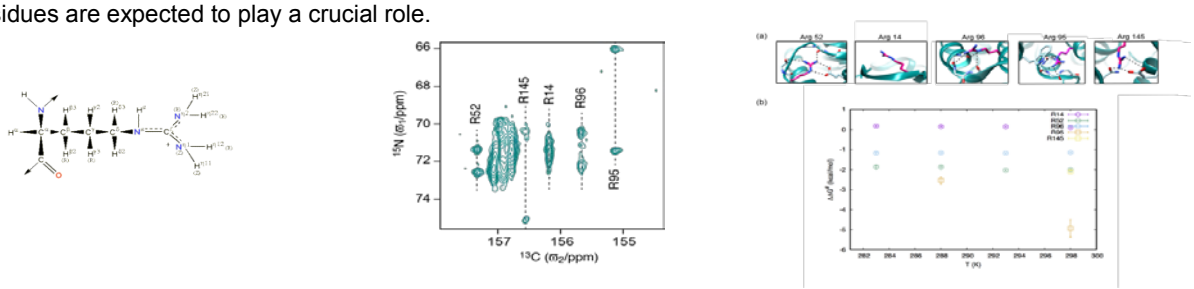

Figure 1: Positive terminal guanidino group in Arg (left); $^{13}C_\zeta$-$^{15}N_\eta$ spectrum of T4L99A at 18.8 T, 298 K (centre); (right) the local environments of Arg in the crystal structure of T4L99A. Hydrogen bonds are depicted as dotted lines. (b) Plot of $\Delta\Delta G^{\ddagger} = \Delta\Delta G^{\ddagger}$(Arg) - $\Delta\Delta G^{\ddagger}$(free) as a function of temperature

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Non-internalizing antibody-drug conjugates release potent cytotoxic agents at the tumor site upon proteolytic linker cleavage

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The use of cytotoxic agents still represents a fundamental pharmacological approach for the treatment of cancer. The conjugation of these toxins to specific antibodies, capable of specific binding tumor-associated antigens, has been proposed as strategy to increase the drug accumulation at the tumor site, sparing normal tissues and leading to better anticancer effects.[1] Although a large number of antibody-drug conjugates (ADCs) are now running clinical trials, only two ADCs have gained market authorization so far, indicating that the current state of the ADC technology is still far from optimal.

In addition to the antibody and drug moieties, the choice of a suitable linker (i.e., the chemical structure responsible for drug release from the immunoglobulin) is fundamental for the therapeutic activity of the ADC product. Both antibodies and linker-payload combinations have often been selected on the basis of their potential to internalize into tumor cells after antigen binding and to be processed by intracellular agents.

However, the strict requirement for antibody internalization has been recently questioned. Our group as shown that non-internalizing ADC products directed against components of the tumor extracellular matrix (i.e., alternatively spliced isoforms of fibronectin and tenascin C) can efficiently liberate their drug in the extracellular milieu, mediating promising therapeutic activity *in vivo*.[2]

The potential of ECM-targeted ADCs has been extensively investigated, and the use of different drug and linker moieties was found to modulate significantly the therapeutic window of non-internalizing immunotoxins (**Fig. 1**).[3]

Our data reinforce the concept that potent payloads can be released from non-internalizing antibodies in the tumor extracellular space, when suitable linkers are used.

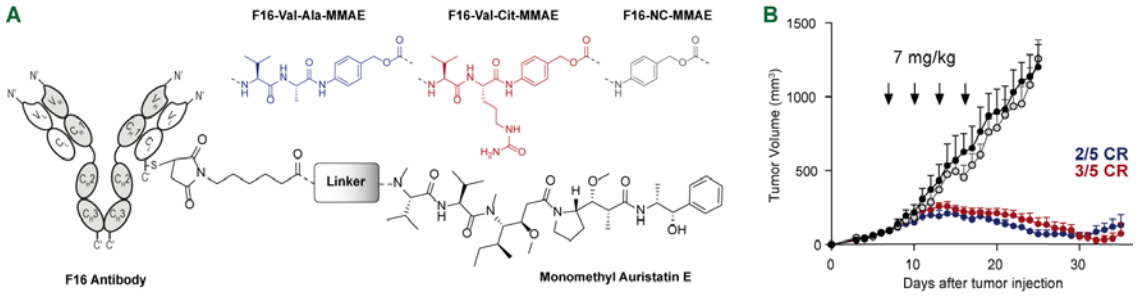

Figure 1: A) Molecular structure of three ADCs composed by the F16 antibody (target: oncofetal tenascin C), monomethyl auristatin E as cytotoxic payload and the Val-Ala, Val-Cit and non-cleavable (NC) linkers. B) Therapeutic activity against A431 human epidermoid carcinoma xenografted in Balb-c nude mice (black: mice treated with PBS).[3]

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Selective, Rapid and Reversible *N*-Terminal Cysteine Functionalisation with 2-Formylbenzeneboronic acids (2FBBA)

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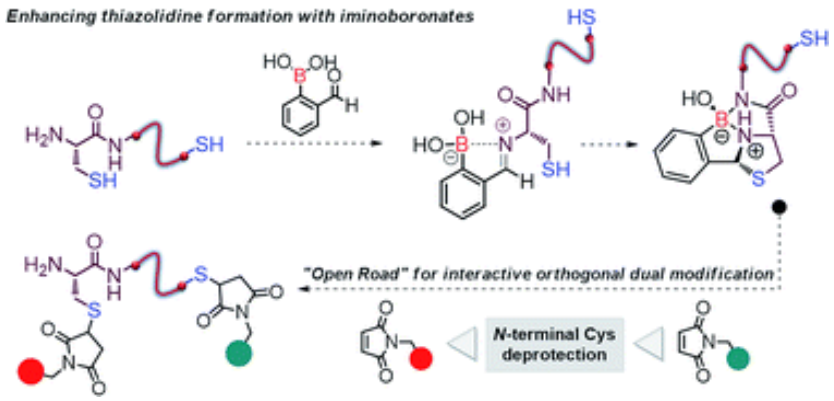
In recent years several methods for facile and selective modification of peptides and proteins were disclosed and become a powerful strategy to study fundamental biological processes, to construct therapeutics and functional hybrid materials without the need for more specialized techniques.[1a]However, among these methods, those that can reversible on command are scarce.[1b]

Recently our group showed that 2-acetyl benzeno boronic acids (2ABBA) reversible functionalize protein exposed lysine residues *via* the formation of iminoboronates.[2] We envisioned that the condensation reaction of aldehydes with *N*-terminal Cys residues could also be significantly improved by generating a transient iminoboronate *en route* to the cyclization (**Scheme 1**).[3]Herein we will demonstrate that this process is fast, selective for *N*-terminal Cys and results in the formation of thiazolidine constructs under mild aqueous conditions. These constructs can be easly reversed in the presence of benzyl hydroxylamine, leading to the deprotection of the for *N*-terminal Cys. The dynamic nature of this system can be used to differentiate between in chain and *N*-terminal Cys residues allowing their selective modification with different maleimide probes (**Scheme 1**).



Scheme 1: Selective for *N*-terminal Cys modification with 2FBBA, allowing an interactive installation of two different maleimides.

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Affinity materials for medical and biotechnological applications

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Over the past 40 years monoclonal antibodies and derived structures became the standard binding proteins representing powerful tools in biotechnology and biomedicine, namely on protein purification. Other protein binding scaffolds, with the robustness and versatility required, have also been explored[1]. We employ biological and chemical combinatorial libraries supported by computational design tools to develop robust peptidomimetics based on different scaffold molecules. The scaffold molecules range from small synthetic ligands, to artificial β-hairpin peptides and small protein domains produced chemically[2–5]. We studied the potential of these scaffold affinity reagents to find binding partners against several targets (e.g. recombinant proteins, phosphorylated peptides, and virus-like particles)[6], to develop affinity-based purification processes, and stimuli-dependent imaging nanoprobes[7]. For these applications, it is critical to combine affinity ligands with several materials, including magnetic nanoparticles and hybrid materials based on biological polymers.

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Smart Polymer Fibers for Stem Cell Cultivation

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Stem cell (SC) therapies are frequently compromised due to problems related to cell recovery from cultivation subtracts. The main goal of this work is to produce stimuli-responsive networks designed from fibers with nano/micro diameters that match the dimensions of the natural niche fibrous proteins where SC inhabit.[1] Electrospinning is a simple and highly versatile method for generating fibers. This technique has attracted tremendous recent interest in both academia and industry, owing to its unique ability to produce ultrafine fibers of different materials in various fibrous assemblies.[2] The desirable smart behavior of this new material is achieved by the presence of copolymer chains of 2-(2′-methoxyethoxy)ethyl methacrylate (MEO2MA) and oligo(ethylene glycol) methacrylate (OEGMA), that are thermoresponsive and especially suitable for biomedical applications.[3]

Here we present a bottle brush like copolymer based in a cellulose acetate (CA) backbone grafted with thermo-responsive polymer chains (P(MEO2MA-co-OEGMA-b-AHMA)). This polymer presents a LCST behavior, resulting in a conformational coil-to-globule transition (CGT) on the polymer chains, thus affecting the solubility upon a temperature stimulus. The thermo-responsive polymer was synthetized by reversible addition fragmentation transfer (RAFT) methodology and was grafted to previously propargylated CA, by a "click-chemistry" reaction (**Fig. 1**).[4] The final product was characterized, by NMR, FTIR and DSC, and turned into fibers (**Fig. 2**), trough electrospinning technique, to produce a thermo-responsive fibrous membrane. The membranes are being characterized by SEM, AFM and submitted to mechanical characterization.

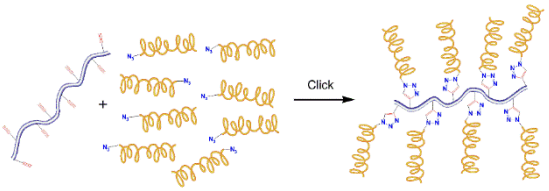

Figure 1: Schematic representation of click-chemistry reaction between azide and propargyl groups

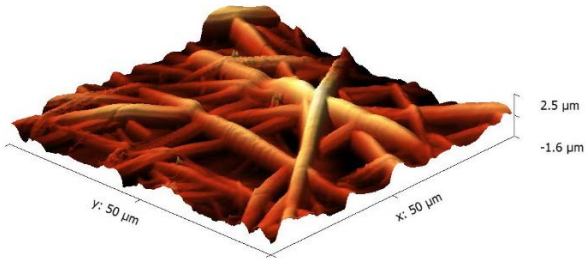

Figure 2: AFM image of fiber morphology

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Recycling of Valuable Metals from Spent End-of-Life Materials: Research on the Liquid-Liquid Extraction of Palladium

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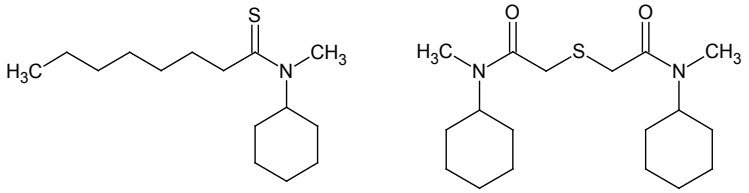
The mineral deposits of platinum-group metals (PGMs) are generally scarce in the earth surface, furthermore being located in specific geographic areas. For instance, South Africa (95%) and Russia (2%) are the almost exclusive primary producers of platinum, palladium and rhodium worldwide.[1]

Due to their extensive applications in several top technological devices such as electrical and electronics equipment and automotive and industrial catalysts, to mention only a few, PGMs are considered critical raw materials; in accordance with the last European Union report on the subject, PGMs are likely to exhibit small deficit supplies in 2020.[2a] To prevent ore exhaustion due to current and short-term industrial demand, the development of PGMs recycling practices from end-of-life materials (the so-called urban mining) is essential, both from environmental and economic points of view.[2b]

When hydrometallurgical PGMs recycling is considered, liquid-liquid extraction is the conventional unit operation usually applied to separate, purify and concentrate these metals from leaching solutions. With the aim of contributing to the development of integrated environmentally-friendly and cost-effective hydrometallurgical processes, the search for innovative extractants to efficiently and selectively recover PGMs from model and real spent catalysts leaching solutions, through liquid-liquid extraction, has been a goal of this research group for more than 10 years.[3,4a,b]

This communication aims to present a summary of the most representative achievements found in literature, and recently attained in the group, regarding palladium recovery from complex hydrochloric acid solutions by liquid-liquid extraction. Two types of diamide derivatives revealed to be adequate to accomplish the efficient and selective separation of palladium, namely *N*-methyl-*N*-cyclohexyloctanthioamide and *N,N*'-dimethyl-*N,N'*-dicyclohexylthiodiglycolamide, *e.g.*, compounds (1) and (2), respectively (**Figure 1**).



(1) **(2)**

Figure 1: Structures of the organic compounds used for Pd(II) extraction from HCl solutions described in this work.

In addition to the assessment of the practical aspects determining their promising performance, *e.g.*, loading capacities and reutilization profiles, the collected distribution and spectroscopic data allowed relevant information about the involved Pd(II) extraction reactions by the two sorts of extractants.[5a,b]

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Magnetic Ionic Liquids - MILs

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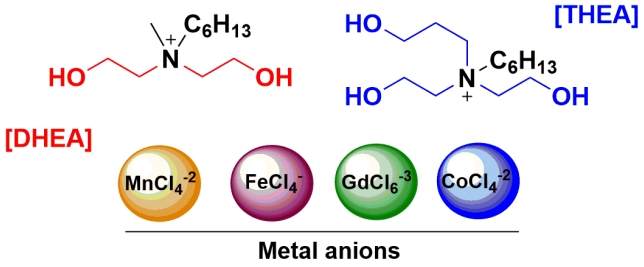
In 2004 was described a new type of magnetic materials based on paramagnetic metal salts - Magnetic Ionic Liquids (MILs). [1] Several MILs have been reported as combination of different organic cations with anionic metal complexes possessing magnetic properties.[2]All presented similar magnetic moments and shown a strong response to external magnetic fields. Although, due to the high propensity to crystalize of the anionic metal complexes, there are only few reported MILs that are liquid at room temperature. When the cation is a strong hydrogen bond donor (like imidazolium based cations), the formation of an organized network of hydrogen bonding is enhanced resulting in a more organized structure. Consequently the crystallization of the salt is enhanced. On the other hand cations that don't have this hydrogen bonding network, such as the bulky tetraalkylphosphonium or tetralkylammonium, have a low tendency to crystalize [3], although these cations can be quite toxic.[4]Different applications have been reported for MILs, for example, in collaboration with this laboratory, Prof Crespo have reported the preparation of supported MILs membranes for CO_2separationand also observed a remarkable reduction of the MILs viscosity in the presence of an applied magnetic field.[5]

In this work is presented a new family of cholinium based ILs (**Scheme**) that are liquid at room temperature, even in combination with paramagnetic anions $FeCl_4$,$CoCl_4$, $MnCl_4$ and $GdCl_6$.[6]We have studied the viscosity of these MILsand it was very interesting to observe that the insertion of one and two ethanol chains([DHEA] and [THEA]) largely decreases the viscosity of the MILs, indeed at 298 K, [THEA]Fe presents a viscosity of 142 mPa s, which is lower than the reported value for $[P_{6,6,6,14}]Fe$, 650 mPa s. Additionally, we have also reported that these new family of MILs are prone to generate low toxicities on human cell lines (even at high concentrations)[4,6]and we have evaluated their ecotoxicity towards the luminescent bacteria *Vibrio fischeri*.[7]



Scheme: Synthesis of Magnetic Ionic Liquids based on cholinium cations.

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Synthesis and physical-chemical characterization of novel anthocyanin-lipophilic bioactives

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Anthocyanins and their derivatives are natural flavonoid pigments present in many foodstuffs that have attracted the scientific community due to both their health promoting properties and appealing colors (from orange to blue). Despite their great interest, there are some drawbacks that have been limiting technological applications of anthocyanins such as their low chemical stability, which is affected by several factors (light, temperature, pH) as well as their low solubility in lipophilic media. One of the approaches followed to increase their lipophilicity consists in introducing long-chain fatty acids in the flavonoid structure. While the structural modification of other flavonoids for technological purposes by chemical and enzymatic methods is widely reported, the derivatization of anthocyanins is practically unknown mostly due to their lower stability, and therefore remains a challenging task.

In this work, novel amphiphilic molecules based on anthocyanin-fatty acid conjugates were developed and characterize in terms of their lipophilicity and antioxidant features (**Figure 1**).[1-4] Ongoing studies of the chemical equilibria of these anthocyanin derivatives in lipophilic models (micellar systems such as anionic SDS, cationic CTAB and neutral Triton) towards pH variations are being performed. The knowledge of the stability of the different species at a wide pH range is crucial to assess their effective application in lipophilic systems such as lipid-based food and cosmetic formulations.

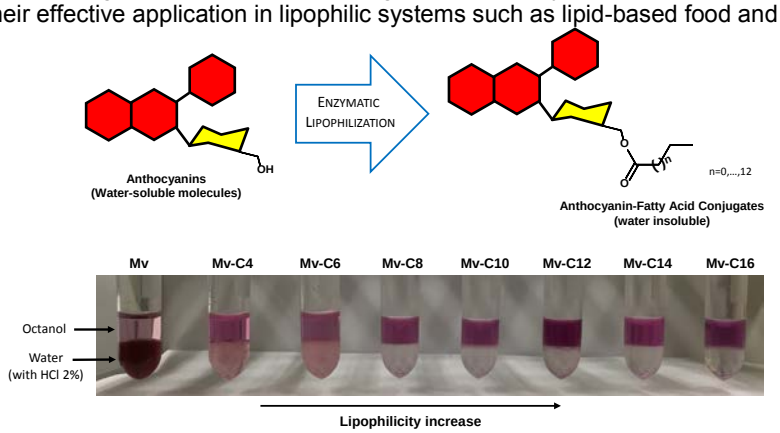

Figure 1. Enzymatic lipophilization of anthocyanins and determination of their lipophilicity.

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Ohmic Heating Assisted Synthesis of 1,3-Disubstituted-quinolin-4(1*H*)-ones by C-C Cross Coupling Reactions in Aqueous Media

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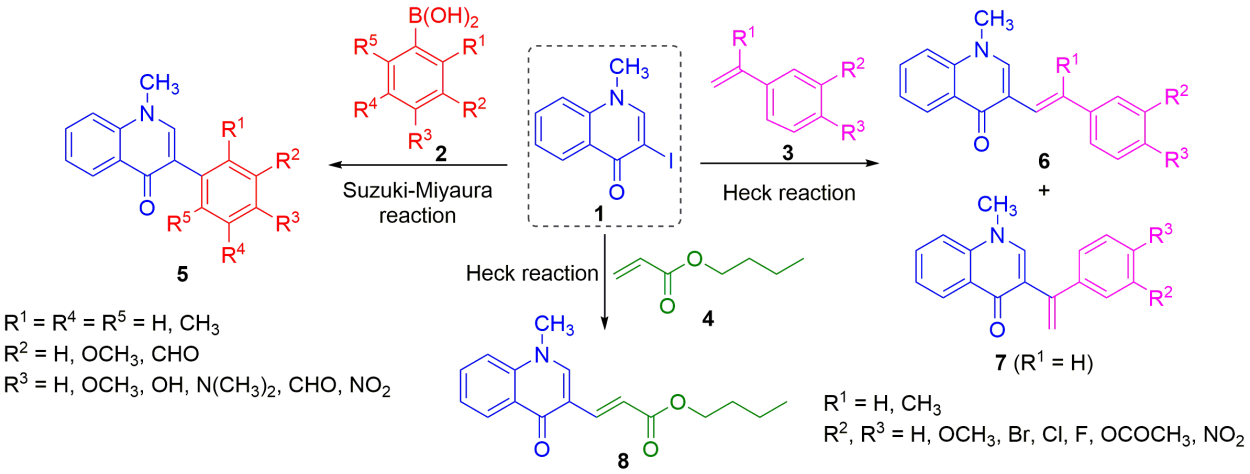
Quinolin-4(1*H*)-one, a common scaffold found in natural products , is considered a privileged structure in medicinal chemistry. In particular, some 3-substituted-quinolin-4(1*H*)-ones have displayed antimalarial activity at low to single digit nanomolar concentrations[1] whereas 3-phenylquinolin-4(1*H*)-one demonstrated an excellent inhibitory effect against AA-induced platelet aggregation, superior to that of indomethacin and aspirin.[2]

In the last years our group has been focused on the development of new and sustainable methodologies for the synthesis of biologically active compounds, including new quinolin-4(1*H*)-ones, using ohmic heating.[3] This is a highly-energy efficient heating method in which heat is generated directly within the reaction medium (by Joule effect) as a result of the passage of an AC electrical current of high frequency through it. Heating is less dependent on the heat transfer step from the surroundings (hot plate) to the reaction medium which results in a fast, volumetric and uniform heating, increased dynamics of charged species in solution, leading to shorter reaction times and better yields.[3]

Herein we present a series of potentially bioactive 1,3-disubstituted-quinolin-4(1*H*)-ones **5-8** which were synthesized following an efficient, ligand-free protocol developed for the C-C cross coupling reactions of 3-iodo-1-methylquinolin-4(1*H*)-one **1** with arylboronic acids **2** (Suzuki−Miyaura reaction),[4] with styrenes **3** and butyl acrylate **4** (Heck reaction)[5] in water, under phase transfer catalysis conditions, using an ohmic heating reactor (**Scheme 1**). Good yields and substrate generality, short reaction time and ease experimental procedures make this method exploitable for the synthesis of several 1,3-disubstituted-quinolin-4(1*H*)-ones for further biological evaluation.



Scheme 1: Synthesis of 1,3-disubstituted-quinolin-4(1*H*)-ones **5-8** by C-C cross coupling reactions using ohmic heating.

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Alpha-glucosidases and cholinesterases inhibition

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The design, synthesis, inhibition and toxicity assays, as well as docking studies (including homology modelling) for *S.cerevisae*'s and Rat (intestinal) α-glucosidases were performed for analogues of deoxinojirimicin (DNJ) and 1,4-dideoxy-1,4-imino-D-arabitol (DAB-1). These studies rendered sensitive information about both ligands and enzymes' structural features and have been reported[1-4].

An interesting structural relation was noted between phtalimide and indolinone derivatives[5], the latter being both acetylcholinesterase and butyrylcholinesterase inhibitors, therefore of strong clinical interest, leading to indolone analogue synthesis, inhibition assays, STD-NMR and docking studies, already reported[6-10]. Our current developments, with emphasis on new docking studies, will be shown here.

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Separation of Nadolol Racemates by Fixed-bed and Continuous Preparative Liquid Chromatography using C18 Columns

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Nadolol is a pharmaceutical drug marketed as a mixture of four stereoisomers, used to treat cardiovascular diseases. However, its prescription is also related with some severe risks such as heart failure. Its chemical structure has three stereogenic centers which allows for eight possible stereoisomers. However, the two hydroxyl substituents on the cyclohexane ring are fixed in the cis-configuration, which precludes four stereoisomers. Nadolol is presently marketed as an equal mixture of the four stereoisomers.

It is well known that pure enantiomer separation is important to control chiral drugs safety. Recently, our research group reported the pseudo-binary separation of nadolol by simulated moving bed (SMB) chromatography using both coated Chiralpak AD and Chiralpak IA immobilized chiral stationary phases (CSP).[1,2] This technology is generally based on the use of chiral adsorbents which must have enough recognition for all the chiral species.

In this work it is proposed an alternative strategy, implementing a first achiral separation step, to be followed by two subsequent parallel chiral separation steps.[3,4] In this first achiral step, C18 columns are used to perform the separation of the two pairs of nadolol enantiomers ("racemate A" from "racemate B") under reversed-phase mode. The C18 achiral adsorbent allows the separation of the two pairs of nadolol diastereomers, i.e., the first racemate (composed by the nadolol compounds 2 and 3) co-eluting in the raffinate, and the second racemate (composed by the nadolol compounds 1 and 4) to be obtained in the extract SMB stream. After this preliminary achiral separation step, two parallel SMB runs must be carried out using a chiral stationary phase to achieve the complete separation of all the four nadolol stereoisomers.

Extensive experimental and simulation results will be presented including solvent screening, measurement of equilibrium and kinetic data, and both fixed-bed and SMB preparative separations.

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De novo computational design of a protein catalyst for the Beckmann rearrangement reaction

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The CHImerASE project aims to create *de novo* enzymes with non-naturally occurring and industrially-relevant catalytic activity. Of particular interest is the Beckmann rearrangement mechanism (BkR), which is widely used in industry as an intermediate step for the production of high-value chemicals. We have developed a computational model of the BkR adapted for biocatalysts and used it to screen and design a set of candidate protein scaffolds using the Rosetta software package.[1] Extensive analysis of the designs allowed to evaluate their potential catalytic proficiency based on a set of catalytic descriptors (**Figure 1**). For this, we used an active Kemp Eliminase design (KE07)[2] as a control to guide the selection of the best putative scaffolds (SID1s). A set of 11 sequence variants of SID1 scaffold have been experimentally characterized and showed no detectable catalytic activity. We are now increasing our set of candidate scaffolds and employing additional computational methodologies to characterize them, such as molecular docking, molecular dynamics simulations and catalophores.[3] By integrating these computational methodologies we aim at developing improved catalytic predictors of the proficiency towards BkR for a given scaffold and thus speed up the development of efficient biocatalytic systems for industrial processes.

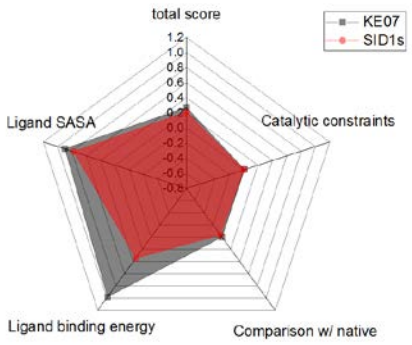

Figure 1: Comparison between active (KE07) *vs* inactive (SID1s) computational designs based on Rosetta descriptors of catalytic activity.

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Characterization of the Chemiexcitation Step of Marine Imidazopyrazinone Chemiluminescence

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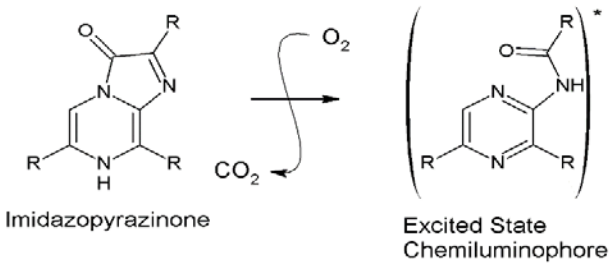
Chemiluminescence is a process in which thermal energy is converted into excitation energy due to a chemical reaction.[1] This is a widespread process in nature, particularly in marine species. While there are more than 700 *genera* known to produce chemiluminescence, ranging from fireflies to fungi, about 80% of luminescent organisms (as bacteria and fishes) reside in the ocean. The majority of marine species use imidazopyrazinone-based compounds as chemiluminescent substrates, as their oxidation result in excited state emitters (**Scheme 1**).[1]

Given very attractive properties (as high quantum yields, no excitation source, sensitivity, etc.), imidazopyrazinone-based systems have gained several health-related applications. These compounds have been tested as excitation sources in photodynamic therapy (PDT) of cancer, opening the door for self-illuminating PDT approaches.[1] These compounds have also been used as reactive oxygen species (ROS) probes, which are potential biomarkers for diabetes mellitus, and play significant roles in several chronic diseases including cancer, inflammation and aging.[2]

Inspired by these applications, we aimed to the elucidation of the chemiexcitation step of imidazopyrazinone-based chemiluminescence. Such knowledge is essential for the development of novel health-related applications and the improvement of existent ones. This was achieved by a combined spectroscopic and theoretical in-depth analysis of different imidazopyrazinone compounds.[3-5] Chemiexcitation occurs due to the stepwise-biradical thermolysis of a dioxetanone intermediate. It was also found that chemiexcitation is achieved with both the neutral and anionic form of the dioxetanone intermediate. However, this process is more efficient with the neutral form, as this species decomposes by homolytic bond cleavage with limited charge/electron transfer, which gives access to a region of the reaction energy surface where the ground and excited states are nearly-degenerated. Analysis of the substituent effect provides information as to how to improve the chemiexcitation yield of new chemiluminophores.



Scheme 1: Representation of the chemiluminescent reaction of imidazopyrazinone compounds.

Acknowledgement to projects PTDC/QEQ-QFI/0289/2014, NORTE-01-00145-FEDER-000028 and POCI-01-0145-FEDER-006980.

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Development of Chemistry Education Research in Portugal: The Emerging Picture from the Papers Published in the *Journal of Chemical Education*

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Chemistry is a central science with a pivotal role in the resolution of the major challenges facing modern society, such as global climate change, alternative sources of energy, sustainable production, world hunger, and the need for new and improved drugs.

Chemistry Education Research (CER) has the crucial task of translating the recent discoveries in the field of chemistry into the classroom, in the form of lectures, demonstrations, and/or laboratory activities, motivate life-long-learning and promote competency-based knowledge, with experimentation being at the heart of Chemistry and Chemistry Education. Current challenges and opportunities of teaching and learning Chemistry in the 21st century include implementation and consolidation of research-based teaching practice, the globalization perspective, and the growing role of new technologies in CER – from the use of the Web to Chem Apps on tablets and smartphones – not only in the delivery of information but also in enhancing conceptual understanding in Chemistry.[1] Chemistry Education has thus become a global endeavour leading to changing perspectives in the Chemistry Curriculum both at the High School and at the University level that calls for innovative strategies, original educational laboratory experiments and introduction of new technologies and modern instrumentation into the educational laboratory setting.[2]

This communication focuses on the development of research in Chemistry Education in Portugal through a content analysis of the CER papers published in the *Journal of Chemical Education* in the new millennium (from 2000 to 2017), ranging from reports on classroom and laboratory practices to educational research, mainly at the undergraduate level.[3]Researching and writing a CER manuscript is a major effort and the main features required for a successful outcome in the publication process will also be addressed based on the author's own experience.[4]

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Flash Communication

Science outreach activities from early grades to high school

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The dissemination of science to pre-university students has become increasingly frequent. However, this disclosure to the public, and to young people in particular, is also extremely important as it allows to stimulate the development of a scientific culture in general. As far as children are concerned, this is more like a long-term bet, but if we can simply contribute to a better understanding of the surrounding world, it's already rewarding. This has been the premise of Química para osmaisNovos, a scientific experiments column published since 2011in QUÍMICA, the Portuguese Chemical Society bulletin.[1]

Aiming at older students and the execution oflaboratorial chemistry classes, alternative strategies have been proposed such as the use of smartphones in substitution of lab equipment. At the present time smartphones are an almost constant presence and as such we can take advantage of their sensors. Several possible applications will be highlighted where smartphones can be used as colorimeters, spectrophotometers or microscopes.[2]

Acknowledgement to projects PTDC/QEQ-QFI/0289/2014, NORTE-01-00145-FEDER-000028 and POCI-01-0145-FEDER-006980.

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HEALTH CHALLENGES POSTER COMMUNICATIONS

XXV ENCONTRO NACIONAL
Sociedade Portuguesa de Química

Determination of fluoxetine in hair by high-pressure liquid chromatography with fluorescence detection

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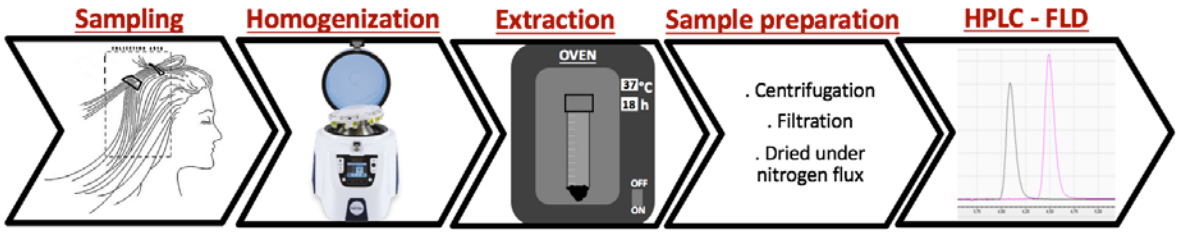
Blood and urine are the most common matrices used for the detection of toxic or illicit drugs. However, blood collection can only be carried out by invasive procedures, urine is a biological fluid known by a high risk of adulteration and the analysis of both matrices has a small detection window, of only a few days. The use of hair as an alternative biological matrix for toxicological analyses has several advantages, namely the non-invasive collection procedure, the sample resistance to adulteration and the possibility of monitoring time and extent of drug exposure depending on hair length [1]. Moreover, hair analysis can also provide a retrospective history of an individual's drug use. These properties are particularly important in a wide variety of clinical and non-clinical situations including doping control in athletes, driving license renewal, drug-facilitated crimes, *postmortem* investigations or the use of illegal drugs by expectant mothers [2].
In this context, a screening methodology for detection of fluoxetine in hair was developed. Briefly, the analytical procedure consists on sampling and homogenizing hair samples using a mixer mill [3], followed by solid-liquid extraction with a mixture of methanol:acetonitrile:ammonium formate (pH 5,3) [4] and analysis of the organic extract by HPLC with fluorescence detection (**Scheme 1**).
Considering the goals of the study, patients under psychiatric treatments with fluoxetine were selected to supply hair samples. The results obtained show that fluoxetine is present in these patients' hair, suggesting that the adopted methodology has the potentiality to be implemented in routine analysis.



Scheme 1: Hair as an alternative matrix in bioanalysis.

Acknowledgements: This work was financed by the European Union (FEDER/COMPETE) and FCT (UID/QUI/50006/2013).

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A quality-by-design approach for the understanding of the effect of model antigen mannose on PLGA nanoparticles

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The incidence of melanoma is growing at a faster rate than practically all other cancers. The reduction of this incidence through improved methods of early detection and prevention of melanoma will be the responsibility of clinicians. Traditional forms of treatment demonstrate severe side effects and do not target tumour cells. Thus, there is a need for innovative therapeutic strategies such as nanoparticle-based therapeutic vaccine, which target tumour cells and are immunotherapeutic.[1]

Poly (lactic-co-glycolic acid) nanoparticles (PLGA NPs) containing mannose (MAN) as model antigen with polyvinyl alcohol (PVA) or d-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) and labelled with cyanine5.5 carboxilic acid (Cy5.5) prepared by double emulsion with solvent evaporation technique were investigated for suitability as advanced drug delivery system. To modify physicochemical characteristics of nanoparticles, variations were made in several properties including the amount of incorporated mannose in the internal aqueous phase. Implementing a quality-by-design approach for the development of NPs is step towards a more robust manufacturing process ensuring that quality is sustained. Average size (Z-ave) and polydispersity index (PdI) were assessed by dynamic light scattering (DLS) and zeta potential (ZP) was determined by laser doppler velocimetry. Nanoparticle Z-ave varied from 184.6 to 194.0 nm and surface charge varied from -2.51 and -1.09 mV. For a better understanding of critical process parameters and critical quality attributes, a multivariate modelling approach was used. Factors such as the percentage of mannose and different responses (Z-average, PdI, ZP) were correlated. A causal predictive model showing the importance of all factors and their interactions was established. A design-space was created resourcing to the developed models considering target properties of the nanoparticulate system.[2]

Acknowledgments: Authors would like to acknowledge Fundação para a Ciência e Tecnologia, Ministério da Ciência e Tecnologia for the iMed.ULisboa grant UID/DTP/04138/2013.

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Bioactivation of the anti-HIV drug etravirine to reactive metabolites: *in vivo* and *in vitro* approaches

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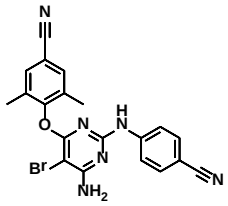
Etravirine, (ETV, **Figure 1**), approved by the US FDA in 2008, was the first second-generation Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) to reach the market. The conformational flexibility of ETV enables this drug to inhibit HIV-1 strains carrying common NNRTI-resistance mutations, which makes it a therapeutic option for HIV patients who developed resistance to the first-generation NNRTIs. Additionally, ETV came into market aiming to overcome some adverse effects associated with the previously used efavirenz (neurotoxicity) and nevirapine (hepatotoxicity) therapies. Nonetheless, post-marketing reports of severe ETV-induced skin rash and hypersensitivity reactions (HSR) have prompted the U.S. FDA to issue a safety alert.[1] Since patients who start ETV-based therapies are typically debilitated by a history of virus resistance and previous drug-induced side effects, administration of a potentially toxic drug must be considered carefully. The development of reliable prognostic tools for early risk/benefit estimations is therefore urgent.

The reasons for the toxicological events associated with ETV administration are currently unknown; however, similarly to what happens with other therapeutic drugs, metabolic activation to reactive electrophiles is likely to be involved in the initiation of toxic responses. To search for potential bioactivation pathways, high resolution mass spectrometry-based metabolomics approaches were integrated with MS^3 experiments for the identification of potential ETV bioactivation pathways. Two distinct strategies were followed: 1) *in vitro*, upon incubation of this NNRTI with human and rat liver S9 fractions in the presence of Phase I and II co-factors and glutathione, as a trapping bionucleophile; and 2) *in vivo*, using urine samples from HIV patients on ETV who gave their informed consent following approval from the Ethic Committee of Hospital Prof. Doutor Fernando Fonseca. We obtained evidence of multiple bioactivation pathways leading to the formation of covalent adducts with glutathione and *N*-acetyl-*L*-cysteine. These results suggest that similar reactions can occur with cysteine residues of proteins, supporting a role for ETV bioactivation in the onset of the toxic effects elicited by this anti-HIV drug.



ETV

Figure 1. Etravirine.

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Ionic Liquids as functional ingredients in Lipidic Implants

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Ionic liquids (ILs) can be placed in water, oils, or hydroalcoholic solutions and thus they may be used as functional ingredients for the development of pharmaceutical and cosmetic formulations, by increasing drug solubility and influencing drug release.
Since lipid implants may provide drug protection as well as accurate and targeted release, they present an enormous potential as parenteral controlled drug delivery systems. However, they may present inflexible drug release profiles and it is crucial to find ways to overcome this drawback.
The aim of this work was to study the effect of an ionic liquid (IL), at non-toxic concentrations, in the release profile of two model drugs from lipid implants, a hydrophilic and a lipophilic drug. The studied IL was (2-hydroxyethyl) trimethylammonium-L-phenylalaninate [Cho][Phe].
Several implant batches were produced with a drug content of 10% (w/w) and containing Dysasan; Dynasan:Gelucire; Dynasan:Sucrose; Dynasan:Gelucire:IL or Dynasan:Sucrose:IL.
The results showed a good content uniformity and a satisfactory homogeneity in all batches, for both actives.
In general results showed that the presence of the IL enhances drug release. Furthermore, implants containing Dynasan:Gelucire:IL presented higher drug release rates when compared with the implants containing sucrose.
Hence results indicate that ILs may act as functional ingredients since they influence drug release and may thus aid in achieving the desired drug release profile.

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Semisynthetic derivatives of monoterpene natural compounds: preparation and evaluation of cytotoxicity

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Research on natural products continues to explore a variety of lead structures, which may be used as templates for the development of new drugs.
There is an enormous variety and quantity of monoterpene compounds which have given evidence of their biological effects by acting as antibacterial, sedatives, anti-tumor and anti-inflammatory agents.[1]
Carvone is a monoterpenic compound found naturally in many essential oils from a variety of plants, being abundant in plants as caraway, dill and mint. This monoterpene appears in nature in its enantiomeric forms: R-(-)-Carvone and S-(+)-Carvone, and has proven its potential pharmacological effects, as well as some of its semisynthetic derivatives.[2]
In this work, we synthesized some derivatives of both isomers of carvone (isomer R and S). Initially, we obtained epoxy derivatives (resulting from the oxidation of exocyclic double bond or α,β – unsaturated ketone), which was opened, both by reductive conditions and by means of nucleophiles. We obtained several derivatives with the epoxide function, alcohol function and ether function, besides the ketone and double bond function observed in the carvone enantiomers.
In the second part of this work, we evaluated the cytotoxicity profile of the semisynthetic derivatives of carvone previously obtained. For this, the murine macrophage cell line, RAW 264.7, was cultured in the presence of various concentrations of the test compounds and cell viability assessed by the method of resazurina reduction. The results obtained were used to set up structure-activity relationships regarding the cytotoxicity potential of the carvone derivatives obtained. We studied the compounds at the concentrations of 12.5, 50 and 200 μg/mL and it was observed that compounds having an epoxy group in their structure exhibit the highest cytotoxicity at concentration of 200 μg/mL. These results establish the basis for future pharmacological studies of these compounds, namely as anti-inflammatory agents.

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Mass Spectrometry Methods for Phenolic Compounds Identification

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Liquid chromatography coupled to mass spectrometry (LC-MS) is an extremely versatile analytical technique, since it combines the power of chromatography separation with the capacity of mass spectrometry identification.[1] Electrospray ionization is a preferred source due to its high ionization efficiency for the majority of chemical structures, such as phenolic compounds.[2]

Phenolic compounds are associated with the prevention of several health conditions, including cardiovascular diseases, diabetes, cancer and stroke.[3] These compounds are present in vegetables, fruits and beverages, such as blueberries, strawberries, tea and wine. Phenolic compounds can be mainly divided in four classes: phenolic acids, flavonoids, stilbenes and tannins.

The objective of this work was to create a database of phenolic compounds through the analysis of different standards by LC-MS and direct infusion in positive and negative ionization modes. The equipment used was a HPLC Surveyor Plus coupled to a LCQ Duo ion trap mass spectrometer equipped with an ESI source from Thermo Scientific (**Figure 1**). Phenolic compounds were chosen due to their recognized importance in the scientific community including our group (GEMAB, Faculdade de Ciências, Universidade de Lisboa, Portugal).

Figure 1: Liquid chromatograph coupled to mass spectrometer.

Acknowledgements: This work was supported by projects UID/MULTI/00612/2013 and REDE/1501/REM/2005 from Fundação para a Ciência e Tecnologia.

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Synthesis of New Curcumin Analogues with Potential Biological Properties

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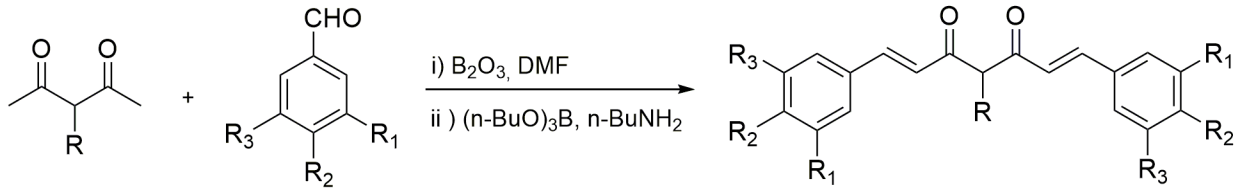
Curcumin, the most active component of turmeric (extracted from *Curcuma longa*), has been used in traditional and Ayurvedic medicine for thousands of years. This compound has numerous pharmacological properties such as anti-inflammatory, antioxidant, antibacterial, antifungal, anticancer, antiviral, among others. One of the little known therapeutic properties of curcumin is as anti-diabetic, reducing glycemic and hyperlipidemia in rodent animals.[1] Furthermore it is quite safe and inexpensive, but highly insoluble and instable in aqueous media. [2]
In order to try the improvement of properties of curcumin as a potential antidiabetic agent and also to increase its solubility and stability in water, curcumin analogues with amino and carboxylic groups in the curcuminoid structure were obtained following the synthetic strategy presented in **Scheme 1** and characterized by the usual spectroscopic and X-ray techniques. Solubility and stability studies in buffer solutions were also performed.
The introduction of the hydrogen bond donor groups in the curcumin skeleton also facilitates the use of cocrystallization techniques in order to improve the physicochemical properties of the synthetized compounds specially the solubility in water.[3]



Scheme 1: General synthetic strategy for symmetric curcuminoid derivatives.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (project UID/QUI/00100/2013) and the IST-UL NMR Network for facilities.

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Design and synthesis of novel multi-targeted directed triazene based hybrid molecules as potential anticancer agents

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Hybrid molecules with combined functionalities can be rationally designed to achieve synergistic effect for efficient cancer treatment. Triazenes are DNA–alkylating agents particularly useful in the treatment of metastatic melanoma and glioma.[1,2,3] However, the high toxicity and lack of selectivity and resistance, severely limits their therapeutic application. Combination of triazenes with homologues of tyrosine (sulfur, sulfuramine and others) will produce hybrid molecules that are expected to overcome these drawbacks.

Herein we reported the synthesis of novel triazene hybrid compounds simultaneously acting on two targets, and selectively activated by tyrosinase in tumour cells. Compounds are also expected to possess better potency and less toxicity than the parent compounds. The optimization of the conventional method for the synthesis of N-heterocyclic triazenes and the *in vitro* anticancer properties of these compounds will also be presented.

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Structural insights on immune checkpoint blockade: An *in silico* strategy towards cancer immunotherapy

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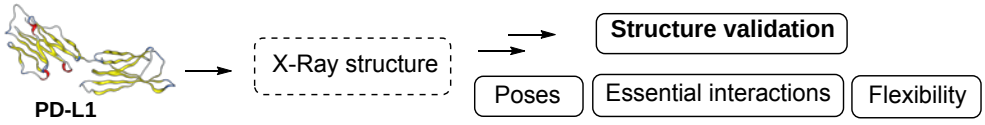
Immunotherapy is nowadays a powerful strategy in cancer therapy. Several approaches to activate antitumor immunity have been reported. In particular, blockade of immune checkpoint receptors have shown very exciting outcomes. Immune checkpoints are immune regulators that limit proliferation and activity of T cells and other immune cells enrolled in these signaling pathways. Under normal conditions, they are essential in maintaining self-tolerance and ensuring adequate duration and amplitude of physiological immune responses in peripheral tissues, avoiding collateral tissue damage[1]. However, they are also one of the major mechanisms used by tumors to evade immune system recognition and destruction. Thus, blockade of immune checkpoints enhance the function of T cells. To date several immune checkpoint receptors have been identified and used as therapeutics in oncology. Programmed cell death protein 1 (PD-1) is one of them, with enthusiastic clinical outcomes in the treatment of melanoma patients. When engaged by one of its ligands (PD ligand 1 (PD-L1) and PD ligand 2 (PD-L2)), PD-1 limits autoimmunity being a major immune resistance mechanism within the tumor microenvironment. The use of immune checkpoint targeting agents in cancer immunotherapy was encouraged by finding that PD-1 ligands are upregulated in distinct human cancers and their blockade could lead to activation and expansion of T cells and therefore enforce tumor recognition[3]. 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. The new antibody therapies are demonstrating impressive activity. However, despite their outstanding success, they still have numerous disadvantages, including severe side effects and low response rates.
Recently, the hypothesis of small-molecule modulators as safe therapeutic alternatives has been raised[3]. However, limited efforts have been directed to the development of small molecules toward these targets in part due to limited structural information. Here, we report a detailed structural characterization of PD-L1 based on *in silico* studies. From the crystal structures available on Protein Data Bank of PD-L1, we addressed the relevant structural features that are essential for the development of new checkpoint inhibitors, such as structural flexibility, gating and binding pockets (Scheme 1). Molecular docking and molecular dynamics simulations will be performed and results will be discussed.



Scheme 1: General approach.

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Synthesis of asymmetric 1,3-diazetidinediones as inhibitors of HNE to target COPD

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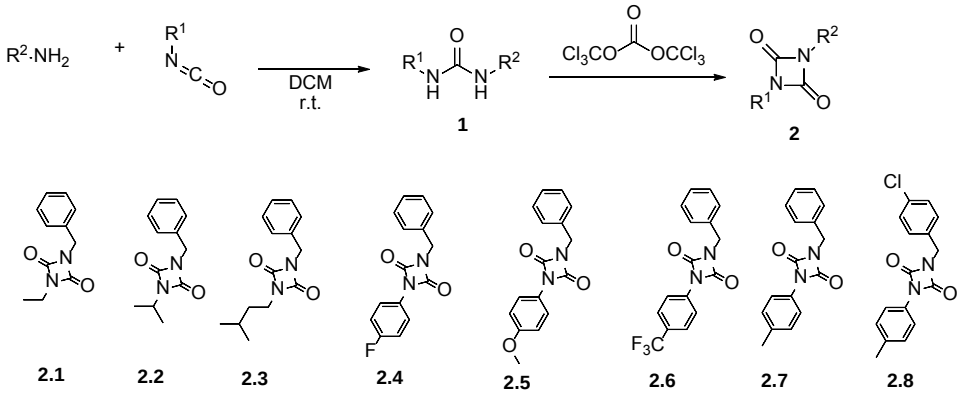
Chronic Obstructive Pulmonary Disease (COPD) is a noncurable lung disease and it is one of the fastest growing causes of death, however current treatment strategies aim only at improving symptoms. No specific assessment tool or biomarker for COPD condition has been developed and validated to date.[1] Human neutrophil elastase (HNE) is an important serine hydrolase in the development of COPD. It is a serine protease released by neutrophils in sites of inflammation as a defence mechanism, assisting the neutrophil in its migration to the site of inflammation and participating in the destruction of pathogens.[2] Several compounds have been studied as inhibitors of HNE, in this field there is a focus in study of lactams derivatives as inhibitors of HNE and as based to build activity-based probes.[1] In this context 1,3-diazetidinediones (DazD) were studied as inhibitors of some important enzymes, between them HNE, and show interesting results.[3] However only symmetric DazD are described in the literature, so this study has as an objective the synthesis of asymmetric DazD. During this study, a novel synthethic strategy was developed with aim to synthesize several asymmetric DazD. This strategy is based on a cyclization using a urea and triphosgene to obtain a 4-membered ring. The urea allows a large structural diversity, changing the substituent group between aromatic and alkyl. After the synthesis of the group of compounds 2 they will be tested as inhibitors of some important serine hydrolases. **(Scheme 1)**



Scheme 1.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia, Portuguese Agency for Scientific Research for financial support through the project PTDC/BBB-BEP/ 2463/2014.

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Nucleoside based N-Heterocyclic Carbenes: Base-Pairing Effects of Carbene Formation

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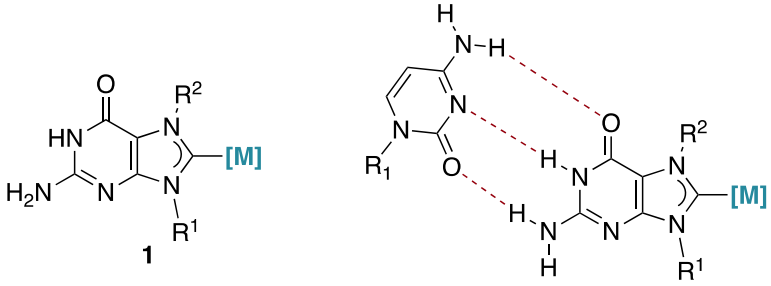
Nucleic acid damage induced by alkylation is a process by which a nucleobase is modified by the introduction of an alkyl group at a specific position of the purine/pyrimidine.[1] This process is induced by endogenous or exogenous sources and is a central modification of the genome involved in the regulation of cellular processes, from epigenetics to the formation of carcinogenic mutations.[2] Once formed, most adducts bear a positive charged due to the quaternization of one of the nitrogens of the nucleobase and show an enhanced reactivity, which can induce modifications on DNA structure and functions. From an organometallic chemistry perspective, alkylated nucleobase adducts are N-heterocyclic carbene (NHC) precursors with a very labile C-H bond. In fact, NHCs are proposed as intermediates in a variety of processes occurring during DNA damage, but their active role in these processes is nevertheless poorly understood. We have examined the formation of NHCs within nucleosides, stabilized by palladium and platinum, and evaluated their stability, behavior in solution and base-pairing properties. These results will be discussed in this communication.



R_1= ribose, desoxyribose
R_2= H, Me
[M]= $Pd(PPh_3)Br$, $Pt(PPh_3)Br$

Figure 1: Metallated guanine adduct **1** and corresponding aggregate with cytosine.

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Cork polyphenols, an alternative strategy against amyloid-beta fibrillization

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Alzheimer disease (AD) is a genetic-based neurodegenerative disorder characterized by progressive impairment in memory. Aging is the primary cause behind the increase in the prevalence of neurodegenerative disorders (where neural cells suffer functional or sensory loss). The hallmark of AD is the presence of amyloid beta peptide in senile plaques and the presence of neurofibrillary tangles.[1] Natural polyphenols with pyrogallol and galloyl groups present in several natural tea catechins, has been referred as effective against peptide aggregation and as a promisimg protector of neuronal loss in AD patients.[2]

Based on these knowledge, we extracted and purified natural polyphenols from cork (e.g. castalagin and vescalagin) and we tested them for their antioxidant activity (AO) and capacity to inhibit amyloid-beta fibrillization. We found that the isolated polyphenols present a AO similar to other natural polyphenols (e.g. EGCG) and are able to inhibit the aggregation/fibrillization of amyloid-beta.[3]

Our results confirm that cork polyphenols, such as, castalagin and vescalagin, while presenting AO in vitro, are also able to rescue the metabolic activity of SH-SY5Y human neuroblastoma cells in the presence of Abeta42. These polyphenols also inhibit amyloid-beta fibrillization, as shown in aggregation assays monitored by circular dichroism, fluorescence spectroscopy, electron microscopy and atomic force microscope. We observed a concentration-dependent decay of Abeta42 fluorescence that paralleled a significant aggregation decrease monitored by electron microscopy and atomic force microscopy. Most importantly, castalagin and vescalagin rescued SH-SY5Y cells from Abeta42-induced cytotoxicity, favoring higher cell viability than epigallocatechin gallate (EGCG). Based on its powerful antioxidant and anti-fibrillization properties we suggest these polyphenols might used as part of a treatment strategy for AD.

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Extracts and new derivatives of anthocyanins as potential cosmetic ingredients – *a skin-barrier model optimization using ECIS*

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There is a growing market demand for the incorporation of plant-derived ingredients in new products of the cosmetic industry. Anthocyanins are polyphenols arising from plant secondary metabolism that have been shown to display many bioactive properties such as free radical scavenging, metal-chelating, antimicrobial, wound healing and chemopreventive activities.[1] The ability to prevent oxidative damages has led to the incorporation of natural bioactives in lotions and facial creams to prevent skin diseases and premature ageing,[2] therefore the biological activities of anthocyanins make them potential novel compounds for cosmetic formulations. However, native anthocyanins present a low solubility in lipophilic media, which compromises their effective application.

In this work, anthocyanins from industrial wastes were recycled and used in their genuine forms. Enzymatic lipophilization was performed by addition of selected chain fatty acids [3,4] to improve their solubility in lipophilic systems. Their biological activities were then assessed by developing a new skin barrier model using keratocytes living cells (HaCat cell line). This model was developed by monitoring continuously the behavior of HaCat cells with a microelectrode-based biosensor device, referred to as Electric Cell-Substrate Impedance Sensing (ECIS).[5] The optimization of cell culture conditions **(Figure 1)** was performed by testing different experiment settings, such as the protocol development for cleaning and coating of the ECIS arrays, as well as choosing the medium, cellular density at which cells are inoculated and time of confluence. This new system allowed a real-time, simple and reliable screening of compounds' cytotoxicity. Wound healing assays were also performed to analyze the effect of anthocyanins and their new derivatives towards skin care.

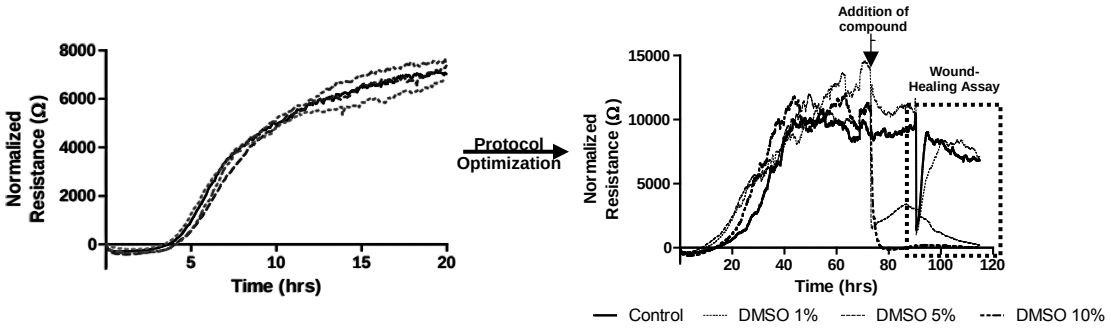

Figure 1: Protocol optimization was performed considering the minimization of confluence time and reproducibility, testing the influence of different media, cellular density of inoculation and preparation of ECIS arrays. An example of ECIS data is shown for a positive control performed with DMSO to validate skin-barrier model in ECIS.

Acknowledgements: This research was supported by a research project grant (PTDC/AGR-TEC/3078/2014) with financial support from FCT/MEC through national funds and co-financed by FEDER, under the Partnership Agreement PT2020 (UID/QUI/50006/2013 – POCI/01/0145/ FEDER/007265). Luís Cruz and Iva Fernandes gratefully acknowledge the Post-Doc Grants from FCT (SFRH/BPD/72652/2010 and SFRH/BPD/86173/2012, respectively).

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Reactivity study and biological activity of royleanones from *Plectranthus spp.*

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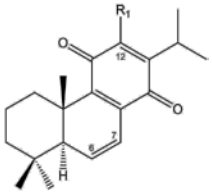
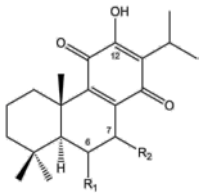
The rapid emergence of resistant bacteria occurring worldwide compromises the efficacy of existing antibiotics. This antibiotic resistance crisis has been attributed to the overuse and misuse of these medications as well as lack of new drug development by the pharmaceutical industry.[1] Natural medicinal products have been used for many years to treat multiple illnesses and developing countries population usually rely on traditional medicine for their primary healthcare.[2] Several plant's secondary metabolites hold antimicrobial properties. Among secondary metabolites, diterpenoids show interest due to their biological activity and possible use as templates for synthesis.[3] Royleanones are abietane quinones commonly isolated from *Plectranthus* spp. and hold interest due to their antimicrobial activity.[4] This study is focused on the synthesis of new abietane diterpenoids using royleanones isolated from *Plectranthus* spp. **(Figure 1)**. The 12-(prop-2-yn-1-yloxy)-abieta-6,8,12-trien-11,14-dione **(3)** was obtained by Mitsunobu Reaction using 6,7-dehydroroyleanone **(1)** as starting material, isolated from *P. madagascariensis*. The 6-hydroxyroyleanone **(4)** was obtained by hydrogenation of 7α-acetoxy-6β-hydroxyroyleanone **(2)** isolated from *P. grandidentatus.*



(1) R_1: OH

(3) R_1: OC_3H_3



(2) R_1: OH R_2: OAc

(4) R_1: OH R_2: H

Figure 1 - Royleanones derivatives.

The MIC values of the natural royleanones and the new derivatives were determined through the microdilution method against methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *Staphylococcus aureus* (MSSA). The results showed that the removal of the acetoxy group of **2** increased MIC value from 3.91 to 62.50 µg/mL and from 0.98 to 62.50 µg/mL for MRSA and MSSA, respectively. Therefore, the oxidation at C-7 position is important for the antibacterial activity. Regarding the insertion of the propargylic alcohol at C-12 position of **3**, the MIC value for MSSA increased from 15.63 to 62.50 µg/mL, however for the MRSA strain MIC values decreased from >250 to 62.50 µg/mL. The preliminary toxicity was evaluated through the brine shrimp assay and the lethality test showed that **1** was the most toxic abietane (36.68 %). The toxicity of the new synthesized compounds **3** and **4** was reduced compared to the starting material.

Further studies are required to understand the structure-activity relationship between several diterpenoids and therefore improve the antibacterial activity.

Acknowledgements: This project is supported by the grant PADDIC 2016 and 2017, from ALIES-COFAC and part of the PhD Program in Health Sciences from U. Alcalá and U. Lusófona. Fundação para a Ciência e a Tecnologia (FCT) (ref. SFRH/BPD/98053/2013)

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Luz10, a new water-soluble bacteriochlorin photosensitizer: Photochemical, *in vitro* and *in vivo* characterization

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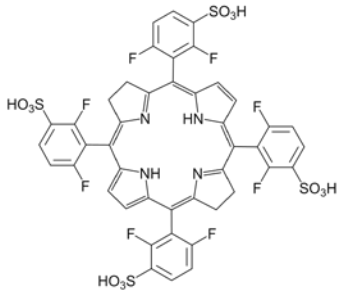
Photodynamic therapy (PDT) is a therapeutic strategy that combines the administration of a drug – the photosensitizer (PS) molecule – followed by the irradiation of the target tissue using light with an appropriate wavelength. The combination of light with PS in the presence of molecular oxygen leads to the formation of reactive oxygen species (ROS) which lead to the selective destruction of target tissue.[1,2,3]
Bacteriochlorins have been increasingly used as photosensitizers due to some of their characteristics such as the affinity for tumours[1], and the intense absorption band in the phototherapeutic window (650 - 800 nm), which is the range of wavelengths in which the laser light has a higher tissue penetration depth.[4]
In this work, a sulfonated and fluorinated bacteriochlorin (LUZ10) was studied regarding its photochemical, *in vitro* and *in vivo* properties. The photochemical characterization covered properties such as infrared electronic absorption spectrum, triplet state lifetime, photostability and singlet oxygen and fluorescence quantum yields. The in vitro studies made use of the CT26 (mouse colon carcinoma) cell line, where the toxicity of LUZ10 was studied in terms of the lethal dose in the presence and absence of excitation light. In vivo studies were performed on BALB/c mice with subcutaneously implanted tumors. Through an ascending escalation of PS and light doses, the best therapeutic dose was determined. A biodistribution and pharmacokinetic study identified the location of the PS in the mice organs over time. Pharmacokinetic parameters such as the maximum plasma concentration and the PS elimination half-life were also obtained. An in vivo phototoxicity study was performed in Wistar rats, where we aimed to understand the skin photosensitivity resulting from solar simulation exposure, at various times after the intravenous administration LUZ10.
This study revealed that LUZ10 has good properties as a photosensitizer for use in oncology. In particular, LUZ10 is soluble in aqueous media, which reduces the burden to the organism compared with other molecules of the same class. The solubilizers needed to administer most photosensitizers, and are often associated with unwanted side effects that can be avoided with a water-soluble photosensitizer such as LUZ10.



Acknowledgements: The Coimbra Chemistry Center is supported by the Fundação para a Ciência e a Tecnologia (FCT), Portuguese Agency for Scientific Research, through the project PTDC/QUI-QUI/120182/2010 and project Pest-OE/QUI/UI0313/2014.

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Non-enzymatic modifications of human serotransferrin and the dyshomeostasis of systemic iron transport

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Modifications under stress conditions affect the structural and functional integrity of proteins and have been implicated in a series of diseases and biological ageing. The most common non-enzymatic post-translational modifications (PTMs) of proteins are oxidation, resulting from the action of reactive oxygen species, and glycation, from the exposure to hyperglycemia.

Herein, we explore how these modifications affect systemic body iron transport in the blood plasma. In healthy individuals, virtually all plasma iron is bound to transferrin; but in clinical conditions as disparate as the iron overloading disease hereditary hemochromatosis (HH) and *diabetes mellitus* toxic non-transferrin-bound iron species (NTBI) can be observed. Commonly, the presence of NTBI is concomitant with partial values of transferrin saturation, a fact not easily explained if the much higher iron-binding affinity of transferrin over alternative plasma ligands is considered.

We have performed a detail study of transferrin modification by glycation.[1] A total of 29 transferrin glycation sites were identified by liquid chromatography coupled to mass spectrometry (LC-MS) in apo- and holo-Tf and we have undertaken a structural protein analysis in order to understand what determines the modification sites. Furthermore, we have thus proceeded with the characterization of the oxidative metabolites of transferrin in HH patients and healthy individuals. Results show that oxidation levels are independent of iron loading. Methionine (M) is the most commonly modified amino acid, followed by tryptophan (W). A total of 129 different oxidation sites were identified, with average modification rates below 5%. Never-the-less, and despite the moderate oxidation levels encountered, the micro-heterogeneity induced by non-enzymatic PTMs might have significant implications for the protein function as the body iron carrier.

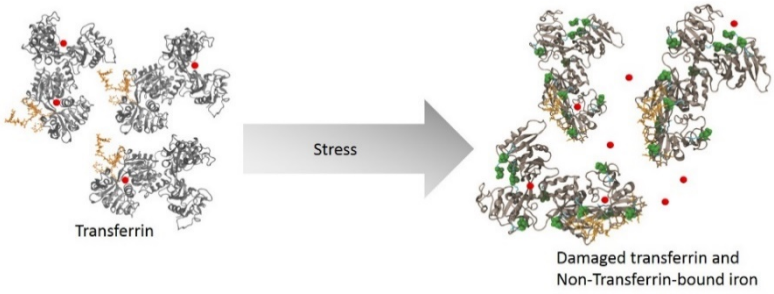

Figure 1: In healthy individuals, virtually all blood plasma iron is bound to transferrin, but in many pathological conditions this protein becomes spontaneously modified and unusual iron species (NTBI) arise even in situation where transferrin-binding capacity is only partially saturates.

Acknowledgements: This work received financial support from the European Union (FEDER funds through COMPETE) and National Funds (FCT, Fundação para a Ciência e Tecnologia), under the Partnership Agreement PT2020 through project NORTE-07-0162-FEDER-000048 UID/Multi/04378/2013 and NORTE-01-0145-FEDER-000024.

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Identification of potential inhibitors against Influenza A virus targeting the RNA-binding domain of NS1

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Influenza A virus cause contagious respiratory disease in humans and are responsible for the periodic widespread epidemics, or pandemics, that cause high mortality rates.
Though vaccination is the primary means of preventing and controlling the disease, still antiviral drugs play an important role in containing the disease during epidemics and pandemics by checking the virus spread and alleviating the symptoms. Currently the antiviral drugs approved are Oseltamivir and Zanamivir, two known neuraminidase inhibitors and Amantadine and Rimantadine, two inhibitors against M2 ion channel inhibitors. But the influenza A virus strains emerged are resistant against all of these antivirals.
In addition to hemaglutinin and neuraminidase, non-structural protein 1 (NS1) of influenza A virus is a key factor for virulence, and participates in both protein-RNA as well protein-protein interactions. The increased lethality observed in influenza A strains has been partly attributed to NS1.[1] This highly conserved and multifunctional protein is composed of two distinctive structural domains, a 73-residue N-terminal double stranded RNA-binding domain (RBD) and a C-terminal effector domain (ED), separated by a flexible linker region (LR).[2]
In order to discover compounds endowed with ability to inhibit NS1 activity, we have started a new research program combining computational and experimental approaches. First, and to allow the experimental validation of new inhibitors, we have independently cloned and characterized the RBD and ED domains of NS1. Additionally, we have initiated computational work for the identification of *druggable* hot spots in RBD-NS1, i.e. putative pockets on the protein surface capable of binding drug-like molecules with high affinity. We proceeded by creating pharmacophore models of the identified hot spots, which are now being used for fragment and virtual ligand screening.

Acknowledgments: The authors wish to acknowledge the support of the ERDF (European Regional Development Fund) through the COMPETE Programme (Operational Programme for Competitiveness) and National Funds through the FCT (*Fundação para a Ciência e a Tecnologia*), grant UID/QUI/00313/2013 (to Coimbra Chemistry Centre). NMR data were collected at the UC-NMR facility, supported in part by grants REEQ/481/QUI/2006 and RECI/QEF-QFI/0168/2012.

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Synthesis of *N*-Glycosylsulfonamides from Ribose and 2-Deoxy Glucose: Exo-anomeric Effect and Furanose/Pyranose Isomerization

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Mimetics of *O*-glycosides, such as thioglycosides, *C*-glycosyl or *N*-glycosyl derivatives, have attracted considerable interest in medicinal chemistry due to their relative stability to enzymatic hydrolysis and propensity for inhibition of therapeutically relevant carbohydrate-processing enzymes, namely glycosidases.[1] Moreover, *N*-glycosyl sulfonamides exhibit higher stability than most of glycosylamines and have shown interesting biological properties, such as antitumor activities due to their ability to inhibit cancer-associated carbonic anhydrases.[2,3]
Thus, we were motivated to explore the synthesis of novel anomeric sulfonamides (**figure 1**) derived from ribose and 2-deoxy glucose and to study the stereochemical and conformational outcome of the reactions involved in their synthesis. The methodology was based on the *N*-glycosylation of methanesulfonamide with 1-*O*-acetyl glycosyl donors. Interestingly, the deacetylation of *N*-ribofuranosyl methanosulfonamide occurred with isomerization to the pyranose form. Moreover, it was observed that all the deprotected derivatives were in the β-anomeric configuration, most likely due to the exo-anomeric effect.
The synthetic details and results will be presented and discussed.

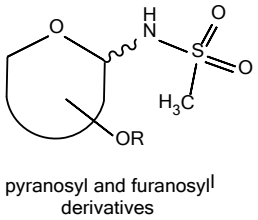

Figure 1: General structure of the target molecules.

Acknowledgements: We thank the Fundação para a Ciência acknowledged for funding (IF/01488/2013/CP1159/CT0006 and CQB strategic project UID/MULTI/00612/2013).

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The Search for New Anti-Cancer Molecules: Catalytic Synthesis of Novel Chiral Oxindole Derivatives

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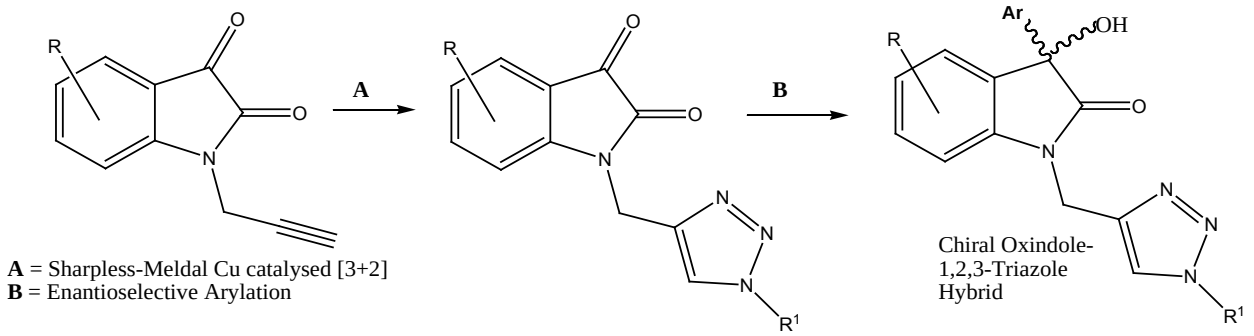
Oxindoles and triazoles are very privileged frameworks in medicinal chemistry, and are thus ubiquitous in numerous medicines and natural products.[1] Molecules that contain both these privileged structures are highly desirable. We have developed a sequential catalytic route that involves the Sharpless-Meldal Cu-catalyzed alkyne-azide cycloaddition (CuAAC) followed by a catalytic arylation reaction to afford families of *N*-(1,2,3-triazolmethyl)-3-hydroxy-3-phenyloxindoles starting from cheap biomass derived isatin. We successfully obtained these compounds with good yields and good enantioselectivities. The reaction is very versatile, tolerant of a wide range of functional groups and broad in reaction scope **(Scheme 1)**.[2]
The compounds were then screened for anti-cancer activity, and showed very promising anti-proliferative activity for a variety of tumor cell lines. These results will be discussed in this presentation.



Scheme 1: New catalytic route to chiral oxindole-triazole hydrids with anti-cancer properties

Acknowledgements: We thank the Obra Social “la Caixa” (project OSLC-2012-007), MINECO, Junta de Castilla y León, Spain (CTQ2014-58812-C2-2-R and BU042U16, FEDER Funds, respectively) and FCT (project UID/QUI/0619/2016) for generous support. C.S.M. thanks FCT for the award of a post-doc grant (SRH/BPD/92394/2013).

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Covalent Functionalization of Nano-Graphene Oxide with Glycol Porphyrins: Synthesis and Effects

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Nano-graphene oxide (NanoGO) and its functionalized derivatives have attracted great interest in nanomedicine due to its own intrinsic properties, all the dimensions lower than 100 nm and a singular chemical structure, which allows interesting possible biomedical applications such as drug delivery, tissue engineering, hyperthermia cancer therapy and photodynamic therapy.[1] However, the toxicity of NanoGO nanosheets is not yet well-known and it is necessary to understand its entry mechanisms into mammalian cells in order to avoid cell damage and human toxicity. Concerning NanoGO administration, although NanoGO colloids are soluble in water, they need further functionalization with molecules which improves the material dispersion and stability in aqueous solutions.

In the present study NanoGO has been covalently functionalized with glycol porphyrins through esterification reactions. The resultant hybrid materials are characterized by scanning electron microscopy, atomic force microscopy, X-ray photoelectron spectroscopy, Fourier transform infrared, ultraviolet-visible absorption and fluorescence spectroscopy **(Figure 1)**.

Preliminary studies on the behavior of hybrid materials after being in contact with different cell types were developed. The effects of materials on cell proliferation, cell morphology and cytokine release were analyzed. Moreover, the production of reactive oxygen species (ROS) was also measured.

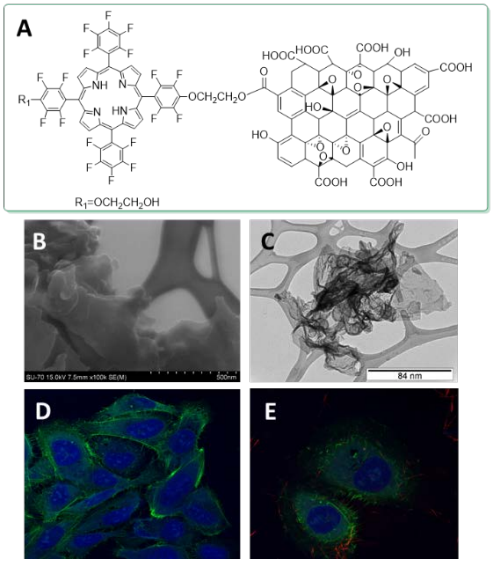

Figure 1: (A) Glycol Porphyrin-NanoGO hybrid material; (B) SEM image, (C) TEM image, (D) and (E) Morphology evaluation by confocal microscopy.

Acknowledgements: Financial support from FCT (SFRH/BPD/75782/2011, SFRH/BPD/105478/2014, IF/00759/2013 and PD/BD/127805/2016).

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2-Benzylchromones: Synthesis of novel potential biologically active compounds

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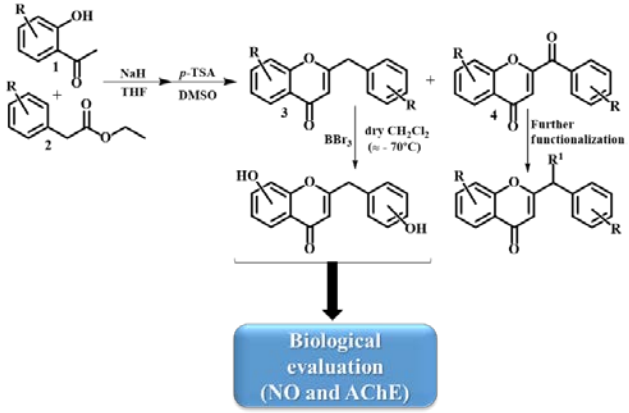
The quest for new and safer drugs is still the focus of several medicinal chemistry programs. Chromones (4*H*-chromen-4-ones) are a group of naturally occurring compounds ubiquitous in plants.[1] This singular ring system has proven to be a privileged scaffold in medicinal chemistry, due to its unique structural features and diverse biological activities[2], with emphasis to its anti-inflammatory activity.[3]

Our project was therefore intended to synthesize new chromone derivatives and evaluate some of its biological activities. To do so, numerous 2-benzylchromones **3**, with distinct substitution patterns, were synthesized through a Baker-Venkataraman rearrangement, using 2'-hydroxyacetophenones **1** and ethyl 2-phenylacetates **2** as starting materials **(Scheme 1)**, allowing us to understand the influence of different substituents in the efficiency of the developed synthetic procedure. This novel series of chromone derivatives **3** was then evaluated towards its cytotoxicity, capacity to inhibit nitric oxide (NO) production and acetylcholinesterase (AChE).

The biological results allowed us to define a few structural features relevant for the potency of both anti-inflammatory and anti-acetylcholinesterase activities. Though a very interesting discovery occurred during the synthetic procedure, in which some by-products **4**, with an extra carbonyl group, appear (Scheme). Besides its potential biological activity, these by-products may also enable the development of new synthetic routes, facilitating further functionalization of the 2-benzylchomone scaffold.



Scheme 1. Synthesis of novel 2-benzylchromone derivatives and biological evaluation.

Acknowledgments: Thanks are due to the University of Aveiro and Fundação para a Ciência e a Tecnologia (FCT) FCT/MEC for the financial support of the QOPNA research Unit (FCT UID/QUI/00062/2013) through national founds and, where applicable, co-financed by the FEDER, within the PT2020 Partnership Agreement.

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Electrophilic derivatives of estrogens from oxidation by Dess-Martin periodinane: evaluation of reactivity toward amino acids

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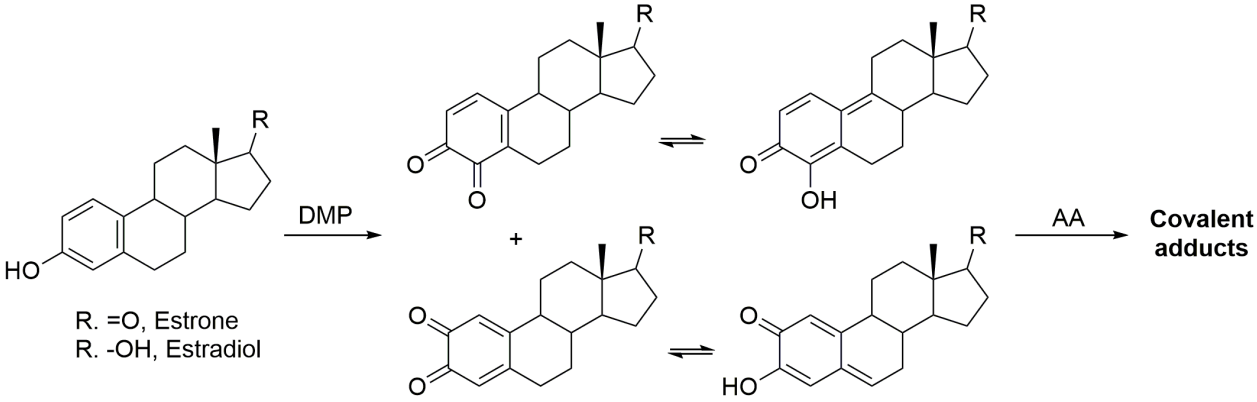
Exposure to estrogen has been associated with the occurrence of Parkinson's disease, breast cancer and autoimmune diseases, among others. Nonetheless, the mechanisms underlying most of these correlations is yet to be established. Endogenous estrogens (estradiol and estrone) undergo oxidative biotransformation via cytochrome P450 enzymatic system yielding catechol estrogens (CEs). The resulting metabolites can undergo further oxidation to the corresponding catechol estrogen quinones (CEQs) that are Michael acceptors capable of reacting with biomacromolecules. In addition, the formed *ortho*-quinones can isomerize to quinone-methide intermediates to give the unsaturated estrogen derivatives that can also form stable covalent adducts (**Scheme 1**).[1]

The nature of products formed by oxidative conversion of CEQs by the direct oxidation of estrone or estradiol with Dess-Martin periodinane (DMP) [2] to the quinones was for the first time studied and compared with the profile obtained under metabolizing competent systems. Subsequent reaction of these electrophilic species with amino acids (AA) presenting different nucleophilic side chains (S-, N- or O-based) can provide a better understanding of the conjugation chemistry behind the reactivity of the quinones with distinct bionucleoplhiles. Moreover, the synthesis and structural characterization by NMR and MS of these synthetic standards will allow to further expand the knowledge about the biological significance of these adducts as possible biomarkers of exposure to CEQs.



Scheme 1: Oxidation pathway of estrogens leading to the formation of reactive metabolites capable of reacting with bionucleophiles.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (PhD grant SFRH/BD/102846/2014, IF/01091/2013/CP1163/CT0001 and UID/QUI/00100/2013) and the Portuguese NMR and MS networks (IST node) for providing access to the facilities. A.M.M.A. also thanks Programa Operacional Potencial Humano from FCT and the European Social Fund (IF/01091/2013).

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Exploratory studies on the synthesis of novel spiro-γ-lactams

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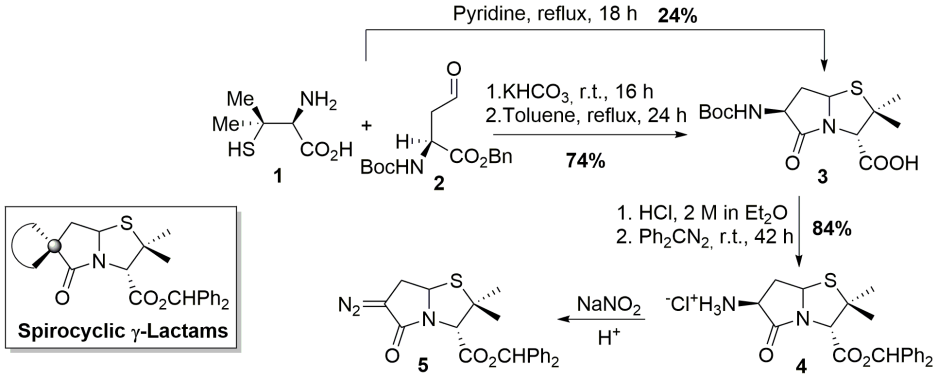
Previous research on the synthesis and biological evaluation of spirocyclic-β-lactams led to the discovery of lead compounds with remarkable anti-HIV and anti-Plasmodium berghei properties.[1] However, life-threatening hypersensitivity reactions are a major problem in the use of β-lactams, therefore the manufacture of these drugs is subjected to ever increasing demanding requirements to avoid cross-contamination of other drugs. To overcome these potential problems, we further aim to obtain non-β-lactam derivatives (γ-lactams) with similar antimicrobial properties of the ones observed for spirocyclic-β-lactams.[2]

In this context, we decided to look into the synthesis of diazo-γ-lactam **5** and explore its 1,3-dipolar cycloadditions as a route to spiro-γ-lactams, compounds having a chiral spiro carbon which is an important criteria for biological activity of known natural spirocyclic compounds.

Following the methodology developed by Baldwin *et al*. for related systems, bicyclic compound **3** was prepared using *D*-penicillamine as starting α-amino acid.[3] However, our optimized reaction conditions allowed the synthesis of the target amine in higher yield. Deprotection of the amino group followed by the synthesis of the corresponding benzhydryl ester derivative afforded γ-lactam **4**, which was converted into diazo-γ-lactam **5.** The reactivity of this compound as dipole was explore leading to novel spiro-γ-lactams (**Scheme 1**). In this communication, details of this study will be disclosed.



Scheme 1: Synthetic pathway to diazo-γ-lactam **5** from *D*-Penicillamine.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia (FCT), Portuguese Agency for Scientific Research (Coimbra Chemistry Centre through the project UID/QUI/00313/2013 and post doctoral grants SFRH/BPD/84413/2012 and SFRH/BPD/102229/2014) for financial support. We acknowledge the UC-NMR facility for obtaining the NMR data (www.nmrccc.uc.pt).

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The New Modular Fluorescent BASHY Platform: Stability in Aqueous Media

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The quest for flexible and modular approaches that enable the construction of electronically tunable and environmentally responsive fluorophore platforms is vital for the development of functional dyes for bioimaging, sensing, and probing applications.[1] Very recently, our group disclosed a new family of modular photostable fluorescent dyes [boronic acid salicylidenehydrazone **(BASHY)**], obtained by the assembly of structurally diverse boronic acids with Schiff base ligands.[2] As a result, BASHY fluorescent dyes already emerged as a powerfull tool for site-selective live cell bioimaging.[3] Herein our interest focus a dye synthetic scope in order to unveil the best structural core for biological conditions **(Figure 1)**. By varying the BASHY core we expect to obtain distinct stability properties that will be discussed in detail.

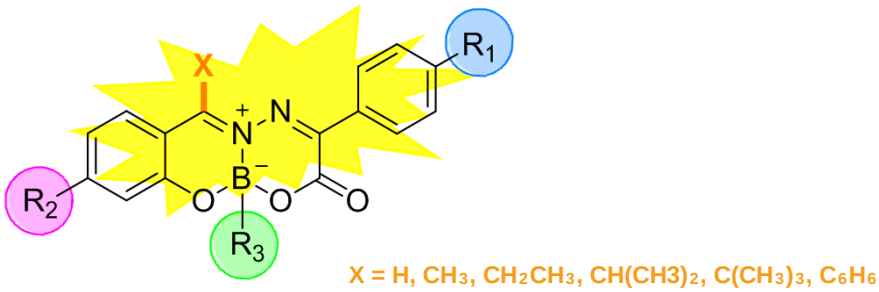

Figure 1: Chemical Structure of the BASHY Modular Core.

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Chitobiose as starting material to bacterial cell Wall oligosaccharides

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Complex oligosaccharides are today a synthetic challenge due their structural variability, high biological activity and presence. Most of the strategies to synthesize this structures are multi-steps requiring the synthesis of both glycosyl donor and acceptor.[1,2] One of the relevant oligosaccharides structures present in bacterial cell wall is peptidoglycan (PGN), a well-known immunopotentiator. PGN is composed by polysaccharide chains of *N*-acetyl glucosamine (NAG) and *N*-acetylmuramic acid (NAM) linked by a β(1-4) glycosidic bond. Each NAM unit have peptide chains linked creating a three-dimensional structure. Isolation of this structure in a significant amount to study is very difficult by natural sources lead to the challenging task to develop new synthetic strategies more sustainable and efficient as possible.[3]
Chitin is a polysaccharide by-product of shrimp and crab industry composed by NAG units linked by a β(1-4) glycosidic bond and chitosan, present in cell walls of certain fungi and can be obtained by deacetylation of chitin have an attractive building blocks to PGN synthesis.[4] Oligosaccharides construction relies on time-consuming protection/deprotection steps, glycosylation reactions, and several approaches have been developed in order to efficiently simplify the synthetic methodologies.[5]
Our group has been developing strategies to assemble NAG derivatives, including one-pot regioselective protection and orthogonal approaches towards NAG derivatives.[3,6] In recent work we envisaged to use chitobiose obtained from chitin, as starting material to attain the desired compounds. Taking advantage of our preliminary work, we report our advances on the modification of chitobiose towards relevant disaccharides.[7]

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support. PTDC/QEQ-QOR/2132/2012 and for the fellowship LAQV/BI/022/2016 - UID/QUI/50006/2013.

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Investigating Selective Cytotoxicity of Cancer Cells

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The main drawback of conventional cancer therapy is its lack of selectivity, which results in an array of adverse drug reactions. The ultimate goal in cancer therapy is to design new treatments which selectively target cancer cells and do not harm the surrounding healthy tissue. If this “targeted-delivery” strategy is achieved then no side effects will be observed and much lower doses of drug will be required. We are investigating the targeted delivery of cytotoxic drugs to cancer cells using two novel methods:

Method 1) A ligand-drug conjugate (LDC) designed to treat prostate cancer (PC) is being developed. The devised construct will pioneer targeting overexpressed calcium channels to achieve selective cytotoxic payload delivery. The project first involves chemical synthesis to build ligand-dye/drug conjugates. These molecules will then be evaluated *in vitro* to study biology and potential efficacy of the pharmacodelivery system. *In vivo* studies will be carried out to assess biodistribution of the molecules and tumour treatment efficacy.

Method 2) An original and innovative approach to cytotoxic drug delivery is being explored. A known cytotoxic will be fragmentized and assessed in toxicity assays. A pair of innocuous fragments will be selected and a bio-orthogonal ligation, specific to cancer cells, will be devised to selectively reinstate activity. This project involves chemical synthesis of fragment-like entities installed with ligation handles. Proof-of-concept will be achieved with imaging, biochemical and biophysical techniques.

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Neisseria gonorrhoeae Cytochrome c Peroxidase and the physiological electron donor, the Lipid-modified Azurin

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Neisseria gonorrhoeae is an obligate human pathogen that causes the sexually transmitted infection gonorrhea. This pathogenic bacterium has multiple enzymes to deal with reactive oxygen species originated both endogenously and exogenously, in particular from the host immune system defenses[1]. One of these enzymes is the bacterial cytochrome *c* peroxidase (*Ng*BCCP), a dihemic enzyme that reduces hydrogen peroxide to water. These enzymes require as electron donors small redox proteins, either small *c*-type cytochromes or type I copper proteins. The lipid-modified azurin (LAz), a type I copper protein, has been proposed to be the electron donor of *Ng*BCCP.[1]

*Ng*BCCP and LAz were heterologously expressed and purified, and it was performed a biochemical characterization of both proteins by: UV-visible and EPR spectroscopies, enzymatic assays, and potentiometric titration. *Ng*BCCP is a 38 kDa protein that exhibits a monomer/dimer equilibrium in solution dependent on concentration and calcium ions, similar to other dihemic bacterial peroxidases studied up-to-date, though this equilibrium is not dependent on ionic strength. It has catalytic activity, dependent on reductive activation and calcium ions, using LAz as electron donor. The structure of mixed-valence *Ng*BCCP was solved by X-ray crystallography and based on this structure a catalytic mechanism for dihemic bacterial peroxidases was proposed, in which the conserved Gln108 and Glu118 residues, at the catalytic site, play a key role.[2]

LAz is a 13.6 kDa monomer in solution and it is an efficient electron donor at physiological pH and temperatures. It is capable of activating the peroxidase, while a synthetic electron donor, such as $ABTS^{2-}$ is not. The formation of the electron transfer complex is dependent on hydrophobic effects and possibly water-mediated polar interactions. The solution structure of LAz has been determined recently [3, 4] and was used to identify the interaction surface with *Ng*BCCP by NMR titration. A model of the complex was produced by molecular docking simulations and it was proposed that His118 that coordinates LAz copper atom, is the exit point of the electrons to *Ng*BCCP.

Better understanding of *Ng*BCCP functional mechanism and of the *Ng*BCCP/Laz interaction will allow us to further understand their mechanism and to determine how to make *Ng*BCCP a potential target immunization against gonorrhea since this enzyme is highly conserved in this species and a *ccp* knockout has been shown to be more sensitive to oxidative stress.[5]

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (PTDC/BIA-PRO/109796/2009 to SRP, and SFRH/BD/87878/2012 scholarship to CSN).

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The photostability and interaction with Biomolecular Targets of Indirubin

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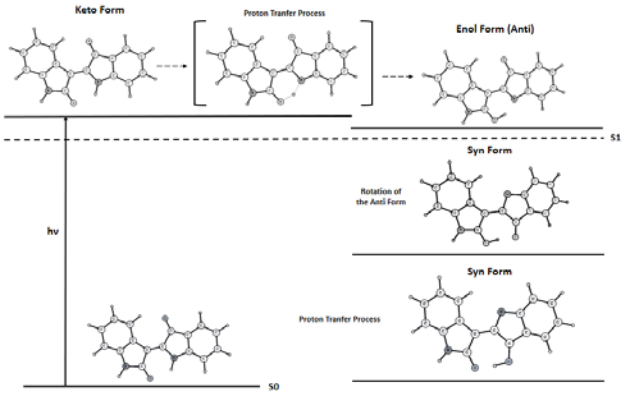
Indirubin and indigo are the core representatives of a rather small category of bisindole alkaloids belonging to the family of indigoids. Indirubin is one of the structural isomers of indigo and in the (red) shadow of this compound. Its relevance (besides the red tone that it imparts to indigo denims) is linked to the use, known for millennia, in traditional Chinese medicine for the treatment of Leukemia. Indirubin has been found to be the active ingredient of a traditional Chinese Medicine - *Danggui Longhui Wan* - used to treat the symptoms of leukemia. Indirubin and its derivatives have demonstrated a vast range of biological effects in stem and cancer cells, cardiac, renal, and pancreatic cells. These effects can be can explained by the interaction of indirubin with important molecular targets such as the members of the family of protein kinases (GSK-3, CDKs, and Aurora kinases) and the aryl hydrocarbon receptor, placing them among the most promising nature derived drug candidates. [1] In Indigo, as with indirubin, the excited state deactivation is known to be dominated by radiationless processes (the internal conversion quantum yield is >99.9%).[3] In indigo the mechanism is associated to a fast intramolecular (single) proton transfer.[2] The excited state mechanism involves the formation, by light excitation, of an instantaneously formed keto form which proton transfers to an enol form that decays to the ground state.[4] In this work indirubin was investigated by both steady-state and transient (time-resolved fluorescence and fs-TA) techniques, together with TDDFT calculations aiming to further understand the mechanism behind this extremely efficient non-radiative process. In comparison with indigo, indirubin shows a more efficient radiationless deactivation due to the fact that the excited state pathway to the CI is downhill whereas with indigo is uphill. In practical terms, this means that with indigo enol form tends to cross the barrier towards the reactant (the keto form) whereas in indirubin the enol form tends to rotate (irreversibly) to the syn conformation. Indeed, from TDDFT calculation it is predicted that the excited state enol form of indirubin is more stable than the excited state keto form **(Scheme 1)**.



Scheme 1: Indirubin's mechanism of deactivation.

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Novel hybrid drugs approach based on peroxides for Leishmaniasis

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Leishmaniasis is a parasitic disease caused by *Leishmania* spp., present in several countries, including Portugal. The control of the disease still relies on chemotherapy but the drugs currently prescribed against leishmaniasis have their use limited due to lack of efficacy, severe adverse reactions, increasing parasite resistance and elevated cost.[1] For these reasons, new antileishmanial drugs or therapeutics are required.

Protozoan parasites of the *Trypanosoma* and *Leishmania* genera stand out by their complex redox metabolism. The latter depend on the flavoenzyme trypanothione reductase (TR) as a defense against oxidative stress.[2] Thus, the development of potent inhibitors of TR could lead to new drugs to treat the various forms of leishmaniasis.

In this context, and as a paradigm for a novel approach to combination antiparasitic chemotherapy, we propose novel endoperoxide-based hybrid compounds incorporating novel TR inhibitors. Endoperoxides, such as 1,2,4,5-tetraoxane, are reductively activated by iron(II)-heme to form carbon-centered radicals, ROS and carbonyl species.[3,4]

This approach is applicable to any infectious agents that acquire high levels of iron at critical steps of their life cycle, such as *Leishmania*, which is dependent on an iron pool for amastigote differentiation and virulence.[5] The proposed strategy uses an endoperoxide-based hybrid to selectively deliver TR inhibitors.

In this presentation, we will describe the synthesis of 1,2,4,5-tetraoxanes-based of hybrid compounds and their characterization by usual NMR techniques (1D and 2D). We will also discuss the kinetics of activation by iron(II) performed by HPLC, using biomimetic systems.

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Synthesis of novel spirooxadiazoline oxindoles and evaluation as anti-cancer agents

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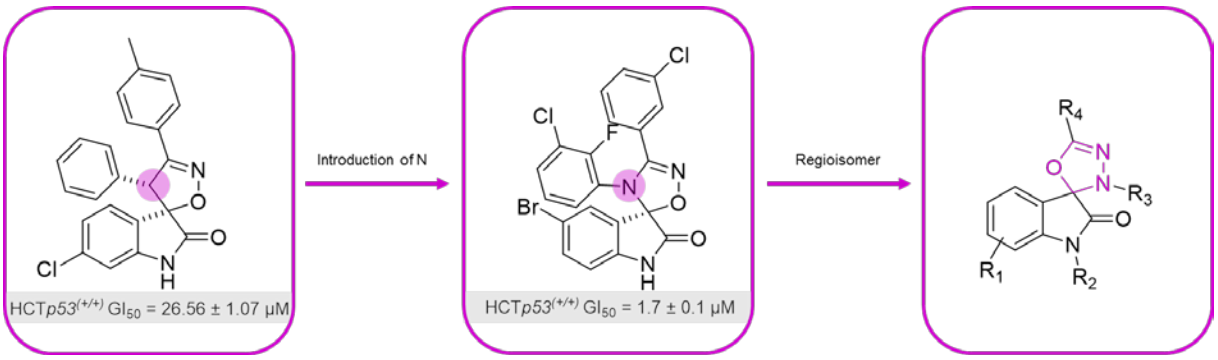
Cancer is one of the modern world's most common and deadly non-infectious disease. According to WHO Cancer Report of 2015, it is one of leading causes of morbidity and mortality worldwide with 8.8 million deaths in 2015 and it's expected to rise about 70% over the next 20 years.[1] The non-selectivity and acute toxicity of many antitumor agents has prompted the search for new antitumor agents with improved tumor selectivity, efficiency and safety.
In this area of research, we have been working in the development of spirooxindole scaffolds that possess promising *in vitro* anti-tumor activities in colon cancer cell lines **(Scheme 5)**.[2] In this communication, we report the synthesis of a novel library of spirooxadiazoline oxindoles, by 1,3-dipolar cycloaddition of isatin derivatives with different hydrazonyl chlorides, as well as the results obtained from the screening of this library in breast cancer cell lines.



Scheme. 5 membered ring spirooxindoles optimization.[2]

Acknowledgements: This work was supported by FCT (Fundação para a Ciência e a Tecnologia) through iMed.ULisboa (UID/DTP/04138/2013). M. M. M. Santos would like to acknowledge Fundação para a Ciência e a Tecnologia (FCT, Portugal), "Programa Operacional Potencial Humano" and the European Social Fund for the IF Program (IF/00732/2013).

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Synthesis of benzopyran-indole dyads with potential cannabinoid activity

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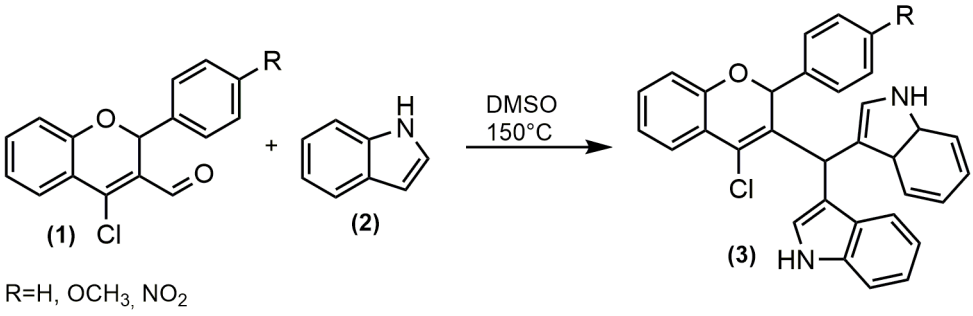
The endogenous cannabinoid system comprises the cannabinoid receptors CB1 and CB2, which are G-protein coupled. CB1 receptors are found predominantly in the brain, while the CB2 are found in the immune system and tumour cells, consequently the cannabinoid receptors are associated with brain, cardiovascular disorders and cancer. Cannabinoid receptors are an attractive target for the development of new therapeutic agents and have aroused great interest among the scientific community.[1]

The known cannabinoids are part of two groups, the natural cannabinoids, where are included the endocannabinoids, and the synthetic cannabinoids. Among which Δ^9-tetrahydrocanabinol (THC), the principal psychoactive component of *Cannabis sativa* L., can be highlighted. THC is a natural and classical cannabinoid which contain a skeleton with a tricyclic dibenzopyran [2] and shows analgesic effects by activating the CB1 and CB2 receptors, nevertheless its adverse psychotropic effects prevents its clinical application.

In this way, the synthesis compounds with cannabinoid activity is still in demand and in this project was envisioned the synthesis of benzopyran-indole dyads expecting to obtain compounds with potential cannabinoid activity. The benzopyran moiety was chosen due to its similarity with THC whereas the indole was chosen due to the fact that several derivatives present interesting biological applications. Adapting a simple procedure [3] was possible to obtain in good yields the desired dyads **3 (Scheme)**. The 4-chloro-2-phenyl-2*H*-chromene-3-carbaldehyde **1** reactivity was evaluated using different substituents. The results and structural characterization will be discussed.



Scheme: Synthesis of 4-chloro-3-bis(1*H*-indol-3-yl)methyl-2-(4-substituentsphenyl)-2*H*-chromene.

Acknowledgements: Thanks are due to the University of Aveiro, to the FCT/MEC and POPH/FSE for the financial support of the QOPNA research Unit (FCT UID/QUI/00062/2013) through national founds and, where applicable, co-financed by the FEDER, within the PT2020 Partnership Agreement and to the Portuguese NMR Network.

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Synthesis of new G-quadruplex ligands

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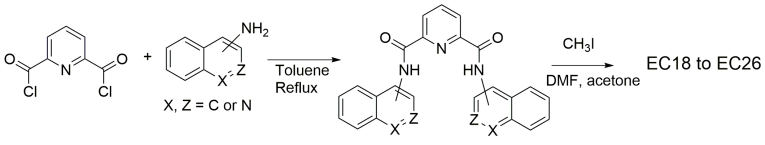
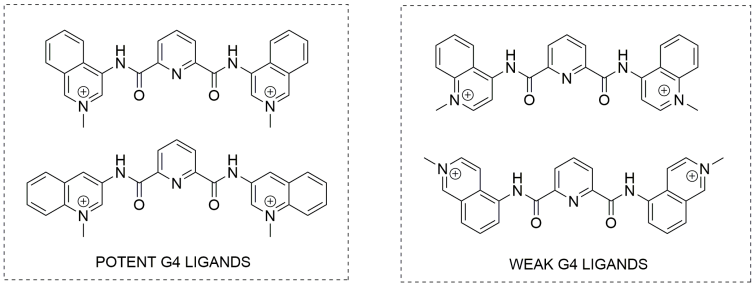
The formation of secondary non-Watson-Crick nucleic acids structures, such as G-Quadruplexes (G4), has a central role in controlling the telomere elongation and *in-vivo* replication. Several guanine-rich sequences besides the telomere has been discovered in many important human proto-oncogenes like *c-MYC* and *k-RAS* and identified as promising anticancer drug targets.[1] The propose of this work is to synthesize analogues of a powerful, already described ligand, ***360A*** [2], in order to identify relevant SAR to apply to the design of other G4-interactive small molecules.

The molecular structure of these V-shape compounds has *pyridine-2,6-dicarboxamide* as central core, linked to different positions of quinoline or isoquinoline ring. A second series of compounds was obtained by methylation of quinoline or isoquinoline nitrogen. The method used for the synthesis of the compounds [2,3] (**Scheme 1**) takes advantage of the extremely low solubility of the products on the solvent (Toluene for EC01 to EC14; DMF/Acetone mixture for EC18 to EC26), avoiding purification by chromatography. All the compounds were isolated pure by filtration and washing (with acetone for EC02 to EC14; with cold MeOH for EC18 to EC26). The yields of isolated pure compounds varied from 50% to 90%. In order to evaluate the capacity of these compounds to stabilize G4s and inhibit DNA replication, we used two different assays: FRET-melting assay and Polymerase stop assay, with different G4-forming sequences (h-telo, k-RAS, c-MYC*)*. As expected, the non-methylated compounds have a much lower activity than the methylated ones. Among methylated compounds we found that relative position of positive charge in relation to the central core has a major influence on the binding, stabilization of G4 structures and inhibition of polymerase.



EC01 to EC14



Acknowledgements: This work was supported by FCT, Portugal (grant No. PEst-OE/SAU/UI4013/2014, SAICTPAC/0019/2015) and New England Biolabs, USA.

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Modular Construction of Reversible Multivalent Targeting Drug Conjugates

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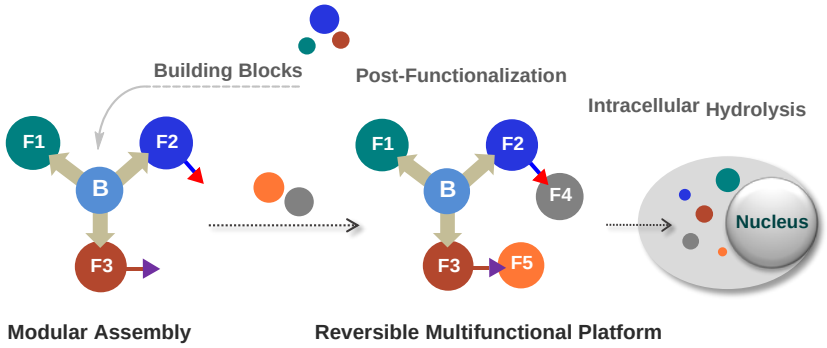
Recent developments of human biology allowed a more clear understanding of the intricate pathogenesis of complex diseases such as cancer. The evolution of normal cells to a neoplastic state is a multifaceted biological process in which normal cells acquire capabilities of sustaining proliferative signalling, evading growth suppressors, resisting cell death, enabling replicative immortality, inducing angiogenesis, activating invasion and metastasis. Consequently, the most recent strategies to tackle cancer, aim at interrupting one or more of these stages using multifunctional constructs.[1]

Targeting drug conjugates, like antibody (ADCs) and small-molecules (SMDCs), are multivalent conjugates that combine the lethality of potent cytotoxic drugs with the targeting ability of specific biomolecules that elicit a high affinity for antigens overexpressed in cancer cells.[2]

Herein is described a new modular platform to construct cancer cell targeting drug conjugates (**Scheme 1**). Tripodal boronate complexes, featuring reversible covalent bonds, were design to accommodate, a cytotoxic drug (bortezomib), polyethylene glycol chains and folate targeting units. The B-complex core was assembled in one step, and proved stable in different biocompatible conditions, namely human plasma (half-life up to 60 h) and reversible in the presence of glutathione (GSH). The stimulus responsive intracellular cargo delivery was confirmed by confocal fluorescence microscopy and a mechanism for GSH induced B-complex hydrolysis was proposed based on mass spectrometry and DFT calculations. This platform enabled the modular construction of multifunctional conjugates exhibiting high selectivity towards folate positive MDA-MB-231 cancer cells with IC_{50}'s in the nanomolar range.[3]



Scheme 1: Modular and reversible assembly of multifunctional targeting drug conjugates promoted by boron.

Acknowledgements: The authors thank Fundação para a Ciência e a Tecnologia (FCT), Portugal (grants: SFRH/BD/94779/2013, PTDC/QEQ-QOR/1434/2014, PTDC/QEQMED/5512/2014, SAICTPAC/0019/2015, UID/DTP/04138/2013 (iMed.ULisboa), UID/QUI/00100/2013 (LFV). Patent rights granted to Hovione SA PT109941.

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3. Submitted manuscript.

An innovative approach towards bacterial cell Wall oligosaccharides

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An innovative approach for the synthesis of oligosaccharides related to peptidoglycan - the carbohydrate basic skeleton of most bacterial cell surfaces will be presented. Peptidoglycan (PGN), a major component of the bacterial cell wall, is made of repeating N-acetylglucosamine (NAG) − N-acetylmuramic (NAM) disaccharide units (red), linked via [NAG-(β-1,4)-NAM] linkage, with stem peptides (black) whose composition is specific for each bacteria species, are attached to the D- lactyl (Lac) moiety of each NAM (**Figure 1**).[1]
We and others have explored several synthetic routes to prepare PGN fragments, whose synthesis are quite lengthy, time consuming and re-quire tedious protecting-group manipulations.[2-4]
Herein we will present our latest approach towards the synthesis (NAG-NAM) containing oligomers that relies on a chemical modification of a natural polymer. The strategy involves a chemoenzymatic approach as a simple route for an easy access to bacterial cell wall fragments – biologically important targets.

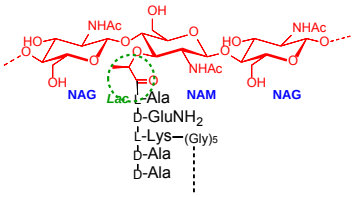

Figure 1: Structure of the S. aureus PGN (a Lys-type PGN).

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support. PTDC/QEQ-QOR/2132/2012 and for the fellowship PD/BD/109632/2015.

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Flow assisted synthesis of bicyclic aziridines *via* photochemical transformation of pyridinium salts

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Photochemistry is a very exciting area of organic chemistry as it allows the access to novel transformations which would otherwise be inaccessible through classical methods. However, photochemical reactions present a series of drawbacks, mainly due to the complexity of the processes and the difficult scale-up. Scalability is hampered due to the attenuation effect of photon transport which prevents the use of a simple dimension-enlarging strategy for scale-up. If larger reactors are used, over-irradiation of the reaction may become an essential issue as the reaction times are substantially increased, resulting in the formation of unwanted byproducts. An increasingly popular solution to solve the aforementioned problem is the development of continuous-flow reactors.[1] Our group has been working on the ring opening of aziridines in water under mild conditions [2] and the formation of these aziridines from pyridine salts are a classical example of a photochemical reaction, thus being envisioned as a perfect transformation to be optimized under flow conditions.
We hereby present the development of two new photochemical reactors and their performances in comparison with the batch processes.

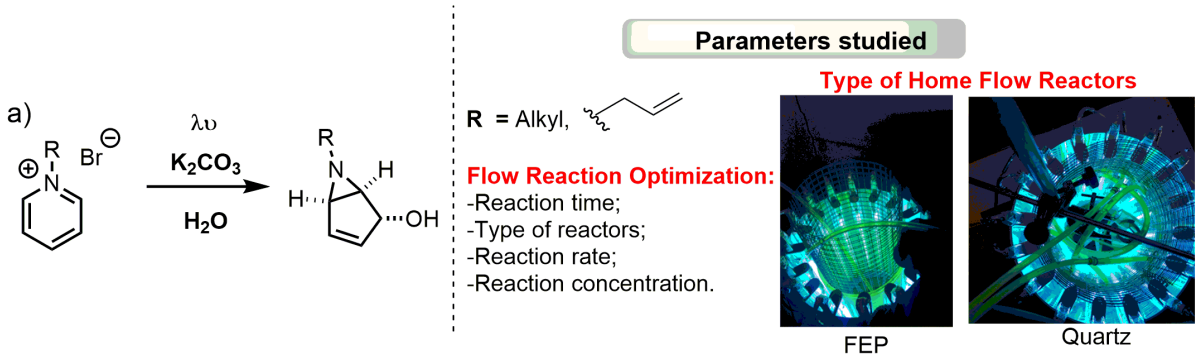

Figure 1: a) Photochemical transformation of pyridinium salt to bicyclic-aziridines.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia (SFRH/BPD/88666/2012, SFRH /BD/128239/2016 and SFRH/BD/120119/2016) and European Research Area Network; ERANet LAC (ref. ELAC2014/BEE-0341) for financial support.

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Pharmacophore modeling of novel EZH2 inhibitors

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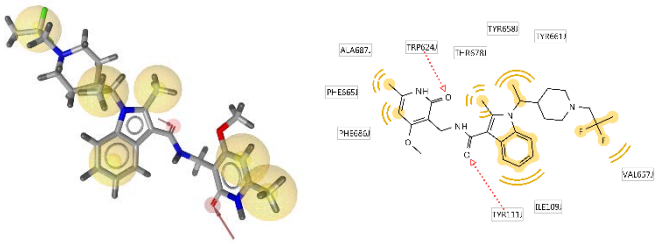
Epigenetic pathways play a key role in cancer disease development and progression, with the main focus on gene expression regulation. Polycomb repressive complex 2 (PRC2) is an epigenetic regulator that catalyzes the trimethylation of lysine 27 in Histone 3 (H3K27me3), a process that facilitates chromatin 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.[2] Thus, the development of new small-molecule inhibitors of EZH2 is a challenge that offers promising opportunities.

Our group is exploring several computer aided drug design approaches to identify new EZH2 inhibitors. With this aim, we generated several pharmacophoric models using LigandScout Advanced 4.1.4 software.[3] 3D-chemical feature-based pharmacophore models were generated based on experimentally derived X-ray data of protein ligand complexes (structure-based). The most relevant structure-based pharmacophore (SBP) was derived from interactions found in the active site of the J chain of the X-ray protein structure (PDB-ID 5LS6). The SBP contains 8 interaction features, most of them hydrophobic units (**Scheme 1**). Ligand-based pharmacophoric models were also created from a set of active ligands without using any active-site information. One of the generated ligand-based pharmacophores (LBP) included 14 features, 4 of them optional. Additionally, some models were obtained by merging features or creating models with only the features that are shared (both geometrically and by type) of SBP and LBP models. All models were validated using a test set that contained known inhibitors of EZH2, inactive molecules and decoys. The most predictive models were optimized by systematic modification on the features of the models. The testing of the modified models reveals important information about the key features associated with bioactive molecules that interact with this target. This information will be crucial to design more accurate and reliable pharmacophores for the remaining steps of the computational campaign.



Scheme 1: (A) SBP model generated from the EZH2 inhibitor found in the active site of the J chain of 5LS6 using LigandScout Advanced 4.1.4. Hydrophobic features and hydrogen-bond acceptor features are represented by yellow spheres and red arrows, respectively. (B) 2D-depiction of the interactions formed between the Ligand and the amino acids of the J chain active site.

Acknowledgements: We thank Fundação para a Ciência e a Tecnologia for financial support (PD/BD/128320/2017, UID/QUI/00100/2013, UID/DTP/04138/2013 and SAICTPAC/0019/2015). We also thank InteLigand GmbH for providing LigandScout license. This communication is based upon work from COST Action CA15135, supported by COST.

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Synthetic optimization process of mesoporous nanoparticles for protein extraction in biological samples

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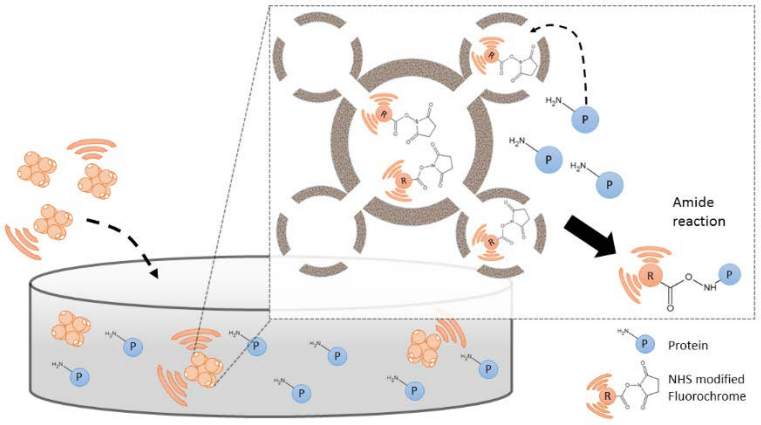
Since its discovery in the 1970s [1,2], mesoporous silica nanoparticles ($mSiO_2$) have been widely applied in many domains, namely in biochemistry and medicine, due to their unique ordered pore structure, high easy-to-functionalize surface areas, wide range of morphologies, great chemical stability and biocompatibility. MCM-41 and SBA-15/16 are solid materials with hundreds of empty mesoporous channels able to absorb/encapsulate large amounts of bioactive molecules. Considering their properties, herein it is proposed the optimized synthesis of SBA-16 $mSiO_2$ nanoparticles capable of, whether by pore size modulation or fluorescent dyes encapsulation, selectively extract peptides and proteins from biological samples.

SBA-16 nanoparticles are synthesized following an adapted non-ionic route, proposed by A. Katiyar et al. [3], with a triblock copolymer – pluronic F127 – as directing agent. Particle and pore size modulation is attained by addition of a swelling agent and control over reaction's time and aging temperature. The resulting nanoparticles capacity to absorb bioactive molecules is then tested with a set of well-known proteins, with the aid of a NHS-modified fluorochrome [4]. (**Scheme 1**).



Scheme 1: Cubic-phase functionalized, with NHS-modified fluorochrome, $mSiO_2$ extracting nanoparticles in pure biological sample.

Acknowledgements: This work was supported by the Unidade de Ciências Biomoleculares Aplicadas-UCIBIO (project MultiNANO@Tox), which is financed by national funds from FCT/MEC (UID/Multi/04378/2013), Scientific PROTEOMASS Association (Portugal) and LAQV/REQUIMTE (UID/QUI/50006/2013). EO acknowledges the Post-Doctoral grant from Fundação para Ciência e Tecnologia (FCT-MEC) Portugal SFRH/BPD/108660/2015 and to Foundation L'Oreal (UNESCO and FCT) for the Prize For Women in Science 2015, "Medalhas de Honra L'Oréal Portugal para as Mulheres na Ciência". H.M.S. is funded by the FCT 2015 Investigator Program (IF/00007/2015).

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Health Challenges

Indole diversity-oriented synthesis (DOS) based on a promising antimalarial scaffold

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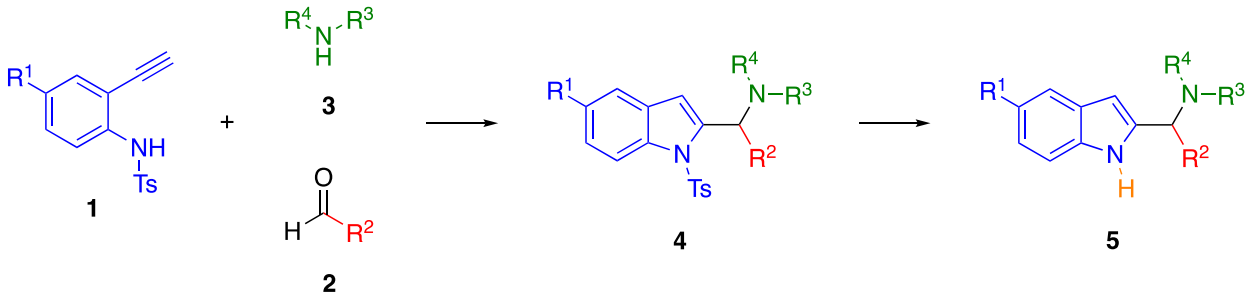
Diversity-oriented synthesis is a common strategy to discover novel and biologically interesting small molecules, enabling the generation of a structurally-related library of compounds based on a bioactive scaffold.[1] Previous results from our research group have identified a C2-functionalized indole active against blood stage malaria parasites in the low micromolar range, which instigated the design of other synthetic analogues.
In this communication, we report the synthesis of a small library of C2-functionalized indoles **5** via copper-catalysed A^3 coupling (and cyclization) of 2-ethynylanilines **1**, aldehydes **2** and secondary amines **3**, followed by *N*-detosylation of the indole synthetic intermediate **4** (**Scheme 1**), inspired by the work of Ohta and co-workers.[2] The influence of different secondary amines, aldehydes and 2-ethynylanilines in this three-component reaction, as well as the influence of the substituents R^1-R^4 on the antimalarial activity will be discussed.



Scheme 1: Copper-catalysed A^3 coupling (and cyclization) of 2-ethynylanilines **1**, aldehydes **2** and secondary amines **3**, followed by *N*-detosylation of the indole synthetic intermediate **4**.

Acknowledgements: This work was supported by Fundação para a Ciência e Tecnologia (FCT) through iMed.ULisboa (UID/DTP/04138/2013). Thanks are also due to University of Aveiro and FCT/MEC for the financial support to the QOPNA research project (FCT UID/QUI/00062/2013) financed by national funds and when appropriate co-financed by FEDER under the PT2020 Partnership Agreement, and to the Portuguese NMR Network. We also thank FCT for additional financial support: IF/00732/2013 (M.M.M. Santos), SFRH/BPD/108807/2015 (V.L.M. Silva) and SFRH/BD/103412/2014 (G. da Silva).

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Nitromethane conjugate addition to 2-[(1*E*,3*E*)-4-arylbuta-1,3-dien-1-yl]-4*H*-chromen-4-ones

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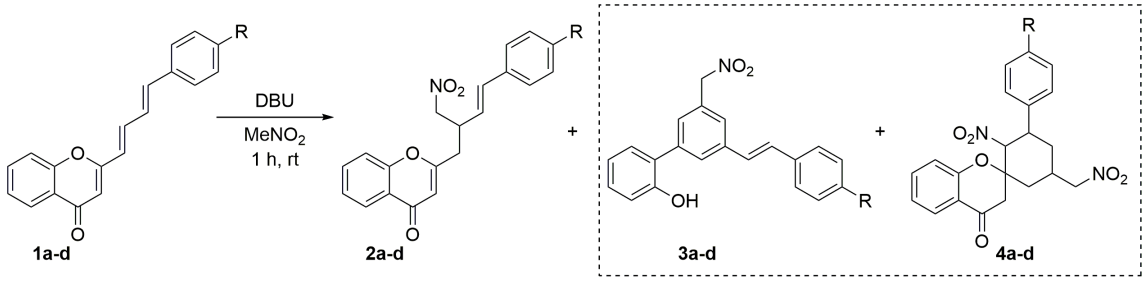
Chromone are a group of oxygen-containing heterocycles, which are often associated to important biological activities.[1] Chromone derivatives are also seen as interesting scaffolds to input further functionalizations,[2] most of them through chemical transformations such as oxidation, condensation, Diels-Alder or conjugate addition. Conjugate addition of carbon nucleophiles to electron-deficient alkenes is one of the most important methods available for carbon–carbon bond-forming reactions. A wide range of carbon nucleophiles easily undergo conjugate addition with various substrates such as chalcones, cinnamylideneacetophenones or styrylchromones.

Following previous work of our research group involving the 1,6-conjugate addition of nitromethane to (*E*)-2-styrylchromones,[3] herein we report the first reactivity studies in the nitromethane conjugate addition to the extended unsaturated π-system of 2-[(1*E*,3*E*)-4-arylbuta-1,3-dien-1-yl]-4*H*-chromen-4-ones **1** (Scheme 1). The DBU catalyzed nitromethane addition reaction afforded the corresponding β-(nitromethyl)chromones **2** (1,6-conjugate addition) as major products. (*E*)-5'-(Nitromethyl)-3'-styryl-[1,1'-biphenyl]-2-ol **3** and 3'-aryl-2'-nitro-5'-(nitromethyl)spiro [chromane-2,1'-cyclohexan]-4-one **4** derivatives were also isolated as minor products, which result from the addition of two nitromethane molecules, through tandem processes.



a) R = H, **b)** R = Cl, **c)** R = OMe, **d)** R = Me

Scheme 1: Nitromethane conjugate addition to 2-[(1*E*,3*E*)-4-arylbuta-1,3-dien-1-yl]-4*H*-chromen-4-ones **1**.

Acknowledgements: Thanks are due to University of Aveiro and FCT/MEC for the financial support of the QOPNA research unit (FCT UID/QUI/00062/2013) through national founds and, where applicable, co-financed by the FEDER, within the PT2020 Partnership Agreement, and to the Portuguese NMR Network, as well as to the Polytechnic Institute of Bragança. H.M.T.A. is grateful to FCT for his PhD grant (SFRH/BD/86277/2012).

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Dipolar Reorientations in the Amorphous Phase of the API Efavirenz: Some insights from the dielectric TSDC and DRS techniques

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Active Pharmaceutical Ingredient (API) is the therapeutically active compound that is integrated in the production of a pharmaceutical dosage form. Most active pharmaceutical drugs present low water solubility and consequently a decrease of the bioavailability, which is a key issue to the therapeutic effectiveness. Among different strategies developed to improve the water solubility, amorphization of the API has appeared as a promising alternative. This is due to the fact that amorphous substances exhibit a higher molecular mobility than crystalline, which can facilitate the interaction with water molecules. However, inherent to the amorphous form of a substance is the tendency for recrystallizing which is a consequent of being out of the thermodynamic equilibrium. In this context, a deeper understanding of the molecular mobility on amorphous materials is a desired issue for a reliable evaluation of the amorphous stability.

The present work dedicated to efavirenz (Figure 1) is part of a research program developed in Lisbon for the study of slow molecular mobility in low molecular weight glass formers. This particular API is a non-nucleoside reverse transcriptase inhibitor (NNRTI) used for the treatment of human immunodeficiency virus type 1 usually sold under the brand name Sustiva®. By combining the dielectric techniques of thermally stimulated depolarization currents (TSDC) and dielectric relaxation spectroscopy (DRS) the study of the slow molecular mobility in the amorphous solid state of efavirez were achieved. The combination of both techniques allows access to molecular motions with characteristic frequencies between 10^{-3} and 10^{6} Hz, corresponding to a wide temperature range that comprises the storage and use temperatures of this drug.

We will present and discuss in a detailed way some aspects related to the molecular dynamics of amorphous efavirenz probed by the two dielectric techniques. The obtained results will be also used to predict the potential utilization of this API in the amorphous state based on their physical stability ground.

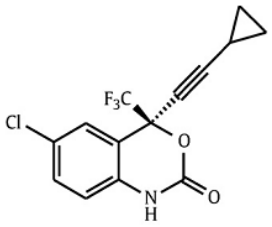

Figure 1: Chemical structure of efavirenz

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Ionic liquids in the polymorphic control of drugs: Are we solving a pharmaceutical industry problem?

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The development of new active pharmaceutical ingredients (API) is expensive and time consuming. In this sense, the pharmaceutical industry is interested on improving the efficacy of old drugs by enhancing their physicochemical properties (solubility, dissolution rate and bioavailability). Approximately 95% of the APIs are marked as solid dosage forms, and 50% of them are salts. However, solids are often strongly affected by polymorphic conversions (different crystalline packing arrangements of the same molecule), which have a direct impact on the bioavailability and thus the drug efficacy, imposing great financial and patenting issues.[1] Taking this in consideration, it is extremely important to control this solid-state phenomenon, or even avoid it, recurring to new and effective alternatives.

The approaches normally used to tackle API polymorphism issues involve crystallization screening using different solvents.[1] In recent years, ionic liquids (ILs) started to be used, not only as green solvents for the synthesis and crystallization of organic compounds, but also as possible drug delivers (API-ILs).[1]

Gabapentin (GBP) is an amino acid-based drug used to treat neurodegenerative diseases, such as epilepsy. This API exhibits three polymorphs (Forms II, III and IV) that are easily interconverted, affecting the physicochemical behavior of GBP and thus its bioavailability.[2]

Here we report a new and challenging approach for controlling polymorphism using imidazolium-based ILs as crystallization directing agents of GBP.[3] We also synthesized new API-ILs, combining GBP with biocompatible counter-ions (Figure 1).[3] The results from the crystallization process, point towards the influence of ILs on driving the formation of specific polymorphs. These results were supported by molecular dynamic simulations where it was possible to discriminate the GBP···ILs interactions. The synthesized room temperature GBP-ILs avoid polymorphism, transforming the solid API into a liquid. All the compounds were characterized by NMR, DSC and MS.

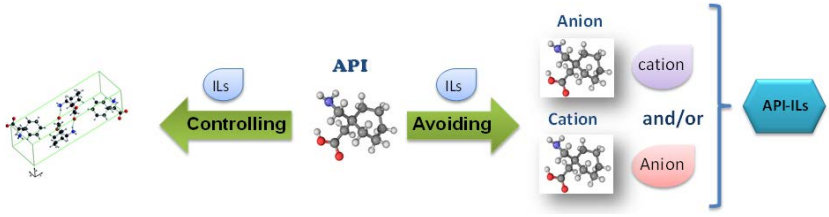

Figure 1: Schematic representation of the use of ILs in polymorphic control.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support of the projects UID/QUI/00100/2013 and SFRH/BD/93140/2013.

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Exploring the Chemistry of Nitroso- and Azoalkenes for the Synthesis of Bilanes

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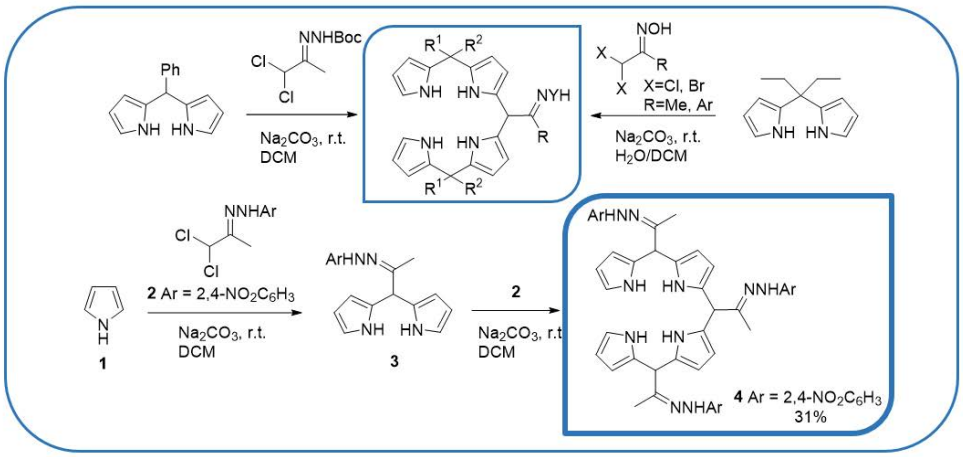
In recent years, open-chain oligopyrroles have attracted extensive attention as promising intermediates in synthetic porphyrin chemistry,[1a] as coordinating ligands for constructing supramolecular assemblies[1b] and as ion sensors.[1c] Tetrapyrrolic bilanes are usually used in the preparation of unsymmetrical porphyrins and are the main building blocks of porphyrin analogs such as corroles. Typical bilanes are obtained directly in an acid-catalyzed condensation reaction of pyrrole and aldehyde or by coupling two dipyrromethanes. Nevertheless, most bilanes are very unstable toward oxygen and acids. Therefore, there is an increasing interest in developing new synthetic methods using mild conditions, which do not involve strong acids.

Recently, we have demonstrated that the base-mediated dehydrohalogenation of α,α-halo-oximes and α,α-halo-hydrazones in the presence of pyrrole allows the synthesis of dipyrromethanes via bis-hetero-Diels-Alder reaction of nitroso- and azoalkenes, respectively.[2a] Furthermore, it was also shown that calix[4]pyrroles and bilanes, bearing hydrazone moieties, can be obtained from the reaction of α-haloazoalkenes with dipyrromethanes.[2b] In this communication, results on the use of this chemistry for the synthesis new bilanes, including derivatives incorporating oxime groups, will be presented (Scheme 1). Further developments on this study will be disclosed.



Scheme 1: Synthesis of bilanes by hetero-Diels-Alder reaction of azo- and nitrosoalkenes with dipyrromethanes.

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Does the antiepileptic drug carbamazepine need bioactivation to react with bionucleophiles?

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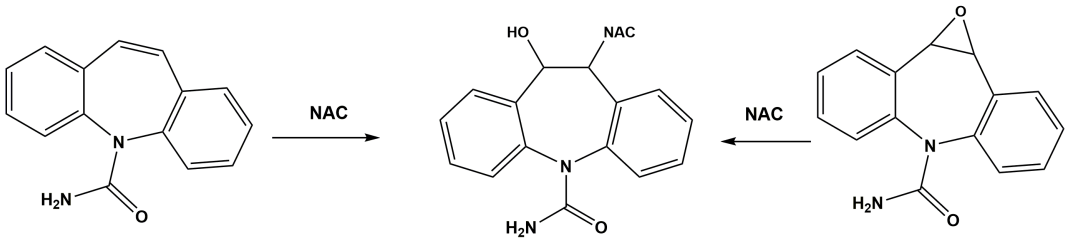
Epilepsy is a chronic neurological disease that affects about 50 million people of all ages worldwide. Carbamazepine (CBZ, 1), is one of the most widely used antiepileptic drugs for both adults and children. In addition, it is also used in the treatment of chronic pain, bipolar disorders and schizophrenia. Despite its widespread use, CBZ is associated with central nervous system toxic events and severe hypersensitivity reactions, which raises concerns about its chronic administration. While the precise mechanisms of CBZ-induced toxic events are still unclear, the metabolic activation to its major metabolite, carbamazepine-10,11-epoxide (CBZE, 2),[1] has been thought to play a significant role in the toxic responses elicited by the drug.[2]

We report herein evidence of direct covalent binding between CBZ and sulphur-derived bionucleophiles (*eg*. *N*-acetyl-*L*-cysteine, glutathione) yielding multiple products, namely 3, the same product obtained upon ring-opening of the main CBZ metabolite, CBZE. Interestingly, when compared with CBZE, the CBZ reaction is faster and more efficient, particularly in the presence of oxygen. These results suggest that under hyperoxia conditions the bioavalibility of the drug can be compromised. Furthermore, the adducts obtained with these bionucleophiles suggest that similar reactions with cysteine residues of proteins can occur, which supports a role for CBZ, without the need of bioactivation, at the onset of the toxic effects elicited by this antiepileptic drug.



(**1, CBZ**) **3** (**2, CBZE**)

NAC - *N*-acetyl-*L*-cysteine

Figure 1: Adduct **3** is obtained both from direct reaction of the bionucleophile *N*-acetyl-*L*-cysteine with CBZ (**1**) and with its main metabolite, CBZE (**2**).

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A simple fabrication procedure of ecological screen-printing biosensors for diabetics' monitorization

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Diabetes mellitus is a metabolic disorder in which glucose levels in the blood are not in the normal range (0.8 g/L - 1.1 g/L) as a result of disturbances related to the production or use of insulin. The need for monitoring blood glucose in patients with diabetes mellitus, and the possibility of this being done by themselves with the aid of point-of-care (POC) devices have led to the development of sensors allowing its detection.[1] Widely used at present in clinical diagnostics, the glucose sensors coupled POC, allow a quick and easy monitoring of glucose levels. However, their use is not free of risks. The lack of specificity and the susceptibility to temperature and humidity variations, and sensitivity to substances which are present in biological fluids, have been referred as weak points of these devices. In this context, the hyperglycaemia or hypoglycaemia diagnostic, obtained by the use of POC using blood samples, may not be true, since interfering substances present in blood, can contribute to an increase or decrease in the detected value, suggesting a false hyperglycaemia or hypoglycaemia, which leads to errors in clinical diagnosis and inadequate treatment.[2]

One possibility to obtain reliable diagnose is to determine not only the glycaemia but also the ketonaemia. With this aim we developed biosensors that can be used to fulfil this requirement. In this research work, a glucose screen-printing paper biosensor, was fabricated using simple manufacturing procedures that did not require drastic chemical or physical treatments. The first biosensors fabricated with this procedure used not only the glucose oxidase incorporated in the working electrode but also mediators, that could be soluble (ferrocene carboxylic acid) or insoluble (ferrocene) in water. Then third generation biosensors were designed and printed using only glucose oxidase incorporated in the working electrodes. The simple preparation procedure facilitated the preservation of the native protein conformation and the enzyme catalytic activity. It was found that there was no significant change in the behaviour of glucose oxidase incorporated in the working electrode comparing with its behaviour in solution[3]. The parameters acquired in these experiments indicate that at the working electrode surface a quasi-reversible redox process controlled by diffusion was found. Using this paper-based amperometric biosensor it was possible to detect glucose in a range between 0.036 g/L to 1 g/L. These values permit the use of this biosensor with blood or saliva samples (glucose normal physiological range in saliva: 0.005 g/L – 0.20 g/L), allowing the use of non-invasive methods to collect biological samps.[4] In order to prove the concept, a 3-hydroxybutyrate dehydrogenase third generation electrode was also fabricated using the same procedure, and its behaviour in the presence of the subtract 3-β-hydroxybutyrate was analysed. The parameters obtained in these experiments reflect a quasi-reversible redox process, controlled by diffusion and a formal potential of $E^{0'}$= (-26.±10) mV *vs* Ag/AgCl. A linear fit was obtained between 1mM and 3 mM of β-hydroxybutyrate. This detection range is useful to perceive the ketonaemia and can be used for clinical measurements since in healthy individuals the normal amounts of 3- hydroxybutyrate are below 1 mM, and in individuals with hyperketonaemia these values can range from 1 mM to 3 mM. [4]

The use of these third generation electrodes will reduced the glucose monitorization effective cost but also will increase the reliability of medical diagnostics.

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ANTHO4SKIN – Recycling anthocyanins for cosmetic applications

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Consumers are becoming more aware and curious and hence more likely to be attracted to natural products, especially from the Mediterranean diet which is usually associated with health-promoting effects. Natural cosmetic market demands for plant-derived ingredients that can be extracted from industrial byproducts. Red wines and red-fruits and vegetables are rich in powerful antioxidants helping to account for the anti-aging and UV-damage protection in the cosmetic industry. Cosmetic industry yearns for new dermal cosmetics with the ability to maintain skin homogeneity and a healthy look due to effective skin cell renewal and protection.

According to the literature polyphenols (monomeric and polymeric flavan-3-ols) from wines and from skins and seeds of red fruits have guaranteed the stabilization and enhanced the affinity of these powerful antioxidants with human skin.[1,2] Research suggests that polyphenols from grape seeds are beneficial in many areas of health, especially in delaying premature skin aging because of its antioxidant effect, promoting youthful skin, cell health, elasticity, and flexibility, help the protection from sun damage and to improve blood circulation.[2]

In this work, anthocyanins from industrial wastes were recycled and used in their genuine forms. Their biological activities were then assessed by developing a new skin barrier model using keratocytes cell line (HaCat). This model was developed by monitoring continuously the behavior of HaCat cells with a microelectrode-based biosensor device, Electric Cell-Substrate Impedance Sensing (ECIS).[3] This new system allowed a real-time, simple and reliable screening of the cytotoxicity and wound-healing effect of the extracts. As to the bioactivity towards skin enzymes, some *in vitro* assays to evaluate the bioactivity of the anthocyanin extracts towards some enzymes involved in biochemical events related to skin-beneficial properties were performed.

After selecting the extracts with best bioactivities, some tests will be made for their incorporation into cosmetic formulations aiming at their applications in skin care products.

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Synthesis of Smart Biocompatible Nanoparticles for Bio-Applications

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Luminescent inorganic mesoporous silica nanoparticles (QDs@mSiO_2) are a new generation of nanocarriers acting as all-in-one diagnostic and therapeutic tools due to their excellent biocompatibility, biodegradability, and high surface area[1,2,3]. Among all fluorescent agents, inorganic SiliconQDs emerged as a new promising biocompatible emissive nanomaterial with low toxicity.[4,5,6] Regarding such aspect, the synthesis and characterization of a new generation of biocompatible luminescent inorganic mesoporous nanomaterials (SiQDs@mSiO_2), and their further application as drug delivery systems in biological samples are explored. (**Figure 1**).

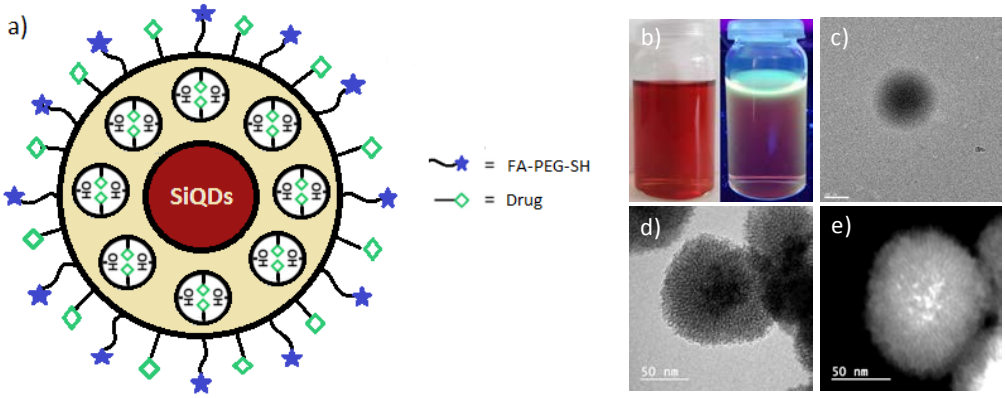

Figure 1: a) Targeted conjugate SiQDs@mSiO_2 nanomaterial; b) SiQDs; c), d) and e) TEM image of mSiO_2 at different angles showing the hexagonal pore structure.

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Health Challenges

Development of new boron based fluorescent dyes as hydrogen sulphide probes

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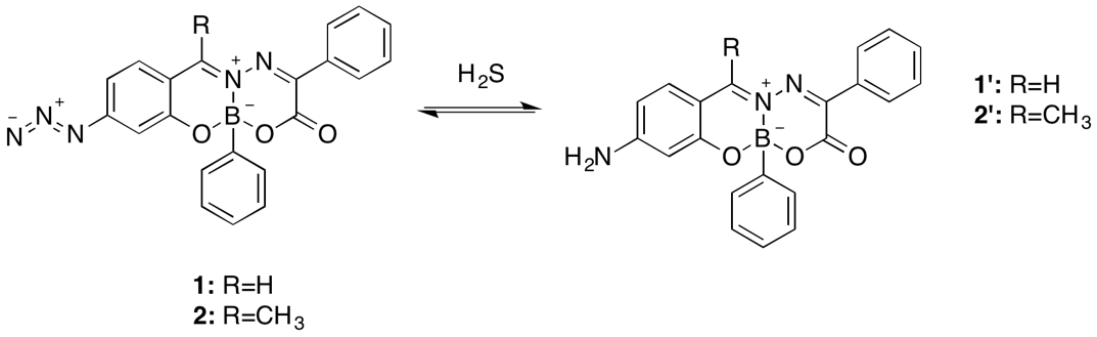
Hydrogen sulphide, known as the third gasotransmitter, is a recognized signalling molecule in the cardiovascular system and is a potential biomarker of ischemia and injury. [1] The scientific progress in the area of fluorescent probes and bioimaging have led to the construction of more demanding probes, particularly the design of probes able to provide information about organelle-specific mechanisms. In respect to H_2S, it is necessary to clarify the regulation of lipid homeostasis signalling, in this context, boronic acid salicylidenehydrazone (BASHY) dyes may be adequate, considering their affinity and accumulation on lipid droplets. [2]

Our lab has been focus on the development of the fluorescent dyes BASHY, which are iminoboronates based heterocycles, constructed in a modular fashion. These dyes have shown marked brightness and photostability. In biological tests, BASHY were cell permeable and were accumulated in specific organelles, namely lipid droplets. Considering the intramolecular charge transfer (ICT) nature of BASHY dyes, the spectroscopic properties may suffer alteration through changes in π-conjugation or in intermolecular electron density distribution. Thus, we present the development of two BASHY probes containing an azide group strategically added on salicylhydrazone moiety, which may be reduced to amine group in the presence of H_2S. This switch is followed by an alteration in electronic character and consequently, in spectroscopic properties, allowing the signalization of hydrogen sulphide. [3] **(Scheme 1)**



Scheme 1: BASHY probe reduction in the presence of hydrogen sulphide.

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Functionalization of betulinic acid through Heck reactions

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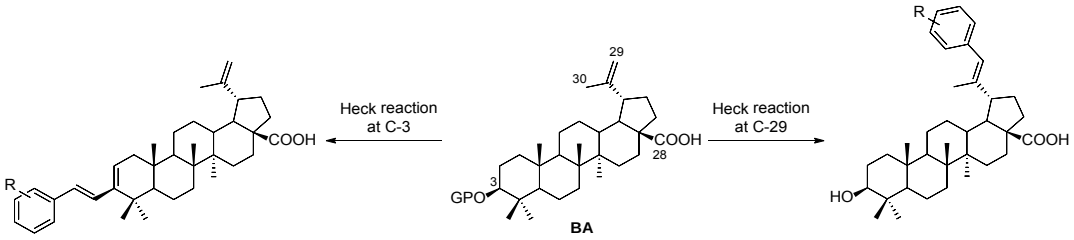
Betulinic acid (BA), a lupane-type pentacyclic triterpenoid, is present in many plants and displays important biological activities.[1] Furthermore, BA showed to be an interesting natural scaffold for functionalization, mainly at positions 3, 28, 29 and 30, through click chemistry, Diels-Alder reactions, palladium-catalysed cross-coupling reactions, among others.[2] Some of these new BA derivatives have been developed as twin drugs (two pharmacophores in the same molecule) or prodrugs. For example, Thi *et al.* synthesized 1,2,3-triazole-linked BA–AZT hybrids, which displayed a promising potential for further elaboration toward novel anticancer agents.[3] As part of our ongoing research project "MultiBiorefinery", aiming at valorising biomass derived compounds, we will use BA to synthesize new BA–flavonoid hybrid compounds with enhanced biological properties, based on the hybrid drug concept.[4]
In this communication, we will present our preliminary results in the functionalization of BA at C-3 and/or C-29 through palladium-catalysed cross-coupling reactions with model substrates (**Scheme 1**). To the best of our knowledge, this is the first report on the modification of the BA skeleton by means of Heck reactions. The experimental and spectroscopic characterization details will be presented and discussed.



PG: protecting group

Scheme 1: Heck reactions at C-3 and C-29 of BA.

Acknowledgements: Thanks are due to FCT/MEC for their financial support of QOPNA (UID/QUI/00062/2013) and CICECO (UID/CTM/50011/2013) through national funds; co-financing, where applicable, came from FEDER within the PT2020 Partnership Agreement. We also thank the Portuguese NMR Network. J.L.C.S. is grateful to the "MultiBiorefinery" research project (POCI-01-0145-FEDER-016403) for her post-doc grant. C.S.R.F. also acknowledges the FCT/MCTES for a research contract under the Program Investigador FCT 2012.

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Novel neutrophil elastase inhibitor-loaded starch-based nanocapsules with improved pharmaceutical performance: *in vitro* and *in vivo* studies

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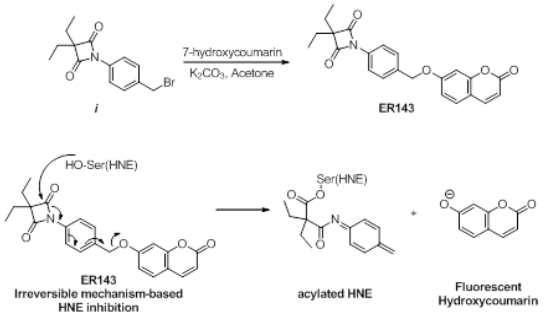
Psoriasis and atopic dermatitis diseases have an excessive amount of elastase in peripheral blood neutrophils and epidermal plasminogen activator. The high levels of this enzyme inactivate the endogenous inhibitor barrier thus, the search for new human neutrophil elastase (HNE) inhibitors are required. HNE is an attractive therapeutic target and the design of new HNE inhibitors is a demanding field that has been extensively investigated in order to provide inhibitors with new molecular architectures, including the potent oxo-β-lactam class.[1,2]

In this context, a promising novel synthetic human neutrophil elastase (HNE) inhibitor (ER143) [2] was associated to a starch-based nanoparticulate system (StNC) with improved pharmaceutical performance, using a quality by design (QbD) approach to support product development and optimization.

The drug selected for this study is a novel inhibitor of human neutrophil elastase (HNE) **(scheme 1)**, presenting low water solubility and putative anti-inflammatory action. HNE is a proteolytic enzyme that is thought to play a central role in diverse inflammatory diseases. An imbalance between HNE and its endogenous inhibitors lead to severe tissue injuries triggering various disease as for instance rheumatoid arthritis, chronic obstructive pulmonary disease, psoriasis or delayed wound healing.[3] The HNE is present inside the migrating neutrophils in the reticular dermis and dermal papillae, as well as outside the cells in micro-abscesses in psoriatic skin. Hence, psoriatic skin contains low concentrations of specific elastase tissue inhibitor, which results in an excessive *in vivo* hydrolytic activity of neutrophil elastase released from migrating cells.[4]

The resulting formulation was characterized in terms of and in vitro release, permeation and retention studies in newborn pig skin, using Franz diffusion cells revealing the StNC have the ability to control the drug release rate and contribute to a high skin retention and/or permeation profiles. Moreover, the anti-inflammatory activity accessed in vivo using the croton oil-induced ear inflammation model in mice showed that erythema and edema were attenuated in 98% following local application.

These observations suggest the association of ER143 to the StNC promotes a deeper skin penetration and retention, also confirming StNC as a potential topical delivery system.



Scheme 1: Synthetic approach to ER143 and mechanism of action against HNE.

Acknowledgements: This work was supported by the Fundação para a Ciência e a Tecnologia, Portugal (UID/DTP/04138/2013 to iMed.Ulisboa, SFRH/BDE/51599/2011 to J Marto, IF/00472/2014/CP1254/CT0004 to SD Lucas).

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Synthesis of pyrimidine-based chemical probes to study the biology of liver stage malaria parasites

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Antimalarial drugs in current use address few targets and their efficacy is being undermined by parasite resistance. Development of antimalarial drugs has been traditionally focused on the blood stage (BS) of the malaria parasite that causes clinical symptoms. The liver stage (LS) of Plasmodium infection is an obligatory step in the maturation and replication of mosquito-delivered parasites toward generating the erythrocyte-infective forms that cause malaria symptoms[1]. To target the hepatic stage is therefore highly desirable in the context of malaria eradication, not only because its asymptomatic nature makes it ideally suited for prophylactic intervention[2], but also because only few chemical tools are available to investigate the LS biology and the liver can serve as a reservoir for P. vivax and P. ovale hypnozoites, that may lead to relapses long after the initial blood infection has been eliminated[3].
It is known that only a few number of drug targets are fully validated for liver stage, so we now report the synthesis of pyrimidine-based chemical probes designed to be used in biorthogonal reactions with fluorescent tags for target imaging. These probes can be seen inside living infected hepatocytes and, allow a better understanding of the mechanism of action as well as identify the target for this class of liver stage inhibitors. The structural assignment of these compounds was made by usual NMR characterization techniques as 1H and 13C NMR (1D, 2D).

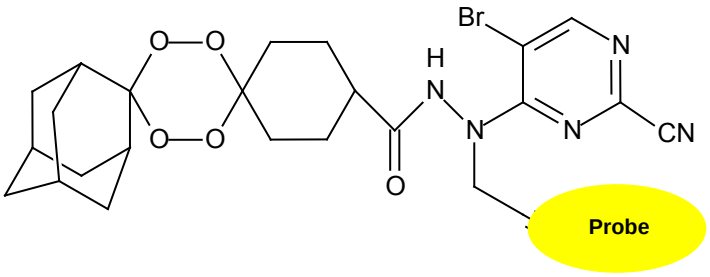

Figure 1: General structure of Tetraoxanes-Pyrimidine Nitriles Probes

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Permanent digital maps of the blood serum proteome for diagnostics and prognostics in multiple myeloma and lymphoma

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The development of non-invasive methods to detect and monitor tumours continues to be a major challenge in oncology[1]. In this work, we aim to develop a methodology to assist diagnostics of Multiple Myeloma and Lymphoma, using non-invasive liquid biopsies. This is achieved by using Matrix Assisted Laser-Desorption Mass Spectrometry (MALDI MS) to generate digital maps of the protein content of the liquid biopsies, which are then probed with bio-statistical tools to unravel disease-characteristic protein signatures for diagnostics and follow-up of disease treatment. The samples were chemically-depleted [2] of high abundance proteins using different amounts of acetonitrile (25%, 35%, 45%, 55%), digested with trypsin and, then, analysed by MALDI-TOF-MS. The MALDI-MS spectra were then examined using the Mass-UP Software using Principal Component Analysis and Hierarchical Clustering [3].

This experimental work has shown that optimal classification of patients with Multiple Myeloma and Lymphoma is achieved when the liquid biopsy samples are depleted with acetonitrile concentrations higher than 45% (v/v). This treatment allows for differentiation of patients using principal component analysis and hierarchical clustering. The use of chemical depletion mediated by acetonitrile (45%, 55% (v/v), Figure 1) combined with MALDI-MS analysis has proven to be effective indistinguishing liquid biopsies from Multiple Myeloma and Lymphoma as well as from healthy donors. Moreover, the protein content of the liquid biopsies has been digitized into permanent digital profiles containing m/z information, and we are working towards enriching the digital profiles with quantitative and identity information.

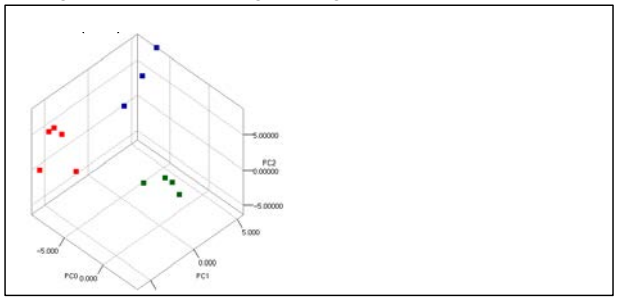

Figure 1: Principal component analysis of the MALDI MS profiles: Green - Healthy control; Red - Multiple Myeloma and Blue – Lymphoma.

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Azaindole derivatives in structure based drug design for the discovery of new anti-apoptotic protein inhibitors

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Programmed Cell Death (PCD), also referred to as apoptosis, is a genetically defined mechanism that prevents the survival and proliferation of abnormal cells, such as cancerous cells. Bcl-2 family proteins are pivotal in the PCD's intrinsic pathway and can be divided into anti-apoptotic and pro-apoptotic members. Bcl-2 protein has been reported has being overexpressed in several types of cancer, namely breast, lung and lymphomas, allowing cancerous cells to escape apoptosis and resist to chemotherapeutic agents[1,2]. Bcl-2's anti-apoptotic function comprises the inhibition of pro-apoptotic member, Bax, through protein-protein interactions with Bax's BH3 domain. To increase the vulnerability to chemotherapy of cancerous cells, small molecules were considered to target Bcl-2's binding site to Bax. Souers *et al.* reported venetoclax (commercial name) as a potent Bcl-2 inhibitor (K_i < 0.01 nM)[3]. This compound has an azaindole moiety which augments its binding affinity and specificity to Bcl-2, when compared to the compound from which it was derived. Our goal is to structurally characterize the interaction of azaindole derivatives with Bcl-2 and contribute to the rational design of new molecules that can inhibit Bcl-2 with less side effects than the ones reported for venetoclax[4]. In this work, we used molecular docking, protein crystallography and biophysical methods, as thermal shift assay (TSA), isothermal titration calorimetry (ITC) and polyacrylamide denaturing urea electrophoresis, to study protein-ligand interaction (Figure 1). Through docking studies, we located venetoclax and azaindole derivative preferred binding site, which corresponds to the physiological binding site of Bcl-2's partner, Bax. Predicted inhibitory constant of the tested azaindole derivative is not as good as of venetoclax, despite of being already in the μM range (0.54 μM). TSA and denaturing electrophoresis proved to be efficient methods to test the binding of inhibitors to Bcl-2 and are going to be used with a library of azaindole molecules. Preliminary co-crystallization attempts of Bcl-2 with the azaindole derivative yielded small crystals using MPD as precipitant.

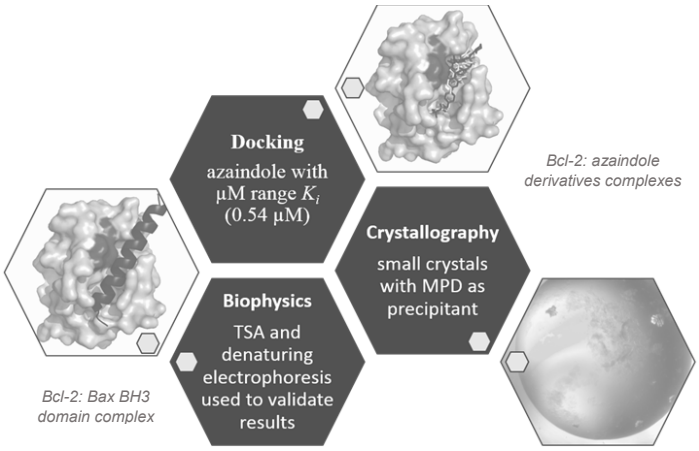

Figure 1: Schematic representation of the used strategy and preliminary results.

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Micromorphological, phytochemical profile and antibacterial evaluation of two Rutaceae species

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Throughout their evolution plants have developed several functional and metabolic mechanisms to survive. One of the major adaptations is the biosynthesis of a large diversity of secondary metabolites which includes terpenic compounds, alkaloids, flavonoids and phenolics, among others. The objective of this work was to carry out preliminary studies on the micromorphology, the phytochemical profile and the antibacterial activity of two Rutaceae species, *Zanthoxylum zanthoxyloides* (leaves and roots) and *Zanthoxylum leprieurii* (roots).

Microscopic characters are important in species discrimination and are considered in Pharmacopoeias. In this way, a micromorphological study of the leaves of both species was carried out. Similar characteristics were found: i) polyhedral epidermal cells on the upper and lower surfaces; ii) hypostomatic leaves; iii) internal secretory structures with a lipid nature. The most significant difference in leaf anatomy is the leaves thickness, thinner in *Z. leprieurii*. Despite this, in this species it is common to find large internal secretory structures and idioblasts with druse type calcium oxalate crystals in the parenchyma cells.

Fifteen extracts of leaves and roots, with increasing polarities, were prepared and their antibacterial activity against three Gram-positive (*Enterococcus faecalis* and *Staphylococcus aureus*, sensitive and resistant strains) and two Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa)* were evaluated. The best results were obtained with *Z. zanthoxyloides* non-polar leaves extracts that presented the lowest MIC values (15-30 µg / mL) against the Gram-positive strains. This may be related to the high content of terpenes and flavonoids detected in those extracts. None of the tested extracts was active against the Gram negative strains.

These are preliminary results that point to the validation of the use of these plant species in traditional medicine and emphasize the worthwhile of additional studies.

Investigation of novel sulfonylation methods

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As time goes by, there has been an ever-growing interest in the use of hypervalent iodine reagents in organic synthesis. This iodine based compounds were traditionally used as oxidizing reagents but, in the last decade, its potential as a transfer agent of numerous groups has arose.[1] Nowadays, benziodoxole-based compounds are used not only as oxidizing reagent but to transfer trifluormethyl group, alkynes, among many others.[2] In this work, we propose the use of an iodine (III) benziodoxole-based compound as an SO_2-surrogates.

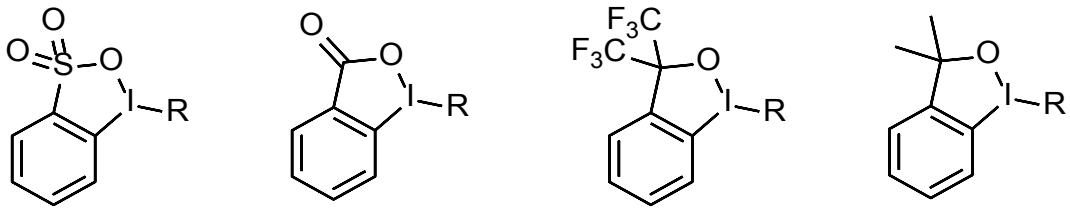

Figure 2: Benziodoxole-based compounds.

The SO_2 group is present in a wide variety of compounds, from polymers to drugs or pesticides. To date most methods to prepare sulfonyl containing compounds use sulphur dioxide gas.[3] So, it is of upmost importance to discover cheaper and greener sulfonylation integration methods. In this presentation, our synthetic achievements will be presented.

Acknowledgements: This work was supported by the Associated Laboratory for Sustainable Chemistry- Clean Processes and Technologies-LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007265). The NMR spectrometers are part of The National NMR Facility, supported by Fundação para a Ciência e Tecnologia (RECI/BBB-BQB/0230/2012).

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Incorporation of cimetidine in mesoporous silica nanoparticles

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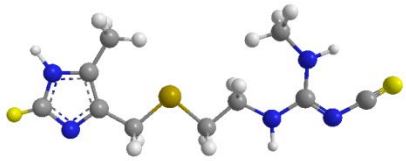
Cimetidine (Scheme 1) is an H_2-receptor antagonist that is used for prevention of heartburn and peptic ulcers; it belongs to class III of Biopharmaceutical Classification System (BCS), i.e. it presents high solubility and low permeability. In order to improve the latter, the incorporation in polymer matrixes with nanometric dimensions has been recently tested with success.[1]

In the present work, we decided to explore this strategy changing the polymer matrix for mesoporous silica nanoparticles (MSN). In fact, the advantages of these biocompatible materials with high surface areas and pore volumes, controlled particle size, morphology, and porosity, exhibiting high chemical stability, have been progressively brought to the field of pharmaceutical science to host pharmaceutical drugs.[2] For this aim, spherical MSN of around 80 and 30 nm with cylindrical pores around 3 nm were prepared. Cimetidine was encapsulated in the nanopores from a concentrated cimetidine/ethanol solution.

The amount of cimetidine incorporated in the silica nanoparticles after removing the solvent was determined by Thermogravimetric Analysis (TGA) and ^{1}H-NMR (the latter, after dissolving the silica matrix and by using an external standard).[2] The amount of loaded cimetidine in the matrixes was found to change between 5 and 10wt%.

Differential Scanning Calorimetry (DSC) and Dielectric Relaxation Spectroscopy (DRS) were used to investigate the physical state of cimetidine inside nanopores and the release kinetics of three samples of SiNP/Cimetidine were followed by UV-Vis spectroscopy, using a cuvette fitted with a dialysis membrane in a spectrometer with Peltier temperature control. The obtained release profile was analyzed taking into account the models described in the literature and compared with the dissolution of bulk drug.



Scheme 1: The chemical structure of Cimetidine.

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A new reversible clickable linker for protein bioconjugation

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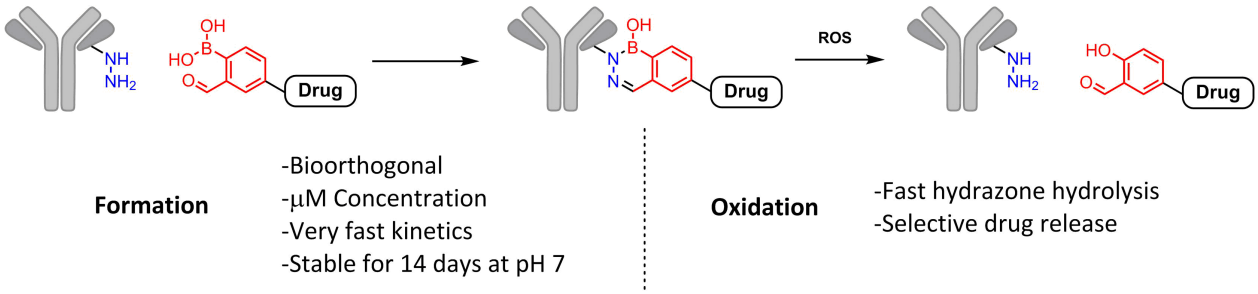
A new paradigm has been emerging in medicinal chemistry, where the focus of research has been shifting from the discovery of new chemical entities, to the optimization of the current ones. Drug targeting is one of the most successful approaches where a very powerful drug is selectively delivered to its site of action through the addition of a targeting moiety, commonly a biomolecule such as a protein or a carbohydrate. The importance of this strategy has been demonstrated by the FDA's approval of Antibody-Drug Conjugates (ADCs). The biggest challenge of this approach is the development of functional linkers which are stable in physiological conditions but, at the same time, capable of releasing the payload under very selective conditions. We hereby present a bioorthogonal clickable linker which is reversible selectively under oxidative conditions.

Despite been known since early XX century, very recently Bane [1] and Gillingham [2] have demonstrated the formation of a boron-nitrogen heterocycle in water, with exceptional kinetics through the reaction of hydrazines with o-formylphenylboronic acids. We envisioned the possibility of using these heterocycles as a clickable linker to conjugate drugs with targeting peptides. At the same time, the oxidation of boronic acids to phenols in the presence of oxidative conditions has been described several times in literature.[3] We proposed that the same could happen with these compounds and provide an innovative mechanism to add reversibility.

Herein, we performed the reaction of different hydrazines with formyl and acetyl boronic acids and evaluated the kinetics and stability to select the optimal linker for bioconjugation. The selected pair formed a very stable heterocycle (over 14 days) with extraordinary kinetics (less than 5 minutes) and with close to 100% conversion. Several model peptides were easily tagged with fluorescent probes using this technology. Upon the addition of hydrogen peroxide, it was possible to observe the oxidation of the boron-nitrogen ring and sequential hydrolysis of the hydrazone, thus releasing the payload. We are presently working on conjugating a cytotoxic drug to a targeting peptide and evaluating its activity.



Scheme 1: The reaction of a hydrazine-tagged protein with a formylboronic acid produces a very stable linker which can be selectively reversed under oxidative conditions.

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Macrocyclic ligands incorporating a pyridine moiety and their copper(II) and nickel(II) complexes: antifungal activity in Fluconazole-resistant pathogenic yeasts

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Antifungal drug resistance is a multifaceted clinical challenge, and a primary cause of treatment failure in patients with severe fungal infections. The increasing resistance rates and a narrow antifungal armamentarium have contributed to the research of novel therapeutic strategies. In this context, several drugs emerged as possible antifungal agents.[1]
Macrocyclic compounds and their transition metal complexes play a key role in several essential biological systems and present highly favourable drug-like properties. In this work, three pyridine-containing polyaza macrocycles (**L1 -** py[14]aneN$_4$; **L2 -** py[15]aneN$_5$: **L3 -** py[16]aneN$_5$) and their copper(II) and nickel(II) complexes were synthesised and characterized, as reported in our previous works.[2]
The macrocyclic ligands and their copper(II) and nickel(II) complexes were tested for their antifungal activity against Fluconazole-resistant *Candida* strains by broth microdilution method (E.DEF.7.3 method of the European Committee on Antimicrobial Susceptibility Testing).[3]
For the compounds that exhibited the best antifungal activity and in order to investigate the action mechanism we have assessed their action against the cell wall (Sorbitol Protection Assay), and for ergosterol interaction related interference (Ergosterol Affinity Assay).[4]

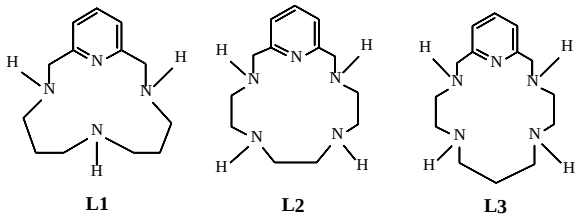

Figure 1: Chemical structures of the macrocycles.

Acknowledgments: This work has been funded by iMed.ULisboa (UID/DTP/04138/2013) from Fundação para a Ciência e Tecnologia (FCT), Portugal.

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Dielectric constants of fluid lipid bilayers measured through the pyrene Ham effect: experimental caveats in fluorescence measurements

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Pyrene fluorescence is advantageous to study biophysical phenomena in fluid lipid bilayer due to its high quantum yield, long lifetime, and precise solvatochromic effects.[1] The physical-chemical properties of pyrene (apolar and rigid bulky group) settle its distinct location as a free molecule within lipid bilayers, allowing obtaining correct information about diverse physical-chemical properties of model membranes.[2,3] Therefore, its location in the ordered section of the methylenic palisade defines the values of equivalent dielectric constants of lipid bilayers, averaged transversally in space (defined by the longest axis of pyrene, ~10 Å) and laterally in time (due to the lateral diffusion of pyrene during its excited singlet lifetime, ~150 ns in aerated aqueous liposome suspensions). To do so, the fluorescence spectra must be corrected for the spurious effects of light scattering from liposome aqueous suspensions that fatally affects the measurements of fluorescence intensity at 371 nm (I_1) and 382 nm (I_3), besides paying the due care to other experimental details, such as pyrene concentration, that renders the fluorescence measurements self-consistent.[4] Analogous procedure is adopted to set up a reference plot for pyrene fluorescence in homogeneous alcohols of known dielectric constants at 20 °C. This plot will make available a regression equation of (I_1/I_3) *vs.* the dielectric constants of standard alcohols that allow retrieving the equivalent dielectric constants of fluid model membranes. If the experimental caveats in fluorescence measurements are not dully fulfilled, only qualitative assessment of bilayer polarity will be attained.[2]

The bilayer polarity of pure POPC and their binary mixtures with cholesterol were monitored using the pyrene Ham Effect (I_1/I_3). Pure POPC exhibits higher dielectric constant than the mixtures at high cholesterol proportions, pointing to features perceived in the thermal phase diagrams available in literature for POPC/Chol mixtures.[5] The values measured for dielectric constants of model membranes are helpful for the comprehension of membrane phenomena like lateral phase coexistence, permeability of water and ions, membrane dipolar potential, and mostly membrane-bound redox and electron transfer reactions. Dielectric changes in lipid bilayers may also affect the structure and functioning of intrinsic membrane proteins with voltage-sensing domains as well, as the surface and transversal distribution of membrane components in biological membranes.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for the financial support through the project CBMR – UID/BIM/04773/2013.

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Human serum transferrin binding of $V^{IV}O^{2+}$ complexes - a computational assessment of the transferrin ability to transport drugs

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Highly proliferative cells have a dramatically increased need for iron which results in the expression of an increased number of human transferrin receptors. This insight makes the transferrin receptor on these cells an excellent candidate for targeted therapeutics. It is well known been shown that human serum transferrin, hTf, is able to accommodate various metal oxyanions, and it has been demonstrated that hTf is able to bind $V^{IV}O^{2+}$ complexes. The knowledge on the binding of vanadium ions and complexes to serum proteins and how vanadium might be transported in blood and up-taken by cells has received much attention during the last decade.

A number of vanadium complexes displays good results in prevention and treatment of cancer in *in vivo* models[1], and this has led to the development of a number of studies focusing on the ability of hTf to transport these complexes and deliver them *in situ* to cancer cells via transferrin receptors.

We have approached this problem by applying a state-of-the-art semi-empirical computational approach, by studying the specific interactions between various vanadium oxyanions and vanadium complexes and the three conformations of hTf (iron-bound, oxalate-bound and free).[2]

Results show that $V^{IV}O^{2+}$ and its complexes are able to bind hTf in active conformations, and that the preference between iron-bound and oxalate-bound hTf if mainly determined by the geometry of the binding complex, as the oxalate-bound conformation of hTf displays a more relaxed binding site. More importantly, the complexes interact with the same residues responsible for iron binding but also with *second-shell* residues, and, when synergistic anions are invoved, they are strongly bound to the aminoacid residues via extensive networks of hydrogen bonds. Energetically, the binding of all tested ligands to hTf agrees with available experimental dissociation data and bioactivity test results.

Results are discussed in terms of the structural characteristics associated with stronger binding, allowing their incorporation in the design of new vanadium complexes with prospective use on cancer therapies via hTF-mediated delivery.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (UID/QUI/00100/2013) and research grants (SFRH/BPD/108258/2015).

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Health Challenges

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

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Of the 850 new therapeutic products registered in the last decade, only 5 (0.6%) were indicated for neglected tropical diseases (NTDs), none of them being a new chemical entity or vaccine. One important approach to overcome this gap is generically referred to as drug repurposing, namely by exploitation of existing drugs in different therapeutic areas.[1]
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 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.[2] 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 disclose Torin2, an ATP-competitive mTOR kinase inhibitor,[3] 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.[4] 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). Based on 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.

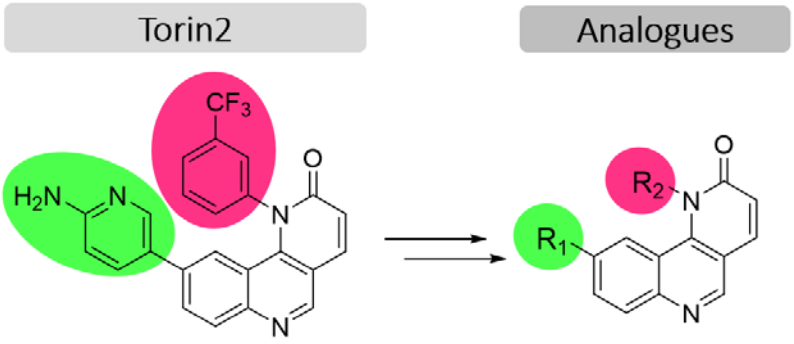

Figure 1: Probing the chemical space around Torin2 scaffold.

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Synthesis of new scaffolds from oleuropein derived building blocks

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Olive tree (*O. europaea*) is a natural source of oleuropein **(Figure 1)**, a secoiridoid present only in plants from *Oleaceae* family. Although it can be found in fruits and small branches, oleuropein is present in higher amounts in olive leaves, which are considered a cheap and easily available source of oleuropein, since are industrial by-products with no practical applications. Oleuropein has potent biological and pharmaceutical properties: anticancer, cardioprotective, neuroprotective, gastroprotective, anti-diabetes and anti-obesity, in large part attributed to its antioxidant and anti-inflammatory effects.[1]

Extraction and analytical methods have been developed and widely reported for qualitative and quantitative studies of olive polyphenols, including oleuropein. Published transformations of oleuropein are generally related to the removal of hydroxytyrosol and glucoside moieties. Since few research has been done at this level [2], we will describe the synthesis of new scaffolds from oleuropein at the level of elenolic acid unit, through semi-synthetic transformations.

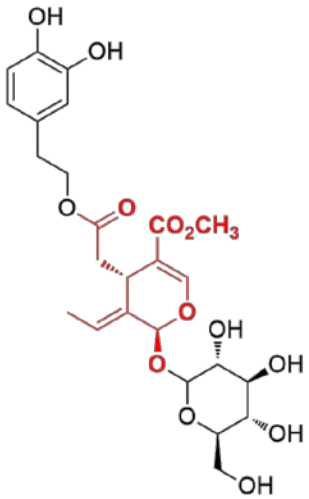

Figure 1: Molecular structure of oleuropein. Elenolic acid unit highlighted (red).

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Synthesis of novel 4-(pyran-3-yl)pyrano[3,4-*b*]-4*H*-chromene: role of catalyst and solvent

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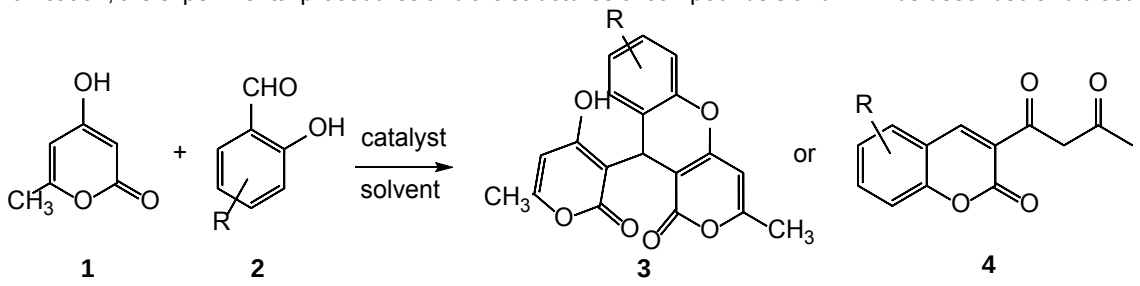
Compounds containing coumarin and pyrone moieties are ubiquitous in a variety of important compounds and potent drugs presenting a variety of biological properties, such as anti-inflammatory, anticoagulant and anti-angiogenesis activity and also as HIV protease inhibitors. Besides, they are also known to display a wide range of antimicrobial and antioxidant activities.[1]

As part of our ongoing research on the synthesis of bioactive compounds,[2] herein we report the reactions of 4-hydroxy-6-methylpyran-2-one **1**with salicylaldehyde **2**, being the selectivity of the multicomponent reactions controlled by the use of diverse catalysts and solvents (**Scheme 1**). This transformation results in two different series of heterocyclic compounds, which have a coumarin and pyranochromene patterns. Using ethanol or acetonitrile as solvent, the Knoevenagel condensation of **1** and **2** followed by a pyranone ring opening gives 3-(3-oxobutanoyl)-2*H*-chromen-2-ones **4**. However, using an acid catalyst, there a conjugate addition of another molecule of **1** to the Knoevenagel condensation product and subsequent cyclisation to the chromone nucleus to give the new product **3**. In this communication, the experimental procedures and the structures of compounds **3** and **4** will be described and discussed.



1 **2** **3** **4**

Scheme 1: Synthesis of 4-(pyran-3-yl)pyrano[3,4-*b*]-4*H*-chromenes **3** or 3-(3-oxobutanoyl)-2*H*-chromen-2-ones **4**.

Acknowledgements: Thanks are due to University of Aveiro, FCT/MEC for the financial support to the QOPNA research Unit (FCT UID/QUI/00062/2013), through national funds and where applicable co-financed by the FEDER, within the PT2020 Partnership Agreement, and also to the Portuguese NMR Network. We would like to thank the Ministry of Higher Education and Scientific Research of Algeria for awarding an exchange scholarship.

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A Chemoproteomic approach to validate Human Neutrophil Elastase as a Biomarker of Chronic Obstructive Pulmonary Disease

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Chronic obstructive pulmonary disease (COPD) is characterized by progressive and self-sustained lung inflammation resulting in non-reversible limitation of lung airflow. New biomarkers to diagnose and evaluate COPD are urgently needed. We propose that the inflammatory process in COPD modulates proteolytic enzymes in the lung environment, like human neutrophil elastase (HNE), which are critical for disease development and are a potential source of new biomarkers. Our main goal is the validation of HNE as a new biomarker of COPD. Based on our previous experience with the development of small molecules for HNE inhibition[1] we synthesized a library of HNE inhibitors and activity-based probes (ABPs)[2] based on the 3-Oxo-β-Sultam warhead[3] using Cu(I)-catalyzed Huisgen azide-alkyne 1,3-dipolar cycloaddition[4]. Our library proved to be very potent, with HNE inhibition values in the nanomolar region. ABPs selectively target only the active form of HNE and are currently being validated in gel-based assays. Once validated, ABPs will be applied in a library of nasal brushing and bronchoalveolar fluid human-derived samples and target identification will be achieved by mass spectrometry and proteomics techniques (Figure 1). The outcome of this project will ultimately lead to important advances for diagnostic tool development and biomarker discovery in COPD.

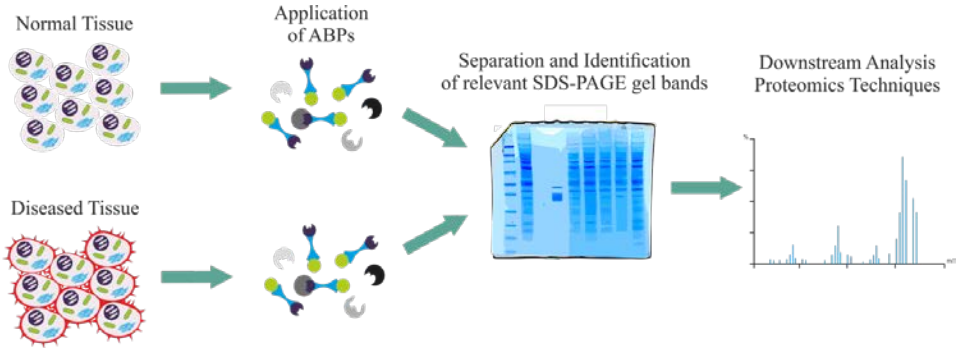

Figure 1. ABPs are applied in human-derived samples, followed by in-gel analysis and target identification using mass spectrometry.

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Synthesis of metabolites from the Benzo Fury's drugs of abuse

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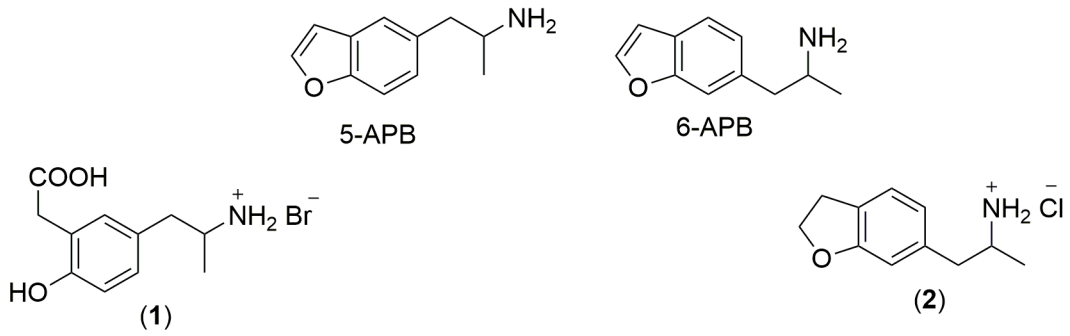
Amphetamines are neuro-stimulants capable of increasing dopamine doses in certain regions of the brain. 5-(2-Aminopropyl) benzofuran (5-APB) and 6-(2-aminopropyl) benzofuran (6-APB) sometimes informally called "Benzo Fury´s" and part of the growing group of designer drugs, belong to the so-called novel psychoactive substances (NPS) being a serotonin–norepinephrine–dopamine reuptake inhibitor. Metabolites of these compounds may involve the reduced and ring opening benzofuran products[1]. From our knowledge some of the proposed metabolites of these drugs like 2-(5-(2-aminopropyl)-2-hydroxyphenyl) acetic acid (**1**) and 1-(2,3-dihydrobenzofuran-6-yl)propan-2-amine (**2**) were never synthetized before. The synthesis of standards for toxicological studies is of crucial importance and here we present our synthetic approach for these two metabolites. The outlined synthesis to **1** starts with 2-hydroxyphenylacetic acid using a method previously reported by us for the synthesis of MDMA metabolites[2], whereas **2** was achieved through catalytic hydrogenation of 6-APB.



Scheme 1: 5-APB and 6-APB designer drugs and two of their metabolites 2-(5-(2-aminopropyl)-2-hydroxyphenyl) acetic acid (**1**) and 6-(2-aminopropyl) benzofuran (**2**).

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Synthesis of benzophenone derivatives by the reaction of nitromethane with (*E*)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-ones

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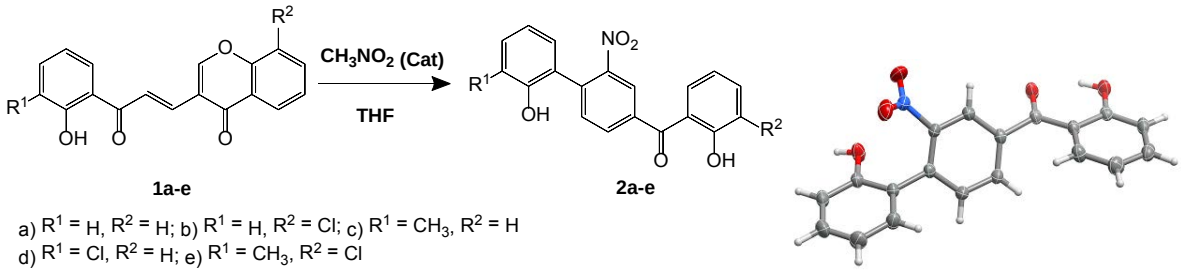
Benzophenone-based compounds are widely present in Nature. Several compounds belonging to this class exhibit a multitude of biological properties,[1] such as antimicrobial, antifungal, anticancer and anti-HIV inhibitory activities.[2] Because of the growing medicinal interest on benzophenone based compounds[3], several methodologies for the synthesis of derivatives with new biological profiles have been developed and reported in the literature. In the present work, we explore the synthesis of benzophenone derivatives taking advantage of the reactivity of (*E*)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-ones **1a-e**. Compounds **2a-e** are formed through a tandem reaction with nitromethane (**Scheme 1**) involving a Michael addition/intramolecular process, followed by subsequent dehydration/aromatization. In a preliminary evaluation of antitumoral activity, MDA-MD-231 cell line cultures were exposed to different concentrations (100 µM-10 ηm) of compounds **2**. Compounds **2a**, **2b** and **2d** displayed significant cytotoxic effects with an IC_{50} of 26.6 µM, 28.1 µM and 50.2 µM, respectively. The effect of 10 µM of these compounds was further studied in a cell wound assay where they did not stimulate migration.



1a-e **2a-e**

a) R^1 = H, R^2 = H; b) R^1 = H, R^2 = Cl; c) R^1 = CH_3, R^2 = H
d) R^1 = Cl, R^2 = H; e) R^1 = CH_3, R^2 = Cl

Scheme1: Synthesis of benzophenone derivatives **2a-e** and single-crystal X- ray structure of **2a.**

In this communication, we will summarise the experimental conditions, the structural characterization of the prepared benzophenone derivatives **2a-e (**^{1}H and ^{13}C NMR and X-ray) as well as the proposed reaction mechanism.

Acknowledgements: Thanks are due to University of Aveiro and FCT/MEC for the financial support of QOPNA (FCT UID/QUI/00062/2013) and iBiMED (UID/BIM/04501/2013) research units as well as CICECO – Aveiro Institute of Materials (UID/CTM/50011/2013) through national founds and, where applicable, co-financed by the FEDER, within the PT2020 Partnership Agreement, and to the Portuguese NMR Network. L. Saidi is grateful for financial support from The Ministry of Higher Education and Scientific Research (Algeria), the University of Sciences and Technology Houari Boumediene (Algeria).

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Site-selective protein chemistry and its therapeutic relevance

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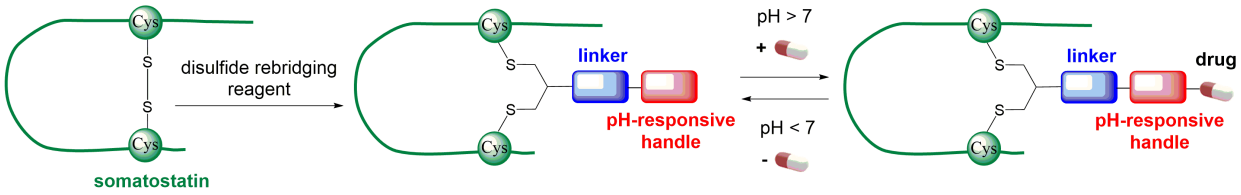
The overexpression of certain receptors on the surface of cancer tissues offers potential of exploiting correspondent peptides and proteins as carriers of therapeutics for selective drug delivery. The selective modification of disulfide bridges in therapeutically relevant peptides and proteins such as somatostatin (SST) and antibodies is attractive since they consist of at least one S-S bond.[1] Furthermore, the adaptation of a contemporary disulfide rebridging strategy results in well-defined and homogenous conjugates of peptide/protein and drug which is crucial for biosafety assessment and activity profile.
To impart stimuli responsiveness to the conjugates for controlled release of drugs in the acidic environment of tumour cells, we have capitalized on the pH responsive salicylhydroxymate group (SHA) - boronic acids (BA) dynamic covalent interaction.[2] We present herein the preparation of SST conjugate with a SHA handle and its application for delivery of BA-containing drugs for cancer therapy.



Scheme 1: Synthetic scheme of site-selective somatostatin modification and pH responsiveness of a salicylhydroxymate handle.

Acknowledgements: We thank the Marie Skłodowska-Curie ITN for a Research Scholarship.

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Validation of cleaning procedures in batch manufacturing of medicines

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In the manufacture and handling of pharmaceuticals it is essential to ensure the cleanliness of equipment and instruments used in the manufacturing, transport, handling and administration. Ensuring the integrity of medicinal products is supported by standards to be followed by stakeholders from the manufacturing process to the administration. In the specific case of drug production this is a critical situation due to two main facts: the large volumes of drugs involved in the production of a batch and the use of the same manufacturing equipment in the sequential production of different drugs.
In large-scale factory production, the contamination of a batch implies the spreading of this contamination throughout a large number of packages whose distribution would have to be withdrawn from the market with the costs of traceability, collection, treatment and follow-up of the patients to whom the nonconforming product was administered. The traditional methods to ensure the integrity of a product manufactured in batch processes are based on the validation of the cleaning process of the equipment with the periodic verification of the existence of contaminations. In this work, a new strategy of validation of the process of cleaning the material used in the manufacture of medicines was conceived and investigated. This new method guarantees the non-contamination of the drug produced by the research of residues of the cleaning agent, and also of the product previously produced, in the first fractions produced. The research of contaminant residues was performed through HPCL analysis with previously optimized and validated methods.

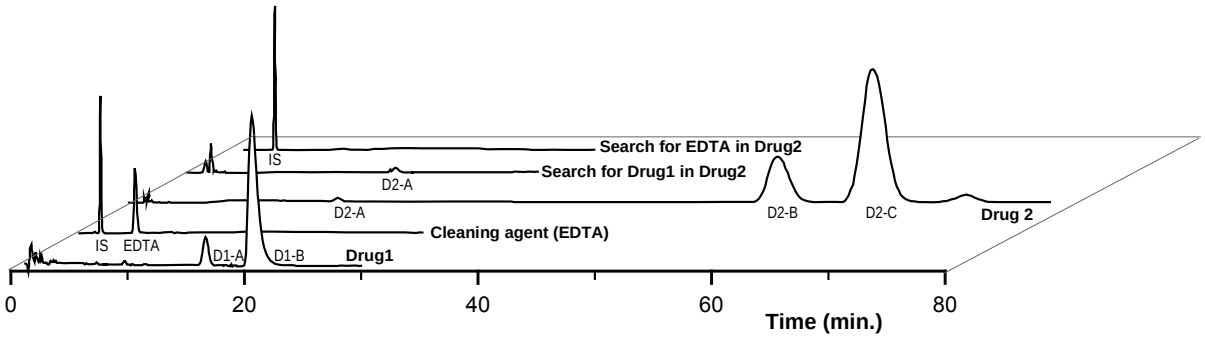

Figure 1- HPLC chromatograms for the sequence: Drug1, Cleaning, Drug2, Cleaning.

The validation of this new method of cleaning makes it possible to detect the contamination of the medicinal products during the initial stage of manufacture, thus preventing great losses of products. For companies, it could be a new tool for early detection of contamination and allowing the manufacturing process to be corrected even during its execution. The detection of contamination can also save the costs of compensation and legal responsibilities by preventing the entrance of a contaminated product in the market. The process can be even more rapid using the UPLC technique instead of HPLC.

NMDA receptor antagonists: an alternative approach to treat neurodegenerative disorders

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N-Methyl-D-aspartate (NMDA) receptors belong to the family of ionotropic glutamate receptors (iGluRs) and are localized in the cell membrane of neurons.[1] These receptors are fundamental for the normal function of the central nervous system (CNS), play a vital role in the normal development of the nervous system, and are extremely important in sustaining healthy memory, learning, and cognitive processes. The over-activation of these receptors leads to neuronal loss associated with major neurological disorders such as Parkinson's disease, Alzheimer's disease, schizophrenia, and epilepsy.[1] For this reason, the development of effective NMDA receptor antagonists is a promising therapeutic approach to fight these diseases.[1]

Here we present our latest results on the hit optimization of bicyclic lactams as NMDA receptor antagonists. Twenty-two novel enantiopure bicyclic lactams were designed, synthesized, and evaluated as NMDA receptor antagonists. To evaluate the potential of the synthesized compounds as NMDA receptor antagonists, we measured their capacity to inhibit NMDA-induced increase of intracellular Ca^{2+} levels in *in vitro* cultures of embryonary rat cortical neurons, using the Ca^{2+}-sensitive fluorescent dye Fluo-4. Most of the new compounds displayed NMDA receptor antagonism, and the most promising compound (**1a**) showed an IC_{50} value of 27 μM, on the same order of magnitude as that of memantine (47 μM), an NMDA receptor antagonist in clinical use for the treatment of Alzheimer's disease. Further biological evaluation indicated that this compound is brain permeable (determined by an *in vitro* assay) and non-hepatotoxic.[2]

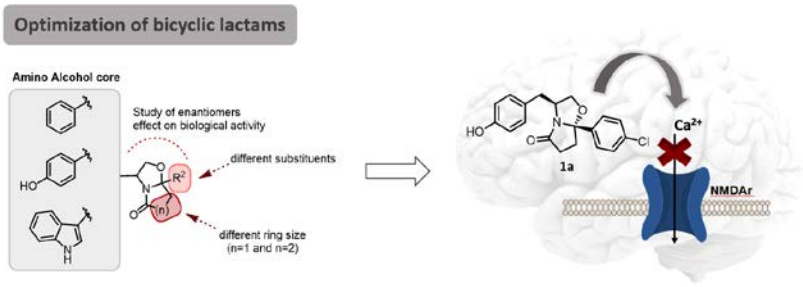

Figure 1: Synthetic strategy for the optimization of bicyclic lactam **1a,** an NMDA receptor antagonist.

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Targeted Mass Spectrometry-Based Metabolomics: From Biomarkers in Biofluids to Mechanistic Studies in Drug Discovery

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Targeted-metabolomics provide invaluable information concerning drug effects on cellular responses to signal transduction, protein function or homeostasis. Microvesicular steatosis is a chronic hepatocellular change associated with certain xenobiotics and it has been unequivocally associated with mitochondrial dysfunction and decreased fatty acid beta-oxidation (mitFAO).[1,2] We addressed the impairment of mitFAO associated with a histone deacetylase inhibitor, valproic acid (VPA), a worldwide used antiepileptic drug, nowadays intensively re-investigated as an anti-cancer drug. The carnitine conjugation pathway is of crucial importance to buffer the concentration of transient acyl-CoA accumulation, namely by interference with branched-chain amino acids oxidative metabolism.[3]

The present work aims to understand the hepatotoxicity and steatosis mechanisms associated with valproate-induced mitochondrial dysfunction, unveiling the added value for cancer treatment and repurposing of the drug. We investigated the prime interference of this drug treatment *in vivo* with mitFAO, through metabolites profiling using liver tissue of Wistar rats and respective biofluids, and also human plasma samples.

The qualitative and quantitative analysis of thirty individual free fatty acids (FFA) was achieved using GC-MS in SIM detection mode. A quantitative study of amino acids (AAs), free carnitine and forty different acylcarnitines (AC) was undertaken in liver tissues using tandem mass spectrometry (ESI-MS/MS). Quantification of NAD^+ and related metabolites was performed in liver by a novel methodological approach based on reverse-phase UHPLC-MS/MS.[4] The samples were obtained from Wistar rats subjected to a single intra-peritoneal injection or a subchronic regimen with the drug. VPA-treated animals revealed a significant increase in plasma levels of dicarboxylic acids as compared to controls. There was a significant dose-related increase of free carnitine and total acylcarnitine fraction in the liver, at the onset of treatment. In rats subjected to subchronic treatment, the hepatic levels of specific AC were different from controls. Activation of ω-oxidation seems to be an important pathway in rats, as in humans, to rescue mitochondrial FFA oxidation inhibited by VPA. Treatment with VPA is associated with a decrease in hepatic levels of the essential cofactors NAD^+ and $NADP^+$ after a single dose of the drug. Results contributed to elucidate the potential effects of the HDACi drug valproate *in vivo* on hepatic mitochondrial acetylated proteins (mitAcK) clarifying the relation with NAD^+ cellular content. Novel insights into the understanding of mechanisms underlying pharmacotoxicology and liver function were obtained through validated methods and MS-based analytical platforms. Small molecules and metabolites profiling are invaluable tools to the comprehensive understanding of human metabolism, which is of utmost importance for phenotyping in Health and Disease or at any stage of the drug discovery and development process.

Acknowledgments: FCT, Lisboa, Portugal (SFRH/BD/25913/2005; SFRH/BD/69062/2010).

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HPLC-DAD-HRMS characterization of the bioactive phenolic compounds in aqueous extracts of *Origanum vulgares L.*

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The oregano (*Origanum vulgare L.*), an aromatic plant of the Lamiaceae family has been used since ancient times as a fresh or dried culinary herb, Oregano is also a rich source of volatile aromatic compounds, as carvacrol, and the essential oil has been widely used in a variety of flavoring applications and cosmetic industries. It is known that the alcoholic extracts present notably bioactive, but scarce studies with aqueous extracts have been report. The antioxidant activity of the alcohol extracts of oregano is generally attributed to the presence of rosmarinic and caffeic acid derivatives. Herein, the antibacterial activities of the oregano aqueous extracts obtained by Soxhlet extraction and Microwave Assisted Extraction (MAE) methodologies were tested against MRSA ATCC43300 and *Pseudomonas aeruginosa* PAO1 by determining the MIC and MBC (broth microdilution method). Both extracts were active against MRSA with MIC=0.0015g/mL, MBC=0.003 g/mL (soxhlet) and MIC between 0.006 - 0.0017 g/mL, MBC between 0.006 - 0.007 g/mL (microwave). Cytotoxicity assays were conducted in human healthy bronchial/tracheal epithelial cells and fibroblasts. Cytotoxicity in normal human cells was less noticeable when extracts were obtained from microwave extraction. The main phenolic compounds of the oregano aqueous extracts obtained by MAE were fully characterized by HPLC-DAD-ESI-HRMS. Detection was carried out in DAD using 280 and 350 nm as preferred wavelengths, and the mass spectrometer was operated in the ESI negative mode. Identification and peak assignment of individual polyphenols was based on comparison of their retention times, MS spectra and MS/MS fragmentation patterns with those of standards, or published data together with accurate mass measurements. The extract was rich in rosmarinic acid and derivatives, namely lithospermic acid B. The presence of syringic acid and derivatives of protocatechiuc acid was also identified. An intense peak at *m/z* 421 was attributed to a dihydroxybenzoyloxymethyl)phenyl-β-D-glucopyranoside isomer, previously reported on *O. vulgare*.[1] Among the flavonoids, apigenin and its apigenin-7-*O*-glucuronide, apigenin-6,8-*C*-glucoside, luteolin and its luteolin-di-*O*-glucuronide, and eridictyol were also present in the extract, as shown in Figure 1.

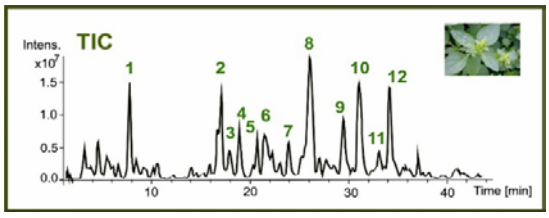

Figure 1. HR-total ionic chromatogram obtained in the ESI negative mode of an aqueous extract of *O. vulgare*: (**1**) syringic acid (*m/z* 197.0433); (**2**) n.i. (*m/z* 387.1650); (**3**) dihydroxybenzoyloxymethyl)phenyl-β-D-glucopyranoside isomer (*m/z* 421.1120); **(4)** apigenin-di-C-glucoside (*m/z* 593.1490); (**5**) hydroxybenzoic acid derivative (*m/z* 567.1697); (**6**) luteolin-di-*O*-glucuronide (m/z 637.1032); (**7**) luteolin-7-*O*-glucuronide-3´-*O*-glucoside (m/z 623.1225); (**8**) dihydroxybenzoyloxymethyl)phenyl-β-D-glucopyranoside isomer (*m/z* 421.1120); (**9**) luteolin-7-*O*-glucuronide (m/z 461.0707); (**10**) epi-lithospermic acid B (m/z 717.1481); (**11**) lithospermic acid B (m/z 717.1478) (**12**) rosmarinic acid *(m/z* 359,0780).

Acknowledgements: This work was supported by Fundação para a Ciência e a Tecnologia (FCT, Portugal) (RECI/QEQ-MED/0330/2012 and UID/QUI/00100/2013). The Portuguese MS network is also acknowledged for providing access to the facilities.

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Carotenoids content of soups consumed in Portugal

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Introduction and Objectives: There are many studies showing strong correlations between diets rich in carotenoids, both with the improvement of the immune system and with the reduction of the risk of some degenerative diseases such as cancer, cardiovascular diseases, cataract and macular degeneration. Fruits and vegetables are the main source of carotenoids. Portugal is one of the largest consumers of soup in the world and soup is a great way to ingest vegetables. The main objective of this work was to evaluate the α-carotene, β-carotene, β-cryptoxanthin, lycopene, lutein and zeaxanthin content of soup samples representative of the Portuguese consumption.
Methods: The soups were selected accordingly to the results of the AEVPP09 study[1] and were prepared according to the habits of the Portuguese using ingredients acquired in markets, super and hypermarkets in region of Lisbon or were acquired in restaurants/hypermakets of the same region. Each pooled sample, representative of each soup, was prepared from 12 independent sub-samples. The identification and quantification of carotenoids in food were done by a reverse phase HPLC method using a DAD-UV-Vis detector, external standard calibration and internal standard[2].
Results: From the analysed soups, cabbage and beans soup and watercress soup had the highest content of α-carotene (244 – 447 µg/100 g), β-carotene (543 – 702 µg/100 g) and lutein (169 – 220 µg/100 g). Tomato soup showed the highest content of lycopene (28.6 – 157 µg/100 g) and zeaxantine (11.0 – 25.3 µg/100 g). Green kale soup, chicken soup and shrimp cream soup presented moderate total carotenoid content (115 – 242 µg/100 g).
Conclusions: The analytical method used in this work allowed the quantification of the carotenoids under study in the chosen soups. The results showed that the Portuguese soups can be good sources of carotenoids. From the results of this work it was also possible to conclude that carotenoid content of soups varies greatly with its ingredients being the carotenoid-rich soups based on cabbage/kale, carrots and/or pumpkin.

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HPLC-DAD-MS characterization of *Carpobrotus edulis* L. extracts processed by an integrated Green Chemical approach

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The natural plant *Carpobrotus edulis* L. (*C. edulis*), a weed pant widely spread along the coastal zone of Portugal, is considered a fast growing weed with pronounced medicinal potential. Quantitative phytochemical analysis of the *C. edulis* extracts revealed a high percentage of the phytochemicals from phenolic family (up to 50-60 %) with appreciable amount of flavonoids sub-family, which is known to have strong antioxidant properties and high biological activities.[1]
In the present study, C. *edulis* was chosen as a renewable low feedstock for an advanced processing development. An advanced scheme was integrated at close loop of the green processes development to produce both the phytochemicals (with emphasis on flavonoids sub-family) using the Microwave Assisted Extraction (MAE), and the bio-fertilizer *via* residual biomass (waste after extraction) processing using Microwave Assisted Activation (MAA) approaches. Conditions of the plant microwave assisted processing and properties of the resulted bio-products (either phytochemicals or biochar) were optimized and compared with well-known conventional approaches, such as Soxhlet extraction and slow/flash pyrolysis of biomass in term of time, energy efficiency, safer solvents usage, and products yield. It was concluded, that the major advantages of MAE are decrease of a process time by 7-8 times and increase of energy efficiency up to 97%. The yield of liquid product – extracts was found to be of 43%, from which 8.5 % is due to the flavonoids sub-family; while solid biomass yield is of 57%, from which the yield of the bio-fertiliser is of 65%.
The main phenolic compounds of the *C. Edulis* aqueous extracts obtained by MAE were fully characterized by HPLC-DAD-ESI-HRMS (Figure 1). The chromatographic profiles exhibited the separation of 12 compounds that, based on absorption maxima observed in the UV spectrum, fall into two subclasses of phenolic compounds. The first seven not well-resolved peaks, with a maximum wavelength of around 280 nm, were attributed to procyanidin, a class of oligomers of flavan-3-ols units (+)-catechin and (-)-epicatechin. The five compounds separated between 330-350 nm. were attributed to *O*-methylated flavonol derivatives, based on their MS and MS^n fragmentation behavior under ESI negative ion mode analysis.

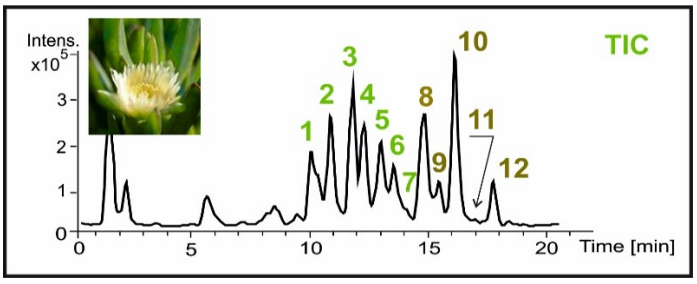

Figure 1. HR-total ionic chromatogram obtained in the ESI negative ion mode of an aqueous extract of *C.edulis*: (**1** and **3**) B-type procyanidins (*m/z* 577.1368); (**2, 4** and **6**) procyanidin tetramers PD4 (*m/z* 1153.2621); (**5**) procyanidin trimer PC2 (*m/z* 865.2015); (**7**) B-type procyanidin hexamer (*m/2z* 864.1925); (**8**) laricitrin-rutinose (m/z 639.1582); (**9**) isorhamnetin-rutinose (m/z 623.1633); (**10**) syringetin-*O*-di-glycoside (m/z 653.1747); (**11** and **12**) laricitrin- and syringetin-*O*-tetra-glycosides (*m/z* 947.2491 and 961.2636).

Acknowledgements: This work was supported by Fundação para a Ciência e a Tecnologia (FCT, Portugal) (RECI/QEQ-MED/0330/2012 and UID/QUI/00100/2013). The Portuguese MS network is also acknowledged for providing access to the facilities.

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Synthetic strategies in the design of new photosensitizers based on tetrapyrrolic derivatives

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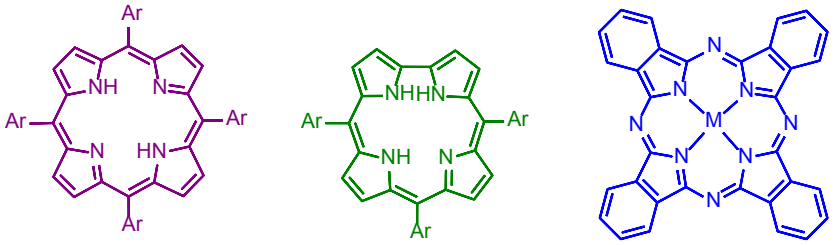
Porphyrins and analogues have been developed as powerful tools for applications in various fields namely in medicine due to their advantageous photophysical properties like strong light absorption, high emission, and an efficient ability to generate cytotoxic oxygen species. These applications are strongly dependent on the availability of compounds with adequate and specific structural features which can explain the high number of studies related with the preparation and modification of natural and synthetic porphyrin derivatives. In particular, the use of synthetic macrocyles like *meso*-tetraarylporphyrins, corroles and phthalocyanines (Figure 1) has been considered a good alternative to the use of natural porphyrins due to their less complex structures and easily synthetic accessibility. The usefulness of this type of derivatives can be improved through the adequate functionalization at β-pyrrolic positions or at *meso* positions.
In this communication, it will be discussed how simple transformations conducted in this type of templates can afford compounds with high PDT efficiency towards cancer cells and to photoinactivate microorganisms.[1-3]



Porphyrin **Corrole** **Phthalocyanine**

Figure 1

Acknowledgements: Thanks are due to the University of Aveiro and FCT (Fundação para a Ciência e a Tecnologia) for the financial support to the QOPNA research project (FCT UID/QUI/00062/2013) through national funds and where applicable cofinanced by FEDER under the PT2020 Partnership Agreement, and also to the Portuguese NMR Network. ATPC Gomes, NMM Moura and JFB Barata thanks FCT for their postdoctoral grants, SFRH/BPD/79521/2011, SFRH/BPD/84216/2012 and SFRH/BPD/63237/2009 respectively. Kelly A. D. F. Castro also thanks CNPq for the post-doctoral scholarship (Process 201107/2014-7).

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Evaluation of several phytochemicals as ligands/probes for copper chelation using UV and fluorescence spectroscopy

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Introduction: Polyphenolic compounds (PPCs) are a large family of phytochemicals. Some of them like gallic acid, methyl gallate and ellagic acid, are nutraceuticals reported as beneficial in the prevention and slowing down of symptoms in the early stages of Alzheimer and senile dementia[1]. They are non toxic and easily commercially available. Tannic acid, that can be found in red wine, tea and spinach among other foods and a ellagitannin rich extract obtained from *Quercus pyrenaica* bark, an endemic tree of Portugal, used to make barrels for wine and brandy, were also investigated. It is already known that small amounts of the tannins of the bark dissolve in the alcoholic beverage increasing its organoleptic properties. Recently it was found that divalent and monovalent copper ions are involved in brain in the oxidative damage of proteins increasing the formation of amiloid peptides[2]. The presence in chemical structures of vicinal hydroxyl groups make the above compounds good candidates as copper and zinc quelators and fluorescent probes for these complexes.
Aim: To investigate some polyphenolic compounds (PPCs) as fluorescent probes for the detection and quantification of copper (II) and zinc ions in solution.
Materials and methods: Aqueous solutions of gallic acid, methyl gallate and ellagic, tannic acid and a ellagitannin rich extract obtained from *Quercus pyrenaica* bark were investigated using a Luminescent spectrometer Perkin Elmer LS 55 before and after addition of copper(II) and Zn^{2+}. Pre-scan excitation and emission spectra were recorded in the range of 200 to 800 nm and 200 to 900 nm respectively. UV spectra were obtained in a Shimadzu 1603 Spectrophotometer.
Results: Ellagic acid, tannic acid and ellagitanin extract showed different excitation spectra in the presence of copper (II) and zinc ions, when compared with the spectra of these substances alone. The differences in maximum intensities were very important for tannic acid and the bark extract and moderate for ellagic acid. The presence of copper ions greatly increase the intensity of peaks of tannic acid being similar the spectra in the 1:5 and 1:10 proportions. The increase in the intensity of peaks due to the presence of zinc ions is only important in 1:10 mixture. Presence of both divalent ions also increases the intensity of peaks in ellagitanin excitation spectra being the effect a slightly higher with zinc ion. The presence of these ions greatly affected the intensity and position of bands of ellagic acid UV spectra, with disappearance of bands at 254 and 356 nm and a bathochromic shift of the band at 280 nm. Excitation spectra of gallic acid and methyl gallate showed no differences in presence or absence of divalent ions.
Conclusion: The techniques used confirmed that ellagic acid, an important nutraceutical, tannic acid and also *Q. pyrenaica* bark ellagitanin, have the ability to complex divalent copper and zinc ions preventing the damages due to the excess of these ions in the body.

Acknowledgements: This project was supported by Fundação para a Ciência e Tecnologia (FCT), Portugal (UID/MULTI/00612/2013)

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An overview on the biological properties of Ag(I) camphor complexes

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In the last decades scientific achievements in the areas of diagnostic and therapy contributed to a considerable improvement in global human health. However, the fight against diseases is never finished and actually there are several types of infections by bacteria, fungi and virus as well as cancer for which there is no suitable treatment. Such threats are challenges to find new substances with antimicrobial and/or anti proliferative properties.
Aiming at contributing to face the problem, new camphor derived Ag(I) complexes were synthesized and their biological properties evaluated. The choice of camphor derivatives as ligands to coordinate silver was based on the known antimicrobial and insect-repellent properties of camphor and on the fact that a wide variety of camphor derivatives with distinct stereochemical and electronic characteristics can be synthesized. Camphor imines ($OC_{10}H_{14}NY$), camphor sulphonimines ($SO_2NC_{10}H_{13}NY$) and bicamphors ($(OC_{10}H_{14}N)_2Y$) (Figure 1) were used as ligands to prepare complexes of formula $[Ag(NO_3)L]_n$ and $[Ag(NO_3)L_2]$.

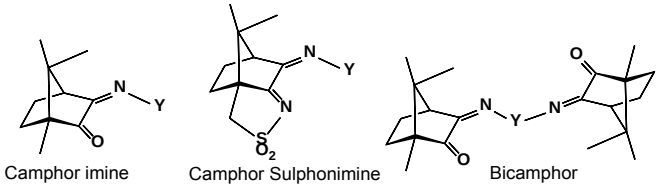

Figure 1: Camphor derived ligands (L)

The biological data obtained till now, shows that Ag(I) camphor complexes display anticancer activity against *cisplatin*-resistant A2780cisR and A2780 cells and antimicrobial activity against bacteria and fungi. The cytotoxic activity against the *cisplatin*-resistant A2780cisR cells is specially relevant since the IC_{50} values of the complexes are one order of magnitude lower than that of *cisplatin*.[1] The complexes also behave as bactericide[2] against Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli, Pseudomonas aeruginosa, and Burkholderia contaminans*) bacteria and as fungistatic against Candida species. Furthermore, the extremely low MIC values (2 μg/mL)[3] calculated for Candida spp (*C. glabrata*, *C. tropicalis* and *C. parapsilosis*) suggest the complexes as as promising alternatives to the existing antifungals.

Acknowledgements: Financial support by FCT-Fundação para a Ciência e Tecnologia through projects UID/QUI/00100/2013.

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Can inhibition of glycolysis increase the selectivity of photodynamic therapy towards cancer cells?

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The selectivity of treatments used in cancer therapies is essential to enable drugs to kill cancer cells while sparing normal ones. Most approaches to improve selectivity aim at targeting the tumor through chemical modifications of the drug. This leads to new drugs and lengthy regulatory pathways for marketing authorization. Alternatively, the combination of different drugs may potentiate the efficacy and selectivity of a treatment leading to the administration of lower doses, thereby minimizing adverse effects, and facilitate clinical approval.

This work presents the combination of photodynamic therapy (PDT) with other drugs to improve efficacy and selectivity in cancer treatments.

PDT uses a photosensitizer and light with an appropriate excitation wavelength that activates the photosensitizer in the presence of oxygen to produce reactive oxygen species.[1] Tumor cells have an alteration in glucose metabolism, characterized by an increase in glycolysis pathway, even in environments with normal oxygen concentration (Warburg Effect).[2] This modification has been explored, including in clinical trials, with the expectation that the inhibition of glycolysis should alter especially the metabolism of tumor cells.

2-Deoxyglucose (2DG), a compound that is phosphorylated to 2-deoxy-D-glucose-6-phosphate, which is not metabolized and accumulates in the cell, inhibiting glycolysis.[3] 3-Bromopyruvate (3BP) inhibits hexokinase (an enzyme of the glycolytic pathway) and also has effects on mitochondria, inducing cell death.[4] Oxythiamine (OXY) is an analogue of thiamine and a noncompetitive inhibitor of transketolase (an enzyme of pentose phosphate pathway). Transketolase plays a vital role in the synthesis of important molecules for cell survival, directly correlated to glycolytic pathway. The inhibition of this enzyme leads to apoptosis of cancer cells.

The hypothesis investigated in this study is that the inhibition of glycolysis, trough these molecules, increases oxidative stress due to an increased production of hydrogen peroxide and superoxide ion, which may increase the sensitivity to the oxidative stress produced by PDT.

In vitro combination studies were performed in both cancer and normal cell lines, CT26 (colon carcinoma – mouse) and NIH/3T3 (fibroblasts – mouse), respectively. We started our studies with the evaluation of IC50 of redaporfin[6] in the different cell lines and then co-incubation with 2DG, 3BP and OXY at nontoxic concentrations, in order to examine which combination was more effective than the individual effects. Inhibition of glycolysis seems to increase the susceptibility of the cancer cell line to PDT. On the other hand, fibroblasts seem to be less responsive to the combination with PDT with glycolysis inhibition. Further studies are required to assess the feasibility of transferring this combination to in vivo studies.

Acknowledgements: This work was financially supported by the Portuguese Science Foundation (Pest-OE/QUI/UI0313/ 2014 and PTDC/QEQ-MED/3521/2014).

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Platinum Complexes Bearing Guanosine Derived N-Heterocyclic Carbenes

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Cisplatin was the first platinum-containing compound used in cancer therapy and continues to be employed worldwide. However, its clinical use is restricted due to the frequent development of drug resistance, the limited spectrum of tumours against which the drug is active and severe normal tissue toxicity[1-3]. Taking this into account, it is of upmost importance to develop more effective metallodrugs, with improved selectivity and reduced side effects. Guanine is a purine base present in DNA and RNA, which provides an excellent recognition tool due to its base pairing properties, both for self-aggregation, or for well-known Watson-Crick base pair interactions. Due to these properties, we envisaged that the utilization of guanine derivatives as ligands for the development of novel anticancer metallodrugs would provide more selective compounds. The metal centre via should be bounded in a coordination mode that allows the purine base to retain all its base pairing sites. One such way is through the formation of an M-C bond, inducing a coordination via N-Heterocyclic carbene at C8. Herein we report the synthesis and characterization of novel organometallic compounds derived from guanosine (**Figure 1**), along with the preliminary evaluation studies of their base-pairing properties.

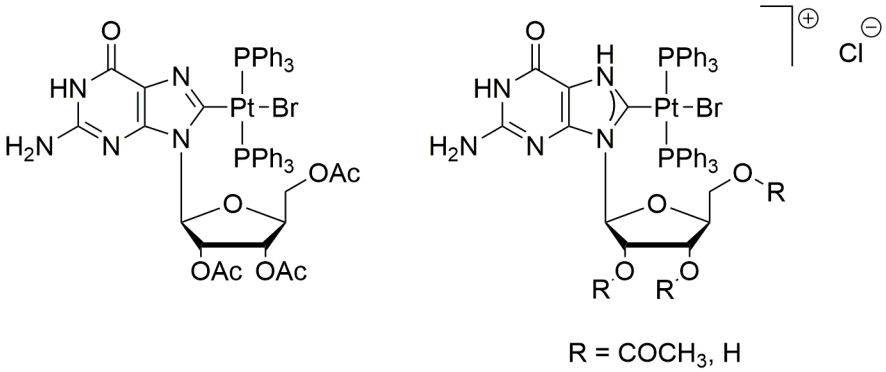

Figure 1: Structure of the anionic (left) and of the carbene (centre) compounds herein reported, and numbering scheme.

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Orthogonal *N*-Terminal cysteine modification *via* thiazolidine cyclization

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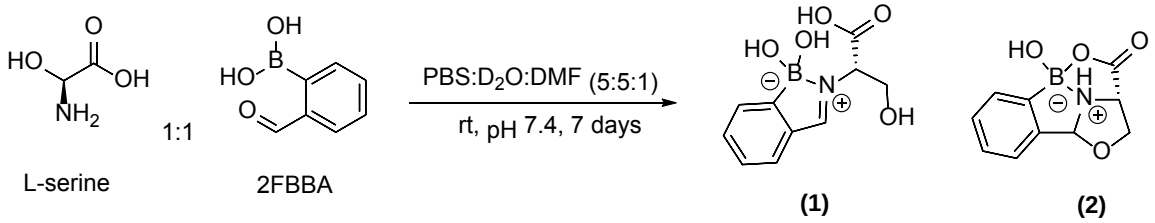
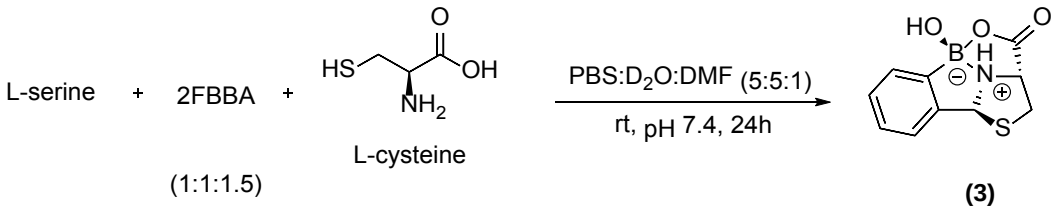
By far the most explored property has been the nucleophilic reactivity of amino acid residues with respect to proteins bioconjugation. In fact, lysine and cysteine have been the election targets especially due their own reactivity since they bear the most reactive nucleophiles in their residue chain.[1] 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).

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Influence of procyanidin B3 in gliadin digestion under different gastro-intestinal conditions

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Phenolic compounds are in a widespread of vegetables resulting of their secundary metabolism. They have a strong focus of research interest because of their health effects in the prevention and/or treatment of several chronic diseases. Anticarcinogenic, antiatherogenic, antirombotic, anti-inflamatory, antiulcer, antiallergenic, anticoagulant, antimicrobial, vasodilatory and analgesic activities are attributed to the consumption of food phenolic in humans.[1] Moreover, some harmful effects have also been reported for these compounds. In fact, polyphenols were often described in the past as antinutritional factors since they can negatively affect animal production.[2] These xenobiotic functions are mainly attributed to the tannin subgroup. Indeed, vegetal tannins are able to bind and inhibit digestive enzymes such as lipases, α-amilases and α-glucosidases [3] and even proteases [4] as well as dietary proteins leading to the formation of relatively less digestible complexes. Celiac Disease (CD) is a heritable chronic inflammatory condition of the small intestine caused by the ingestion of gluten proteins from widely prevalent food sources such as wheat, rye, barley and to lower extent, certain oat varieties. Due to the high proline content of gluten proteins and because human proteases are unable to hydrolyze amide bonds when they are adjacent to conformationally constraint proline residues, relatively stable gluten-derived peptides are allowed to reach the intestinal mucosa at unusual high concentrations exerting toxic effects. It was previously demostrated that procyanidin B3, a common food tannin, can interact with gluten-derived peptides.[5] Therefore, tannins can potentially influence gliadin digestion by two ways: inhibiting the digestive enzymes or through the interaction with gliadin-derived peptides. The aim of this study was to verify the influence of procyanidin B3 in gliadin digestion at different conditions. Enzymatic inhibition was also evaluated. The presence immunotoxic peptides was determined at the intestinal digestive phase to verify the potentially toxicity of each digested protein fraction and to evaluate the effect of procyanidin B3 in the amount and nature of the resulting peptides. Qualitative and quantitative differences were found between fractions in terms of CD T-cell epitopes as well as in the number of peptides containing them. When procyanidin B3 was added to the assay, the number of released immunotoxic peptides was significantly reduced. Altogether, this study provides valuable insights about the benefit of food tannins ingestion and influence during the digestion of dietary allergenic proteins as it supports the potential applicability of polyphenols as nutritional protective agents on a CD point of view.

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Flavonols isolated from *Hedychium gardnerianum* leaves

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Hedychium gardnerianum Sheppard ex Ker Gawl (Zingiberaceae) is a Himalayan rhizomatous perennial herb, brought to the Azores Islands in the 19th century as an ornamental plant.[1] It is an aggressive invasive weed capable of spreading rapidly and dominating large areas in the Azores. Other *Hedychium* spp. were used in traditional medicine, *e.g.* leaves of *H. coronarium* are used in Bangladesh to treat stomach ailments, and rhizomes of the same species are used in traditional Chinese medicine to treat headache, diabetes, contusion, inflammation and sharp pain due to rheumatism.[2] The anti-acetylcholinesterase effects of the essential oils of *H. gardnerianum* was reported previously.[3] Phytochemical studies on the rhizome of *H. gardnerianum* have led to the isolation of labdane diterpenes, xanthones, salicylic acid and oplopanone.[4] Following our interest in new active natural compounds from plant, we report the isolation by chromatographic techniques, of several secondary metabolites from of *H. gardnerianum*, including four flavonol derivatives **1a**-**1d** (**Figure 1**) from dichloromethane extract leaves, which exhibited anticholinesterase activity in a preliminary screening procedure. The structures of all isolated compounds were elucidated on the basis of detailed spectral analysis (1D and 2D NMR, MS and HRMS). This is the 1st time that flavonols are reported from *H. gardnerianum*.

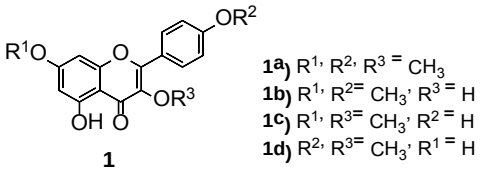

Figure 1: Chemical structure of flavonols isolated from *Hedychium garderianum* leaves.

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Cocrystallization screening of new hydrochlorothiazide cocrystals

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Pharmaceutical industry is facing an enormous problem when dealing with active pharmaceutical ingredients (APIs), which have a desirable pharmacological activity display, but low solubility and therefore limited bioavailability.[1] Cocrystallization is growing up as an approach to facing this problem. Cocrystals are considered as crystalline materials comprised of at least two different components solids at room temperature and held together by non-covalent bonds.[2] The aim of this work is to produce new cocrystals of hydrochlorothiazide (HTZ), an API with low solubility that belongs to class II of the Biopharmaceutical Classification System (BSC).

A screening methodology was attempted using six different coformers (all considered safe for human consumption) in the ratio of API:coformer of 1:1 and 1:2 and seven different solvents. The cocrystallization was performed by ultrasound assisted in a 96-well plate (Figure 1) [3]. The final product was characterized by mid infrared spectroscopy (MIRS) to verify which experimental conditions (API:coformer ratio, coformer and solvent) had influence cocrystal formation. To increase the scale, the selected ones were subject to cocrystallization by slurry. An appropriated amount of solvent was added to the API and coformer in a flask, and placed in a bath at a control temperature of 30ºC with lateral agitation (200 rpm) during 24h. The final product was vacuum filtrated and characterized by near infrared spectroscopy (NIRS) and differential scanning calorimetry (DSC) to confirm cocrystal formation.

In future work the new HTZ cocrystals are going to be subjected to solubility measurements to compare their solubility with HTZ.

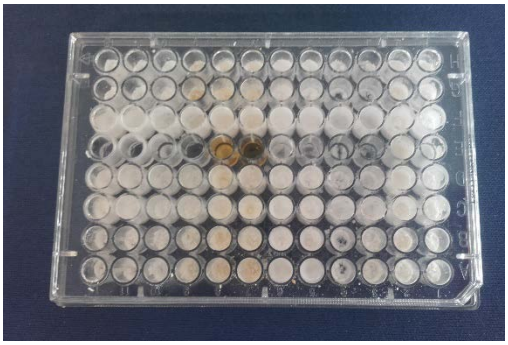

Figure 1: 96-well plate after the cocrystallization by ultrasound assisted.

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Ionic Liquids and Salts of Antibiotic and Antiviral Drugs

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Synthesis of Ionic Liquids from Active Principle Ingredients (API-ILs) has been one of the focus of our group over the last years. The combination of APIs as anions or cations with appropriate organic counter ions can be an innovative solution to the polymorphism behavior of several drugs as well as to improve their water solubility, permeability and corresponding bioavailability and biological activity.[1] Within this context, novel ionic liquids based on antibiotic and antiviral Active Pharmaceutical Ingredients (API-ILs) with enhanced pharmaceutical properties and decreased toxicity will be presented.[1] In this communication, we present our latest developments in the field of API-ILs using antibiotics from several therapeutic groups as anions, namely the β-lactam antibiotics (Ampicillin and Amoxicillin), cephalosporin (Cefuroxime) and carbapenem (Meropenem). These APIs were combined with appropriate biocompatible organic cations (e.g. choline, cetylpyridinium, alkylimidazolium). On the other hand, the anti-tuberculostatic drug Isoniazid was combined as cation with biocompatible anions based on suitable organic acids. Finally, Acyclovir was investigated both as anion and as cation (see Figure 1).[2]

The prepared API-ILs were characterized by standard spectroscopic techniques as well as thermal properties (calorimetric analysis by DSC) to evaluate the mitigation or elimination of the polymorphic behavior presented by the parent APIs.[3] Additionally, the solubility in water and biological fluids as well as the toxicological profile of new API-ILs will be discussed.

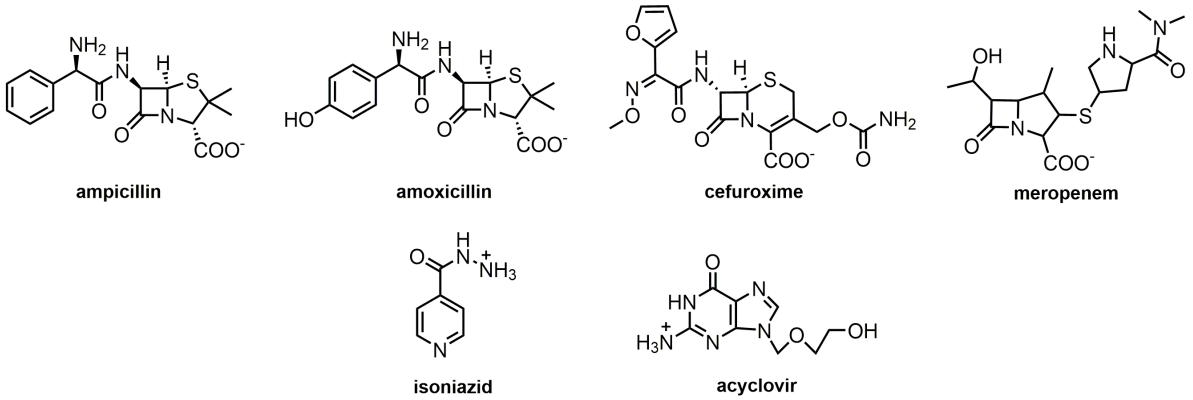

Figure 1: Novel API-ILs based on anionic Ampicillin and bisphosphonates combined with biocompatible organic cations.

Acknowledgements: This work has been supported by Fundação para a Ciência e Tecnologia (PTDC/CTM-NAN/120658/2010; IF/0041/2013/CP1161/CT005; PEst-C/EQB/LA0006/2013, RECI/BBBBQB/0230/2012) and Solchemar company.

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Synthesis, Characterization and DFT Studies of New 2-Arylidene-Thiazolo[3,2-*a*]pyrimidines as Prospective Antitumor Scaffolds

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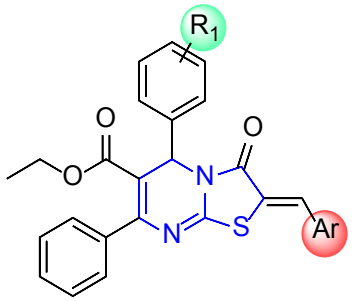
Thiazolopyrimidines and related heteroaromatic compounds are important classes of N-containing fused heterocycles widely used as key building blocks for pharmaceutical agents due to a wide range of biological properties that include antimicrobial activity and also the ability to inhibit kinase enzymes, such as casein kinase 2 and YycG histidine kinase, a property thought to be associated with antitumor activity.[1-5] As part of a program aimed at preparing new bioactive heterocycles, we designed and synthesized a series of thiazolo[3,2-*a*]pyrimidines and their 2-arylidene derivatives (**Scheme 1**). Recent reports suggest that structures of this class are useful bioactive moieties in a plethora of synthetic pharmaceutical scaffolds due to their physico-chemical properties, such as hydrophobicity and steric characteristics. The products were fully characterized by 1D- and 2D-NMR, high resolution ESI-MS/MS and single crystal X-ray diffraction analysis, which indicated a consistent *Z* configuration at the arylidene double bond. Additionally, the optimized geometry and total energies of the *Z*- and *E*-diastereomers were studied by DFT, using Gaussian at the B3LYP/6-31 + G (d) level. The results were fully consistent with the X-ray crystal structure data. Studies are underway to assess the biological activities of the new compounds.



Scheme 1: General structure of the 2-arylidene-thiazolo[3,2-*a*]pyrimidines reported in this work.

Acknowledgements: This work was supported in part by Fundação para a Ciência e a Tecnologia (FCT, Portugal), through grants RECI/QEQ-MED/0330/2012, RECI/QEQQIN/0189/2012, UID/QUI/00100/2013 and SAICTPAC/0019/2015. MYM also thanks the Egyptian Higher Education Ministry, Cultural Affairs and Missions sector, for financial support.

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New Cu(II) complexes with pyrazolyl Schiff base: synthesis and biological evaluation

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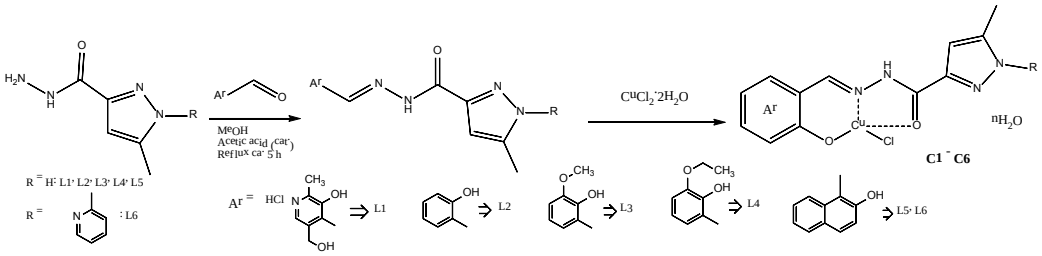
Pyrazole derivatives have gained increasing attention and there are several reports on the anticancer, antibacterial and antiviral activities of pyrazole metal complexes.[1] Moreover, there is a growing interest in developing new anticancer drugs based on endogenous metal ions, such as copper, considered to have less side-effects, improved spectrum of efficacy and lower toxicity.[2] Therefore, we hypothesized that copper complexes of pyrazole Schiff bases could be good candidates as anticancer drugs. The syntheses, structural characterization, interaction with biological macromolecules and cytotoxicity of new copper(II) complexes of pyrazole based "ONO" tridentate Schiff base ligands (see **Scheme 1**) was carried out. All compounds were characterized by analytical techniques; the complexes were found to have square based geometries with $d_{x^2-y^2}$ ground-state. The tridentate ligands coordinate copper forming two chelate rings and the coordination sphere is completed with a chloride atom. Quenching fluorescence experiments showed that all complexes (except **C3**) are able to interact with DNA and HSA. Complexes **C5** and **C6**, with larger aromatic systems, showed much higher cytotoxicity (in the low μM range), than **C1**-**C4**, as well as IC_{50} values much lower than *cisplatin* in the tested cell lines (MCF7 and PC3). For **C6** the results suggest that the mechanisms of cell death do not seem to be mediated by apoptosis, through caspases 3/7 activation, but by involving membrane potential and imbalance in physiological elements such as P, K and Ca.



Scheme 1: Syntheses of the ligands and Cu(II) complexes.

Acknowledgements: This work was supported by Fundação para a Ciência e Tecnologia (FCT) (projects UID/QUI/00100/2013, UID/MULTI/04349/2013, UID/BIO/04565/2013, RECI/QEQ-QIN/0189/2012, RECI/QEQ-MED/0330/2012), Programa Operacional Regional de Lisboa (LISBOA-01-0145-FEDER-007317) and programme Investigador FCT. The Portuguese NMR and Mass Spectrometry IST–UL Centers are acknowledged for the access to the equipment.

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Determination of fluoride in mineral waters and tea consumed by the portuguese population: is there a risk of fluorosis?

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Fluoride is a chemical element typically used in tooth decay treatment and is present in oral hygiene products such as tooth pastes and elixirs. Additionally, fluoride is present in various environmental, clinical and food samples.
As a general rule, small amounts of fluoride are considered to be vital for the human organism, but in larger amounts it can become toxic. In fact, for adults, the lethal dose is 0,20-0,35 grams of fluoride per kilogram of body weight.
On the other hand, fluorosis may be caused by the intake of fluoride over prolonged periods of time. Skeletal fluorosis and dental fluorosis are of two main types: in dental fluorosis the structural integrity of enamel is affected and small pits are left in teeth as it breaks away; skeletal fluorosis is the accumulation of fluoride in skeletal tissues associated with pathological bone formation.
Two important sources of fluoride intake by humans are the consumption of bottled water and tea/infusions. Tea leaves are usually very rich in fluoride and the tea plant (*Camellia sinensis*) takes up fluoride from the soil and accumulates it in its leaves. It is considered a major source of fluoride. A substantial amount of this element is released during tea infusion and nearly all (about 94.9%) of the released fluoride is available to consumers.
In what ground waters it concerns, the main sources of fluoride are minerals found in soil such as fluorospar (CaF_2), cryolite (Na_3AlF_6) and chiolite ($Na_5Al_3F_{14}$). One of the main factors affecting fluoride availability in soil is pH. In fact, acidic conditions (pH<6) favour the solubility of fluoride bearing minerals, increasing its concentration in ground waters.[1]
The motivation and concern behind the present work relies on the increasing consumption of mineral bottled water and tea/infusions by the portuguese population, and therefore the possible risk of fluorosis development. In fact, our group conducted a survey study where 15 commercial samples of mineral waters and 15 commercial samples of tea and infusions were analysed.[2,3] In the case of mineral waters samples were chosen in order to cover different regions of Portugal. As teas and infusions it concerns, the most common ones were analysed including, black tea, white tea, green tea, chamomile, lemon balm, peppermint or lemon verbena, among others. Additionally, the results obtained for the same kind of tea prepared from tea leaves and tea bags, were compared.
The concentrations of fluoride in the studied samples were carried out by direct potentiometry using a fluoride ion selective electrode and an Ag/AgCl reference system.[4]
The obtained results revealed the presence of fluoride in almost all the analysed samples. In fact, in some water samples as well as in some tea samples, the fluoride concentration overcomes the average value recommended by the World Health Organization (regarding the prevention of fluorosis), which is 1,0 miligrams of fluoride per liter of water.

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Synthesis of antibacterial and antitumor alkylaminophenols by Petasis borono Mannich multicomponent reaction

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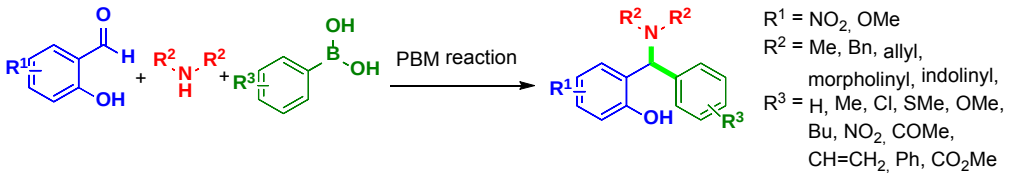
The Petasis borono–Mannich (PBM) reaction, a multicomponent reaction of boronic acids, aldehydes/ketones, and amines, is a remarkable tool for the preparation of complex molecules in a single step from readily available starting materials. The reaction has been used in the preparation of very different classes of compounds spanning from α-amino acids, to imininocyclitols or 2,5-dihydrofurans as well as natural products.[1] A small library of alkylaminophenols obtained from using salicylaldehyde as the PMB reaction aldehyde component was prepared (**Scheme 1**).



Scheme 1: Preparation of alkylaminophenols library

The biological properties of the obtained compounds were assesed (**Figure 1**).[2] Indoline derived alkylaminophenols containing a nitro group at the *para*-phenol position showed considerable activity against several bacteria tested, with minimal inhibitory concentrations (MIC) as low as 1.36 μM against *Staphyloccocus aureus* and *Mycobacterium smegmatis*.[2a] The citotoxicity of the same family of compounds was tested against osteosarcoma (U2OS) and human embryonic kidney cells. A citotoxic effect towards U2OS cell line as potent as IC_{50}=37 μM was determined. Further experiments revealed that the most promising compounds induce cell death by apoptosis and also acted as a migration inhibitors. Analysis of the mitochondrial calcium following treatment with the citotoxic agents on U2OS cells showed a significant reduction in the level of mitochondrial calcium concentration suggesting a mitochondrial calcium-independent mechanism in triggering apoptosis.[2b,c]

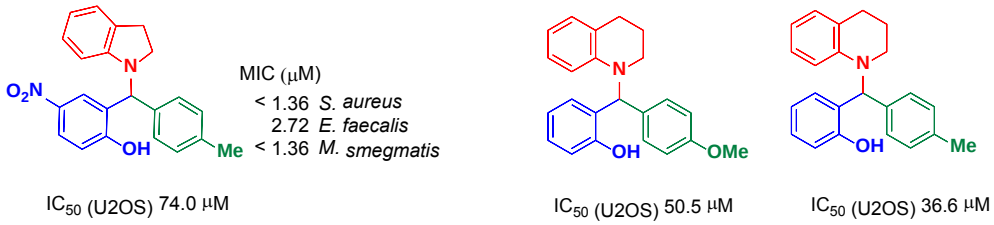


Figure 1: Antimicrobial and antitumour activity of alkylaminophenols

Acknowledgements: Academy of Finland is thanked for financial support.

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Progress towards Neofiscalin A Synthesis, a Potent Antibacterial Agent

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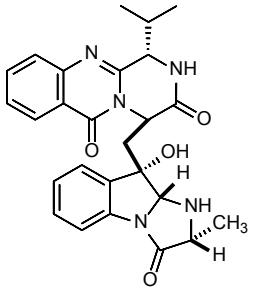
Neofiscalin A (**1**) is a marine natural product with an indolic alkaloid structure, containing a pyrazino[2,1-*b*] quinazoline-3,6-dione moiety, and isolated from *Neosartorya siamensis* with antimicrobial activity and biofilm inhibitory against gram-positive bacteria.[1]Herein, synthetic studies towards neofiscalin A (**1**) were undertaken based on the approach used for total synthesis of fiscalin A[2], starting from the tryptophan- derived scaffold synthesis from the protected D-tryptophan and D-alanine. The coupling of N_{α}-troc-D-tryptophan methyl ester with *N*-Cbz-D-alanine-$PhNO_2$ furnished N_{in}-D-Cbz-alanyl-N_{α}-Troc-D-tryptophan methyl ester in 53 % yield. The coupling product was submitted to a iodination which was treat without purification with the microwave radiation in the condensation reaction and was further oxidized with the Davis' saccharine-derived oxaziridine. Further steps will involve the coupling of the tryptophan-derived scaffold with anthranilic acid and protected L-valine. With this work is expected to obtain neofiscalin A (**1**) in amounts required to proceed with toxicological evaluation.



Neofiscalin A (**1**)

Acknowledgements: Supported through national funds provided by FCT and ERDF and COMPETE under the projects PTDC/MAR-BIO/4694/2014 (POCI-01-0145-FEDER-016790), PTDC/AAG-TEC/0739/2014 (POCI-01-0145-FEDER-016793) and INNOVMAR - Innovation and Sustainability in the Management and Exploitation of Marine Resources, reference NORTE-01-0145-FEDER-000035, Research Line NOVELMAR. P Boonpothong (ALFABET Scholarship) and D Resende (NOVELMAR/BPD_2/2016-019) acknowledge for their grants.

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Chemical characterization of *Pinus pinaster* bark and needles lipophilic fractions: a valuable resource of diterpene resinic acids

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Pinus pinaster (maritime pine) is the main softwood species of Portuguese forest, occupying 23% of continental area (714 x 10^3 ha). This conifer has an important impact in national economy, due to its vast applicability in wood and resin industries.[1] Traditionally, *P. pinaster* bark extracts are used for the treatment of inflammatory diseases and wound healing, mainly ascribed to procyanidins.[2] Monoterpenes and diterpene resinic acids, which exhibit antimicrobial and antiulcer effects, were also reported in *P. pinaster* bark and needles lipophilic fractions,[3-5] however, a detailed chemical characterization of this fraction is still missing. Therefore, this study highlights the composition of lipophilic extractives, derived from *P. pinaster* bark and needles, by analysing the respective dichloromethane extracts via gas chromatography-mass spectrometry.

Diterpene resinic acids were found as the main lipophilic components of *P. pinaster* bark and needles. Dehydroabietic acid was the major abietane resinic acid, followed by abietic, 7α-hydroxydehydroabietic and 15-hydroxydehydroabietic acids (**Figure 1**). Two pimarane resinic acids, namely pimaric and isopimaric acids, were also identified. Minor constituents include monoterpenes, aromatic compounds, fatty acids, long chain aliphatic alcohols and sterols. Overall, these insights can represent an opportunity to valorise *P. pinaster* by-products, as a primary source of bioactive resinic acids for nutraceutical applications.

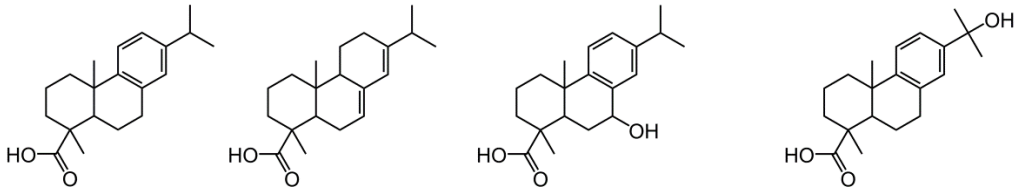

Figure 1: Chemical structures of the main diterpene abietane resinic acids identified in *Pinus pinaster* bark and needles.

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Computational approach to structural characterization of Viral Surface glycoproteins in HIV-2

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The efficacy of some of the available antiretroviral drugs is very limited against HIV-2 and, most importantly, none of the current drugs effectively prevents HIV-2 entry into the cells. HIV envelope glycoproteins mediate binding to the receptor CD4 and to CCR5 and/or CXCR4 co-receptors at the surface of the target cell enabling fusion with the cell membrane and viral entry.[1,2] We are using computational tools to infer the structure of HIV-2 variable regions, in particular V3, and discover new compounds that bind to these regions and prevent HIV-2 cell entry. In the absence of a complete crystallographic structure of HIV-2 envelope gp125 comprising variable domains, computer aided modulation is crucial to identify structural features in the V3 region that correlate with HIV-2 tropism and susceptibility to antibody neutralization.[3]

A 3D structure of C2V3C3 domain of HIV-2_{ROD} gp125 was generated by homology modelling. HIV-2_{ROD} is an X4 T-cell adapted isolate naturally resistant to antibody neutralization and unable to replicate in macrophages. To disclose the importance of the main structural features and compare with experimental results, 3D-models of six HIV-2ROD V3 mutants were also generated (H18L, H23Δ + Y24Δ, K29T, H18L+ H23Δ + Y24Δ, H18L+ K29T and H18L+ H23Δ + Y24Δ+ K29T). These mutations in V3 revealed selective impact in coreceptor use, macrophage tropism and sensitivity to antibody neutralization of HIV2ROD

The H18L variant replaces a basic residue by an hydrophobic one leading to the loss of an aromatic moiety and abrogating any π-π interactions in this position. H23 and Y24 fit on the 23% β sheet content present in WT V3. Y24 can establish π-π interactions and exposition of its hydroxyl group could promote other interactions with the environment. The deletion of these two residues along with the H18L substitution results in the elimination of the parallel β sheets and a major loss of the aromatic system. Experimentally, such changes were associated with X4-to-R5 coreceptor switch and higher sensitivity to antibody neutralization. The substitution of K29 by a T29 reduces the charge of V3 and leads to loss of the interactions with Isoleucine at position 27. This was associated with higher resistance to antibody neutralization and acquisition of macrophage tropism. These new insights into the structure-function relationship will help in the design of better vaccine immunogens.

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Triggering a specific immune response against cancer – activation of NK cells with small organic molecules

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Immunotherapy, a new strategy of cancer treatment, is based on the innate power of the immune system to fight cancer. Because of the immune system's unique properties, these therapies may hold greater potential than current treatment approaches to fight cancer.[1]

Natural killer (NK) cells, a type of cytotoxic lymphocyte intrinsically involved in the immunosurveillance of cancer and critical to the innate immune system, that provides rapid responses to viral-infected and cancer cells, consist of a good target for these therapies. Instead of acting via antigen-specific receptors, lysis of tumor cells by NK cells is mediated by alternative receptors, including NKG2D, NKp44, NKp46 and NKp30.

In recent developments, B7H6, a surface protein present in a broad panel of tumor cells, including lymphoma, melanoma, and carcinoma, was identified as a ligand for the NKp30 receptor. The structure of the NKp30-B7H6 complex has been resolved, showing marked conformational changes that may be a key-factor for the NK-response activation role of B7H6.[2]

Our current work aims at designing a family of small organic molecules (SOMs) capable of mimicking the effect of B7H6 on the NKp30 receptor. The main goal is to obtain a SOM capable of inducing an NK response, through binding to the NKp30 receptor, and structurally amenable to derivatization with tumor-targeting molecular units to produce a specific immune response against cancer cells. A combination of computational ligand-protein docking tools has been intensively used, yielding a multitude of possible lead compounds. These have been tested using state-of-the-art mass spectrometry and NMR spectroscopy tools, allowing the identification of a possible NK-triggering molecule that is now under testing using cell culture methodologies.

Once the suitability of the newly identified molecule has been demonstrated, it will be combined with a tumor targeting molecule and further tested, in more complex disease models. This work is expected to demonstrate the feasibility of using small and easily obtained organic molecules to induce specific, localized and potent immune reactions against cancer lesions.

Acknowledgements: This work has been carried out with financial support from FCT-funded projects RECI/QEQ-MED/0330/2012, RECI/QEQ-QIN/0189/2012, UID/QUI/00100/2013 and SAICTPAC/0019/2015, and grants SFRH/BD/110945/2015 to PFP and SFRH/BPD/108258/2015 to GCJ, and from Liga Portuguesa Contra o Cancro (LPCC/NRS-Terry Fox grant 2015).

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Understanding Proteasome Inhibition: A Molecular Dynamics study

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Ubiquitin proteasome pathway (UPP) plays a pivotal role in intracellular protein degradation and turnover in eukaryotic cells.[1] Crucial in homeostasis UPP is also pivotal in regulating a wide variety of pathways, including cell growth and proliferation, antigen processing, cell differentiation, apoptosis, DNA repair, transcription, immune response, and signalling processes via the degradation of cellular key players, such as cyclins, or tumour suppressors like p53.[2] 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.[3]

During the last two decades academia and pharmaceutical industry made huge efforts to develop natural and synthetic proteasome inhibitors (PI). In 2003 the FDA approved the pioneering dipeptidyl boronic acid derivative PI bortezomib for the treatment of refractory multiple myeloma (MM) and subsequently frontline therapy for MM. Since then, 3 other proteasome inhibitors were approved, carfilzomib, marizomib and ixazomib and several others are now in clinical trials, isolated, or in combination with other drugs (usually anticancer drugs). However, despite the enormous potential of PI, their use is still restricted to certain types of blood cancer and show severe side effects, dose limiting toxicity, particularly peripheral neuropathy, limited activity in solid tumor and innate or acquired resistance.[4]

Our goal is to discover and develop new proteasome inhibitors for cancer treatment. In order to achieve this, we performed a computational campaign exploring the conformational and structural profile of the native proteasome with molecular dynamics, using GROMACS[5] software. The crystallographic structure with high resolution of the 20S human proteasome in the native **(Figure 1)** form and complexed with seven different inhibitors was resolved in the last year. Results will be presented and discussed.

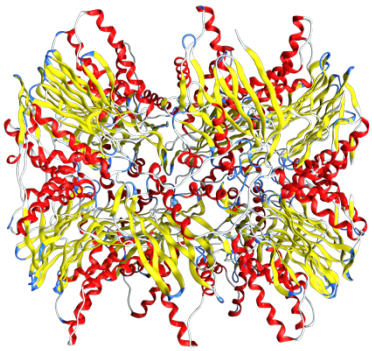

Figure 1. Secondary structure of human native proteasome inner β-rings (PDB ID 5LE5).

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Chemically Activated Writer – "Click-to-Acetylate" Concept

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Post-translational modifications (PTMs) are a tightly controlled system of *in vivo* chemical modification of proteins which are crucial for biomolecules to play specific functions. Examples of such reactions are phosphorylations, glycosylations, methylations or acetylations.[1] These last reactions exhibit their upmost relevance on histones. Histones are proteins wrapped around by DNA that confer structural integrity and are involved in gene regulation whenever specific residues of the protein undertake PTMs. For example, the addition of acetyl groups to histones by a specific enzyme can block the histone-DNA interaction, thus affecting gene transcription.[2] These enzymes are called epigenetic "writer" proteins. Despite its relevance, to perform this tight control artificially and without enzymatic influence has not been done before. Herein, we designed a chemically controlled reaction that directs an acetylation through a nearby click reaction, generating an "artificial writer". Since lysine in position 9 (K9) of histone H3 sequence is a crucial residue where acetylation naturally occurs, this motif was chosen to evaluate the "click-to-acetylate" concept. Hence, peptides with cysteine mutations in residues close to K9 were designed to install the required tag where a specific click reaction can be performed. In two steps, K9 was site-selectively acetylated (Figure 1) and its product was effectively recognized by a H3K9 deacetylase. Thus, we present a procedure to direct an acetylation based on a click reaction that favors the site-selective modification of the closest primary amine. Currently, H3 mutants are being engineered to prove the same in native proteins and from there develop artificial nucleosomes to influence gene transcription *in vitro*.

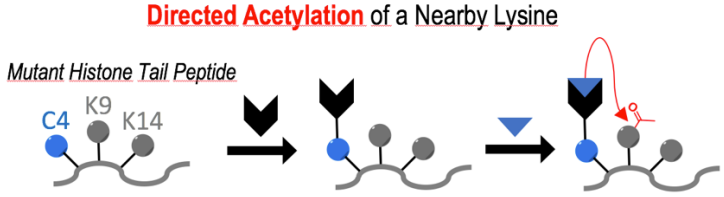

Figure 1: Example of "Click-to-Acetylate" concept on the model peptide.

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Synthesis of co-amorphous drugs by freeze-drying of low solubility drugs

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One of the main challenges of the pharmaceutical industry has been drugs with poor aqueous solubility since they present low bioavailability. The biopharmaceutical classification system (BCS) classifies in four classes drugs according to their solubility and permeability. Class II drugs present high permeability and low solubility and class IV drugs present low solubility and permeability.[1] There are several methods that have been used to increase drugs solubility: one approach is converting drugs from crystalline to amorphous state.[2] The co-amorphous technology has established itself as a promising approach to increase solubility of poorly water-soluble drugs. Although it has potential to become an important technology for the stated end, it is still a new technology and the concept needs to be further established.[3,4] The main goal of this work is to study is to synthesize co-amorphous drugs of poorly soluble drugs by freeze-drying (Figure 1). In particular, it is intended to investigate co-amorphous formulations describing their formation and mechanism of stabilization, study their impact on dissolution performance. For this study furosemide, a BCS class IV drug was used with several different excipients – nicotinamide, ascorbic acid, citric acid, adenine, mannitol and p-aminobenzoic acid with acetonitrile as solvent. Co-amorphous formulations were characterized by near and mid infrared spectroscopy, differential scanning calorimetry and X-ray powder diffraction.

Figure 1. Freeze dryer (Telstar) used in the work.

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Graphene-based magnetic nanocarriers for combined hyperthermia and controlled-responsive drug delivery applications

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The limitations of the current cancer therapies prompt the urgent need for a more effective therapeutic strategy.[1] Magnetic drug delivery systems (MDDS) have been attracting much attention due to the possibility to combine synergistically therapeutic applications, such as magnetic hyperthermia and drug delivery.[2,3] Taking advantage of the unique atomic structure and properties of graphene-based materials, such as thermal and chemical stability, large surface area, biocompatibility and easy functionalization, hydrophilic graphene-based MDDS were developed and functionalized with nitric acid and pluronic F127. These MDDS, comprising a yolk-shell structure, exhibit a combination of properties that allows them to be used as both hyperthermia agent and drug delivery carrier. The magnetite core reveals a superparamagnetic behaviour with saturation magnetization around 70 emu/g, as well as good heating properties under an alternating magnetic field (SAR = 323 W/g $_{Fe}$). Moreover, the graphene-based yolk-shell structure allows an impressive drug loading efficiency of 91 % (doxorubicin, 0.910 mg/mg) with pH- and thermo-responsive drug release of 82 % at an acidic tumour pH environment, and mimicked hyperthermia temperature (45 ºC), after 48 h. These results shed light on the development of new hybrid nanomaterials with high potential to be applied in nanomedicine for the treatment of tumour tissues, combining magnetic targeting, hyperthermia and controlled drug delivery (**Figure 1**).

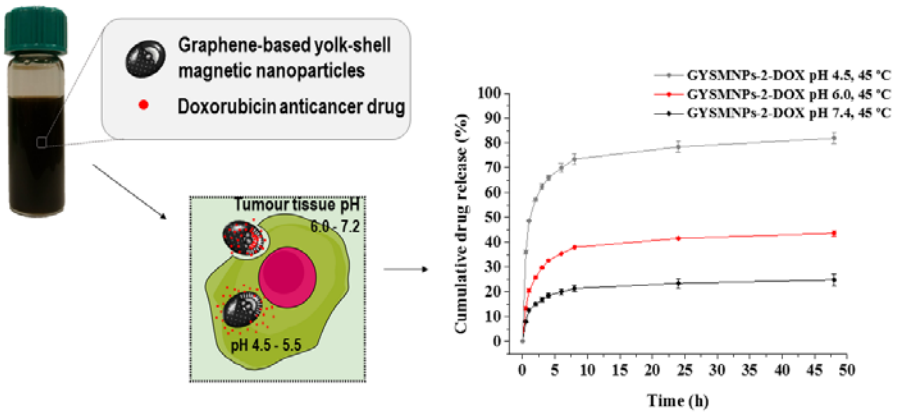

Figure 1: Graphene-based yolk-shell magnetic nanoparticles developed for hyperthermia and controlled drug delivery

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Polyphenols in Celiac Disease Prevention: a Multidisciplinary Study

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Celiac Disease (CD) is now recognized as a worldwide problem, considerably affecting the quality of life of its patients. In genetically susceptible individuals, CD is triggered by the ingestion dietary gluten - a heterogeneous and polymorphic family of closely related storage proteins from wheat, rye, barley and oats. Due to the unusually high content of proline residues, gluten proteins become incompletely digested by gastric, pancreatic and intestinal brush border peptidases, leaving large peptide fragments that can directly affect intestinal cell structure and function by different, strictly related, molecular mechanisms.[1] To date, several poorly digested proline and glutamine-rich peptides from disease-associated grains have been identified.[2] Some of them stand out because of their high immunoreactivity as is the case of a 32-mer peptide described by *Shan et al*. in 2002 as one of the most important CD immunological modulators.[3] Presently, the only effective treatment for CD involves a strict, lifelong adherence to a gluten-free diet. Given its high prevalence and absence of alternative therapeutical means, new solutions are needed.[4]

Polyphenolic compounds are perhaps the most important non-nutrient bioactive group in the human diet. Widely found in fruits, vegetables, grains, spices, herbs and derived foods and beverages, early reports suggested that these compounds were anti-nutritional components of plants by promoting a decreased digestibility of dietary proteins as well as inhibition of digestive enzymes and iron absorption.[5] In some circumstances, however, from both a nutritional and pharmacologic perspective, the interaction of polyphenols with proteins may have important therapeutical implications and therefore outweigh the negative effects. In fact, on a CD context, *Perot et al*. demonstrated very recently that natural polyphenolic extracts are efficient modulators of the immunogenicity and allergenicity of gluten based on their ability to interact with gluten proteins, mask epitopes and impact basophil degranulation.[6] Therefore, polyphenolic compounds appear as promising candidates with a very high potential of being good therapeutical agents for nutraceutical application in CD.[7]

The present work intends to bring molecular insights on the ability of the green tea polyphenol epigalhocatechin-3-gallate (EGCG) to interact and modulate the activity of the major CD immunodominant 32-mer peptide. Characterization of peptide binding was assessed by means of both 1D and 2D ^{1}H-NMR experiments and by molecular dynamics simulations. Accordingly, the EGCG not only exhibits a high reactivity towards the 32-mer but its binding appears to be specific and dominated by both hydrogen bonds and hydrophobic contacts. Structural rearrangements were also detected during the interaction, contributing to a greater stability of the formed complexes. *In vitro* permeability assays on a Caco-2 cell line model were also performed and highlighted the ability of EGCG to prevent monolayer disruption upon treatment with the 32-mer peptide. Overall, his work highlights the potential importance of natural phenolic compounds in a nutritional context to prevent Celiac Disease.

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Optimizing the flavanone core towards a new generation of multiple ABC transporters efflux modulators

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Multidrug resistance (MDR) to anticancer drugs is one of the major impairments in current chemotherapeutic regimens. Aiming at developing new and selective modulators towards the most prominent efflux pumps in MDR, namely P-glycoprotein (P-gp), Multidrug-resistance Protein 1 (MRP1) and Breast Cancer Resistance Protein (BCRP), a small library of naringenin derivatives was built in which nitrogen atoms and aromatic rings were added to the flavanone scaffold to improve its MDR-reversal properties.[1-3] Our results showed that, while selective efflux modulation can be achieved for each pump, some compounds additionally modulate drug efflux in more than one ABC transporter. New structure-activity relationships from ligand- and structure-based approaches allowed the identification of which structural features were intimately related with the herein reported selective inhibition of both efflux pumps. Furthermore, this work provides a proof of concept that the flavanone core can be used as a suitable scaffold for developing new MDR modulators against the most important members related with overexpression of ABC transporters in cancer cells.

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Therapeutic bioconjugates: Evaluation of iminoboronates as payload delivery system for cancer

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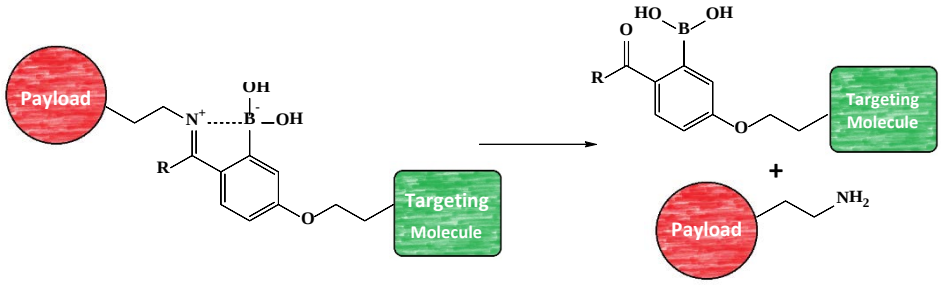
Chemotherapy uses small potent molecules with high activity towards specific tumour targets. However, with such high activity comes high off target toxicity and severe side effects. Fortunately, chemotherapy can be now targeted thanks to powerful linkers that connect a ligand molecule with affinity to interesting biological receptors and a cytotoxic drug. These linkers must have very specific properties, such as high stability in plasma, no toxicity, no interference with ligand affinity nor drug potency, and at the same time, be able to self-lyse once inside the target cell. Bipolar environments as seen between tumoural extracellular and intracellular medias are usually exploited by this linkers in order to release the therapeutic warhead. This work explores a new model for the same task, specific cancer drug delivery.[1] Iminoboronates were studied due to its remarkable selective stability towards a wide pH range and endogenous molecules.[2] Bioconjugates were design to prove this iminoboronate linker's effectiveness. The ability to be uptaken by a cancer cell through endocytosis process and delivery of specific payload are two features expected for this construct. (**Scheme 1**)



Scheme 1: Iminoboronate as payload delivery system model.

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Development of small molecular cores for boronic acid ligation in peptides

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Protein bioconjugation has been one of the hot topics in medicinal chemistry during the recent years, expanding the tools available for biological investigation and bringing innovative therapies to the clinic. In this field, there is an increasing demand for bioconjugations reactions that are not only bioorthogonal, but also reversible under selected conditions, in order to achieve the maximum control possible over the system.[1]
Boronic acids are excellent candiadates for this kind of applications as they are stable under physiological conditions and show in general good biocompatibility, they are also known for reversibly binding to diols in aqueous environment, a feature that we exploited to develop a new biocnjugation technique.[2,3]
Our work revolves around 3-Hydroxy Quinolinones (3HQs), a class of compounds that exist a in tautomeric equilibrium between the amide form and a diphenolic one, with the first one favored over the latter in aqueous environment.[4] The diphenolic form is, however, capable of binding boronic acids, leading to the formation of a highly aromatic structure that results in an overall stabilization of the system.

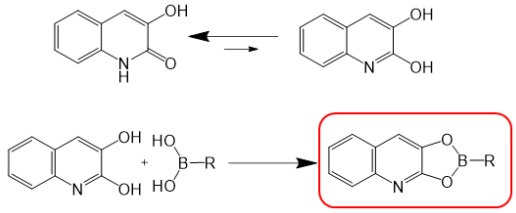

Figure 1 – Tautomeric equilibrium of 3HQs and binding to boronic acids.

Based on this discovery, we developed a series of 3HQs derivatives, these compounds showed remarkable binding capabilities with boronic acids in buffer solution and were further developed to be inserted in peptidic fragments via classic bioconjugation techniques.
The peptides modified with our molecule gained the ability to bind boronic acids in aqueous environment with moderate to good efficiency, thus demonstrating the possibility to use them as functionalization tool for boronic acid ligation.

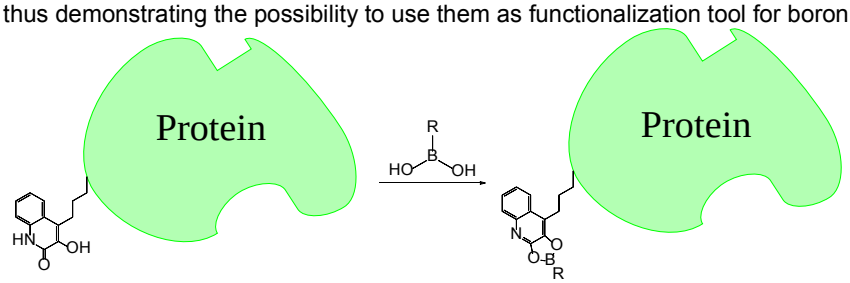

Figure 2: Functionalization of a protein with 3HQs, creating a molecular handle for boron ligation.

Acknowledgements: This work was supported by Marie Sklodowska-Curie actions (MSCA-ITN-2015-ETN-675007) in the framework of the ITN – ProteinConjugates, and the funding from PTDC/QEQMED/5512/2014; PTDC/QEQ-QOR/1434/2014, UID/DTP/04138/2013, SAICTPAC/0019/2015.

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Targeting the human 20S proteasome: finding new inhibitors through a computational-based drug discovery approach and biological evaluation of the selected compounds

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The ubiquitin proteasome system (UPS) is a nonlysosomal pathway by which cells regulate the controlled degradation of several proteins, not just in cell cycle and apoptosis but also in inflammatory and immune responses, carcinogenesis, among others. Usually, in protein homeostasis the defective proteins are ubiquitinated and are proteolysed into short peptides by the proteasome. Proteasome substrates include, for example, signalling molecules, tumour suppressors, cell cycle regulators and transcription factors. 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.[1]

This work relies on a computational-based drug discovery campaign 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 methodologies (i.e. molecular docking and structure-based virtual screening) in order to identify potential hit compounds (**Figure 1**). The selected compounds were tested in cell growth inhibition assays, being also performed inhibition assays for the chymotrypsin-like and trypsin-like activities of purified proteasomes using fluorogenic substrates.

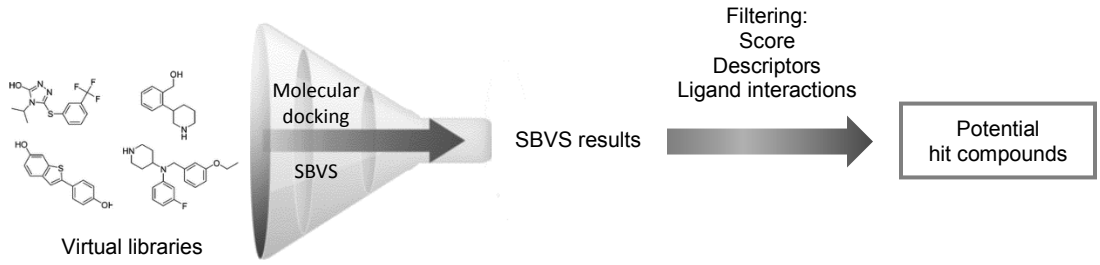

Figure 1: Computer-aided drug design workflow.

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In vitro metabolism studies on synthetic cathinones

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During the last years, the use of novel psychoactive substances (NPS), also known as “recreational drugs”, “legal highs”, or “design drugs”, has been critically increasing. Their intensification of use has happened mostly due to the easy access via the Internet and in smart-shops.

Synthetic cathinones is a large class of NPS that has been widely abused, since the mid-2000s. These substances are derivatives of cathinone, a naturally occurring beta-ketone amphetamine (2-amino-1-phenyl-1-propanone) analogue found in the leaves of the *Catha edulis* (Khat) plant. Due to the ease of synthesis of this compound, as well as to circumvent existing laws on controlled substances, and/or to enhance pharmacological activity, new synthetic cathinones have been constantly synthesized. They have been marketed under several brand names, which includes “pond cleaner”, “plant food” and “bath salts” and are labelled as “not for human consumption” to avoid drug abuse legislation. Synthetic cathinone pharmacological effects may be similar to those of cocaine, amphetamine or (±)-3,4-methylenedioxy methamphetamine (MDMA), can provoke elicit powerful effects such as delusions, hallucinations and potentially dangerous behaviour, but those effects can vary depending upon the class.

One of the main cathinone derivative is the 3’-substituted - buphedrone (2-(methylamino)-1-phenylbutan-1-one, a-methylamino-butyrophenone, MABP). Buphedrone is usually supplied as hydrochloride, and this stimulant can be snorted, smoked or taken orally. The drug has been associated with fatalities in USA and some European countries. Until present, gas chromatography–mass spectrometry (GC-MS) has been used to analyse urine samples in order to detect the use of this NPS class drugs. Parent drugs are usually far less abundant than their metabolites in this type of biological samples and other methodologies as LC-MS have been optimized in order to detect and quantify metabolites in biological samples.

This project aims to access the main metabolites of selected synthetic cathinones like buphedrone. For that propose, in vitro studies were performed in order to detect by LC-MS/MS the main metabolites present in the reaction mixture of selected drugs incubated with liver microsomal preparations, at several time points. Knowledge about the metabolites is of major relevance to allow to detect the consume of this type of drugs and to unveil the metabolic route for assessing the toxicity of the drug in the human body, including associations to genetic variations and drug-drug interactions.

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Tetra-PEGylated bacteriochlorin as potential PDT photosensitizer: Synthesis, characterization and *in vitro* studies

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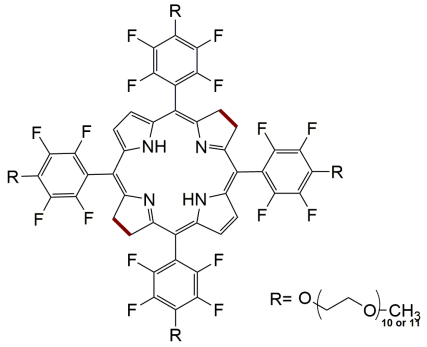
Cancer is one of the deadliest diseases of modern time and throughout the world, billions of euro are spent annually on research for new techniques to improve life-standards of cancer treatment.[1] Photodynamic therapy is an emerging non-invasive modality that has been extensively studied as a promising alternative to the traditional cancer treatments, that can result in serious side effects. This therapeutic strategy involves either systemic or local administration of a photosensitizer, followed by irradiation with red or near-infrared (NIR) light of appropriate wavelength to activate the photosensitizer. The excess energy absorbed by the photosensitizer is transferred to the nearby oxygen molecules, producing short-lived reactive oxygen species (ROS), namely singlet oxygen, that are responsible for the selective tumor destruction, tumor-associated vascular damage, and activation of antitumor immune responses.[2] Porphyrins and related macrocycles present suitable physical-chemical properties, particularly significant electronic absorption in the "phototherapeutic window", high singlet-oxygen-producing ability and tendency to accumulate in solid tumors, making them one the most studied class of molecules for application as photosensitizers.[3] Herein we present the synthesis, photophysical characterization and *in vitro* studies of a new tetra-pegylated bacteriochlorin (**Scheme 1**) in order to evaluate its potentiality as photosensitizer in photodynamic therapy.



Scheme 1.

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Palladium-mediated synthesis of pseudo-*C*-glycosylxanthone and phenyloxybenzaldehyde derivatives of pharmacological interest

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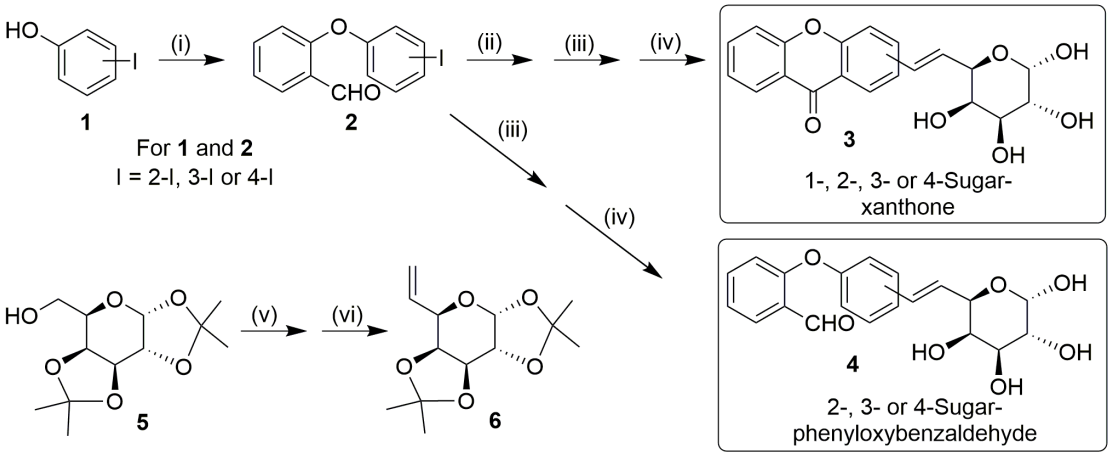
The prominent interest on phenolic *C*-glycosides in medicinal chemistry lies on the combination of the distinguishing hydrolytic stability of their *C*-glycosidic bond and the high hydrophilic character of the carbohydrate unit[1] together with the well-known biological activities of phenolic compounds such as xanthones, which include antioxidant, anti-inflammatory and antitumor activities.[2] This resulting interesting synergic effect[3] has inspired and challenged chemists for the synthesis of novel *C*-glycoside derivatives.[4]

In this communication, it will be presented the synthesis of pseudo-*C*-glycosylxanthone **3** and phenyloxybenzaldehyde **4** derivatives. These new conjugates containing unsaturated linking groups were prepared throughout a key Heck cross-coupling reaction of different iodo-substituted xanthones and phenyloxybenzaldehydes with galactopyranose sugar alkene **6** (**Scheme 1**).



(i) 2-Fluorobenzaldehyde, K_2CO_3, DMF, 100 ºC; (ii) Ferrocene, ^tBuOOH, MeCN, 90 ºC; (iii) **6**, $Pd(OAc)_2$, K_2CO_3, $(Bu)_4NBr$, DMF, 100 ºC; (iv) TFA/water (1:1), rt; (v) Dess-Martin periodinane, CH_2Cl_2, rt; (vi) NaH, CH_3PPh_3Br, THF, rt.

Scheme 1: Synthesis of pseudo-*C*-glycosylxanthone **3** and phenyloxybenzaldehyde **4** derivatives.

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Compounds with antibacterial activity based on camphor and silver

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In February 2017, the Word Health Organization (WHO) challenged the research community to strengthen efforts to find alternative antimicrobials towards twelve families of bacteria which represent serious threats to human health due to increasing resistance to commercially available antibiotics. Aiming at contribute to find new compounds with antibacterial activity several silver complexes ($[Ag(NO_3)(L)_2]$, $[Ag(NO_3)(L)]_n$)[1,2] with camphor derived ligands were synthesized (Fig. 1). The antibacterial activity of a selected number was evaluated based on Minimal Inhibitory (MIC) concentration determination by a microdilution standardized method against Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli, Pseudomonas aeruginosa* and *Burkholderia contaminans*) strains.

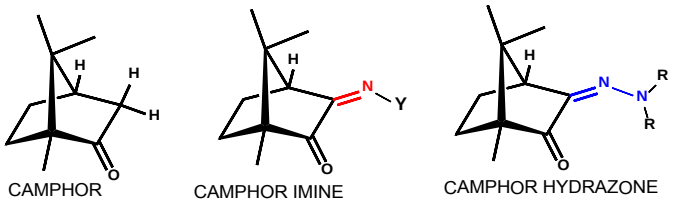

Figure 1

Camphor and camphor ligands (L) types under study:
Y = *p*-HOC_6H_4,*m*-ClC_6H_4, *p*-ClC_6H_4, *p*-FC_6H_4, *p*-MeC_6H_4,3,5-$Me_2C_6H_3$;
R = H, Me

The MIC values were calculated for the complexes and $AgNO_3$ (comparative purposes) were calculated and the more recent results displayed in Table 1.

Table 1 - Average MIC values (μg/mL) calculated for complexes $[Ag(NO_3)(L)_2]$, $[Ag(NO_3)(L)]$ and $AgNO_3$.

			Bacterial Strain			
Compound	Y	R	E. coli ATCC 25922	S. aureus Newman	B. contaminans IST408	P. aeruginosa 477
[Ag(NO3)(L)2]	p-C6H4CH3	-	54	56	97	45
[Ag(NO3)(L)]	-	H	59	107	53	51
[Ag(NO3)(L)2]	m-C6H4OH	-	120	232	110	103
AgNO3	-	-	47	73	74	39

The results show that the all the complexes display antimicrobial activity with MIC values depending on the characteristics of the camphor ligand. Further work is in progress to ascertain on the parameters that drive the biological activity and optimize the system.

Acknowledgments: Financial support by FCT-Fundação para a Ciência e Tecnologia through projects UID/QUI/00100/2013, UID/BIO/04565/2013 and the NMR Network (IST-UTL Node) for facilities are gratefully acknowledged.

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Synthesis of therapeutically useful multivalent boronate complexes

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Medicinal chemists incessantly face the daunting task of discovering new strategies to tackle cancer. Nowadays, the most recent strategies focus at interrupting the evolution of the neoplastic state. Since it involves a variety of biological process, multifunctional constructs that combine the lethality of a cytotoxicity drug with the targeting ability of specific biomolecules, are necessary. Despite conceptually simple, the assembly of multifunctional construct is often hampered by the complexity of the synthetic steps. A promising strategy to create such compounds, known as Cancer Cell-Targeting Drug Conjugates (CCTDC) is the use of Boronic acids (BAs). Based on work of P.Gois et al.[1] we conceived that CCTDC could be easily created by assemblage of simple building blocks promoted by a boron tether. Indeed, boronic acids are planar trivalent Lewis acids able to establish modular and reversible complexes due to their capacity to form negatively charged tetravalent framework with Lewis base donors.[2] In the vision of develop useful CCTDC, suitable propriety of stability, controlled reversibility in biological environment and fluorescence are highly desiderable. Herein we present the development of multifunctional B-core complex. Starting from different building blocks, and based on a one-pot three-component reaction, boronate core complexes have been synthesized; evaluated at physiological and lysosomal pH, and in human plasma, as along as their hydrolysis resistance tested in the presence of glutathione. UV/Vis absorption and fluorescence analysis have been also carried out. The cores showing suitable stability and controlled reversibility will be selected as the components to build the multifunctional conjugates, featuring a cytotoxic drug, a polar small chain and a target unit (**Figure 1**). Finally, the selectivity and cytotoxicity of the synthesized B-core complexes will be evaluated against human cancer cells.

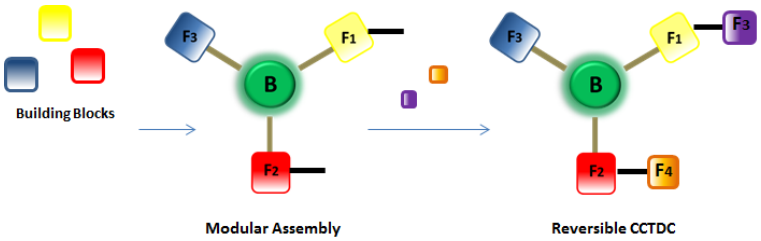

Figure 1: Modular and reversible assembly of CCTDC

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Bis-(thio)urea-based receptors as potential membrane transporters for anions

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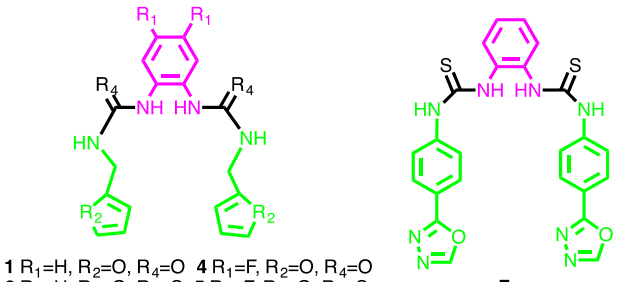
Ion transport across the phospholipid cell membranes is crucial to several biological processes, such as nerve conduction and homeostasis maintenance.[1] A combination of protein ion channels embedded in the membrane establishes and controls the ion concentrations inside and outside the cell.[1] The dysfunction of these channels is currently linked with the occurrence of serious pathologies, including types of male infertility and the prominent cystic fibrosis (CF), caused by a defective transmembrane transport of the chloride and bicarbonate anions.[1] Most of the current treatments for CF aim to manage the disease symptoms, while the cure remains a challenge. Therefore, the development of drug-like transporters with potential to be applied as replacement therapeutics for malfunctioning channels is an imperative demand.

During the last decade, an increasing number of synthetic anion transporters have been synthetised.[2-5] In this context, here we present the syntheses of new oligo(thio)ureas receptors containing two heteroaromatic recognition units linked by an *ortho*-phenylene rigid linker. The ability of these synthetic receptors to bind in solution with fluoride, chloride, bromide, and iodate was investigated using ^{1}H NMR titration experiments in DMSO-d_6.

The strongest binding affinities was found for chloride anion probably due to its best matching size of the receptor cavity which allowed maximizing the number of hydrogen bonds between the anion and the bis-(thio)ureas units of the receptors. Instead, the iodate anion has no interaction with these synthetic receptors. In general, the presence of the fluorine atoms in the aromatic ring of the receptors (**4** and **5**) increases the association constants due to increase of hydrogen-bond acidity. The highest association constants were obtained for the urea receptors however, the thiourea receptor **7** has a high binding constant probably due to the presence of the longer aromatic rings.



1 R_1=H, R_2=O, R_4=O **4** R_1=F, R_2=O, R_4=O
2 R_1=H, R_2=O, R_4=S **5** R_1=F, R_2=O, R_4=S
3 R_1=H, R_2=S, R_4=O **6** R_1=F, R_2=S, R_4=O

7

Scheme 1: Representation of the synthetic receptors.

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A Computational Approach Targeting LRRK2

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Parkinson's disease (PD) is the second most common progressive neurodegenerative disorder, affecting approximately 1.5% of the population above 60 years of age and 4% of the population at the age of 80. Although PD remains rather uncommon, with the general aging of the population, it is expected that its prevalence will quickly increase.[1, 2]
Leucine-rich repeat kinase 2 (LRRK2), also known as dardarin, is a multi-domain serine-threonine kinase belonging to the ROCO protein family, which seems to be involved in a complex array of intracellular processes.[3] Although its biological role remains largely unknown, it is now well established that mutations in this protein are associated with autosomal dominant forms of PD[3]. Therefore, inhibition of LRRK2 kinase activity is considered one of the most promising therapeutic strategies for the treatment of PD[3].
With the aim of discovering new and innovative small molecules that can inhibit LRRK2 and be further used in the treatment of PD, a computational protocol combining virtual screening and structure-based drug design is being developed. Since no LRRK2 X-ray crystal structure is currently available, the first goal of this work was to identify a LRRK2 structure, using homology modelling, which could be used in the rational design of LRRK2 inhibitors. To accomplish this purpose, a series of LRRK2 kinase domain models were generated and optimized. Janus kinase 2 (JAK2)-based LRRK2 homology model was selected and further validated through docking studies on a diverse set of LRRK2 inhibitors. The main results of this studies will be presented and discussed.

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Antitumor Activity of Quinazolinone Alkaloids-Inspired in Marine Products

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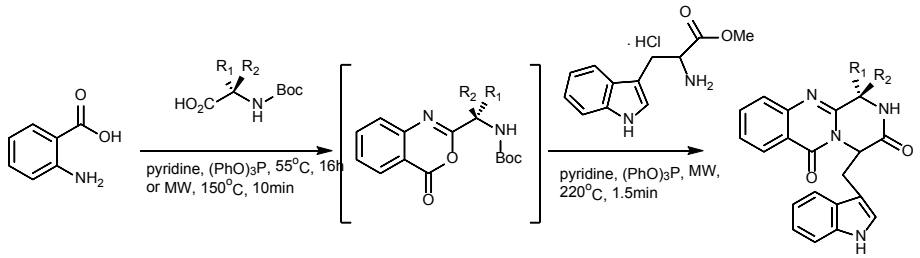
The quinazolinone alkaloids, which contain a pyrazino[2,1-*b*]quinazoline-3,6-dione core linked to an indole moiety have emerged in the last two decades, mainly from marine sources, and have revealed very promising activities, especially in the field of chemotherapics.[1] The purpose of this work was to obtain a library of quinazolinone derivatives to access their antitumor activity and ability to circumvent multidrug resistance mediated by P-glycoprotein (P-gp, a drug efflux pump). Quinazolinone alkaloids with simple tryptophan moiety were obtained via microwave-assisted synthesis, in one-pot procedure. This strategy used chiral *N*-Boc-protected α-amino acids, tryptophan methyl esters, and anthranilic acid to form the core ring of pyrazino[2,1-*b*]quinazoline-3,6-dione (**Scheme 1**).[2] The formation yields of quinazolinones were low, ranging from 7 to 16 %.



Scheme 1: One-pot total synthesis of quinazoliniones

Eight derivatives were tested on non-small cell lung cancer (H460), *colon adenocarcinoma* (HCT-15) and breast cancer (MCF7) human cell lines and showed moderate cytotoxic effects, with GI_{50} concentrations ranging from 30 to 80 μM. Noteworthy, significant differences were obtained between enantiomeric pairs. Future work will consist on the evaluation of their effect in tumor cells with P-gp overexpression and in their drug-sensitive counterparts, in order to study their ability to inhibit drug-efflux mediated by P-gp.

Acknowledgements: We thank to National funds provided by FCT – Foundation for Science and Technology and European Regional Development Fund (ERDF) and COMPETE under the projects PEst-C/MAR/LA0015/2013, UID/QUI/00062/2013), PTDC/MAR-BIO/4694/2014, and INNOVMAR - Innovation and Sustainability in the Management and Exploitation of Marine Resources, reference NORTE-01-0145-FEDER-000035, Research Line NOVELMAR. S. Long thanks Erasmus Mundus Action 2 (LOTUS+, LP15DF0205) for full PhD scholarship.

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Peptide Nanofibers as tools for efficient retroviral gene transfer

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We have developed self-assembling peptide nanofibers (PNFs) as convenient, flexible and effective tools to improve retroviral gene transfer. Retroviral gene transfer is the method of choice for the stable introduction of genetic material into cells and offers many prospects for basic research and for the treatment of genetic disorders, malignancies, and infectious diseases. Retroviral vectors insert the therapeutic gene into the DNA of a host cell, thus allowing stable, long lasting gene expression. This process is termed transduction and its efficacy is unfortunately often hampered by low infection rates due to electrostatic repulsion of negatively charged viral particles and cellular membranes.
The self-assembly of peptides into bioactive supramolecular nanofibrils offers a versatile way to overcome the limitations of retroviral gene therapy. This study focuses on our recently described fragment of the HIV-1 glycoprotein gp120, termed EF-C, which promotes amyloid-like nanofibrils that significantly enhance viral fusion and thus HIV infection.[1] We intrinsically altered the peptide composition in order to elucidate the impact of the amino acid primary sequence on fibril formation and transduction enhancement. Furthermore, we studied the influence of additional functional moieties in the periphery of the assembled nanostructures in order to customize their properties.[2] Our study yielded a library of new amphiphilic peptides which feature potent intrinsic self-assembling capabilities. The peptides instantly form PNFs in aqueous environments and efficiently capture negatively-charged viral particles. The virion-fibril complexes furthermore mediate the viral attachment onto target cells thus promoting increased viral loads on membranes and support their subsequent fusion **(Figure 1)**.

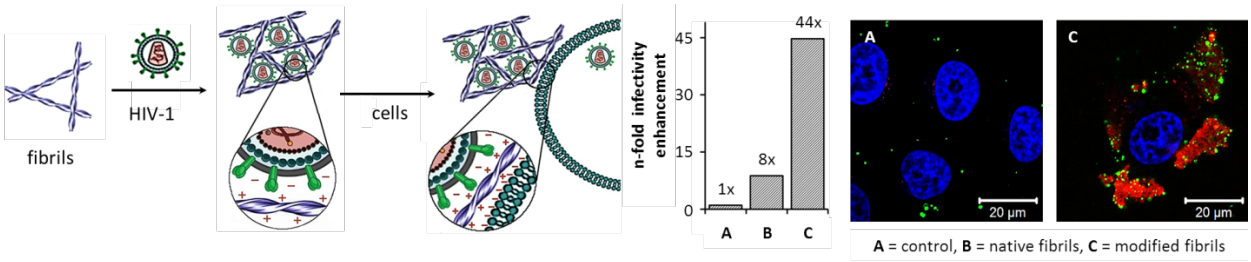

Figure 1: Mesoscaled fibril-virion complexes lead to significant infectivity enhancement when added to cells. The laser scanning confocal images show how fibrils (red) increase viral loads (green) on cellular membranes (cell core stained blue).

EF-C and derived PNFs increase retroviral transduction more efficiently than any other commonly used additive in gene therapy and thus represent a highly interesting class of building blocks for gene delivery as well as other biomedical applications.

Acknowledgements: We are grateful for the financial support of the VolkswagenStiftung

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Hybrid Silica Nanoparticles to Target the Blood-Brain Barrier for Controlled Drug Release

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There is a huge number of neurological disorders responsible for the impairment and the degeneration of several areas of the central nervous system (CNS). Despite the existence of physical and chemical methods used to treat CNS diseases, new strategies have been emerging to successfully overcome the BBB for the treatment of these disorders.[1,2] The use of silica-based nanoparticles has largely increased in the material science and biomedical fields [3]. The use of nanoparticles to overcome the BBB in order to encapsulate a range of therapeutic agents, with low levels of toxicity, and to deliver higher drug ratio in the target CNS compartment in an effective manner has been performed in the last years.[4-6]

The purpose of this work is to design a strategy to treat CNS diseases based on the development of silica nanoparticles with a perylenediimide (PDI) dye in the silica structure for traceability and the surface modified with a peptide that targets the BBB tight junctions.

Particles of different diameter, with low size dispersity and uniform fluorescent intensity for traceability were obtained. **(figure 1a and 1b).** The nanoparticles were surface-modified with a PEPDART (Permeability Enhancing Peptides for the Disruption, Attenuation and Recovery of Tight-Junctions) peptide **(figure 1c)** in order to specifically target the transmembrane protein claudin-5 (cldn-5) expressed on endothelial cells of the BBB, enhancing the permeability of the barrier.

Our results highlight the feasibility of functionalize hybrid silica particles with PEPDARTs to modulate the permeability and disruption of the BBB for imaging of the CNS and drug delivery across the barrier.

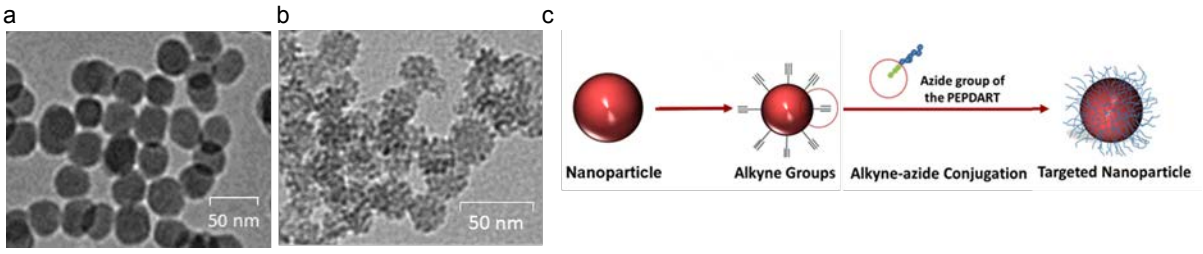

Figure 1: Images of a) non-porous silica nanoparticles and b) mesoporous silica nanoparticles by Transmission Electron Microscopy (TEM) and c) schematic representation of the subsequent functionalization by PEPDART peptide of the non-porous silica particles.

Acknowledgements: We thank Fundação para a Ciência e a Tecnologia (FCT-Portugal) and COMPETE (FEDER) project PTDC/CTM-POL/3698/2014. S. C. thanks FCT and Stem Cell Manufacturing for Bioengineering- Cell Therapies and Regenerative Medicine Doctoral Program for PhD grant PD/BD/105793/2014.

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Synthesis and characterization of 3-hydroxy-4-pyridinone functionalized with hydrophilic chains for treatment of iron deficiency chlorosis in plants

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Successful cultivation of crops with the best nutritional properties is an issue of paramount importance in the Agricultural and Health fields. Iron (Fe) is an essential mineral nutrient and legumes are one of the major sources of Fe. However the absorption of Fe by the roots of plants is compromised when grown in alkaline soil. As a consequence, plants may suffer from iron deficiency chlorosis (IDC), characterized by chlorosis, yield losses, and lower concentrations of Fe in edible plant parts. Soil application of synthetic Fe(III) chelates (e.g. Fe-EDTA or FeEDDHA) remains one of the most common measures to correct IDC.

In previous work[1], we tested the capacity of two tris(3-hydroxy-4-pyridinonate) Fe(III) complexes, [$Fe(dmpp)_3$ and $Fe(mpp)_3$], to amend IDC in hydroponically grown soybean (*Glycine max*) plants, and we compared them to FeEDDHA. This work indicates that [$Fe(mpp)_3$] has potential as an Fe fertilizer that, even at low doses, is able to avoid IDC symptoms development, and that could be economically and environmentally favorable in agricultural contexts.

In the sequence of our research, the design of new ligands, used to further produce Fe complexes, is a topic of interest. The improvement of water solubility of these ligands and complexes, by developing more hydrophilic chelators, remains crucial for such biological application. In our last work, a pegylated highly water soluble 3-hydroxy-4-pyridinone (3,4-HPO) functionalized with a hydrophilic ethylene glycol chain (PEG-HPO) and its respective iron(III) complex were synthetized.[2]

In the present work, we present the design and structural characterization of four novel 3,4-HPO functionalized with hydrophilic chains (**Figure 1**). In the general synthetic approach for the production of the ligands, the amino-terminated chain reacts with the protected pyrone where the oxygen atom of the ring is substituted by the nitrogen of the anime group of the chain, yielding the protected 3,4-HPO. Subsequently, the protecting group was removed under hydrogen atmosphere in the presence of Pd/C (10%) and HCl, to obtain the dihydrochloride salt of PEG-HPO. Ligands were characterized by ^{1}H NMR, ^{13}C NMR and Mass spectrometry Their respective Fe(III) complexes will be formerly synthesized and characterized.

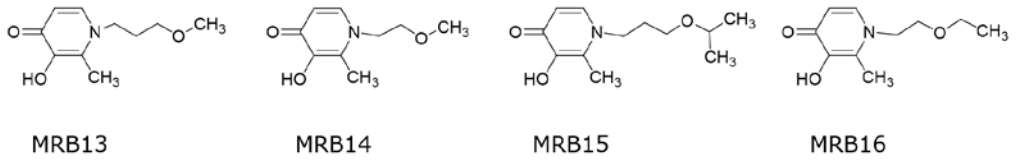

Figure 1: Numbering and formulae of the functionalized 3,4-HPO with amino-terminated chains.

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Tryptophanol-derived oxazoloisoindolinones: promising small molecules to target cancer

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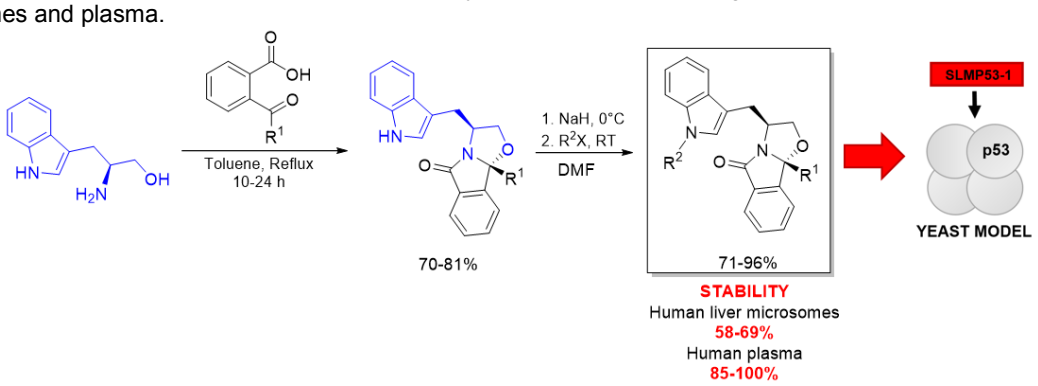
Preparation of enantiomerically pure compounds in a single synthetic step constitutes one of the most demanding subjects in organic synthesis. Due to the clinical advantages that enantiopure drugs offer over the correspondent racemic forms, strategies of asymmetric synthesis to access single-enantiomer compounds have gained importance in pharmaceutical industry. A very useful synthetic methodology for the elaboration of enantiopure compounds is the use of a chiral starting material that will remain included in the structure of the final product. Using this approach, we have developed several biologically active small molecules starting from 1,2-aminoalcohols.[1]

Here we will present our most recent results on the development of a chemical library of enantiopure tryptophanol-derived oxazoloisoindolinones to modulate p53 activity. The target products were obtained in good to excellent yields (**Scheme 1**) through a highly efficient/atom economic cyclocondensation reaction between the aminoalcohol tryptophanol and different oxoacids. The compounds were then screened in Saraiva's lab as p53 activators using a yeast model, followed by validation of the molecular mechanism of action in human tumor cell lines and in human xenograft mice models.[2,3] Furthermore, the stability of the most promising hits was evaluated in human liver microsomes and plasma.



Scheme 1: Synthesis of enantiopure tryptophanol-derived oxazoloisoindolinones.

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Development of new NIR dyes by Pd-catalyzed aminocarbonylation

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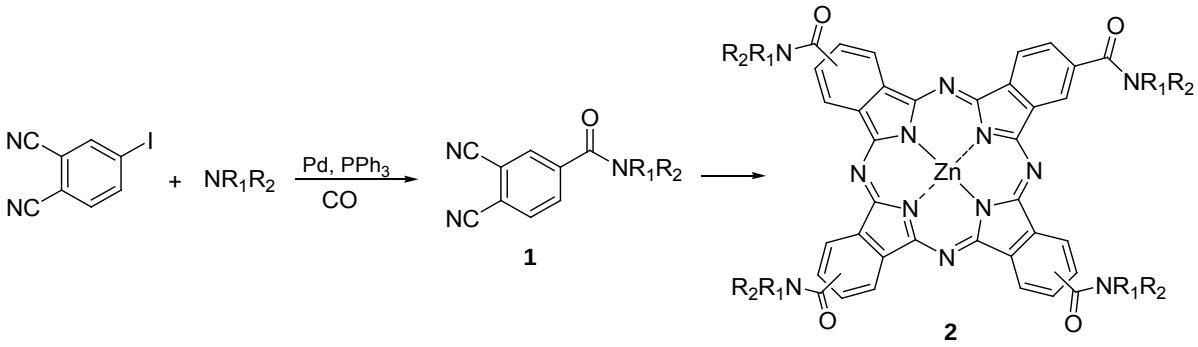
Phthalocyanines largely fulfil a crucial optical requisite, necessary for photomedical applications, including phototherapy and optical imaging, which is a strong absorption in near-infrared (NIR) spectral region (600–900 nm), as light in this region affords the deepest penetration in soft tissue. Considering the increasing number of applications of phthalocyanines in the field of biomedicine, research has been focused on modeling these macrocycles structures in order to increase their biocompatibility. In this context, the amide linkage (peptide bond) is one of the most natural conjugations available,[2] present in many biological synthons, such as amino acids, peptides or proteins, as well as in pharmaceutical drugs. Nevertheless, when compared with other functionalities, amide substituted phthalocyanines are quite rare.[3]

In this study we present a new strategy for direct modulation of phthalocyanine precursors through optimized palladium catalyzed aminocarbonylation reactions of 4-iodophthalonitrile, using different amines as nucleophiles, yielding the desired carboxamide-phthalonitrile derivatives **1** in moderate to good isolated yields (49-80%), and the corresponding zinc phthalocyanines **2** prepared through subsequent cyclotetramerization of **1** (**Scheme 1**). Additionally, we have also evaluated the photophysical parameters of some of the resulting zinc phthalocyanine conjugates **2**, as promising probes to be further exploited as suitable sensitizers in optical imaging.



Scheme 1: Synthesis of phthalonitrile-carboxamide derivatives **1** and the corresponding zinc phthalocyanines **2**.

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Polyurea Dendrimers as Nanocarriers for Ovarian Cancer Therapeutics

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Polyurea (PURE) dendrimers[1] are a new class of intrinsically fluorescent, biocompatible, pH responsive and biodegradable[2] polymers. PURE dendrimers have been used in a wide range of applications, both as sensors[3] and drug[4] and gene[5] nanocarriers. To comprehensively evaluate the use of PURE dendrimers in ovarian cancer chemotherapy, we investigated the biological interaction of polyurea dendrimer $PURE_{G4}$ and new generations $PURE_{G5}$ and $PURE_{G6}$ in the ovarian cancer cell line COV362 and in the normal fibroblast cell line NIH/3T3. We systematically conducted a panel of cell biological assays to explore the generation-dependent effects of PURE-type dendrimers on cell morphology, viability, proliferation, metabolic generation of reactive oxygen species, and modulation of key therapeutic biomarkers. For therapeutic applications, we show that through surface modification it is possible to render these dendritic structures to encapsulate and release *cis*-platin (**Figure 1**) in a time-dependent manner and with high therapeutic efficacy.

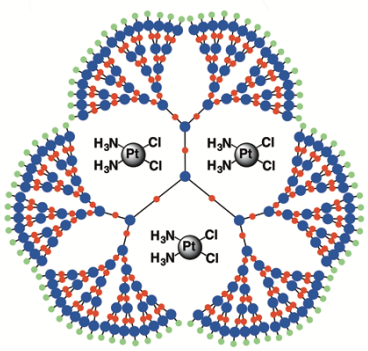

Figure 1: Schematic representation of a *cis*-platin encapsulated generation 6 polyurea dendrimer.

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Synthesis of (Triazolyl)methyl Amide-linked Disaccharide Nucleosides as Potential Inhibitors of Glycosyltransferases

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Glycosyltransferases are enzymes involved in the glycosylation of oligosaccharides, proteins and lipids, leading to glycans and glycoconjugates. These latter molecules are involved in important biological processes, including cell adhesion or signalling. In cancer cells, glycosylation patterns in glycoproteins and in other glycoforms become aberrant and therefore the inhibition of glycosyltransferases is a promising approach for anticancer therapy. [1]

In this work, two analogues of nucleoside diphosphate sugars, natural substrates of glycosyltransferases, comprising a (triazolyl)methyl amide moiety as neutral and potential enzymatically/hydrolytically stable bioisostere of the diphosphate moiety, were synthesized. [2]

Their access was based on a convergent approach involving the synthesis of N-propargyl glucuronamide-containing nucleosides and azido sugar precursors and their further coupling using a click-chemistry protocol. [2] Variations on the regiochemistry of the N-glycosidic bond (N9- or N7-linked nucleosides) as well as on nucleoside ring system A (i.e. furanose and pyranose motifs) were made **(Figure 1)**.

In this communication, the synthetic methodologies leading to the target compounds will be presented and discussed.

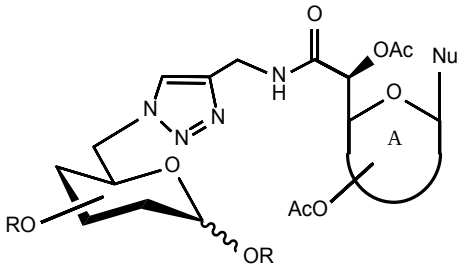

Figure 1: General structure of the synthesised compounds

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support on the projects IF/01488/2013/CP1159/CT0006 and UID/MULTI/00612/2013.

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MATERIALS CHALLENGES POSTER COMMUNICATIONS

XXV ENCONTRO NACIONAL
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Hydrosoluble copper complexes for homogeneous catalysis

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As part of our interest on water soluble transition metal complexes with applications in catalysis,[1] we have obtained novel compounds by reacting Cu(II) or Cu(I) salts with water soluble 3,7-diacetyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane (DAPTA) **(Figure 1)**.[2]
The obtained complexes were fully characterized and applied as catalysts, under mild conditions, for Nitroaldol condensation of aldehydes with nitroalkanes (Henry reaction) and Azide-Alkyne 1,3 dipolar Cycloaddition (Huisgen reaction) in homogeneous aqueous systems to give yields up to 97 % and >99%, respectively.

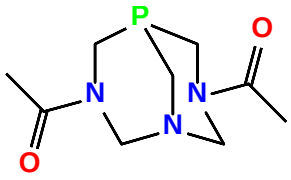

Figure 1: 3,7-diacetyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane (DAPTA).

Acknowledgements: This work has been partially supported by the Foundation for Science and Technology (FCT), Portugal (UID/QUI/00100/2013). A.G.M. is thankful to the CATSUS doctoral program of FCT for his PhD fellowship (SFRH/BD/106006/2014).

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Fluorescent Conjugated Oligomers Based on Calix[4]arene and β-Glucose Units

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Fluorescent sensors based on conjugated polymers (CPs) can be extremely sensitive and selective toward a large variety of analytes. Expeditious sensing schemes have been successfully applied for detection of a wide range of small organic molecules (*e.g.* explosives) and biomacromolecules (*e.g.* proteins and DNA),[1] since the seminal work of Swager.[2] Receptor-based sensors covalently linked to conjugate polymers present additional advantages since the whole structure can be modulated to suit particular envisioned targets.[1]

The introduction of chiral units in conjugated polymer side chains may significantly influence the spatial organization of the whole structure leading to chirality induction on solution/solid states of the macromolecule. As far as this aim is achieved, ways to improve their application as enantioselective sensors or chiral selectors are wide open.[3]

Several calix[4]arene-based conjugated polymer architectures has been previously reported by us,[4] and their ability to behave as highly sensitive sensors demonstrated.

In this communication, we report our efforts to synthesize CPs having calix[4]arene and β-glucose units as recognition elements, being the latter also used to impart chirality to the assembling. It was found that under a variety of polymerization conditions, the attained degree of polymerization (DP) was too low (mean DP~2-3; Fig. 1), probably meaning that strong steric hindrance during the Sonogashira cross-coupling precluded the polymerization progress. Nevertheless, the small linear oligomer I ($M_{n\ GPC}$ = 4400 gmol^{-1}) displayed solvent-dependent induced dichroic signals in its electronic circular dichroism spectra (ECD; Fig. 2) and was highly fluorescent (Φ_F= 0.40, $CHCl_3$).

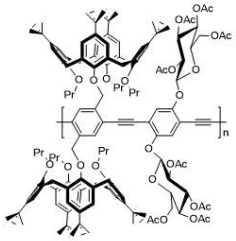

Figure 1. Oligomer I.

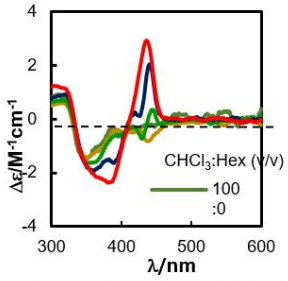

Figure 2. ECD spectra of oligomer I (4x10^{-5} M).

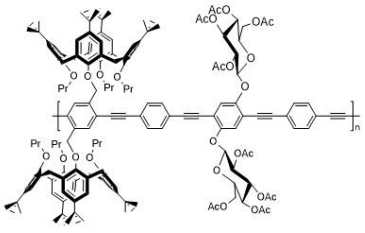

Figure 3. Oligomer II.

In order to enhance the DP, another possibility was evaluated. In this case, an oligomer possessing between 3-5 repeating units was obtained (oligomer II, Fig. 3). Unfortunately, no chiroptical activity was observed for this material in solution. A high quantum efficiency (Φ_F= 0.43, $CHCl_3$) was also registered for II. In the solid state, the oligomer II shows two negative Cottons effects in the π-π* transition regions of the backbone (333 and 414 nm).

Discussion of synthetic details and chiroptical properties of synthesized materials will be presented.

Acknowledgements: We thank FCT/MCTES (PEst-OE/EQB/UI0702/2013 and UID/QUI/00616/2013) for financial support.

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New promising intermetallic, borates and chalcogenides nanofibers

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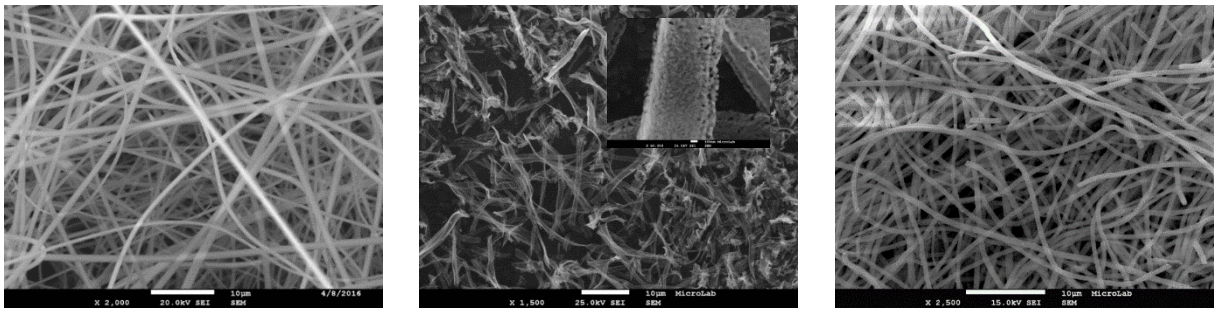
Electrospinning is a technique that has been originally developed to produce high-tech ultra-fine polymer fibers [1]. This route enables low cost production of nanometer scale fibers with tunable surface properties. Such fibers have extremely high surface area, very high porosity, high permeability, low basic weight, the ability to retain electrostatic charges, among others properties [2].
The purpose of this work was to apply electrospinning for the preparation of compounds containing *f*-block elements with nanofibers shape. Moreover, the expected high surface area and low dimensionality can bring benefits to the catalytic, thermoelectric or magnetic properties of these materials, which will be the aim of future studies. Preliminary results showed that nanofibers of some compounds as $DyFe_3$, CuS, and LaB_6, can be successfully produced by this technique, which, to our knowledge, happens for the first time. Examples of SEM images of nanofibers prepared in this work are presented in **Figure 1**.



(a) (b) (c)

Figure 1. SEM images of nanofibers (a) $DyFe_3$-PVP as spun; (b) $DyFe_3$-PVP 800 ºC under air; (c) CuS-PVP as spun.

Acknowledgements: The authors gratefully acknowledge also the FCT support through the UID/Multi/04349/2013 project.

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Self-assembled Molecular Conducting Bilayers

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Organic conductors were initially proposed as possible high temperature superconductivity materials. While that was not achieved a new a class of materials immerged with a very rich diversity of ground states, ranging from antiferromagnets, insulators, to 2D metals, superconductors and physical phenomena that are very sensitive to magnetic field, pressure, and temperature. Since the first family of organic superconductors, the quasi-one dimensional Bechgaard salts $(TMTSF)_2X$ (X = ClO_4, PF_6, AsF_6, etc), and after the quasi-two dimensional compounds $(BEDT\text{-}TTF)_2X$ there has been a remarkable development of bidimensional molecular conducting systems in particular with other derivatives of the electron donor BEDT-TTF.[1] Systems based on double layered structures, potentially more interesting, have however never been explored.

This project aims at exploring bilayer conducting systems based on a new BEDT-TTF derivative, recently prepared in the C^2TN group,[2] and different inorganic anions. This new organic donor was recently found to self-assemble in double layered structures in charge transfer salts with small anions.[3] However a large number of different anions have not yet been explored, namely paramagnetic anions which can lead to conducting magnetic materials where anomalous magneto resistance, quantum interference effects[4] and even superconductivity induced by magnetic fields can take place.[5] There is a variety of mechanisms for magnetoresistance (the change the electrical resistance by a magnetic field) which reflects the electronic structure and may be applied in different devices. Besides the common positive magnetoresistance of metals, there is a negative magnetoresistance[6] in ferromagnets and since 1980's large magneto-resistive in multilayer systems gained importance.

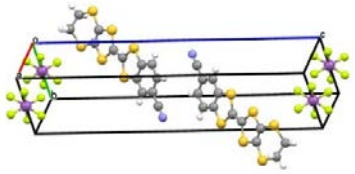

Figure 1: Crystal structure of a new bilayer salt $(CNB\text{-}EDT\text{-}TTF)_4SbF_6$

Acknowledgements: Work partially supported by FCT through contracts UID/MULTI/04349/2013 and RECI/QEQ-QIN/0189/2012 and grants SFRH/BPD/113344/2015 and SFRH/PD/BD/127804/2016, to S.R. and and A.C.G. respectively.

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N-Alkylated porphyrin–thiazolothiazole conjugates

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Porphyrin derivatives have been intensively studied due to their potential applications in catalysis, photodynamic therapy (PDT), new electronic materials, chemical sensors and solar cells.[1,2]
Thiazolothiazoles are a class of heterocyclic compounds with a rigid and coplanar bicyclic scaffold possessing enhanced extended π-electron system and charge transfer capabilities, together with a high environmental stability.[3-5]
Taking advantage of the characteristics of porphyrins and thiazolothiazoles, we decided to synthesize compounds behaving these two units expecting to obtain dyes with improved properties for application in solar cells.
In this work we will report the synthesis of *N*-alkylated porphyrin–thiazolothiazole conjugates under very mild conditions (**Figure 1**).

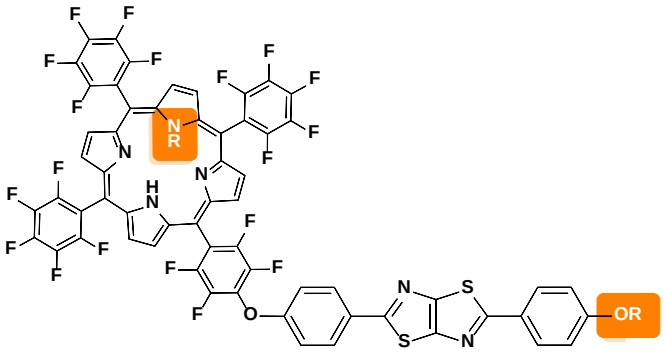

Figure 1

Acknowledgements: Thanks are due to Fundação para a Ciência e a Tecnologia (FCT) for the financial support to project PTDC/QEQ-QOR/6160/2014 and the QOPNA research project (FCT UID/QUI/00062/2013) through national funds and where applicable co-financed by the FEDER, within the PT2020 Partnership Agreement, and also to the Portuguese NMR Network.

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Acrylic Biomaterials for Targeting Bone Infections: a multidisciplinary approach

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Poly(methylmethacrylate) (PMMA) bone cement is considered to be the gold standard biomaterial for total hip replacement procedures. However, when combined with antibiotics, this polymer has a major drawback, which is the incomplete release of the drug resulting in an elevated risk of bacterial infection due to biofilm formation associated with inflammation[1]. Research on novel formulations is urgently needed. In this context, the aim of the present work was to load levofloxacin, a fluoroquinolone with anti-staphylococcal activity and adequate penetration into osteoarticular tissues, on lactose-modified commercial bone cement (BC). This modified BC matrix exhibited improved antibiotic release (during a 7-week period) with antibacterial activity against *Staphylococcus aureus* and *S. epidermidis*. Moreover, for the first time, an original *in silico* approach provided an insight of the drug-biomaterial interaction and demonstrated the existence of both covalent (Figure 1) and non-covalent interactions between levofloxacin and BC. Finally, BC mechanical and biocompatibility properties were maintained[2]. These features justify the potential of levofloxacin-loaded modified-BC as a valuable approach for local targeting of bone infections.

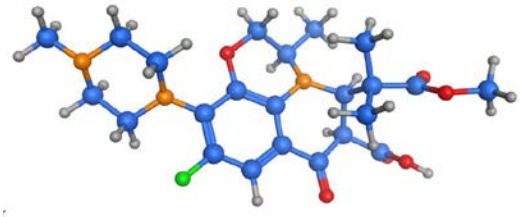

Figure 1: Covalently bonded complex of levofloxacin with polymethylmethacrylate monomer[2].

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support: research project EXCL/CTM-NAN/0166/2012; UID/DTP/04138/2013, COST Action TD1305 (IPROMEDAI).

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A Step Forward In The Control of Monomer/Aggregates Ratio in Hybrid Systems

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The non-covalent self-association of organic dyes is an important phenomenon that leads to the formation of dimers and higher ordered aggregates. In view of the fundamental and technological interest in organized assemblies of dyes, it is vital to gain an in-depth knowledge of aggregation behaviour and structure-property relationships of the dye molecules in different microenvironments.[1] The incorporation of organic dyes into layered inorganic supports has provided a wealth of photo-functional organic-inorganic (OIH) hybrid systems that offer many advantages such as tunable photophysical properties, chemical inertness, high photochemical and thermal stabilities which make them useful as insoluble pigments, light-emitting devices, non-linear optics and sensors.[2,3] In this work, we present some results concerning the intercalation of several dyes individually into layered double hydroxides (LDHs) and layered hydroxy salts (LHS) and also the co-intercalation of dyes with surfactants or another dye with different molar ratios (Fig. 1). A structural and photophysical study was undertaken for the dyes in solution and/or in the solid-state for all materials, aiming to obtain a detailed characterization of the host-guest and guest-guest interactions. It is shown that it was found possible to control the level of aggregation of the dye molecules within the layer cavity by the introduction of an appropriate surfactant[2,3] or a parent dye.

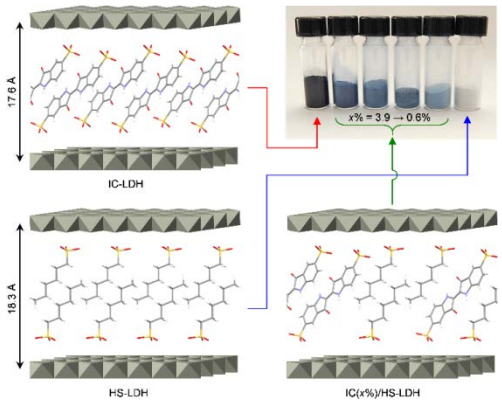

Figure 1: Schematic representation of indigo carmine and a surfactant with different loadings in Zn-Al LDHs.

Acknowledgements: Funding through the FCT within the projects Coimbra Chemistry Centre (PEst-OE/QUI/UI0313/2014) and FCOMP-01-0124-FEDER-029779 (FCT ref. PTDC/QEQ-SUP/1906/2012) is thanked. This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, POCI-01-0145-FEDER-007679 (FCT Ref. UID/CTM/50011/2013), financed by national funds through the FCT/MEC and when appropriate co-financed by FEDER under the PT2020 Partnership Agreement. The FCT is acknowledged for a PhD grant to A.L.C. (SFRH/BD/88806/2012) and a post-doctoral grant to A.C.G. (SFRH/BPD/108541/2015).

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Porphyrins in 1,3-dipolar cycloadditions. Novel synthetic avenues to annulated chlorins and mixed bisadducts

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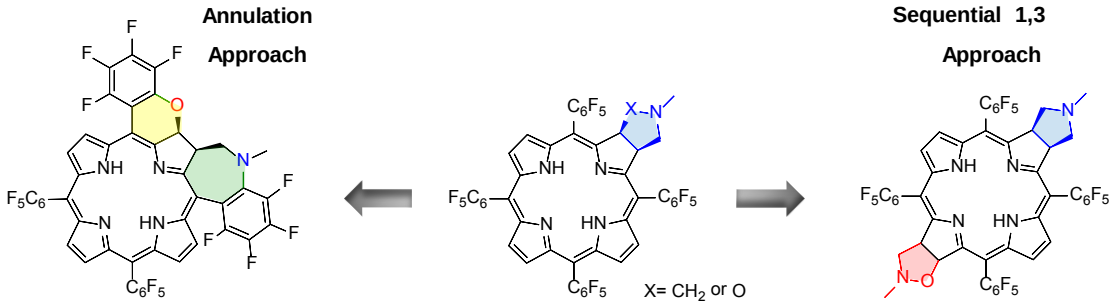
Almost 90 years after the groundbreaking porphyrin synthesis by Hans Fischer, researchers have long acknowledged the various functions performed by this nature-ubiquitous macrocycle, and have successfully applied it in the design of new sensors, catalysis, photocatalysis and photophysical applications.[1] In the biomedical sciences the use of porphyrins, chlorins (7,8-dihydroporphyrins) and bacteriochlorins (7,8,17,18-tetrahydroporphyrins) as photosensitizers (PS) in photodynamic therapy (PDT) is of growing interest.[1]

Here we describe the most recent advances in the design, preparation, and photophysical properties of novel porphyrinic systems by using 1,3-dipolar cycloadditions (1,3-DC). Starting from the adduct of the 1,3-DC of nitrones to *meso*-tetraarylporphyrins, two synthetic routes were investigated, as shown in Scheme 1: (i) mixed bisadducts were obtained, in a site selective approach,[2] from the sequential addition of a nitrone and an azomethine ylide to the porphyrin macrocycle; (ii) a novel *meso*-tetraarylchlorin bearing simultaneously azepine and 2*H*-pyran rings was obtained *via* an annulation approach that involved the cleavage of the isoxazolidine N–O bond followed by two sequential intramolecular nucleophilic aromatic substitutions.[3] Experimental procedures and spectroscopic data of the new macrocycles will be shown and discussed.



Scheme 1: Novel synthetic avenues to annulated chlorins and mixed bisadducts.

Acknowledgements: This work received financial support from FCT/MEC through national funds and co-financed by FEDER, under the Partnership Agreement PT2020, through the projects UID/QUI/50006/2013-POCI/01/0145/FERDER/007265 (LAQV/REQUIMTE), FCT UID/QUI/00062/2013 (QOPNA), PTDC/QEQ-QOR/6160/2014 and M-ERA-NET/0005/2014. The authors gratefully acknowledge the COST action CM1302 (SIPs). A.L. also thanks FCT her grant (SFRH/BPD/85793/2012).

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Photocatalytic Synthesis of Vanillin Through an Energy-Efficient Process

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Vanillin is an organic compound widely used as flavoring and fragrance agent in food, pharmaceutical and cosmetic industries. Currently, the synthesis of vanillin is mostly performed by chemical process, involving toxic substrates as lignosulfonates.[1] Thus, the development of new production routes based on environmentally friendly processes is a challenge to the industry. Heterogeneous photocatalysis has been proving to be a promising alternative to traditional thermal catalytic synthesis processes, due to the possibility to operate at ambient temperature and pressure, to use water as solvent and energy-efficiency and low-cost radiation sources for reaction activation.[2] In the present work, we synthetized composite materials based on zinc oxide (ZnO) and carbon nanofibers (CNF) to be used in the photocatalytic synthesis of vanillin (V) through oxidation of vanillyl alcohol (VA) in aqueous medium under UV-LED irradiation. The effect of the CNF content (from 5 to 20 wt.%) was assessed by monitoring the VA conversion (C), yield (Y) and selectivity (S) towards V production and the composites were dully characterized through several techniques. SEM micrographs of the composite materials show the presence of ZnO tetrapods (**Fig. 1a, zone A**) surrounded by CNF (**Fig. 1a, zone B**). The composite containing 10 wt.% of CNF was the best performing catalyst (**Fig. 1b**), leading to a 50% of VA conversion, and 40% selectivity and 20% yield towards V production after 8 hours of reaction.

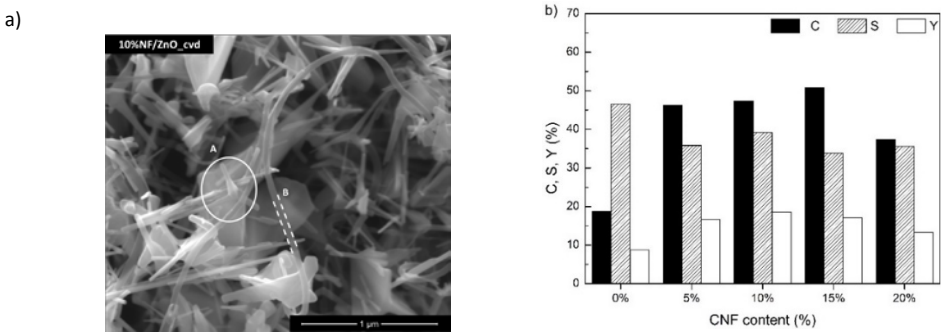

Figure 1: a) SEM micrograph of 10%CNF/ZnO; b) C, S and Y obtained using composite materials with different CNF contents.

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New Trinuclear and Tetranuclear Copper(II) Cores Self-Assembled from Aminoalcohol Ligands

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Multinuclear copper(II) coordination compounds are widely applied in different research areas, ranging from molecular magnetism, bioinorganic and materials chemistry to catalysis.[1–4] In particular, the use of Cu-containing catalysts is primarily governed by the versatile redox properties of this metal, its natural abundance and relatively low cost, and rich inorganic and coordination chemistry. Moreover, copper ions are present in the active sites of diverse oxidation enzymes, thus justifying an extensive research in the fields of copper bioinorganic chemistry and related areas of biomimetic and/or bioinspired catalysis.

In pursuit of our recent research on the design and catalytic use of multicopper(II) coordination compounds,[1–7] the main objective of the present work concerned the self-assembly synthesis and characterization of novel tri- or tetracopper(II) cores driven by the multidentate aminoalcohol blocks and various supporting ligands. Thus, we describe herein two self-assembly reactions, wherein a metal salt {copper(II) nitrate or acetate} is treated, in aqueous alkaline medium at room temperature, with an aminoalcohol {*N,N*-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid or *N*-benzylethanolamine} as a main ligand and in the presence of a supporting ligand source {3,5-dinitrobenzoic acid or sodium thiocyanate}.

The obtained microcrystalline solids were characterized by IR spectroscopy, elemental analysis, and single crystal X-ray diffraction, revealing two novel linear Cu_3 and cubane Cu_4 cores. Synthesis of these compounds as well as their main structural, supramolecular, and topological features will be discussed. Besides, the results on the application of these compounds as bioinspired catalysts for the mild oxidation of cyclohexane to cyclohexanol and cyclohexanone by hydrogen peroxide will be presented.

Acknowledgements: This work was supported by the Fundação para a Ciência e Tecnologia (projects IF/01395/2013/CP1163/CT005 and UID/QUI/00100/2013).

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Metal-free cucurbit[7]uril for the catalytic alcoholysis of epoxides

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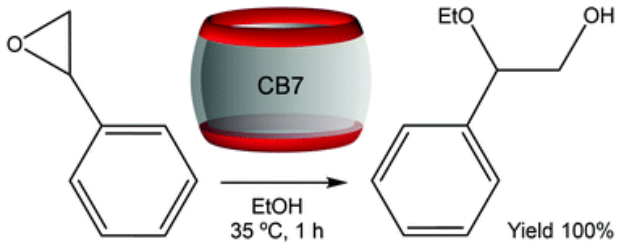
Cucurbit[n]urils (CBn, n = 5–8, 10, 14) are a family of macrocyclic compounds that can be prepared on a large scale by one-pot synthesis from cheap starting materials, glycoluril and formaldehyde.[1] The unique properties of CBs, notably their rigid structure, two highly polar carbonyl-lined portals, a hydrophobic non-polarisable inner cavity, and high binding affinities, have prompted numerous studies within the fields of host–guest chemistry, supramolecular catalysis, drug delivery, molecular machines and electronics, amongst others. Catalytic applications are still waiting to be extensively explored.[2]

We report the use of cucurbit[7]uril (CB7) in the alcoholysis of aliphatic and aromatic epoxides under mild conditions to give β-alkoxy alcohols (**Scheme 1**), which are important intermediates for the synthesis of a vast range of compounds such as bioactive pharmaceuticals.[2] The catalytic process is heterogeneous and the catalyst can be reused in consecutive runs without any reactivation treatment. To date, only a few examples of metal-free heterogeneous acid catalysts have been investigated for the alcoholysis of epoxides, e.g. graphene oxide, mesoporous carbon, and the commercial ion-exchange resin Amberlyst™-15.



Scheme 1: Alcoholysis of styrene epoxide in the presence of CB7.

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Optical and thermal properties of a copper(I)-tin(II) mixture

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A mixture of tin (II) dichloride and copper (I) iodide was manually grinded resulting in a photoluminescent compound that exhibits red luminescence when excited at wavelengths near 400 nm (figure 1). Although it's crystal structure is not yet resolved, this compound showed interesting thermal properties (in its anhydrous and hydrated forms) that were studied by thermogravimetry and differential scanning calorimetry. It's optical properties were also studied using both diffuse reflectance spectroscopy and emission spectroscopy. 2D luminescence maps were created and the quantum yields were measured, with QY reaching as high as 12,57%. Time-resolved spectra were also recorded and the fitted data showed that the system exhibits a single-exponential fast first-order kinetics followed by a slower second order kinetics. This behavior agrees with a semiconductor excitonic recombination which is in contrast with a double single-exponential model followed by Grätzel *et al* [1] when modelling a perovskite life-time.

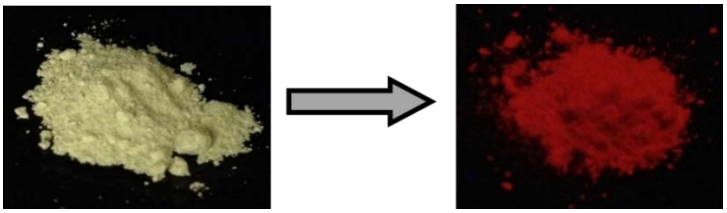

Figure 1: Compound when exposed to visible light (on the left), and to UV light (on the right).

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Sugar Surfactants Niosomes formed by Ethanol and Methanol Injection Method

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Sugar surfactants are the most promissing class of surfactants nowadays. When compared with surfactants derived from petroleum, sugar surfactants present better surface active properties, excellent biodegradability and are derived from renewable sources.[1]

Sorbitan esters (Span) are nonionic surfactants and are one of the most prominent sugar surfactant class, with a wide range of applications. The Span surfactants have low HLB values, which gives them a greater solubility in lipophilic materials, and low solubility in hydrophilic compounds such as water. To overcome this problem, we produced niosomes by ethanol and methanol injection method.

The niosomes are vesicular systems formed by non-ionic surfactants. They are biodegradable, biocompatible and exhibit greater chemical stability when compared with liposomes, once nonionic surfactants are more resistant to hydrolysis and oxidation.[2]

In this work nisomes were obtained by ethanol and methanol injection method, in order to understand the influence of chain length of the solubilizing medium on structure and emulsification ability of vesicular structures formed. The Span used in the study were 20, 40, 60, 65, 80, and 85 and the niosomes were analyzed by DLS and and the emulsification index in the vegetable oil (EI%) was determined.

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Shampoos: new formulations and characterization strategies

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Shampoos are products designed to cleanse, condition, and provide a pleasant fresh, clean residual scent to hair. The shampoo formulation comprises, among others, water, surfactants, thickening agents and other components. The main constituent of hair cleansing product, besides water, is the surfactant due to its detergent properties. With the growth in demand for environmentally-friendly products steadily on the rise, it's natural that only naturally-derived surfactants are a category sparking interest among formulators. Another recent trend has been to use sulfate-free primary surfactants, especially in color protecting shampoos.

The aim of this work was to study the behaviour of new green formulations composed with surfactants that doesn't show any sulphate or any environmental issue in its composition.

To perform this work, ten formulations composed by natural surfactants were prepared, including alkyl polyglucosides (sugar based) formed, in this case, by two different decyl glucoside, coco-glucosides and two different lauryl glucoside. Different thickeners were also used, such as the traditional cocamide DEA and a sugar based composed of PEG-18 glyceryl oleate. All the formulations studied at the level of viscosity, the foaminess and pH. The formulation with sodium laureth sulfate (SLES) was used as control.

The pH was measured with a potentiometer while the foaminess and foam stability were determinate using a vortex for 10 seconds and measuring the foam height for 100 minutes. The viscosity of formulations was determined using a viscometer (Brookfield, digital viscometer) with a needle number 21.

Concerning the pH values, it can be stated that the values vary between 10.04 and 4.95. The formulation with higher pH is the one that has the lauryl glucoside as surfactant and the sugar based thickener while, the formulation with decyl glucoside as surfactant and a sugar based thickener has the lowest pH. There is another formulation whose pH is also of 10.04, this shampoo also have a lauryl glucoside as surfactant, however the thickener is the traditional option.

Concerning the stability of the formed foam, it has been found that all formulations have a good and stable foam formation, varying their values between 0.1 and 0.3 cm during 100 minutes. The formulations with less foam stability are the ones where the decyl glucoside it's used as a surfactant and the traditional and sugar based thickeners are used.

Regarding viscosity, the formulation that presents lower viscosity is the one that contains a decyl glucoside as surfactant and PEG-18 glyceryl oleate as thickener while, the formulation with lauryl glucoside and a sugar based thickener has the highest viscosity.

In conclusion, even natural formulations, sometimes, present an inappropriate pH, the thickeners and naturally-derived surfactants are a major breakthrough in cosmetic technology. These new constituents of shampoos have a great impact in hair cleansing properties of the products.

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Ohmic heating approach in the synthesis of pyridyl analogues of rosamines: Synthesis and photophysical behaviour.

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Rosamines, xanthene derivatives, are excellent backbones to desing fluorescent probes featuring robustness and chemical versatility suited for a wide range of fluorescence measurements and imaging.[1]
Here we prepared a new serie of pyridyl analogues of rosamines (**2a-c**) by employing two methodologies: (i) the conventional approach[2] involving the condensation of a pyridinecarboxaldehyde with 3-(diethylamino)phenol under oil-bath heating and (ii) the novel ohmic heating (ΩH) approach[3] based on the condensation under 'on water' conditions giving triarylmethane intermediates (**3a-c**), followed by oxidative cyclodehydration. The photophysical properties of pyridyl rosamines (**2a-c**) were investigated and compared with the standard rhodamine B. Also a novel *N*-methylpyridinium analogue was obtained from the methylation of rosamine **2a** with methyl iodide. Structural variations, including the position of the nitrogen atom in the pyridine and its cationization, were found to have significant effect on the absorption and fluorescence properties of the fluorophores.
Experimental procedures and spectroscopic data, including NMR, UV-Vis, fluorescence spectroscopy, mass spectrometry and single-crystal X-ray analysis, of the new dyes will be presented and discussed.

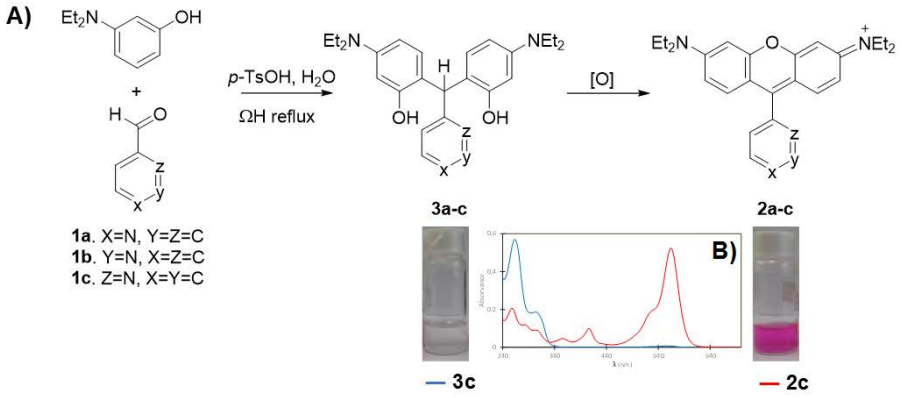

Figure 1: (A) Ohmic heating approach for the synthesis of pyridyl analogues of rosamines (**2a-c**); (B) Absorption spectra of **2c** (red line) and **3c** (blue line), in methanol.

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Synthesis and Characterization of Magnetic and Luminescent Ionic Liquids

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Ionic Liquids (ILs) as tunable organic salts possessing peculiar properties have been applied in many research fields including organic chemistry; catalysis; analytical chemistry; material science; pharmaceutical science as well as electrochemistry and energy topics, among others.[1] Nowadays, a recent class of these salts, the magnetic ionic liquids (MILs), has gained greater attention. These compounds have the advantage of combining ionic liquids properties as well as magnetic materials. This combination allows these organic salts to respond to a strong magnetic field.[2] Discovered and studied by Hayashi and Hamaguchi in 2004, [BMIM][$FeCl_4$] was the first example of MILs and since then magnetic ILs have also been reported with other paramagnetic ions including transition metals such as cobalt (II), manganese (II), ruthenium and some lanthanides, like gadolinium (III) and terbium (III).[3,4] Until a few years ago, magnetic ILs applications have been mainly focused in catalysis but today, MILs have a wide range of applications. Specifically, they have been used in electrochemical and chemical engineering applications including extraction and separation processes.[5] Herein, we have developed more biocompatible magnetic and luminescent ionic liquids based on the combination between choline derivative cations and Mn(II), Gd(III) and Tb(III) anion complexes (Figure 1). All prepared compounds were completely characterized by spectroscopic (NMR, FTIR, UV-Vis, Emission); magnetic susceptibility; solubility profiles and thermal properties. Additionally, Mesoporous silica nanoparticles (MSNs) have been also developed for the most promising compounds in order to improve some of their physical-chemical as well as biological properties. Finally, DTPA complexes and adequate counter-ions are used to develop coordination metal complexes in the presence of adequate counter-ions for further medical or biological applications.

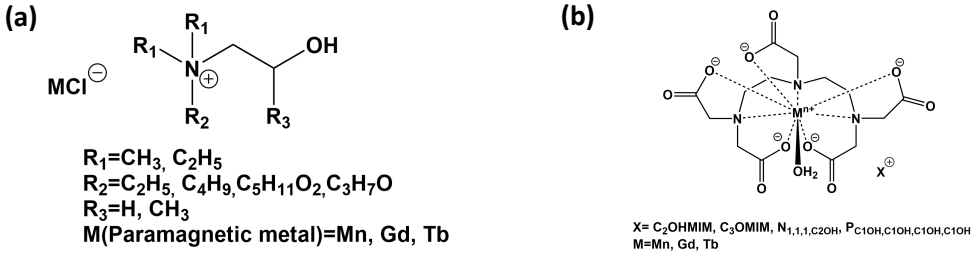

Figure 1*:* (a) Structure of synthesized magnetic ionic liquids based on choline derivatives; (b) DTPA-Metal complexes.

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Exploring unconventional fluorinated anions for efficient CO2/N2 separation using supported ionic liquid membranes

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In the last 15 years, ionic liquids (ILs) have found their place as new functional materials. In particular, they have shown to be extremely successful in CO_2 separation applications, due to their inherent designer nature, that enables the tailoring of their properties by proper selection of cation and/or anion or via the addition of specific functional groups. A broad diversity of ILs has been used to prepare supported ionic liquid membranes (SILMs) and the effect of IL chemical structure on the gas permeation and separation properties of these membranes has been investigated[1]. Since some SILMs have shown potential for industrial applications, particularly for low pressure systems such CO_2 separation from flue gases, many efforts are being put in the development of new task-specific ILs to enhance the already advantageous combination of gas permeability and selectivity of SILMs[2-5]. In particular, the superior performance of ILs bearing fluorinated anions, such as the bis(trifluoromethylsulfonyl)imide $[NTf_2]^-$, tetrafluoroborate $[BF_4]^-$, and hexafluorophosphate $[PF_6]^-$, due to their CO_2-phylic behaviour and high CO_2 permeabilities, is well recognized.
In this work, we explore the gas permeation properties of ILs based on the 1-ethyl-3-methylimidazolium ($[C_2mim]^+$) cation and different unconventional fluorinated anions such as 2,2,2-trifluoromethylsulfonyl-N-cyanoamide ($[TFSAM]^-$), bis (fluorosulfonyl) imide ($[FSI]^-$), nonafluorobutanesulfonate ($[C_4F_9SO_3]^-$), tris(perfluoroalkyl)trifluorophosphate ($[FAP]^-$), and bis(perfluoroethylsulfonyl)imide ($[BETI]^-$) anions. Moreover, the re-design and structural unfolding of the asymmetric anion $[C_2mim][TFSAM]$ through the use of IL mixtures was also investigated. The CO_2 and N_2 permeation properties (permeability, diffusivity and solubility) through all the prepared SILMs were determined using a time-lag apparatus. In order to evaluate trends and considering that IL viscosity and molar volume are significant parameters that impact the gas permeation properties of SILMs, the thermophysical properties, namely density and viscosity, of the tested IL phases were also measured.

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Discovery of new intermetallic compounds: the U_2Sb case

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Intermetallic compounds are solid state materials composed of two or more metals (or metals and nonmetals) that contain metallic bonds and have a defined stoichiometry and ordered crystal structure. They are amazing systems that can present complex crystal structures with more than thousand atoms, but in many cases the structure is simple and highly symmetric. These materials frequently present important technological and/or unusual properties, like high hardness, superconductivity, hard magnetism, complex magnetism, giant magneto-caloric effects, heavy fermion behavior, etc.

The majority of the binary phase diagrams involving metals have been explored and most of them contain intermetallics. The U-Sb is one of the cases where the phase diagram was completely studied up to the liquid phase in the whole composition range. Four intermetallic compounds, USb_2, USb, U_3Sb_4 and U_5Sb_4, were identified in this system.[1] Recently, we decided to explore the ternary U-Fe-Sb phase diagram in order to identify and study the new compounds.[2] Two compounds, $UFe_{1-x}Sb_2$ and $U_3Fe_{3-x}Sb_4$, were identified in this ternary system, but in some uranium-rich samples signs of an extra phase could be seen. Here we present the story of the identification, single crystal growth, and characterization of such new binary compound, U_2Sb (**Figure 1**), that exists in this system.[2]

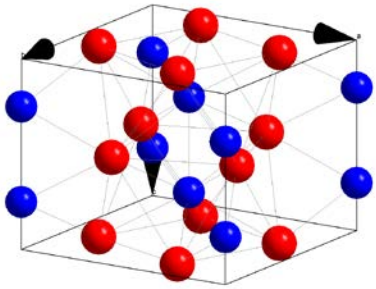

Figure 1: Representation of the U_2Sb unit cell.

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Phosphine-Gold(I)-Alkynyl-Naphthyridine complexes as luminescent sensors for guanine derivatives

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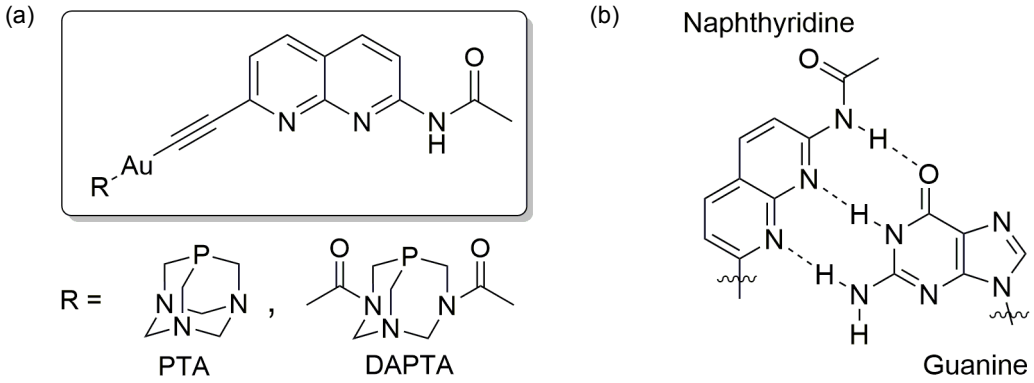
Gold(I)-alkynyl complexes have become an attractive class of compounds towards the development of new systems and materials for sensing based on luminescence changes, not only due to their high chemical versatility and easiness in handling/preparation, but also due to the presence of Au(I)---Au(I) interactions which often induce luminescent behavior.[1] Such advantages allow for the preparation of a large spectrum of derivatives, which present different properties that are largely dependent on the substitution pattern of the organometallic complexes.
Our recent efforts have been focused on designing new molecules which can binding to specific targets and consequently, work as chemosensors for specific analytes. With this in mind, we successfully synthesized two Phosphine-Gold(I)-Alkynyl-Naphthyridine complexes (Scheme 1a).
The naphthyridine moiety is a fluorophore capable of forming hydrogen bonds with Guanine and its derivatives, mimicking Watson-Crick base-pairing interactions (Scheme1b).[2] The phosphine group is responsible for conferring increased water solubility to the final structure.
Herein, we present some of the latest developments regarding the luminescent behavior and sensing properties of our new complexes in the presence of Guanine derivatives.



Scheme 1: (a) Structure of Phosphine-Au(I)-Alkynyl-Naphthyridine complexes; (b) Schematic representation of base-pairing interactions between Naphthyridine and Guanine.

Acknowledgements: This work was supported by the Associate Laboratory Research Unit for Green Chemistry - Technologies and Processes Clean – LAQV, which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265). A.J.M. gratefully acknowledges a postdoctoral grant from FCT/MEC (SFRH/BPD/69210/2010). This research was supported by a Marie Curie Intra European Fellowship within the 7th European Community Framework Programme (R. G.). The SAXS experiments were performed at the NCD beam line at the ALBA Synchrotron with the collaboration of the ALBA staff.

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Difluoroboron complexes of functionalized dehydroacetic acid: Electrochemical and luminescent properties

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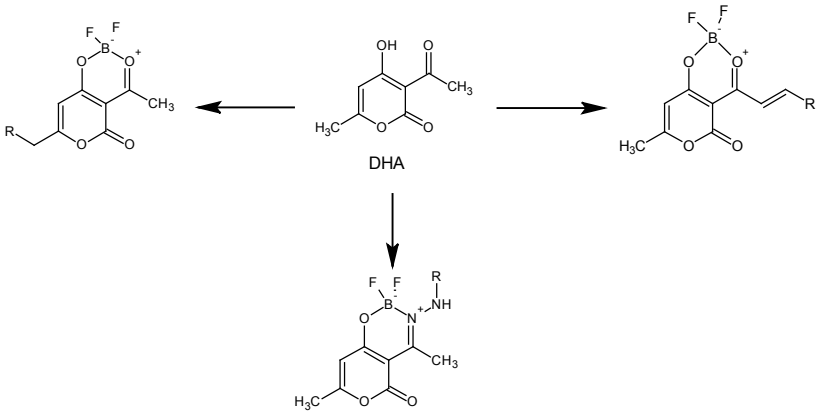
Dehydroacetic acid (DHA) and the Schiff base of DHA can complex difluoroboron moiety and such difluoroboron complexes present two advantages: (i) it enhances the reactivity of DHA itself and (ii) some of these derivatives can exhibit fluorescence properties. We report in this work the functionalization of DHA-BF_2 and Schiff base of DHA-BF_2 by a phenyl ring or an electroactivecore (tetrathiafulvalene or ferrocene) in order to analyse the influence of the electrophore on the fluorophore properties.For that purpose, three approaches were used: i) Wittig reaction at the 6 position involving aldehydes bearing an electroactive unit and a phosphonium salt of DHA, ii) condensation reactions of these aldehydes with DHA BF_2 at the acetyl position and iii) condensation of the aldehydes on the DHA-hydrazone.[1] Depending on the reaction used, the spacer group between the DHA moiety and the electroactive part will be different as well as the position of the connecting part on the DHA core (**Scheme 1**).



Scheme1: functionalization of dehydroacetic acid

The redox and the photophysical properties of obtained derivatives have been studied.

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A thermochromic and a self-organization case studies in an Eu(III) family of Room Temperature Ionic Liquids

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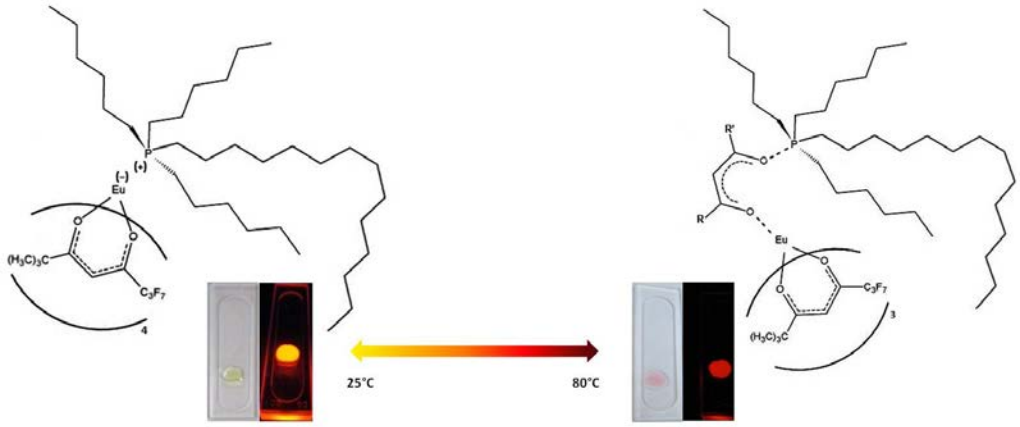
The first example of an observable and reversible case of thermochromism due to the interaction of an alkylphosphonium $(P_{6,6,6,14})^+$ with a β-diketonate (1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionate-fod) of an Eu(III) room temperature ionic liquid (RTIL), $[P_{6,6,6,14}][Eu(fod)_4]$, is described. This thermochromism is characterized by the conversion of a light yellow viscous liquid, at room temperature, to a reddish liquid close to 80 ºC. The reversibility of this optical effect was highlighted by the thermal stability of the Eu(III) complex.[1] The use of a dibenzoylmethanate (dbm) ligand instead of one fod ligand leads to the formation of another RTIL, $[P_{6,6,6,14}][Eu(fod)_3(dbm)]$, with an unexpected thermal behavior explained by uncommon self-organization properties due to the influence of the long chain tetraalkylphosphonium counter ion.



Scheme 1: Schematic structure of the $[P_{6,6,6,14}][Eu(fod)_4]$ RTIL formed upon heating to 80 ºC. Pictures were taken under daylight (left) and under 366 nmUV irradiation (right)..

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Multidisciplinary Approach For Forensic Discrimination Of Latex Gloves

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Latex gloves are frequently used by felons to avoid leaving fingerprints and DNA traces in crime scenes. The majority of felons discard the gloves at the crime scene or nearby[1-3]. Despite being common items, the analysis of latex gloves may provide useful information to crime scene investigators, for instance by comparing gloves found at the crime scene with those seized at a suspect's premises[3].

Latex is a highly regular *cis*-1,4-polyisoprene produced by more than 2000 species. The manufacture of latex gloves includes a compounding step, which allows to improve their final properties[1]. This step and the differences along the general manufacture process may introduce differences that enable distinguishing gloves of distinct origins.

The main objective of this study is the forensic discrimination of latex gloves that are indistinguishable by visual examination, using a multidisciplinary approach, without any sample preparation, combining infrared spectroscopy in attenuated total reflectance mode (FTIR-ATR), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), Time domain-nuclear magnetic ressonance (TD-NMR) and X-ray diffraction (XRD). Twenty four latex gloves, from six different brands, were analyzed at three random sites each. A data matrix was constructed with the results obtained. All data were submitted to multivariate statistical analysis including Principal Component Analysis (PCA) and Hierarchical Cluster Analysis (HCA). Multivariate analysis proves to be effective to interpret the information obtained in the experimental multidisciplinary approach. Blind samples were included in the data matrix and also subject to the same type of analysis. These blind samples were successfully grouped, allowing validation of the results obtained.

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Ligand characterization and functional group conversion in nanostructured silica by ^{1}H-NMR

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Nanoscale materials offer excellent opportunities for bio-imaging and therapeutic applications. Particularly, silica-based nanoparticles (SiNPs) are a promising class of materials due to their well-defined and tunable structures and versatile functionalization chemistry, which improves their chemical and physical properties.[1] An accurate quantification of active functional groups on a nanoparticle surface is important to know the number of molecules that can be linked to the surface. Solid-state NMR methods have been used to investigate functionalized nanomaterials, however, an important drawback of these methods is that they are very time consuming, need a large amount of sample for analysis and are generally carried out on the dried powders.

Here, we present a fast and simple method for quantification of surface ligands and for tracking chemical modifications on silica nanoparticles. This is based on solution NMR spectroscopy, combining in-situ dissolution of the SiNPs and standard ^{1}H-NMR experiments.[2]

Quantitative analysis of the NMR spectra for functionalized SiNPs agrees well with the TGA results **(Table 1)** and the obtained results revealed the sensitivity of solution NMR spectroscopy for tracking small amounts of surface bound ligands on the SiNPs. Extension of this method to other silica based nanomaterials can also be envisaged.

Table 1: Functional group quantification for SiNPs by NMR and TGA.

Sample	NMR (mmol/g)	TGA* (mmol/g)	Surface coverage (molecules/nm^2)
MSN@NH_2	0.38	0.36	2
MSN@SH	0.41	0.43	2
MSN@vinyl	0.45	0.44	2
SSN@NH_2	0.81	0.78	3
SSN@SH	0.14	0.17	0.5
SSN@COOH	0.23	0.21	1

* Corrected for the weight loss due to silica network condensation at high temperatures.

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Enzymatic polymerization of HMF derivatives

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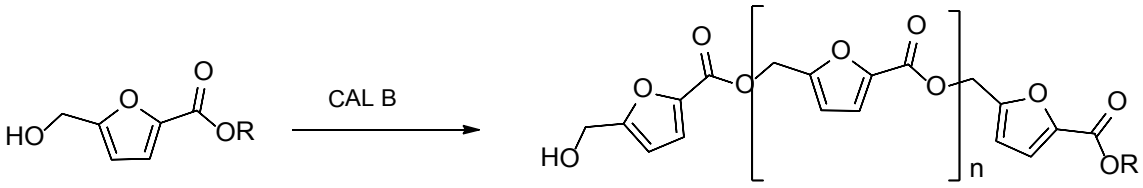
The development of biorenewable chemical building blocks for the production of polymer plastics and resins is an important modern approach in achieving more sustainable methodologies in organic synthesis and processing.[1]
Monomers obtained from renewable sources, like terpenes, lactic acid and sugars, present similar properties. On the other hand, using furan or furan-based molecule this is not observed. This molecules present different properties from theirs precursors, allowing to build a wide variety of macromolecules with different properties. Therefore, it is a good alternative to petrochemical molecules.[2] 5-(hydroxymethyl)furfural (HMF) is considered to be one promising biorenewable building block for the production of monomers.[3]
Recently, continuous flow methodologies have rapidly growing and with it came the opportunity to change the way how synthetic chemistry is performed in academia and industrial level. Also, the combination of continuous processing and biocatalysis have been elected as key green emerging research areas for sustainable manufacturing.[4]
Herein, we will present the synthesis and enzymatic polymerization of key monomers based on HMF in batch and in continuous flow mediated by *Candida Antarctica* lipase B **(Scheme 1)**.



Scheme 1: Enzymatic polymerization of HMF derivatives

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The Molecules of Colour in the Portuguese Postage Stamps (1857-1909)

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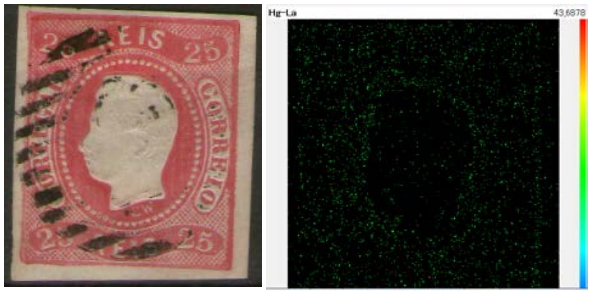
The origin of the pigments or dyes (molecules of color) used to dye the first Portuguese postage stamps remains until nowadays unknown. A single reference to a box with printing inks original from England, without any reference to its content, was received on April 23, 1853.[1, 2] It is known from a previous analysis that we have done to some postage stamps of the United Kingdom that carminic acid, cochineal, (for reds) and the iconic mauveine (for lilacs / purple) were used in UK postage stamps the period ranging from 1847 to 1901.[3] In this work we will present a study, based on an analysis involving different techniques (X-Ray Fluorescence, UV-VIS-NIR spectroscopy, ATR-FTIR, HPLC-DAD-MS, steady and time resolved fluorescence) of the inks used in a selected number of Portuguese postage stamps from the period 1857-1909 with red, rose, purple and orange colours. It was found that these included, amongst others, the inorganic pigments cinnabar (HgS), lead oxides (Pb_3O_4) and chromates ($PbCrO_4$), lead sulphides (PbS) and the organic compounds carminic acid and eosin Y. The use of these molecules of colour, in particular of the inorganics, contrasts with those used in the printing of United Kingdom postage stamps.[3]



22_1866_Rep.1

Figure 1: A red Portuguese postage Stamp (catalogue reference 22 1886) and its XRF mapping of Hg.

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Nonlienar emission in carbon dots

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Carbon dots (C-dots), due to their unique photophysical properties, versatile surface functionalization and good biocompatibility, have recently attracted considerable interest in biomedical applications such as biosensors, drug delivery, bioimaging and theranostics. The origin of photoluminescence in carbon dots is under intense debate. They have been reported to have exceptionally high two-photon brightness, competing with state-of-the art nonlinear fluorophores such as upconversion nanoparticles and semiconductor quantum dots. Understanding the nonlinear photoluminescence mechanism of C-dots is one of the most important issues to be solved in adapting this material to biological applications. Nitrogen doped, crystalline carbon dots have been reported with high Two-Photon Absorption (TPA) values (on the 10^4 GM range).[1] In contrast, very modest values (<100 GM) have been reported for undoped amorphous carbon dots.[2] At the moment, the limited number of studies where the TPA properties have been address in a systematic and quantitative way preclude a conclusive analysis about the critical factors for an effective two-photon brightness. In this paper we discuss the TPA properties of carbon dots produced by either top-down methods, involving the conversion of a graphite based material to graphite oxide sheets, or bottom-up methods, involving the synthesis of quantum dots from the pyrolysis of organic compounds. The material that is produced using different methods can be quite different in terms of structure, crystallinity and types of oxygen containing functional groups decorating the edges or the surface of the carbonaceous core. (**Figure 1**) In this poster we discuss the TPA properties in connection with the structure of the different types of dots investigated.

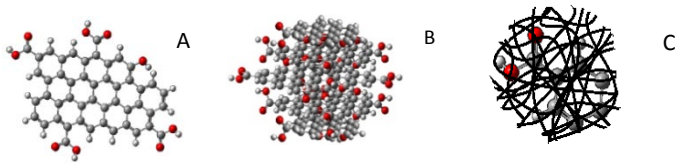

Figure 1: Different types of dots produced, A) sheet like graphene quantum dots, B) crystalline carbon quantum dots and C) amorphous polymer dots.

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Copper Metalloporphyrins As Catalysts For Microwave-Assisted Oxidation Of Secundary Alcohols

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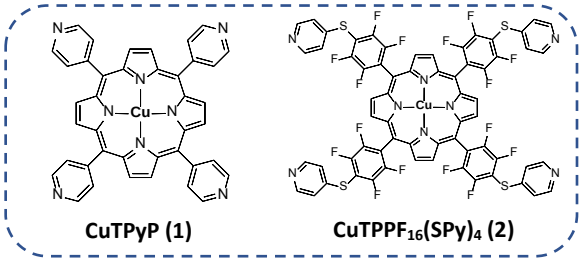
Microwave-assisted oxidation of alcohols is a highly demandable research topic because selective oxidation of alcohols to carbonyl compounds is a vital step in the synthesis of important intermediates and fine chemicals[1]. In comparison to other transition metal complexes, copper catalysts are commercially inexpensive, less polluting and fairly easy to handle/prepare[2]. Moreover, metalloporphyrins are long known for their catalytic performances against a wide variety of substrates[3]. Thus, it would be attractive to test them as catalysts in the peroxidative oxidation of alcohols.

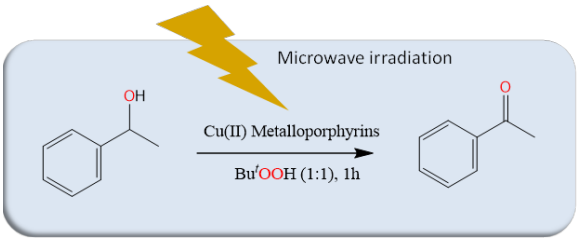
We have recently synthesized two Cu(II)-based metalloporphyrins CuTPyP (**1**) and $CuTPPF_{16}(Spy)_4$ (**2**) prepared in a $CHCl_3$/MeOH (2:1) mixture, using 1.5 equiv. of $Cu(AcO)_2{\cdot}H_2O$ and H_2TPyP (for **1**) or $H_2TPPF_{16}(SPy)_4$ (for **2**) porphyrins (Scheme 1)[4,5]. Full characterization of the final metallated derivatives was obtained through UV-Vis, infrared (ATR-FTIR) and electron paramagnetic resonance (EPR).



Scheme 1

Both complexes act as good catalysts for microwave-assisted peroxidative oxidation of 1-phenylethanol with *tert*-butyl hydroperoxide (*t*-BuOOH), with ketone yields up to *ca*. 70%, in the absence of any added solvent (**Scheme 2**).

The influence of various parameters, such as: reaction time, amount of catalyst, temperature and presence of additives, is also evaluated.



Scheme 2

Acknowledgements: Thanks are due to FCT/MEC for the financial support to CQE (FCT UID/QUI/0100/2013) and QOPNA (FCT UID/QUI/00062/2013) research units, through national funds and where applicable cofinanced by the FEDER, within the PT2020 Partnership Agreement.

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Mono and Di-alkylated Indigo Derivatives: Synthesis and Excited State Characterization

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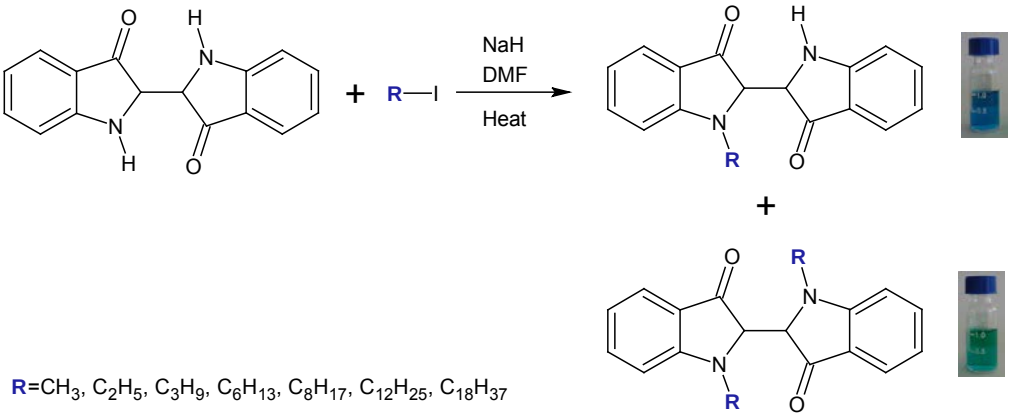
Indigo and its derivatives are included in the most ancient and popular natural dyes.[1] The longevity of indigo is chemically related to its photostability which is linked to an excited state proton transfer.[2] Structural changes in the structure of indigo may tune its photochemical and photophysical properties. Modifications in the chromophoric center, following the methodology reported by Setsune[3], have been accomplished by replacing one or two N-H groups by different alkyl groups, see **Scheme 1**. In the present work seven mono-alkylated indigo derivatives (*N*-methylindigo, *N*-ethylindigo, *N*-propylindigo, *N*-hexylindigo, *N*-octylindigo, *N*-dodecylindigo and *N*-octadecylindigo) and seven di-alkylated indigo derivatives (*N,N'*-dimethylindigo, *N,N'*-diethylindigo, *N,N'*-dipropylindigo, *N,N'*-dihexylindigo, *N,N'*-dioctylindigo, *N,N'*-didodecylindigo and *N,N'*-dioctadecylindigo) have been synthesized and investigated in different media in order to study the influence of the substitution in the photophysical and photochemical properties of indigo. It was found that with the mono-alkylation, the spectral and photophysical properties of the compounds remain approximately identical to those of indigo, whereas dialkyl-substitution promotes significant changes in the photophysical and spectral properties with a strong dependence on the nature of the solvent.



Scheme 1: General synthetic procedure followed by the synthesized indigo derivatives.

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Custom poly(ionic liquids) heading microextraction specificity

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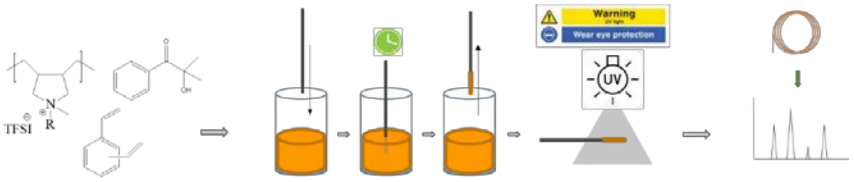
In this work, Poly (Ionic Liquids) (PILs) were synthesized and tested as coatings for SPME devices. ILs are known by their high solvation capacity for a large number of chemically different compounds1 and the combination of their properties with the mechanical and thermal properties of polymers is a promising approach to prepare materials with enhanced and specific properties2,3. A series of PILs, based on divinyl methylamine, vinyl imidazolium and ammonium methacrylate cations bearing different alkyl chain lengths or pendant groups and different nitrogen containing structures such as thiazole, pyridine, triethylamine, morpholine, piperidine or imidazole were synthesized through photo-polymerization (Scheme 1) or co-polymerization with styrene yielding a plethora of materials. The monomers were combined with (trifluoromethanesulfonyl) imide anion ([TFSI]−) not only to increase their thermal stability but also to increase the free volume of the material. Also, polymer blends combining commercial polymers, such as poly(dimethylsiloxane) or poly(ethyleneglycol) with our poly(ILs) were tested. After the characterization of each material, the fiber supports were coated and they have been tested as SPME coatings in a GC-FID against several model samples of standard solutions. Limit of detections, sorption time profiles, specificities, reproducibility and thickness effect of each fiber were accessed and validated. Human urine, contaminated water, food, plants or contaminated soils were used as real matrix for recovery tests. The unique property of Poly(ILs) is their tunable design that can be adjusted to each sample and each specific analyte. This feature makes them extremely valuable in areas were specific separations are needed.



Scheme 1: Workflow for the preparation of SPME fibers trough photopolymerization.

Acknowledgements: FCT grant SFRH/BD/97042/2013 and project PTDC/CTM-POL/2676/2014. COST for financial support.

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Bright nanoparticles for an even brighter future: efficient production of luminescent carbon nanodots from olive mill wastewater

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Carbon nanodots (CNDs) are a very recent class of spherical-shaped nanosized carbon materials possessing average typical diameters < 10 nm. Since the very first reports on carbon dots,[1,2] a variety of methods (top-down and bottom-up strategies), carbon sources and passivating agents, have dealt with their synthesis.[3] The bottom-up approach, encompassing the use of pyrolytic/solvothermal processes, is more amenable for large-scale production and can cope with a large diversity of carbon precursors, either from natural or synthetic sources, typically endowed with acid, alcohol and amine functionalities.[4] Some of the interesting CNDs properties include tunable photoluminescence, outstanding photostability and negligible cytotoxicity. These unique properties have prompted their intense and widespread use in several fields, such as fluorescent bioimaging and nanomedicine, chemo/biosensing, photocatalysis and optoelectronics.[4]

Olive oil is obtained from the fruit of the olive tree (*Olea europaea* L.) by batch press and continuous centrifugation processes. Large amounts (200-1600 L) of olive mill wastewater (OMWW) may be produced per tonne of processed olives, depending on the process. The main organic constituents of OMWW are sugars, pectins, phenols/polyphenols, tannins and lipids. OMWW exhibits phytotoxicity and antimicrobial activity, usually attributed to its phenolic content, leading to very low biodegradability parameters and serious environmental concerns for its uncontrolled disposal.

Following sustainable and expedite hydrothermal processes, we have been able to synthesize highly luminescent CNDs directly from OMWW. The as-prepared CNDs were obtained in excellent yields under a variety of conditions. In order to maximize the quantum yield of the as-synthesized carbon nanoparticles, several operation variables (*viz.* reaction temperature, reactor dwell time and amount/nature of organic additives) were investigated. Certain processing-structure-property correlations have been established and will be presented in this communication, along with the photophysical properties (UV-Vis, excitation and fluorescence emission), surface analysis (FTIR, $^{1}H/^{13}C$ NMR), microanalysis, and morphology (TEM) of selected CNDs.

Under specific synthetic conditions, and without any further purification procedure, the as-synthesized CNDs are deep blue emitters ($\lambda_{em\ max}$ ~ 410 nm; λ_{exc} = 340 nm) reaching notable quantum efficiencies (Φ_F = 0.3-0.4), an extremely high photostability (upon being continuously irradiated at 340 nm), and a pH-responsive luminescence (pH 1-12).

Such luminescent properties of CNDs, allied to the carbon source affordability, their easy synthesis, and excellent dispersion behaviour in aqueous solutions and polar protic and non-protic organic solvents, render them with unique capabilities to be used in several important domains such as bioimaging tools, in sensory analysis, and as organocatalysts and/or nanocomposites components in photocatalysis.

Acknowledgments: We thank Instituto Politécnico de Lisboa (Project NANOLIVE/IDI&CA/2016) and Fundação para a Ciência e a Tecnologia/Ministério da Ciência, Tecnologia e Ensino Superior (UID/QUI/00616/2013) for financial support.

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Cryogenic Nanothermometer Based on the MIL-103(Tb,Eu) Metal Organic Framework

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Microporous metal organic framework MIL-103 doped with Tb^{3+} and Eu^{3+}, formulated as $[(Tb_{0.95}Eu_{0.05})(BTB)(H_2O)]\cdot(solv)_x$ (H_3BTB = 1,3,5-tris-(4-carboxyphenyl)benzene; solv = H_2O, CH_3OH) is shown to be a good platform for luminescent ratiometric thermometry.[1] Although operative in a wide range of temperatures (10 – 320 K, **Figure 1**) this material exhibits, in the cryogenic range (<100 K), one of the best performances among metal organic frameworks, with a relative thermal sensitivity of 2.85 %·K^{-1}, at 14 K. The material presents itself in the form of nanoparticles, suitable for nanothermometry applications (*e.g.,* microfluidics). Moreover, as MIL-103 is nanoporous its use as a multisensing platformdeserves further consideration in the near future. This work adds to the mounting evidence that metal organic frameworks bearing trivalent lanthanides present considerable potential in nanothermometry and, indeed, as multisensing platforms since they combine light emission and nanoporosity.

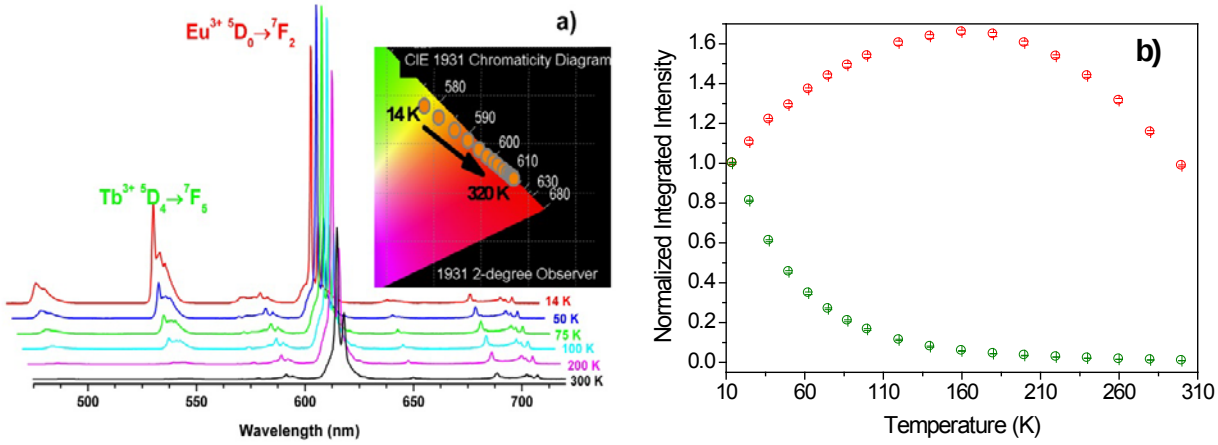

Figure 1: a) Emission spectra (excited at 340 nm) of MIL-103($Tb_{0.95}$,$Eu_{0.05}$) in the 14-300 K range; b) Dependence of the corresponding integrated intensities of the $Tb^{3+5}D_4\rightarrow{}^7F_5$ (green) and $Eu^{3+5}D_0\rightarrow{}^7F_2$(red) emission transitions.The areas were computed by integrating numerically the emission spectra in the 537-570 nm and 600-635 nm ranges, respectively. The corresponding errors result from the maximum difference between the integrated areas computed when the integration limits of each transition is increased or decreased by 1 nm. The maximum relative errors are 0.7% ($^5D_0\rightarrow{}^7F_2$, at 25 K) and 8% ($^5D_4\rightarrow{}^7F_5$ at 280 K).

Acknowledgements: Work financed by national funds through Fundação para a Ciência e a Tecnologia (FCT), [project CICECO, reference number FCT UID/CTM/50011/2013 and potdoctoral Grant to D. A. (SFRH/BPD/95032/2013)], and when applicable co-financed by the Fundo Europeu de Desenvolvimento Regional (FEDER) under the PT2020 Partnership Agreement.

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Bio-based polyols for more ecological adhesive formulation

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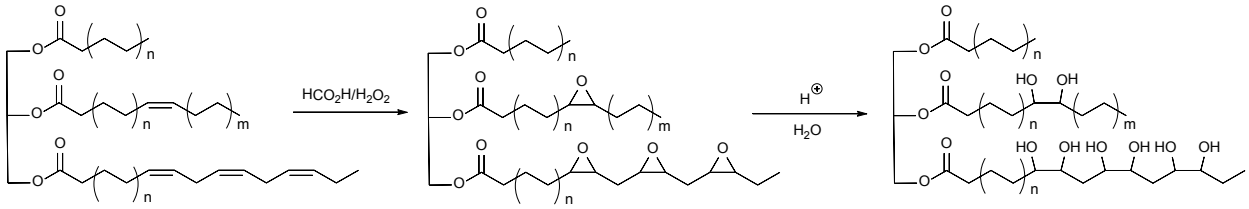
Vegetable oils are an abundant, renewable, and alternative feedstock for polymeric materials. They are constituted by triglycerides and different fatty acids that have carbon-carbon double bonds and carboxyl groups/ester linkages, which can be converted to hydroxyl groups (bio-based polyols). Because of their high versatility, polyols from vegetable oils and their derivatives have been used to produce various polyuretane materials such as foams, elastomers, rigid plastics, and coatings, which have shown properties mostly comparable to those of their petroleum-based analogs. Epoxidation has been one of the most commonly used methods for the functionalization of carbon-carbon double bonds. Polyols are produced from epoxidized vegetable oil by oxirane ring-opening reactions.[1] The main goal of this work is to produce bio-based polyols starting from waste cooking oils in order to obtain a more ecological adhesive formulation. The conversion of triglyceride double bonds to epoxide rings followed by their conversion to the hydroxyl groups occurs in a single step. Epoxidation is carried out by performic acid generated *in situ* with formic acid/hydrogen peroxide and ring opening by water in acidic media (**Scheme 1**).



Scheme 1: Triglycerides epoxidation and ring-opening reactions.

The products obtained are characterized by proton NMR, FT-IR spectroscopy[2], refractive index, acid number and OH number measurement. These polyols can be used to react with isocyanates by polyaddition to obtain more ecological polyurethane-based adhesives.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support.

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Molecular Trends in Surfactant-Assisted Exfoliation and Functionalization of Carbon Nanotubes

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The high aspect ratio and strong van der Waals cohesive forces (~40 $kT{\cdot}nm^{-1}$) of carbon nanotubes (CNTs) results in tightly agglomerated, bundled powders. Surfactants have been used as non-covalent exfoliants and dispersants of pristine CNTs in water, but a fundamental understanding of the dispersing mechanism is still lacking.[1] Well-controlled, systematic dispersing methods and reliable comparative metrics are warranted. This could greatly influence optimization of dispersions and future applications. Herein, we have investigated the ability of several ionic surfactants to exfoliate and disperse single and multiwalled CNTs, resorting to a stringently controlled sonication-centrifugation method. In order to quantify CNT concentration, combined TGA and UV−vis spectroscopy were used. Different single-tailed and double-tailed gemini surfactants, covering a wide range of molecular properties, were studied.[2-4] The dispersibility curves obtained permitted the definition and comparison of several metrics. In turn, this allowed us to assess and rationalize the effect of different molecular properties (aromatic rings, chain length, headgroup charge, *cmc,* covalent spacer length) on the dispersing performance (*viz.* effectiveness and efficiency) of the surfactant.

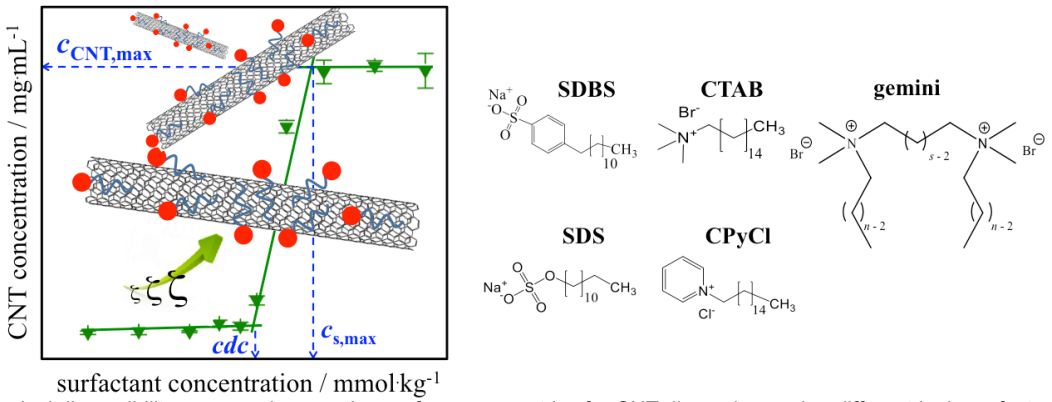

Figure 1: Typical dispersibility curve and respective performance metrics for CNT dispersions using different ionic surfactants.

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Light-Driven Hydrogen Generation Using Hybrids of Porphyrins and Graphitic Carbon Nitride

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Civilization is dependent upon fossil fuels, a non-renewable energy source originally provided by the storage of solar energy. There is an urgent need to develop new materials and renewable energy technologies to alleviate this issue. These technologies should be inexpensive, sustainable and green, using mainly materials or energy sources that are abundant, thereby eliminating secondary pollution production. In this regard, artificial photosynthesis via solar-driven water splitting[1] is of interest for producing clean fuels such as hydrogen (H_2). Considerable effort has been devoted to the development of stable and visible light active photocatalyst semiconductors for H_2 evolution based on the principles of natural photosynthesis.[1] However, the conversion efficiency of the current materials is still low due to weak light absorption ability, rapid recombination of electron-hole charge-carriers and low stability.[1] Due to its features, porphyrin/carbon based functional materials (g-C_3N_4, graphene, carbon nanotubes)[2] linked by covalently or non-covalently approaches are excellent candidates to overcome these shortcomings.

Inspired by the structure of the biological chlorophyll dye, in this study we present the preparation, characterization and photocatalytic application of g-C_3N_4 sensitized with porphyrins for H_2 production. The *free meso*-tetrakis(*meta*-carboxyphenyl)porphyrin (*m*-TCPP) and its Zn(II) complex (Zn-*m*-TCPP) were assembled on g-C_3N_4 by a non-covalent approach and were characterized by several spectroscopic techniques. De-aerated aqueous solutions containing the *as*-prepared hybrid materials, a sacrificial electron donor and Pt as co-catalyst were tested towards H_2 production by irradiation with UV-vis light. The efficient sensitization of g-C_3N_4 with *m*-TCPP and Zn-*m*-TCPP porphyrins was evidenced by UV-vis, infrared and X-ray diffraction analysis. The activity of H_2 evolved over both hybrid materials (Zn-*m*-TCPP/g-C_3N_4 and *m*-TCPP/g-C_3N_4) is significantly higher than that of pure g-C_3N_4. This demonstrates that the assembly between porphyrin and g-C_3N_4 has an important influence on the photocatalytic activity of the g-C_3N_4, besides improving its light absorption.[3] Furthermore, a higher production of H_2 was achieved with the Zn-*m*-TCPP/CN hybrid (272 μmol, 6 h) in comparison to *m*-TCPP/CN (202 μmol, 6 h). Our work shows that the interaction between the porphyrins and the g-C_3N_4 within the hybrid improves the electron transfer efficiency, enhancing the lifetime of the electron-holes pairs at the semiconductor dye interface, contributing therefore for a higher photocatalytic activity of the material, overcoming the limitations of pure g-C_3N_4.

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Multifunctional Lamellar Coordination Polymer

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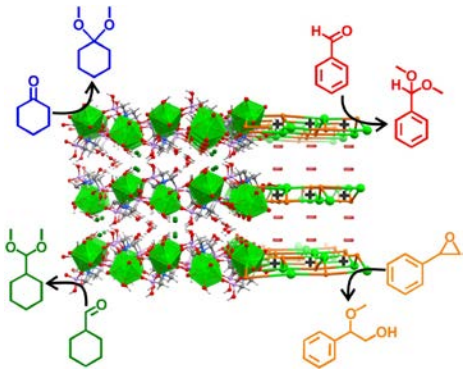
Research on Metal-Organic Frameworks (MOFs), and Coordination Polymers (CPs), is currently driven by the need to employ such materials in important technological areas for society by taking advantage of the high versatility of these networks.[1] Over the last few years our research group has been focusing on the design of novel networks based on polyphosphonic acid ligands and rare-earth cations. This combination of building units, particularly the use of phosphonic chelating units, has been found to induce the formation of highly robust dense networks, some of which exhibit true multifunctionality (*e.g.*, photoluminescence combined with catalytic activity). In this report we describe our most recent efforts to design and prepare the novel crystalline layered MOF $[Gd(H_4nmp)(H_2O)_2]Cl{\cdot}2H_2O$ (**1**) [where H_6nmp stands for nitrilotris(methylenephosphonic acid); see scheme 1]. This material is a heterogeneous and versatile catalyst, exhibiting remarkable activity in four different reactions: alcoholysis of styrene oxide, acetalisation of benzaldehyde, ketalisation of cyclohexanone and, tested for the first time, in the acetalisation reaction of cyclohexanaldehyde. For all reactions, the reported material surpassed or, at least, equalled the catalytic results reported for other related materials studied in the literature. Besides Brönsted acid properties, this new material possesses interesting proton conduction properties. At near ambient temperature and high relative humidity, the measured conductivities of the as-prepared material reaches 1.23×10^{-5} Scm^{-1}.[2]



Scheme 1: $[Gd(H_4nmp)(H_2O)_2]Cl{\cdot}2H_2O$ (**1**) used as heterogeneous catalyst in four distinct reations.

Acknowledgements: We thank Fundação para a Ciência e a Tecnologia (FCT, Portugal), the European Union, QREN through *Programa Operacional Factores de Competitividade* (COMPETE), and CICECO-Aveiro Institute of Materials, POCI-01-0145-FEDER-007679 (FCT Ref. UID/CTM/50011/2013), financed by national funds through the FCT/MEC and co-financed by FEDER under the PT2020 Partnership Agreement. FCT is also gratefully acknowledged for the Ph.D. grants Nos. SFRH/BD/84231/2012 and SFRH/BD/46601/2008 (to RFM and PS, respectively), the post-doctoral grants Nos. SFRH/BPD/89068/2012 and SFRH/BPD/96665/2013 (to MMA and PB, respectively), and the Development grant No. IF/01174/2013 (to FF).

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Simple and solvent-free synthesis of vanadium oxide composites and their catalytic application towards oxidation of benzoin

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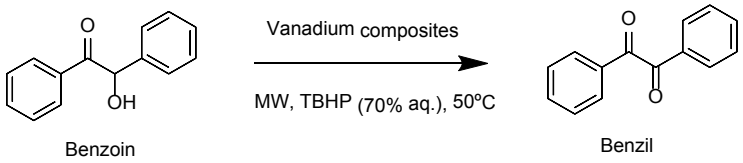
Oxidation of benzoin to benzil has been widely studied for the production of fine chemicals[1]. In general *α*-dicarbonyl compounds are important synthetic intermediates in the synthesis of many heterocyclic compounds. Benzil, in particular, is a standard building block in organic synthesis and is utilized as an intermediate in the synthesis of chiral ligands and biologically active compounds.
The oxidative transformation of an *α*-hydroxy ketone (benzoin) to the corresponding *α*-diketone (benzil) has been accomplished by the use of a wide variety of reagents or catalysts and different reaction procedures. However, in spite of their potential utility, some of the reported methods suffer from drawbacks such as long reaction time, low yields, expensive catalysts, harsh conditions or complexity of workup.
In this work we prepared vanadium containing composites with different ratios of additives (TiO_2, Al_2O_3 or SiO_2) by a simple and solvent-free mechanochemical method, *i.e.*, ball-milling [2,3]. The thus prepared composites materials were characterized by XPS, SEM, FEGSEM, EDX and TEM microscopy techniques and were screened for the microwave-assisted peroxidative oxidation of benzoin to benzyl with TBHP. The effects of time, solvent, temperature and amount of catalyst were optimized to obtain maximum yield. The catalytic activity results demonstrate that these catalytic systems are both highly active and selective for the oxidation of benzoin under mild reaction conditions.



Benzoin Benzil

Scheme 1 - Microwave-assisted peroxidative oxidation (TBHP) of benzoin into benzil

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia (fellowship SFRH/BPD/90883/2012 to A.P.C.R. and the UID/QUI/00100/2013 and PTDC/QEQ-QIN/3967/2014 projects) and the Instituto Politécnico de Lisboa (IPL/2016/MechSynCat_ISEL project) for financial support.

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Charge transfer salts of Dissymmetrical TTF donor with Cyano Coordinating Groups

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The chemical modification of the electron donor tetrathiafulvalene (TTF) has been extensively explored in search for new building blocks suitable for electroactive molecular materials namely organic conductors and superconductores. In our group we recently focused our interest on TTF-derivatives, with cyano units which can be used to coordinate transition metals by N atoms and to form in the solid state segregated and partially oxidized structures.[1]
In this context we have synthesized a new dissymmetrical TTF derivative cyanobenzene-ethylenedithio-tetrathiafulvalene (*4*CNB-EDT-TTF) (**Figure 1**) and prepared by electrocrystallisation and by direct oxidation charge transfer salts with some small anions X= ClO_4^-, I_3^-, affording charge transfer salts with composition (*4*CNB-EDT-TTF)$_2$X at variance with the previously described donor isomer CNB-EDT-TTF which forms salts with stoichiometry 4:1.
This new donor and their charge transfer salts were characterized namely by single crystal X-ray diffraction, cyclic voltammetry, NMR, UV-visible and IR spectroscopic.

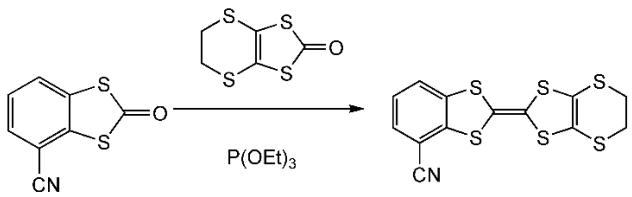

Figure 1: Synthesis of cyanobenzene-ethylenedithio-tetrathiafulvalene (*4*CNB-EDT-TTF).

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Trypsin goes nano! New nano-sized magnetic trypsin for ultra-high effective protein digestion

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Sample preparation in mass spectrometry (MS)-based proteomics is a crucial step for reliable protein identification and quantification in large-scale. A key step for proteomics analysis is the digestion of proteins to generate their peptides. This step can be performed with a wide array of proteases, being trypsin widely used because of its specificity and reproducibility.[1] One common bottleneck in MS analysis of tryptic-digested protein is the existence of peptides resulting from auto-digestion of trypsin, which often interfere with peptide detection. One easy way to overcome this issue is to immobilize trypsin into a solid surface. Immobilized trypsin is an excellent method for digesting a simple or complex proteome over a wide range of concentration, allowing an easy separation between trypsin and the digestion products eliminating trypsin interference in downstream MS analysis.[2] In this work we aim to develop a nano-magnetic immobilized trypsin system for unbiased and reproducible digestion of proteins for mass spectrometry-based proteomics (**Figure 1**). This new system is very exciting because of the large surface-area-to-volume ratio. Our nano-device has an iron core conferring a magnetic propriety to these particles allowing a quick and highly effective separation showing excellent results compared with other available immobilized trypsin.

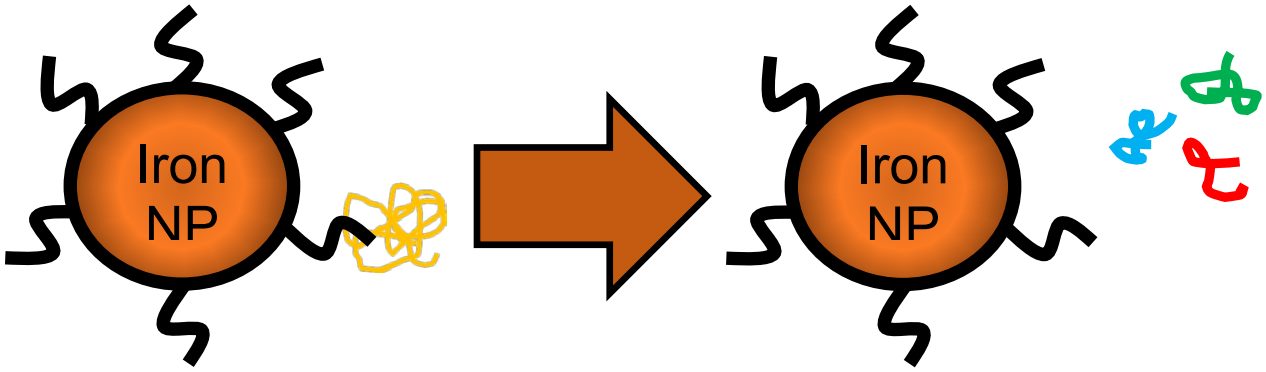

Figure 1: Iron Nanoparticle coated with immobilized trypsin

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Strategies for Thin Films of Hybrid Mesoporous Silica Nanoparticles

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Mesoporous Silica Nanoparticles (MSNs) are very promising structured materials because of their high pore volume and surface area, defined geometric mesostructure and functionalization versatility.[1] Due to their low density and high pore volume, MSNs could accommodate large quantities of conjugate polymers on the pore volume. Additionally, it is possible to incorporate electron acceptor molecules on the silica structure. This way, hybrid MSNs can be used as an ordered scaffold for donor acceptor pairs, providing new opportunities to the organization of the active layer layout in organic photovoltaics devices. The bottleneck of this new approach is the organization of the hybrid MSNs in thin films (below 150 nm).
Our goal is to develop a deposition strategy of hybrid MSN in different surfaces (glass, hydrophobic or hydrophilic) to obtain a homogeneous and compact layer. We tested different deposition techniques (dip coating, drop casting and spin coating) and tuned different parameters (solvent, nanoparticles concentrations and drying environment).
The dip coating and drop casting approaches have shown problems in homogeneity of the final layer, while spin coating exhibit good results in terms of thickness and homogeneity **(Figure 1)**.

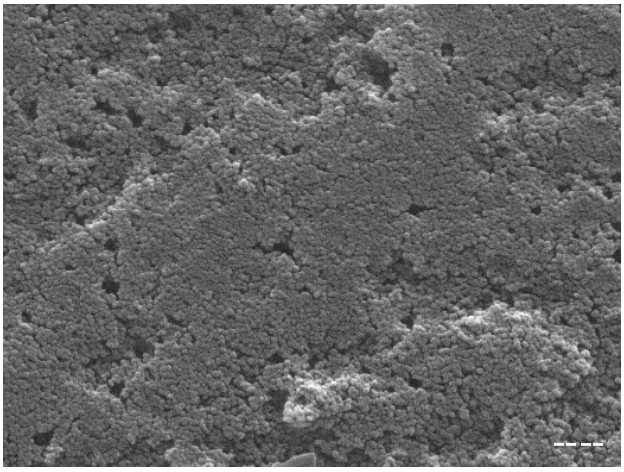

Figure 1: SEM image of hybrid MSNs spin coated onto a glass slide (scale bar: 400 nm).

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Alcohols as Molecular Probes in the study of Ionic Liquids

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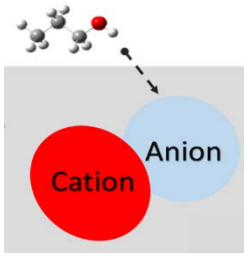
Ionic Liquids (ILs) are compounds composed by salts that are liquid close to room temperature and that have been attracting many attentions both in industry and academy due do their uncommon properties and the possibility to make functionalized ILs. Between the uncommon features of these compounds are its nanostructuration and the complex interplay between their intermolecular forces that explain their peculiar properties.
Alcohols are excellent molecular probes to study ILs as they have a hydroxyl group that can interact with the IL by dispersive or H-bonds interactions and the non-polar tail which can interact with the non-polar moieties of the IL. In a recent publication[1] concerning the use of alcohols as molecular probes to study ILs we demonstrate that the alcohols were preferentially located at the polar domain of the IL and where it was possible to highlight the nanostructuration effect.[1]
In the present work, further results will be presented concerning the effect of the anion, cation and the alcohol itself. Results of the enthalpies of solution/solvation of alcohols in ILs at infinite dilution obtained by Isothermal Titration Calorimetry (ITC) combined with a quantum chemical calculation study of the interaction of alcohols and IL anion in the gas phase will be presented (Fig. 1). Overall, the results allowed a better understanding of the interactions alcohol-IL and unravel the effect of the basicity/acidity in the hydrogen bond interactions.



ITC

Isothermal Titration Calorimetry

Solvation of Alcohols in

Ionic Liquids

Figure 1: Schematic representation of the effect under study Alcohols-ILs interaction.

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Heptagon-containing Nanographenes as a New Alternative to Graphene Quantum Dots

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Graphene quantum dots (GQDs) have been extensively investigated in recent years due to their exceptional optical properties that enabled applications in bioimaging, sensors, optoelectronic devices and nanomedicine. However, due to their uncontrolled synthetic procedures the final material is quite heterogeneous making it impossible to control its properties and engineering the material for specific applications. To overcome this limitation, we initiated the study of the photophysical properties of Polycyclic Aromatic Hydrocarbons (PAHs), also known as nanographene molecules, mimicking the structure of GQD. The step-by-step controlled synthetic procedure of these molecules leads to a homogenous material with well-defined molecular structure.[1] For a set of distorted nanographenes containing non-hexagonal rings on the edge, the effect of the nature of the edge groups, the distortion from planarity and the conjugation length on the photophysical properties were studied, with emphasis on the two-photon absorption and emission. Figure 1 illustrates the typical spectroscopic properties of one of the studied molecules showing a moderate TPA cross section (~ 500 GM).

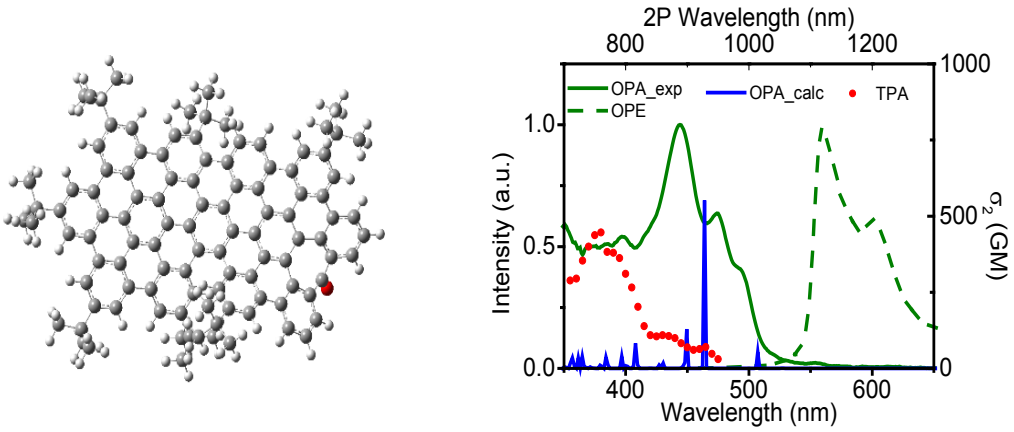

Figure 1: Experimental and calculated One-photon absorption (OPA), experimental Two-photon absorption (TPA) and One-photon emission (OPE) of the molecule represented on the left.

Acknowledgements: We acknowledge A. G.Campaña for providing the compounds. This work was partially supported by Fundação para a Ciência e a Tecnologia (FCT-Portugal) (IF/00759/2013 and post-doc grant SFRH/BPD/75782/2011) and COMPETE (FEDER), project UID/NAN/50024/2013.

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Eutectic Solvents: Expanding Chemical Profiles

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One of the major challenges in modern chemistry and chemical engineering is the formulation of new solvents, which simultaneously meet the Green Chemistry criteria and have the ability to dissolve as large as possible spectrum of solute[1]. Currently two major classes of solvents, ionic liquids (ILs) and eutectic mixtures (DES), are being largely developed and used by academia and industry, with new members being proposed at a fast pace. Regarding ILs, their commercial availability promoted the production of a large body of information concerning their thermophysical and transport properties, toxicity and phase equilibria, and consequently, new applications can now be properly evaluated. Conversely, eutectic mixtures, and in particular deep eutectic solvents, prepared from a salt or an ionic liquid combined with a neutral compound, are still in the infancy, lacking organization and properties systematization[2]. Inspired by this novel advanced class of green ILs, our group has studied a large number of eutectic mixtures from cheap, non-toxic, biodegradable compounds using cholinium chloride and a wide variety of naturally occurring organic acids and carbohydrates. However, these eutectic mixtures are all extremely hydrophylic in nature, hindering their easy and effective application in some processes where hydrophobic solvents are needed. The use of hydrophobic compounds from natural resources, such as L,D-menthol and and long chain organic acids as well as and cations/anions bearing long alkylic chains, and organic salts enabled the development of hydrophobic eutectic mixtures. It is very important to characterize these solvents from the point of view of their thermophysical and transport properties, and also their wáter afinity. Thermophysical properties of the prepared DES, such as densities, viscosities and conductivities, at atmospheric pressure and in a large range of temperatures and with variable water contents will be discussed. Polarity will also be evaluated through the use of solvatochromic probes. Water-eutetic mixtures mutual solubilities will also be presented and discussed.

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Microencapsulation of *Ammodaucus leucotrichus* essential oil using chitosan/ TPP/vanillin chemical system

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A. leucotrichus (Coss. & Dur.) Coss. & Dur., known in Algeria as “Kammûnes-sofi”, is a medicinal plant that finds culinary use by indigenous populations. Among others, it is used against stomach pain, indigestion, diarrhea, vomiting, fever, and to combat high blood pressure. In this work, the essential oil of *A. leucotrichus*, obtained by steam distillation (3h) from fruits collected in March 2015 from Tassili n'Ajjer, a vast plateau in south-east Algeria (25°30'0" N and 9°0'0" E), was chemically and biologically characterized and thereafter microencapsulated using a chitosan/TPP/vanillin system. Chemical characterization allowed the identification of ten constituents representing 98.6% of the whole essential oil composition. Oxygen-containing monoterpenes (87.2 %) were found to be the main group of components, followed by monoterpene hydrocarbons (11.1 %) and oxygen-containing sesquiterpenes (0.35 %). Perilla aldehyde was identified as the main component present in the essential oil accounting for 85.6 % of the total composition. Additionally, the oil presented antioxidant (EC_{50} 28±2 mg/ml, concentration able to scavenge 50% of DPPH radicals), anti-inflammatory (EC_{50} 11.7±0.7 µg/ml, concentration able to inhibit 50% of NO formation) and antimicrobial (against *Escherichia coli*: minimum inhibitory concentration (MIC) 10 mg/ml and minimum bactericidal concentration (MBC) 10 mg/ml; against *Staphylococcus aureus:* MIC 20 mg/ml and MBC 20 mg/ml) activities.*A. leucotrichus* essential oil microparticles were produced using an atomization/coagulation technique with chitosan as the shell material, sodium tripolyphosphaste (TPP) and vanillin as crosslinking agents. Comparatively to the most used chemical systems, this one presents several advantages since all the raw materials are nontoxic and no organic solvents are required. Moreover, the used microencapsulation process allows the microparticles production in a single step, without having the constrains of the traditionally used oil-in-water (o/w) emulsion based techniques. The adopted procedure comprises the following stages: (1) Chitosan solution (CS) preparation (3.0%, w/v) in acidic medium (acetic acid 3%, v/v); (2) Oil-in-water (o/w) emulsion preparation by emulsifying the essential oil (O) with the chitosan solution at O/CS ratio of 0.025 (v/v) with Tween 80 (emulsifier of HLB=15.0, 1.5%, w/v). The emulsion was homogenized at 11000 rpm during 5 min with a CAT Unidrive X homogenizer; (3) Atomization of the o/w emulsion in a Nisco VarJ30 system (flow rate: 0.3 ml/min) under pressurized nitrogen; (4) Coagulation with TPP (10%, w/v at pH 6.0) followed by vanillin crosslinking (1.0% (w/v), 50ºC at 0.5 ml/min during 2 h). Microparticles were recovered by filtration under reduced pressure, washed with distilled water and stored in the hydrated form.The produced microparticles were preliminary analyzed by optical microscopy (OM) using a Nikon eclipse 50i microscope to access size and morphology. This analysis showed the presence of spherical and individualized structures with an estimated particle size between 15 and 75 µm. Moreover, microparticles chemical structure was analyzed by FTIR, the thermal degradation was evaluated by TG and microparticle size distributions were measured by laser diffraction. The results shown the production of viable microparticles, indicating that the chitosan/ TPP/vanillin chemical system is a feasible alternative for a green *A. leucotrichus* essential oil encapsulation, when the atomization/coagulation technique is used. Moreover, taking into account the antimicrobial activity of *A. leucotrichus* essential oil, the produced microparticles can be a good alternative for cosmetic application as preservative.

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Photocatalytic activity of N,S-doped graphene-based multi-composite for the degradation of organic molecules

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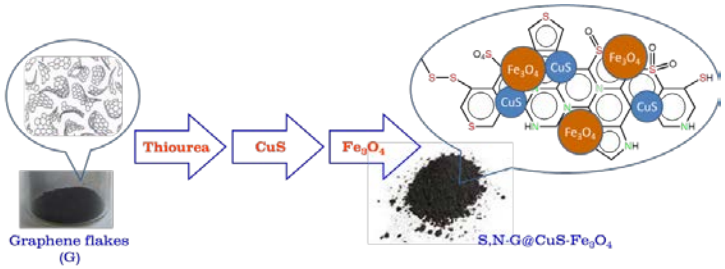
Photocatalytic processes, which make use of the energy of photons to propel useful chemical reactions, have attracted tremendous scientific and technological interest over the last 4 decades. More recently, the groundbreaking isolation of graphene has received significant attention as it shows many novel properties, which ascribed mainly to its unique electronic band structure. [1] Due to its highly tailorable nature, its surface properties can also be favourably adjusted through chemical modification, allowing its use as part of a composite material. The heteroatom doped graphene has been widely prepared and applied in different photocatalytic fields: water splitting, pollutant degradation and CO_2 reduction.[1, 2] Very recently, functionalized graphene-based semiconductor photocatalysts have attracted a lot of attention. [3]

Herein we presented the synthesis and characterization of N,S- dual doped graphene decorated with semiconductor nanoparticles namely copper(II) sulphide, CuS and manganese ferrite, Fe_3O_4 (Scheme 1). The N,S-dual doped graphene was prepared by solvent free ball milling, using thiourea as N and S heteroatoms source, followed by thermal treatment at 600°C. The CuS and Fe_3O_4 were immobilized into the dual-doped graphene flakes by in situ growth methods. The nanomaterials were characterised by FTIR spectroscopy, XPS, TEM and XRD. The results confirmed successful incorporation of the heteroatoms on the graphene structure, as well as the grafting of CuS and Fe_3O_4 nanoparticles. The hybrid nanomaterial was tested in the degradation of 4-Nitrophenol (4-NP) and Methyl Orange (MO) using UV-vis spectroscopy to monitor the reaction evolution; the 4-NP-P25 and MO-P25 systems (P-25, commercial TiO_2) was used to benchmark the prepared catalysts. Control reaction without photocatalyst was also performed.



Scheme 1: Preparation route of double doped graphene decorated with CuS and Fe_3O_4.

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Multivariate statistical analysis based on thermal and spectroscopic data for forensic discrimination of plastic bags

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The purpose of this investigation is to apply a combined approach of instrumental methods of analysis with multivariate statistical techniques for discrimination of plastic bags in forensic context.
A set of twenty-eight plastic bags obtained from seven different brands were analyzed in three random sites by differential scanning calorimetry, thermogravimetric analysis, polarized light microscopy, FTIR spectroscopy in attenuated total reflection mode and X-ray diffraction. Two methods of multivariate analysis were applied in order to explore and interpret the results: hierarchical clustering analysis (HCA) and principal component analysis (PCA). Before this step, a data matrix was constructed using all the results obtained through the methods mentioned above, and considering a large number of variables that characterize the samples. The complementarity of analytical and chemometric methods allowed to observe the presence of natural grouping structures among the set of samples and, consequently, discriminate apparently similar plastic bags, which have significant differences as a result of the manufacture process. [1-3] This statistical analysis was also applied in the investigation of blind samples, which were successfully identified and used to test and validate the statistical method.
This approach is very useful for applications in a forensic chemistry context, since plastic bags consist of a type of polymeric materials, and are often found in crime scenes. They can for example be used to hide the body of a victim or in other crime related purpose, such as packing illicit drugs to be sold in the consumer market. [1,2,4] In cases where illicit drugs are seized, it is important to correlate the seized plastic bags with unused bags, such as those found in the house of a suspect. Thus, it becomes useful to characterize these polymeric items for trace their source and obtain supplementary information that can help forensic investigations. [1,2]

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Photophysics of TADF emitters for bioimaging and sensing applications

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Thermally-activated delayed fluorescence (TADF) occurs in emitters where a triplet state and an excited singlet state lie close in energy, allowing reverse intersystem crossing (rISC) to occur.[1] Thus, TADF has gathered significant interest in the development of OLEDs as a tool to harvest energy from usually dark triplet states without the application of heavy-metal and rare earth complexes, which are expensive and pose toxicity problems.[1] In principle, TADF can be also used in fluorescence microscopy to overcome drawbacks associated with conventional fluorescent probes. With two distinct emission lifetimes (from prompt and delayed fluorescence), TADF emitters can improve the sensitivity of detection by rejecting auto-fluorescence and scattering on a time basis, using time-gated acquisition methods, and obtain ratiometric response, thus independent of concentration.[2,3]

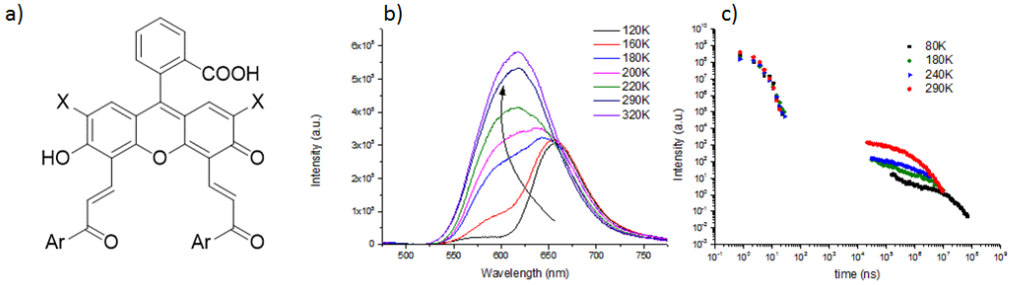

Figure 1. a) general chemical structure of the synthesized compounds; b) change in time resolved emission (delay time 1 ms) upon heating; c) time resolved luminescence decay at different temperatures. Emission collected in vacuum in solid polymeric films

Eosin and fluorescein analogs are water soluble emitters that have previously exhibited TADF emission with long wavelengths, thus being excellent candidates for TADF probes in time-gated fluorescence imaging.[3] Under this light, several fluorescein derivatives were synthesized and their photophysical properties were fully characterized using steady-state and time resolved emission spectroscopy, both in solution and solid state. The effect of chemical derivatization of key positions on the delayed fluorescence quantum yield is discussed and a quantitative structure-property relationship study is described.

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How to help find a needle in a haystack

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The number of scientific publications as well as the number of new compounds found or synthesized has increased significantly in recent years. According to Chemical Abstracts Service there are currently more than 100 million known substances of which 10 million were added in less than one year, corresponding to about 15,000 new substances in each day.[1,2] The experimental properties determination, however, could not set the same pace. Thus, it is crucial to develop methods to predict chemical, physical and when possible biological properties in a reliable way. In last 40 years, Chemoinformatics became a science in its own right making decisive contributions to the development of chemistry despite the fact that there are still many problems to be solved in the area of chemoinformatics.[3] In any case, the quality of the predicted data relies mainly on the size and quality of existing experimental databases. Therefore, it is of top importance to extract all the information available in the literature.
In this communication it is defined an identifier called "Chemical, Physical and Biological properties Identifier", or CPBI, with the structure shown in **Scheme 1**.

CPBI = Standard InChIKey/Property1,Attribute1,Attribute2,Attribute3,Attribute4(Value,Error)/Property2, ...

Scheme 1 – Structure of CPBI

The first part (in purple) is dedicated to the identification of the molecule. For that purpose the Standard InChIKey code, developed by IUPAC will be used.[4] The second part (in brown after the slash) is the acronym for the property, followed by the attributes that define the conditions for which the property was determined. Finally (in green inside parenthesis) the value and error determined for the property. As can be seen, a second or third property for the same compound can be easily added. A list of proposed codes and attributes for properties will be presented as well as some examples to show the advantages of using it. The definition of the identifier was published recently [5] and is also available in a dedicated webpage.[6]

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Synthesis of new acylsilanes

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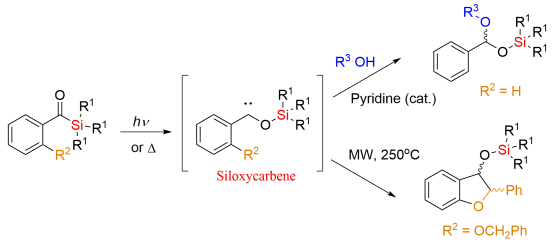
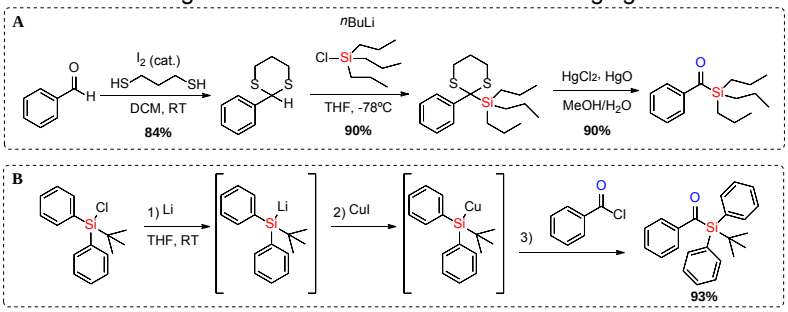
Acylsilanes are an interesting class of organosilanes due to their ability to form reactive siloxycarbenes (**Scheme 1**) after thermo[1] or photochemical conditions.[2] These carbenes have been studied in reactions with alcohols to form mixed acetals,[2] in intramolecular CH-insertion reactions[1] (**Scheme 1**) and other valuable transformations.[3] However, the synthesis of acylsilanes has been focused on carbon-bound silicon compounds, and the effect of silicon-heteroatom bounds in typical acylsilane chemistry has not been investigated so far.



Scheme 1: Examples of siloxycarbene reactions: OH-insertion on alcohols[2] (top) and intramolecular CH-insertion[4] (bottom).

In this work we set out to synthetize new acylsilane with different substituents at the silicon atom. The known dithiane umpolung approach proved to be excellent for simple chlorosilanes such as chlorotripropyl silane (**Scheme 2, A**), but unsuitable for bulky chlorosilanes and for trialkoxide-chlorosilanes, which are needed for the synthesis of desired oxygen-silicon bound acylsilanes. For bulkier silanes, a different methodology involving the lithiation of chlorosilanes was successfully applied (**Scheme 2, B**). However, this methodology is limited by the requirement of an anion-stabilizing phenyl group in the initial chlorosilane, which again restricts the synthesis of acylsilanes with heteroatoms bound to silicon. More studies are being conducted as to obtain these challenging molecules.



Scheme 2: Explored synthetic methodologies for acylsilanes: dithiane umplong substitution (A) and lithiation of chloroslanes (B).

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Crystallographic, thermodynamic and spectroscopic characterization of glibenclamide:tromethamine 1:1 cocrystal synthesized by slow evaporation

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The pharmaceutical industry has been increasingly interested in the search for new cocrystals in the last years as a strategy for enhancement of physico-chemical properties and therapeutical performance of APIs. The synthesis of cocrystals is regarded as a very promising strategy for increasing chemical stability, solubility, dissolution rate and thus bioavailability for active pharmaceutical ingredients (API). A cocrystal can be defined as a crystalline form of a mixture of different molecules, in the simplest form two compounds, an API and a coformer, that are solid at ambient conditions when isolated, and, when mixed at a perfect stoichiometric ratio, form noncovalent bonds. The new crystalline structure is characterized by a crystallographic pattern different from that of the original compounds and presents a thermodynamic behavior of a pure substance.

A cocrystal of glibenclamide (GLB) has been synthesized using tromethamine (TRIS) as coformer in 1:1 molar ratio, by slow solvent evaporation cocrystalization. Glibenclamide (GLB),(5-chloro-N-[2-[4-(cyclohexylcarbamoylsulfamoyl) phenyl] ethyl]-2-methoxybenzamide), is an antidiabetic drug used for the control of glicemia in Type 2 diabetis patients. It is classified as a type II compound according to the Biopharmaceutics Classification System showing low solubility (<0,004 mg mL^{-1} at 37°C and neutral pH), and high membrane permeability. The low solubility is an undesired property, influencing the dissolution profile and consequently the bioavailability.

The characterization of the synthesized product was done resorting to X-ray powder diffraction (XRPD), differential scanning calorimetry (DSC), mid infrared (MIR), near-infrared (NIR) and Raman spectroscopy. The formation of a cocrystal between the API and coformer is consistently observed by the different techniques. The cocrystal is formed through synthons based on the hydrogen bonding between hydrogen in amines of tromethamine and carbonyl and sulfonyl groups of glibenclamide.

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Direct transformation of fructose to 5,5'(oxy-bis (methylene))bis-2-furfural (OBMF) or diformylfuran (DFF) using Preyssler heteropolyacids

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5,5'(oxy-bis (methylene))bis-2-furfural (OBMF) could serve as monomer for further copolymerization reactions. However, the conventional synthesis of OBMF by etherification of 5-HMF involves elevated temperatures (≥373 K), anhydrous conditions, long reaction times, and homogeneous catalysts. Although OBMF can also be synthesized using acid solids from 5-hydroxymethylfurfural. [1] The production of OBMF is directly related to the presence of Brönsted acid sites and the elimination of water, so our research group using Preyssler heteropolyacids (HPA´s) obtained a yield of 84 % to OBMF at 5 h and 343 K.[2] These solids have attracted special attention due to their low toxicity, high thermal and hydrolytic stability throughout a wide pH range (0-12), strong Brönsted acidity (14 H^+), low corrosiveness, and high oxidation potential.[3] Although, 5-HMF is a good candidate to obtain OBMF its commercial availability is yet not reached. For this reason, it is necessary to search other alternatives sources of minor cost. Thus, the transformation of fructose to OBMF in a one pot is hot topic to produce new biomass derived monomers via efficient catalytic routes. In this work, we demonstrated that the reaction of fructose using Preyssler heteropolyacids (HPA´s) can be conducted to OBMF or 2,5-diformyl furane (DFF). At 2 h of reaction the fructose is fully converted to 5-HMF which is posteriorly transformed to OBMF or DFF. A yield of 20% at OBMF and 50% at DFF was obtained at ratio of 1:1 or 1:3 of DMSO:CH_2Cl_2. However, ratios 3:1 and 3:0 of DMSO:CH_2Cl_2 the reaction stops with preferential formation of 5-HMF and DFF. The blank experiments produce OBMF or DFF with yield minors to 10 %. When the reaction was conducted in inert atmosphere the yields at OBMF decreases, hovewer, it seems be that an oxidant atmosphere improves the yield to OBMF (17%) in 4 h the reaction after fructose is fully converted to 5-HMF, also is observated a yield fo 34% to OBMF from the 5-HMF. Further studies is being essayed to determine the effect of oxygen atmosphere to improving the production of OBMF from fructose. The figure 1 displays the progress of reaction in the fructose transformation to DFF and OBMF using DMSO:CH_2Cl_2, 1:1.

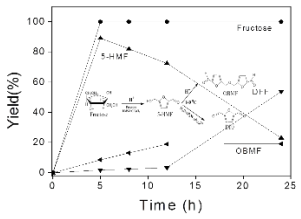

Figure 1. Effect of reaction time on the transformation the furctose using Preyssler heteropolyacids.

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Mesoporous Silica Nanoparticles with pH-responsive Polymeric Shell for Controlled Drug Release

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Recent progress in material chemistry and drug delivery led to the possibility to develop stimuli-responsive devices that deliver a drug with spatial, temporal and dosage control. Implementation of such devices requires the use of biocompatible materials that are susceptible to specific physical stimuli. Nanoparticles have received much attention precisely because they comprise these characteristics. In addition to improving the pharmacokinetics of the loaded poorly soluble hydrophobic drugs by solubilizing them in the hydrophobic compartments, coated with stimuli-responsive polymers, nanoparticles allow the control of drug release in response to disease-specific physiological conditions.[1] Among a variety of inorganic-based nanomaterials, mesoporous silica particles (MSNs) have several attractive features for application as a drug delivery system due to their high surface areas, large pore volumes, high payload, uniform and tunable pore sizes, and a great diversity of surface functionalization options **(Figure 1)**.[2] In this work, we developed core-shell MSNs, coated with a pH-responsive polymer. In addition, by incorporating a high quantum yield fluorescent perylenediimide (PDI) dye in the MSNs pore structure, we could combine diagnostic and therapeutic properties.

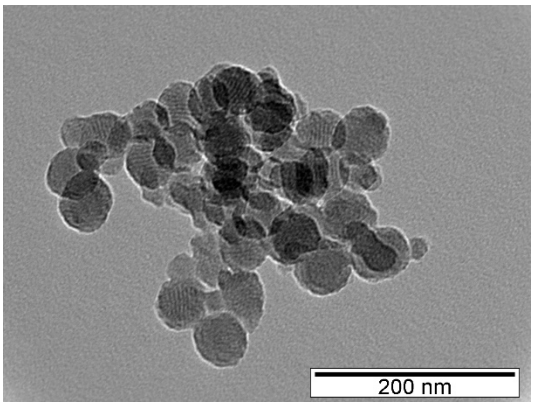

Figure 1: Transmission electron microscope image of MSN-PDI showing morphology and mesostructure. Scale bar: 200 nm.

Acknowledgements**:** This work was partially supported by Fundação para a Ciência e a Tecnologia (FCT-Portugal) and COMPETE (FEDER), UID/NAN/50024/2013 and PTDC/CTM-POL/3698/2014

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Aiming at cancer: Structural and spectroscopic studies of new metalloporphyrins and metallochlorins.

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Chlorins and metallochlorins with high absorption spectra in the visible region and strong fluorescence properties, are excellent chromophores to be applied in the construction of optical sensors for monitoring harmful species, as well as in the treatment of cancer through, for example, photodynamic therapy (PDT).[1] With this in mind, pyrrolidine-fused *meso*-tetraarylchlorin was synthesized via 1,3-dipolar cycloaddition (1,3-DC) of 5-(4-carbomethoxyphenyl)-10,15,20-(pentafluorophenyl)porphyrin with azomethine ylide,[2] followed by hydrolysis in HCl/TFA. Iron, copper, zinc and platinum metal ions were efficiently inserted into the porphyrin and chlorin N4 core with metal chloride and acetate salts by using microwave irradiation. The absorption and emission properties of both metalloporphyrin and metallochlorins' families will be presented as well as the study of the different Cu(II) complexes by EPR spectroscopy. Structural elucidation of possible dimers or trimers were also studied by MALDI-TOF and ESI mass spectrometry.

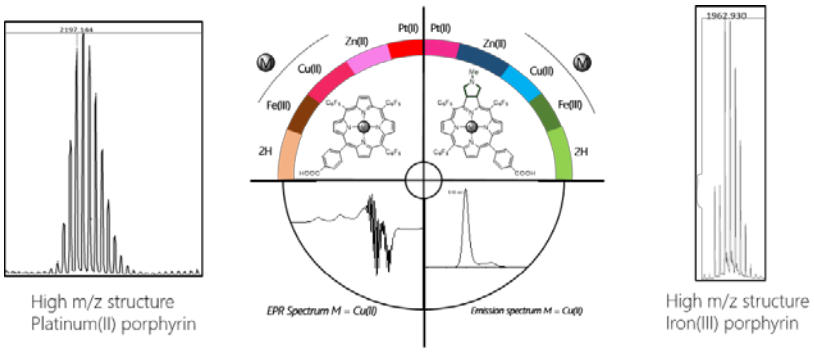

Figure 1: Left: zoom in of a MALDI-TOF spectrum of platinum(II) porphyrin. Center: porphyrin crosshair depicting the different colors of porphyrins, chlorins, metalloporphyrins and metallochlorins synthesized; emission spectrum of copper(II) chlorin and EPR spectrum of copper(II) porphyrin. Right: zoom in of a MALDI-TOF spectrum of iron(III) porphyrin.

Acknowledgements: This work was supported by FCT (Fundação para a Ciência e a Tecnologia, Portugal) through financial support to UID/QUI/50006/2013-POCI/01/0145/FEDER/007265 (LAQV/REQUIMTE), and M-ERA-NET/0005/2014. A.L. also thanks her SFRH/BPD/85793/2012 FCT grant. The authors gratefully acknowledge the COST action CM1302 (SIPs).

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Plasmonic office paper as an alternative cost effective platform for trace analyte detection by Surface Enhanced Raman Spectroscopy

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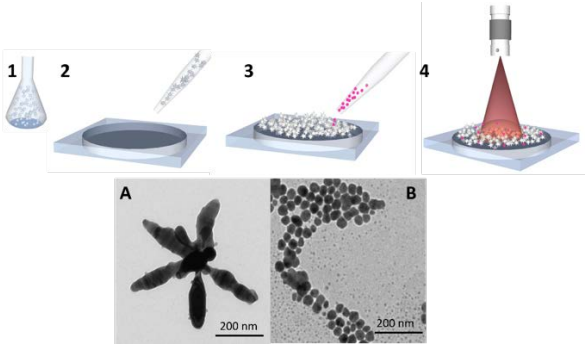
Surface Enhanced Raman Spectroscopy (SERS) is a highly sensitive analytical technique, based on light scattering by analytes near plasmonic nanostructures. For analytical applications in portable sensors to be used in the point-of-need, low-cost SERS substrates using paper as a base, are an alternative. In this work, SERS substrates were produced on two different types of paper: a high porosity paper (filter paper); and a low porosity paper (office paper). Solutions containing spherical silver nanoparticles (AgNPs) and silver nanostars (AgNSs) were separately drop-casted on hydrophilic wells patterned on the papers. The porosity of the paper was found to play a determinant role on the AgNP and AgNS distribution along the paper fibres, with most of the nanoparticles being retained at the illuminated surface of the office paper substrate. Both papers treated with NPs showed no paper-derived fluorescence. A limit of detection for rhodamine-6G as low as 11.4±0.2pg could be achieved, with an analytical enhancement factor of ≈10^7 on the office paper substrate with deposition of AgNS. The well patterning technique allowed a good uniformity of signal inside the wells, and a good reproducibility when different AgNSs synthesis batches were tested (RSD of 1.7%). Besides, these SERS substrates remained highly stable after 5 weeks of storage (RSD of 7.3%) without any type of encapsulation/protection. Also, paper-induced aggregation of AgNPs was found to be a viable alternative to the classical salt-induced aggregation, to obtain in a simple manner a highly sensitive SERS-active substrate.[1]



Acknowledgements: This work is funded by the FCT-MCTES (Portuguese Foundation for Science and Technology) under project DISERTOX, number PTDC/CTM-NAN/2912/2014 and CENIMAT/i3N by FEDER funds through the COMPETE 2020 Programme and National Funds through FCT under project number POCI-01-0145-FEDER-007688, Ref. UID/CTM/50025/2013. Unidade de Ciências Biomoleculares Aplicadas-UCIBIO was financed by Portuguese national funds from FCT/MEC (UID/Multi/04378/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007728) and UID/QUI/50006/2013-POCI/01/0145/FEDER/007265 (LAQV/REQUIMTE), Programa Operacional Regional do Norte (ON.2 - O Novo Norte), under the Quadro de Referência Estratégico Nacional (QREN) and funded by Fundo Europeu de Desenvolvimento Regional (Feder) NORTE-01-0145-FEDER-000024 and NORTE-01-0145-FEDER-000011. A Araújo and M. Almeida were funded by FCT-MCTES through grants SFRH/BD/85587/2012 and SFRH/BD/95983/2013, respectively, in program POCH.

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Molecular modeling of the intercalation of functional molecules into layered double hydroxides

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Layered double hydroxides (LDHs) have general formula $[M^{2+}_{1-x}M^{3+}_{x}(OH)_2]^{x+}$ $(A^{n-}_{x/n})\cdot mH_2O$, where M^{2+}/M^{3+} are di-/trivalent cations and A^{n-} is an anion. Through different synthetic routes it is possible to obtain a large number of tailored compositions with desirable physico-chemical properties. Their positively-charged layers are relatively weakly bonded to the charge-balancing anions in the interlayer region, which allow them to intercalate different functional molecules in the anionic form. The latter can be delivered upon an external trigger and the process of anion release can be initiated by other anionic species in the surroundings. This intrinsic property of LDHs turns them interesting as potential nanocarriers for several applications. One application in which this property assumes a fundamental role is in corrosion protection. In fact, LDHs are able to entrap aggressive species, such as chlorides, and respond to different electrolyte conditions (concentration, pH). This makes them ideal macromolecular containers to be used as additives in self-healing coatings or as nanostructured conversion films formed on top of metallic alloys.
In the framework of project SELMA, we have been performing classical molecular dynamics and quantum density functional theory simulations to interpret different experimental (structural, microscopic and/or electrochemical) results, which made possible to understand the interface between LDHs' conversion films and the metal and the formation of corrosion inhibitors' protective films after their release from LDHs. For the first time, molecular modelling has been used to i) unveil the relation between structure and morphology of nanostructured conversion films based on layered double hydroxides,[1] to propose the mechanisms of formation of the protective films on metal surfaces,[2] and to understand the stability of corrosion inhibitors into LDHs.

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Application of Proteins for organocatalysis

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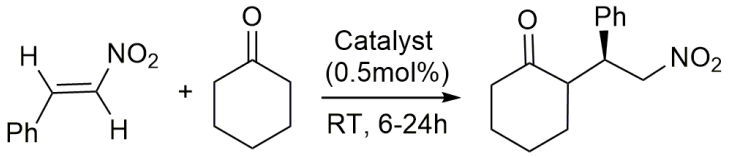
Proteins are large biomolecules consisting of one or more long chains of amino acid residues. Proteins perform an enormous range of functions within organisms, including catalyzing metabolic reactions, DNA replication, responding to stimuli, and transporting molecules from one location to another[1]. The production and applications of proteins have rapidly grown up in different fields such as biochemical research, chemical, food and pharmaceutical industries[2].
Many laboratories have explored simple organic molecules, including simple amino acids and small peptides, as catalysts for organic reactions. It is important to focus the large spectra of application related to proline as efficient catalyst in different asymmetric organocatalytic reactions[3]. Efficient peptide based catalysts possess properties that are difficult to achieve with other catalysts, such as high yields and enantioselectivities. Over the past decade several functionalized peptides have been reported as effective asymmetric catalysts for a range of synthetically useful reactions: acylation, oxidation, ester hydrolysis, aldol reactions, among others[4,5].
Lately, ionic liquids (ILs) have successfully emerged as a great solvent media for enzymatic reactions[6] and other protein based applications. These ILs are organic salts consisting of poorly coordinated ions, due to which they remain in liquid form at temperatures lower than 100°C or even at room temperature (RTILs)[7]. The physical-chemical properties of ILs can be changed according suitable cation-anion combinations. Although, ionic liquids can stabilize the proteins over a wide range of temperatures and the structure of cation and/or anion from IL.
Since the Michael addition of ketone (Michael donor) to nitroalkenes (Michael acceptor) catalyzed by L-proline upraised, many research groups have been concentrated on development of more efficient and selective catalytic systems using CILs derived from natural acids for this functional transformation (**Scheme 1**)[8]. Asymmetric C–C bond formation reactions with peptides are also well-described. Herein, we tested three different proteins (casein, albumin and lysozyme) as organocatalysts for the Michael addition between cyclohexanone to trans-nitrostyrene as model reaction. The preliminary studies proved that it is possible to obtain the desired pure Michael product in moderate to high conversions. The asymmetric version has been also tested to evaluate the potential of this innovative approach.



Scheme 1: Michael Addition of cyclohexanone to trans-nitrostyrene using proteins as catalysts

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (IF/0041/2013/CP1161/CT005) and Solchemar Company.

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Structurally colored photonic pigments by soft lithography droplet microfluidics technology

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Colloidal photonic crystals (PCs) are receiving increased attention due to the fundamental aspects of their formation, their numerous applications (*e.g.,* as waveguides and light manipulators in optoelectronic, photovoltaics and sensoric applications), and also because of their artistic beautiful colors. Their shining structural coloration arises from the modulation of the electromagnetic waves by means of Bragg reflection from photonic band gaps (PBG). The PBGs are due to repeating regions of low and high dielectric constants obtained by the periodical arrangement of nanoparticles that is used to control the propagation of light.[1]

In this work our aim is to develop uniformly sized colloidal spherical assemblies that exhibit structural coloration throughout the visible spectrum light range. To this end we synthesized differently sized colloidal building blocks by emulsion polymerization. The polymeric nanoparticles are composed of a hard core made of cross-linked polystyrene and a soft shell composed of poly(methyl methacrylate-co-acrylic acid) (P(St-MMA-AA)) in a size range from ≈ 100 to 300 nm with very low polydispersity.

To obtain photonic pigments within the spherical confinement of emulsion droplets, we used a bottom-up approach, where the self-assembly of colloidal nanoparticles is controlled by means of microdroplet W/O and W/O/W emulsification in PDMS microfluidic devices. Microfluidic devices were fabricated via conventional soft lithographic techniques. The microchannel architecture was transferred to high resolution aluminum masks and the master mold was fabricated using the negative photoresist SU-8, from which we developed 50 µm height PDMS microchannels.[2] Different sized emulsion droplets can be obtained by adjusting the flow rates of the continuous and dispersed phases. After water evaporation from the emulsion droplets, different photonic pigments can be obtained by using differently sized polymeric nanoparticles.

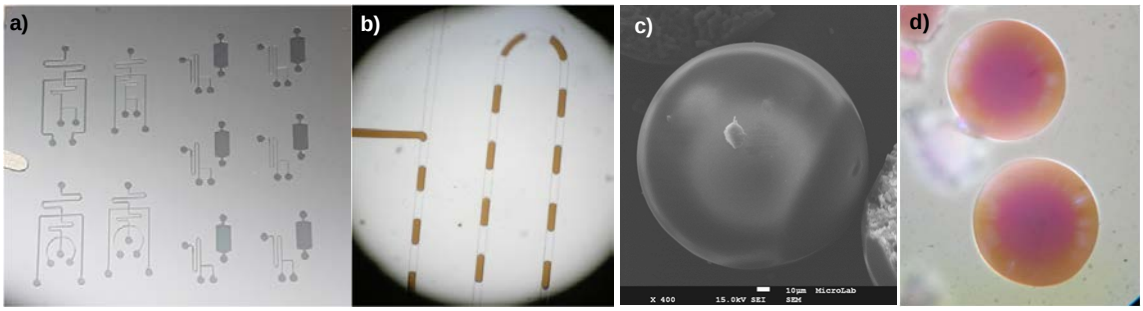

Figure 1: a) Photograph of the SU-8 hard mask; b) Emulsification process for droplet formation inside the PDMS circuits; c) SEM image of a microsphere after water removal and assembling of the polymeric nanoparticles; d) Pink-Orange color displayed by a macrosphere composed of 270 nm polymeric nanoparticles under optical microscope (10x objective).

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Deep Eutectic Solvents and Functional Ionic Liquids for Material Science

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In last years, different functional ionic liquids (ILs) for application in several research topics have been reported[1]. Recently, Deep Eutectic Solvents (DES) as Ionic Liquid analogues have attracted much attention due to the possibility to use as greener alternative solvents as well as promising functional materials. DES can be formed from eutectic mixtures between Lewis and Brønsted acids and bases and it can be comprised by a variety of anionic and/or cationic species[2].

Herein, sustainable approaches for application in Material Science is described:

a) ***Task-Specific ILs seems to be the most suitable lubricant oils for micro and nanoelectromechanical systems (MEMS/NEMS)*** which are miniaturized silicon based devices. ILs containing sulfur based anions have an enhanced tribological performance on silicon surfaces comparing to other oils[3].

b) ***Multi-Stimuli Responsive Electrochromic Ionic Liquids*** based on symmetric and non-symmetric di- and tetra-substituted alkyl- and oxo-bipyridinium cations combined with different anions. The most promising electrochromic bipyridinium ILs have been tested as efficient liquid and solid state electrochromic devices using suitable electrolytes[4].

c) ***Application of Deep eutectic solvents (DES)*** based on choline chloride or lithium chloride with ethylene glycol, Polyethylene glycol and glycerol as low-cost, recyclable and green electrolytes for electrochromic devices[5]***.***

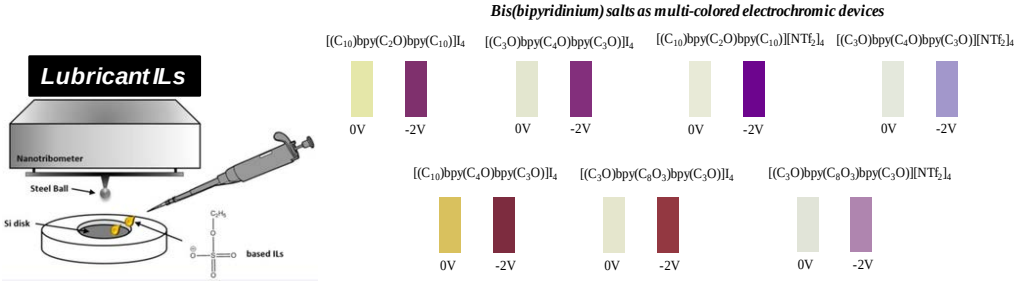

Figure 1: Examples of Lubricant ILs based on ethyl sulfate and bis(pyridinium) salts as multi-coloured elecvtrochromic devices

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Oxidative Catalytic Activity of Carbon Nanomaterials from Cork Industry Wastewater

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Carbon nanomaterials, in particular those with particle sizes of less than 10 nm, the so-called carbon dots (C-dots)[1], are gathering increasing attention in fluorescent bio-imaging and nanomedicine[2], sensory analysis[3] and as photocatalysts[4].
Herein, carbon nanomaterials produced from cork industry wastewater (**Figure 1**) are provided to design improved catalytic processes for selective oxidation reactions of industrial interest such as the oxidation of primary and secondary alcohols to, respectively, aldehydes and ketones (**Scheme 1**).

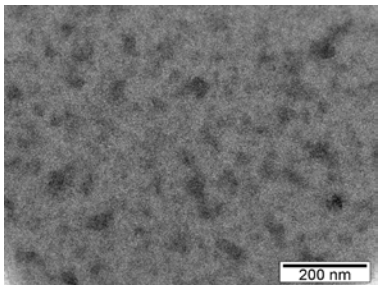
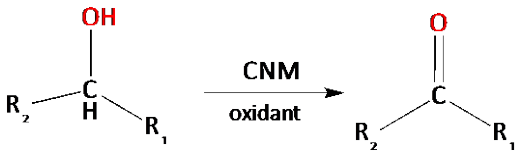


Figure 1: TEM image of a C-nanomaterial prepared from cork industry wastewater.



Scheme 1: Oxidation of alcohols to aldehydes or ketones catalysed by C-nanomaterials prepared from cork industry wastewater.

The activity of the prepared materials was tested in batch and the effects of reaction parameters, such as reaction time, temperature, type and amount of oxidant are reported and discussed.

Acknowledgements: Funding from Instituto Politécnico de Lisboa (IPL/2016/NANOXSUS_ISEL) and Fundação para a Ciência e a Tecnologia (PTDC/QEQ-ERQ/1648/2014 and UID/QUI/00100/2013 projects) are acknowledged.

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Zinc-derived materials for medical applications in orthopaedic implants

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Due to different factors, namely age, lifestyle and activity level, a number of problems can occur in human joints and bones, such as inflammatory diseases and degeneration. These problems affect millions of people, who may require surgery for treatment, which often involve permanent or temporary prostheses. Present orthopedic implants have several problems that include poor osseointegration, stress shielding and/or infections associated bone cell death. Additionally, numerous patients receive orthopedic implants as a result of bone cancer, however current orthopedic materials were not designed to prevent either the occurrence or reoccurrence of cancer. A promising candidate for designing orthopaedic implants will be zinc-derived materials. However, to succeed there is the need to produce topologically-ordered porous zinc-derived nanostructures with controlled porosity, surface chemistry, morphology and structure[1]. They are most frequently prepared by electrodeposition[2] and wet chemistry synthesis. Electrodeposition is a versatile, very-fast and low-cost technique for materials production. In particular, electrodeposition under intense hydrogen evolution, using the so called dynamic hydrogen bubble template (DHBT) has been the focus of an increasing number of papers, as described in a recent review paper[3]. In this study, zinc-derived materials were prepared under controlled electrodeposition conditions from zinc containing electrolytes under the dynamic hydrogen bubbling template. Scanning electron microscopy (SEM) with energy dispersive X-ray spectroscopy (EDS) capability and Raman spectroscopy were used for characterising the porosity, morphology and surface chemistry. With this study was possible to produce zinc-derived materials with different porosity ranges and morphologies such as dendrites and hexagonal crystals. Preliminary studies of biological testing of zinc-derived materials were very promising. It was found that zinc-derived materials can lead to preparation of materials with anti-cancer performance highly comparable to some of the best obtained by other workers[4] who studied novel anti-cancer orthopedic materials.

Acknowledgements: We would like to express our gratitude to the Fundação para a Ciência e Tecnologia (FCT) for the funding under the contracts RECI/QEQ-QIN/0189/2012 and UID/QUI/00100/2013.

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Effect of the heating method on the catalytic properties of SAPO-11 materials synthesized with polyethylene glycol

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Pt-based SAPO-11 material is currently used as heterogeneous catalyst in long-chain alkanes hydroisomerization, due to SAPO-11 moderate acidity combined with its unique 1D pores system (4 x 6.5 Å), allowing good selectivity into desired monobranched isomers. Many strategies can be used to improve SAPO-11 catalytic properties: introduction of secondary mesoporosity, dual templating, use of chemical additive, etc. Polyethylene glycol (PEG) is one example among others: it changes synthesis condition by interacting with SAPO precursors and has been claimed to incorporate crystals, creating extra mesoporosity after removal. Recently, we also verified that Microwave (MW) radiation was a powerful heating method to get SAPO-11 materials with very interesting physicochemical properties.[1]

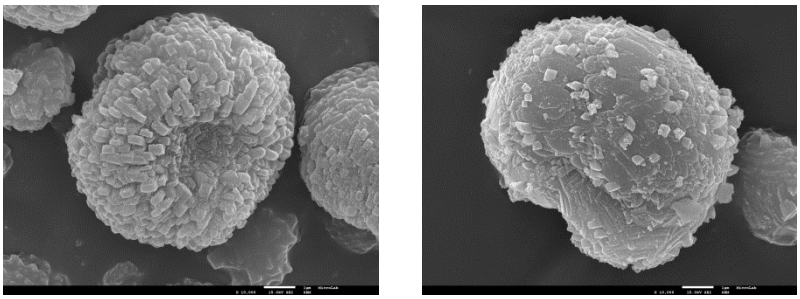

Figure 5. SEM photograph of SAPO-11 materials synthesized without (left) or with (right) PEG (electric heating method).

Here we studied the use of PEG as chemical additive during SAPO-11 synthesis, using conventional (electric) and MW heating. All the final materials were fully characterized using chemical analysis, XRD diffraction, low temperature N_2 sorption, SEM observation and pyridine adsorption followed by FTIR. Materials were also mixed with Pt-Al_2O_3. The catalytic properties were evaluated in in *n*-decane hydroisomerization reaction. In particular, we evaluated the impact of the heating method and how it modifies the role of PEG molecules during SAPO-11 synthesis stage.

Acknowledgements: The authors thank Portuguese FCT for financial support (UID/QUI/00100/2013, UID/MULTI/00612/2013, SFRH/BPD/91397/2012).

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Photoactive MOFs based in Diphenylanthracene Derivatives and obtained by Mechanochemistry for Energy Applications

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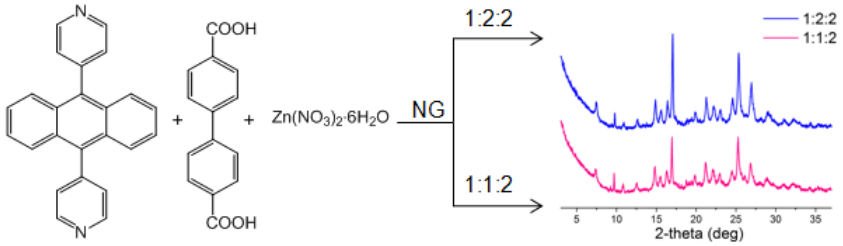
The goal of this work is the conversion of solar energy into electrical energy through photoactive metal-organic frameworks (MOFs), taking advantage of the exciting properties of this class of nanomaterials. Since the discovery of MOF-5 electronic properties [1], more MOFs have shown semiconductor behavior and have been used with success in photovoltaic devices and in other clean energy applications [2]. In our project, two main topics will be addressed: photon capture and host-guest interactions. The strategy to absorb high amount of photons will be focused on the electronic structure of the organic linker, namely diphenylanthracene (DPA) derivatives (dipyridyl anthracene and 4,4′-(9,10-anthracenediyl)dibenzoic acid). DPA and its derivatives exhibit a planar structure and upon incorporation in the MOF structure is expected to lead to long range π-π interactions. In addition, these molecules have already revealed electroluminescent (EL) properties and application in organic light-emitting diodes (OLEDs) [3]. We expect good charge mobility in the new DPA-MOFs nanomaterials. Mechanochemistry will be used to prepare the DPA-MOFs, affording a greener behavior to the synthesis approach, with solvent free and room temperature conditions. A comparative study will be developed using the solvothermal approach to correlate and identify new crystalline 3-D structures by powder X-ray diffraction (PXRD) or single crystal. Scheme 1 presents a first synthetic approach for the new DPA-MOFs by mechanochemistry.



Scheme 1- Schematic representation of the first reactions by neat grinding to obtain the DPA-MOFs.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support within the Materials Chemistry PhD program (PD/BD/127983/2016). This work was partially supported by Fundação para a Ciência e a Tecnologia (FCT-Portugal) and COMPETE (FEDER), projects PTDC/CTM-NAN/6249/2014, RECI/QEQ-QIN/0189/2012, UID/QUI/00100/ 2013 and UID/NAN/50024/2013.

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Calcium and Phosphorous Incorporation in Silica Nanoparticles for Stem Cell Differentiation in Bone Regeneration

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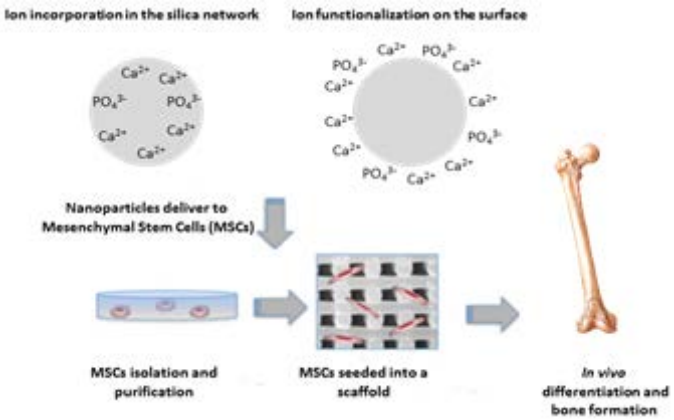
The application of adult stem cells in regenerative medicine requires the spatiotemporal control of their differentiation and of new tissue production. The differentiation is usually performed *in vitro*, by exposing the stem cells to specific factors. Alternatively, one can use carriers containing such factors, that can be internalized by the cells. In this case, the cells can be immediately implanted or further manipulated without the need for incubation in a culture media containing the factors. Calcium and phosphorous ions, once released inside adult stem cells induce bone cell proliferation and differentiation, and also stimulate the expression of growth factors.[1] The goal of this work is to develop silica nanoparticles (SiNPs) containing calcium and phosphorous ions, incorporated in the silica network during the synthesis of the nanoparticles, or at their surface in a post-synthetic procedure (Scheme 1). We have tested different calcium precursors: calcium hydroxide, calcium oxide, calcium acetate and calcium methoxyethoxide. In the case of phosphate we use triethyl phosphate (TEP) or ammonium phosphate dibasic. The nanoparticles were characterized by TEM and DLS, and the ion incorporation degree and releases kinetics were accessed by ICP. The influence of the precursor and functionalization on the particle morphology, degree of functionalization and releases kinetics profiles will be discussed.



Scheme 1 - Representation of bone regeneration approach (Adapted).[2]

Acknowledgements: This work was partially supported by Fundação para a Ciência e a Tecnologia (FCT-Portugal) and COMPETE (FEDER), projects UID/NAN/50024/2013 and PhD grant PD/BD/114019/2015.

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Naproxen Incorporation in Organic Silicas as a Strategy to Achieve Guest Amorphization

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This work aimed to study the behavior of naproxen, a pharmaceutical drug with anti-pyretic and anti-inflammatory properties[1], when loaded in three organosilicas (Periodic Mesoporous Organosilicas, PMOs)[2] with different bridging organic units in the mesoporous walls as byphenylene, with pore size of d_p= 3.42 nm, and phenylene with pore diameters of, respectively, d_p= 2.80 nm and d_p= 3.14 nm. Drug solubility has been a topic of interest for the pharmaceutical industry since it's adsorption in the organism may depend on this property. To boost the solubility of poorly-water soluble crystalline drugs one of the potential methods is to prepare them in the amorphous form, since it is an higher energetic state relative to the crystalline counterpart, and thus making it more advantageous in the dissolution rate[3,4,5]. Therefore naproxen amorphization by loading in PMOs was used as a strategy to simultaneously improve its solubility and stabilize its amorphous form. Before loading, silica activation was carried out in order to remove water and impurities by heating up to 150 ºC during 7 hours under vacuum. Naproxen was loaded from a chloroform solution under vacuum conditions. To evaluate the guest's physical state, different techniques were used as: differential scanning calorimetry (DSC), dielectric relaxation spectroscopy (DRS) and attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy. After the first heating run, DSC confirmed full naproxen's amorphization by the detection of a glass transition, located between ~0ºC and 20ºC and the absence of melting that, for the native drug, occurs at 156 ºC. The mobility of the amorphous pharmaceutical drug loaded inside these silica pores, was probed by DRS. The extrapolation of the temperature dependence of the estimated relaxation times to 100 s (τ(Tg) = 100 s usually found in other glass formers[6]), allowed estimating a dielectric glass transition temperature in good agreement with the calorimetric one. The in vitro drug delivery profile, at pH = 6.8 to simulate intestinal fluid, was monitored using high-performance liquid chromatography (HPLC). The different analyses showed that naproxen was successful incorporated in the pores of the organosilicas, and that it was possible to stabilize the amorphous state of the drug at least for 2.5 months, turning these composites promising as controlled drug delivery devices.

Acknowledgements: This work was supported by the Associate Laboratory for Green Chemistry LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265). M. T. Viciosa acknowledges to Fundação para Ciência e Tecnologia the scholarship SFRH/BPD/110151/2015.

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Strategies to Stabilize High Energetic States of Pharmaceutical Drugs

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Currently marketed compounds and novel drug candidates remain poorly water-soluble[1] with unwanted side effects to the patient, due to excessive dosage, and negative impact to the environment (water and soils). A solution for this hurdle is to obtain the drug in states of higher internal energy as amorphous, or metastable polymorphs, whose intrinsic disorder relative to the more thermodynamically stable crystalline form, can improve solubility. However, since the amorphous form is a high energetic state, it is thermodynamically unstable and so a strategy is needed to overcome this instability. Several approaches have been explored, among which the use of inorganic mesoporous matrices as hosts for the drug. Therefore, it was adopted in the present work, bringing the advantages of the unique, high specific and tuneable structural properties of these silica materials to the field of pharmaceutical science and industry. Previous studies by dielectric relaxation spectroscopy (DRS) with pharmaceutical drugs loaded in these mesoporous silica matrices[2], unravelled two molecular populations with different dynamical behaviour: one with hindered mobility due to the guest adsorption at the pore wall and another one with accelerated mobility due to reorientational motions of guest molecules in the pore core. The inter-play between the different motional regimes allows tuning drug delivery making such systems suitable for drug delivery. Another approach for the stabilization of drugs is the formation of a DES. DES is a mixture of two or more compounds that present a much lower melting point than the individual components, becoming in most cases liquid at room temperature. The recent inclusion of a drug as at least one of the eutectic mixture constituents, designated as therapeutic deep eutectic solvent (THEDES), represents a step further towards pharmaceutical and biomedical applications, due to their ability to enhance drugs solubility and to improve permeation and absorption, thus potentially overcoming low bioavailability of poorly water-soluble drugs. It is already recognized the enhancement of the permeation of THEDES involving mixing the ibuprofen drug with terpenes as menthol and camphor[4]. Hence, the combination of a drug to form a THEDES is the second strategy explored in the present work. Two case studies of high crystallisable drugs will be presented for which amorphization was successfully achieved.

Acknowledgements: This work was supported by the Associate Laboratory for Green Chemistry LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265). M. T. Viciosa acknowledges to Fundação para Ciência e Tecnologia the scholarship SFRH/BPD/110151/2015. Nitrogen absorption analysis was obtained by the Laboratório de Análises/Requimte of the Chemistry Department - Universidade Nova de Lisboa (http://www.dq.fct.unl.pt/en/analytical-services).

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Does co-crystallization prevent or enhance polymorphism?

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The use of molecules in co-crystals or salts was initially thought to prevent the phenomenon of polymorphism, making pharmaceutical production more predictable and controllable, but recent studies have shown that co-crystals can also crystallize in different forms. The different polymorphic forms may arise from different hydrogen bond motifs or synthons or from conformational flexibility of one or more of the co-crystal components, or even from differences in three-dimensional crystal packing, without significant changes in conformation of the molecules or in the H-bonded network. We present here the study of the polymorphic behaviour of a co-crystal composed of neutral molecules through a multidisciplinary approach using differential scanning calorimetry, polarised light thermomicroscopy, infrared spectroscopy and X-ray single crystal and powder diffraction. Two new major polymorphic forms have been identified and for one of them the crystal structure was revealed. Smaller polymorphic modifications were also found. The relative stability of three polymorphic forms was established.

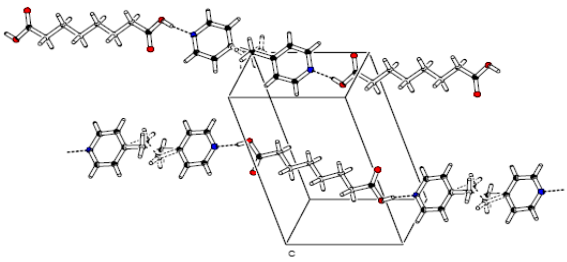

Figure 1: Two of the chains in which the neutral molecules assemble (in one of the polymorphic forms).

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HPLC-DAD and Chemometric Analysis of the Molecules of Colour in Blue Pen Inks

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Despite the fast development of the digital technology, paper documents continue to be the main information source in various fields. A common method of forgery of a document (more often of its signature) usually forgets the constitution of the used ink.[1] Analysis of the constituents of the inks can therefore constitute a trace for the detection of faked documents. [2,3]

Forensic scientists often face the following question: how many analytical methods should be considered sufficient to discriminate different inks in a document.[4]

In this work we will show an investigation of a selected number of blue pens by HPLC-DAD aiming the analysis of its main colouring constituents. These have been compared with known standards, such as Crystal Violet. Indeed, this dyes seems to be present in the great majority of the inks analysed. The analysis of the different HPLC-DAD chromatograms was further analysed by PCA and HCA.

Figure 1 depicts the HPLC-DAD chromatogram of a blue pen ink and of the standard Crystal Violet, which can be considered the main colouring matter of this pen.

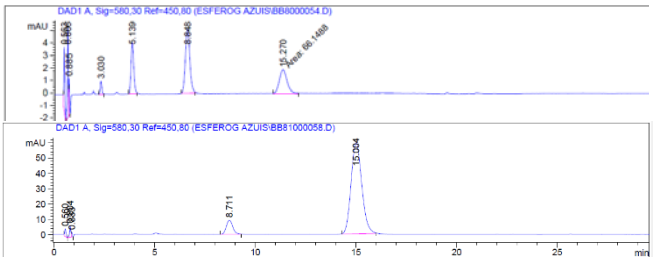

Fig. 1 – Top: HPLC-DAD chromatogram of the blue pen BIC, model “Cristal GRIP” (Q-H-19)

Bottom: HPLC-DAD chromatogram of Crystal Violet.

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Cellulosic nanostructured materials: an inelastic neutron scattering study

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As a response to the limited availability of fossil fuels and a globally growing concern on the future of our environment, the demand for sustainable alternatives to oil and oil-based products is constantly increasing. Alternative resources to replace current raw materials are sought by the industry and, at the same time, sustainable materials are gaining more and more interest among consumers around the world.

Potential raw materials to meet these challenges can be found in cellulosic biomass, which forms the feedstock for second-generation biorefineries. In order to utilize the full potential of the available resources, to improve the current processes and to develop new ones, a better understanding on the cellulose fundamental structural aspects, which is relatively limited should be attained[1,2].

Cellulose has a complex, multi-level supermolecular architecture. This natural polymer is built from superfine fibrils having diameters in the nano-scale and each such nanofibril contains ordered nanocrystallites and low-ordered nano-domains[3]. Accessibility of cellulose plays a crucial role in many kinds of chemical and physical reactions. Especially for molecules or enzymes of nanometer dimensions, the physical structures formed by cellulose microfibrils may have a considerable limiting effect on this accessibility.

Therefore, methods to characterize the nanometer scale morphology and packing of cellulose microfibrils and their bundles are highly desired. Cellulose from various sources is all the same at the molecular level but they differ in the crystalline structures and bindings by other biochemicals. It is this difference that makes possible a persistent research on cellulose.

In this contex*,* inelastic neutron scattering (INS) will be applied to gain a deeper insight at the molecular level by characterizing the nanoscale structure of cellulose from a variety of sources (bacterial and natural cellulose). Model compounds such as the cellulose derivatives -carboxymetylcellulose sodium salt and acetylcellulose will be used for comparison. Special attention will be devoted to the analysis of low frequency modes that should probe differences in the structural packing of cellulose.

Acknowledgements: this work was developed within the scope of the project CICECO-Aveiro Institute of Materials, POCI-01-0145-FEDER-007679 (FCT Ref. UID /CTM /50011/2013), financed by national funds through the FCT/MEC and when appropriate co-financed by FEDER under the PT2020 Partnership Agreement

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Novel magnetic scorpionate materials

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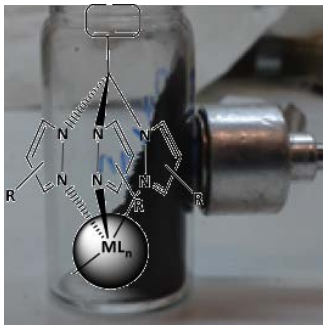
The aim of this work was to prepare a novel magnetic scorpionate material (MScorp). The method of preparation is based in microwave irradiation, providing sustainable alternative method for producing magnetic ferrite based materials, with significant advantages over the conventional current impregnation processes in terms of safety, simplicity, energy saving, time consuming, and economical and environmental concerns[1].
Experimental parameters, such as reactional time or irradiation power, were optimized.
The new scorpionate material was characterized by SEM and TEM, elemental analysis and magnetic susceptibility.



Acknowledgements: Funding from FCT (Fundação para a Ciência e a Tecnologia, Portugal) (UID/QUI/00100/2013, PTDC/QEQ-ERQ/1648/2014 and PTDC/QEQ-QIN/3967/2014 projects). APCR also acknowledges FCT for the SFRH/BPD/90883/ 2012 grant.

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Biocompatible Heater-Thermometer Nanoplatforms for Hyperthermia

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Plasmonic nanostructures concentrate light and heat within a small volume at the nanoscale, offering potential applications in areas such as biomedicine, *e.g.,* hyperthermia. However, the precise quantification of the actual temperature rise in the vicinity of such nanosystems is a considerable challenge. Here, gold nanorod heaters and $(GdYbEr)_2O_3$ nanorod thermometers join in to form nanoplatforms for efficient plasmon-induced optical heating and accurate upconversion temperature sensing (**Figure 1**), upon 980 nm laser excitation, at low power densities (up to 102.0 W cm^{-2}).[1] The local temperature rise, 302–548 K (maximum temperature sensitivity 1.22% K^{-1}, uncertainty 0.32 K and repeatability >99%), is assessed using Boltzmann's distribution of the Er^{3+} $^2H_{11/2}\rightarrow{}^4I_{15/2}/{}^4S_{3/2}\rightarrow{}^4I_{15/2}$ intensity ratio. Comparing with similar nanoplatforms that use spherical Au nanoparticles,[2] rather than Au nanorods, the plasmon-induced heating efficiency increases very significantly due to shifting of the localized surface plasmon resonance of Au nanorods into resonance with the excitation. Therefore, much lower laser power densities (8.3–24.8 W cm^{-2}) are used to achieve thermal heating in the physiological temperature range (302–330 K). The nanoplatforms are imaged within osteoblast-like MG-63 cells by hyperspectral microscopy, and they are biocompatible, with potential applications in hyperthermia.

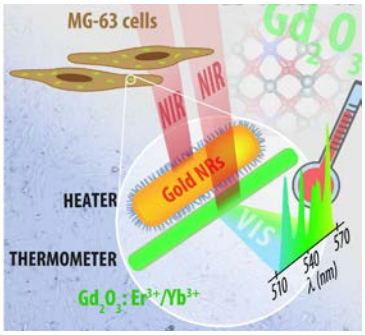

Figure 1: Optical image of MG-63 cells treated with nanoplatforms (background) and schematic representation of the heater-thermometer nanoplatforms inside MG-63 cells excited with NIR laser and emitting in the visible spectral region used for ratiometric nanothermometer.

Acknowledgements: This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, POCI-01-0145-FEDER-007679 (Fundação para a Ciência e a Tecnologia - FCT, Ref. UID/CTM/50011/2013), financed by national funds through the FCT/MEC and co-financed by FEDER under the PT2020 Partnership. Financial support of FCT (PTDC/CTM-NAN/4647/2014 and POCI-01-0145-FEDER- 016687) is also acknowledged. MLD (SFRH/BPD/93884/2013) and CDSB (SFRH/BPD/89003/2012) thank Fundação para a Ciência e Tecnologia (Portugal) for the post-doctoral grants.

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Preparation of ZnO nanoparticles and their application in transesterification reactions

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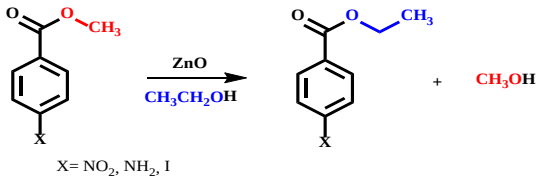
The development of sustainable catalytic systems is a keystone for the achievement of industrial processes based on the green principles.
Zinc oxide (ZnO), a solid catalyst that can act either as acid or base in large organic transformations, has provided a tremendous impact in view of its non-toxicity, friendliness preparation, high chemical stability, large surface area and high catalytic properties.[1]
An attractive class of organic synthesis is the transesterification reaction, as a feasibility of transformation (interchange) of an ester to another. The development of eco-friendly catalytic conditions for such reaction, in which harsh homogeneous systems are normally used in industry, is a matter of interest.[2]
This work started with the easy preparation of the promising ZnO nanoparticles by a simple precipitation method. The prepared nanocatalyst was tested in the transesterification of different methyl benzoates with ethanol. The reaction conditions, such as catalyst concentration, time and temperature, were optimized. Screening of transesterification with different alcohols was established. The obtained results will be presented.



Scheme 1. Transesterification reaction of methyl benzoate with ethanol

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia (fellowships SFRH/BPD/90883/2012 and PD/BD/114400/2016 to A.P.C.R. and M.M.A.S. and the UID/QUI/00100/2013 project) and the Instituto Politécnico de Lisboa (IPL/2016/MechSynCat_ISEL project) for financial support.

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Materials Challenges

New Access to Furanocoumarin Type Structures

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Furanocoumarines constitue a class of natural compounds, and display a wide range of biological activities such as antibacterial, anticancer, anti-HIV and anti-inflammatory activities.[1]
Various methods have been developed for the synthesis of this class of heterocycles, *via* cyclization of allylic coumarins under acidic conditions, mainly in the presence of sulfuric acid, with low yields.[2]
In this work, we present a new method for the one-step synthesis of furanocoumarine derivatives. In a model reaction, 4-hydroxycoumarin **1** reacts with methallyl acetate **2**, under metal triflate ($M(OTf)_n$) catalysis, leading to the awaited porduct **3** with 93 % yield (**Figure 1**). The protocol was extrapolated to the preparation of other heterocycles, such as pyranocoumarines and pyranochromenes.

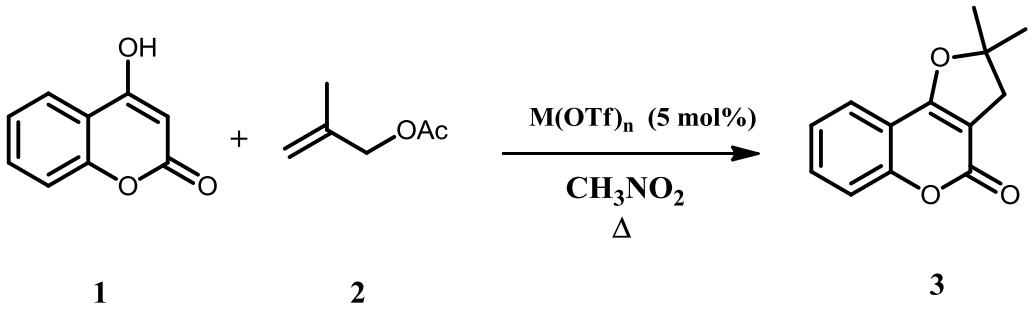

Figure 1: Synthesis of furanocoumarine derivatives.

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Advanced Supported Materials for efficient Lignin Oxidation

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Lignin is a natural polymer primarily used in paper industry as biomass, having smaller applications as well as the production of resins, foams, and other applications. In addition, it is the only renewable resource that has in its composition high volume aromatic compounds that can be used in the chemical industry. Given its molecular structure and complex modification, the production of high-value products from lignin is not common, so its valorization represents a great challenge in the environmental sustainability context reducing the dependency of oil. The modification of lignin can be achieved by oxidation reactions, which bring advantages due to the production of aromatic compounds with additional functionalities or its conversion directly to target fine chemicals. Nevertheless, in the context of green chemistry, novel advanced oxidative catalysts with high selectivity, recyclability and efficiency at mild conditions are required.[1-3]

In this work, new heterogeneous catalysts based on polyoxometalates and ionic liquids (POMs-ILs) supported on mesoporous silica nanoparticles (MSNs-POM-ILs) have been prepared (Figure 1). Their analogous homogeneous compounds were also prepared for comparison and characterized by elemental and thermal analyses (TGA and DSC), *solution and solid-state NMR spectroscopy (*^{1}H, ^{13}C and ^{31}P), vibrational spectroscopy (FT-IR and FT-Raman) and mass spectrometry techniques (ESI or MALDI-TOF techniques), to confirm the expected structures and the purity levels as well to evaluate thermal properties (e.g. glass transition temperature, melting point and decomposition temperatures). Additionally, the supported catalysts were characterized by DLS, SEM and TEM techniques, Powder XRD, N_2 adsorption-desorption isotherms in order to evaluate their size, morphology, aggregation and textural properties. The most promised supported catalysts will be tested in the oxidation of lignin and their catalytic performance should be compared.

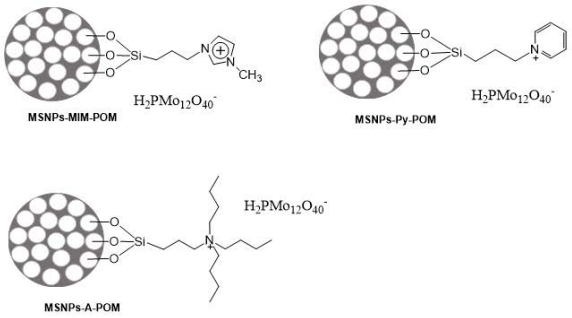

Figure 1: Heterogeneous Catalysts prepared with different cations supported, methylimidazolium (MIM), pyridinium (Py) and ammonium (A), and phosphorus-molybdenum heteropoly acid $[H_2PMo_{12}O_{40}]^-$ (POM) as anion.

Acknowledgements: This work was supported by the Associate Laboratory Research Unit for Green Chemistry - Technologies and Processes Clean - LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265).

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Valorization of biomass ash and sludge from pulp and paper industry: characterization of waste materials and new products

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Currently the EU is working towards a transition from a linear economy to a more circular economy where existing resources such as nutrients and organic matter present in materials classified as waste are effectively being recycled.[1] In fact, the re-use of raw materials that are now disposed of as waste is one of the key principles underlying the launch of the revision of the Fertiliser Regulation by the EC in 2016.[2] Clearly the re-use of such materials in agriculture calls for strict quality control and safety protocols to avoid introduction or accumulation of potentially toxic chemicals in soil and subsequent transfer to (arable) crops and/or surface waters. Among these waste materials are bottom ash (BA) and fly ash (FA) from biomass combustion to heat and power production, as well the sludge from the pulp and paper industry (PPI). At present, these materials from PPI are classified as a solid waste according the European List of Wastes[3] and a current practice is the disposal in landfills.[4] In view of the transition to a more circular economy however, the beneficial properties of these materials for soil amelioration warrant a more careful re-assessment of this status of waste materials.

Ash from residual forest biomass combustion produced in thermal plants from the PPI in Portugal show pH values between 12.0 and 13.7, relatively high contents in Ca, Mg and K, and generally relatively low contents in potentially toxic elements, as recently discussed by Cruz *et al.* (in press).[5]

In this context, in an attempt to material valorisation of these wastes, mixtures of biomass ashes with biological sludge were processed to obtain new soil improvers to be tested in the recovery of degraded soils (correction of acidic pH and input of organic matter and plant nutrients). In total, 23 ash materials, including 8 BA samples and 15 FA samples, 4 biological sludge materials were collected at a PPI in Portugal in four sampling campaigns and tested in this study.

In this work is discussed the influence of the type of residual forest biomass used as fuel on the properties of ashes produced and consequently on the characteristics of the new developed soil improvers produced (as well as on their capacity to improve degraded soils). The pre-treatment and processing operations as well as the methods and operational conditions to obtain mixtures of ash and sludge that can effectively and safely be used for soil correction are analysed and discussed.

Acknowledgements: Authors acknowledge the financial support of European Commission, and LIFE programme through the project No_Waste - Management of biomass ash and organic waste in the recovery of degraded soils: a pilot project set in Portugal (LIFE14 ENV/PT/000369) and CESAM (Centre for Environmental and Marine Studies).

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Materials Challenges

Functional Systems Based on Switchable Host-Guest Complexes

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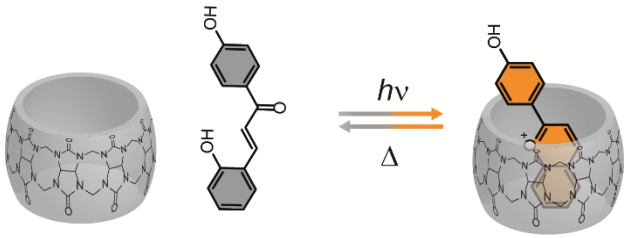
Inclusion of small molecules inside the nanometric cavities of artificial or natural receptors may lead to the emergence of new behavior, properties and functionalities. Under the topic of inclusion phenomena, we are interested in the investigation of stimuli-responsible host-guest systems with applications in drug-delivery, molecular switches, molecular machines, supramolecular polymers, etc. In particular, we have devoted special attention to cucurbituril-flavylium binding pairs. On the one hand, cucurbiturils are water-soluble macrocyclic receptors that display ultra high binding affinities (beating the avidin-biotin biological pair) and selectivity for specific guest molecules while, on the other hand, flavylium compounds provides some features that are particularly attractive to devise functional host-guest complexes. In this presentation, the formation of photo and pH-switchable host-guest systems between flavylium compounds and cucurbiturils will be discussed and some examples of their potential applications for molecular machines and drug-delivery vehicles will be presented.[1–4]



Scheme 1: Photoswitchable host-guest complex formed form cucurbituril and a flavylium compound.

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Halogen bond and luminescence in supramolecular architectures

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Halogen bonding[1] is a relatively new supramolecular interaction, and plays an important role in diverse fields including chemistry, biology and crystal engineering. The development of new synthons using this interaction is a difficult but important step in the design of supramolecular architectures. In the search of all-organic luminophores efficient in the solid state, halogen bonds have emerged as an important factor, promoting inter-system crossing through the heavy atom effect, and thus inducing phosphorescence emission of a purely organic solid.[2] To develop solid-state organic luminophores, aggregation-induced emission enhancement (AIEE)[3] effect has also been an efficient strategy. Here we present an attempt at combining these two approaches. We designed, synthesized and studied chalcone and benzophenone derivatives decorated with electron-donating substituents and halogen atoms (Figure 1).[4] The crystal structures of the halobenzophenones showed that the formation of a halogen bond is not the driving force for the organization of the compounds in the solid state, but rather a consequence of the crystal packing. Although halogen bonds may occur, unfortunately they do not promote luminescence in these compounds. In the case of the halochalcones, no halogen bonds are observed in the crystals. But the compounds are luminescent in the solid state, and the halogen atoms are important to maximize the emission of the solid through aggregation-induced emission enhancement (AIEE). This study highlights the difficulty in predicting the crystal packing of small molecules and the formation of halogen bonds in the solid state. It also demonstrates that closely related molecules can exhibit very different luminescent properties in the solid state.

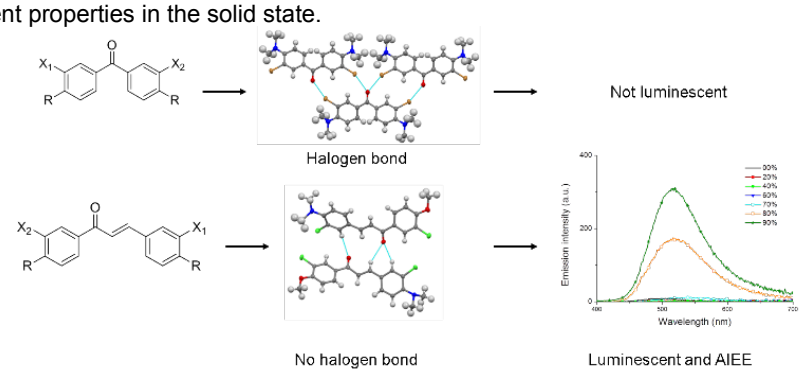

Figure 1: Study of halogenated chalcones and benzophenones.

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Bis-calix[4]arene-carbazole conjugates for Protein Sensing and Recognition

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Calixarenes are among one of the most investigated macrocyclic scaffolds for molecular recognition. Owing to their well-defined cavity, ease of derivatization of their upper and lower rims, and conformational properties, calixarenes and their derivatives are versatile hosts for numerous guest species, including ions and neutral molecular species.[1] Recently, an increased interest has been shown in the design of calixarene-based ligands for biomolecular recognition.[2] Herein we report the use of two fluorescent chemosensors based on bis-calixarene-carbazole conjugates functionalized with hydrophilic carboxylic acids at their lower rims, but differing on the type of substitution at the carbazole rings (**CALIX-CO$_2$H-CBZs**),[3] in the detection of specific proteins.[4]

It was found that **CALIX-CO$_2$H-CBZs** show a high sensing ability and selectivity toward hemic proteins, particularly for cytochrome *c* (h-cyt *c*) in aqueous-based medium as evaluated by a Stern-Volmer analysis.

In fact, several spectrofluorometric experiments performed in two solvent systems (organic and aqueous) shown that these synthetic receptors are capable of efficiently discriminating heme proteins (cytochrome *c* vs. myoglobin) and non-heme proteins (lysozyme) in an aqueous medium. Additionally, the results strongly suggest that in an organic medium a Förster-type resonance energy transfer controls the extinction of **CALIX-CO$_2$H-CBZs** emission upon contact with heme proteins while in an aqueous medium a specific photoinduced electron transfer mechanism prevails.

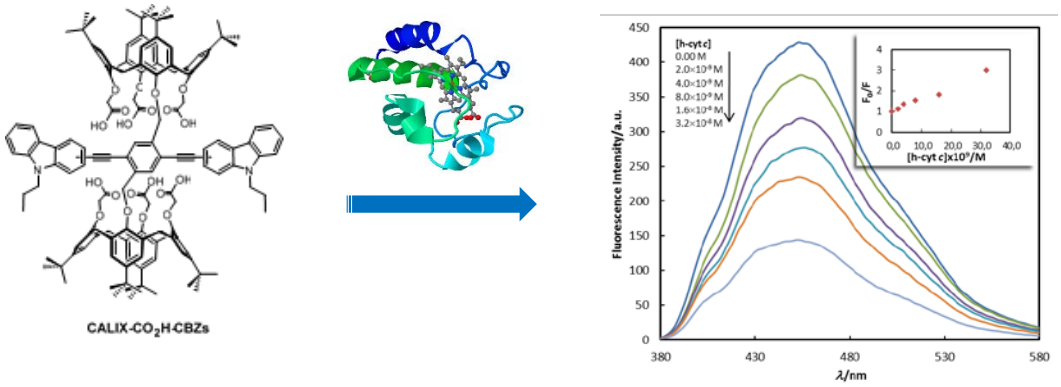

Figure 1: Fluorescence spectra of **CALIX-CO$_2$H-2-CBZ** and Stern–Volmer plot in the presence of increasing amounts of h-cyt *c* in phosphate buffer: DMF (9 :1) solution.

Acknowledgements: We thank Fundação para a Ciência e a Tecnologia/MCTES (Portugal) (PEst-OE/EQB/UI0702/2011-2014 and UID/QUI/00616/2013) for financial support.

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Stabilization of Amorphous Cimetidine by Loading in Silica Matrices

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The work aims to achieve the amorphization of drugs, since the amorphous state has a higher intrinsic disorder and therefore a greater solubility that could favour therapeutic activity[1]. It is noteworthy to mention that the existence of drugs in multiple physical forms provides the opportunity to select the preferred form of the material. The pharmaceutical drug, cimetidine, a member of the histamine blocker family, was used as target drug, which inhibits gastric secretion and reduces the production of pepsin. To stabilize this drug in the amorphous form, it was loaded in mesoporous inorganic silicas, (MCM-41) with pore size of 3.2 nm and in a phenylene bridged periodic mesoporous organosilica[2] (C_{14}-PMO) with a pore size of 2.3 nm. To eliminate water and impurities, the unloaded matrices were heated up to150ºC during 7 hours under vacuum. Then the drug was loaded from an ethanol solution into the matrices, at room temperature, under vacuum. The unloaded matrices, native drug and the obtained composites were characterized by a variety of experimental techniques such as Differential Scanning Calorimetry (DSC), attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) and dielectric relaxation spectroscopy (DRS). By DSC, it was observed that, when cooled from the molten state (T_m = 139 ºC), native cimetidine easily avoids recrystallization and a glass transition is detected; the onset and midpoint glass transition temperatures (T_g) are, respectively, 43 ºC and 47 ºC. An amorphous fraction is detected when cimetidine is loaded in both inorganic and organic matrices. However, melting is also observed at a temperature close to the native one, indicating that some crystalline fraction still exists outside pores. The broadening of the N-H absorption band as seen in ATR-FTIR spectra, provide further evidence of partial amorphization inside pores. The overall spectrum of composites corresponds to the sum of absorption bands originated by native crystalline, amorphous cimetidine and matrix itself. The mobility of the loaded drug in MCM-41 was probed by DRS in a frequency window from 0.1 to 10^6 Hz and in a temperature range -110 and + 170ºC. By comparing the relaxation behaviour of native cimetidine with the loaded one, it was concluded by a delay of the relaxation time of the latter due to surface effects that hinder the guest mobility. This composite was taken for further drug release studies. The cimetidine delivery in phosphate buffer at physiological pH of 6.8 to simulate intestinal fluid, was conducted in an orbital shaker at 100 rpm, maintained at 37 ºC, being monitored by UV-VIS spectroscopy (218 nm), evidencing that full release occurs after the first 15 minutes[3].The cimetidine/MCM-41 composite revealed promissory behaviour to be further used a drug delivery system.

Acknowledgements: This work was supported by the Associate Laboratory for Green Chemistry LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265). M. T. Viciosa acknowledges to Fundação para Ciência e Tecnologia the scholarship SFRH/BPD/110151/2015.

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Inelastic Neutron Scattering study of Reline: shedding light on the hydrogen bonding network of deep eutectic solvents

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The solids choline chloride and urea, mixed in a 1:2 molar proportion, form the iconic deep eutectic solvent “Reline”. A combination of computational and vibrational spectroscopy tools, including inelastic neutron scattering (INS), have been used to probe intermolecular interactions in the eutectic mixture. Reline’s experimental spectra were estimated using discrete and periodic ab-initio calculations of a molecular aggregate with two choline chloride and four urea units. This is the minimum size required to achieve satisfactory agreement with experiment, as smaller clusters cannot represent all of Reline’s significant intermolecular interactions. The INS spectrum of Reline, compared with that of pure choline chloride, reveals a displacement of chloride anions away from their preferred positions on top of choline’s methyl groups, whose torsional movement becomes less hindered in the mixture. Urea, which adopts a planar (sp2) shape in the crystal, becomes non-planar (sp3) in Reline, a feature herein discussed for the first time. In Reline, urea is expected to associate strongly with chloride anions while preferring softer contacts with other urea molecules. Chloride’s interactions with choline are fairly conserved at the hydroxyl end while becoming weaker at the cationic headgroup. The interplay of soft and strong interactions confers flexibility to the newly formed hydrogen-bond network and allows the ensemble to remain liquid at room temperature.

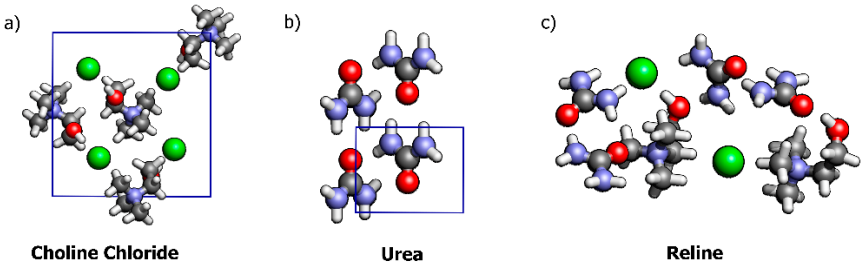

Figure 1: Molecular representation of the crystal lattices of a) choline chloride and b) urea along with c) the optimized geometry of Reline’s model..

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Near-infrared spectroscopy for the assessment of mechanical properties of cork disks used for the manufacturing of sparkling wine stoppers

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Portugal is one of the main world producers of cork, representing a high weight in exports. It's necessary to produce a product with the highest quality, capable of placing itself on the market at a level of excellence. Industrially the quality control of production is directly connected to the success of sales, the manufacturer wants to guarantee the best quality, avoiding to the maximum any fault that can lead to rejection.[1] Cork is as a material with incredible physical properties, has a complex three-dimensional structure in it's matrix, being able to recognize by eye a high heterogeneity.[2] This heterogeneity is especially relevant when dealing with the production of cork stoppers, namely for the sparking wines market (e.g., Champagne) that are increasingly demanding in terms of quality. The material properties heterogeneity and complexity result in some variability in the quality of cork stoppers that cannot be fully perceived during the manufacturing process. The incorporation of non-invasive and non-destructive systems for the quality control of cork is of especially interest in this context. Near infrared spectroscopy plays an important role in this context as it allows extremely fast measurements (range of milliseconds), is non-destructive and can provide valuable chemical and physical information simultaneously.

In this study, cork disks used in the manufacturing process of cork stoppers for the sparkling wine industry were tested in terms of several mechanical properties using a material testing press (Lloyd LR50K, Ametek, USA). Disks were evaluated against several properties (e.g., compression force, resilience...) aiming at estimating elastic and plastic behaviour.[3] The goal was to scan multiple cork disks from different material grades unveiling the heterogeneity in terms of these mechanic properties. In parallel the same cork disk samples were measured on a near infrared (NIR) spectrometer (FTLA2000, Bomem, USA) in diffuse reflectance mode. NIR measurements were performed in multiple locations of the cork disks. Resourcing to multivariate analysis (partial least squares and feedforward neural networks), NIR spectra were modelled against the different mechanical parameters determined from cork disks. Results indicate that the NIR spectroscopy method is able to model the variability observed in most estimated mechanical parameters indicating that it can be a viable methodology for in-line implementation as a process analytical methodology for ensuring high quality product.

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The Key Role of Solvent in Ion-Pair Halogen Bonds: Building Efficient Receptors for Halide Recognition in Solution

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Halogen bonds (XB) represent a specific type of non-covalent interactions involving a halogen atom (X = Cl, Br, I) and a Lewis base (B), where X acts as an electrophilic species. The nature of these interactions has been predominantly explained from an electrostatic standpoint, due to the existence of a localized region of depleted electron density at X (named σ-hole), while evidence for significant contributions from charge-transfer have been the subject of intense debate. In recent years, the potentialities of XBs have found increasing application in material sciences such as crystal engineering, ionic liquids, supramolecular chemistry and anion recognition in solution, amongst other fields.[1,2] In the context of anion recognition, the haloimidazolium or halotriazolium motifs have been widely employed in the construction of diversified supramolecular architectures, some of which are capable to act as strong anion-binding entities in competitive aqueous environment, *via* charge-assisted halogen bonds.[1]
In this communication, we studied this specific type of ion-pair systems by quantum mechanical calculations,[3] highlighting the key role of the solvent on the XB nature and strength, and its importance for the correct prediction of interaction energies (**Figure 1**).

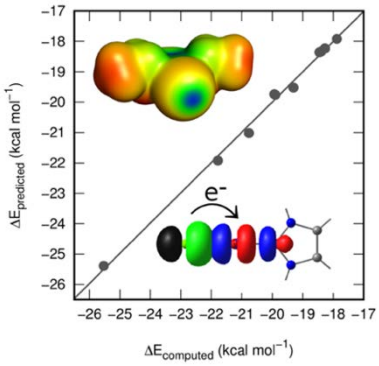

Figure 1: The interaction energy of 2-halo-functionalized imidazolium derivatives with a chloride anion can be predicted accounting for both electrostatics and charge-transfer effects, their relative contribution being modulated by the solvent environment.

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S-doped carbon nanotubes: a solvent-free methodology

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Carbon nanotubes (CNTs) have been intensively investigated as catalysts or catalyst supports in the fields of renewable energy and environmental technologies[1]. The surface of carbon materials can be modified by doping with heteroatoms such as oxygen, nitrogen, sulfur, boron or phosphorus increasing the role assumed by carbon nanomaterials and extending their application to a wide range of processes[2]. Incorporation of O- and N-surface groups has been extensively studied, but S-doped carbons materials only started to receive attention in the last few years[3]. Several approaches have been developed to incorporate sulfur into the carbon matrix; however, these methods implicate high energy consumption and multi-step procedures, which increase the catalyst manufacturing cost, limiting their practical application. Hereby, we present an easy to handle, solvent-free post-doping method to incorporate S-functionalities onto the surface of CNT, involving a mechanical treatment under ball-milling followed by a thermal treatment under inert atmosphere (N_2) (**Figure 1**). Thiourea, sodium thiosulfate and sodium sulphite have been used as S-precursors. Nitrogen adsorption was used to assess the changes in the textural properties induced by the applied treatments, while the nature and amounts of the surface groups incorporated onto the CNT were determined by suitable methods, such as X-ray photoelectron spectroscopy (XPS), Elemental Analysis and also thermogravimetry.

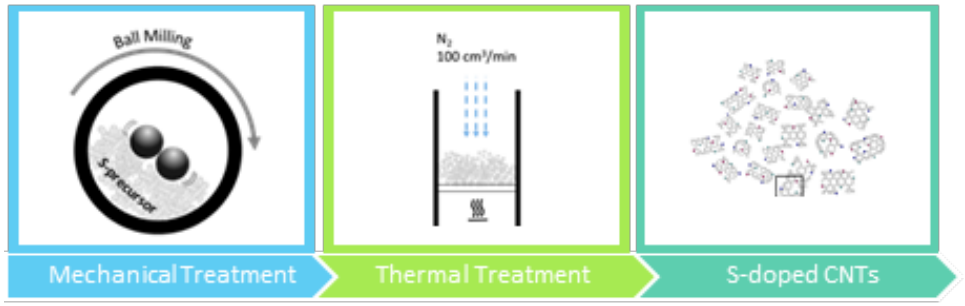

Figure 1: Illustration of the solvent-free method to prepare S-doped carbon nanotubes.

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Revisiting the study of solvent effects: Grunwald-Winstein vs. TAKA approaches

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Grunwald-Winstein plots[1] have been extensively used over time to rationalize solvent effects in solvolysis reactions. The underneath model equation is usually written as

$$log\left(\frac{k}{k_0}\right) = mY + lN + c$$

where *k* is the rate constant of an RX substrate in a given solvent, k_0 is the corresponding rate constant in a reference solvent, usually 80% (v/v) ethanol/water, *l* is the sensitivity of the solvolysis to changes in solvent nucleophilicity (*N*), *m* is the sensitivity of the solvolysis to changes in solvent ionizing power (*Y*) and *c* is a (residual) constant term. *N* and *Y* are supposed to translate a single effect. However, several of these scales had to be improved over the years to accurately interpret the behavior of each substrate, suggesting that neither of these are truly pure solvent parameters[2]. The TAKA model equation[3], offers a different approach to analyse solvent effects over different types of reactions, including solvolysis, but it does not presuppose any reference solvent or substrate. It relates, instead, *k* with a set of solvent parameters,

$$\log k = a\alpha + b\beta + p\pi^* + c$$

where α refers to the solvent's hydrogen bond donor ability, β refers to the solvent's hydrogen bond acceptor ability and $\pi*$ relates to the solvent's dipolarity/polarizability.

To our knowledge, very little has been done to correlate both sets of parameters in order to understand if the G-W *N* and *Y* scales are indeed pure and/or if they deliver the same mechanistic information as the TAKA model parameters. -Moreover, the few works found in the literature were based on a small set of pure solvents[4]. One reason for this might be due to the fact that there are limited, scattered and inconsistent data in the literature regarding solvatochromic parameters for typical Grunwald-Winstein (G-W) mixtures *i.e.*, among others, the aqueous solvent systems ethanol, methanol, acetone and trifluorethanol, and also the mixture trifluorethanol/ethanol.

In this work, Kamlet-Taft solvatochromic parameters ($\pi*$, α and β) have been determined at 298.15 K on the basis of the spectroscopic shifts of five solvatochromic probes (betaine (30), 4-nitrophenol, 4-nitroanisole, 4-nitroaniline and *N,N*-dimethyl-4-nitroaniline), for 42 of the referred G-W solvent mixtures, in order to establish a coherent matrix of solvatochromic parameters.

Good correlations between several *N* and *Y* scales with $\pi*$, α and β scales have been found revealing that G-W parameters can indeed be expressed as linear combinations of the TAKA parameters, thus showing the similarity of both approaches.

Acknowledgements: The authors are grateful to Fundação para a Ciência e a Tecnologia, Portugal, for financial support under project UID/MULTI/00612/2013.

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Synthesis and characterization of a new copper-phthalocyanine dye

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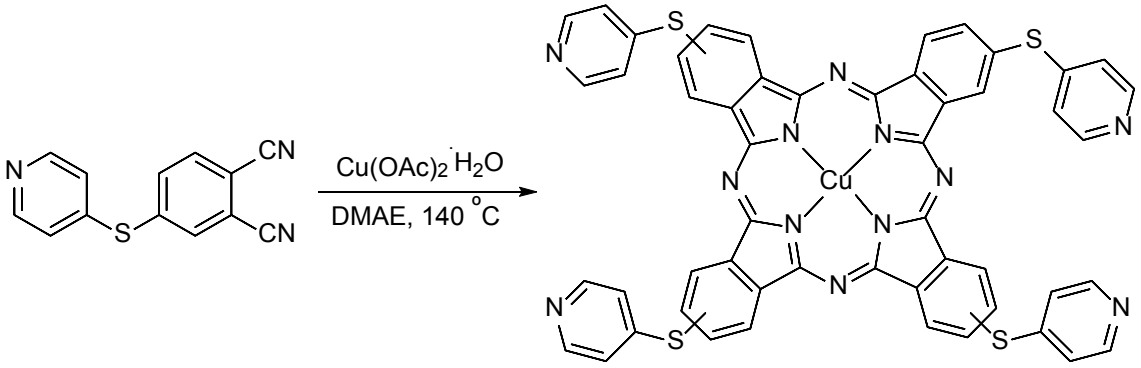
Phthalocyanines (Pcs) have been prepared to be used as valuable (photo)catalysts which can be useful in industrial and cleaning anthropogenic waste.[1] For that, multi-substituted Pc dyes have also been prepared to be used as (photo)active molecules in more complex materials, such as coordination polymers.[2] This work aims the synthesis and characterization of a new copper(II) tetra-substituted mercaptopyridine-phthalocyanine (**Scheme 1**). The UV-Vis absorption, FTIR-ATR spectroscopy and mass spectrometry will be discussed. Also, simulation of catalytic conditions, such as pH and time of exposure to light will be presented and discussed.



Scheme 1

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Studies of insertion/desinsertion of K+ and Cs+ in copper hexacianoferrate modified electrodes

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The behaviour of thin films of copper hexacyanoferrate (CuHCFe) on glassy carbon electrodes and platinum electrodes has been studied in K+ and Cs+ aqueous electrolytes. These modified electrodes have been characterized by cyclic voltammetric and ac impedance measurements, as well as by XPS and neutron activation analyses. Attention has been given to the reversible exchange of potassium cations and caesium cations between film and aqueous solutions, as well as to the charge transfer mechanism. The cyclic voltammetric studies revealed that the behaviour of the films is affected by the cation present in the electrolyte:

- In K+ containing electrolytes the system is reversible, adiffusional and quasi-stationary.
- In Cs+ containing electrolytes the system is quasi-reversible, diffusional and transient.

Self Assembled Bilayer Molecular Metals (Cnb-Edt-Ttf)$_4$X; Polymorphism And Superconductivity

Rabaça S.,[a] Oliveira S.,[a] Gonçalves A.C.,[a] Lopes G.,[a] Gama V.,[a] Lopes E.B.,[a] Santos I.C.,[a] Paixão J.A.,[b] Belo D.,[a] Canadell E.,[c] Almeida M.[a]

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In this contribution a new type of 2D molecular conductors with a bilayer structure of the donors, based on the dissymmetrical ET derivative cyanobenzene-ethylenedithio-tetrathiafulvalene (CNB-EDT-TTF)[1], is described. Through an efficient network of electrostatic and hydrogen bond assisted dimeric interactions, involving the cyano groups of these donors, it is promoted the formation of partially oxidized donor bilayers in salts with composition (CNB-EDT-TTF)$_4$X with different small anions such as X= ClO_4^-, PF_6^-, I_3^-, BF_4^-, ReO_4^-, SbF_6^-. However different polymorphs of salts with the 4:1 stoichiometry, depending on the solvent and crystallization conditions can be obtained. [2,3] These 4:1 charge transfer salts present 2D metallic properties with unusual characteristics derived both from the unusual stoichiometry and the weak interaction between paired donor layers. As predicted by band structure calculations these properties, which will be discussed in detail, are related with high band filling, large electronic effective masses and quasi degenerated 2D Fermi surfaces and in agreement with electron transport measurements in single crystals. Depending on the donor packing pattern some of these 2D metals can present superconductivity at temperatures close to 4K.[1]

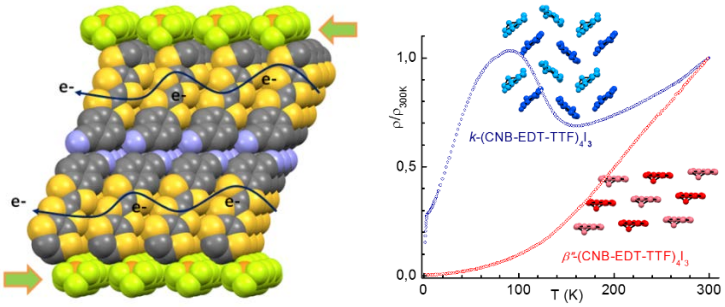

Figure 1: Bilayer molecular metals *β"*- and *κ*- (CNB-EDT-TTF)$_4$X..

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support SFRH/BPD/113344/2015.

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New BioMOFs based on azelaic acid: Synthesis, Characterization and Stability studies

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In the last years, Bioinspired Metal-Organic Frameworks (BioMOFs) have emerged as new promising drug delivery systems that can tackle the drawbacks of the traditional ones, such as low drug-storage capacity, uncontrolled delivery and potential toxicity. In this work, we embraced the challenge of synthesizing novel BioMOF structures based on biocompatible cations and active pharmaceutical ingredients (API) as constitutive linkers, recurring to mechanochemistry, an original and totally green technique for the synthesis of this type of solids.[1]
Four new 3D BioMOFs were synthesized using azelaic acid, an API commonly used to treat skin disorders, and several safe metals such as Mg, K, Na and Ag (**Figure 1**). These novel materials were structurally characterized by using a combination of experimental techniques (Single-crystal and Powder X-Ray diffraction, FT-IR, SEM, TGA and DSC). In addition, their thermal and chemical stability was assessed under different conditions (temperature, time and humidity), some of them relevant for their cutaneous administration as antibiotic. Some of these solids present water molecules in the coordination metal sphere, exhibiting a reversible dehydration/rehydration associated to structural changes. Finally, the release of the active constitutive moieties from some of these materials under physiological conditions has been monitored, making these systems promising candidates for antibiotic cutaneous release.

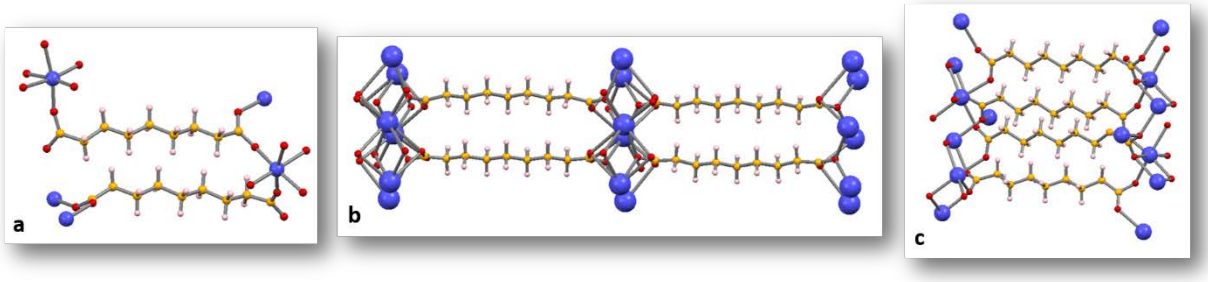

Figure 1: Molecular structure view of the new compounds with azelaic acid and a) Mg, b) K and c) Na

Acknowledgements: Authors acknowledge funding to Fundação para a Ciência e a Tecnologia (PEST-OE/QUI/UI0100/2013, RECI/QEQ-QIN70189/2012, SFRH/BPD/78854/2011, SFRH/BD/100024/2014) and “Ramon y Cajal” funding (ENE2016-79608).

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Molecular Tuning: Halogen influence on crystal structure and properties

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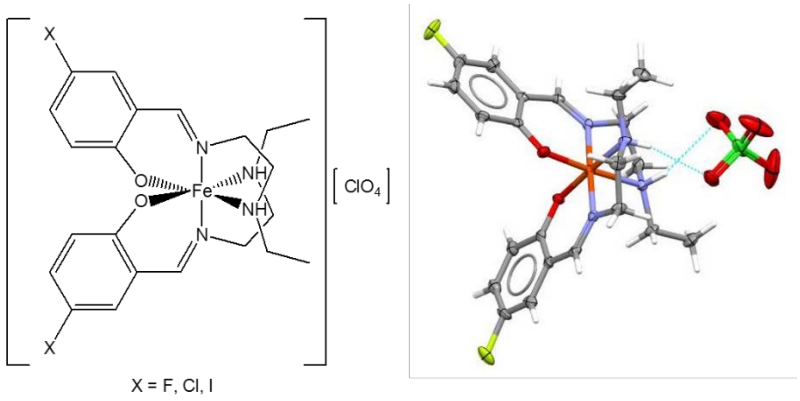
Spin crossover (SCO) compounds are very relevant mainly due to their broad possible applications such as molecular switches, memory devices, sensors and bio-compatible machines. d^4-d^7 transition metal compounds have the ability to switch from a low-spin (LS) state to high-spin (HS) and reverse through several different stimuli like temperature, pressure, light or an electrostatic field. This spin transition is accompanied by a geometry adjustment, since the metal-ligand atom bond lengths are greater in the HS state. This geometry arrangement may result in a phase transition.[1]
We have recently reported the thermosalient effect (where crystals suddenly jump, bend, twist or explode upon undergoing a thermally activated phase transition) of a Salen-based iron(III) compound, $[Fe(5\text{-}Br\text{-}SalEen)_2]ClO_4$,[2] and we are now exploring the magnetic behaviour and structural properties of the parent compounds with three other halogens (**Scheme 1**).[2]



X = F, Cl, I

Scheme 1

Acknowledgements: This work was supported by Fundação para a Ciência e a Tecnologia (FCT), Portugal (Projects UID/MULTI/00612/2013 and UID/MULTI/04046/2013 and PTDC//QEQ-QIN/3414/2014 and Grants SFRH/BD/90386/2012 and SFRH/BPD/73345/2010). The SCXR determinations were performed at the Unidade de Ciências Biomoleculares Aplicadas-UCIBIO which is financed by national funds from FCT/MEC (UID/Multi/04378/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007728).

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Hybrid nanoparticles with application in photovoltaic solar cells

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Solar energy conversion based on organic photovoltaic (OPV) cells is a promising clean and sustainable source of energy and exciting research area. A major challenge in the development of better OPV is the trade-off between light absorption and photogenerated exciton collection, requiring that the polymer film has both high absorbance and low thickness. One promising approach to enhance light harvesting in OPVs is based on the use of noble metal nanostructures such as gold or silver, which can act as local field enhancers[1,2] and/or light scattering centers[3].
Here, we prepared and characterized gold nanoparticles (spheres and stars) and coated them with insulating silica shell of 7 to 20 nm to avoid charge recombination (**Figure 1**). A high quantum yield perylenediimide (PDI) dye was attached to the silica surface of the nanospheres avoiding fluorescence quenching. We predicted emission enhancements of 5 to 30 times without change in the dye emission lifetime, attributed to the increased local electromagnetic field around the metal.[1] The nanoparticles were incorporated in the active layer of a OPV device, in order to study the interfacial charge and energy transfer processes at the nanoscale.

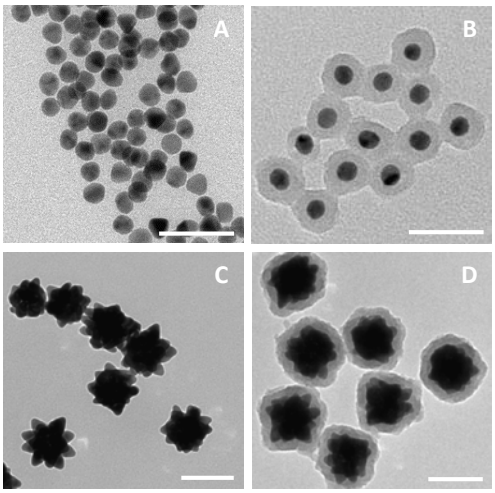

Figure 1: TEM images of hybrid core-shell nanoparticles with gold spheres (A) and gold stars (C) in the core encapsulated with a silica shell (B and D). Scale bar: 50 nm (A and B), 100 nm (C and D).

Acknowledgements: This work was partially supported by Fundação para a Ciência e a Tecnologia (FCT-Portugal) and COMPETE (FEDER), projects UID/NAN/50024/2013, RECI/CTM-POL/0342/2012, PTDC/CTM-POL/3698/2014 and grant SFRH/BPD/96707/2013.

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New Water Soluble PDIs for Bioimaging

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Due to its extraordinary properties, several PDIs have found their way into industrial-scale production, especially in fiber applications and in high-grade industrial paints. In 2009 a new method for the functionalization of the ortho-positions (2,5,8,11-positions) of perylenediimides was discovered[1]. The opportunity to selectively alkylate the perylene core was demonstrated across the Murai alkylation protocol via a one-step metal catalyzed reaction, resulting in a incredible influence on the solubility, intermolecular packing and solid-state fluorescence compared to the parent unsubstituted PDIs. The excellent optical properties of PDI's, such as near-unity fluorescence quantum yield, excitation in the visible region, strong and reversible electron-accepting character, high photochemical stability and high electron mobility, lead to a burst in the development of high performance optical molecular probes based on the PDI core for Near-InfraRed (NIR) imaging techniques. Despite the fact that NIR organic probes usually suffer from poor hydrophilicity and low quantum yields, recent progress in strategies and synthetic methods for the development of water soluble PDI have been made.

In our group, we have developed several visible and NIR PDIs with different imide and bay substituents[2]. The synthesis of PDIs derivatives, starting from the commercially available perylene-3,4,9,10-tetracarboxylic acid dianhydride, allows the introduction of substituents in the imide group (affecting the aggregation, solubility or immobilization), in the bay region (substituents affect electronic and optical properties) or in the ortho position (affecting the solubility) (Figure 1).

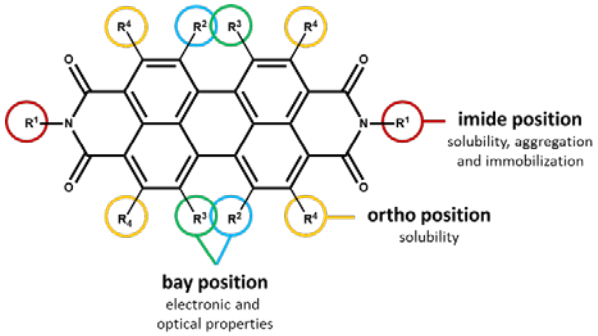

Figure 1: General structure of PDIs and influence of the different substituents position.

Acknowledgements: This work was partially supported by Fundação para a Ciência e a Tecnologia (FCT-Portugal) and COMPETE (FEDER), project UID/NAN/50024/2013 and project PTDC/CTMNAN/6249/2014.

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A Self-Separating Catalysts Based On Molybdenium

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An important goal in transition metal catalysis science is the development of systems that combine the advantages of homogeneous catalysts with those of heterogeneous catalysts[1]. The principal approach to solving this problem has been the immobilization of molecular catalysts onto organic, inorganic or hybrid organic-inorganic supports.[2] In the period 2001-2003 only two papers reported on a new approach involving catalyst self-separation or self-precipitation. The first report, by Xi et al., described reaction-controlled phase-transfer catalysis for propylene oxidation to propylene oxide.[3] Exhaustion of the oxidant led to spontaneous precipitation of the catalysis that could be recovered and used again. The second approach, developed by Dioumaev and Bullock, consisted on alternative solid-liquid-solid phase separation that relied on the differences in solubility of the catalyst in the liquid substrate and product.[4] Since the publication of these two landmark papers, progress on self-precipitating transition metal catalysts has been slow.
In the present work, we describe a new type of self-separating catalyst based on a molybdenum oxide hybrid material. The material $[MoO_3(trz)_{0.5}]$ (trz = 1,2,4-triazole), which was first reported by Zubieta and co-workers[5], was chosen for study as part of our ongoing investigations into the catalytic properties of Mo(VI) and W(VI) oxide-organonitrogen hybrid materials.[6] We know that depending on the structure and composition of these hybrids, as well as the catalytic reaction conditions, the materials typically act either as sources of soluble active species or (more rarely) as heterogeneous catalysts. In a manner similar to that reported with polyoxometalate salt reference 3, a solid-liquid-solid phase transfer takes place, with spontaneous reassembly and self-precipitation of the original molybdenum oxide-triazole solid upon completion of the reaction. Results with Mo(VI) hybrid are compared with those for the corresponding W(VI) compound, and the catalytic performances of both materials have been further examined for the oxidation of benzyl alcohol and benzaldehyde.

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Mesoporous and biocompatible locust bean gum aerogels for controlled drug delivery

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In the pharmaceutical industry, there is a demand to convert the crystallinity of drugs into the respective amorphous state due to better dissolution and bioavailability of the latter. However, as the amorphous state is thermodynamically instable, during processing or storage, drugs may spontaneously convert back to the crystalline form[1]. One way to promote and maintain the amorphous form is to load the drug in a porous carrier[2]. In the present study, aerogels made of the polysaccharide locust bean gum (LBG) were used to incorporate naproxen, a nonsteroidal anti-inflammatory drug, practically insoluble in water. LBG is a biopolymer biodegradable, easily modifiable, biocompatible, and its degradation products are easily excreted[3]. The use of polysaccharides has a long tradition in pharmaceutical industry as excipients. Nowadays, the concept evolved and the polysaccharides are seen as bioactive materials, being used as drug delivery carriers in order to favour the interaction of a nanostructure with a specific biological surface[4], providing the delivery of a defined dose, at a controlled rate and to a given biological site[3]. The matrices used in this work for hosting naproxen were performed using LBG and two ionic liquids ([BMIM][Cl] and [C_2OHMIM][Cl]) and also water as dissolution media for the polysaccharide and as templates that determine the pore size. Differential scanning calorimetry (DSC) was used to access the guest physical state in the prepared composites allowing to probe its conversion from the crystalline state to the amorphous one; this was confirmed by ATR-FTIR. It was found that naproxen is full amorphous in LBG:[bmim][Cl]$_{naproxen}$ and partially amorphous in LBG:[C_2OHmim][Cl]$_{naproxen}$ and LBG:[H_2O]$_{naproxen}$. The bimodal nature of the calorimetric glass transition detected for all composites, was taken as an evidence of the existence of two molecular populations: one adsorbed at the inner pore walls with hindered mobility and another one in the pore core with enhanced mobility. The drug release from aerogels was monitored in pH=6.8 media and quantified through HPLC. A complete release of drug was achieved for the three composites. These findings reinforce the suitability of LBG aerogels as matrices for controlled drug delivery. The cytotoxicity of composites were assessed using confluent and undifferentiated Caco2 cells. This cell model shares some characteristics with crypt enterocytes and thus it has been considered as an accepted intestinal model widely implemented to evaluate the effect of chemical and food compounds on the intestinal function[5]. Result suggested that all composites were not cytotoxic in Caco2 cells for the range of concentrations tested and after 24h of incubation. As expected, free naproxen did not present cytotoxic effect in this cell line.

Acknowledgements: This work was supported by the Associate Laboratory for Green Chemistry LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265). M. T. Viciosa acknowledges to Fundação para Ciência e Tecnologia the scholarship SFRH/BPD/110151/2015. Nitrogen absorption analysis was obtained by the Laboratório de Análises/Requimte of the Chemistry Department - Universidade Nova de Lisboa (http://www.dq.fct.unl.pt/en/analytical-services).

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Design of Bioinspired Copper(II) Aminoalcohol Complexes and Coordination Polymers for Mild Oxidative Functionalization of Alkanes

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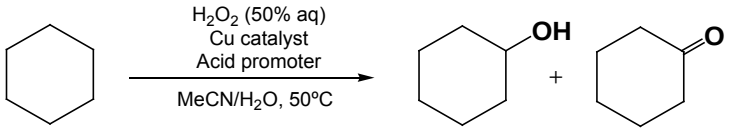
As a continuation of our recent research on the synthesis and catalytic application of bioinspired multicopper(II) cores,[1] the main aim of the current work consisted in the self-assembly generation of new copper(II) compounds bearing aminoalcohols as principal *N*,*O*-ligands. Their catalytic function toward the mild homogeneous oxidation or hydrocarboxylation of cycloalkanes to give the corresponding cyclic alcohols and ketones or carboxylic acids was also investigated.

N-benzylethanolamine (Hbea), triisopropanolamine (H_3tipa), *N*,*N*-dimethylethanolamine (Hdmea), or *N*-ethyldiethanolamine (H_2edea) were applied as *N*,*O*-building blocks for the self-assembly generation of five novel copper(II) compounds: $[Cu_2(\mu\text{-bea})_2(Hbea)_2](NO_3)_2$ (**1**), $[Cu_2(H_3tipa)_2(\mu\text{-pma})]\cdot 7H_2O$ (**2**), $[\{Cu_2(\mu\text{-dmea})_2(H_2O)\}_2(\mu_4\text{-pma})]_n\cdot 4nH_2O$ (**3**), $[\{Cu_2(\mu\text{-Hedea})_2\}_2(\mu_4\text{-pma})]_n\cdot 4nH_2O$ (**4**), and $[\{Cu(bea)(Hbea)\}_4(\mu_4\text{-pma})]_n\cdot 2nH_2O$ (**5**) {H_4pma = pyromellitic acid}. All products were isolated in good yields and fully characterized by IR spectroscopy, ESI–MS(±), elemental analysis, and single-crystal X-ray diffraction. Synthesis and structural features of **1**–**5** will be discussed.

Compounds **1**–**5** act as highly efficient pre-catalysts for the mild homogeneous oxidation of various cycloalkanes (C_5–C_8) to the corresponding alcohols and ketones by aqueous H_2O_2 in acidic MeCN/H_2O medium at 50 °C (**Scheme 1**). Overall product yields up to 45% (based on cycloalkane) were achieved and the effects of various reaction parameters were investigated, including the type and loading of pre-catalyst, the amount and kind of acid promoter (HNO_3, H_2SO_4, HCl, or CF_3COOH), the influence of water, and the substrate scope (**Scheme 1**).[2,3] Although water typically strongly inhibits alkane oxidations due to the reduction of H_2O_2 concentration and lowering of the alkane solubility, in some catalytic systems we observed a significant growth of an initial reaction rate in the cyclohexane oxidation on increasing the amount of H_2O in the reaction mixture. This unusual water promoting effect will be discussed in detail. Compounds **1** and **2** also catalyze the hydrocarboxylation of C_5–C_8 cycloalkanes, by CO, $K_2S_2O_8$, and H_2O in a water/acetonitrile medium at 60 °C, to give the corresponding cycloalkane carboxylic acids in up to 38% yields based on cycloalkanes.[3]



Scheme 1: Cu-catalyzed oxidation of cyclohexane to cyclohexanol and cyclohexanone.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (IF/01395/2013/CP1163/CT005, RECI/QEQ-QIN/0189/2012, UID/QUI/00100/2013, SFRH/BPD/119980/2016, SFRH/BPD/78854/2011, and REM2013).

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Synthesis of Monodisperse Hybrid Nanoparticles for Structural Colour

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Structural colour can be observed from the interaction of light with periodically arranged structures and can be found in nature from the feathers of peacocks, humming birds, pheasant or even in small bugs like beetles. In contrast to pigmentary colour, structural colour does not work through light absorption mechanism and therefore it does not photodegradate. Besides, it presents properties that can be used in many applications, such as low-cost non-toxic coloured pigments, full-colour paper-like displays, cosmetics and many others, replacing the use of dyes or pigments[1]. Here we describe the synthesis of several monodisperse polymer nanoparticles of different sizes that will serve as building blocks for photonic crystals exhibiting structural colour. Hybrid monodisperse polymer nanoparticles were successfully prepared by emulsion polymerization, adapting a method previously described in the literature[2]. Styrene, methyl methacrylate and acrylic acid were used as comonomers, potassium persultafe as initiator, sodium dodecyl sulphate as surfactant and sodium hydrogen carbonate to stabilize the pH.
The nanoparticles were analysed by dynamic light scattering (DLS), nanoparticle tracking analysis (NTA) and transmission electron microscopy (TEM), confirming sizes between ≈ 100 to 300 nm with low polydispersity index (PDI < 0.1)[3] as observed on Figure 1.

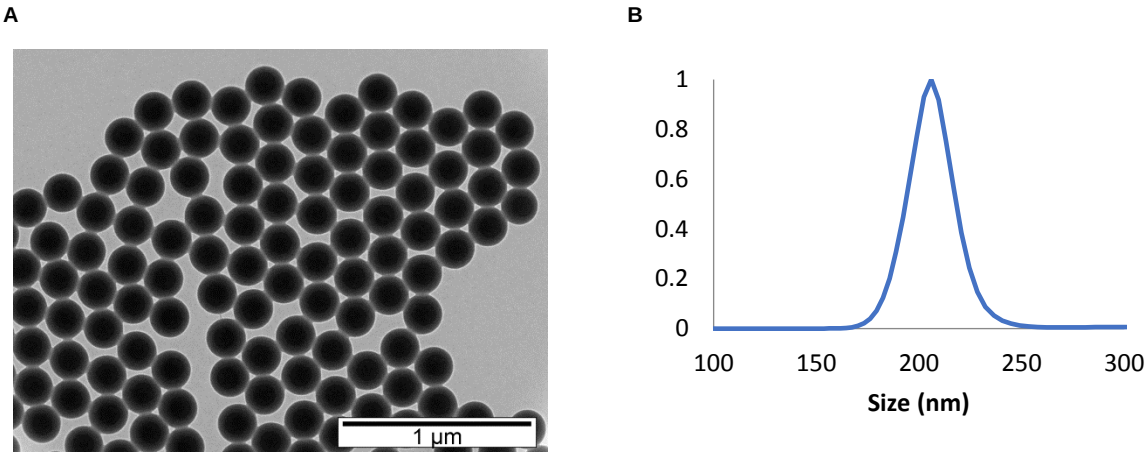

Figure 1 – A) TEM images of nanoparticles with 200 nm of diameter. B) Size distribution obtained by NTA, with PDI of 0.01.

Acknowledgements: This work was partially supported by Fundação para a Ciência e a Tecnologia (FCT-Portugal) and COMPETE (FEDER), projects UID/NAN/50024/2013 and PTDC/CTM-POL/3698/2014.

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Fluorescent Organoboron Chelates and Their Use in Bioimaging

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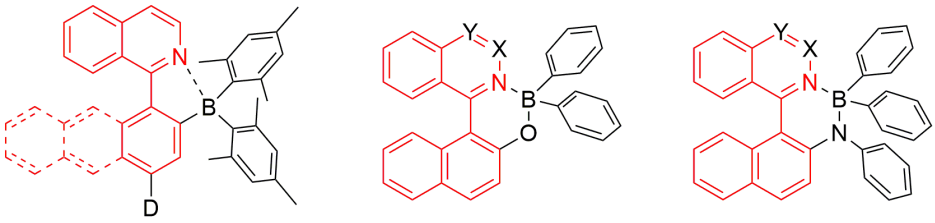
An important challenge for organic chemists is the preparation of new fluorophores which satisfy the requirements for potential applications in functional materials or in bioimaging. In our laboratories we have been developing fluorescent tetracoordinate organoboron N,*C*-, *N*,*O*- or *N*,*N*-chelates, containing an arylisoquinoline skeleton (**Scheme 1**).[1,2] Due to their large Stokes shifts these organoboron chelates could be an alternative for the well-known boron dipyrromethene dyes (BODIPY).[3] In addition, the compounds show high fluorescence quantum yields in solution, pronounced solvatochromic effects, high photostability, and sometimes significant two-photon absorption cross sections. In the present contribution, we focus on the preparation, photophysical characterization, and application in bioimaging of some of these dyes.



D: Electron donor

X = Y = CH
X = CH, Y = N
X = N, Y = CH

Scheme 1: Structures of arylisoquinoline-derived tetracoordinate organoboron chelates.

Acknowledgements: The presenting author gratefully acknowledges financial support by the Spanish MINECO (CTQ2014-54729-C2-1-P), the European Union (FEDER), and the Junta de Andalucía (P12-FQM-2140 and postdoctoral contract within P08-FQM-3685).

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Facile one-step synthesis of POM@MOF(Fe) nanocomposites by using *in situ* approach

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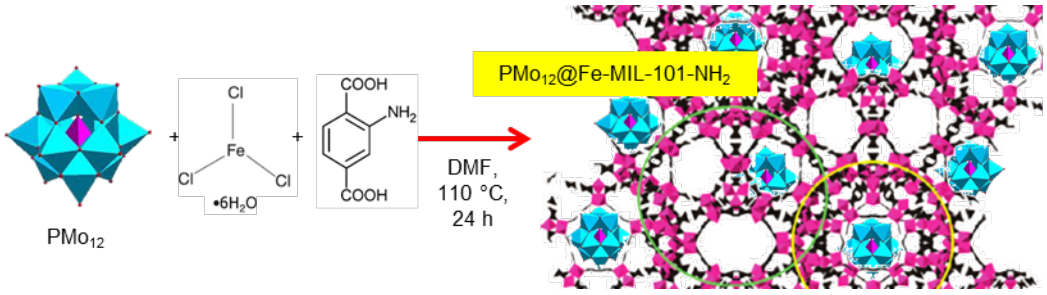
Metal-organic frameworks (MOFs) are a new type of emerging materials consisting of metal ions coordinated organic ligands to form an ordered 3D structure. Specifically, Fe-MIL-101-NH_2 represents a very interesting MOF material due to several properties: high specific areas, large cage/pores sizes, and the presence of iron (earth-abundant metal with non-elevated cost and significant catalytic activity).[1] In addition, amino groups can enhance the interaction capacity of the MOF with other materials and eventually play the role of nitrogen source for the fabrication of N-doped porous carbons derived from MOF carbonization. On the other hand, polyoxometalates (POMs) are polyatomic anions that consist of three or more transition metal atoms linked together by oxygen atoms, exhibiting attractive electrocatalytic properties.[2] Taking in account the favorable features of the two presented materials, the development of efficient strategies to the combination of MOF and POM materials into nanocomposites is very desirable.
In this work, an easy one-step approach to the preparation of PMo_{12}@Fe-MIL-101-NH_2 and $PMo_{11}V$@Fe-MIL-101-NH_2 composites has been explored. This approach is based on an 'in situ' solvothermal synthesis of Fe-MIL-101-NH_2 in presence of the corresponding and previously prepared POM material (**Scheme 1**). Hexahydrate iron(III) chloride and 2-aminotherephtalic acid have been used as Fe source and organic ligand, respectively. These MOF precursors were mixed with the corresponding POM in DMF and transferred to an autoclave and heated at 110 °C for 24 h. The presence of POM into the resulting material has been confirmed by FTIR-ATR, while the absence of peaks assignable to POM in the XRD patterns suggests that they are mainly located in the inner cages of the MOF. Moreover, metal-containing N-doped porous carbon materials have been obtained by controlled pyrolysis of the previously synthetized POM@MOF composites. For the complete characterization of the different materials, diverse analysis techniques (XRD, FTIR-ATR, SEM/EDX, ICP) have been employed.



Scheme 1: 'In situ' one-step synthesis of POM@MOF nanocomposites.

Acknowledgements: The work was funded by Fundação para a Ciência e a Tecnologia (FCT)/MEC under FEDER under Program PT2020 - project UID/QUI/50006/2013-POCI/01/0145/FEDER/007265 and project "UniRCell", with the reference POCI-01-0145-FEDER-016422.

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Synthesis of diketopyrrolopyrrole derivatives for dye-sensitized solar cells

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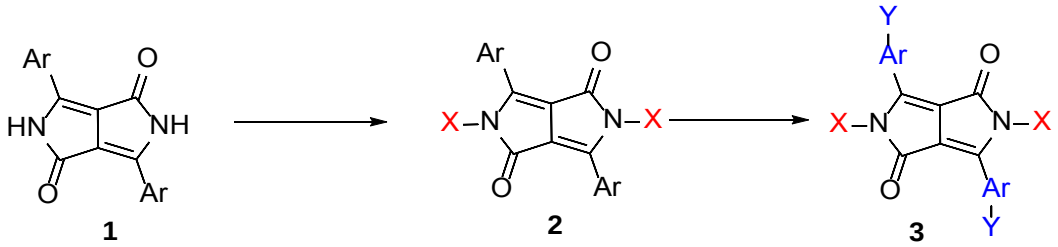
The construction of dye-sensitized solar cells (DSSCs) requires a photostable organic dye that absorbs a large part of the visible light or a mixture of dyes absorbing in different regions of the visible spectrum.[1]

In the last years, the bicyclic diketopyrrolopyrrole (DPP) system has been increasingly used as an active building block in materials (polymers and small molecules) used in solar cells. That is mainly due to its high environmental stability (mainly photostability) and charge transfer capabilities. Despite its infancy, the results already achieved have shown the tremendous potential of diketopyrrolopyrroles in solar cells.[2,3]

In this work, we report the synthesis of DPP derivatives functionalized both at the NH groups and at the aryl substituents in order to obtain compounds of types **2** and **3** (**Scheme 1**). All new compounds were characterized by NMR and MS.



Scheme 1. Functionalization of DPP at the NH groups and at the aryl substituents

Acknowledgements: Thanks are due to Fundação para a Ciência e a Tecnologia (FCT) for the financial support to project PTDC/QEQ-QOR/6160/2014 and the QOPNA research project (FCT UID/QUI/00062/2013) through national funds and where applicable co-financed by the FEDER, within the PT2020 Partnership Agreement, and also to the Portuguese NMR Network.

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Ferrocene Modified Bakelite

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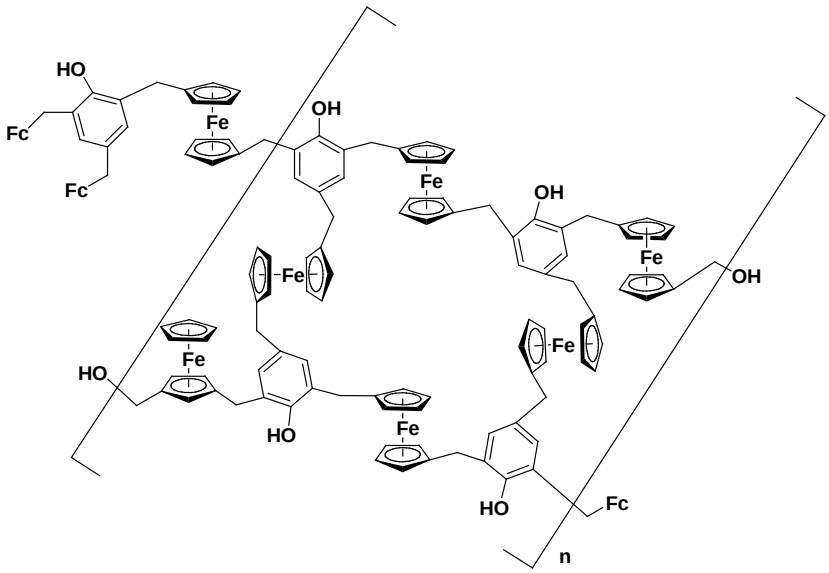
Phenol formaldehyde resins (PFR) are synthetic materials obtained by condensation of phenol or substituted phenols with aldehydes or formaldehyde, which were first produced in the XIX century. In 1909, Baekeland made the first plastic (bakelite) and PFR was the first commercial and synthetic resin (plastic) produced industrially.[1] Although PFR are still used for production of some synthetic materials, since late 1940 they became largely replaced by other polymers. Nowadays, they are used in about one tenth of all plywood and particle board industries. However, there is a tendency to substitute some reagents in PFR synthesis by other compounds in order to reduce their cost or toxicity (e.g. lignin in place of phenol).[2]

We came to the idea to prepare ferrocene modified bakelite for potential electrochemical applications. After several attempts, we managed to produce a polymer whose structure consists of a ferrocene unit introduced into bakelite (**Scheme 1**). The obtained compound is a crystalline polymer with low diffraction angle (16º on XRD) and currently characterized by solid state NMR and IR spectroscopy.



Scheme 1: Ferrocene Modified Bakelite.

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ENVIRONMENT CHALLENGES
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Environmental fate and behaviour of (2-hydroxy-4-methoxyphenyl)-(2-hydroxyphenyl)-methanone in aqueous solution

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Ultraviolet (UV) filters are the primary components of many personal care product formulations and pharmaceuticals, as they absorb, reflect or scatter UV radiation, consequently protecting human skin and health from its nefarious effects. They are now part of a new class of environmental contaminants, named emerging pollutants (EPs), a group whose compounds have not yet been the focus of thorough and environmentally-centered research, are presumed or expected to display potential eco-toxicological implications, and are not yet bound by water-quality regulations.[1-4]

There are more than 40 UV filters currently used and regulated worldwide, the vast majority of which are synthetic organic, with two inorganic compounds currently regulated.[5] The premise for its widespread application in numerous commercial products, besides cosmetics, is predicated on its assumed general stability. However, it is known that these compounds experience degradation, disinfection-induced, through contact with disinfection agents such as chlorine, and also photo-induced, through exposure to UV radiation.[6-9]

Degradation reactions are a topic of paramount significance in regards to these compounds, since these will yield by-products with potentially concerning eco-toxicological profiles: such as disinfection by-products (DBPs), that is, halogenated structures of the parental compounds as well as halogenated structures subsequent to the degradation of the original compound; or by-products of photo-degradation (photolysis and photo-isomerization), such as free radicals or other highly reactive particles, which may penetrate the skin and damage cells and tissues, but also photo-isomers, which will no longer exhibit the UV-protective characteristics of the filters themselves.[1,2,7,9,10]

In an ongoing project, the environmental fate of EPs that are present in natural waters and undergo chlorine disinfection, is being investigated. In this communication, the degradation reactions of the UV filter (2-hydroxy-4-methoxyphenyl)-(2-hydroxyphenyl)-methanone (known as benzophenone-8, BP-8) in aqueous solution will be presented and discussed, including the kinetic parameters and degradation mechanisms. Moreover, the formation of DBPs will be ascertained.

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Environmental fate and behaviour of caffeine in aqueous solution

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The 3,7-dihydro-1,3,7-trimethyl-1H-purine-2,6-dione, or as it is trivially known, caffeine, has gathered much attention in the last years, given its massive use and frequent detection in the aquatic, environmental compartments, from waste water treatment plant (WWTP) effluents to other superficial, natural or artificial water courses, such as swimming pools, rivers and lakes.[1,2]

Caffeine, is a natural alkaloid, present in countless plants, namely tea, coffee and cacao, as the most famous. Although it represents a naturally-occurring compound, caffeine's rising levels in the aquatic ecosystems are essentially attributed to human action.[2] There are several studies focused on the detection of caffeine in natural waters, both superficial or ground water courses, and overall the compound is reported amongst the most prevalent and prominent worldwide.[1]

The most relevant sources of caffeine consumption, are naturally coffee, tea, soft or energy drinks, but it is also found in significant proportions in chocolate, pastries and dairy-related desserts.[2] Additionally, caffeine is also often associated with common active principles in pharmaceutical formulations, since it is known to enhance the analgesic action of pain medication, and to be an important cardiac, cerebral and respiratory stimulant, besides being also used as a diuretic.[3]

Despite its continuous detection in natural and artificial, superficial and ground water courses, the fate and behaviour of caffeine has seldom been the subject of thorough and comprehensive environmental research.[3] Consequently, it is paramount that caffeine's degradation reactions, both disinfection-induced and photo-induced, can be evaluated and potential by-products identified.

In an ongoing project, the environmental fate of emerging pollutants (EPs) that are present in natural waters that undergo chlorine disinfection, is being investigated. In this communication, the degradation reactions of caffeine in aqueous solution will be presented and discussed, namely the kinetic parameters and degradation mechanisms. Moreover, the formation of disinfection by-products (DBPs), particularly chlorinated, will be ascertained.

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Theoretical Characterization of Brown Carbon Chromophores Generated by Catechol Heterogeneous Oxidation

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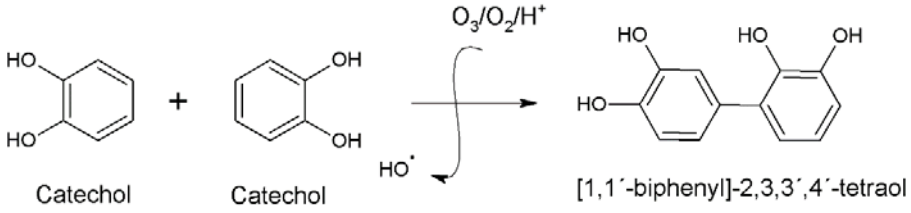
The effect of light-absorbing atmospheric particles (as black carbon, BC) have been extensively studied and incorporated into climate models.[1] However, there is significant differences between model predictions and measured data on aerosol absorption and radiative forcing. These discrepancies are explained by recent studies that show that optical absorption by organic aerosol components (also known as Brown Carbon, BrC) also occurs, and so, should be included in radiative forcing models.[1b]

BrC constituents are present both in primary aerosols emitted from combustion sources, and in secondary organic aerosols (SOA). However, little is known regarding the relationship between optical properties and BrC's chemical compositions, as their optical properties and chemical composition evolve significantly, due to oxidation, solar irradiation and changes in temperature.[1c] This obviously results in high uncertainties in predicting their climate effects.

Dihydroxybenzenes such as catechol are the most common gas-phase organic constituents (~50 ppbv) resulting from biomass burning, pyrolysis and combustion.[1c] Cloud water collected from brown clouds also contains molecules as catechol, substituted with different groups. The surfactant properties of these species favor their accommodation at interfaces of aerosols, where they are prone to undergo photooxidation.[1c]

Given this, we have characterized the optical properties of catechol (**Scheme 1**) and known heterogeneous oxidation products (under humid tropospheric conditions). To this end was used a theoretical approach, based on density functional theory (DFT).[2] While experimental characterization requires a number of steps, as synthesis, separation/purification, and characterization, a theoretical calculation can be carried out more quickly and less expensively than experimental methods.[2] While catechol absorb in the UVB region (5% of solar radiation), we have identified several polyaromatic derivatives with significantly higher absorption and that absorb in the UVA region (95% of solar radiation). Thus, this approach allowed us to obtain information that can be useful for radiative forcing modelling, and helped us to identify harmful SOAs.



Scheme 1: Example of the heterogeneous oxidation of catechol.

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Direct conversion of carbohydrates into 5-ethoxymethylfurfural (EMF) and 5-hydroxymethylfurfural (HMF) catalyzed by oxo-molybdenum complexes

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The decrease in fossil fuel reserves and the resulting high price of petrochemicals has imposed the search for renewable resources as alternatives to fossil fuels resources. Biomass is the most attractive alternative and is considered as a sustainable raw material for the production of many chemicals and fuels.
In continuation of our research on the use of oxo-molybdenum complexes as efficient catalysts for organic chemistry,[1,2] in this work we report the first methodology for one-pot synthesis of 5-ethoxymethylfurfural (EMF) and 5-hydroxymethylfurfural (HMF) from various carbohydrates catalyzed by oxo-molybdenum complexes. The best EMF yields (53-60%) were obtained using a mixture of ethanol/THF (5:2) catalyzed by $MoO_2Cl_2(H_2O)_2$ at 120ºC, after 17 h (Figure 1). This dioxo-molybdenum complex also promoted the synthesis of EMF from other carbohydrates such as inulin and sucrose. The selective conversion of fructose into HMF was achieved in good yield (75%) from fructose using $MoO_2Cl_2(H_2O)_2$ in DMSO at 120ºC after 30 minutes (**Figure 1**). This novel methodology has the advantages of using an inexpensive, environmental friendly and air stable catalyst with an easy preparation.

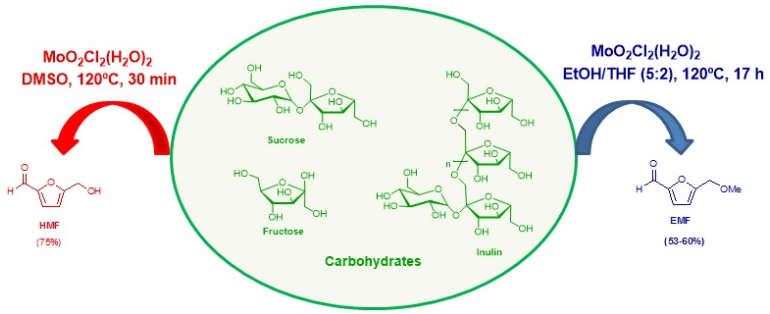

Figure 1: Direct conversion of carbohydrates into EMF and HMF catalyzed by $MoO_2Cl_2(H_2O)_2$.

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New insights about *Citrus* genus revealed by infrared spectroscopy

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Citrus trees are one of the most cultivated plants around the world with high economic impact. The wide sexual compatibility among relatives gave rise to a large number of natural and artificial hybrids which are difficult to discriminate. This work sought to explore the ability of infrared spectroscopy to discriminate among *Citrus* species and/or hybrids and to contribute to the elucidation of its relatedness. Adults leaves of eighteen distinct *Citrus* plants belonging to eleven species and/or hybrids (*Citrus reticulate*; *Citrus sinensis*; *Citrus medica*; *Citrus japonica*; *Citrus paradisi*; *Citrus limonia*; *Citrus aurantifolia*; *Citrus latifolia*; *Citrus microcarpa*; *Citrus limon* and *Citrus reticulata* x *Citrus sinensis*) were included in this work. Near and mid infrared spectra of the leaves were acquired immediately after harvesting and after a drying period of one month**.** Spectra were modelled by principal component analysis (PCA) and partial least squares discriminant analysis (PLSDA). The scores of the PLSDA model were further used for clustering purposes towards the elucidation of the samples relatedness. Both infrared techniques revealed a high potential for the discrimination of the species and/or hybrids included in this work (78.5-95.9 % of correct predictions) being the best results achieved with near infrared spectroscopy and air-dried leaves (95.9%). Regarding species and/or hybrids relatedness, spectra were clustered in two main groups, one including *C. latifolia*, *C. aurantifolia*, *C. japonica* (through near infrared spectroscopy) and *C. medica* (through mid infrared spectroscopy) and another including the remaining species. Infrared spectroscopy was able to successfully discriminate several *Citrus* species and/or hybrids. Our results also contributed to enhance the insights about the *Citrus* species and/or hybrids included in this work. Despite the benefit of including additional samples, the results herein obtained clearly pointed infrared spectroscopy as a reliable technique for *Citrus* species and/or hybrids discrimination.

Acknowledgements: This work received financial support from the European Union (FEDER funds POCI/01/0145/FEDER/007265) and National Funds (FCT/MEC, Fundação para a Ciência e Tecnologia and Ministério da Educação e Ciência) under the Partnership Agreement PT2020 UID/QUI/50006/2013. Ricardo Páscoa was supported by a postdoctoral grant (SFRH/BPD/81384/2011) and Clara Sousa was funded through the NORTE-01-0145-FEDER-000024 – "New Technologies for three Health Challenges of Modern Societies: Diabetes, Drug Abuse and Kidney Diseases". Thanks are due to Eng. Paulo Lúcio Gomes for providing *Citrus* leaves.

Enhancing alkane oxidation using Co-doped SnO_2 nanoparticles as catalysts

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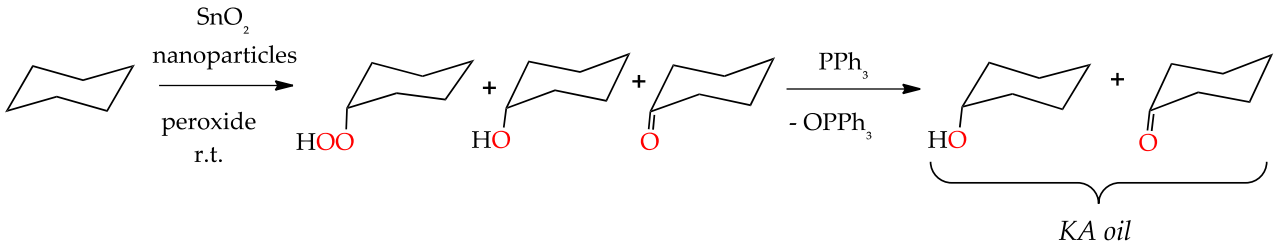
The development of sustainable catalytic processes for the oxidation of abundant and inexpensive alkanes into high-added-value products remains a great challenge for both academic and industrial purposes. A novel eco-friendly KA oil synthesis at room temperature (up to 25% yield) via solvent-free cyclohexane oxidation using $Sn_{1-x}Co_xO_{2-\delta}$ (x = 0, 0.01 or 0.05) nanoparticles as catalyst (TON up to 2×10^3) is here reported. (**Scheme 1**) These nanoparticles are the first SnO_2-*based* material able to catalyze the oxidation of alkanes.[1]

Effects of the type of oxidant, of Co content, oxidant-to-nanocatalyst molar ratio, amounts of nitric acid, of solvent and of alkane, and reaction time, on the catalytic reaction were investigated and discussed.

The most active nanocatalyst was $Sn_{1-x}Co_xO_{2-\delta}$ NPs with a Co/Sn ratio of 5%, using TBHP as oxidant in acidic medium, allowing an easy recovery and reuse, at least for five consecutive cycles, maintaining high selectivity concomitant with 92% of its initial activity.

The oxidation appears to proceed mainly via radical mechanisms involving both carbon-centred and oxygen-centre radicals, as shown by radical trap experiments, allowing us to propose a mechanistic pathway.



Scheme 1: Cyclohexane oxidation to KA oil catalyzed by $Sn_{1-x}CoxO_{2-\delta}$ (x = 0, 0.01 or 0.05) nanoparticles.

Acknowledgements: This work has been supported by the Fundação para a Ciência e a Tecnologia (FCT), Portugal (FCT project PEst-OE/QUI/UI0100/2013). BGMR is grateful to FCT for the PhD fellowship (SFRH/BD/52370/2013) of the CATSUS PhD program.

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Fruit peels as low cost sorbents to remove priority pollutants from water

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The sustainable management of water resources in a context of population growth, economic development and climate change is currently a challenge. One of the main stressors for water quality is the release of industrial and mining wastewaters, containing contaminants such arsenic, lead, mercury and cadmium, which present toxicity even at low levels and a persistent character in the environment.

Currently, there are no cost-effective water decontamination methods capable of removing these elements, which are classified as priority hazardous substances by the US Agency for Toxic Substances and Disease Registry[1] and by the European Water Framework.

Biosorption, namely the use of sorbents developed from agroindustry wastes and by-products, largely available and with no commercial value have emerged as a promising alternative for water decontamination[2]. However, till date most of works followed an idealistic approach, i.e. focused on the removal of a single contaminant from synthetic solutions with extremely high and unrealistic concentrations.

In this work fruit peels were applied in the removal of priority pollutants (As, Cd, Hg and Pb) from contaminated water. The biosorbents were used with no chemical modification, keeping it an economic process, and evaluated under realistic conditions (environmental relevant concentrations of pollutants, short sorption times and multi-contaminant systems). The influence of drying process in the biosorbent performance was also assessed.

Results showed that apple and pear peels (0.5 g/L, d.w) are extremely efficient biosorbents of Hg and Cd, achieving more than 80% of removal in only 6 hours of contact. The biosorbents exhibited a similar selectivity toward the target metals: Hg > Cd >> Pb > As. Air-dried peels performed better than freeze-dried peels in removing Hg.

Overall, it can be concluded that fruit peels may be used to reduce the levels of priority pollutants in water, in a simple, cost-effective and environmentally friendly way. The proposed methodology will allow the reuse of treated water for further purposes, with lower requirements of water quality (e.g. agriculture irrigation, recreational uses or industrial applications).

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Mecanochemistry for the of sustainable synthesis of porphyrins

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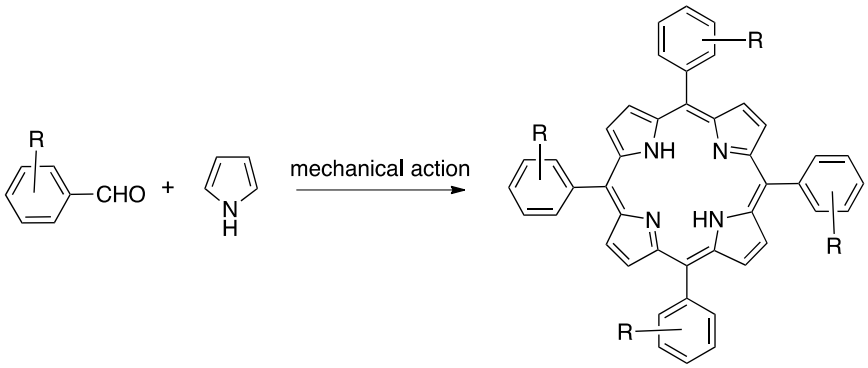
The recognition that porphyrins had essential functionalities in nature stimulated the interest in multiple scientific domains, which comprise analytical uses, dye-sensitized solar cells, molecular electronics and non-linear optics, sensors of small molecules, catalysts in oxidation and photo-oxidation reactions, and several biological applications such as photodynamic therapy for cancer treatment, imaging and boron neutron-capture therapy. The remarkable popularity and versatility of porphyrins and their derivatives relies in a great length on the development and improvement of synthetic strategies over the years that make possible the huge availability of these compounds.[1]
The classical methodologies for the synthesis of porphyrins involve the use of large quantities of halogenated solvents and/or toxic oxidants being far from be sustainable processes adequate to the new philosophy of organic chemistry. The development of novel technologies, such as microwave, allowed the exploration of new reaction conditions that in the case of the synthesis of porphyrins culminate with the synthesis of porphyrins using water as solvent and oxidant, improving the sustainability of the process to levels never attained in this area.[2]
Herein, we present the synthesis of porphyrins under mechanical action, **Scheme 1**, and the discussion of the contribution for the improvement of the sustainability of the porphyrin synthesis.



Scheme 1: Synthesis of *meso*-substituted porphyrins under mechanical action

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Long Range Theoretical Study On LiH_2

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The lithium chemistry has received a great attention in recent years due to the importance that LiH molecules and its ionic variants can have in the primordial universe.[1,2] The reaction LiH + H → Li + H_2 is considered to contribute to LiH depletion, while the hydrogen-exchange reaction LiH + H → LiH + H leads to the retention of LiH in this process.
In this work we report our recent studies on the long-range interactions between the reactants of those reactions. For the LiHH system, the main contribution for the long-range interactions is the dispersion interaction. To modeling the dispersion interaction, the parallel and perpendicular values of the polarizabilities, α, for the diatomics (H-H and Li-H) have been calculated and fitted (see **figure 1**).

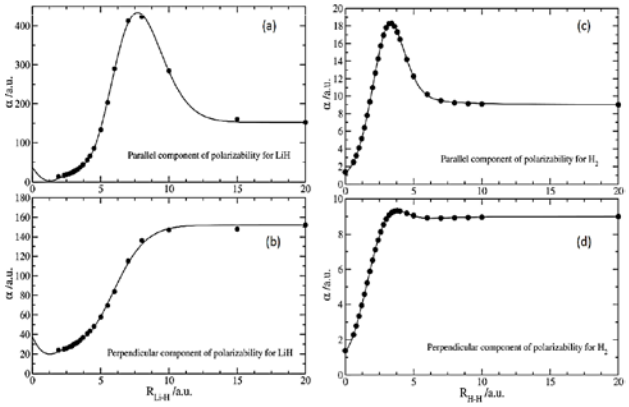
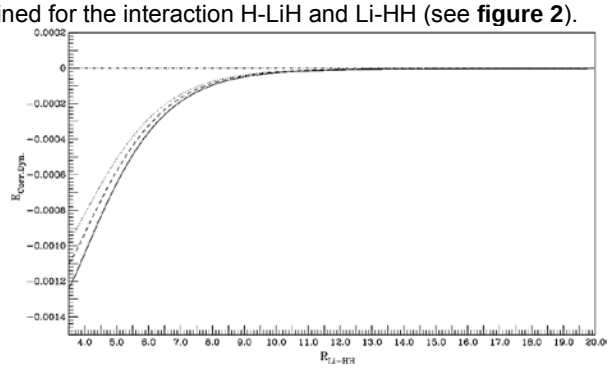


Figure 1: Parallel and perpendicular components of polarizabilities, α, for LiH ((a) and (b)) and H_2 ((c) and (d)). Solid lines are the functional form fit to the ab initio calculations (solid dots).

The dispersion interaction coefficients C_6 have been computed as C_8 and C_{10} have been semiempirically estimated from C_6 using a universal correlation. The total dispersion interaction was obtained as a function of C_n and inter-atomic distances.[3] The dynamical correlation energy has been obtained for the interaction H-LiH and Li-HH (see **figure 2**).

Figure 2: Total dynamical correlation energy for the interaction Li-HH at 0º, 45º and 90º.



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Camellia japonica cultivars discrimination through FTIR-ATR

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Camellia japonica cultivars are very difficult to discriminate due to their small phenotypic characteristics variation among species members. Also, their genotypic characteristics are very similar making difficult its discrimination. This work aims to explore the ability of Fourier transform infrared spectroscopy with attenuated total reflectance (FTIR-ATR) to discriminate among 10 distinct cultivars of C. japonica. Adult leaves of 23 distinct plants belonging to 10 cultivars ('sophia'; 'etoile polaire'; 'duchesse de nassau'; 'augusto leal gouveia pinto'; bella portuense'; bella milanese'; 'conde do bomfim'; 'mathotiana'; 'maria irene' and 'roi des belges') were included in this work. FTIR-ATR spectra of the leaves were acquired immediately after harvesting and after a drying period of 6 weeks. Spectra were modelled by partial least squares discriminant analysis (PLSDA). The scores of the PLSDA model were further used for clustering purposes towards the elucidation of the samples relatedness. The total of correct predictions obtained through the PLSDA model were above 85% being the best results achieved with the dried leaves. Despite the benefit of including more cultivars and/or robust the included ones with additional samples from distinct plants, the results obtained in this work clearly shown the ability of this infrared based technique to discriminate C. japonica cultivars.

Acknowledgements: This work received financial support from the European Union (FEDER funds POCI/01/0145/FEDER/007265) and National Funds (FCT/MEC, Fundação para a Ciência e Tecnologia and Ministério da Educação e Ciência) under the Partnership Agreement PT2020 UID/QUI/50006/2013. Ricardo Páscoa was supported by a postdoctoral grant (SFRH/BPD/81384/2011) and Clara Sousa was funded through the NORTE-01-0145-FEDER-000024 – "New Technologies for three Health Challenges of Modern Societies: Diabetes, Drug Abuse and Kidney Diseases".

New Green Solvents for water purification

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One of the major problems of modern society is to be able to provide clean water to everyone, or in another words, to develop efficient wastewater treatment processes and simultaneously reduce the hazardousness of the current pollutants present in different kinds of wastewater as a result of domestic, industrial and agricultural water activities.[1] Recently, a class of new ionic solvents, deep eutectic solvents (DESs), has been emerging as an easy-to-prepare, inexpensive, environmentally-benign media having potential for applications in various areas of chemistry.[2] DESs succeed as analogues of Ionic Liquids (ILs), which are solvents that have been gaining a lot of attention especially due to their solvation properties and the capacity to fine tune these properties, as a consequence enhancing extraction efficiencies and selectivities.[3]

Inspired by this novel advanced class of green ILs, the aim of this work focuses on the development of new deep eutectic solvents (DESs), as cheap extractants for the removal of pollutants, such as pesticides and pharmaceuticals, from water environments. Different classes of hydrogen bond donors and acceptors have been used to develop hydrophobic DES and phase diagrams will be presented and discussed. In particular, two different families of DESs, one based on natural neutral ingredients (DL-Menthol and natural organic acids) and the other based on quaternary ammonium salts and organic acids were prepared. Finally, extraction efficiencies will be presented and DES's recycling evaluated.

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Iridium(I) Catalyzed C(sp2)-H activation and intramolecular addition to alkenes and alkynes

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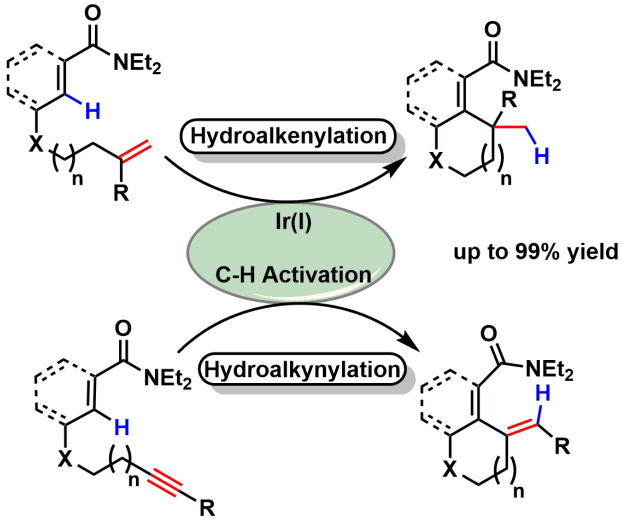
C-H bond activation is an active field of research because it enables the access to very challenging scaffolds without need of substrate pre-activation using shorter and atom economical protocols. Low valence transition metals (Rh(I), Ru(0), Co(0), Ni(0), Pd (0), etc.) are widely used to perform catalyzed C-H functionalizations assisted by heteroatom containing directing groups.[1]

The intermolecular Ir(I) catalyzed hydroalkenylation and hydroalkynylation is well known using different directing groups and scaffolds, however the intramolecular version is not yet explored.[2]

Herein is presented a cationic Ir(I) catalyzed C(sp2)-H activation-hydroalkenylation or hydroalkynylation process yielding a new series of cyclic scaffolds including the enantioselective formation of quaternary centers.



Scheme 1: Ir(I) catalyzed C(sp2)-H activation followed by intramolecular hydroakenylation or hydroalkynylation

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The denitrification pathway of *Marinobacter hydrocarbonoclasticus*

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Anthropogenic emissions of nitrous oxide (N_2O) to the atmosphere are one of the main concerns of the 21st century.[1] Nitrous oxide is a very potent greenhouse gas that can be detoxified by nitrous oxide reductase (N_2OR), in a metabolic pathway named denitrification, during which nitrate is reduced, via nitrite, to nitric oxide and nitrous oxide, and lately to the inert dinitrogen gas. Part of of the atmospheric N_2O arises from incomplete denitrification that occurs in acidic environments.[2]

N_2OR has two copper centers, CuA the electron transfer center and CuZ the catalytic center. CuZ is a tetranuclear copper-sulfide center, unique in biology that has been isolated as CuZ*(4Cu1S) or as CuZ(4Cu2S) (**Figure 1**). [3, 4]

The work presented here, includes a study of the effect of environmental acidification on the denitrification pathway, using *Marinobacter hydrocarbonoclasticus*, as a model of marine organisms. The pH effect on the growth cultures were evaluated by the gene expression profiling, quantification of denitrification metabolites, as well as measurement of the activities of enzymes involved in denitrification pathway. The results indicate an accumulation of nitrite and a very low rate of N_2O reduction by the whole-cells at low pH.

Furthermore, the effect of growth pH on nitrous oxide reductase was investigated. The enzyme isolated from growths performed at different pH was biochemically and spectroscopic characterized. Our data shown that N_2OR isolated from acidic cultures presents its catalytic center as CuZ*(4Cu1S), which exhibits high activity *in vitro*.

This study reveals a clue to identify the active form of nitrous oxide reductase *in vivo*, as well as pin-points possible molecular mechanisms involved in the release of nitrous oxide due to environment acidification.

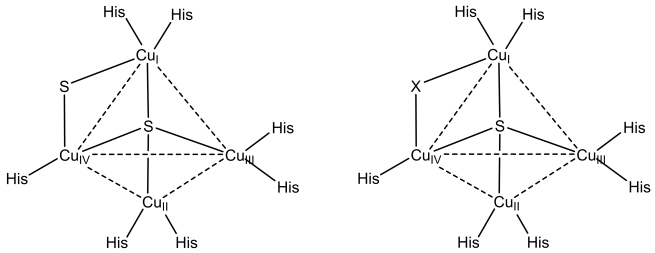

Figure 1: Two forms of the catalytic center of N2OR: CuZ(4Cu2S) and CuZ*(4Cu1S)

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Environmental fate and behaviour of paracetamol in aqueous solution

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The compound N-(4-hydroxyphenyl)-ethanamide, commonly known as paracetamol, is one of the most prominent analgesic and antipyretic pharmaceuticals used worldwide in order to treat fever and localized or general physical pain. Its structure is somewhat analog to that of other organic pollutants, with a central benzenic ring substituted with a hydroxyl group and also an unsaturated side-chain in the opposite position.[1,2]

Analgesics and anti-inflammatory compounds like paracetamol, represent quite a significant role in the list of emerging pollutants (EPs), which also includes human and veterinary anti-microbials, anti-epileptics, psychiatric drugs and even personal-care products like sunscreens (pharmaceuticals and personal care products - PPCPs). EPs are of paramount importance and relevance, since they represent a large group of compounds that are believed to display potentially threatening eco-toxicological effects, have not been the subject of meticulous and comprehensive research in the context of their fate and behavior in the aquatic ecosystems, and are not yet covered by water-quality regulations.[3]

EPs are biologically active compounds, and they exhibit a significant proclivity towards persistence and accumulation in the aquatic environment and food chain.[3] In parallel to the harmful characteristics of EPs, the compounds are known to experience degradation and transformation within the aquatic environment, yielding a series of potentially more threatening compounds, such as disinfection-induced or photo-induced by-products.[3,4] Additionally, eco-toxicological data remain scarce and still converge solely on the most predominantly prescribed and used drugs worldwide.[5]

In an ongoing project, the environmental fate of EPs, in particular PPCPs that are present in water and undergo chlorine disinfection, is being investigated. In this communication, the degradation reactions of paracetamol in aqueous solution will be presented and discussed, namely the kinetic parameters and degradation mechanisms. Moreover, the formation of disinfection by-products (DBPs), particularly chlorinated, will be ascertained.

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Assessment of pharmaceuticals in the Lis River (Leiria, Portugal)

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A wide spectrum of pharmaceuticals have been detected in the aquatic environment, mainly in surface and ground waters.[1] Different sources of environmental contamination have been identified though Wastewater Treatment Plants (WWTP) are recognized as the main route by which pharmaceuticals reach the aquatic environment due to their incomplete elimination during sewage treatment.[2]

The Lis river suffers a high impact of anthropogenic activities, such as agriculture, industrial activities (e.g. tannery, mineral mining) and livestock production, mainly piggeries. Two WWTPs also discharge their effluents into the river. Thus, pharmaceuticals belonging to non-steroidal anti-inflammatory drugs (NSAIDs)/analgesics, antibiotics, and psychiatric drugs were the target of the present study. Five points in the stretch of the river as well as the influent and the effluent of the two WWTPs that discharge into the Lis River were monitored. Sampling campaigns were performed monthly, embracing eleven sampling periods in the Lis River from August 2013 to June 2014, and nine in the WWTPs from October 2013 to June 2014. A total of 91 samples were analyzed.

Six pharmaceuticals and one metabolite were never detected, neither in river water nor in wastewaters, namely enrofloxacin, ofloxacin, sulfamethoxypiridazine, sulfadimethoxine, acetylsalicylic acid, nimesulide, and the metabolite norsertraline. A total of 20, 21, and 23 out of 33 pharmaceuticals were detected in the Lis River, in the WWTPs effluent, and in the WWTPs influent, respectively. Pharmaceuticals belonging to NSAIDs/analgesics and psychiatric drugs were the most frequently detected.

NSAIDs/analgesics were the therapeutic group with a high contribution to the total mass load of pharmaceuticals entering the Lis River, followed by psychiatric drugs, and antibiotics. WWTP effluents contributed with a total mass load of pharmaceuticals into the Lis river between 470 and 2317 mg/d/1000 inhabitants. An increase in the concentration of pharmaceuticals was noticed downstream of the WWTPs.

In Lis River, carbamazepine, fluoxetine, ibuprofen, ketoprofen, and salicylic acid had 100% of detection frequency, followed by acetaminophen (98%). Antibiotics showed a low detection frequency, not exceeding 18% (azithromycin).

It was possible to detect pharmaceuticals in all the extension of the watercourse, including in the source of the river though usually the highest concentrations were found in the lower part of the river, when it is getting near to the mouth. Different possible sources of contamination of the Lis River were identified, such as WWTP effluents, untreated wastewaters, and livestock production. In general, these were related with the metabolism/excretion of pharmaceuticals by humans or animals, showing a high impact of anthropogenic activities in the Lis River.

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Ferromagnetic particles for the removal of arsenic from water

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Arsenic is one of the most toxic elements introduced in the environment by natural and anthropogenic sources. The pollution arising from the presence of this element in waters presents serious environmental problem due to their toxicity, persistent character in the environment and bio-accumulation and bio-amplification along the food chain. [1]
Consequently, in the last decades have been an increasing interest in the development of new methodologies for reduce the levels of arsenic contamination in the aquatic systems. The sorption method have been widely applied for the treatment of contaminated waters as a simplest, cost-effective and user friendly technology. And a wide variety of sorbents have been developed in order to obtain materials with a high efficiency and selectivity to reduce the levels of this contaminant. Advances in nanoscale science and engineering are providing opportunities to develop more cost effective and environmentally acceptable water purification processes. [2]
This communication presents magnetic sorbents for the uptake of As from waters. Magnetic materials are of increasing interest as an important class of sorbents for removal of water contaminants, not only because they can be easily separated from solution by applying an external magnetic field, but also due to the possibility of controlling the morphological characteristics and the ability for surface modification, thus conferring better efficiency to these materials. In this context, we prepare ferrites such as $MnFe_2O_4$, $CoFe_2O_4$ and Fe_3O_4 for removal of arsenic from waters. Batch stirred tank experiments were carried out by contacting a volume of solution with known amounts of particles, aiming to investigate the effect of sorbent dose, pH and salinity. The sorbents tested showed high performance for capture arsenic in different matrices and present a potential treatment method at industrial scale. In addition, the process requires small amounts of sorbents to decrease the As concentration to values lower than recommended values for drinking water and allows fast separation of the sorbents from water by applying an external magnetic field.

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Enantioselective Palladium-Catalyzed [3+2] and [4+3] Cycloaddition Reactions

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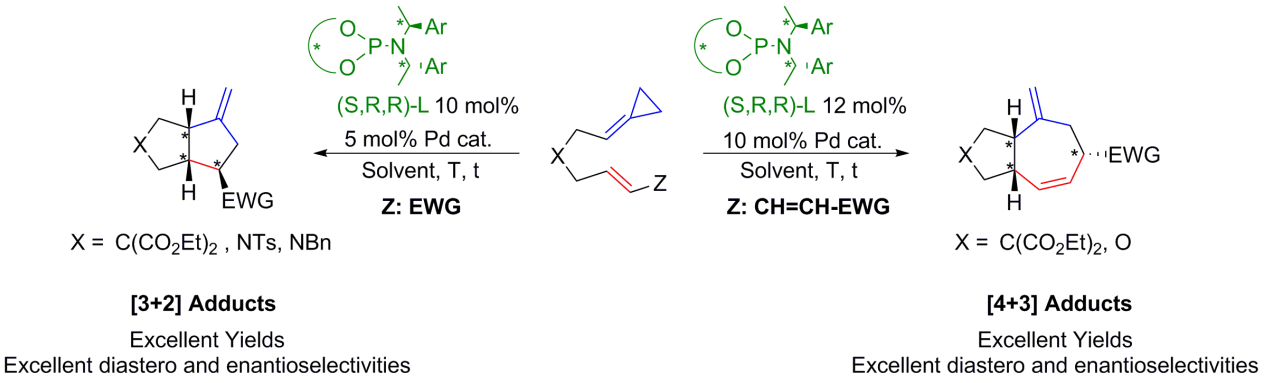
Transition metal catalyzed cycloaddition reactions are particularly attractive synthetic methods that allow for the rapid assembly of complex hetero-and carbo-cyclic systems from very simple acyclic precursors. In this context, during the last years our group developed racemic variants of novel palladium-catalyzed cycloadditions using alkylidenecyclopropanes as three-carbon components.[1,2] Herein, we will show our efforts on the development of enantioselective variants of these processes by using chiral phosphoramidite-based Pd catalysts (**scheme 1**), thus providing an asymmetric entry to a variety of 5,5- and 5,7-fused bycyclic systems, which can be obtained with good yields and moderate to excellent diastereo- and enantio-selectivities.



Scheme 1: Novel asymmetric Palladium catalyzed [3+2] and [4+3] cycloaddition reactions.

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Magnetic deep eutectic solvents in refinery desulfurization: comparison between liquid-liquid extraction and ultrasound assisted liquid-liquid microextraction

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Sulfuric compounds in fossil fuels have become one of the main sources of environmental pollution. Terms like “deep desulfurization” and “ultra-low sulfur fuel” became very important in order to follow the strict regulations that have been legislated around the world. Currently, the sulfur content on the highway fuels is limited to less than 10 ppm, in many countries.[1]

Hydrodesulfurization is the conventional industrial process for removing sulfur from fossil fuels. However, its drawbacks, such as, high cost of operation and low effectiveness removing refractory heterocyclic sulfur compounds (e.g. dibenzothiophene) are prompting the development of innovative complementary technologies for fuel oil desulfurization.[2] Extractive desulfurization (EDS) is one of the most promising desulfurization processes due to its simple operation and low cost. Nevertheless, the commonly used extractants are organic solvents, which brings environmental and health concerns due to their volatility and flammability. Ionic liquids (ILs) have been widely explored as alternative solvents for sulfur removal, and although they have many desirable properties, such as non-flammability, non-volatility and high tunability, they also present major disadvantages like, high cost and, in some cases, toxicity. To overcome these limitations, Deep Eutectic Solvents (DESs) have been proposed as alternative to ILs, since DES can be seen as a low cost and more environmentally friendly ionic solvent. [3,4]

In this work, a series of $FeCl_3$-based deep eutectic solvents have been synthesized and studied as key players for sulfur removal using two different extractive approaches: simple liquid-liquid extraction (LLE); and ultrasound assisted liquid-liquid microextraction (UALLME). In both cases, the extraction of thiophene and dibenzothiophene from model oils with sulfur content of 500 ppm was considered. It is important to note that, in the case of UALLME, the magnetic property of the synthetized DESs was crucial in the facile separation of the two phases. For the most promising systems, the recycling and re-using of the DESs is under study.

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Effect of the activated carbons characteristics on phenolic compounds removal from aqueous media

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Activated carbons (AC) are widely used in different applications. Depending on the preparation conditions and precursors, they can exhibit exceptional characteristics, such as highly developed pore structures, high adsorption capacities and versatility for adsorbing both organic and inorganic compounds, with the possibility to be regenerated and reused [1,2]. Most of the available activated carbons are derived from lignocellulosic precursors by chemical activation or by physical activation with carbon dioxide or water vapour. The search for efficient AC remains very active, and new precursors and methods of preparation have been tried to reduce the cost of AC production. Also, a diversity of AC post treatments have been tested to improve textural and chemical characteristics.

Phenolic compounds are frequently found in effluent wastewater arising from many chemical industries. Particularly, phenol is a weak acid that causes an unpleasant odour, but more importantly it is highly toxic even at low concentration and difficult to be biodegraded. The concentration of phenolic compounds in potable waters is regulated as less than 1 μg L^{-1}. Therefore, wastewater containing phenolic compounds must be treated to reach the limits accepted for its disposal. Among the diversity of processes used, those based on adsorption are the most common and the AC are the most extensively used adsorbents for this purpose. It is generally believed that the incorporation of basic groups, such as those containing nitrogen, in activated carbons improves the adsorption of phenolic compounds from aqueous media.

The objective of this work was to evaluate the effect of the activated carbons characteristics on phenolic compounds removal from aqueous media. To achieve our purpose, a series of AC was produced, by chemical activation with KOH, at 973 K, from recycled poly(ethyleneterephthalate) (PET), a low cost precursor. We used urea as nitrogen source in order to introduce nitrogen directly during the preparation and to increase the pore volume. The AC produced from PET with KOH and urea exhibit very high micropore volumes when compared with that prepared without urea. Significant increase in the nitrogen content was also observed. Selected AC were tested for adsorption of phenolic compounds, including *p*-nitrophenol (PNP) and phenol (P), and presented excellent adsorption capacities. We found that phenolic compounds adsorption performance is complex. Nevertheless, the increase of the pore volume, in particular of the narrower microporosity, always improved the AC performance. Increasing nitrogen content also had a positive effect on the adsorption of PNP.

Acknowledgements: This work was funded by the Fundação para a Ciência e a Tecnologia (project UID/QUI/0619/2016) with National (OE) funds.

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Synergistic Gold and Enamine Catalysis: Intermolecular α-alkylation of Aldehydes with Allenamides

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Enamine-mediated organocatalysis has proven to be a invaluable tool for the asymmetric α-functionalization of carbonyl derivatives as electrophilic partners.[1] Considering the well-known ability of gold (I or III) complexes to activate C-C unsaturated bonds,[2] we envisioned that being able to combine such activation with enamine orcanocatalysis might offer the opportunity to discover new and valuable chemical transformations.

Herein, we describe our recent results on the development of new intermolecular process involving the synergistic action of an amine organocatalyst and a gold(I) catalyst. The reaction consists of the α-alkylation of aldehydes with N-allenamides, and can be even achieved in an asymmetric fashion by using Proline-derived organocatalysts (**Figure 1**).[3]

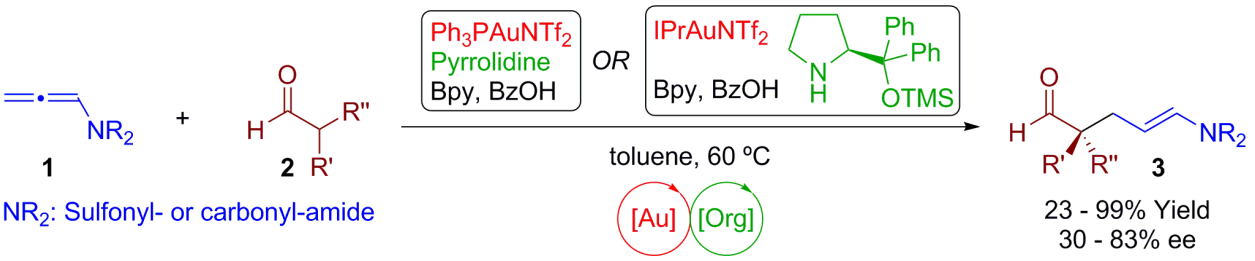

Figure 1: α-Alkylation of aldehydes with allenamides by means of dual catalysis.

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Metabolic Flexibility Towards Nutrient Availability Allows *Desulfovibrio desulfuricans* ATCC 27774 Adaptation to Ecological Niches

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Sulfate-reducing bacteria (SRB) are a diverse group of anaerobic microorganisms that obtain their energy from dissimilatory sulfate reduction [1]. The interest on SRB is extended over distinct research areas. These microorganisms have been linked to health issues since they can have a role in inflammatory bowel diseases [2]. They play an essential role in the sulfur cycle and regulate various environmentally important processes due to the production of high levels of H(2)S [3]. For example, they are involved in corrosion of metal equipment and souring of petroleum reservoirs, which can cause serious economic problems in the oil industry [4]. Furthermore, SRB's ability to reduce toxic heavy metals might be valuable for bioremediation [5,6]. The implications in such diverse areas are surely a consequence of the adaptability of the bacteria to alternative substrates, i.e. to different environmental conditions and strongly compel studies regarding the understanding of its versatile metabolism.

In this work, we studied *Desulfovibrio desulfuricans* ATCC 27774 (*D.desulfuricans*), which grows in the presence of nitrate (end product: ammonium) with higher rates and yields to those observed in sulfate containing medium (end product: sulfide). Yet, in the presence of both substrates, the cells prefer the thermodynamically less favorable, sulfate [7]. In order to identify the tools involved in the respiratory flexibility of *D.desulfuricans*, we performed a differential proteomic analysis based on 2D electrophoresis (2DE) combined with mass spectrometry (MS) based protein identification and transcript analysis.

The most remarkable difference in the 2DE maps is the high number of spots exclusively represented in the gels from the nitrate medium. Most of the proteins with increase abundance in this condition are involved in the energy metabolism and the biosynthesis of amino acids (or proteins), especially those participating in ammonium assimilation processes. qPCR analysis performed during different stages of the bacterium's growth showed that the genes involved in nitrate and nitrite reduction (*napA* and *nrfA*, respectively) have different expressions profiles: while *napA* did not vary significantly, *nrfA* was highly expressed at a 6 h time point. Nitrite levels measured along the growth curve revealed a peak at 3h, which means the initial consumption of nitrate and concomitant production of nitrite must induce *nrfA* expression.

Thus, we propose that in order to adapt to the nitrate medium, *D. desulfuricans* activates additional pathways involving amino acid and/or protein biosynthesis, whereas in the presence of sulfate the bacterium solely expresses the proteins required for its constitutive energy metabolism. The activation of alternative mechanisms for energy production, aside several N-assimilation metabolisms and detoxification processes, solves potential survival problems in adapting to a different environment and contributes to higher bacterial growth rates.

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Studying the pressure dependence of the termolecular Areaction H + O2 + M → HO2 + M

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The pressure dependence of the termolecular reaction H + O_2 + M → HO_2 + M is one of the main sources of uncertainty when modelling hydrogen combustion chemistry[1]. This reaction is initiated by a H + O_2 collision giving a long lived excited HO_2^* radical that can react to products, O + OH, which is endothermic, dissociate back to reactants, H + O_2, or be stabilized by collision.

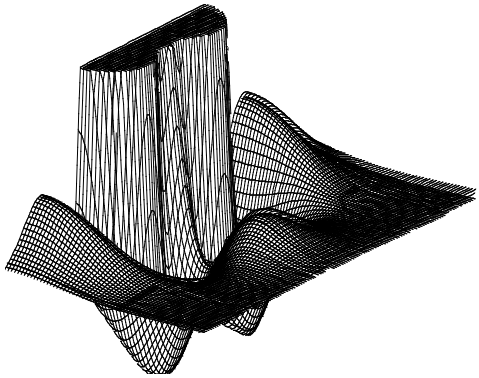

Figure 1: An H atom around an O_2 molecule.

The long-lived nature of this radical is a result of its electronic structure. At collinear and perpendicular geometries this radical correlates with a hydrogen atom in a 2p state. By this way, the dissociation back to H+OH has energy barriers in these directions. In Figure 1, we display the energy of a hydrogen atom around an oxygen molecule at its equilibrium geometry.

Being a termolecular reaction, it cannot be studied using normal classical trajectory programs. We have adapted the program MReaDy[2] to study this reaction at 2 000K and pressures of 10, 20 and 50 atm. We start with hydrogen atoms and oxygen molecules. By collision they form excited HO_2* radicals whose time evolution is followed all along. When an excited HO_2* radical is formed, the H atom stays trapped and needs to find a way to dissociate and may experiment several collisions before dissociation or stabilization.

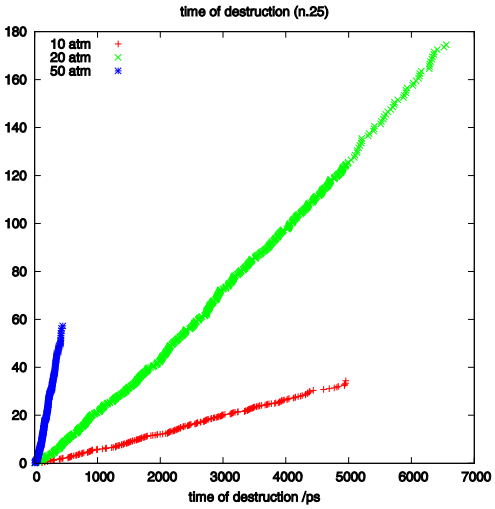

Figure 2: Number of HO_2 radicals stabilized by collision at 10, 20, and 50 atm.

We can count how many of the excited HO_2* radicals are stabilised by collisions at different pressures and temperatures. Counting the number of radicals that are stabilized as a function of time, we can calculate the formation rate of stable HO_2 radicals, see Fig.2. Using a simple mechanism and the steady state approximation, we can estimate the rate constant for the process HO_2* + M --> HO_2 + M.

In Figure 2 we display preliminary results for this process showing a clear increase of the rate constant with pressure. From this simulation we are able to study the rate constants of the different processes presented and propose a mechanism for this termolecular reaction.

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Bifunctional Cr^{3+} modified ion exchange resins as efficient reusable catalysts for the production and isolation of 5-hydroxymethylfurfural from glucose

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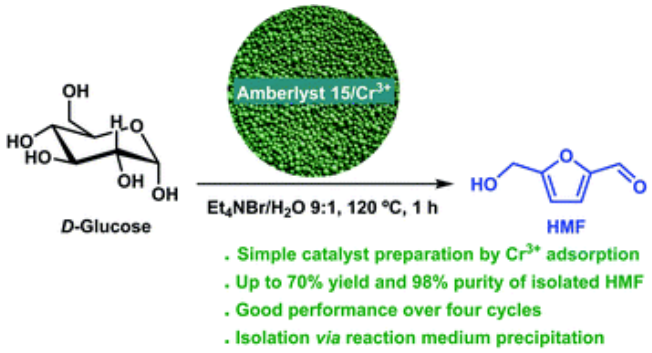
5-hydroxymethylfurfural (HMF) has been recognized as a key biorefining building block derived from carbohydrates, such as cellulose, glucose, inulin, fructose, etc. Among them, fructose is currently the only carbohydrate that can be readily dehydrated into HMF, typically in high yield and selectivity.[1,2] However, fructose has a low abundance in nature resulting in high cost, whereas glucose has much higher abundancy and is readily available from non-food cellulosic biomass, thus being a highly desirable feedstock.[3] Conversion of glucose to HMF is a twostep process where first the glucose is isomerized to fructose and the last undergoes subsequent dehydration to form HMF. The isomerization step is typically enzymatic, base or metal salt catalysed, while dehydration is an acid catalysed process. In the recent years a considerable number of bifunctional catalysts have been reported allowing this one pot transformation. Tetraethyl ammonium bromide (TEAB)/water is an efficient reaction media for fructose dehydration, which allowed quantitative HMF isolation via simple TEAB crystallization and subsequent recycling of both TEAB and organic solvents.[4,5] Herein we report Cr3+ modified readily available cation exchange resins explored as heterogeneous bifunctional catalysts for the dehydration of glucose to 5-hydroxymethylfurfural (HMF) in tetraethyl ammonium bromide (TEAB)/water as reaction medium. Excellent HMF isolated yields of up to 70% were achieved using simple crystallization of the reaction medium (TEAB) from ethyl acetate/ethanol which allowed the isolation of HMF in high purity. The best identified catalyst (Amberlyst 15/Cr3+) exhibited high activity over 4 cycles. The loss of activity was attributed to the decreased number of acidic sites of the catalyst, thus a simple treatment of the catalyst with 10% HCl efficiently restored its activity in the following cycles.



Scheme 1. Production and isolation of 5-hydroxymethylfurfural from glucose using Bifunctional Cr^{3+} modified ion exchange resins

Acknowledgements: The authors acknowledge Fundação para a Ciência e a Tecnologia (FCT) (ref. SFRH/BPD/109476/2015, SFRH/BD/120829/2016 and UID/DTP/04138/2013), European Research Area Network; ERANet LAC (ref. ELAC2014/BEE-0341), and REDE/1518/REM/2005 (FF-UL) for the mass service.

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Methanation of CO_2 over bimetallic Ni - 5f block element oxides

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Many studies have been developed using emission greenhouse gases, namely CO_2, in different processes for the production of value-added chemicals such as hydrocarbons and alcohols [1]. In this work, the study of carbon dioxide methanation over bimetallic nickel-5f block element oxides was undertaken. The compounds were prepared by controlled oxidation under dry air using intermetallic binary compounds ($AnNi_2$, An=Th, U) as precursors [2]. The best results were those obtained over the thorium-based catalyst that present an activity and selectivity equivalent to that of a commercial supported rhodium catalyst on alumina (5wt% Rh/Al_2O_3). The catalysts present also an unusual long stability in the gaseous stream and were characterized by different techniques (XRD, SEM/EDS, H_2-TPR). To our knowledge, this is the first time that bimetallic nickel-f block element oxides were tested for the carbon dioxide methanation.

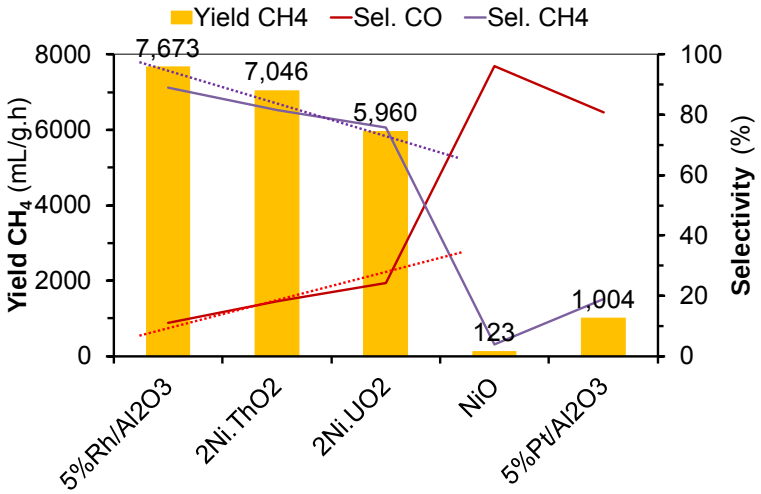

Figure 1: Methanation of CO_2 over bimetallic nickel-actinide oxides at 450 ºC (CO_2 / H_2 =1:4 mol/mol; GHSV=15000 mL of CO_2 per g of catalyst and per h).

Acknowledgements: C2TN/IST authors gratefully acknowledge also the FCT support through the UID/Multi/04349/2013 project

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Adsorption of lipophilic pollutants from biphasic systems by using modified activated carbon materials

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A commercial activated carbon (AC: Norit ROX 0.8, D = 0.8 mm) was chemically and thermally modified by following the procedures described elsewhere.[1] The materials were assessed as adsorbents for the removal of a lipophilic dye pollutant, Sudan IV (S-IV), using a biphasic medium water in oil in order to simulate contaminated petroleum mixtures with water. The AC was modified in successive steps considering: (1) grinding and sieving (< 250 μm) and (2) treatment with nitric acid, followed by hydrotreatment with urea and thermal treatment at 800 ºC under continuous flow of N_2 (100 $cm^3STP \cdot min^{-1}$), resulting in the adsorbents PAC and PACNAUT, respectively. Modelling of the kinetic and equilibrium S-IV adsorption onto the activated carbons was developed by employing a nonlinear method with successive numerical iteration to fit the model equations. Kinetic adsorption was evaluated by implementing Lagergren, Ho & McKay, Weber-Morris, Dunwald-Warner, Bangham, Elovich, Double-exponential and Avrami equations. Equilibrium adsorption was modelled by fitting the Langmuir, Freundlich, Jovanovic, Harkins-Jura, Tempkin, Dubinin-Radushkevich, Toth, Radke-Prausnitz, Sips, Brouers-Sotolongo and Vieth-Sladek models. The equations from Avrami kinetic model and Vieth-Sladek equilibrium model showed the best statistical parameters to represent the adsorption of S-IV onto activated carbons, so these models were the most suitable equations to describe the kinetics and equilibrium adsorption (**Fig. 1**), respectively. PACNAUT sample shows the higher adsorption capacity (q_e) and rate constant (k).

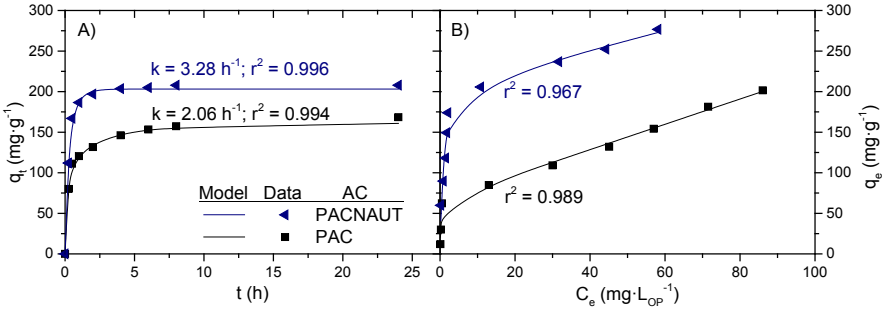

Figure 1: Evolution of adsorption capacities of modified activated carbon with (A) time and (B) equilibrium pollutant concentration, considering 2.5 $g_{adsorbent} \cdot L_{oil}^{-1}$, 50 ºC, initial S-IV concentration of 500 $mg \cdot L_{oil}^{-1}$ and W/O=1:10.

Acknowledgements: This work is a result of project "AIProcMat@N2020 - Advanced Industrial Processes and Materials for a Sustainable Northern Region of Portugal 2020", with the reference NORTE-01-0145-FEDER-000006, supported by NORTE 2020, under the Portugal 2020 Partnership Agreement, through FEDER and of Project POCI-01-0145-FEDER-006984 – Associate Laboratory LSRE-LCM funded by FEDER through COMPETE2020 - POCI – and by national funds through FCT. A.M.T. Silva acknowledges the FCT Investigator Programme (IF/01501/2013), with financing from the European Social Fund and the Human Potential Operational Programme.

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Environmental Challenges

Gas-Phase Studies of the Relative Affinities of N- and O-Donor Bases toward Ln(III) Ions

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The coordination chemistry of lanthanides (Ln) and actinides (An) with N- and O-donor ligands is a topic of current research associated to Ln/An separations within advanced nuclear fuel cycles. These comprise the development of advanced processing techniques for the separation (partitioning) of minor actinides (e.g. Am and Cm) from fission products (e.g. lanthanides) for their subsequent transformation (transmutation) into shorter-lived radionuclides, either in fast reactors or in accelerator-driven systems, therefore reducing long-lived radioactive waste inventories.[1-4]
Comparative studies of the gas-phase affinities of different N-donor bases (L = 1,10-phenanthroline, 2,2'-bipyridine, pyridazine, 1-methylimidazole, imidazole, 1-methylpyrazole, pyrazole and pyridine) and O-donor bases (L = triphenylphosphine oxide, dyphenylsulfoxide, dimethylsulfoxide, dimethylformamide and benzophenone) as models/building blocks of ligands in use, to Ln(III) (Ln = several from La to Lu, except Pm) ions by electrospray ionization quadrupole ion trap mass spectrometry (ESI-QIT/MS) have been performed. The aim is the identification of basic effects that may contribute to observed selectivities in Ln/An separations.
Complexation/association studies were performed with ethanol solutions of lanthanide nitrates and equimolar amounts of selected base pairs yielding mainly the ions $[Ln(NO_3)_2L_x(H_2O)_y]^+$ (x=1-3) (y=0, 1) and $[Ln(NO_3)_2L^1L^2]^+$. Competitive collision induced dissociation (CID) experiments in the QIT involving the mixed $[Ln(NO_3)_2L^1L^2]^+$ ions revealed the relative gas-phase affinities of the N-donor ligands and the relevant gas-phase factors behind the observations: phenantroline > bipyridine > pyridazine > methylimidazole > imidazole, methylpyrazole, pyrazole, pyridine. In general this ordering is in agreement with known density functional theory calculations.[5,] In the gas-phase bidentate ligands have a higher coordination power than the monodentate. The first potentially monodentate example in the scale with the highest affinity for Ln^{3+} is pyridazine for which a η^2 coordination mode seems to prevail, leading to a stronger bonding.[6] The results of competitive CID experiments of the mixed complexes containing O-donor ligands pointed out the following range of affinities: triphenylphosphine oxide > dyphenylsulfoxide > dimethylsulfoxide > dimethylformamide > benzophenone.

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Manganese N-Heterocyclic Carbene Complexes in the Reduction of CO_2

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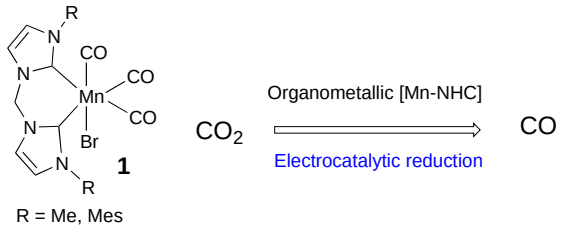
Utilisation of CO_2 as cheap and abundant C1 raw material is a promising strategy to mitigate global warming. In this context, development of catalysts capable to activate CO_2 for the formation of chemicals is a topic of increasing interest. In particular, the use of cheap, earth-abundant and non-toxic metals such as Mn as catalysts would have a significant impact.[1] Herein, we present our results on electrocatalytic studies for the reduction of CO_2 performed with Mn-NHC complexes of general type [MnBr(bis-NHC)$(CO)_3$] (**1**). Experimental data showed that complexes **1** are highly active catalysts for the reduction of CO_2 in the absence of acids. Combined UV-Vis and IR spectroelectrochemical experiments help us not only to provide mechanistic insights of the reductive pathway under inert atmosphere, but also to confirm the remarkable activity under CO_2. Preliminary results also suggest good selectivity for the conversion of CO_2 to CO.



Scheme 1: Electrocatalytic reduction of CO_2 to CO with Mn-NHC.

Acknowledgements: We thank FCT- Fundação para a Ciência e Tecnologia through project UID/Multi/04551/2013, and the National NMR Facility supported by the FCT (RECI/BBBBQB/0230/2012). We thank FCT for consolidation contract IF/00346/2013 (B. R.), PhD grant PD/BD/105994/2014 (M. P.) and COST Action STSM 42, COST CM1205.

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Simultaneous determination of Pt and Rh at ultra-trace levels: a step towards the current understanding of Pt and Rh cycles and fate in the environment

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Platinum (Pt) and rhodium (Rh), as well as other Platinum Group Elements (PGE), are severely depleted in the earth's crust: 0.4 ng g^{-1} for Pt and 0.06 ng g^{-1} for Rh. Yet they have been increasingly explored and used over the past decades in several applications. The automobile industry is the main sector responsible for the PGE global demand, representing approximately 45 % Pt and 5 % Rh in 2016. The reason for this stands on the use of PGE in automobile catalytic converters to reduce the emissions of other pollutants, and as a result the anthropogenic emissions of PGE grew over the last decades. Particles released from catalytic converters result in widespread distribution of PGE at the same time, mainly near high traffic roads. Thus, accumulation of PGE has been observed in sediments and vegetation, exceeding largely the natural background levels[1]. The determination of Pt and Rh in relevant environmental matrices is a challenging task and the need for extremely sensitive and accurate analytical tools for their simultaneous determination is demanding.

In this work, we have applied the second derivative signal transformation in a single scan for the simultaneous determination of ultra-trace Pt and Rh by Adsorptive Cathodic Stripping Voltammetry (AdCSV) in the presence of formazone (**Figure 1**) The experimental conditions were optimised in terms of electrolyte composition, deposition time (t_d) and deposition potential (E_d). Interferences from other metal ions in solution were also assessed. The method was successfully applied in the simultaneous determination of Pt and Rh in sediments from Tagus estuary and for the first time dissolved Rh was determined in water samples of a waste water treatment plant[2].

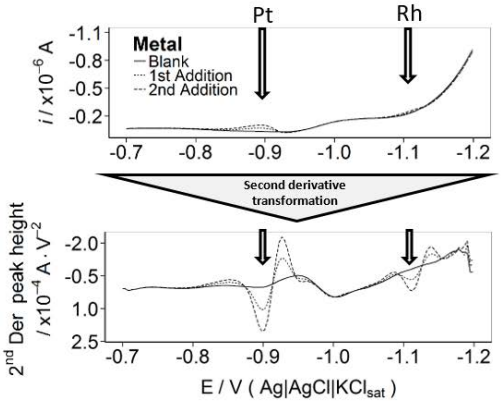

Figure 1: (a) Original and (b) second derivative voltammograms of a calibration curve obtained in the optimised conditions. Electrolyte: 0.25 M H_2SO_4, 0.05 M HCl, 0.01 M FA and 0.5 mM HZ; t_d =120 s and E_d = –0.75 V.

Acknowledgments: This work was financed by the Portuguese Foundation for Science (FCT) project UID/QUI/001002013, C.E. Monteiro FCT PhD grant SFRH/BD/111087/2015 and the COST Action TD1407.

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Synthesis and Anion Binding Properties of Hexahomotrioxacalix[3]arene Trinaphthylurea Derivative

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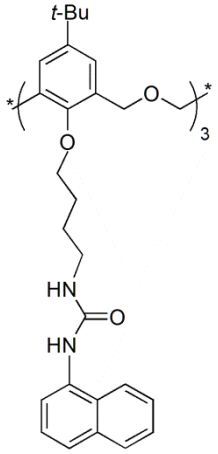
Calixarenes represent an extremely versatile class of macrocyclic receptors, able to bind and selectively transport ions and neutral molecules. Lately, the study of anion receptors based on calixarenes has considerably increased.[1] The important role of anions in both biological and environmental areas is one of the reason for this growth. The NH groups of urea derivatives are strong hydrogen bond donors, and this property has been widely used for the construction of neutral anions receptors.

In the course of our studies on cation binding properties of homooxacalixarenes (calixarene analogues in which the CH_2 bridges are partly or completely replaced by CH_2OCH_2 groups),[2] we have recently extended our research into the study of anion complexation.[3,4]

In the present work we report the synthesis, the NMR conformational analysis and the complexation properties of *p-tert*-butylhexahomotrioxacalix[3]arene trinaphthylurea derivative **1** toward a large variety of anions of different geometries. ^1H, ^{13}C and COSY NMR experiments carried out in $CDCl_3$ at r.t. indicated the partial cone conformation for **1**. Its complexation properties were assessed by proton NMR, UV-Vis absorption and steady-state fluorescence studies.



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Solution enthalpies of 3-methylimidazolium tetrafluoroborates: a QSPR study

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Ionic liquids (ILs) are a class of chemical compounds that have been extensively studied in the last years.[1] This interest is due in part to their potential use in areas as diverse as electrochemistry, biotechnology, organic synthesis, extraction processes, energy and pharmaceutical industry. Many of these studies are focused on their unusual properties, *e.g.*, their low vapor pressure, high thermal stability and high dissolution capacity. Despite this attention, most studies are directed towards their role as solvents and not as solutes.

In previous works, we have used a quantitative structure-property relationship (QSPR) methodology to understand how different solutes interact with specific solvents.[2,3], In this study we have monitored the behavior of ~~re~~ of three ionic liquids, 1-Butyl- , 1-Hexyl-, and 1-Benzyl-3-methylimidazolium tetrafluoroborates (Figure 1) as solutes, and have determined their enthalpies of solution in 11 solvents with different functionalities. The observed differences were rationalize using as framework the referred QSPR approach. The best found model equations allowed the identification of the dominant solute-solvent interactions. Results highlighted the relevance of the disruption of solvent-solvent interactions and of the solvent´s Lewis acidity in the solution process of these ILs.

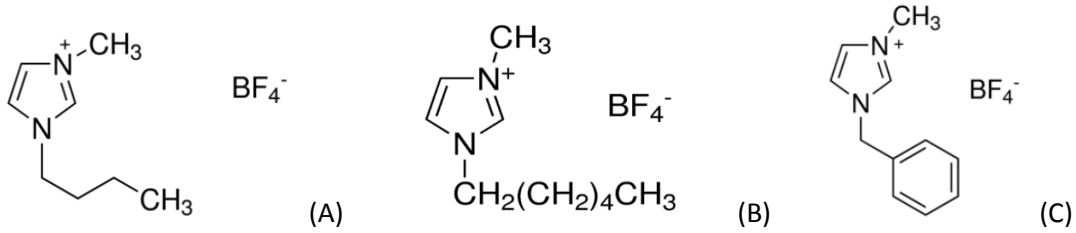

Figure 1: (A) 1-Butyl- (B) 1-Hexyl- (C) 1-Benzyl- 3-methylimidazolium tetrafluoroborates

Acknowledgements: We thank Fundação para a Ciência e Tecnologia for financial support through under project UID/MULTI/00612/2013.

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Cationic porphyrin-terpyridine derivatives: Synthesis, characterization and biological evaluation

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Porphyrins are receiving a special attention from the scientific community due to their unique features to be used as catalysts, drugs, electronic materials and sensors.[1] In particular, this type of macrocycles are being exploited with high success as photosensitizers (PS) in Photodynamic Therapy of tumours (PDT) or in the Photodynamic Inactivation of microorganisms (PDI). In both cases, the cell destruction by oxidative stress is induced by the cytotoxicity of highly reactive oxygen species (ROS) resulting from the combined action of light, PS and molecular oxygen. Nowadays, due to the continuing rise of drug resistant microorganisms, PDI is being considered an efficient alternative to the more conventional techniques in the inactivation of microorganisms.[2,3]
Herein, we report the synthesis, characterization of a series of neutral and cationic porphyrins bearing terpyridine units in one of their beta-pyrrolic positions and their ability to photoinactivate bioluminescent *E. coli* (**Figure 1**).[4]

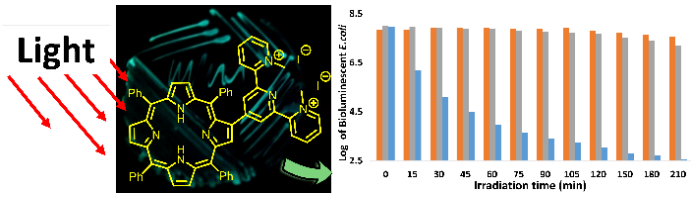

Figure 1: Representation of the photoinactivation of bioluminescent *E. coli* by cationic porphyrin-terpyridine derivatives.

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Banana peel as a low cost sorbent for cleaning contaminated waters

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Metal contamination is a worldwide concern due to severe toxicity of most of those elements and their persistent action in the ecosystem. Various anthropogenic activities have been responsible for the rejection of trace elements potentially toxic to the environment. Indeed, elements such as arsenic, lead, mercury and cadmium are still in the top list of the hazardous substances established by The Agency for Toxic Substances & Disease Registry in 2015[1] and there is still the need to find new methods to remove these elements from waters.

Biosorption has emerged as an area of great potential for the removal of metal ions from wastewaters, since the materials used are cheap, environmental friendly and available in large quantities in nature. However, the majority of the biosorption studies found in literature tests the efficiency of the materials under metal concentration far above realistic values and uses large mass of biosorbents[2]. Furthermore, these studies focus mainly on a single-element and only a few of them addresses real wastewater conditions[3].

In this work we studied the sorption capacity of a low cost food residue – banana peel – toward multi-contaminant systems of mercury, lead, cadmium and arsenic in natural tap water, using low amount of material under realistic contaminants concentration.

The efficiency of the material was tested in quaternary systems of Hg, Cd, Pb and As with concentrations equal to 50 µg/L, for all the contaminants. Hg analysis was performed by cold vapor atomic fluorescence spectroscopy (CV-AFS) while Cd, Pb and As were quantified by inductively coupled plasma mass spectrometry (ICP-MS).

Under the experimental conditions studied it was possible to conclude that the affinity of banana peel to the selected contaminants is in the order Hg>Pb>Cd>>As. Banana peel proved to be an efficient sorbent material with high percentages of removal for Hg and Pb (95% and 80%, respectively). The efficiency of removal for cadmium was a slight lower, being around 65%. In the case of arsenic, the sorbent material was not efficient in removing this element from contaminated waters.

This work highlights the valorization of a low cost and widely available food waste, without pre-treatment associated costs, allowing to significantly reduce the levels of contaminants in a polluted tap water.

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Anion Binding by Partial Cone Dihomooxacalix[4]arene-Based Receptors Bearing Urea Groups at the Lower Rim

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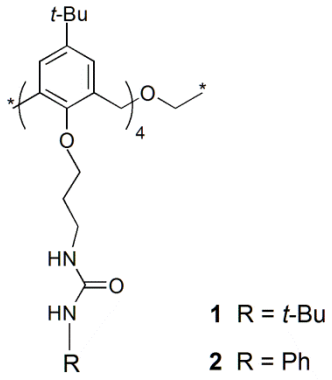
The study of anion receptors based on calixarenes, as well as on other macrocycle compounds, has considerably increased, mainly due to the important role of anions in both biological and environmental areas.[1,2] In biological systems, anions are essential to normal metabolic function. Concerning environmental pollution, anions such as phosphate and nitrate can be harmful pollutants. Organic-based receptors have been developed and only use hydrogen donor units, such as ureas and thioureas, to bind anions.

Following our interest in the synthesis and study of dihomooxacalix[4]arene-based receptors for cationic species, we have recently extended our research into the study of anion complexation.[3,4]

This work reports the binding properties of two *p-tert*-butyldihomooxacali[4]arene tetra-substituted derivatives with *tert*-butyl (**1**) or phenylurea (**2**) moieties at the lower rim via a propyl spacer, towards a large variety of anions (spherical, linear, trigonal planar and tetrahedral geometries). The binding properties of **1** and **2**, in the partial cone conformation, were assessed by proton NMR and UV-Vis absorption spectrophotometric studies. The results are discussed in terms of the nature of the substituent (alkyl/aryl) at the urea moiety.



1 R = *t*-Bu

2 R = Ph

Acknowledgements: Authors thank the Fundação para a Ciência e a Tecnologia, Project ref. PTDC/QUI/69858/2006.

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Oxidative β-Functionalization of Secondary Amines with Furan Derivatives: From Biomass to Potentially Active Highly Unsaturated Imines

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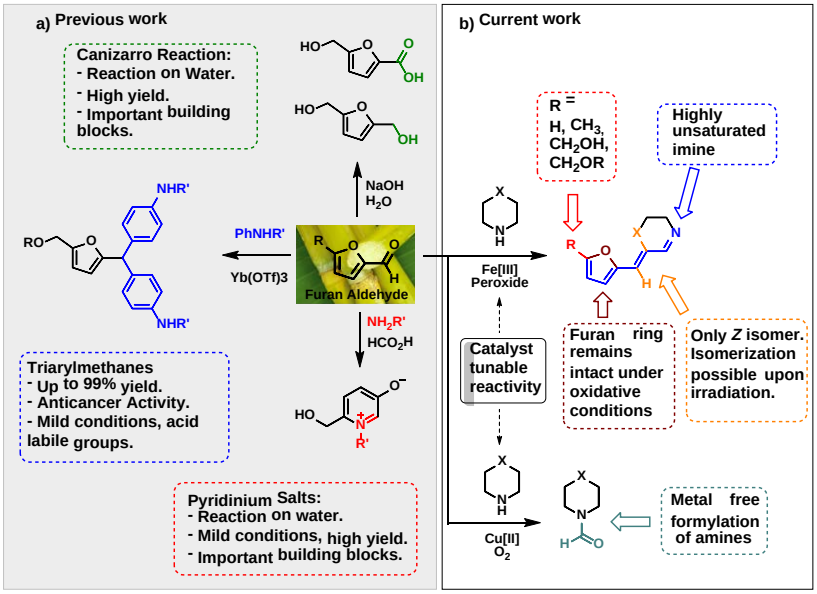
The ever increasing population growth, aligned with the concomitant industrial development leads to an increased demand for chemicals and energy. The fact that oil reservoirs are being depleted is a concern and the increased demand will hasten this depletion. New sustainable sources for fuels and bulk chemicals are of the highest interest, and biomass is the most attractive alternative for oil based products. Furan aldehydes such as 5-hydroxymethylfurfural (HMF) and furfural, easily obtained from fructose or glucose, are included in the U.S. Department of Energy top 10+4 list of biobased materials.[1] We have been involved on the synthesis of HMF[2] and the transformation of this important furan to other interesting building blocks such as dihydroxymethylfuran (DHMF), hydroxymethylfurancarboxylic acid (HMFCA), pyridinium salts, dimers[3] and more recently the transformation of HMF to bioactive anticancer triarylmethanes .[4] Herein we report the first methodology for the direct oxidative β-functionalization of secondary amines, with different biomass derived furan aldehydes providing interesting highly unsaturated imines. We can tune the reactivity by changing the catalyst, achieving the formylation of the amine up to 99% yield, and changing the aldehyde to a benzaldehyde derivative, achieving the oxidative amidation of the aldehyde group.



Scheme 1: Catalyst tunable oxidation of biomass derivatives containing furan ring.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support and European Research Area Network; ERANet LAC (ref. ELAC2014/BEE-0341).

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Lupanine removal from lupin beans detoxification wastewater

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Alkaloids are a group of naturally occurring chemical compounds, ubiquitously found in different parts of the plants, namely in seeds, roots and leaves. Among them is lupanine, a toxic tetracyclic quinolizidine alkaloid that is present in the seeds of *Lupinus albus*, known as lupin beans (**Figure 1**). Our interest in lupanine recovery relates to the fact that lupanine can be easily converted into sparteine, a compound of great interest for its application in asymmetric synthesis, which has also pharmaceutical properties.[1]

The purpose of the present work is to investigate separation techniques commonly used in biotechnology for the development of less expensive and more environmentally friendly methodologies to extract and isolate lupanine from lupin beans detoxification wastewater.[2] These methodologies should allow the easy recovery of lupanine in multigram-scale quantities for its further valorization and, at the same time, the decontamination of large volumes of water before they are released to the environment.

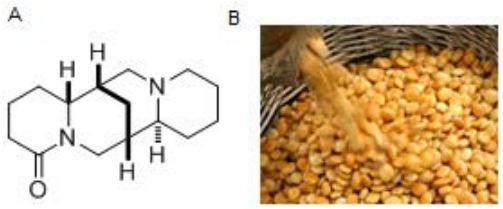

Figure 1: Chemical structure of lupanine (A), the main alkaloid found in lupin beans (B).

Acknowledgements: We thank WaterWorks2014 and FCT through Water JPI/0001/2014 and PTDC/QEQ-PRS/4157/2014.

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Microwave-assisted Transfer Hydrogenation using Fe-NHC Based Catalysts in Glycerol

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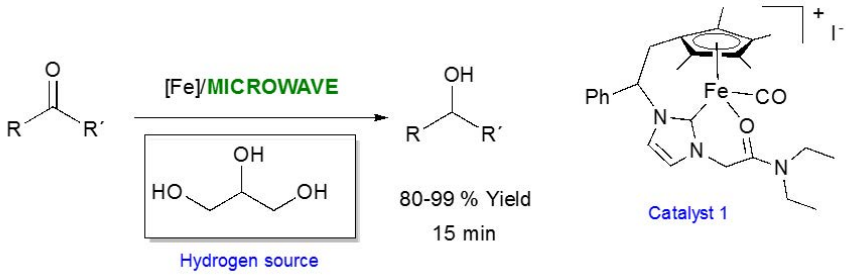
Metal-catalysed transfer hydrogenation (TH) is a powerful method for the reduction of carbonyl groups. The operational simplicity of this approach, avoiding the use of highly flammable molecular hydrogen has made TH an elegant tool for hydrogenation of unsaturated molecules. In the last few years, we have been involved in the development of iron N-heterocyclic carbene (NHC) complexes for their application in the reduction of functional groups through transfer hydrogenation and hydrosilylation processes.[1-3] Herein, we present a new highly efficient iron-based catalytic system for the reduction of ketones using glycerol as hydrogen source and microwave heating. Glycerol is an extraordinary low cost and non-toxic recyclable liquid manufactured from renewable sources, which provides important environmental benefits. We observed that the use of microwave has a tremendous impact in shortening the reaction time of the catalytic reactions. Complex **1** resulted to be a very active catalyst under those conditions, yielding high yields of the corresponding alcohols in 15 min of reaction. Notable, catalyst **1** allowed the synthesis of interesting bioactive alcohols, including steroids and chalcones.



Scheme 1: Transfer hydrogenation with Fe-NHC catalyst in glycerol.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support through project UID/QUI/00100/2013 and CQC (PEst-OE/QUI/UI0313/2014), grant fellowship SFRH/BD/52373/2013 (R.L), and B. R. thanks for IF/00346/2013.

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Identification of the transformation products of citalopram, an emerging compound in the environment, by mass spectrometry

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Citalopram, a selective serotonin reuptake antidepressant inhibitor (SSRI), has a high consumption in the world for the treatment of depression.[1] There are numerous studies that have detected this drug in effluents and surface waters but there are few studies of the fate and transformation products (TPs) in the environment or in the wastewater treatment plant (WWTP).[2,3] The processes of formation of TPs are important pathways for emerging compounds in environment: These TPs may be stable, remain in the water and present higher toxicity than the original contaminant. Since most of these compounds are unknown, their identification is fundamental to understand the risks that may cause in the environment.

The objective in this study is to identify the formation of TPs of citalopram that might be found in the environment by means of simulations processes under controlled conditions that may occur in the aquatic environment and in the wastewater treatment plant: hydrolysis; photo-degradation under ultraviolet (UV) irradiation and chlorination. Blank superficial water was spiked with citalopram (purity was >98%) and the pH was monitored but not modified to simulate the real environmental condition. The experiments consisted of withdrawn aliquots of 1 mL in determined times (0 to 3 days) and were stored for further analysis at -60 °C.

TPs were identified and elucidated by ultra-high-performance liquid chromatography (UHPLC) coupled to a hybrid quadrupole time of flight mass spectrometer (QTOF MS) operating in both positive-ion and negative-ion mode. The system was equipped with an electrospray ionization source. Samples were analyzed in full-scan mode and in broadband collision-induced dissociation (bbCID) acquisition mode, (MS)n were performed with low energy function, where (de)protonated molecules are intact and with high energy function, where fragmentation occurs.

The experiments resulted in 15 possible identified TPs and some TPs were formed in more than one degradation process. There was an increase in TPs formation by photolysis named TP1 ($C_{19}H_{18}N_2O_2F^+$), TP2 ($C_{20}H_{20}N_2O_2F^+$) and TP4 ($C_{20}H_{22}N_2O_3F^+$) over time. Others TPs named TP5 ($C_{20}H_{20}N_2O_3F^+$, chlorination) and TP3 ($C_{19}H_{20}N_2OF^+$, hydrolysis) showed stability over time. Desmethylcitalopram ($C_{19}H_{19}N_2OF$), citalopram N-oxide ($C_{20}H_{21}N_2O_2F$), human metabolites, were detected in these experiments and showed that the compounds can be formed under environmental conditions. The probable structures of TPs were established based on two prediction tools softwares: EAWAG-BBD: Pathway Prediction and Bruker MetabolitePredict. Analyses were based on accurate mass and on the fragmentation observed in the MS spectra and the mass errors were less than 5 ppm. A possible degradation pathway was proposed for the formations of TPs and the stability and formation of TPs was monitored in the experiments.

Acknowledgements: This work was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for PhD grants (99999.000845/2014-00) Fundação para a Ciência e a Tecnologia (FCT), Portugal (Projects UID/MULTI/00612/2013)

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Application of a new sensing material for the construction of surfactant potentiometric sensor

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Anionic surfactants (ASs) are commercially the most widely used group of surfactants. They are used in industry, households and research.[1] ASs have exceptional cleaning properties, can improve efficiency of active compounds in various commercial products and are biologically active.[2-4] Their annual production was 7686 KT in 2014. Due to their widespread use, it is necessary to find simple, rapid and accurate method for monitoring ASs concentrations in commercial products, during the industrial processes and in environmental samples. The two-phase titration is the reference method for ASs determination in products where the higher concentrations of ASs are expected.[5] In the effluents and in samples with lower ASs concentration, the standard method for determination is Methylene Blue Active Substances method (MBAS).[6] Both of these methods are tedious procedure, time-consuming and require a large consumption of organic solvents. Considering the above, ASs selective electrodes as sensors during the potentiometric titrations represent great alternative to the standard methods.[7] In the last years, great efforts are invested in construction of the electrodes having the best analytical and functional properties and finding the new components of the electrode membrane that can improve sensor characteristics.[8, 9]

The new electrode for ASs determination was made using tetraoctadecylammonium-tetraphenylborate as sensor material incorporated in liquid type of membrane. The response characteristics of the new sensor material were tested using dodecyl sulfate and dodecylbenzenesulfonate ions. The new sensor responded in approximately 5 s after an abrupt change of AS concentration.

The applicability of the new electrode was tested over a wide pH range and there was no significant potential deviations. Finally, the sensor was used for ASs determination in three commercial products with different concentration of ASs and the results were compared with those obtained using the two-phase titration.

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Smart Polymeric Nanoparticles for Boron Scavenging

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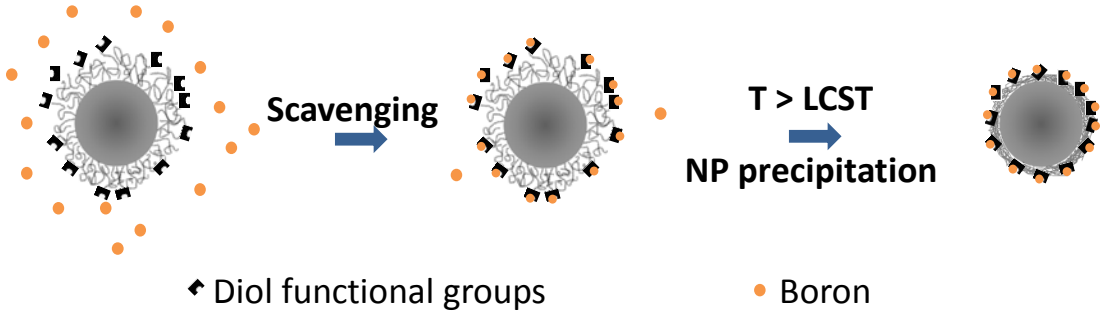
Boron is a trace element essential to human health and agriculture in trace quantities, but becomes toxic when in excess.[1] Boron compounds are used in many industries, including in the manufacture of glass and ceramics, semiconductors, fertilizers, insecticides, pharmaceutical drugs, high duress compounds, soaps and detergents, and flame retardants. A high boron contents in water might be a result from industrial wastewaters or leaching from rocks and soils containing borates and borosilicates.[1]
It is difficult to detect [2,3] and remove boron from water,[4] a step which is sometimes required in the treatment of residual waters. We have synthesized thermoresponsive core-shell polymer nanoparticles containing vicinal diol groups for boron scavenging. The particles have a core of poly(methyl methacrylate) (PMMA) and a thermosensitive shell with a brush composed of a copolymer of N-isopropylacrylamide (NIPAM), 2-aminoethyl methacrylate (AEMH), and either D-gluconoamidoethyl methacrylate (GAEM) or monodiol methacrylate (MDM) boron-chelating diol-containing monomers. The nanoparticles revealed good boron chelation capacity, both for the removal of boric acid and phenylboronic acid from water. At temperatures above about. 35ºC the particle shell collapses, inducing particle flocculation that facilitates particle separation. We observed boron removal efficiencies of up to 96%.[5]



Scheme 1: Boron scavenging process.

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Manganese N-Heterocyclic Carbenes in Catalytic Reduction Reactions

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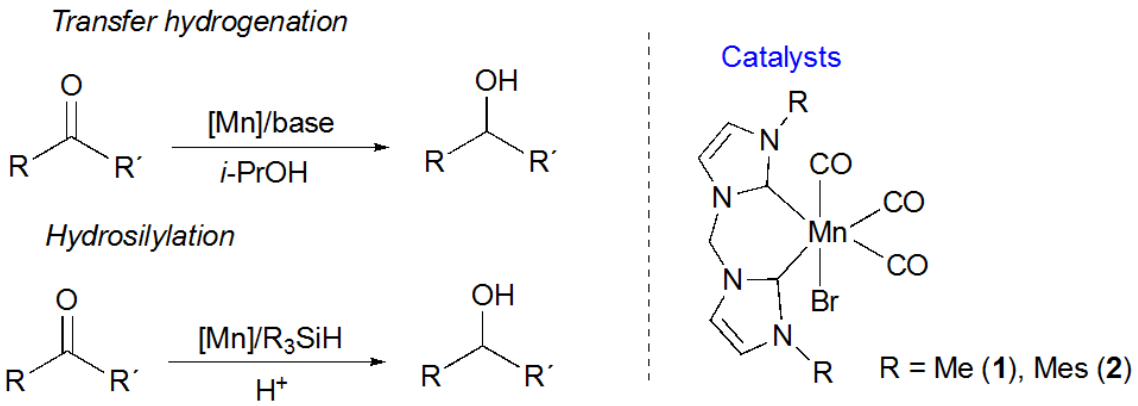
The development of catalytic reduction processes using Earth–abundant, low cost and non-toxic first-row transition metals is attracting enormous interest in both academic and industrial researchers. [1] In our research group, we have developed Fe and Ni N-heterocyclic carbene (NHC) complexes for their application in a variety of catalytic reactions.[2] Recently, we become interested in extending our studies to Mn-NHC complexes. Herein, we present the synthesis and characterisation of a new series of Mn-NHC complexes of general type [MnBr(bis-NHC)$(CO)_3$] and their application as catalysts in transfer hydrogenation and hydrosilylation processes (**Scheme 1**). We have found that complexes **1** and **2** displayed an excellent catalytic activity in the reduction of carbonyl groups. Quantitative reduction of cyclohexanone was obtained by using isopropanol as a hydrogen source, with 5 mol% of catalyst **1** in the presence of catalytic amounts of base, in 4 h at 90 °C. The scope of the reaction and the mechanistic details of these processes will be presented.



Scheme 1: Reduction of carbonyl groups with Mn-NHC catalysts.

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Evaluation of the effect of organic matter on the dissolution of Cu from CuO nanoparticles in soils

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The development of new nano-enabled pesticides and fertilizers is an active field of research. These nanopesticides or nanofertilizers can offer a targeted delivery, controlled release and enhanced solubility and increased efficacy of active ingredients, and considerably reduce the amounts of agrochemical products applied to crops and soils when compared to conventional formulations. Copper-based nanoparticles (NPs), such as copper oxide (CuO) NPs are currently being used as fungicides due their antimicrobial properties, and as fertilizers due their ability to deliver micronutrient-Cu to plants.[1] The increasing interest on these agro-enabled agrochemicals raised however several questions regarding potential environmental risks arising from their application. Recent studies suggest that differences in the dissolution of Cu-based NPs relative to Cu salts may alter their impact and eventually their toxicity to soil organisms.[2] Soil properties including pH, dissolved organic matter (DOM), and inorganic ligands can play an important role on the dissolution rate of Cu-based NPs in soils.[3]

In this study we evaluated how natural organic matter (NOM), and most particularly properties of DOM affect the temporal variability of the dissolution and extractability of Cu from soils amended with CuO NPs. Pots containing LUFA 2.1 or LUFA 2.2 standard soils were amended with distilled water (controls); a suspension of CuO NPs (Sigma, 50 nm) or $CuSO_4$ solution ([Cu]=50 or 250 mg kg^{-1} in soil, dry weight) and kept for 30 days at constant moisture content (50% of WHC). Soil pore water samples were collected in selected days throughout the experiment using two different methods: low-pressure method using Rhizon samplers and soil extraction by 0.01M $CaCl_2$. Levels of dissolved organic carbon (DOC) were analyzed by a Shimadzu TOC analyzer, and DOM in both pore water and soil extracts was characterized by UV-Vis and Molecular Fluorescence spectroscopy. Concentrations of total Cu in pore water and soils extracts were determined by ICP-MS.

Preliminary results showed that DOC concentrations in pore water samples collected from LUFA 2.2 soil were higher (38.1-127 mg C L^{-1}) than those in LUFA 2.1 soil (30.0-43.6 mg C L^{-1}). After 30 days, the levels of dissolved Cu in pore water samples from LUFA 2.2 soil amended with CuO NPs (250 mg Cu kg^{-1}) reached similar values (41 μg Cu kg^{-1}) as those from LUFA 2.2 amended with $CuSO_4$ (57 μg Cu kg^{-1}) at the same concentration. For pore water samples from LUFA 2.1 soil amended with CuO NPs also at the higher concentration, the dissolved Cu never reached levels as those obtained from LUFA 2.1 soil amended with $CuSO_4$. Our findings clearly indicate that the dissolution of Cu from CuO NPs in amended soils is determined by DOC levels and DOM composition. The evaluation of the effect of the variability of DOM composition on Cu dissolution in soils will be further discussed in this presentation.

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Validation of Heavy Metals Determination in Marine Sediments: A comparison of uncertainty evaluation approaches

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Statistics point to 85 % of heavy metals released into the aquatic environment are accumulated in sediments surface[1], which makes sediments the major pollution receptor and a potential source of this type of pollutants in aquatic systems. Marine sediments can be dredged and applied in beaches recharge[2]. Since some metals are strongly toxic and bioaccumulative, these resources must be monitored before their use.

The Division of Marine Chemistry and Pollution of Instituto Hidrográfico has developed procedures to determine metals in sediments. The determination of metals concentration involves a microwave digestion of samples using OSPAR method or the empirical EPA 3050B method before Atomic Absorption Spectrometry (AAS). In this context, the analytical procedures must be validated to verify if produced measurements are fit for the intended use.

The validation process involves defining analytical requirements and the metrological assessment of measurements ability to fulfil these requirements, in particular, the ability to produce results with adequately small measurement uncertainty. The estimated measurement uncertainty provides information on result quality[3]. GUM, Eurachem and Nordtest guides propose approaches for measurement uncertainty evaluation. The first two describe the bottom-up approach for uncertainty evaluation that involves the detailed assessment of the measurement process and used references.

In chemical analysis, frequently, the bottom-up approach is difficult to apply due to the complexity of some analytical steps (e.g. sample digestion step). Additionally, the combination of the uncertainty of many input quantities is not straightforward due to the need to fullfil combination models assumptions such as the linearity of measurement function given the input variables uncertainty. Monte Carlo Simulation comes up as a solution to overcome this issue. Unfortunately, for some, this numerical method is still unknown, although many advantages have been claimed[4].

This work developed a new user-friendly tool for the bottom-up evaluation of measurements of heavy metals in sediments by AAS where uncertainty components are combined using Monte Carlo Simulations. The Monte Carlo Method involves generating pseudo-numerical simulations for all measurement parameters in order to estimate their impact on measurement uncertainty. This powerful tool allows an accurate estimation of the true values of the measurand (i.e. the quantity intended to be measured) as a probability density function.

Furthermore, top-down evaluations of the measurement uncertainty were performed for comparison.

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Engineered MAO-N for the enantioselective synthesis of bioactive tetrahydroisoquinolines

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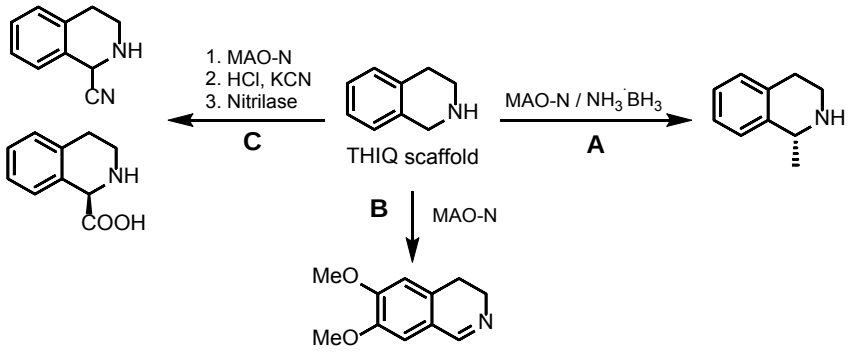
The chemical industry is under increasing pressure to change its environmental policy, shifting towards sustainable processes while maintaining product quality and production cost. However, the use of classical synthetic methods severely limits this change by requiring a compromise between yield, purity and waste generation. Biocatalysis represents an attractive alternative to these methods, employing enzymes or whole microorganisms in the fast synthesis of complex molecules. Moreover, enzymatic bioprocesses usually present great yields and selectivities in water, at low temperatures and ambient pressures. The mild reaction conditions disfavour the presence of secondary products and therefore simplify further purification processes.

Monoamine oxidase from *Aspergillus niger* (MAO-N) catalyses the deamination of primary amines in fungi. A "toolbox" of MAO-N variants has been developed at the Manchester Institute of Biotechnology for the oxidation and deracemisation of chiral amines, exhibiting high activities towards 1,2,3,4-tetrahydroisoquinoline (THIQ). Remarkably, a MAO-N catalysed dynamic kinetic resolution procedure allows 100% yield in the conversion of racemic amine to one enantiomer, a significant improvement over classic resolution methods **(Scheme 1 – A)**.[3]

In this work, MAO-N variants were screened with different THIQs to determine the influence of the presence and position of substituents in the enzyme's activity, allowing the first model to approximately predict its substrate scope. None of the variants tested presented significant activity with compounds containing a catechol or dimethoxy group in the sixth and seventh positions, limiting its application in industrial synthesis. To solve this problem, the mutations in known variants were combined to design MAO-N D13, the first reported variant capable of oxidizing 6,7-dimethoxytetrahydroisoquinoline with great yield and complete *(S)* selectivity **(Scheme 1 – B)**.

Finally, a one-pot three-step process was developed for the novel C1 functionalization of THIQs through oxidation, cyanation and hydrolysis reactions, presenting good yields and great selectivities in water and at mild conditions **(Scheme 1 – C)**. The energy-saving and environmental advantages of this enzymatic process, as well as the direct use of intermediate products in the following reactions, suggest a future application of this process in the chemical industry with great benefit for the environment.



Scheme 1: Biocatalysis in the synthesis of enantiopure 1,2,3,4-tetrahydroisoquinolines.

Acknowledgements: Thanks are due to the University of Aveiro and Fundação para a Ciência e a Tecnologia (FCT) FCT/MEC for the financial support of the QOPNA research Unit (FCT UID/QUI/ 00062/2013) through national funds and, where applicable, co-financed by the FEDER, within the PT2020 Partnership Agreement.

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Rate Constants from elementary reactions may fail for combustion kinetics models

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Kinetics models use available kinetic data, rate constants and their variation with temperature to model complex mechanisms and have been successfully applied to model combustion processes. They rely on the assumption that the number of collisions between reactants and intermediates is large enough to achieve thermal equilibrium.
Recently, we proposed a method to model complex reactive systems incorporating accurate PESs, reactive and nonreactive, and concurrently integrating the equations of motion of the chemical species present in the bulk1. This is accomplished by defining a global Potential Energy Surface (gPES) integrating various PESs, each one of them representing an elementary reaction that is expected to play a role in the chemical process. Multi-process Reactions Dynamics, MReaDy, is a program that builds an overall PES for the process in question and performs reactive classical dynamic calculations on it.
To test the distribution of the reaction partners, we have followed the evolution of the hydroxyl radical in its ground electronic state, OH (2Π), which is an important and very reactive intermediate during the combustion of a equimolecular mixture of oxygen and hydrogen, started at 3000 K and 2 atm, until 2 ns, using the MReaDy program. The overall results of this calculation have shown to be in reasonable agreement with similar kinetic model results[1].
To follow the OH radical, the MReaDy program has been modified in order to print out the identification, the position and the velocity of each O and H atom of a OH radical, every time a OH radical is “formed” or “consumed”. Using this information, we have been able to decompose the energy of this radical in its translational, vibrational and rotational components.
In this work we present preliminary results of that study. They show that, in spite of the occurrence of a large number of collisions, these are more efficient in rotational and translational energy transfer than in vibrational quenching. As a consequence, the OH radical has shown to be vibrationally excited, having an average energy which is twice the rotational. The non-thermal distribution of the internal energy of intermediate radicals in hydrogen combustion has recently been experimentally confirmed.[2]

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INDUSTRIAL CHALLENGES POSTER COMMUNICATIONS

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Blackberry anthocyanins: Impact of β-cyclodextrin on their stabilization

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Currently, as a consequence of consumer's preferences as well as legislative action, there is a worldwide trend towards the development of food colorants from natural sources.[1] Although anthocyanins are potential food colorants due their colors and their biological properties, their low stability has limited the technological application of these natural colorants.[2]

In this work, we have assessed the interaction between β-cyclodextrin and cyanidin-3-*O*-glucoside and the impact of this binding on anthocyanin's color and on the thermal and gastrointestinal stability of blackberries anthocyanins. It was observed that the addition of β-cyclodextrin resulted in the fading of anthocyanin solution and this fading effect was greater at higher β-CD concentration. This interaction was showed to affect the equilibrium and kinetic constants of the network of chemical reactions taking place in cyanidin-3-*O*-glucoside, resulting on the increase of the hydration equilibrium constant (K_h) which is in agreement with the fading of anthocyanin solution. This inclusion also induced a thermal stabilization of the pigment with a decrease on the degradation rate constant (k) and an increase of the half-time values ($t_{1/2}$) in the presence of β-cyclodextrin. Despite the rapid degradation of anthocyanins observed within the first minutes of simulated intestinal digestion, complexation with β-CD allowed anthocyanins degradation to be slowed down (**Figure 1**).

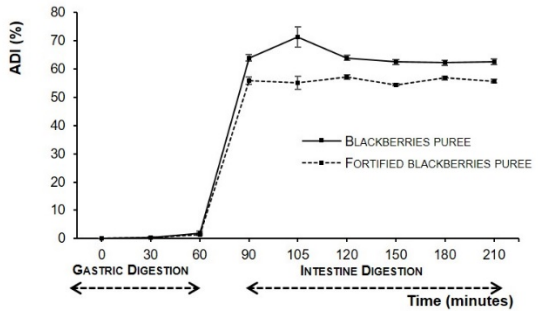

Figure 1: Anthocyanin degradation index (ADI) during the mimicked gastric and intestinal digestion of blackberries puree and β-CD fortified blackberries puree. Data (means SD of n=3) is presented as percent of anthocyanin degradation (degraded amounts vs. initial anthocyanin concentration).

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Pathway to the synthesis of 1,3-diamines a high value added compound

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1,3-Diamines are important structural motifs existing in many natural products and pharmaceuticals. In particular, chiral 1,3-diamines are important chiral building blocks that have been widely used for the synthesis of bioactive molecules such as marine alkaloids batzelladines, natural bromopyrrole alkaloid manzacidin A, and HIV-1 protease inhibitors A 74704. Preliminary results from our group, recently submitted to publication, shows an unexpected and unusual reactivity of 2-methyl imidazolium salts (1) towards aryl aldehydes, whereas 1 can act as an oxidant to the final conversion to the carboxylic acid. Unexpectedly when DBU is used as base, 1 catalysed the ring opening to a caprolactam-based 1,3-diamines scaffold (2) which is reduced to the 1,3-diamine (3) a high value added compound (**Scheme 1**). Reaction is being extended to other amidine and guanidine bases.
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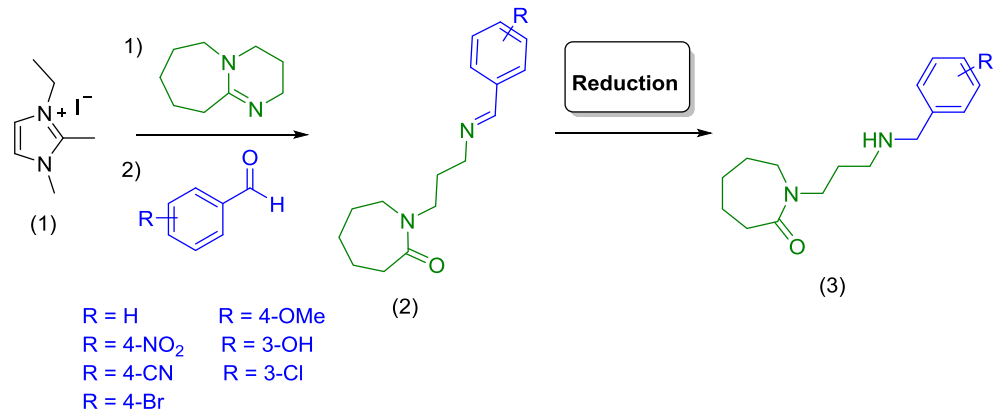

Scheme 1: General procedure for the synthesis of caprolactam-based 1,3-diamines scaffold.

Acknowledgements: This work was supported by the Associated Laboratory for Sustainable Chemistry - Clean Processes and Technogies LAQV which is financed by national funds from FCT/MEC(UID/QUI/50006/2013) and cofinanced by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007265). The NMR spectrometers are part of The National NMR Facility, supported by Fundacão para a Ciência e Tecnologia (RECI/BBB-BQB/0230/2012). La-boratório de Análises REQUIMTE for the technical sup-port on mass spectrometry analyses.

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Increase of the bioactive compounds in pineapple by-products through postharvest abiotic stresses

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Heat treatments and cut are investigated as abiotic stresses to promote bioactive synthesis of pineapple (*Ananas comosus*) by-products (shell). The shell was cut into rectangles of 30x20 mm with sharpened knives and the portions of shell were packaged in bags PA/PE/PE film 90 µm thickness. The by-products within the bags were submerged in a water bath (Selecta, Spain) at temperature 30 °C, 40 °C and 50 °C during 15 minutes and stored at the temperature ± 5 °C for 8 and 24 hours and then they were frozen to -80 °C. The heat treatment was not applied to the control samples. The samples were lyophilized. Total phenolic content was determined by the Folin–Ciocalteu method.[1] The determination of the antioxidant activity was done according to the methods of DPPH (2,2-diphenyl-1-picrylhydrazyl) [2], FRAP (ferric reducing antioxidant power) [3] and ABTS (2,2-azinobis (3-ethyl-benzothiazoline-6-sulfonic acid) [4] with some modifications. Intending to research a less time consuming analytical methodology, spectra (32 scans per spectrum) of the lyophilized pineapple core were collected in the mid infrared wavenumber range from 4000 to 400 cm^{-1} at a resolution of 4 cm^{-1}. The FT-IR spectrometer Alpha-P (Bruker Optik GmbH, Ettlingen, Germany) with a diamond ATR (attenuated total reflection) single reflection accessory was used.

The control sample after 24h of storage time shows higher levels of phenolic compound and antioxidant activity than the initial by-product and the control sample after 8h of storage time, which indicates that superior storage times after cut benefit the synthesis of phenolic compounds. The effect of the cut has more influence than the time/temperature of the heat treatment on the behavior of phenolic compounds and antioxidant activity, although the thermal treatments with moderate temperatures promoted the synthesis of these compounds. Thermal treatments at 50 ºC showed lower phenolic compounds and antioxidant activity for storage time of 8 and 24 h, which indicates that the temperature was excessive and decreased phenylalanine-ammonia lyase (PAL) activity [5]. The temperature of 40ºC promote a higher synthesis of phenolic compounds and antioxidant activity by the FRAP method for the shortest storage time (8h), although for longer storage times (24h) the temperature of 30ºC presented higher phenolic compounds content and antioxidant activity by the FRAP method. The temperature of 30 ºC showed higher values of antioxidant activity by the DPPH and ABTS methods than the treatments at 40 ºC, independently of storage time. Fourier transform infrared spectroscopy separates in the first principal component (99.08%) the samples with the highest content of phenolic compounds, as obtained by physicochemical analyzes.

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Solvent-free Suzuki–Miyaura reaction by mechanical milling catalyzed by metalla-aminocarbene palladium(II) complexes

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Metal-mediated coupling between equimolar amounts of *cis*-[$PdCl_2(CNR)_2$] (R = Xyl or Cy) and the amino acid esters L-HTyrOMe, L-HProOtBu or L-$HProNH_2$ proceeds at room temperature in chloroform yielding the complexes *cis*-[$PdCl_2$(CNXyl){C(*L*-TyrOMe)=NHXyl}] (**1**), *cis*-[$PdCl_2$(CNR){C(*L*-ProOBu*t*)=NHR}] (R = Xyl **2** or Cy **3**) or *cis*-[$PdCl_2$(CNXyl){C(*L*-$ProNH_2$)=NHXyl}] (**4**) with full conversion within *ca*. 48 h.[1]
The Pd-catalyzed formation of carbon-carbon bonds using ball mills as reactors for cross-coupling reactions namely the Suzuki–Miyaura reaction have been developed throughout the last decade.[2]
Complexes **1**-**4** exhibit a high catalytic activity, under mild ball milling and in alkaline conditions (K_2CO_3), for the Suzuki-Miyaura cross-coupling reaction of iodoanisole or bromoanisole with phenylboronic acid. Molar yields up to 80 % were achieved after 0.5 h at room temperature.

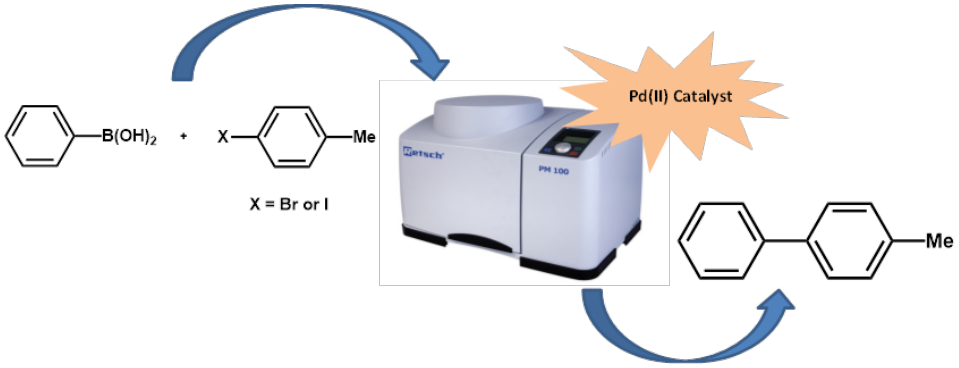

Figure 1: Pd(II)-catalyzed Suzuki-Miyaura reactions in a ball mill reactor

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Formaldehyde-Scavenging Nanoparticles for High Performance Resins

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Mesoporous silica nanoparticles have been developed in order to carry a strong acid, used as a catalyst, into the curing step of urea formaldehyde (UF) resin synthesis.
One of the challenges of this process is the reduction of formaldehyde emissions (a carcinogenic agent)[2]. In the final product, different attempts to decrease the emissions have been tried in the plywood industry, in particular the reduction of formaldehyde: urea molar ratio[4] and the use of melamine as a resin fortifier agent[3]. Both approaches were unsuccessful in their final goal because of the loss of mechanical properties and the increase of the product cost, respectively.
By using a strong acid as a catalyst, formaldehyde emissions can be efficiently reduced. However, the acid must be encapsulated until the hot pressing/curing of the resin in order to avoid pre-curing.[1] Mesoporous silica nanoparticles with thermo-responsive behaviour are a promising solution to catalyse the resin at the right moment.
Mesoporous-nanoparticles with 50 nm diameter were filled with a strong acid and coated with a polymeric shell. The morphology was evaluated by TEM and the stability in water and upon drying was determined by Dynamic Light Scattering (DLS).

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An efficient approach for chemical process development using kinetic modeling in batch and continuous mode

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Traditionally the majority of active pharmaceutical ingredients have been manufactured in batch mode however the pharma companies express increasing interest in continuous processing. Apparently continuous manufacturing is an attractive alternative due to its benefits such as reduced development time, greater process safety when employing hazardous chemistries or extreme conditions, reduced operating costs, improved process control and product quality. Kinetic modeling plays an important role in the development stage of a chemical process regardless of the operation mode. Precise knowledge of the kinetic parameters is necessary for the scale up from laboratory to industrial scale and for the design of robust and safe processes.

This work describes an efficient approach for the development of a reaction in an API synthesis. The approach includes screening of the reaction conditions, estimation of the kinetic parameters both in batch and flow mode and their comparison, and also fine-tuning optimization applying Design of Experiments.

Due to the previous knowledge about the process the yield and the impurity content were targeted to be improved. During the screening phase, applying both conventional and microwave heating we found the most favorable conditions resulting in excellent yield and we analyzed the possibilities for a continuous process. Specific sets of experiments were performed and kinetic parameters were then obtained and assessed to determine if the studied variables impacted the impurity formation. The model was used to predict conversion values and impurity levels for different conditions. In the last stage optimization studies were carried out in order to determine the Design Space ensuring the product quality within specifications.

We demonstrate our methodology applied for a case study following the Quality by Design concept, including experimental data and also simulations. This approach can be used for the development of batch or continuous processes in the future. The use of kinetic modeling allowed deeper understanding of the reaction and its influential factors, resulting in shorter development time and enhanced confidence level regarding the impurity formation.

Influence of ionic liquids on phase diagrams behavior and protein partitioning within the PEG 3350-$(NH_4)_2SO_4$ aqueous two-phase system.

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Aqueous two-phase systems (ATPS) are recognized as a relevant alternative liquid-liquid extraction (LLE), separation and purification technique of diverse range of biomolecules,[1] providing mild conditions that do not harm unstable compounds. Despite the advantages offered by commonly used polymer-salt based systems, such as low interfacial tension, rapid separation of the phases and low cost, they present restricted range of applicability, due to the difficulty in overcoming the limited polarity range of these systems. The introduction of ionic liquids (ILs) in the implementation of ATPS greatly changed this scenario and enabled to finely tune the properties of the aqueous phases in equilibrium.[2]
In this context, the influence of different ionic liquids on the phase equilibria of PEG 3350 – ammonium sulfate ($(NH_4)_2SO_4$) ATPS at 25ºC is studied in this work. The addition of small amounts (5 wt%) of chemically different ILs has different effects on the phase equilibria. In particular, we are searching for ILs that can lead to an increase of two-phase region, therefore leading to a decrease of concentrations of compounds needed for the liquid-liquid demixing. Moreover, these IL-based ATPS were tested in the separation/concentration of myoglobin from aqueous solutions.
The obtained results indicate that myoglobin preferentially partitions for the salt-rich phase in PEG-salt ATPS. However, extraction studies with presence of ILs demonstrate that the ILs have ability to tune the polarity of the PEG-rich phase, thus leading to an increase in the partitioning of this protein. The effect greatly depends on the chemical structure of the IL used.
Therefore, the results presented in this work show that the addition of a fourth compound, Il in the present case, to PEG–salt-H_2O ATPS constitutes a viable alternative to improve the extraction of proteins, such as myoglobin.

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In-silico Approach for Process Safety and Scale-Up

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Modern simulation techniques have emerged as a valuable tool to cope with today's pharmaceutical industry standards (**Figure 1**). In process safety assessments and scale-up or tech-transfer, mixing conditions are very often found to influence the process outcome [1-2]. Thermal stability and reaction calorimetry studies are used side-by-side with process modelling tools such as VisiMix®, to generate powerful hazard assessments – the manufacturing reactor performance during exothermic reactions can be predicted and ultimately help engineers selecting the proper safety measures. These tools are not only used for hazard assessments but also for process development and optimization. In the specific case of liquid-liquid reactions, it is possible to search for correlations between relevant scale-up factors and process outcomes such as yield and purity. Large scale reactors mixing conditions can be scaled-down to bench scale for process troubleshooting and very often simple solutions can be found in detriment of more complex ones. The *in-silico* approach described can fill in the gap between laboratory reactors and manufacturing performance by allowing scientists and process engineers to anticipate manufacturing scenarios avoiding unsafe and/or less robust processes. This leads to safer and faster processes delivering new medicines to patients.

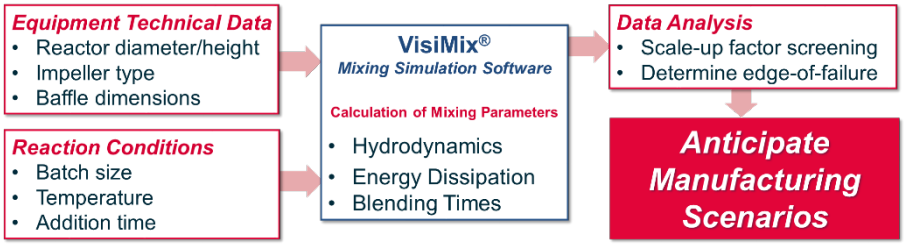

Figure 1: Mixing simulations workflow to predict manufacturing batch reactors performance.

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Organocatalysis by supported cyclic aminoguanidinines

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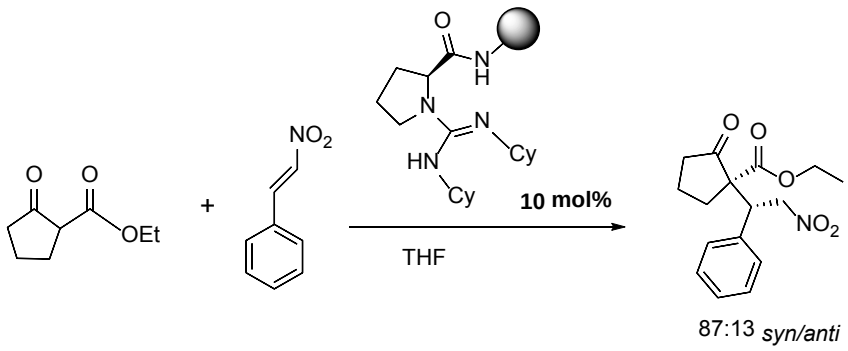
Guanidines are of the most basic organobases and supramolecular oxoanion hosts, usually recognized as good supporting ligands in organometallic and coordination chemistry, as also good catalysts. In recent years chiral guanidine catalysts have found application in asymmetric synthesis, namely in Michael, Mannich and Diels-Alder reactions among others.[1] As so guanidines have a crucial role as enantioselective organic catalysts due to the ion-pair interaction and hydrogen bonding they promote which accelerate the reaction rate and/or provide chiral induction. In the case of chiral catalysts, which are often expensive, or obtained from a complex synthesis, the immobilization on a solid support represents an attractive methodology that allows the recovery, and possibly the recycling of the catalytic species, developing 'metal-free' alternatives to established 'metal-based' catalytic processes. Here we present a new solid support proline-guanidine based catalyst immobilized on an (aminomethyl)polystyrene resin for the model Michael reaction between β-keto esters and nitroolefins (**Scheme 1**).[2]



Scheme 1: Solid support proline-guanidine based catalyst immobilized for the Michael reaction between β-keto esters and nitroolefins.

Acknowledgements: This work was supported by the Associated Laboratory for Sustainable Chemistry - Clean Processes and Technogies (LAQV) which is financed by national funds from FCT/MEC(UID/QUI/50006/2013) and cofinanced by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007265). The NMR spectrometers are part of The National NMR Facility, supported by *Fundacão para a Ciência e Tecnologia* (RECI/BBB-BQB/0230/2012). Laboratório de Análises REQUIMTE for the technical support of mass spectrometry analyses.

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Managing protein haze formation in white wines.

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Despite the extensive research performed during the last decades, the multifactorial mechanism responsible for white wine protein haze formation is not fully characterized. After testing different metabolites (1) and model wine solutions containing different protein fractions (2) a new model was proposed by our group which is mainly based on the experimental identification of sulfur dioxide as the non-proteinaceous factor that induces white wine protein haze formation upon heating.
Unlike other reducing agents, addition of sulfur dioxide to must/wine upon heating cleaves intraprotein disulfide bonds, hinders thiol-disulfide exchange during protein interactions, and leads to formation of novel interprotein disulfide bonds. The formation of these new bonds together with hydrophobic interactions between unstable proteins are ultimately responsible for wine protein aggregation following a nucleation-growth kinetic model (Fig. 1). The model was tested in wine model solution (using total and fractionated wine proteins) and validated under real wine conditions (2).
The results achieved may open the way to develop new techniques not only on fining and stabilization technology but also in new analytical methods to predict the protein haze susceptibility of a wine.

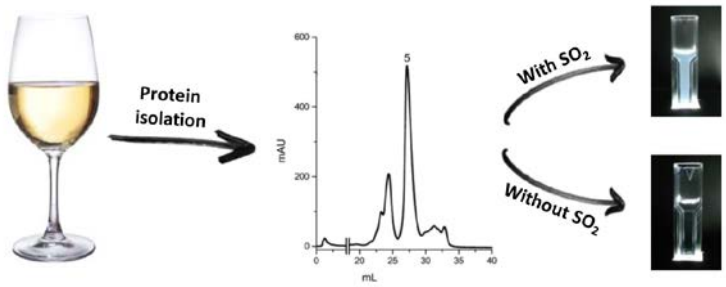

Figure 1: Representation of white wine proteins aggregates after heat stress in the presence or absence of sulfur dioxide.[2]

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Ultrasonic metal welding – splice replacer connector

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Since their discovery, in the middle of XX century, ultrasonic metal welding are being widely used on the industry in applications that involve softer and high conductivity alloys or metals like copper or aluminum. [1,2] In this process the metals are joined by the application of high frequency vibrations, under moderate pressure, in which the vibrations are applied parallel to the interface between the parts. The high frequency relative motion between the parts forms a solid-state weld through progressive shearing and plastic deformation over the surface asperities that disperses oxides and contaminants and brings an increasing area of pure metal contact between adjacent surfaces.[3] The biggest benefit of this technology is that addition materials are not needed. However, on automotive industry, for applications that involve the ultrasonic welding of cables this is not completely true since after performing the welding a tape or a heat shrinking tube is needed in order to guarantee the performance of the ultrasonic welded splice. Moreover it has been seen that for small configurations, using small cross section cables, the performance of the splices is often under the expectations, causing problems of broken splices with loss of continuity. After several studies trying to understand the reason for damaged splices on serial production we came out with the idea to check the possibility of using a connector that replaces totally the ultrasonic welding on small splices and guarantee the demands on that matter (Fig. 1). The connector is still being developed by 3D printing using ABS (Acrylonitrile butadiene styrene), but when compared with ultrasonic welded splice some benefits can be identified. Even considered a part that need to be purchased, it cost is significantly low when produced by injection molding and there is no need of adding tape or shrinking tube and corrosion is prevented by the sealant included on the connector.

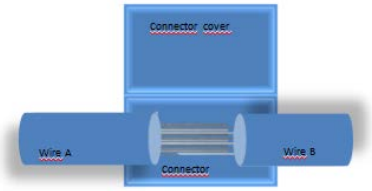

Fig.1 – Splice replacer connector

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TEACHING CHALLENGES POSTER COMMUNICATIONS

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About the new SI framework and the mole

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In 2018, the International System of Measurement Units (SI) will officially adopt a new wording for the definition of all the seven base units that will be based on defining constants, and not on artefacts any more. Consequently, the amount-of-substance unit, the mole, will be defined explicitly with the Avogadro constant, and not from the mass unit, the kilogram. Here is its new wording published by the International Bureau of Weights and Measures (BIPM) SI Brochure 9th edition draft: "The mole, symbol mol, is the SI unit of amount of substance of a specified elementary entity, which may be an atom, molecule, ion, electron, any other particle or a specified group of such particles. It is defined by taking the fixed numerical value of the Avogadro constant N_A to be 6.022 140 857 × 10^{23} when expressed in the unit mol^{-1}" [1]. This new wording that has been officially elaborated since 2011 was caused by the observed trend over 100 years of the International Prototype Kilogram (IPK) which lost 50 micrograms. Consequently, in order to be adopted, the new definitions need to be consistent within some parts in 10^8 with the present definition to ensure continuity of mass values[2]. This means that the numerical values of the defining constants will be adopted after experimental results reaching the required degree of consistency. Continuing with the example of the kilogram, this corresponds to consistent results of three independent experiments with smaller than 5 10^{-8} relative uncertainty (and, at least, one result with smaller than 2 × 10^{-8} relative uncertainty) and metrological traceability to IPK. The deadline for the publication of the new values by the Committee on Data for Science and Technology (CODATA) is on July 1, 2017[2].

In response to criticisms made against the new SI framework[3,4] and the redefinition of the mole[5], by metrologists and chemists, explanations were also published[6].

The main purpose of this communication is to discuss some of the questions raised by the new SI, namely the role of the constancy in science[7] and the special role played by Avogadro constant, N_A, considered as a scaling factor between a number of entities, i.e. a discrete kind-of-quantity and an amount of substance, which is a continuous quantity. So, the mole is not of the same kind of unit as the meter, the second or the kilogram[8]. Concomitantly to the need for an adequate notation for such huge number[9], it seems that its use for any kind of particles be still questionable[10].

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Detection and Separation of Pigments in Flower Petals: a new and sustainable chromatographic approach

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The decrease of the demand for Chemistry courses has been encouraging joined efforts of Schools, University and Chemical Technology for the development of more effective pedagogical tools to improve young students motivation in the study of this science.
Science experiments play a crucial role in the teaching/learning process because it develops the curiosity, the critical sense and it generates a great enthusiasm in the student through the discovery by doing himself. The use of high impact experimental activities demonstrating that chemistry is present in everything around us is definitely the key to the success in the Chemistry Education and may influence students to choose Chemistry for a future career.
The colours of the plant world have a vital importance in our lives. The plant pigments not only provide colour to our lives, but they are also important in food, medicine, clothing and cosmetics, among other products or activities of our daily life. Their pretty colours, wide-ranging physicochemical properties and particular safety provide to these pigments unique capacities to design attractive and sustainable experimental activities for teaching purposes. The chemistry of plant pigments is a crosscutting theme in the teaching of sciences that will enable students to establish and understand the relationship between Chemistry and everyday life.[1]
As extension of a previous work,[2] the pigments present in several flower petals were studied in order to develop a new and sustainable problem based practical activity to be implemented in basic and secondary schools. In the newly developed activity the students observe the flowers in the school garden, investigate the pigments responsible for their colours and learn how to detect and separate these molecules through environmentally friendly chromatographic techniques using more accessible and greener materials. This project provides a major pedagogical tool because it allows the teaching/learning of several key concepts of the Chemistry Curricula listed for Basic and Secondary Education: mixtures, substances, polarity, intermolecular forces, solvents, Organic Chemistry, Green Chemistry and sustainability. The colours achieved in this activity cause an excellent visual impact and the experimental procedures demonstrate a more proactive chemistry and impart the knowledge and awareness necessary to develop solutions in a sustainable and socially responsible science.
The experimental results obtained with this sustainable approach will be presented and compared to traditional methods.

Acknowledgements: We thank the Universidade do Minho and Fundação para a Ciência e Tecnologia for financial support.

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Chemistry e-lab online courses in Portugal

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Teaching nowadays is, as always, a challenge. Science is inherently experimental, and students can gain a better feel for the subject, and perhaps a greater insight into its principles, if they are active participants in scientific discovery.

In chemistry education, often a clear understanding of theory is largely dependent on experimentation. To view the real phenomenon is sometimes of crucial importance, to understand but also to stimulate. Thus, the importance of real laboratories in chemistry classes is stressed. When this is not possible the use of remote and virtual labs could be a good solution. In addition to promoting inquiry, experimentation can help students to acquire higher-order cognitive skills such as critical thinking, applying, synthesizing, decision making, and creativity, among other scientific skills. The e-lab is a remotely controlled laboratory that allows students of primary and secondary school to consolidate their knowledge in science and hence develop their scientific skills.[1]

The e-lab is a platform designed to support teaching and learning which calls for both laboratory work and technologies available in http://elab.ist.eu. It has already proved its contribution to the increased motivation and interest of students towards scientific subjects, both within and outside the classroom.[2]

For the first time, in 2014 two chemistry online courses were made, one for high school students (that was also implemented), and one for physics and chemistry teachers. We can find the results in 2.

Recently, between February 20 and April 13 of 2017, the two online courses were reformulated, considering the feedback received both by the students who took the course in 2014 and by invited professors and researchers who tested the course.

The courses were performed in Moodle platform and the promotion was made only through two Portuguese teachers Facebook groups, where 33 teachers and 58 students have shown interest in the course. The main results of the participants that conclude the course showed that teachers and students have interest and were motivated to do the course.

These online courses aim to stimulate students and teachers to know, learn, explore and use technological resources to support the use of experimental methods in science education, in chemistry. The e-lab experiment worked in the course allow to verify the Boyle-Mariotte Law, topic that is integrated in the chemistry Portuguese curriculum.

The courses have the following structure: (i) presentation of e-lab platform; (ii) testing e-lab platform; (iii) reading and investigating on the e-lab experiment “Verification of Boyle-Mariotte Law”; (iv) launching trials and data collection using a task protocol; (v) data analysis; (vi) perform three assignments and submit them electronically; (vii) final evaluation inquiry.

Although the experimental nature of chemistry presents severe challenges for its distance teaching, the obtained results are encouraging.

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Facing the hard problem of convincing the public and students to appreciate the real importance of chemistry in our world: a personal view

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In the twentieth-first century, the public image of chemistry is facing a subtle paradox: the public accepts the relevance and need of chemistry in a broad sense,[1] but do not seem to appreciate its real importance for the well-being of humankind and sustainability of the planet.[2]
The real importance of Haber-Bosch's synthesis of ammonia is not, in general, grasped by the public, students, and even instructors. Although a central theme in the secondary syllabus, most students have difficulty in associate this process with the possibility of having much more food available, through artificial fertilizers. In fact, it is estimated that around one-third of the population is alive due to this process.[2]
Having more food available, easy access to safe water, hygiene, antibiotics, vaccines, new medicines, pill, sustainable green processes, etc., does not seem to excite much the public and the students. A bold although truthful statement as "chemistry saved one-third of humankind" has a small effect!
Conversely, when faced with statements such as “chemistry saved the whales”, the public and students are, in general, surprised and become prone to love or hate, and thus, remember, discuss, and accept. Surprise and even discomfort can also be created by having in hands the apple of **Figure 1**: "What if apples have a label with the chemical composition?" Again, from surprise, feelings can arise, and bonds can be created.
Other examples used by the author: trying to establish a real appreciation for Green and Sustainable Chemistry, through well know daily substances, as indigo - "most people in the room are using this molecule bellow the waist" and ascorbic acid - "its lack can be found in 'Os Lusiadas' of Luis de Camões"; use connections with literature; tell a story, use the history and biographies of the characters involved in the discovery of natural and semi-synthetic penicillins to create an appreciation for chemical analysis and synthesis, and the way chemists work.
The hard problem of the public and students' lost of “love for chemistry” is not new nor simple. My approach is to use surprise, rise feelings, create bonds, show connections, tell a story, introduce the characters, invite to be a part.

Figure 1: Apple's label with the chemical composition used in popularization and outreach activities (author's photo).

Acknowledgements: The Coimbra Chemistry Centre is supported by Fundação para a Ciência e Tecnologia (FCT), the Portuguese Agency for Scientific Research, through the projects Pest-OE/QUI/UI0313/2014 and POCI-01-0145-FEDER-007630, co-financed by FEDER, through COMPETE 2020.

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