



SOCIEDADE PORTUGUESA DE QUÍMICA

3PYchem

3rd Portuguese Young
Chemists Meeting

9 - 11th May
Faculdade de Ciências
Universidade do Porto

Book of abstracts





3PYChem

3rd Portuguese Young Chemists Meeting 2012

Book of Abstracts of the 3rd Portuguese Young Chemists Meeting

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Joana Reis

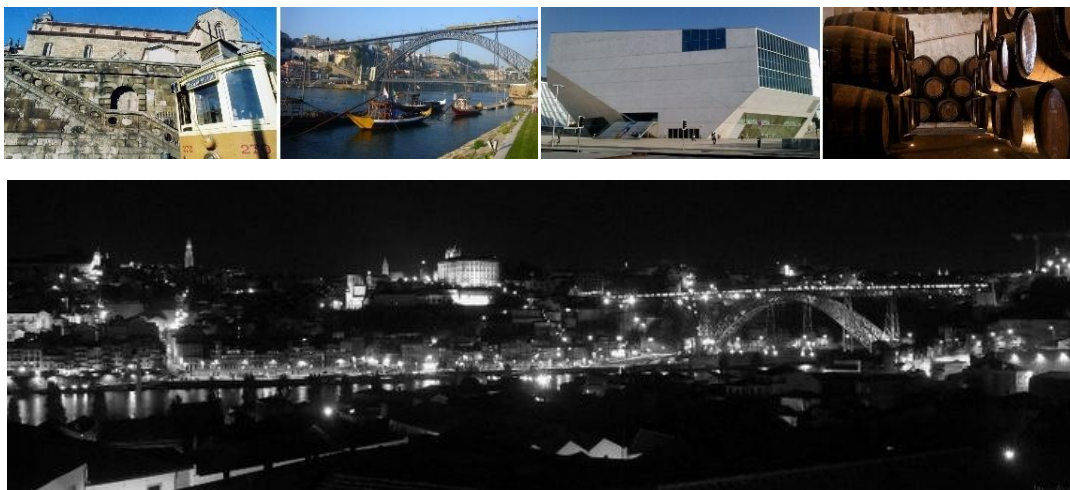
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This book is a compilation of the abstracts submitted by the authors for presentation at the meeting. There were introduced only minor editing alterations that do not change the scientific content.

The scientific content is sole the responsibility of the authors.



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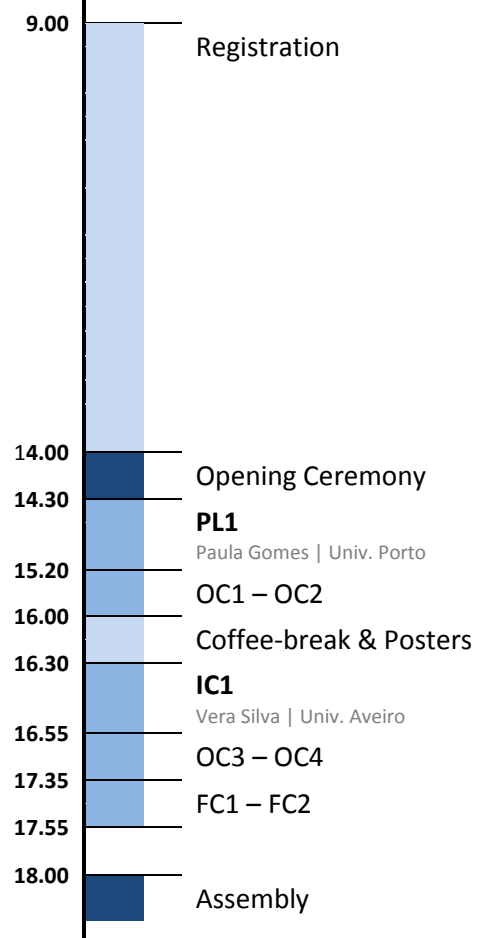
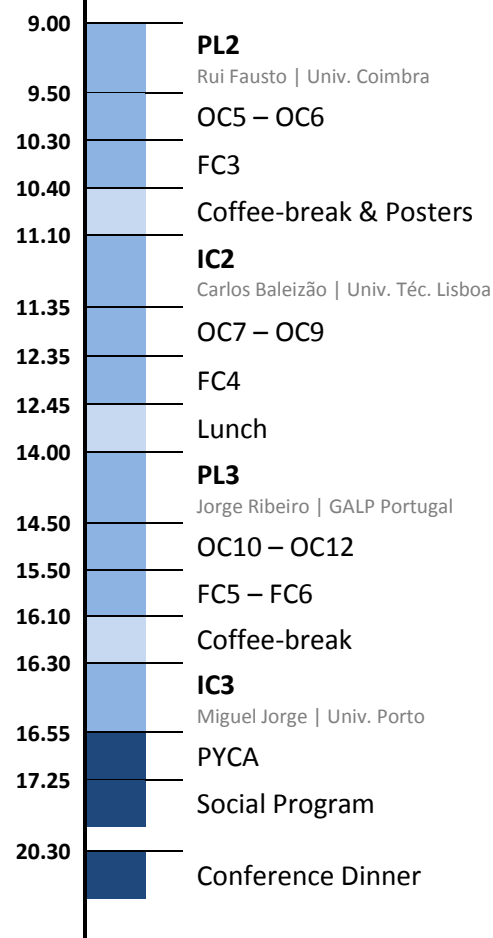
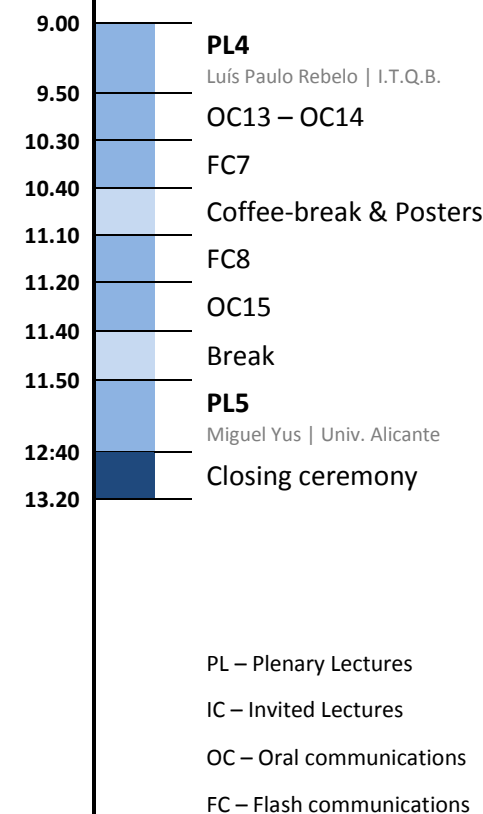
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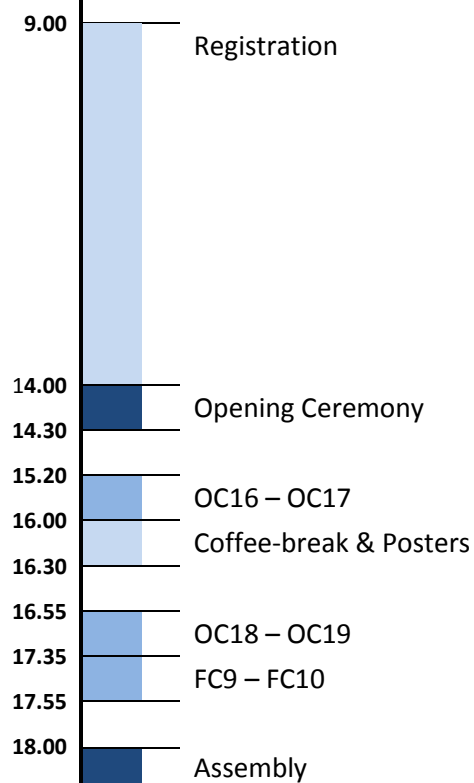


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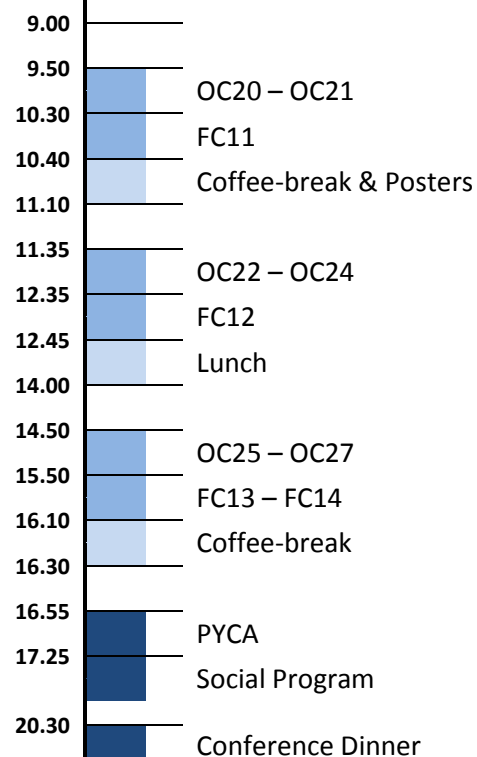
Room A2

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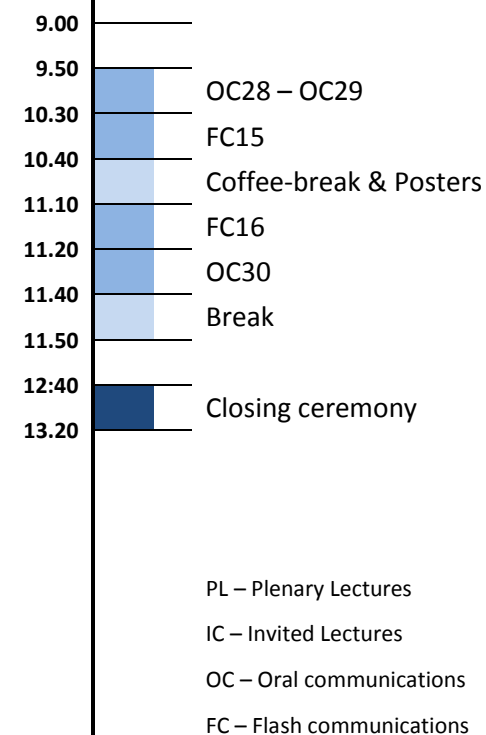
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DETAILED PROGRAM

Wednesday, May 9th

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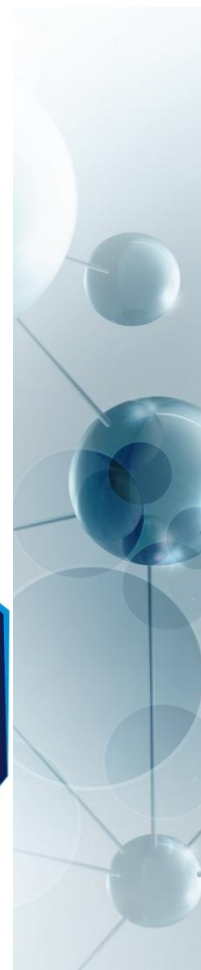
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Plenary Lectures



Old drugs with new faces: Chemical strategies to cover primaquine unpleasant traits while preserving its attractive antimalarial attributes

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Despite the worldwide efforts of Organic and Medicinal Chemists in the arena of malaria chemotherapy since the 1950s, 66-year-old drug **primaquine** (PQ) is still the only antimalarial in clinical use that is active against all exo-erythrocytic stages of *Plasmodia*, including latent liver forms (hypnozoites) responsible for infection relapse. However, PQ is hemotoxic and presents unfavourable pharmacokinetics [1-3]. A major factor behind this last aspect is extensive first pass-metabolic inactivation of PQ by oxidative deamination of the drug's aliphatic chain [3]. This requires frequent administration of high doses of PQ, which brings about serious toxicity issues, as PQ metabolism generates highly reactive oxygen species (ROS) underlying oxidative stress in human cells, namely, red blood cells (RBC). Thus, PQ-based therapy is often associated with hemotoxicity due to abnormal accumulation of methemoglobin in RBC, ultimately leading to hemolytic anemia. This adverse effect is particularly harmful for individuals with deficiency in NADH methemoglobin reductase or in glucose 6-phosphate dehydrogenase (G6PD), the latter being a common trait in African men. Due to this problem, PQ cannot be administered to pregnant women or newborns, as G6PD deficiency cannot be diagnosed in early stages of human life. This is a critical issue in malaria chemotherapy, given that 86% of the fatal malaria cases in 2011 were of children under five years old.

For almost a decade, we have been working on the chemical synthesis and evaluation of peptidomimetic and organometallic derivatives of PQ, designed to be resistant to oxidative deamination while preserving the antimalarial activity of the parent drug; this led to novel PQ derivatives with promising features as drug leads against exo-erythrocytic malaria parasites [4].

Acknowledgements: This work was mainly supported by Fundação para a Ciência e a Tecnologia (FCT, Portugal) and FEDER (European Union), refs. PTDC-QUI-65142-2006 and FCOMP-01-0124-FEDER-007418. The authors thank FCT also for financial support to CIQ-UP research unit. NV holds a post-doctoral grant from FCT (SFRH/BPD/48345/2008). The authors are grateful to all project's research collaborators.

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Light induced reactions in cryogenic matrices

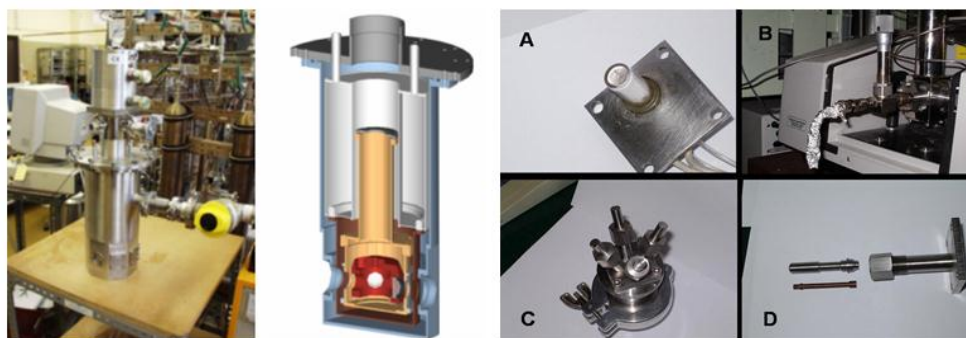
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This lecture will stress the power of the matrix isolation technique, coupled with infrared spectroscopy, to study chemical reactivity.

Since its invention by George Pimentel in 1954 [1], matrix isolation has been given an enormous contribution to the study of molecular reactivity. Nowadays, the investigation of light induced reactions in cryogenic matrices is a hot topic of research both in chemistry and physics [2]. For example, interesting chemical systems with potential application as molecular optical devices have been described [3-5], and new materials, such as stable covalently bound noble gas containing molecules, have been produced and characterized [2,6]. Moreover, in recent years, besides the more classic photochemical processes involving UV-visible excitation and electronic excited states, studies have also included hot vibrational chemistry processes, in which vibrationally excited molecules in their ground electronic state undergo chemical transformations upon IR excitation. Matrix-isolation spectroscopy has been the main technique used in these investigations, revealing itself to be specially powerful in the identification of reaction intermediates and establishment of reaction mechanisms. Interestingly, the success of this approach may also be ascribed to the concomitant development of computational chemistry, which provides sound theoretical foundations for the interpretation of the experimental data, and the availability at relatively low cost of tunable lasers that could be used as adequate irradiation sources to investigate specific processes in an elegant and powerful way.

Besides a general introduction to matrix isolation, in this lecture a series of case studies will be presented which illustrate the use of the method in the investigation of chemical processes induced by both UV-visible and IR light.



Acknowledgements: Members of the Laboratory of Molecular Cryospectroscopy and Biospectroscopy and our research partners involved in the studies described in this lecture are acknowledged. Financial support has been provided by Fundação para a Ciência e a Tecnologia (FCT, Projects PTDC/QUI/71203/2006 and PTDC/QUI/111879/2009).

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Collaborative R&D between GALP Energia and university as a factor to promote competitiveness

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GALP Energia S. A. is an enterprise group which integrates companies in the business segments of exploration and production of oil and natural gas, refining and marketing oil products, natural gas, electrical and thermal power generation and marketing and sales in the energy segment.

Its activity is predominantly developed in Iberian Peninsula, Africa, Asia, North and South America. Produces and commercialize more than forty different products, regarding gases and liquefied products from petroleum, aviation/navy/auto fuels, lubricants and base oils, bitumen, waxes and paraffin's, high purity chemicals and solvents.

The interaction between industry and university plays an important role due to the high activity of this diverse competitive industrial sector, which demands new challenges for the chemical technology which requires an increased investment in innovation. Our company developed and is promoting collaborations with the academic community, under the EngIQ program. These collaborations aim to meet the technological requirements as well as, to train highly qualified professionals, to promote the fundamental and applied knowledge.

The use of NMR spectroscopy in industrial process control, the application of ionic liquids in extraction processes, the development of bitumen and its production process, the design and construction of an apparatus for evaluation of the thermophysical properties of paraffin's, are some examples of investment in R&D and ongoing projects in collaboration between our company and the universities, which are a key factor for the technological and scientific based support of Galp Energia competitive strategy for the future.

Novel ionic liquids – New flexibility

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A short, recent overview of some aspects of the field will be provided. It will be followed by two topical issues - making ionic liquids even more ionic or turning them to be active pharmaceutical ingredients. Ionic liquids are distinct from other chemical substances because they may be designed and engineered in such a fashion that all chemical tools already known to exist in all other chemicals may be present.

Making them more organic-like has been a major task. However, providing ionic liquids with an even greater ionic (salt-like) character, without losing their liquid status, has not been exploited [1].

Most drugs are solid. Solids often present distinct polymorphic forms and many drugs are composed of several of these polymorphs; however, oftentimes, only one is medically effective. Thus, liquid pharmaceuticals are generally superior. In a joint ITQB-Requimte project, we have used ampicillin as the anion and several biocompatible cations to develop novel ionic liquids with antibiotic properties [2].

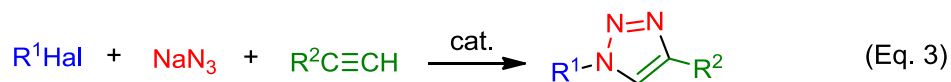
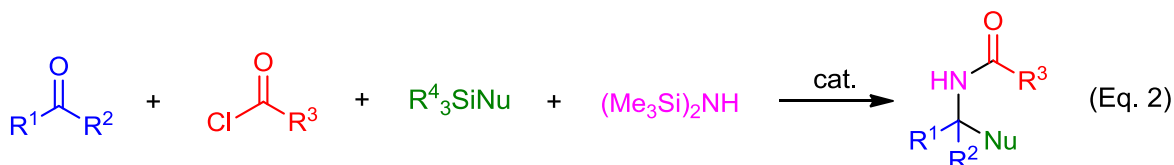
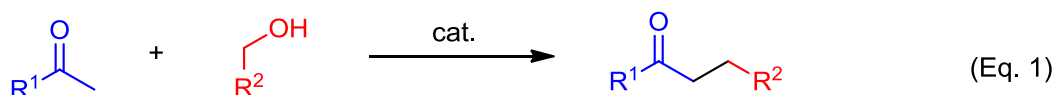
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Efficiency in Chemistry: From hydrogen autotransfer to multicomponent catalysis

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One important task concerning any chemical process has to do with the so-called atomic efficiency (AE), which can modify considerably the concept of yield corresponding to a chemical reaction: even working with a high chemical yield a reaction can be not efficient when the main part of the reactants structure is not included in the final product [1]. Two interesting processes will be the subject of this presentation: (a) The hydrogen autotransfer reaction [2], in which an alcohol is used as electrophilic component, for instance, in the alkylation of a carbonyl compound, water being the only byproduct in the process, that is, therefore, of great value from an atom efficiency point of view (Eq. 1); and (b) the multicomponent [3] reaction, such as the aza-Sakurai reaction (Eq. 2), or the 1,3-dipolar cycloaddition of alkynes and in situ generated alkyl azides ('click' chemistry) (Eq. 3), of considerable interest from a step efficiency point of view [4].

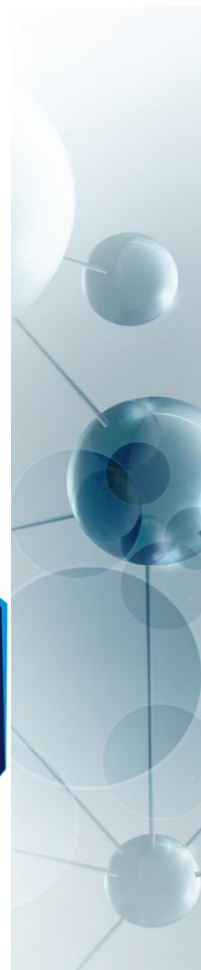


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Invited Lectures



Development of synthetic methodologies for new biologically active heterocyclic compounds

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Nitrogen and oxygen containing heterocyclic compounds are key building blocks used to develop compounds of biological or medicinal interest [1,2]. A vast number of nitrogen containing heterocyclic building blocks have applications in pharmaceutical and agrochemical research and drug discovery. Heterocyclic compounds also have a practical use in industry as components in dyes, antioxidants, copolymers, bases and ligands [1,2]. Here we present the synthetic methodologies we have developed for pyrazoles (**I**, **II**) [3], indazoles (**III**) [4], quinolones (**IV**) and acridones (**V**) [5], which are heterocyclic compounds with a high biological importance. The first preliminary structure-activity relationship (SAR) analysis of a group of novel pyrazole-based synthetic cannabinoids (**II**) will be presented. These analyses were performed in *post-mortem* human brain membranes and led to the evaluation of the pharmacological affinity of these pyrazoles for CB¹ receptors.

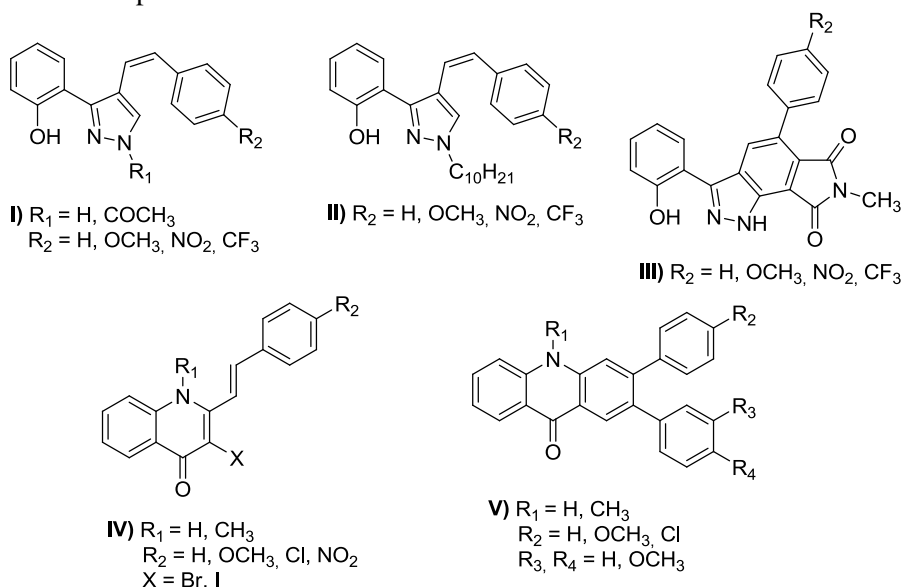


Figure 1. Some nitrogen and oxygen containing heterocyclic compounds synthesized in our group.

Acknowledgements: Thanks are due to the University of Aveiro, “Fundação para a Ciência e a Tecnologia” (FCT) and FEDER for funding the Organic Chemistry Research Unit (project PEst-C/UI0062/2011) and to the Portuguese National NMR network funded by FCT. V. L. M. Silva also thanks the FCT for the grant (SFRH/BPD/27098/2006).

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Perylenediimide based functional hybrid materials

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Perylene-3,4,9,10-tetracarboxylic acid diimide derivatives (also called perylenediimides, PDIs) have been widely used as industrial pigments for tissues and paints. The synthesis of PDIs derivatives (Figure 1), 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) or in the bay region (substituents affect electronic and optical properties) [1].

Since the first report in 1913 of N,N'-dimethyl PDI [2] several PDIs have found their way into industrial-scale production and use since early 1950s [3], especially in fiber applications and in high-grade industrial paints [4]. PDIs show other interesting properties, such as near-unity fluorescence quantum yield, excitation in the visible region, strong and reversible electron-accepting character, high thermal, oxidative and photochemical stability and high electron mobility [5]. Therefore, in recent years, PDIs have been extensively studied in various electronic and optical applications such as organic field-effect transistors, fluorescent solar collectors, organic photovoltaic cells, and imaging [6].

This lecture will focus on the latest progresses achieved at CQFM-IST on the development of new PDIs and their incorporation in functional hybrid materials, including silica nanoparticles and organic frameworks, for application in imaging and solar cells.

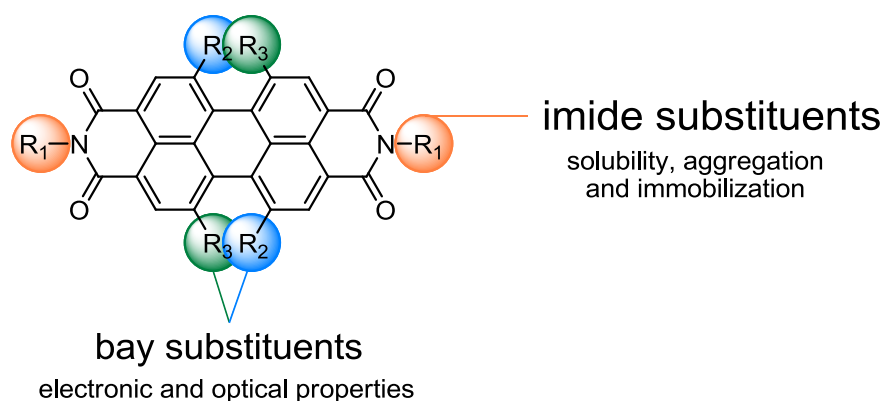


Figure 1. Substituted PDIs.

Acknowledgements: This work was supported by Fundação para a Ciência e a Tecnologia (FCT-Portugal) and COMPETE (FEDER) within project PTDC/CTM/101627/2008.

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Molecular simulation of hybrid organic-inorganic nanoporous materials: synthesis and adsorption predictions

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Nanoporous materials play an important part in many applications, ranging from separation processes, to optoelectronics, to controlled drug delivery. Recently, hybrid porous materials that combine the resilience of inorganic matrices with the versatility of organic moieties have unfolded their extraordinary potential for a wide range of applications. Among these novel materials are Periodic Mesoporous Organosilicas (PMOs) [1] and Metal-Organic Frameworks (MOFs) [2]. Apart from their attractive properties, these materials offer the possibility of tuning the pore structure and the surface chemistry by a judicious choice of inorganic and organic building blocks [3]. This feature is extremely promising for the *a priori* design of nanoporous materials to suit a particular application.

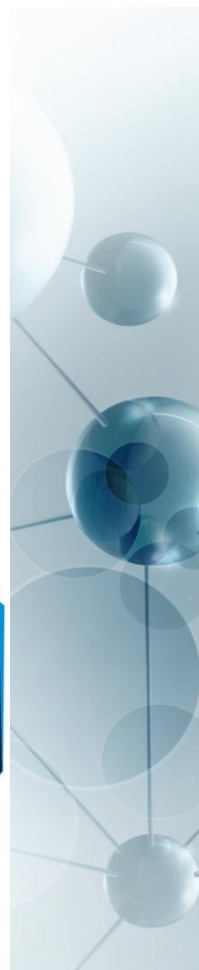
In this context, molecular simulation methods have played an increasing role in the elucidation of the mechanisms by which these materials are synthesised [4] and in the prediction of the material's performance in the chosen application [5]. This communication reports some of our most recent results on the application of classical molecular simulations and quantum chemical methods to those two aspects of the material design process. In particular, we begin by presenting a systematic molecular dynamics study of the synthesis process of PMO materials, clarifying the role of silicates and organic linkers in the mechanism of PMO formation. New molecular models are developed by incorporating information from Density Functional Theory of organosilicate precursors. We then present predictions of adsorption and separation selectivity on MOF materials by Monte Carlo simulation, focusing on highly challenging olefin/paraffin separations. We demonstrate that although good predictions can be obtained for alkanes using standard molecular models, those models fail for the adsorption of alkenes. We circumvent this limitation by developing a new approach whereby information from DFT is directly incorporated into the classical Monte Carlo calculations. With this new approach, we are able to accurately describe preferential adsorption of the olefin on unsaturated metal centres, thus obtaining good adsorption predictions. Our results highlight the potential of molecular simulation in the characterisation and design of hybrid nanoporous materials.

Acknowledgements: Financial support from FCT and FEDER, through project PTDC/EQU-EQU/099423/2008.

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Oral Communications



New chromene scaffolds for adenosine receptors: synthesis and pharmacology

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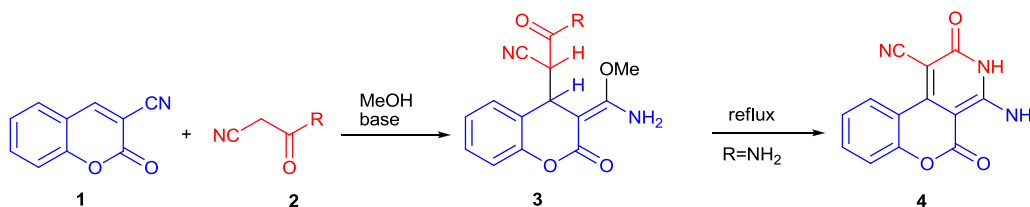
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Adenosine receptors are distributed throughout the body, regulating different cellular functions and can be considered attractive targets for therapeutic agents [1,2]. Different compounds proved to be active on these receptors, displaying pharmacological activity namely for the treatment of cardiovascular, inflammatory or neurodegenerative diseases and cancer [1,2]. The active molecules usually belong to the purine family, but compounds with the pyrazolo-triazolo-pyrimidine, dihydropyridine and quinazoline-urea core unit were also identified as active.[1] To our knowledge, the interaction of chromene derivatives with adenosine receptors was never reported.

Naturally occurring chromene-based compounds are often used as valuable leads for the design and synthesis of new active analogs with potential therapeutical applications, namely as anti-HIV, anti-tuberculosis, anti-inflammatory and anti-fungal agents [3].

Herein we report a one-pot procedure for the synthesis of novel chromene derivatives **3** and **4**, generated from the reaction of 2-oxo-2H-chromene-3-carbonitriles **1** and cyanoacetamides **2** (Scheme 1). These new scaffolds proved to be active at adenosine receptors and several hits were identified in this study with affinities in the submicromolar range. A detailed discussion of the scope of the synthetic method and affinities of the compounds will be presented.



Scheme 1. Synthesis of compounds **3** and **4**.

Acknowledgements: we gratefully acknowledge the financial support from University of Minho and FCT through the Portuguese NMR network (RNRMN), the Project F-COMP-01-0124-FEDER-022716 (ref. FCT PEst-C/UI0686/2011) FEDER-COMPETE and BPD grants awarded to Marta Costa (SFRH/BPD/79609/2011) and Filipe Areias (SFRH/BPD/26106/2005).

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Marine biomaterials on the origin of biomedical applications

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On marine environment one can find an uncountable diversity of materials, bearing all kinds of biological and chemical features, some of which are unique, without equivalent in terrestrial organisms.

Inspired by marine organisms, the authors have been deeply enrolled in raising the potential of marine materials for several applications, in particular by creating new marine biomaterials, further used on the development of biomedical applications [1].

Marine (*Blue*) Biotechnology is being explored towards the valorisation of marine resources, where several materials have been isolated and further used in tissue engineering context. In this perspective, emphasis will be given to chitosan produced from squid pens, which has been used on the development of porous structures for engineering of bone and cartilage tissue (Figure 1). In addition, the development of polymeric structures with collagen obtained from fish skins will be also addressed, namely its cross-linking to achieve porous structures and hydrogels.

Marine biomaterials are thus being presented as a valuable alternative to other compounds on the development of health-related applications, with lower risk of associated diseases to pose to humans.

This approach definitely contributes to the strategy Europe 2020 (smart, sustainable and inclusive growth) and to the accomplishment of the strategic objectives outlined in the position paper European Marine Strategy [2], by providing new opportunities to exploit natural marine resources in a sustainable way.

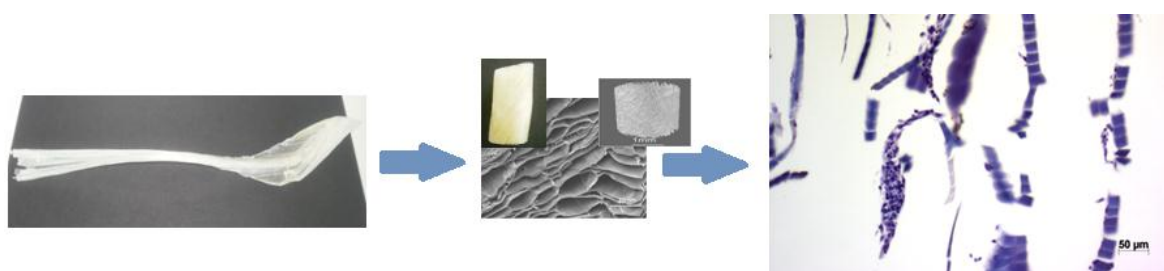


Figure 1. Squid pens are the raw material for extraction of chitin, further converted into chitosan and processed into porous structures to be used in Tissue Engineering approaches.

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New synthetic approach towards miharamycins sugar moiety

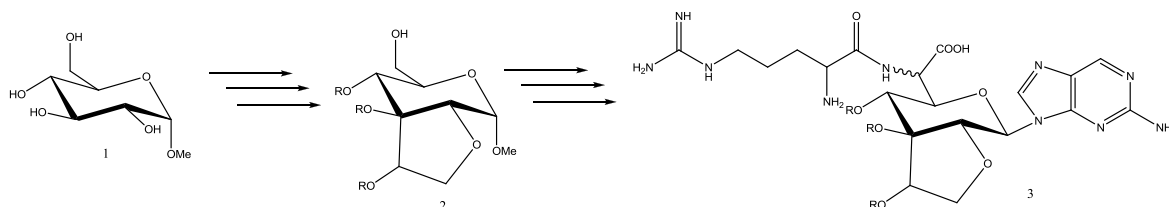
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Pyricularia oryzae is a fungus responsible for the disease known as rice blast, that is the most devastating disease affecting rice worldwide, both in terms of distribution and damage caused. It affects about 85 countries, where rice is usually cultivated, and its remarkable ability to overcome plant defenses is responsible for the destruction of an amount of rice crops that would feed 60 million people annually. Since rice is an important food source around the world it is imperative that a potent antibiotic is developed [1].

Miharamycins are natural products with structure type **3** isolated from *Streptomyces miharaensis* that exhibit a potent antimicrobial activity against various microbes, particularly *Pyricularia oryzae* [2]. Total synthesis of the miharamycins core was reported by our group [3] and we found that related nucleosides do not inhibit cholinesterases [4], which is an important feature for agrochemicals [5]. Although various syntheses have been proposed for its sugar moiety, they usually give mixtures of isomers that are difficult to separate and use toxic reagents. In this work we present a synthesis for the miharamycins saccharidic moiety **2** with simple and stereoselective reactions starting from **1**.



Scheme 1. Synthetic route towards the miharamycins.

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Mechanosynthesis: a new pathway for the synthesis of metallodrugs and metallopharmaceuticals

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The quest for new crystal forms of active pharmaceutical ingredients (API) is one of the most challenging topics in solid-state chemistry and has attracted much attention over the last years. New crystal forms often display different physico-chemical properties, often leading to improvements in drugs' performance, processing and marketing, and thus represent a great opportunity for intellectual property protection [1].

The search for polymorphs, salts, co-crystals and solvates of API has been extensively studied in the last decade, but coordination complexes of pharmaceuticals are a much less developed family of pharmaceutical forms. Such complexes can be roughly divided into two groups: (i) metallodrugs in which the metal ion is also the biologically active component and (ii) metallopharmaceuticals in which the metal ion plays mainly a role of a carrier for the API molecule [2].

New API crystallines are pursued by a judicious choice of synthetic and crystallization conditions, which include both solution and mechanochemical techniques. Mechanochemistry has proved to be a great alternative to the traditional solution methods, often leading to higher purity and yields. A well-known example of metallodrug is the bismuth subsalicylate complex. Rapid, efficient and selective synthesis of three different forms of bismuth salicylate, which differ in the stoichiometric ratio of bismuth and salicylic acid, was successful by ion- and liquid-assisted grinding (ILAG) and the first crystal structure of a bismuth salicylate without auxiliary ligands was unveiled [3]. API coordination complexes (metallopharmaceuticals) are another recent pathway for the development of improved crystal forms and precursors to new bio-inspired materials, in which the pharmacological activity of the API may be improved by changing its properties and/or by taking advantage of the metal benefits. Two complexes of the antibiotic 4-aminosalicylic acid with silver and one complex coordinating piracetam to nickel were disclosed [4].

Mechanochemistry has indeed emerged as an excellent experimental approach to rapidly and efficiently screen for and synthesise metallopharmaceuticals and metallodrugs.

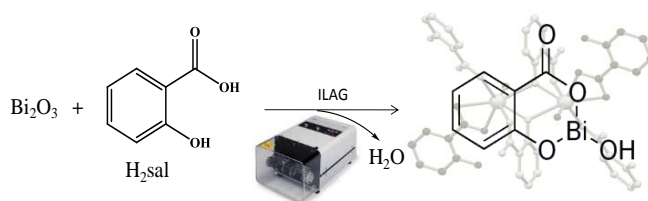


Figure 1. Mechanochemical synthesis of the metallodrug bismuth subsalicylate

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The Sulfur-shift: the activation mechanism of mononuclear Mo enzymes

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In this communication we will explore by theoretical means the importance in mononuclear Mo enzymes of an interesting mechanistic phenomenon that we have called the sulfur-shift. This mechanism is characterized by a displacement of a sulfur atom in the metal site that allows the enzyme to exchange between two states: an inactive form, in which the access to the metal ion is blocked by the formation of a pseudo-dithiolene ligand and an active form that opens a free-coordination position at the metal site that can be occupied by the substrate [1,2]. This specific rearrangement provides an efficient mechanism to lower the activation barriers for ligand exit or entrance processes and at the same time to protect the metal site from other molecules that can potential destroy or inactive it, including the solvent. This mechanism has been recently validated by experimental means and has many similarities to the well-known carboxylate-shift mechanism. All these data seems to reinforce the idea that the enzymes in which the metals are involved in the catalytic process have a particular self-protecting mechanism that allows them to maintain a constant or nearly constant coordination number of the metal throughout an entire catalytic pathway and at the same allows them to protect the metal from other molecule capable of destroying it.

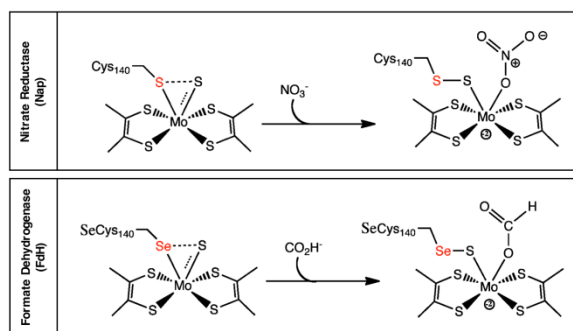


Figure 1. The sulfur-shift mechanism found in Mo dependent enzymes: top - Nitrate Reductase ; bottom- formate dehydrogenase.

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Manganese porphyrins as catalysts in the oxidation of diclofenac

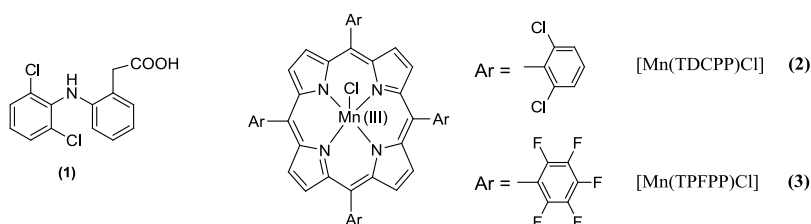
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Diclofenac (**1**) is one of the most frequently used anti-inflammatory drugs, which is metabolized in humans by cytochrome P450 (CYP) enzymes to hydroxy-derivatives: 4'-hydroxydiclofenac, the major metabolite, and 5-hydroxydiclofenac [1]. Other metabolites resulting from oxidative decarboxylation of (**1**) mediated by CYP enzymes have also been reported [2]. Metalloporphyrins (MPs) are known as excellent catalysts able to mimic oxidation reactions catalyzed by CYP enzymes [3]. The hydroxylation of diclofenac using MPs as catalysts has already been demonstrated [4]. However our work will show the formation of new diclofenac derivatives, initially resulting from oxidative decarboxylation of (**1**), similarly to what happens *in vivo*. Chloro [5,10,15,20-tetrakis(2,6-dichlorophenyl)porphyrinato]manganese(III), [Mn(TDCPP)Cl] (**2**), and chloro [5,10,15,20-tetrakis(pentafluorophenyl)porphyrinato]manganese(III), [Mn(TPFPP)Cl] (**3**) are the manganese (III) porphyrins tested. Compounds resulting from the oxidation of (**1**) in the presence of hydrogen peroxide will be presented and characterized.



Acknowledgements: Thanks are due to the University of Aveiro, “Fundação para a Ciência e a Tecnologia” (FCT) and POCI 2010 (FEDER) for funding the Organic Chemistry Research Unit (Project PEst-C/UI/UI0062/2011) and CICECO (Project PEst-C/ CTM/LA0011/2011).

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Light-activated delivery of inorganic and organic phosphates: using metal nanoparticles for the release of caged compounds in aqueous media

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Controlling the activation or delivery of therapeutic agents at the cellular level has become a major target for research in the past few decades, mostly due to the significant advances made in the field of nanotechnology. One of the most promising approaches to achieve this goal is the use of “caged molecules”, i.e. molecules whose therapeutic effect can be activated through light [1]. Our current efforts are focused on designing a system based on metal colloids, typically Ag/Au alloys or Ag@Au nanoparticles (NPs) which can be functionalized with a caged molecule to the nanoparticle surface [2]. Apart from its influence due to Near-Field Enhancement effect [3], the nanoparticles assume an important role as scavengers of the undesired organic photoproducts to the media, which may disrupt biological activity within cells [4]. With this in mind, we designed a molecule with (1) a cage for phosphates (inorganic or organic, e.g. ATP) based on a coumarin chromophore; (2) a spacer, namely a tetraethyleneglycol chain; and (3) a thiol group, to allow covalent immobilization at the surface of NPs via stable Au-S bonds. The molecules were fully characterized in solution and at the NPs surface with regard to the efficiency of the photochemical events as well as the compatibility with enzymatic activity of RNA/DNA polymerases.

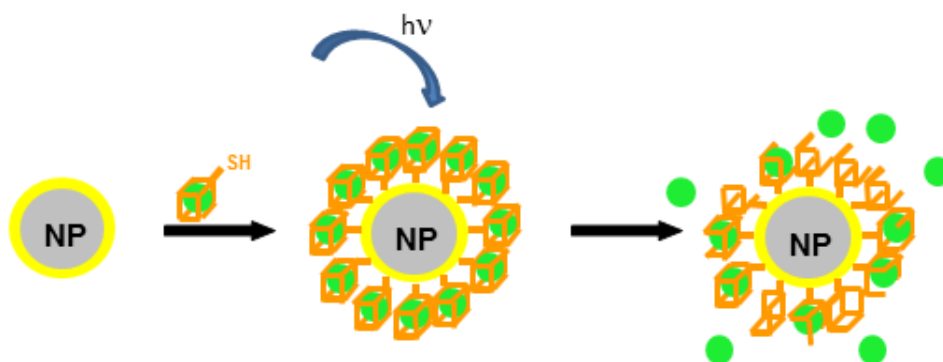


Figure 1. Schematic for the release of caged molecules at the surface of metal NPs.

Acknowledgements: The authors gratefully acknowledge the financial support from Fundação para a Ciência e Tecnologia (Post-doc grant SFRH / BPD / 69210 / 2010, PhD grant SFRH / BD / 69210 / 2008 and project NANOLIGHT, ref. PTDC/ QUI-QUI/ 112597/ 2009).

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Encapsulation of resveratrol in lipid nanoparticles: formulation and characterization

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Nowadays, the problems related to obesity and overweight have gained utmost importance for the population, especially in developed countries where cardiovascular diseases are increasing dramatically, and are now the leading causes of death. As a result, there is a rising interest from health professionals in nutraceuticals like resveratrol which is a natural polyphenol that, among other sources, occurs in grape skin and seeds. In this context, resveratrol is pointed out as a possible contributor to the cardiovascular protection conferred by red wine consumption, the so called “French Paradox”. Therefore, the interest in resveratrol has increased due to its pharmacological effects that include cardio and neuroprotection, antioxidant and anti-inflammatory effects and chemopreventive properties. Despite the therapeutic effects of resveratrol, its pharmacokinetic properties are not so favorable since this compound has poor bioavailability being rapidly and extensively metabolized and excreted [1].

In order to overcome this problem, the main goal of this work was to develop resveratrol loaded lipid nanoparticles which are biocompatible and capable of transporting and protecting this important bioactive compound against degradation, increasing its physical stability and enhancing its bioavailability. The lipid nanoparticles (LN) tested were solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) and were produced using a modified hot homogenization technique by optimization of some parameters (time of stirring; time of sonication and sonication intensity). In order to evaluate the quality of the developed nanoparticles, LN were characterized according to their: surface morphology by scan electron microscopy (cryo-SEM); particle size parameters i.e., the average diameter size and polydispersity index using dynamic light scattering (DLS); zeta potential determined using electrophoretic light scattering (ELS); pH; degree of crystallinity and lipid modification (polymorphism) using a differential scanning calorimetry (DSC). Drug loading and release were measured by UV-Visible spectroscopy and *in vitro* resveratrol release was evaluated in the shelf conditions of storage (room temperature) using dialysis bag diffusion technique under sink conditions. The stability of the nanoparticles was also verified periodically, by measurements of particle size and zeta potential.

In conclusion, the work developed consists in a complete characterization of lipid nanocarriers containing resveratrol to confirm the viability of the application of these developed nanosystems as nutraceuticals, to increase the nutritional value of food and beverages.

Acknowledgments: A. N. thanks FCT for the fellowship (SFRH/BD/73379/2010). The authors are grateful to Dr. Daniela Silva (CEMUP, UP) for expert help with scanning electron microscopy.

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Monitoring heavy metals in urban soils at Lisbon

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In the year of 1999 “leaded petrol” was abolished in Portugal and a significant decrease of environmental lead contamination was expected in the following years.

Since 1998 our group has followed the contamination by lead on poplar leaves in the city of Lisbon and verified that the lead content in this bio-indicator specie decreased significantly in the years following the abolition of “leaded petrol”, but kept their content almost unchanged thereafter [1]. This led us to consider the existence of high levels of lead and other heavy metals in soils that would be the cause of the high levels of lead in the poplar leaves. The soil has a high retention capacity for heavy metals, but when this capacity is exceeded, the metals become bio-available. Therefore they can contaminate the food chain or be leached to groundwater. The contamination can also prevent the use of these soils for the so fashionable urban gardens. Because heavy metals are the cause of various diseases of the nervous system, kidney dysfunction, immune system compromising and lung cancer [2], we have considered this study of Lisbon soils very important. In this communication the results of lead, cadmium, nickel and chromium levels in soils from Lisbon area, collected from 2003 to 2011 are present. In Figure 1 we can see the results of lead between 2003 and 2010. The heavy metals content of soils was determined by graphite furnace atomic absorption spectrometry (GFAAS) after aqua regia digestion [3].

The real knowledge of soil conditions in terms of pollution by heavy metals is extremely important [4], because it allows better decision making in relation to its use and also to consider the implementation of remedial actions if necessary.

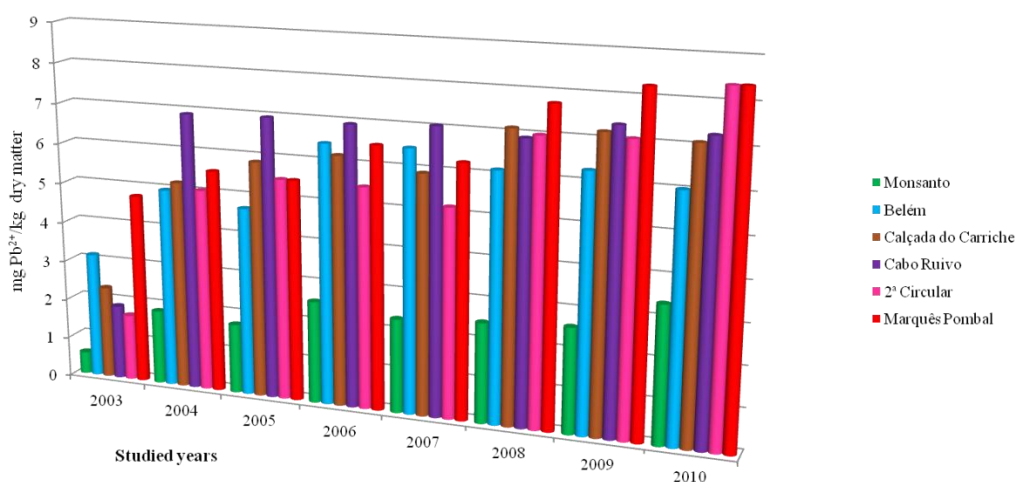


Figure 1. Levels of lead in Lisbon soils between 2003 and 2010.

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Dow human element, fostering an innovation culture

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New products and technologies are vital to the success and future prosperity of a modern corporation. While some executives still look to cost cutting as the way to improve bottom lines, these periodic downsizing exercises have proven ineffective in the long run.

As we begin this new millennium, the growth game is still on – faster and more competitive than ever. Driven by rapidly advancing technologies, globalization of markets and increasing competition at home and abroad, effective new product development is emerging as the major corporate strategic initiative of the decades ahead. Corporations that fail to develop excellent new products and technologies will eventually disappear or be globed up by the winners [1].

Organizational culture is a fundamental element of sustained innovativeness and financial performance. Although many companies appreciate the important role culture plays in making an innovation successful, it is not easy to change culture [2].

At Dow we understand the difference between innovation and invention. Invention is important, it is the beginning and it is the spark. But innovation is where we actually create value for Dow, for the society and for the world. In Dow laboratories from Indianapolis to Shanghai, the best of minds are just dealing with the most promising inventions, practicing the discipline, the science [3].

Science requires immense creativity because the process that we are trying to address for tomorrow are not going to be obvious. No process can make up for the lack of creativity or curiosity. The unwritten truth of the scientific method, it is that it requires curiosity. At Dow we are constantly searching for how to use our fundamental knowledge of chemistry to solve these difficult problems. At Dow we can take our plastics expertise to be able to make a better solar shingles that will reduce the price of photovoltaic solar energy. The journey from need, to hope, to discovery is driven by curiosity and guided by science.

The same 117 elements do the fundamental work of chemistry; the difference is the one element that is the catalyst for innovation. The one element that changes everything, it is the human element.

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Photoacoustic waves based technology using light absorbing thin films for transdermal drug delivery

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This innovative method refers to a device capable of rapidly and efficiently converting the energy in a laser pulse into a high-impulse broadband pressure wave [1]. Its applications include the transient permeabilization of a biological membrane, including the outer layers of the skin and cellular membrane without causing damage or discomfort.

The distinctive features of the device are the use of thin films (thickness <200 μm) strongly absorbing the light of pulsed, affordable and portable ND:YAG lasers, such as low energies lasers (<50 mJ). The films are constituted of associations between polymer-calorimetric references or titanium dioxide-calorimetric references. The device produces pressure waves with rise times lower than 50 ns at low optical power densities (<40 MW/cm²), of a very high frequency (up to 200 MHz) and with amplitudes peaks of 12 atm (energy-to-pressure conversion yield of 30%).

The device has been tested with healthy volunteers, for a period of 2 minutes for each one of them. It was shown to increase the transepidermal water loss (TEWL) of the skin by a factor of 3 without causing any pain or discomfort, and it then returned to normal in one minute, leaving no marks.

It has shown that molecules heavier than 1 kDa were delivered with an initial flow 3 times larger with this device than with an optimized topical formulation. The onset of large molecules delivery like Green Fluorescent Protein (GFP) was tested in minipigs with large accumulations in the viable epidermis. In both cases fluorescence microscopy and confocal microscopy showed that the stratum corneum was intact after the 20 minutes delivery.

Transdermal drug delivery of high molecular weight molecules can be achieved with the aid of pressure waves produced with relatively low energy laser pulses.

Acknowledgements: The author wishes to thanks the FCT for financial support.

[1] Device for the efficient delivery of compounds to or through the skin or biological barriers, using light-absorbing thin films. S, G. F. F.; Serpa Soares, C. A. L.; Arnaut Moreira, L. G. S., Universidade de Coimbra. PT Patent Application no. 105635, 19 de Abril de 2011.

Use of solid phase extraction in a sequential injection system for the determination of alkaline phosphatase activity in plant roots

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Phosphorus (P) is an essential nutrient to all organisms and in soils P is the most limiting nutrient that controls living processes in plants. Dissolved inorganic phosphate is readily available for assimilation by organisms such as bacteria and plants. For that reason, when dissolved inorganic phosphate is depleted compared to other nutrients both in water and soil, phytoplankton, plants and bacteria have the ability to obtain phosphorus from dissolved organic compounds due to the production of an enzyme named alkaline phosphatase. This enzyme hydrolyzes phosphate monoesters releasing inorganic phosphate and organic matter. Its production is regulated by inorganic phosphate concentrations and internal P levels so the values of alkaline phosphatase are an excellent indicator of P status.

In this work, a sequential injection methodology was developed for the determination of alkaline phosphatase activity in root plants. The enzymatic activity was assessed using *p*-nitrophenyl phosphate as substrate and measuring the absorbance of the colored product, *p*-nitrophenol. The alkaline phosphatase is an extra/intra cellular metalloenzyme, as it requires metal ions in the active site to carry out the catalytic activity. Exploring this feature of the enzyme and aiming for the low levels found, a step for the in-line pre-concentration was included. As alkaline phosphatase needs Zn^{2+} ions in the active site, a resin, Nitrilotriacetic Acid (NTA) Superflow, was charged with Zn^{2+} to retain the enzyme.

The proposed methodology allowed the determination of alkaline phosphatase activity in plant roots within a range between 0.044 – 0.441 unit cm^{-3} enzyme activity and 19 – 280 $\mu\text{mol dm}^{-3}$ *p*NP. A determination rate of 17 h^{-1} and detection limits of 0.025 unit cm^{-3} enzyme activity and 1.9 $\mu\text{mol dm}^{-3}$ *p*NP were obtained. The activity was assessed with a minimal incubation time (≈ 12 s).

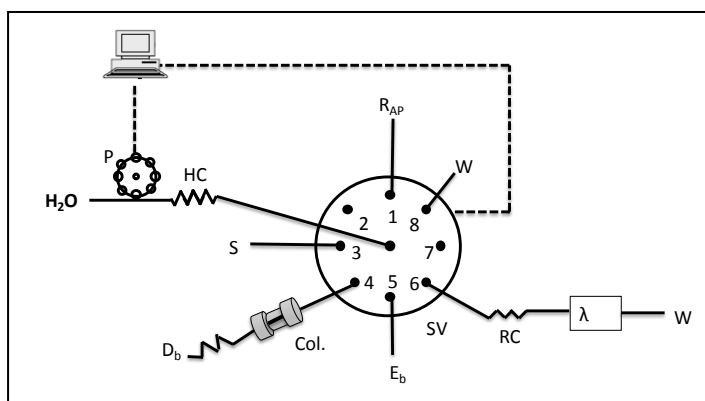


Figure 1. Sequential injection manifold for the spectrophotometric determination of alkaline phosphatase activity: P, peristaltic pump; SV, eight-port selection valve; HC, 4.25 m holding coil; S, sample or standard; Col., column with NTA Superflow resin charged with Zn^{2+} ions; R_{AP} , *p*NPP or *p*NP; E_b , eluting buffer; D_b , diethanolamine buffer; RC, 0.95 m reaction coil; λ , spectrophotometer (405 nm); W, waste.

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Preparation and characterization of ionic liquids based on thioflavin T

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Thioflavin T is a basic yellow biological compound used as a dye to detect and quantify the amyloid fibrils that are normally associated with several neurodegenerative diseases such as Alzheimer's and Parkinson's [1,2].

Recent studies showed that Room Temperature Ionic Liquids (RTILs) can effectively trigger amyloid fibril formation, being their monitoring process carried out using Thioflavin T fluorescence assay [3]. In the sequence of this observation, we have prepared different Ionic Liquids based on Thioflavin T in order to check their biological properties.

Ionic Liquids (ILs) as organic salts are compounds whose melting point is below 100°C, being many of them liquids at room temperature (RTILs) [4]. Thioflavin T as an organic cation was combined with different anions such as bis(trifluoromethylsulfonyl)imide (NTf₂), docusate (AOT), trifluoromethanesulfonate (OTf) and dicyanamide (DCA) in order to prepare novel ILs (Figure 1)

Novel Thioflavin salts were characterized by NMR (¹H, ¹³C and ¹⁹F), FTIR and elemental analysis. Some physical-chemical and thermal properties were also evaluated in particular their rheological (viscosity), spectroscopic (UV-Vis and emission spectra) and calorimetric (melting point, glass transition and decomposition temperatures) behavior.

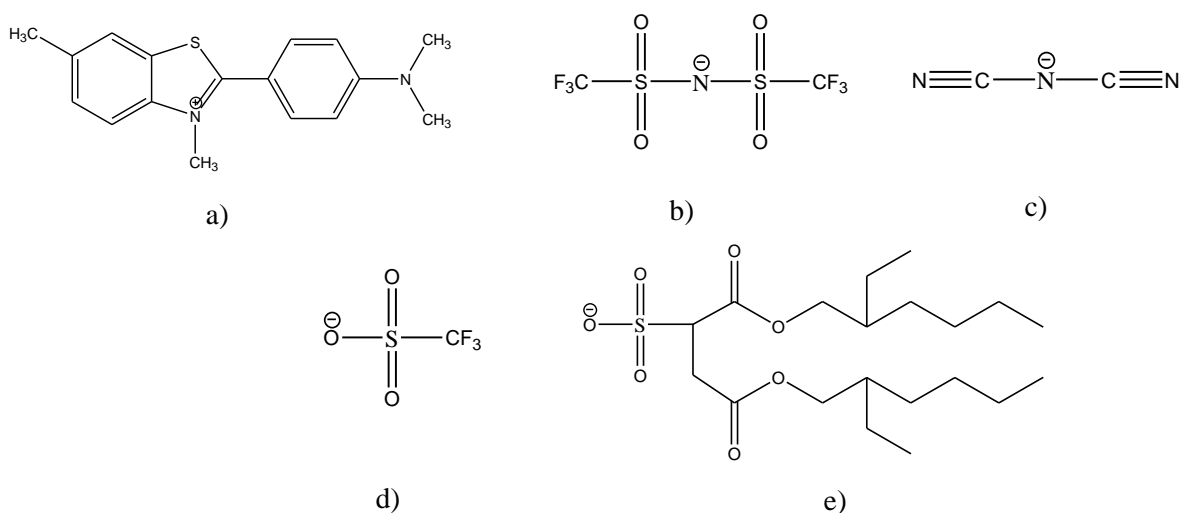


Figure 1. Structures of selected compounds: a) Thioflavin cation T; Anions: b) bis(trifluoromethylsulfonyl)imide (NTf₂); c) dicyanamide (DCA); d) trifluoromethanesulfonate (OTf); e) docusate (AOT).

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PDLC devices that consume lower power and are environmentally friendly

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Polymer dispersed liquid crystal (PDLC) films are a mixed phase of nematic liquid crystals (LC), usually E7 [1], commonly dispersed as inclusions in a solid polymer. They have remarkable electro-optical behaviour since they can be switched from an opaque (OFF state) to a transparent state (ON state) simply by application of an electric field [2]. PDLC have attracted attention as novel class of optical applications such as flexible information displays and light shutter devices. A new type of electro-optical response with a high transparency state is obtained for a long period of time at room temperature even after the applied voltage has been switched off, starting from an opaque state and after reaching a transparent state (figure 1), has been studied by us.

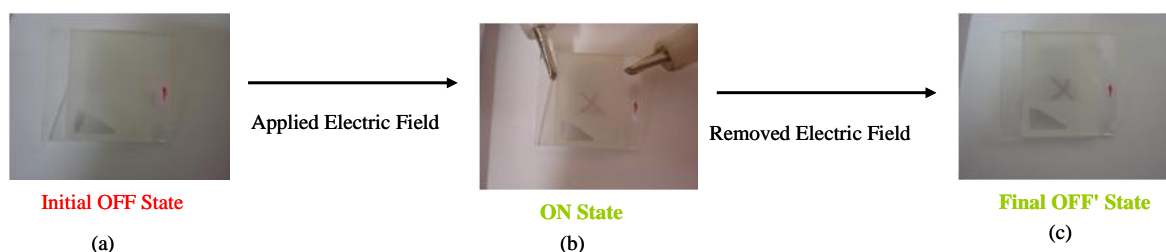


Figure 1. Images of PDLC devices with permanent memory effect: (a) initial OFF state, (b) upon applying electric field and (c) OFF state after removed electric field.

The PDLC film with this electro-optical response has a permanent memory effect and this still remains a poorly understood aspect of PDLC electro-optical behaviour. This electro-optical response is very revolutionary in the study of PDLC because allow a switch in transparency and the new state is kept without the need for any more energy to be spent, the only energy required is that needed to switch the PDLC from the OFF state to the ON state. They can be used in memory devices, they consume lower power and are environmentally friendly. Various factors can influence the performance of a PDLC and therefore the permanent memory effect. However, the most frequently explanation mentioned in literature is related with the polymeric conditions and molecular structure of polymerisable monomers used in the preparation of PDLC films. Therefore, series of new thermal and photochemical polymerisable monomers with structurally diverse functionalisation were previously synthesised and applied on PDLC films [3,4]. However, the commercial acrylates and methacrylates monomers with long carbon chain seem to be candidates to those devices. We obtain a 70% of the permanent memory effect that is, to our knowledge, higher than the values reported in the literature.

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A GC-MS method for the simultaneous identification and quantification of amino acids, fatty acids and sterols in marine organisms

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In this work a fast and simple multi-target gas chromatography-mass spectrometry (GC-MS) method for the simultaneous detection and quantification of amino acids, fatty acids, and sterols in marine organisms is proposed. The method does not use hazardous solvents and was applied to the characterization of the echinoderm *Marthasterias glacialis* (sea star) extracts, collected along the Portuguese coast. The main factors influencing the extraction of target compounds were evaluated by using different extraction procedures, solvent systems and temperature conditions. Good analytical parameters were obtained for all 39 compounds under analysis (15 amino acids, 16 fatty acids and 8 sterols). Variations in samples from different seasons and geographical origin are reported. Moreover, due to the fast and wide character of the proposed method it is suitable for implementation as routine analysis both in the food and biomedical industry.

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Photophysics of push-pull oxazolones derivatives with nonlinear optical properties

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Two-photon absorbing fluorophores are molecules that absorb simultaneously two photons, accompanied by the transition of an electron from a lower energy level to a higher level. The absorbed photons can be up-converted into emitted photons with twice the energy. This type of nonlinear molecular material have found applications in very diverse areas such as microfabrication, data storage, photodynamic therapy, optical power limiting and sensors [1,2].

Oxazol-5-(4H)-ones (referred as oxazolones) are small and simple molecules with potential applications as labels in bioimage, and as nonlinear activated optical sensors. In order to produce an highly conjugated π -system with push-pull geometry, which allows to an increase in the two-photon absorption capability of molecules, a series of oxazolones with different electron donor and acceptor groups and the same active center have been synthesized and their linear and nonlinear properties analyzed. Figures 1a and 1b present the general structure of these molecules and the linear absorption and emission spectra and two-photon absorption spectra of one of the oxazolone synthesized, respectively. In general, these molecules have quite reasonable two-photon absorption cross-sections (up to 540 GM, 1 GM= 10^{-50} cm⁴s) but low emission quantum yield due to non-radiative processes of different nature. By changing the electron donor group of the molecule we were able to obtain a molecule with a two-photon absorption cross section of \approx 320 GM and a high emission quantum yield (0.79). The performance of this optimized oxazolone can be compared with that of the commercially available fluorophores used in bioimaging, which have at best two-photon absorption cross sections around 100-200 GM and quantum yields of 0.4-0.9.

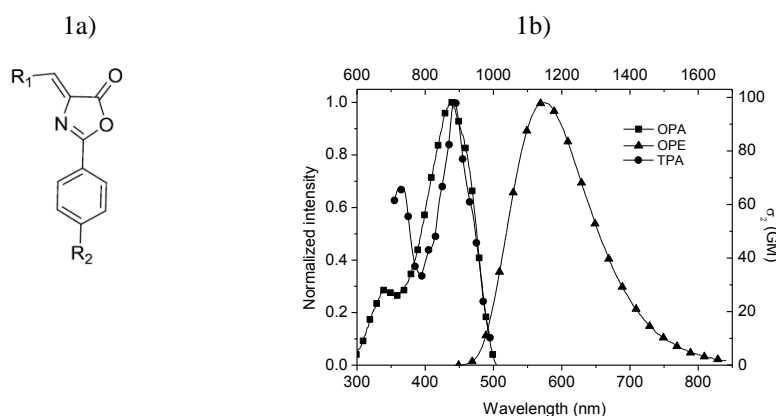


Figure 1. a) General structure of oxazol-5-(4H)-ones, b) linear absorption and emission spectra and two-photon absorption spectra of an oxazolone molecule in THF.

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New porphyrin materials for optoelectronic and PET applications

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Porphyrins and related compounds are ubiquitous in nature, and are responsible for several biological centres involved in energy or charge transport. In the last 50 years an enormous number of applications for porphyrins, both natural and synthetic, have emerged. These include artificial light harvesting, energy conversion systems, photodynamic therapy, positron emission tomography (PET), nonlinear optics, together with molecular photonic devices such as solar cells and photon-gated molecular wires [1-4].

Multiporphyrin arrays have become the focus of considerable attention, resulting, in particular, from possibilities of incorporating different functionalities [5]. The combination of synthetic accessibility, excellent electronic properties and their ability to complex many types of metal ions, makes porphyrins matchless as building blocks for the synthesis of both straight-chain and branched extended molecular systems designed for specific advanced applications.

Here, we report the synthesis and photophysical properties of a small library of porphyrin based materials with applications in sensing [6], solar cells, melting point modulation [7] and PET.

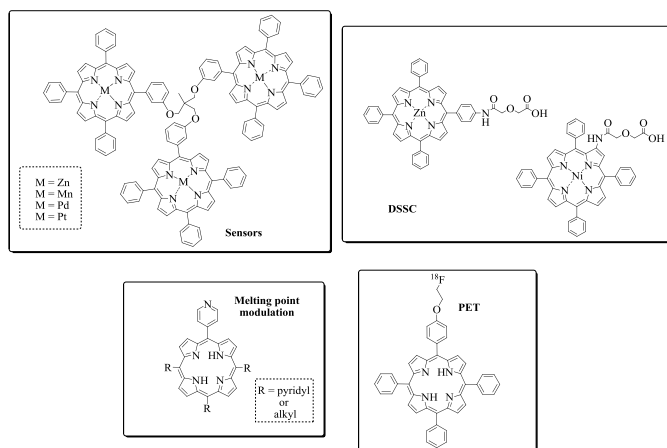


Figure 1. Examples of the porphyrin compounds synthesised.

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Clay materials for the storage and release of nitric oxide for therapeutic purposes

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NO is implicated in a wide range of medical processes, for example, vasodilation, prevention of blood platelet aggregation and thrombus formation or neurotransmission in wound healing [1].

A significant proportion of therapies involving NO require systems to enhance delivery of this molecule at specific sites of the body. In this sense, it has been studying the development of nanoporous materials to their use in storage and subsequent release of NO in therapy [1,2].

This study explores the possibilities of clay materials containing cobalt ions in its structure in the storage and release of NO. The choice of cobalt, besides the known biocompatibility of the metal, was due to the existing literature references mentioning that cobalt ions can promote interaction with nitric oxide, thereby increasing the adsorption capacity of the material.

The samples were characterized by X-ray diffraction (Bruker AXS D8) and nitrogen adsorption at -196°C (Micrometrics, mod ASAP 2010). The adsorption and desorption curves of NO were obtained at 25°C in an adsorption microbalance (CI Electronics, Disbal) associated with a high-vacuum producing system.

The isothermal nitrogen adsorption-desorption show a high specific surface area, as recorded in Table 1, which is the result of a finely divided structure. In this table there are also the values of basal spacing (d_{001}). The peak corresponding to basal spacing differs from the equivalent of natural clays, likely consequence of its disorganized structure.

The data on the adsorption and adsorption kinetics of nitric oxide, in CoClay-2 (as an example), is in Figure 1. It appears that the amount of NO adsorbed is about 4.3% by mass, while its release takes place only partially.

Table 1. Textural parameters of studied samples.

Material	$A_{\text{BET}} (\text{m}^2 \text{g}^{-1})$	$d_{001} (\text{\AA})$
CoClay-1	219	14,22
CoClay-2	253	5,12
CoClay-3	272	2,13
CoClay-5	264	8,00

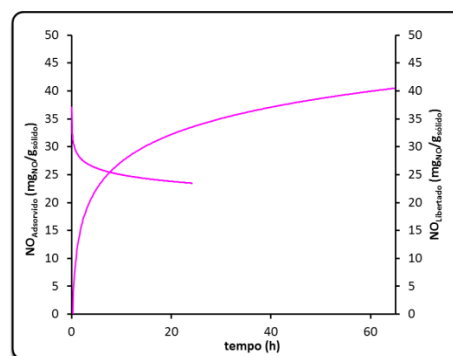


Figure 1. Adsorption and release of NO on CoClay-2.

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On the voltammetry of chalcones: trans-chalcone, cardamonin and xanthohumol

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Chalcones (1,3-diphenyl-2-propene-1-one, whereas 2 aromatic rings are connected by a 3-carbon link, Fig. 1) are a particular subclass of flavonoids. Chalcones are an example of compounds present in many plants with a high therapeutic and preventive potential of many diseases. Chalcones are particularly interesting for their chemopreventing properties, one should keep in mind that cancer is one of the major death causes worldwide and such even tends to increase. Moreover, these compounds could be easily introduced in human's diet or in pharmaceutical formulations with great added value considering that they are not synthesized by the human body [1].

In this study, electrochemical analysis was applied to three chalcones (xanthohumol, cardamonin and trans-chalcone) in order to obtain qualitative and quantitative information about them. This was performed by cyclic voltammetry (CV) on a hanging mercury drop electrode (HMDE) [2,3].

The reduction of these chalcones seemed to be an overall irreversible process and a mixed adsorptive and diffusive response was obtained. Also, for major times of accumulation was showed a stagnation of the adsorptive effective. This method proved to be selective and was calculated a calibration straight. This study provided a double reduction profile depending on the pH, i.e. proton concentration.

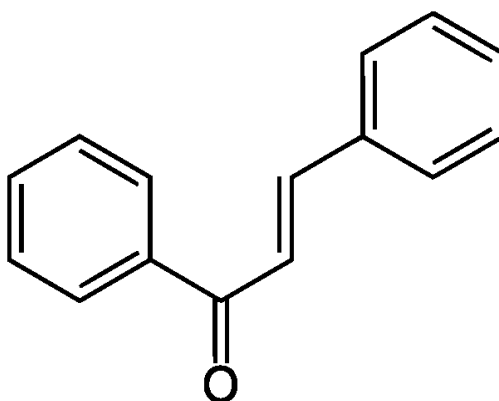


Figure 1. Basic chalcone structure.

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Computational studies on the aspartic protease Renin

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The aspartic protease renin (REN) catalyzes the rate-limiting step in the Renin-Angiotensin-Aldosterone System (RAAS). This cascade is a central regulator of cardiovascular and renal homeostasis, beginning with the release of REN by the kidney which converts circulating angiotensinogen into angiotensin I (angI). The latter is then cleaved into the potent vasoconstrictor angiotensin II (angII) by the angiotensin-converting enzyme (ACE). Following its synthesis, angII interacts with the AT₁ receptor, mediating cardiovascular events such as vasoconstriction, inflammatory response, aldosterone secretion and salt retention [1-3].

Although combined blockade of the RAAS is an attractive therapeutic strategy for the treatment of hypertension and cardiovascular diseases, REN inhibitors are actually the most advantageous drugs to reduce the healthcare impact of these conditions. However, until now, the FDA approved only one direct REN inhibitor - aliskiren (Tekturna®) [3]. Taking this into account, theoretical and computational approaches were used to research new generation drugs targeting REN.

On the one hand, the theoretical catalytic mechanism of human and mouse REN were assessed to identify efficient ways of inhibiting their activities and subsequently design Transition-State (TS) analogue molecules with potential clinical use. For that, we used the hybrid ONIOM method (DFT:AMBER calculations), and the whole enzyme systems were subdivided into two regions studied at different theoretical levels (QM/MM) [4]. Our data suggests that the first step in the reaction is the rate-limiting one, where a protonated carboxyl group acts as a general acid to donate its proton to the substrate scissile carbonyl, whereas the other unprotonated carboxyl group acts as a general base to accept a proton from a water molecule. Additionally, the comparison of the active site surrounding regions of each enzyme (human and mouse) justifies the high specificity for the respective substrate.

On the other hand, Molecular Dynamics simulations were performed to understand the correct binding mode between REN and its unique substrate angiotensinogen, as well as with two well known inhibitors (aliskiren and remikiren) [5]. Alanine Scanning Mutagenesis studies were also carried out to check the most important residues to the interaction between both proteins [6]. Our calculations identified some flexible regions and specific amino acids that are crucial to an efficient REN activity. In sum, our results are preminent to future drug design studies directed to these specific target regions.

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Ciprofloxacin and norfloxacin spectrophotometric determination in a fully automated multi-pumping flow system

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A flow-based methodology was developed for the determination of ciprofloxacin and norfloxacin in pharmaceutical products, based on the oxidation with N-bromosuccinimide in acidic medium [1,2]. The procedure was implemented in a multi-pumping flow system, which established a pulsed flow, inherent to the micro-pumps actuation and promoting a sample-reagent mixing more efficient and a faster and enhanced reaction development. The high level of automation of multi-pumping flow system (MPFS) with all parameters under computer control allowed the manipulation of the reaction zone, including added volumes, sequence of addition and sample zone focusing, avoiding superfluous sample and reagent consumption, less waste generation and an increased sampling rate [2].

The use of solenoid micro-pumps as the sole insertion, propulsion and solution commutation devices, allowed working with different flows and different sampling strategies, making it easy to adjust the system parameters for development purpose. The nature of the pulsed flow guaranteed a good homogenization with dispersion reduction and less time for the reaction to take place.

Linear calibrations were obtained for ciprofloxacin and norfloxacin concentrations ranging from 5 to 70 mg L⁻¹ with R. S. D < 2.2% (n=10). Detection limits (3σ) were 0.27 mg L⁻¹ and 0.99 mg L⁻¹ for norfloxacin and ciprofloxacin, respectively. The overall figures of merit were improved [3].

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Efficient synthesis of new spiroisoxazoline oxindoles

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Compounds possessing a spiro-oxindole core represent attractive synthetic targets due to their interesting biological properties and consequently with potential application in medicinal chemistry [1]. In particular spiropyrrolidine oxindole derivative MI-219 (Figure 1) is already entering phase I clinical trials as anticancer agent through inhibition of p53-MDM2 interaction [2].

The initial synthetic design of the present work was devised as a consequence of a methodology developed in our group applied to the synthesis of naphtho[2,3- d]isoxazole-4,9-diones, in which a new isoxazole ring was formed when primary nitro compounds were employed (Scheme 1) [3].

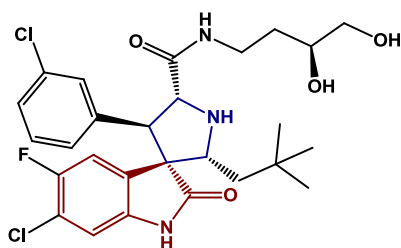
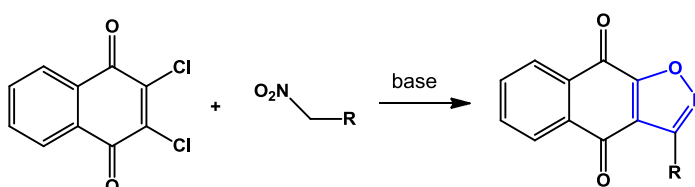


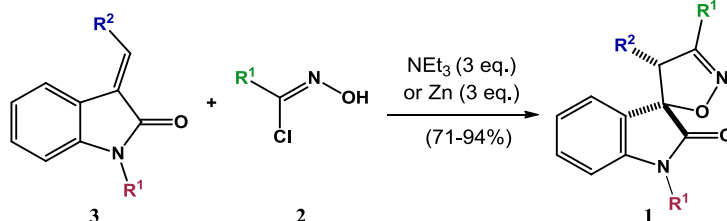
Figure 1. MI-219.



Scheme 1. Synthesis of naphtho[2,3- d]isoxazole-4,9-diones.

We report here a novel synthetic strategy for the synthesis of spiroisoxazoline oxindoles **1**, through the reaction between 3-methylene indolin-2-ones **2** and chlorooximes **3** in the presence of triethylamine or zinc (Scheme 2). This new efficient method represents the first time that zinc is used as the dehydrochlorinating agent in a 1,3-dipolar cycloaddition reaction [4].

Due to the structure similarity to MI-219, a library of spiroisoxazoline oxindole compounds as potential inhibitors of the p53-MDM2 interaction, using the above methodology, is currently under construction.



Scheme 2. Synthesis of spiroisoxazoline oxindoles.

- 1a** R¹=Me, R²=CO₂Et, R³=CO₂Et;
1b R¹=Me, R²=CO₂Et, R³=Ph;
1c R¹=Me, R²=CO₂Me, R³=Ph;
1d R¹=H, R²=CO₂Et, R³=Ph;
1e R¹=H, R²=CO₂Me, R³=Ph;
1f R¹=Me, R²=CO₂Me, R³=CO₂Et;
1g R¹=H, R²=CO₂Et, R³=CO₂Et;
1h R¹=H, R²=CO₂Me, R³=CO₂Et;
1i R¹=H, R²=CO₂Et, R³=CO₂Me;
1j R¹=H, R²=CO₂Et, R³=pOMePh;
1k R¹=Me, R²=CO₂Et, R³=pOMePh;

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New composites based on polyoxometalates and porous MOFs as active catalysts for liquid phase oxidation

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Metal-Organic Framework (MOFs) materials have been one of the most important materials family presently studied, due to their application in important areas such as gas separation [1] and catalysis [2, 3]. Their infinitive networks result of the bonding of metal centers to multifunctional organic molecules, often leading to porous 3D frameworks. These structures have considerable mechanical and thermal stability and have claimed considerable attention because of their high porosities, large surface areas, and the ability to accommodate guest molecules [2, 4]. One of the possible guests are polyoxometalates (POMs) that are a class of compounds formed by bulky clusters of transition metal oxide anions. POMs are well-known efficient homogeneous catalysts and have been broadly applied in oxidation reactions [5]. However, the necessities to recover and recycle the catalysts has led to an increasing effort to immobilize the POMs on solid supports in the last years. In the present work, we have prepared composite materials through the encapsulation of POMs within the porous cages of MIL-101. The composite materials were characterized by vibrational spectroscopy (FT-IR and FT-Raman), ³¹P solid-state NMR and electronic microscopy. The results show that the POM structure is retained inside the metal-organic framework porous. The composite materials were tested as heterogeneous catalysts for oxidation reactions using H₂O₂ as oxidant. The robustness of the composites was confirmed and the presence of POMs inside the MIL-101 cages seems to promote the stability of these hybrid materials under oxidative environment.

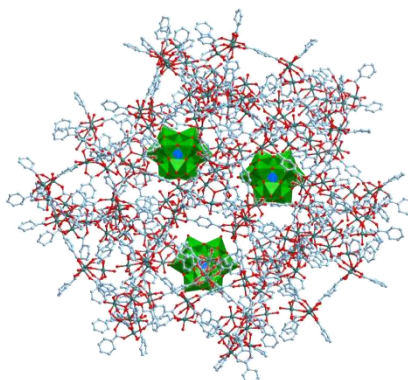


Figure 1. Representation of POMs incorporated at porous MIL-101.

Acknowledgements: the authors are grateful to the Fundação para a Ciência e a Tecnologia (FCT, MEC, Portugal) for general financial support by the strategic project no. Pest C/EQB/LA0006/2011 (REQUIMTE), the R&D projects PTDC/CTM/100357/2008 and PTDC/EQU-EQU/121677/2010, and the fellowships SFRH/BPD/73191/2010 (CG) and SFRH/BD/46601/2008 (PS).

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Iron oxide/gold core/shell nanoparticles and screen printed carbon electrode for sensitive detection of *Salmonella typhimurium*

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Salmonella typhimurium is a gram negative bacterial pathogen and is one of the most common pathogens of foodborne disease worldwide [1]. It is estimated that *Salmonella* causes 93.8 million human infections and 155.000 deaths annually [2]. Sensitive and rapid detection of *Salmonella* is of outmost importance in the field of food safety, bio threat prevention and public health. There is an urgent need for rapid methods to detect pathogenic bacteria in food products as alternatives to the current laborious and time-consuming culture procedures. Among the available biosensor platforms, electrochemical approach has received remarkable attention due to its high sensitivity, fast response, low cost and suitability to miniaturization [3]. The use of electrochemical immunoassay has attracted considerable interest for *Salmonella* determination.

In this work, an ultrasensitive immunosensor assay using iron oxide/gold core/shell nanoparticles conjugated with anti salmonella monoclonal antibodies is developed. The gold shell provides a well established platform for conjugation of biomolecules. An electrochemical transducer based on screen-printed carbon working electrode with onboard carbon counter and silver chloride pseudo-reference electrode for *Salmonella* detection is used. A magnetic field is applied to quickly bring nanoparticle attached with salmonella from a solution to an electrode surface and to improve detection level of *Salmonella* at very low concentration. The stepwise assembly procedure of the immunosensor was characterized by means of square wave voltammetry (SWV) and impedance. The $K_3[Fe(CN)_6]/K_4[Fe(CN)_6]$ was used as a marker to probe the interface and to determine the amount immune-captured *Salmonella* on the electrode surface.

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e-lab: a didactic interactive experiment. An approach to the Boyle-Mariotte law.

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An experimental interactive resource to explore the validity of the Boyle-Mariotte law ($PV = \text{const}$) is the main subject of this communication. The resource used is a remotely controlled laboratory called *e-lab*, freely available in <http://www.e-escola.pt/elab.asp>, physically located at the Instituto Superior Técnico campus in Lisbon, and can be used at primary, secondary or higher education level.

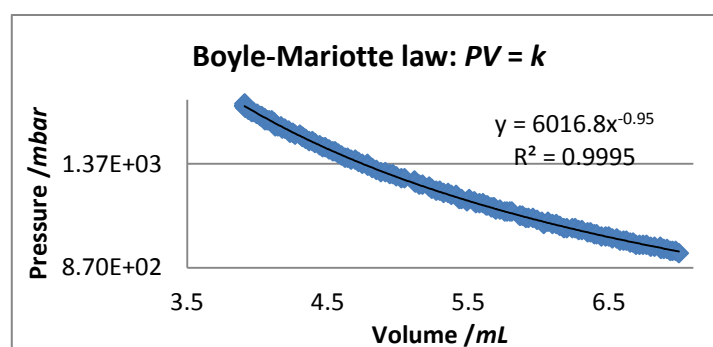


Figure 1. Numerical fit of the plot Pressure Vs Volume (exponent not exactly -1).

The e-lab is an e-learning platform to support teaching and learning of Physics and Chemistry that has been tested in the last years in the classroom in basic (seventh and eighth years) and secondary (twelfth year) level. It has proven to be an important tool in stimulating students to scientific subjects, holding their attention and increasing their motivation and interest in science contents, as seen by the pilot study already conducted [1,2]. The pilot study occurs in the years where the Boyle-Mariotte law is integrated in Portuguese pre-university curricula.

The e-lab Boyle-Mariotte experiences permit the verification of the law with very satisfactory results and allow a correct interpretation of it. The raw data may be processed in Excel, checking the Boyle-Mariotte law by calculating the pressure and volume product (verifying that it remains approximately constant) as well as by appropriate graphical representations.

The fact that the platform itself has the resources for the preparation, operation and implementation of various experiences is an asset for teachers to work with students scientific skills [1]. The ability to use a laboratory tool any day, any time, according to the availability of the teacher and students is also an asset, as well as the possibility of using the b-learning turns e-lab an excellent tool to use in class.

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Dual complexation mode of cucurbit[7]uril and cationic surfactants

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Cucurbit[*n*]urils are pumpkin-shaped cavities composed of *n* glycoril units linked by a pair of methylene groups. Their two identical carbonyl-fringed portals have a considerable negative charge density, which facilitates the binding of metal ions and cationic organic compounds, while the inner cavities are relatively hydrophobic and can host neutral molecules that fit within [1].

In the present communication we show the assembly of host-guest complexes of CB7 with a series of alkyltrimethylammonium surfactants (C_nTA^+ , $n = 6-18$), characterized in solution by NMR spectroscopy, isothermal titration calorimetry and kinetics measurements. Our studies have shown the existence of CB7: C_nTA^+ complexes with stoichiometries 1:1 and 2:1 for alkyl chains with more than 12 methylene groups. The binding constants for the 1:1 complex are independent of the alkyl chain length of the surfactant [2], whereas a relationship was found for the 2:1 complex between $K_{2:1}$ and the chain length of the surfactant. Competitive experiments, as well as NMR studies have shown that CB7 binds the cationic surfactants without the need for forming an inclusion complex.

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The conducting polymer based electrochemical sensors and biosensors with autocatalytical stage and the description of their work

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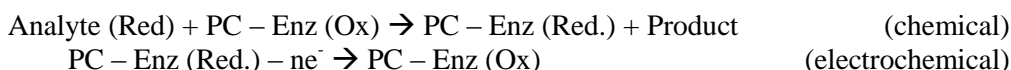
The electroanalytic chemistry, being one of the most important branches of chemistry, because it uses the electrochemical methods in detection of different substances, and one of the most investigated in the epoch. One of the objects of this science is the preparation of sensors, capable to detect exactly the minimal quantities of different substances. It begins the application of nanotechnology and the conducting polymer chemistry in electroanalytical processes.

For the last decades the conducting polymers have been intensively studied and the facility in modification let us use them for different purposes, including the electrochemical sensors. In this work we describe the sensors and biosensors, the implementation of which contains the autocatalytic stage.

For the “direct transfer” case the conducting polymer, that implements either the functions of the active substance, or the mediating functions, contains the fragments of enzyme factors, that oxidate the analyte.

The electrochemical instabilities occur in electroanalytical processes very frequently, manifesting themselves on the sensor response, for example, in the form of the oscillatory behavior [1] (Fig. 1) and the mathematical model, capable to describe the sensor’s work, could determine the instabilities causes.

The sensing function contains two stages:



and the first one is autocatalytic. The conducting polymer may be used either in its normal, doped form, or on its overoxidized form.

Using the mathematical model of the sensing function, we determined that the oscillatory behavior might be caused by the influence of the electrochemical oxidation to the double electric layer and also by the effect of the autocatalytic reaction on the first stage.

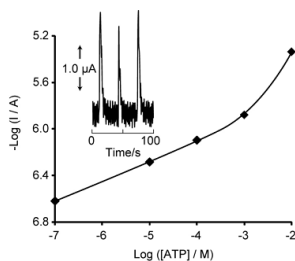


Figure 1. The oscillatory response, obtained during the ATP detection with usage of overoxidized polypyrrole.

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One-step three-component vs two-step two-component microwave assisted synthesis of 4,6-diaryldehydropyrimidinethiones

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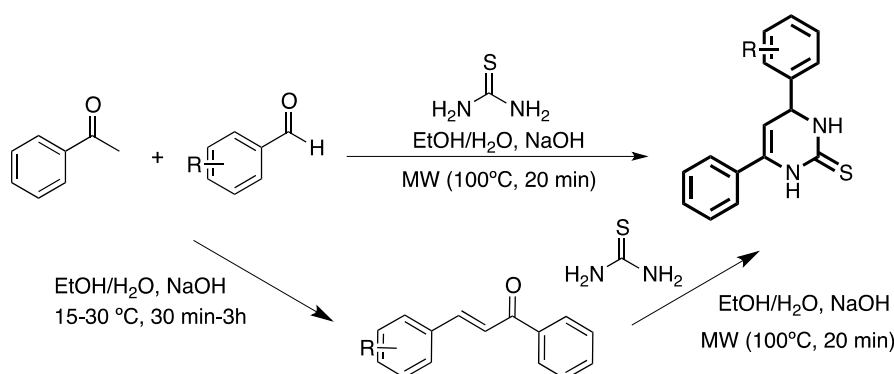
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4,6-diaryldehydropyrimidinones can be obtained in a three-component reaction using acid catalysts such as ZnI_2 under microwave irradiation [1] or FeCl_3 under conventional heating [2], however, these methods fail for the synthesis of the corresponding thione derivatives. The synthesis of 4,6-diaryldehydropyrimidinethiones **5** has attracted less attention, and to the best of our knowledge only four methods have been reported, two of them using conventional heating [3,4], one under ultrasound irradiation [5] and one under microwave irradiation [6]. In all these reports the pyrimidinethiones were obtained in base-mediated reactions from the corresponding previously synthesized 1,3-diarylporpenone **4** and thiourea, **3**.

Here we report the first three-component microwave assisted synthesis of 4,6-diaryldehydropyrimidinethiones. Comparison with the two-component two-step synthesis of these compounds and with the use of conventional heating is made, and a discussion of the reaction mechanism will be presented.



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Molecular imprinted polymer on graphene nanosheets modified glassy carbon electrode for norfloxacin detection

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Fluoroquinolones have been widely applied in veterinary and human medicine since they were developed in the 1980s. Norfloxacin, 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolonecarboxylic acid, is a drug mainly used for the treatment of urinary tract infections [1]. This drug is also used in a wide range of gastrointestinal and respiratory tract infections; ocular and skin infections as well as in patients with intra abdominal infections in combination with anti anaerobic agents.

In this work, the preparation of a molecularly imprinted polymer film and its recognition properties of norfloxacin was investigated. Molecular recognition with a molecularly imprinted polymer is attributed to the uptake of an analyte with a complementary shape of the imprinted sites. A graphene nanosheet-modified glassy carbon electrode was fabricated to deposited the imprinted polymer layer. We developed a direct route to synthesize a norfloxacin imprinted polypyrrole film. Electrochemical polymerization of pyrrole was performed on the electrode surface in presence of template molecule norfloxacin. The over oxidation of polypyrrole film was performed by cyclic voltammetry in the presence of 0.1M NaOH as supporting electrolyte [2]. The voltammetric behaviour of norfloxacin on imprinted and non-imprinted films was investigated by square wave voltammetry. This sensor was applied to detect norfloxacin in urine samples.

Acknowledgments: This work has been supported by Fundação para a Ciência e a Tecnologia through grant no. PEst-C/EQB/LA0006/2011.

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Gold(I)-catalyzed intermolecular (4 + 2) and (2 + 2) cycloadditions of allenamides

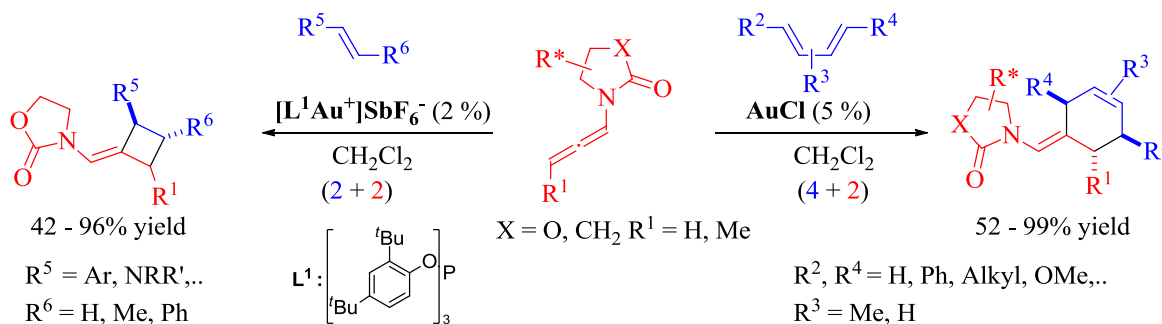
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In recent years there have been extraordinary advances in the development of gold-catalyzed processes. The high carbophilicity of gold complexes as well as their ability to stabilize carbocationic intermediates has allowed the development of a great variety of previously unfeasible transformations. [1] In this context, our group has recently demonstrated the possibility of using allenes as three or two carbon components in intramolecular Au-catalyzed [4C+3C] and [4C+2C] cycloadditions.[2]

Herein, we report our results on a gold-catalyzed (4 + 2) intermolecular cycloaddition between a variety of conjugated dienes and allenes. An initial reactivity screening allowed to identify allenamides as suitable allene partners, and AuCl as the most selective and efficient catalyst for these annulations.[3] Curiously, in some cases, (2 + 2) cycloaddition products were also detected as minor side products. On these bases, and considering the synthetic and medicinal relevance of these cyclobutanic frameworks, we specifically pursued the development of a gold-catalyzed intermolecular (2 + 2) cycloaddition. We have recently found that these (2 + 2) cycloadditions between allenamides and alkenes (i.e. enamides or styrenes) can be efficiently achieved by using a gold complex incorporating a bulky phosphite ligand, and provide excellent yields of a variety of (2 + 2) adducts, with complete regio-, chemo- and stereoselectivity.[4] Different mechanistic scenarios for both types of cycloadditions will be discussed.

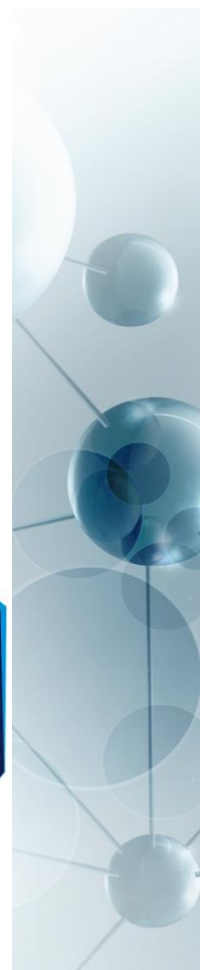
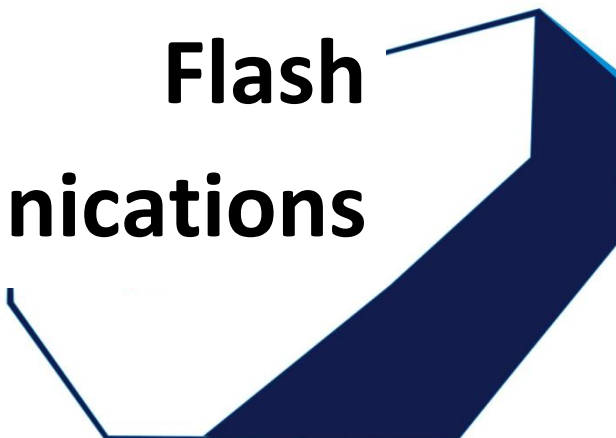


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Flash Communications



Thermochemistry of 1-methylimidazolium nitrate

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Ionic liquids (ILs) are defined as salts which melt at temperatures below ~373 K [1]. They are generally classified into two classes: aprotic (AILs) and protic (PILs). PILs are formed by proton transfer from a Brønsted acid, AH, to a Brønsted base, B, to yield, strictly speaking, a [BH⁺][A⁻] species [2], while AILs contain substituents other than a proton (e.g. alkyl groups) at the site of the acidic proton in PILs.

The study of the energetics of vaporisation of ILs became an important topic of research because of its relevance for purification/recycling processes involving distillation and also due to its direct relationship with the cohesive energies of ILs. These (often represented by standard molar enthalpies of vaporisation, $\Delta_{\text{vap}}H_{\text{m}}^{\circ}$) constitute one of the most important pieces of information needed for the development and validation of the force fields employed in molecular dynamics simulations and their trends are also very useful to define strategies for the design of task-specific ILs.

The available studies on the energetics of ILs refer almost exclusively to AILs [3]. Recently our group proposed a simple methodology to determine enthalpies of formation and analyse the energetics of vaporisation of PILs based on reaction-solution and Calvet-drop calorimetry measurements [4]. The method was tested using 1-methylimidazolium ethanoate, [Hmim][O₂CCH₃], which was the only PIL system known to us whose the vaporisation mechanism, involving the formation of 1-methylimidazole and ethanoic acid, had been unequivocally demonstrated by different methods and for different pressure ranges [5].

Here we will present an extension of these studies to the more ionic PIL 1-methylimidazolium nitrate, [Hmim][NO₃].

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On the synthesis of dehydropregnenolone derivatives: reactivity as dienophile in the Diels Alder reaction

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16-Dehydropregnenolone acetate (16-DPA), Figure 1, has a very versatile skeleton which has allowed the synthesis of different steroidal drugs such as dexametasone or β -metasone [1]. Only a few examples are known for the Diels Alder reaction involving this compound as dienophile [2,3] or diene [4].

Aiming to synthesize new dehydropregnenolone derivatives we used 1,3-diarylpropenones and 1-acetylcyclopentene as a reactivity model and explored its capabilities as dienophile for the Diels-alder reaction under different reaction conditions. The influence of the solvent and the catalysts were studied under conventional heating and under microwave irradiation. The best reaction conditions, affording the highest yields, were used to derivatize the steroid. Yields, characterization of the final products and discussion on the selectivity of the reaction will be presented in this communication.

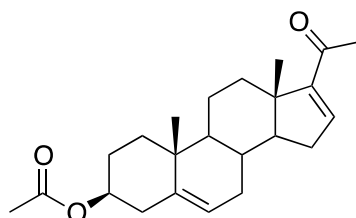


Figure 1. 16-dehydropregnenolone acetate.

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Dicarboxylate recognition by two macrobicyclic receptors: selectivity for fumarate over maleate.

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The carboxylate functionality is part of a wide range of biologically and environmentally active entities, in many cases accounting for their chemical and biological properties [1]. Not surprisingly supramolecular chemists have strived to design new synthetic receptors for this class of substrates since the early days of this relatively young field of research [2].

Among the most successful groups of receptors for the binding of carboxylate anions in aqueous medium there are the polyamine macrobicyclic compounds, as they have well defined three-dimensional cavities and can be protonated to provide the necessary positive charges to interact with the substrates and to impart water solubility [3].

In this work, two ditopic polyamine macrobicyclic compounds have been studied as receptors for the recognition of dicarboxylate anions of varying chain length in aqueous solution. One of the receptors consists of two tris(2-aminoethyl)amine derived binding subunits separated by *p*-xylyl spacers while the other is a heteroditopic compound, combining two different head units, a tren derived and a 2,4,6-triethylbenzene derived one, also separated by *p*-xylyl spacers. The acid-base behaviour of the compounds as well as their binding ability with oxalate, malonate, succinate, glutarate, maleate and fumarate dicarboxylate anions were studied by potentiometry at 298.2 K in aqueous solution and at ionic strength 0.10 M in K₂SO₄. NMR studies were also performed to obtain structural information in solution on the supermolecules formed by association of the protonated macrobicycles with the dicarboxylate substrates. The results revealed that both compounds are able to form stable associations with the dianionic substrates in competitive aqueous solution, with unprecedented selectivity for fumarate over other dicarboxylate competitors, including its *cis* isomer maleate. In addition it was found that although the selectivity pattern is unaffected by the introduction of the 2,4,6-triethylbenzene head unit, the affinity towards dicarboxylates is significantly reduced. Therefore, the comparison between the binding behaviour of these two receptors showed the effect of the increased rigidity and lipophilicity of the receptor with the 2,4,6-triethylbenzene head unit in the binding properties and the selectivity pattern.

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Effect of extraction conditions for chlorogenic acid determination in lamb's lettuce

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Lamb's lettuce (*Valerianella locusta*), a member of the family *Valerianaceae*, commonly used in salads, has been attaining some relevance as an important source of antioxidant compounds, namely chlorogenic acid (CGA) [1]. CGA belongs to a family of esters formed between certain *trans*-cinnamic acids and (-) quinic acid which have been described as major phenolics in coffee, strawberries, pineapple, apple, sunflower, blueberries. The most common individual CGA is 5-O-caffeoylquinic acid (5-CQA) [2]. Reports indicate that CGA compounds have antioxidant properties which are suggested to play an important role in preventing various diseases associated with oxidative stress, such as cancer, cardiovascular, aging and neurodegenerative diseases [3].

The aim of this work was to evaluate the influence of some parameters such as the extraction pH, the use of a grinding mill and consequently the ground size on the recovery of CGA from lamb's lettuce. Thus, an ultrasound extraction of CGA was applied to fresh and freeze-dried samples. Then, the extracts were analyzed by high-performance liquid chromatography with UV detection (HPLC/UV). The results obtained clearly showed that pH influences the extraction yield. HPLC analysis showed that both samples (fresh and freeze-dried) extracted at low pH (2 and 3.5) achieved the highest CGA content (469.0 – 970.3 mg CGA/100 g FW/DW). Furthermore, some differences were detected between fresh and freeze-dried extracts, namely in the phenolic profile. Work is in progress in order to identify and characterize these compounds by LC-ESI-MS analysis.

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Understanding the mechanism of resistance of HIV-1 RT to tenofovir

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HIV-1 Reverse Transcriptase (HIV-1 RT) is one of the enzymes responsible for HIV-1 replication as it converts the single-stranded viral RNA into double-stranded DNA. Different types of RT inhibitors are available at the moment (Nucleoside, Nucleotide and Non-nucleoside Reverse Transcriptase Inhibitors) and it is known that RT develops two general mechanisms of resistance to them: (i) Discrimination at the time of incorporation, in which resistance mutations prevent incorporation of the inhibitor while the enzyme retains the ability to incorporate the natural dNTP substrates and (ii) RT efficiently incorporates the inhibitor, which temporarily blocks DNA synthesis, but it is subsequently removed (excised) unblocking the NRTI-terminated primer [1].

Tenofovir (TDF) is one of the most common used HIV-1 RT inhibitors. In one of the reported crystal structures of TDF in complex with RT and a DNA template-primer, TDF adopts two different conformations at the priming site (P-site), in which the adenine base of tenofovir is flipped by 180° from the first conformation [2].

As HIV-1 RT inhibition is such a crucial step in the fight against AIDS it prompted us to investigate the mechanism of resistance behind one of its most common inhibitors: tenofovir. We conducted molecular dynamic (MD) simulations of the complexes of HIV-1 RT with both the natural ligand (deoxynucleoside triphosphate, dNTP) and the different TDF conformers at the P-site, as well as MM-PB/GBSA calculations, in order to understand the factors behind the smaller excision rate of TDF compared to other inhibitors such as AZT. We hypothesize that the flexibility that lead to the different TDF conformations at the P-site prevent the retrotranslocation to the N-site, which is necessary for an ATP-based mechanism of excision, thus reducing the excision rate.

We are also studying several mutations associated with TDF resistance, in particular the K65R mutation [3], and its effects on the incorporation rate / excision mechanism due to the restriction of structural adaptability of key nucleotides, like Arg65 and Arg72.

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Mannosylated nanoparticles for targeted delivery of amphotericin B towards visceral leishmaniasis

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Current therapies against visceral leishmaniasis, a neglected tropical disease caused by obligate intracellular protozoa, are associated with emergence of resistances and elevated toxicity. In that way is important to develop alternative treatments, like nanotechnology-based drug delivery systems which may reduce toxicity and side effects of the drug, and enhance their efficacy.

The purpose of this work was to prepare mannose coated nanoparticles by different techniques and do their biophysical characterization in order to see which of those techniques is more advantageous in the preparation of these nanoparticles. The nanoformulations cytotoxicity towards macrophages and their activity against the *Leishmania infantum* parasite were also evaluated.

Empty poly(lactic-co-glycolic acid) nanoparticles (PLGA-NPs) were prepared by the nanoprecipitation method [1] and mannose was attached to the PLGA-NPs by three different techniques: physical adsorption, one-step chemical reaction and two-steps chemical reaction. Physicochemical characterization of the nanoformulations included size, shape, polydispersity index and zeta potential determined by transmission electron microscopy and dynamic light scattering. The produced uncoated nanoparticles were about 240 nm and after mannose coated their size was about 200 nm, negatively charged (~-20 mV). We also use Fourier transform infrared spectroscopy to confirm the structure of M-PLGA NPs and the lectin binding assay to assess the surface orientation and availability of mannose ligand after formation of the NPs. Mannose was indirectly quantified by chemical reaction with about 2 mg/mg of polymer. The biological effect was evaluated on THP1 differentiated macrophages, *L. infantum* promastigotes and intracellular *L. infantum* amastigotes. Encapsulation of amphotericin B was successfully obtained and quantified by a UPLC method (yield of ~20%). *In vitro* release of amphotericin B under distinct pH conditions was observed and their antileishmanial activity quantified on an *in vitro* model of visceral leishmaniasis.

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The role of ionizable amino acid residues on peptide and protein folding: a time-resolved photoacoustic calorimetry experiment

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Time-resolved photoacoustic calorimetry (TR-PAC) has been applied to investigate diverse problems in biochemistry, organic and organometallic chemistry [1]. In particular, TR-PAC can reveal metal-ligand bond enthalpies, reaction enthalpies for highly reactive species such as radicals, and also provide insights on the dynamics and energetics of protein-ligand interactions and protein folding on short time scales. The information contained within the photoacoustic waves is indeed rich and it is possible to obtain dynamics, magnitude of enthalpy changes as well as changes in molecular volume associated with chemical processes in one single experiment [2]. Here we propose to use TR-PAC combined with the laser-pulsed pH-jump technique to provide new insights on site-specific folding processes that occur within the nanosecond to microsecond time scale and to investigate the role of ionizable residues on folding events.

Proteins are mainly composed of two major secondary structural features: α -helices and β -sheets. It is observed that 40-70% of secondary structure in proteins falls within these two elements [3]. Formation of secondary structures such as α -helices and β -hairpins play an important role in the early stages of protein folding and may occur on the nanosecond to low microsecond time scale. In order to make it experimentally accessible we use TR-PAC associated with a laser-pulsed pH-jump technique. In the present work, we selected short aqueous soluble peptides that fold into α -helix and β -hairpin structures and exhibit pH-dependent conformational dynamics. We induce destabilization on site-specific regions of our peptides using a laser-pulsed pH jump. The proton gradient formed will protonate amino acid residues such as histidine, glutamic acid or aspartic acid, and as a consequence conformational changes occur. The pH-jump technique also allow us to understand the role of salt-bridges within acid and basic amino acid residues and critical hydrophobic contacts such as interactions between histidine and aromatic acid residues, crucial in the stabilization and folding of secondary structure elements in proteins.

In order to completely describe our peptide model systems we started by studying the isolated amino acids present in the peptide sequences that may be ionizable upon pH jump. From the photoacoustic waves it is possible to identify two processes: the volume and enthalpy change associated with the fast proton release (~ -5 ml/mol) and a slower process related with the amino acids protonation. Our results show that the protonation of aspartic acid and glutamic acid is accompanied by an expansion (~ 5 ml/mol) while for the protonation of histidine a small contraction (~ -2 ml/mol) is detected. In our peptide model systems, the additional process associated with the structural changes that occur during the folding or unfolding events promoted by the protonation of the amino acid residues may also be observed. The dynamics of volume changes can be combined with CD and NMR characterization of folded/unfolded species coexistent in different pH conditions to obtain a comprehensive picture of the structural and dynamic roles played by ionizable residues in proteins.

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Chemistry at the university: an approach to science dissemination for youngsters

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Science, and particularly Chemistry, has an important role in finding solutions to many challenges that humankind is facing nowadays – from fighting sickness to constructing a sustainable environment – so its dissemination has never been so important. However, the dissemination of Chemistry should be done not only amongst adults, since today's youth are tomorrow's adults. Under this perspective, the University of Porto has promoted the Junior University project with the goal of contextualizing the students in the university environment giving them a more objective view of the potential of every scientific discipline. In particular, through the Department of Chemistry and Biochemistry, of the Faculty of Science of Porto, projects focused on the dissemination of Chemistry among young people have given excellent results [1].

In Chemistry, the concepts are often abstract, so the performance of laboratory experiments, contextualized in topics related to daily life, simplifies its understanding and contributes to the improvement of teaching and learning. The project “Química: Uma Ciência Sem Fronteiras” (Chemistry: A Science Without Borders), assembled in 2011, intended to contribute to the broad dissemination of the important role of Chemistry, generating the interest of young people and motivating them for its study.

While structuring this project there was a concern to use a didactical approach compatible with the social reality and the knowledge level of students. This was made in order to encourage and motivate them, arousing their interest, criticism, creativity and curiosity, with the intention of foster their active participation and commitment to achieve the objectives which were set [2].

Looking forward to new Chemistry activities for the University Junior, a next project for 2012 will meet the educational needs on chemistry for students of 8th and 9th grades. The new project will implement his work on trying to increase interdisciplinary.

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Application of the QuEChERS methodology for the extraction and determination of volatile phenols in beverages

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QuEChERS (acronym of Quick, Easy, Cheap, Effective, Rugged, Safe) technique was developed by Anastassiades *et al.* [1] for the analysis of pesticide residues in fruits and vegetables. So far, the QuEChERS methodology has been used mainly for the extraction and determination of pesticides in solid samples. However this technique can be equally useful for other applications. In fact the two involved techniques in this procedure (liquid-liquid and solid-phase extractions) are commonly but separately used for the analysis of liquid samples. The direct analysis of complex samples (such as wine, beer, juices) could be the simplest way to obtain a result. However, the sample matrix could have a deleterious effect especially in chromatographic systems. In fact obtaining a clean extract is very important in order to avoid the long term degradation of the chromatographic columns.

This work presents an application of the QuEChERS procedure to the analysis of important ageing markers in beverages, the volatile phenols, by liquid chromatography with fluorimetric detection. The sample preparation procedure comprises two main steps: (1) a liquid-liquid extraction and (2) a dispersive solid-phase extraction (d-SPE). In the first stage, the analytes are extracted from the sample by liquid-liquid extraction using a fixed volume of acetonitrile. After vigorous shaking, a mixture of salts is added in order to displace the extraction equilibrium towards the organic phase, while simultaneously facilitating phase's separation. After centrifugation, an aliquot of the organic supernatant is added to the dispersed sorbent to remove matrix interferents. The main objective of this step is to retain the matrix components while the analytes remain in the liquid phase. The mixture is then manually shaken and centrifuged [2].

The results showed a variable amount of phenols in the analysed samples (beer, wine and fruit juices). 4-ethylphenol and 4-ethylguaiaicol were the compounds found in higher amounts varying in the range 5–995 µg/L and 130–174 µg/L, respectively.

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Syngas production over M-Ni nanoparticles (M = Pr, Gd, Th and U)

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The Partial Oxidation of Methane (POM) constitutes a proper way to produce syngas ($\text{CO} + \text{H}_2$) and provides a suitable H_2/CO ratio for the methanol and Fischer-Tropsch synthesis. Nickel catalysts supported on ceria [1] and lanthanum oxide [2] has been investigated for partial oxidation of methane to syngas. They were reported to be active catalysts for this reaction.

The bimetallic oxides compounds were synthesized by modified sol-gel methods to obtain nanoparticles (<50nm) (Fig. 1). The purpose of this work was to study the performance of bimetallic oxides for partial oxidation of methane from 350°C at 800°C. This study was performed for a high GHSV (8500 $\text{mL}_{\text{CH}_4}/\text{g}_{\text{cat}}\cdot\text{h}$). At 650 °C, the activity expressed as percentage of methane converted is: Pr-Ni-O oxide (26%), Gd-Ni-O oxide (72%), Th-Ni-O oxide (68%) and U-Ni-O oxide (74%), with a higher selectivity to syngas.

All catalysts are more active than nickel oxide and comparable with a commercial catalyst as 5%Pt/ Al_2O_3 with selectivities to H_2 and CO superior at 85% and 80% respectively, and H_2/CO ratio of 2. Fig. 2 shows the conversion of methane over Gd-Ni-O as a function of the time on stream at different temperatures. No deactivation was observed during 70 h on stream. The conversion of methane was very stable, whereas the selectivities to CO and H_2 and the formation of CO_2 was residual.

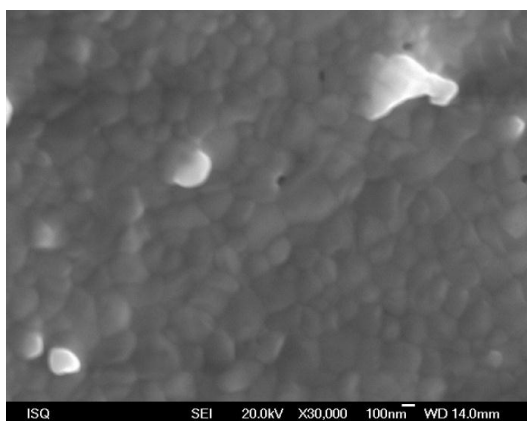


Figure 1. SEM of Gd-Ni-O.

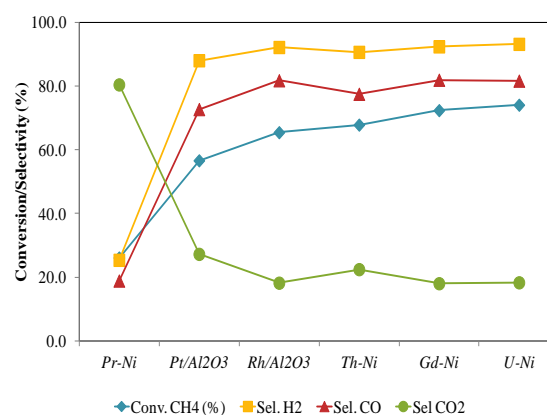


Figure 2. Partial oxidation of methane over M-Ni (M=Pr, Gd, Th and U) catalysts at 650°C.

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Characterization and antibacterial studies of a copper(II) lomefloxacin ternary complex

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Antimicrobial resistance is currently considered a global public health problem. Different classes of antibiotics have seen their efficiency reduced and even compromised due to the existence of resistant strains which make some antibiotics completely unsuccessful against certain pathogenic bacteria. The over and unnecessary use of antibiotics, as well as the easy spread of resistant strains in hospitals and agriculture, has contributed to the aggravation of this problem, which began in mid-twentieth-century [1].

Due to their wide use, there has been an increasing menace of bacterial resistance to quinolones, which led to the need to improve existing antimicrobial drugs and/or develop new ones. In this quest of producing new antimicrobial agents the concept of metal complexes, as novel derivatives of fluoroquinolones, also called metalloantibiotics, has been pushed forward with promising results which indicate that they can play an important role in this field with evidence that these complexes have a potentiated effect on the antibacterial activity of fluoroquinolone antibiotics [2].

In this work the study of the solution behavior of the fluoroquinolone lomefloxacin (lmx) with Cu^{2+} in the presence and absence of 1,10-phenanthroline (phen) was performed. The values obtained for the stability constants of the binary and ternary divalent metal ion complexes are very high and clearly show that the ternary complexes are more stable than the binary ones. Furthermore the distribution diagrams indicate that only the copper(II) ternary species are stable at physiological concentrations and pH.

Studies of the antibacterial activity of these compounds are also being conducted, by determining their MICs (minimal inhibitory concentration) in *Escherichia coli* strains. These results will be very important to conclude about the possible use of the ternary complex as a metalloantibiotics. Furthermore the determination of MICs for porin-deficient *E. coli* strains will allow us to confirm the entry pathway of these compounds.

Preliminary studies of the interaction of this ternary complex with liposomes are going on, to try to understand the uptake mechanism of these compounds at a molecular level.

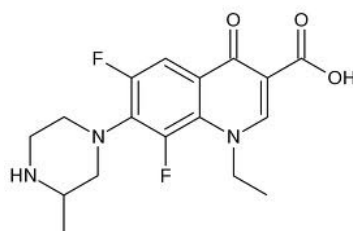


Figure 1. Structure of lomefloxacin.

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Conception of glycerophospholipid hydrated bilayer models through computational modeling

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Biological membranes are crucial elements to cells and organelles. Beyond the architectural role of these entities they are also functionally relevant structures, adsorbing and anchoring 30 % of the total protein content, and controlling different transport phenomena. We wish to develop biological membrane models of glycerophospholipid bilayers, taking benefit of Molecular Dynamics (MD) simulations. The MD parameters developed are consistent with the General-AMBER Force Field (GAFF) [1], which has no consistent glycerophospholipid parameters.

We have modeled 12 different glycerophospholipid bilayers. The Molecular Dynamics (MD) simulations were carried out for systems containing 200 glycerophospholipids and TIP3P water model, in an NPT ensemble. The simulations were performed using the General Amber Force Field (GAFF) [1] and up to 80 ns dynamics were conducted for each of the bilayer systems created.

An extensive protocol validation, as well as a broad structural and dynamic analysis was performed for the 12 glycerophospholipid models. We have found great stability of the bilayer systems throughout the computational simulations and a great similarity on both the volume per lipid quantity and lipid lateral diffusion coefficients regarding experimental data. We have also observed that the applied methodology tends to overestimate the bilayer thickness and underestimate the area per lipid.

All things considered we have described a set of consistent parameters for the description of biological membrane models that present a high pharmacological interest. All the simulations were developed without imposing any constraints (often used in this type of systems).

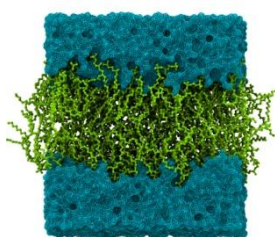


Figure 1. DOPC hydrated bilayer model. Water phases in blue and DOPC glycerophospholipids in green.

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Synthesis of novel bipyrrolic compounds with potential application in anion binding

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The synthesis of materials that may establish supramolecular interactions with anions is an important field of research in organic chemistry, with an increasing interest due to the need to find, for instance, compounds that can bind and transport anions across lipid bilayer membranes or cleaner methods for waste treatment [1].

For this purpose, pyrrole units are particularly attractive since the N–H protons remain in place over a wide pK_a range making possible their use as a hydrogen bond donor group within a large pH window. Also, the reasonably easy functionalization and incorporation into elaborate cyclic and acyclic systems are reasons to have into account when synthesizing this kind of receptors [2]. Recently, attention has turned towards acyclic receptors and several types of pyrrole-containing anion binding systems have been reported such as guanidinium-containing amidopyrroles and pyrrole-2,5-dicarboxamides [1a,3].

As part of our studies, we report here the synthesis, structural characterization and anion binding properties of bipyrrolic units functionalized with 1,3-indanedione (**1**) and malononitrile (**2**) through Knoevenagel reactions (Fig. 1). It is expected that these compounds will support the formation of new anion complexes and provide for a range of new application opportunities.

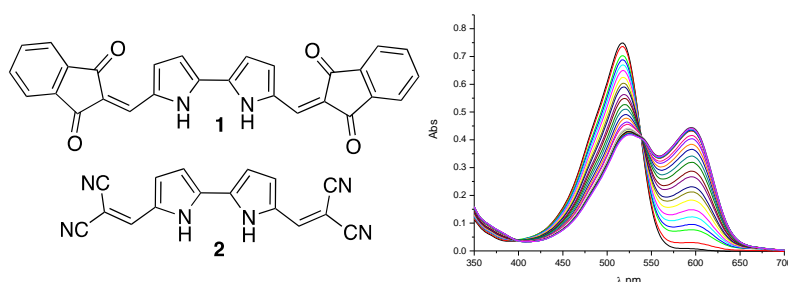


Figure 1. Left: novel bipyrrolic structures **1** and **2**; Right: UV-vis titration of **1** with dihydrogen phosphate anion in DMSO.

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On the complexation between bovine serum albumin and manganese porphyrin

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Serum Albumin is the most abundant protein in blood plasma and probably the most studied protein. Among its multiple functions Serum Albumin are carriers, distributors and metabolizing agents of multiple ligands [1]. Porphyrins are organic molecules composed of a tetrapyrrole macrocycle. They have numerous applications, such as electron transport, biochemical sensors, photodynamic therapy agents and catalysis [2]. The inclusion of manganese in the porphyrin ring greatly affects its photophysical behavior, favoring the non-radiative decay channels. Photoacoustic Tomography is a very promising technique for medical imaging [3] whose more general applicability depends on the availability of contrast agents that release as heat all the energy contained in an absorbed pulse of light.

We intend to label BSA with 5,10,15,20-tetrakis(4-sulphonylphenyl)porphyrinate manganese (III) acetate (MnTPPS) and then expose the labeled protein to nanoseconds laser pulses. Each laser flash should result in considerable heat deposition into a small volume in a short period of time. This heat deposition gives rise to a pressure wave whose detection constitutes the basis of Photoacoustic Tomography. It can also happen that the quite substantial local temperature rise could be enough to denature (or otherwise inactivate) the protein [4]. We intent to use time-resolved photoacoustic calorimetry to fully characterize the heat release behavior of BSA bound MnTPPS.

We started to study of the interaction between MnTPPS and BSA in aqueous solution of buffered PBS (pH=7.4) using fluorescence spectroscopy. BSA fluorescence quenching ($\lambda_{exc}=280$ nm) with the addition of MnTPPS indicates that the interaction between them occur in the region of the tryptophan residue. Using the fluorescence spectra, the Stern-Volmer modified equation can be applied to get the values of the binding constant at temperatures of 281 K, 288 K and 293 K [5]. The observed K_a values are between 10^6 - 10^7 L.mol⁻¹, indicating a strong interaction between BSA and MnTPPS. Using the values of $\ln K_a$ at these three temperatures in a Van't Hoff Stern-Volmer modified plot, we obtained the thermodynamic values ΔG° , ΔH° e ΔS° [6]. The negative value of ΔG° is consistent with the spontaneity of the binding, the positive value of ΔH° indicates that the binding process of porphyrin is endothermic, and the positive value of ΔS° shows that the type of interaction between the porphyrin and BSA is hydrophobic.

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Halogen ... Cyano group interaction: an energetic and structural analysis of monohalogenated benzonitrile isomers

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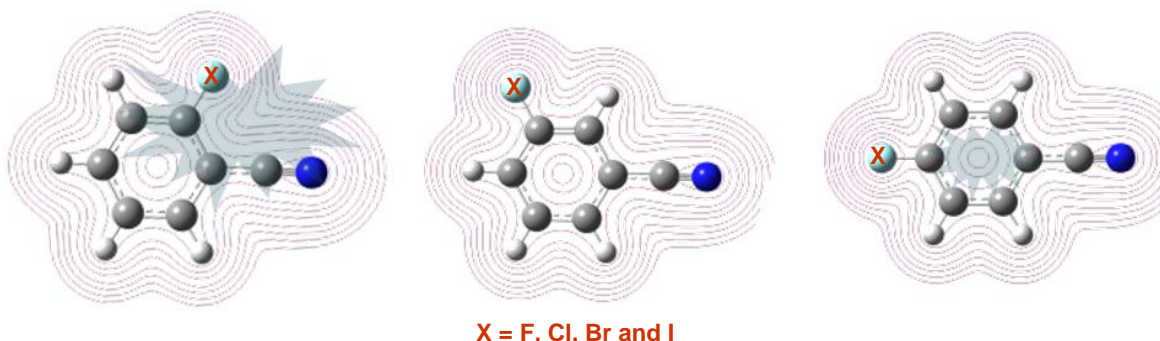
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Across the years, the energetic of several halogenated benzene derivatives has been subject of study in our research group [1-4]. Due to the lack of knowledge of the energetic parameters of the benzonitrile derivatives, the present work is dedicated to the study of the interaction of the halogen atoms with the cyano group of the benzonitrile.

The standard ($p^\circ = 0.1$ MPa) molar enthalpy of formation, in the gaseous phase, at $T = 298.15$ K, allows to establish correlations with structural properties of a molecule, since the effects of intermolecular forces do not apply in the gaseous phase. This energetic parameter was calculated combining the respective standard molar enthalpies of formation, in the condensed phase, at the same temperature, measured by rotating-bomb combustion calorimetry, and the standard molar enthalpies of phase transition, at $T = 298.15$ K, using the mass-loss Knudsen effusion technique or the Calvet microcalorimetry.

In this work, the experimental thermochemical study of the monohalogenated benzonitrile was complemented with their electronic parameters, using several computational methodologies such as Nucleus-Independent Chemical Shifts (NICS), Natural Bond Orbital (NBO) and Mulliken population analysis, in order to understand the energetic nature of the bonds and the change of the electron density of benzonitrile when hydrogen is replaced by a halogen atom in different positions.



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Structural and thermodynamic study of nonlinear polyphenyls

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This work involves the thermodynamic and structural study of four nonlinear polyphenyls (Fig. 1): *ortho*-quaterphenyl, *meta*-quaterphenyl, *ortho*-quinquephenyl and *meta*-quinquephenyl. The compounds were synthesized using the Suzuki-Miyaura methodology [1] and structurally characterized by single crystal X-ray. The temperatures and standard molar enthalpies of fusion were measured by DSC, and the standard molar entropies of fusion were derived. The heat capacities, at $T = 298.15$ K, were measured by means of a precise drop heat capacity calorimeter [2]. The enthalpies of sublimation, at $T = 298.15$ K, were determined using the Calvet microcalorimetry drop method and enthalpies of combustion, for the *ortho* and *meta* isomers were measured by mini-bomb combustion calorimetry [3]. The energetic and structural studies were interpreted in order to evaluate *ortho* and *meta* isomerization effect in the thermodynamic properties. It was found that, with the exception of terphenyls isomers, the temperature of fusion of the *ortho* series is always higher than the *meta* isomers, highlighting an odd/even effect in fusion equilibrium in the *ortho* series. For the *ortho* series, it was also found an indication of an odd/even effect in the gaseous phase energetics that could be related with the $\pi \cdots \pi$ intramolecular interaction.

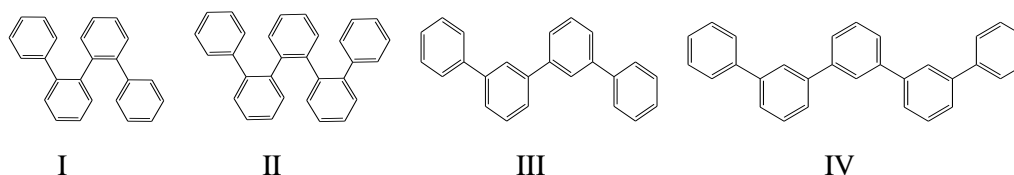


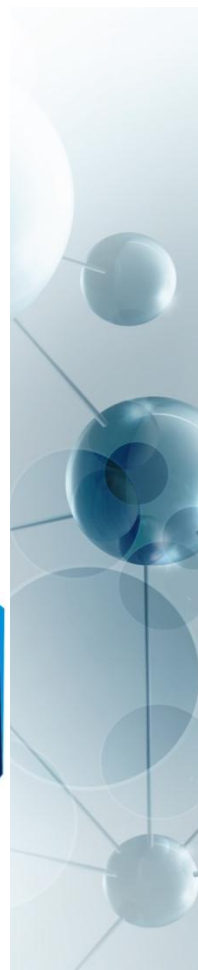
Figure 1. Schematic Structure of: (I) *ortho*-quaterphenyl; (II) *ortho*-quinquephenyl; (III) *meta*-quaterphenyl; (IV) *meta*-quinquephenyl.

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Posters



Synthesis of 9-methyl-6-methylamino-2-arylpurines as potential new ligands to adenosine receptors

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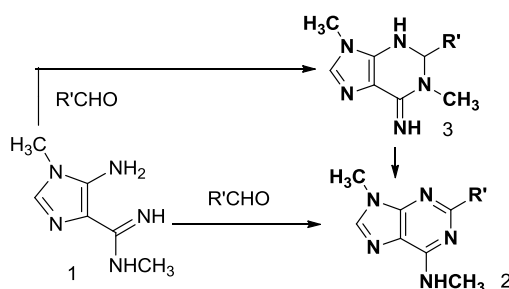
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The adenosine receptors are important therapeutic targets due to their role in the process of regulation of the heart, kidneys, immunological system, central nervous system and cellular growth [1,2]. Recently, in the literature, it has been suggested that the adenosine receptor A_{2A} has an important role as a therapeutic target for Parkinson's disease [3].

In our research group a new set of purine derivatives was identified as active on adenosine receptors, however the selectivity was low [4].

In this communication we report the synthesis of new purine derivatives **2** potentially active on adenosine receptors. The new compounds were obtained from the 5-amino-4-cyanoformimidoyl-9-methylimidazole **1** in two sequential steps. The reaction conditions and the mechanism of the reactions will be presented.



Acknowledgements: Thanks are due to University of Minho and *Fundação para a Ciência e Tecnologia* for financial support (project n°F-COMP-01-0124-FEDER-022716 (ref. FCT PEst-/QUI/UI0686/2011) FEDER-COMPETE, FCT-Portugal. The NMR spectrometer (Bruker 400 Avance III) is part of the National NMR Network supported with funds from FCT.

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Chiral HPLC method for determination of the enantiomeric purity of new xanthone derivatives

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The development of new methodologies for chiral discrimination and enantiomeric purity determination has been of great concern. Among the most useful and versatile chiral columns described in the literature in recent years are the coated polysaccharide derivatives. Thousands of different chiral compounds have been efficiently enantioresolved by polysaccharide-based columns [1] including xanthonolignoids [2].

This work describes a chiral HPLC method for determination of the enantiomeric purity of ten new chiral xanthone derivatives (CXDs) (Figure 1) on polysaccharide-based columns.

The selection of the appropriate column and mobile phase for a given separation is normally a difficult task. Thus, our first effort was to resolve enantiomeric mixtures of CXDs under different elution conditions using four different polysaccharide-based phases. The amylose tris-3,5-dimethylphenylcarbamate coated onto APS-Nucleosil was found to be the most efficient. All the CXDs were enantioresolved with high enantioselectivity and resolution (for example, $\alpha = 1.78$ and $R_s = 2.41$).

The optimized chromatographic conditions allowed the measuring of the enantiomeric ratios of all the CXDs, usually higher than 99%.

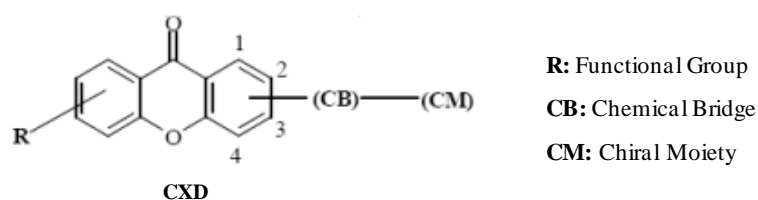


Figure 1. Schematic representation of a CXD.

Acknowledgements: CEQUIMED-UP (PEst-OE/SAU/UI4040/2011), for financial support.



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Synthesis of new pyrimido[5,4-*d*]pyrimidines derivatives as potential antitubercular agents

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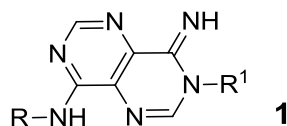
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Infection with *Mycobacterium tuberculosis* affects much of the world population, despite the fact that drugs for treating tuberculosis (TB) were available since the 60s. The current TB treatment takes 6-12 months and requires a combination of three or four drugs that were developed almost half a century ago. The narrow choice of antibiotics, lengthy treatment regimens, and patient noncompliance has provided conditions for acquired antibiotic resistance that led to worldwide emergence of strains resistant to virtually all available drugs [1-3]. Since mid-1985s a renewed interest in the discovery of new antitubercular drugs led to the appearance of new classes of compounds active against *M. tuberculosis* [4-6]. However, new clusters of extensively drug resistant tuberculosis may always appear and, currently, there is still an urgent demand for new and more effective anti-TB drugs possessing new modes of action.

Recently our research group reported a new class of antitubercular compounds, with the pyrimido[5,4-*d*]pyrimidine core structure **1** [7]. The activity of these compounds was dependent on the substituents R and R¹.

In this communication we present the synthesis and characterization of new derivatives of pyrimido[5,4-*d*]pyrimidines **1** with more lipophilic groups as substituents R and R¹.



Acknowledgements: Thanks are due to University of Minho and *Fundação para a Ciência e Tecnologia* for financial support (project n°F-COMP-01-0124-FEDER-022716 (ref. FCT PEst-/QUI/UI0686/2011) FEDER-COMPETE, FCT-Portugal. The NMR spectrometer (Bruker 400 Avance III) is part of the National NMR Network supported with funds from FCT.

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Biotransformation of primary aromatic amines by laccases

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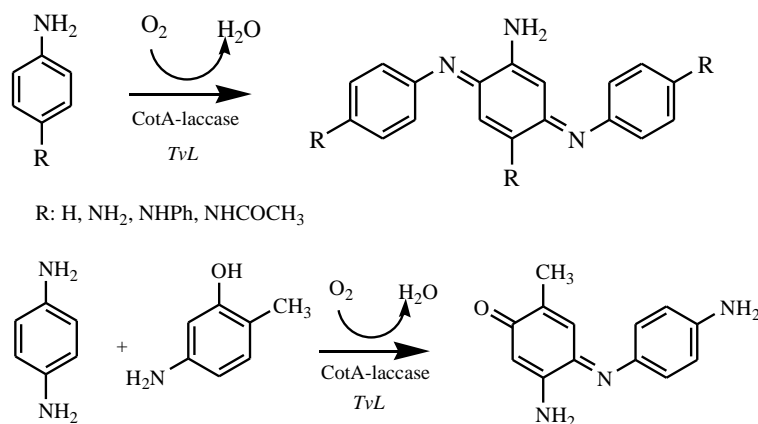
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The use of enzymes as biocatalysts has increased enormously in the past years and represent an important field in green chemistry. Laccases are multi-copper oxidases (EC 1.10.3.2), widely distributed in fungi, higher plants and bacteria with a broad spectrum of substrates such as substituted aromatic structures (phenol derivatives, aminophenols and substituted aromatic amines). Their capacity to catalyse transformations in organic synthesis, such as phenols and aromatic amines oxidations, homomolecular and heteromolecular coupling reactions with formation of C-C and C-N bonds, is well known and reported [1,2]. These synthetic biotransformations occurs under mild reaction conditions of pressure and temperature, in aqueous or biphasic systems, and appear as alternative routes to the conventional organic synthetic methods.

In this work we present the ability of two different laccases a bacterial laccase from *Bacillus subtilis* (CotA-laccase) and a fungal laccase from *Trametes Versicolor* (TvL), to oxidise several *p*-substituted primary aromatic amines. The first enzymatic step, leading to a radical which further undergo to an instable primary *p*-quinonediimine intermediate, is followed by several homo and/or heterocoupling reactions (scheme 1). The sequential oxidation of substrates results in the formation of dimers and trimers, which were characterized by spectroscopic techniques (FTIR and 1D, 2D-NMR).



Scheme 1. Homo and heterocoupling reactions.

Acknowledgements: This work was supported by PTDC/BIO/72108/2006 from FCT. Authors thank the Portuguese NMR Network (IST-UTL Center) for providing access to the NMR facilities.

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Oxidative coupling of methane using nitrous oxide as oxidant over calcium-rare earth oxides nanoparticles

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The oxidative coupling of methane (OCM) to light hydrocarbons using oxide catalysts has been investigated for many research groups in the last decades. Recently, the nitrous oxide has been shown to be an excellent oxidant for performing some difficult oxidation processes [1,2], but for production of C2 hydrocarbons have never been referred in literature. The use of a number of calcium oxide-based catalysts [3-5] for the OCM has been reported in the literature.

The main objective of this work was to study the performance of $\text{CaO-Ln}_2\text{O}_3$ nanoparticles for conversion of methane with nitrous oxide into C2 hydrocarbons (ethylene and ethane). The nanoparticles of calcium-rare earth oxides were active and selective for production of C2 at 750 °C. The activity is lower (13-20% for different rare-earth) but the selectivity to C2 hydrocarbons is higher than 60%, except for Ca-Ce oxide (Fig. 1).

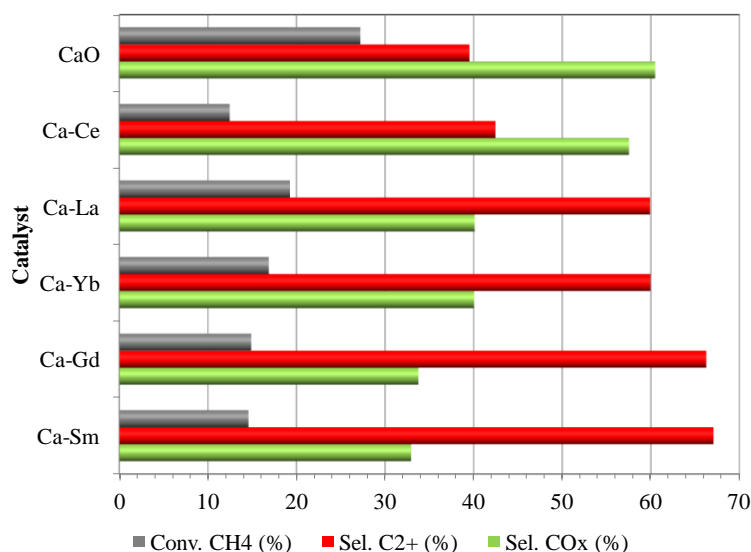


Figure 1. Activity/Selectivity of Ca-Ln catalysts for OCM at 750°C.

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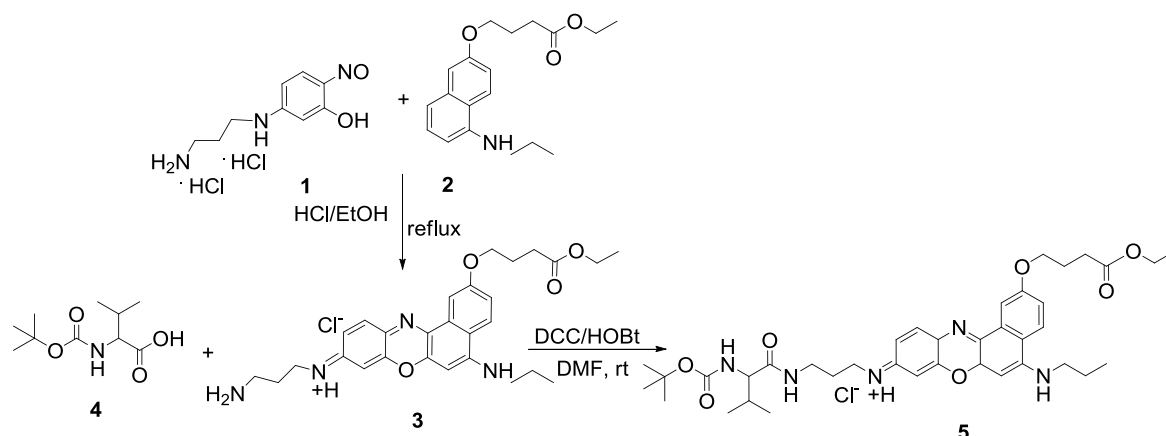
Fluorescent labelling of valine with a new benzo[*a*]phenoxazinium chloride functionalized at 2- and 5-positions

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Fluorescent derivatization has been considered one of the most sensitive methods for the determination of analytes at low concentrations. Bearing in mind the importance of the research in this area and also our recent interests [1-3], the present work describes the synthesis of a new benzo[*a*]phenoxazine derivative possessing two functional groups, namely the carboxylic ester and the amine function. Consequently, this compound is capable of covalent linkage to (bio)molecules, and can also be linked to another entity. As a preliminary study, 3-amino-*N*-(2-(4-ethoxy-4-oxobutoxy)-5-(propylamino)-9*H*-benzo[*a*]phenoxazin-9-ylidene)propan-1-aminium chloride **3** was efficiently used in the derivatisation of L-valine at its carboxylic group. Evaluation of absorption and emission properties of benzo[*a*]phenoxazinium **3** and the corresponding conjugate **5** synthesised was performed in ethanol, at physiological pH and distilled water.



Scheme 1. Synthesis of benzo[*a*]phenoxazinium chloride **3** and covalent labeling of valine **4**.

Acknowledgements: We are grateful to the Foundation for Science and Technology (Portugal) for its financial support to Centre of Chemistry (University of Minho) through the FCT project PEst-C/UI0686/2011 (F-COMP-01-0124-FEDER-022716), FEDER-COMPETE, FCT-Portugal. The NMR spectrometer Bruker Avance III 400 is part of the National NMR Network and was purchased within the framework of the National Program for Scientific Re-equipment, contract REDE/1517/RMN/2005 with funds from the POCI 2010 (FEDER) and FCT.

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Solvent-free microwave synthesis of 2-, 5- and 9-substituted benzo[*a*]phenoxazininium chlorides

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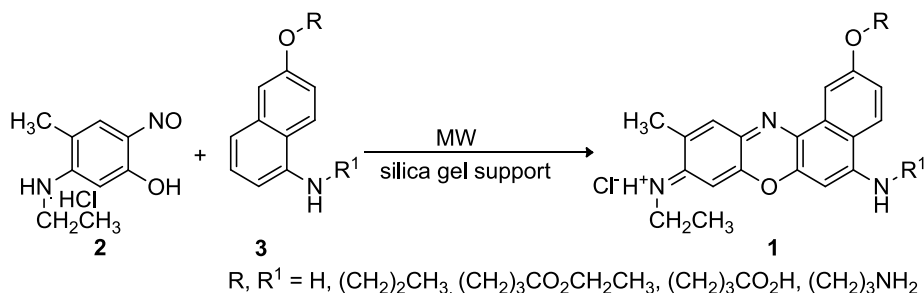
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Benzo[*a*]phenoxazininium salts are usually synthesised by condensation reaction of nitrosoanilines or nitrosonaphthylamines with 1-naphthylamines, 3-aminophenols or 2-naphthol. In the last case, monoaminosubstituted benzo[*a*]phenoxazininium salts should be transformed into the diaminosubstituted derivatives by reaction with amines in the presence of an oxidation agent.

The use of a strong mineral acid, such as perchloric or hydrochloric acids, in *N,N*-dimethylformamide, methanol or ethanol as a solvent, under reflux conditions, is frequently reported for the cyclisation [1-6].

As a continuation of our previous research [3-6], the present work describes for the first time the efficient synthesis of benzo[*a*]phenoxazininium chloride **1** by condensation reactions of nitrosophenol **2** and 5-aminonaphthalen-2-ol or its derivatives **3** under microwave irradiation in solvent-free conditions or using *N,N*-dimethylformide, in comparison to conventional heating conditions. These new compounds possess a combination of substituents at the tetracyclic ring that includes the hydroxyl, aminopropoxyl, as well as amine groups, and monoalkylated amines.



Scheme 1. Synthesis of benzo[*a*]phenoxazininium chlorides **1**.

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Thermochemical study of the some fluoronitrophenol isomers

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The chemistry of phenols has attracted continuing interest in the last centuries. Phenol and phenolic derivatives have achieved considerable importance as the starting material for numerous intermediates and final products, which have several indispensable applications in our daily life. Phenolic derivatives constitute, among others, an important class of antioxidants that inhibit or reduce the rate of the oxidative degradation of organic materials including a large number of biological aerobic organisms and commercial products. This antioxidant property can be related to the ability of phenols to trap the peroxy radicals via the hydrogen transfer reaction. Hence, calculations of the hydrogen–oxygen bond strengths of the phenolic hydroxyl groups on various phenols allow for predictions of their potential as antioxidants [1-4].

The current work presents a thermochemical study of the four isomers of fluoro-*ortho*-nitrophenol. The standard gas-phase enthalpies of formation of two fluorinated isomers of *ortho*-nitrophenol have been experimentally determined, and have also been predicted by means of computational (G3(MP2)//B3LYP level). Combustion calorimetric studies were used to determine the standard molar enthalpies of formation of 3-fluoro-6-nitrophenol and 4-fluoro-2-nitrophenol isomers, at $T = 298.15$ K, in the crystalline state as $\Delta_f H_m^\circ(3\text{-F-6-NO}_2\text{Phenol, cr}) = -(398.9 \pm 1.3)$ $\text{kJ}\cdot\text{mol}^{-1}$, and $\Delta_f H_m^\circ(4\text{-F-2-NO}_2\text{Phenol, cr}) = -(391.2 \pm 1.3)$ $\text{kJ}\cdot\text{mol}^{-1}$. The Knudsen mass-loss effusion technique was used to determine the standard molar enthalpies, entropies and Gibbs energies of sublimation, at $T = 298.15$ K, of those compounds. The standard molar enthalpies of sublimation of the two isomers were also measured by Calvet microcalorimetry. The combination of the obtained $\Delta_f H_m^\circ(\text{cr})$ and $\Delta_{\text{cr}}^\circ H_m^\circ(298.15 \text{ K})$ values, yielded to the standard ($p^\circ = 0.1$ MPa) molar enthalpies of formation in the gaseous phase, at $T = 298.15$ K, of the two isomers: $\Delta_f H_m^\circ(3\text{-F-6-NO}_2\text{Phenol, g}) = -(320.2 \pm 1.8)$ and $\Delta_f H_m^\circ(4\text{-F-2-NO}_2\text{Phenol, g}) = -(314.5 \pm 1.4)$ $\text{kJ}\cdot\text{mol}^{-1}$.

The results are analyzed and interpreted in terms of enthalpic increments and molecular structure of the compounds, and compared with computational ones. Furthermore, the molecular structure of the four molecules was established and the structural parameters were determined at the B3LYP/6-31G(d) level of theory. The computational study was also extended to the determination of O–H bond dissociation enthalpies.

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Thermochemical study of 2-methylbenzoxazole and 2-methylbenzothiazole

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Organic compounds containing five-membered heterocyclic rings, having nitrogen, oxygen and sulfur heteroatoms, are widely distributed in nature and often play an important role in various biochemical processes. Compounds exhibiting the functionality of benzoxazole and benzothiazole have been employed in drug synthesis [1,2] and, recently, they have been studied in several other research areas, such as on electronics (organic light-emitting diodes, OLED) [3] and materials (liquid crystals) [4].

The present work reports an experimental study on 2-methylbenzoxazole (**1**) and 2-methylbenzothiazole (**2**), in order to evaluate the energetic effects associated to the replacement of the heteroatom of oxygen by a sulfur atom on the ring.

We present the results for the energies of combustion of 2-methylbenzoxazole (**1**) and 2-methylbenzothiazole (**2**), at $T = 298.15$ K, obtained from static and rotating bomb calorimetry measurements, respectively. The enthalpies of vaporization for these two compounds were measured by high temperature Calvet microcalorimetry. These values were corrected for $T = 298.15$ K, using the corresponding C_p 's of the compounds, estimated at the B3LYP/6-31G* level of theory, with a scaling factor of 0.9614, for the vibrational frequencies. The standard ($p^\circ = 0.1$ MPa) molar enthalpies of formation of 2-methylbenzoxazole (**1**) and 2-methylbenzothiazole (**2**), in condensed and gaseous states, were derived. The results obtained are discussed in terms of energetic-structural relationships.

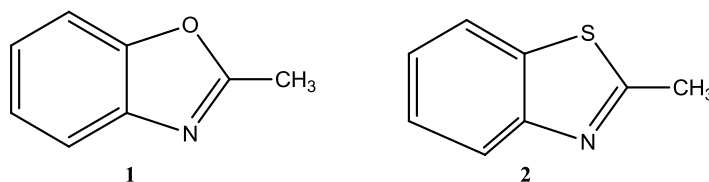


Figure 1. Structures of 2-methylbenzoxazole (**1**) and 2-methylbenzothiazole (**2**).

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Force field parameterization of cobalt-containing metalloproteins

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Cobalt-containing metalloproteins, such as Vitamin B12, play a vital biological role, participating in a variety of biological processes [1]. Thus, the study and characterization of metalloproteins with cobalt coordination centers is an important topic of research. The aim of this research project is to determine molecular mechanics force field parameters for cobalt coordination centers present in metalloproteins, within a bonded-model approach [2], as to enable further computational studies, by molecular dynamics simulations and related methodologies (in particular thermodynamic integration). Force constants were calculated with B3LYP/SDD:6-31G(d), with RESP charges derived at the B3LYP/6-311G++(3df,3pd) level of theory, on models of the metal coordination sphere obtained from high-resolution structures available from the Protein Data Bank. The use of the Stuttgart-Dresden pseudopotentials for the treatment of Cobalt presents several advantages for this specific case, into which protrude not only the excellent cost *vs.* computational time but also the accuracy of the results [3].

The obtained results so far display the variation of the force constants associated to the several bonds and angles that involve cobalt, with the type of residue and geometry. A database containing these molecular mechanical parameters in an easily accessible format for use with popular molecular dynamics codes is currently in preparation, with plans existing to extend these studies to metalloproteins involving other metal atoms.

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Pressure waves generated by light-absorbing thin films

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Ultrasound wave sources are used in a wide range of clinical applications, including diagnostics, therapeutics, and imaging. Clinical uses of ultrasound may be further advanced by the availability of broadband ultrasound sources extending the generation of ultrasound to higher frequencies because they may discriminate between tissues by selective absorption and attenuation. High frequency ultrasound waves generated by laser light irradiation can permeabilize biological barriers, such as the skin [1] or cellular membranes [2], with a reversibility that allows skin to recover its protective function and cells to remain viable [3].

In this work we develop materials capable of rapidly and efficiently converting the energy in a laser pulse into a high-impulse broadband pressure wave [4]. Photoacoustic reference compounds are incorporated in appropriate polymers and cast into thin films to obtain materials that strongly absorb light at the wavelength of laser, convert all the energy absorbed into heat within the laser pulse duration, and produce in intensity photoacoustic waves.

We describe methods to produce homogeneous dye-polymer blended thin films with micrometer thicknesses by cast coating and characterize the photoacoustic properties of the new films. The polymers chosen were polystyrene and elastomeric polydimethylsiloxane, and the dyes selected were Mn^{III} complexes of *meso*-tetraphenylporphyrin (MnTPP), amaranth, allura red, brilliant blue and new coccine. Our results show that homogeneous thin films incorporating amaranth and new coccine efficient produce ultrasound, but photostable thin films are only obtained with MnTPP. Pressure waves formed upon conversion of laser light irradiation were evaluated in terms of intensity, frequency and dependence on the films thickness and absorbance.

Acknowledgments: We thank RedEmprendia for financial support through AVCRI/LaserLeap project.

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Thermodynamic study of phase transitions in methyl esters of *ortho*-, *meta*- and *para*-aminobenzoic acids

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A static method based on capacitance gauges [1] was used to measure the vapor pressures of the condensed phases of the methyl esters of the three aminobenzoic acids. For methyl *o*-aminobenzoate the vapor pressures of the liquid phase were measured in the range (285.4 to 369.5) K. For the *meta* and *para* isomers vapor pressures of both crystalline and liquid phases were measured in the ranges (308.9 to 376.6) K, and (332.9 to 428.0) K, respectively. Vapor pressures of the latter compound were also measured using the Knudsen effusion method [2] in the temperature range (319.1 to 341.2) K.

From the dependence of the vapor pressures on the temperature, the standard molar enthalpies and entropies of sublimation and of vaporization were derived. Differential scanning calorimetry was used to measure the temperatures and molar enthalpies of fusion of the three isomers. The results enabled the estimation of the enthalpy of the intermolecular (N–H \cdots O) hydrogen bond in the crystalline methyl *p*-aminobenzoate. A correlation involving the temperature of fusion and the enthalpy and Gibbs energy of sublimation of benzene, methyl benzoates and benzoic acids was derived.

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Monovacant polyoxometalates @ MIL-101: synthesis and heterogeneous catalytic studies

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Coordination polymers, also known as Metal-Organic Frameworks (MOFs) are extended materials formed by metal or metallic cluster centers interconnected by organic molecules (ligands), leading to infinite one-, two- or three dimensional (1D, 2D or 3D respectively) hybrid networks. In addition to the remarkable structural features, their properties give them high potential for industrial and technological applications, such as heterogeneous catalysis, gas storage and separation, and others [1]. In the present work, a porous 3D MOF material, chromium(III) terephthalate, herein named MIL-101, was investigated as solid support for the preparation of active heterogeneous catalysts.

MIL-101 was prepared by hydrothermal synthesis using terephthalic acid and chromium(III) nitrate nonahydrate, and was characterized [2]. Afterwards, two distinct monovacant polyoxometalates, $K_7[PW_{11}O_{39}] \cdot n(H_2O)$ (PW_{11}) and $K_8[SiW_{11}O_{39}] \cdot m(H_2O)$ (SiW_{11}), were incorporated in the porous of the MOF leading to the formation of two unprecedented composite materials, $PW_{11}@MIL-101$ and $SiW_{11}@MIL-101$, respectively [3]. These materials were structurally characterized by FTIR spectroscopy, powder XRD and electronic microscopy (SEM/EDS).

The catalytic activity, selectivity and reusability of the two composite materials were investigated for the oxidation of geraniol, using hydrogen peroxide as oxidant. The two materials revealed to be active heterogeneous catalysts, capable to be reused in various consecutive cycles. Higher yield of 2,3-epoxygeraniol was found when $PW_{11}@MIL-101$ was used, however both catalysts showed 100% of selectivity for this epoxide.

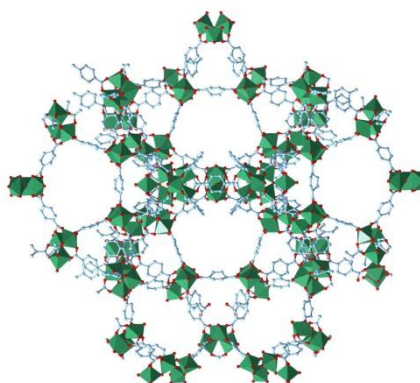


Figure 1. Structure of the porous Metal-Organic Framework MIL-101.

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Isolation and quantification of labdanolic acid from *Cistus ladaniferus*

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Natural products continue to provide unique source of inspiration for advances in organic chemistry and disease treatment [1]. Particularly, labdane-type diterpenes [2] are an excellent example of natural products with important applications in medicine. Several of these derivatives possess a wide range of relevant biological properties, such as anti-fungal and anti-bacterial, anti-mutagenic, cytotoxic, anti-inflammatory or analgesic activities. Our interest in the study of labdane-type diterpenes emerged recently due to the possibility of isolation of appreciable quantities of a specific diterpene, the labdanolic acid (LA), from a Portuguese natural resource, i.e., the plant *Cistus ladaniferus*. From the extract of this plant has been identified near 300 compounds, including fragrances such as Ambrox and diterpenes like labdane derivatives [3]. However, LA is one major compound which has been isolated in high quantities (1.1 g per 100 g of air-dried twigs) by extraction with diethyl ether followed by aqueous basic extraction and normal column chromatography [4].

Through this investigation we have focused our efforts on the development of an analytical method for the quantification of LA. The process depends on the derivatization of LA to form the benzylic ester that can be analysed by HPLC. This investigation aims for the study of the variation of LA present in *Cistus ladaniferus* during the year and the results obtained will be present and discussed in this communication.

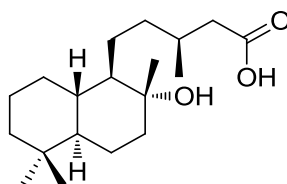


Figure 1. Labdanolic acid (LA).

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Application of geochemistry software to corrosion studies

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“The need for a consistent evaluation of complex geochemical systems resulted in a rapid increase of interest in the field of geochemical modeling, leading to the creation of Geochemical Modeling Software (GMS). The chemical speciation in aqueous environment, mineral balance and solute transport are some of the calculations that can be performed by GMS. These programs are well suited for direct application to corrosion studies, namely those related to atmospheric corrosion, corrosion in submerged environments or even corrosion at high temperature. In all of these cases, the interactions are of geochemical nature, i.e. the reactions are the same as those encountered in natural waters or in high temperature magmatic systems.

The analytical ability of GMS allows the user to model real situations and predict how materials behave when exposed to different environments. Although geochemical modeling can provide a better understanding of the causes and results of corrosion reactions and processes, the GMS have been rarely applied to the study of corrosion.” [1]

In this communication, two examples are presented in order to illustrate the work that is currently being undertaken in our laboratory using GMS applied to corrosion problems. The corrosion of a pure zinc disc electrode (1 mm in diameter) immersed in near neutral aerated 0.05M NaCl was characterized experimentally using potentiometric microelectrodes. Values of corrosion potential, pH and pZn ($-\log a_{\text{Zn}^{2+}}$) were obtained in selected points of the corroding sample. The experimental data was compared with the predictions given by stability and Pourbaix diagrams generated using GMS (commercial and freeware), making a correlation between results and the kinetic and thermodynamic information present in databases from the programs. A second example is the kinetic study of the oxidation of Fe^{2+} to Fe^{3+} based from the work of Singer and Stumm [2].

Acknowledgements: The authors acknowledge funding from FCT and the European project AtCorAS.

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Micro-electrochemical techniques to study localised corrosion

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Many methods and techniques are used to study and monitor corrosion. Among the most widely used, electrochemical techniques are very suited and versatile. Typically, electrodes of centimeter size are employed and the measured quantities give the net response of the overall sample. This becomes a problem when characterizing localized corrosion processes like pitting, crevice and galvanic corrosion, as well as, defects in protective films and inclusions in technical alloys. The use of microelectrodes can overcome this problem. The major advantage is the spatial resolution obtained. Diverse complementary localized techniques can be used. The Scanning Vibrating Electrode Technique (SVET), for example, detects charged species in solution and is able to map the corrosion activity, discriminating the anodic and cathodic regions on the surface of a corroding metal. It is “blind” to uncharged species and gives no information about the nature of the charges present. This information can be obtained by potentiometric and amperometric microelectrodes that sense chemical species of interest, like metal ion concentration, dissolved oxygen, pH, etc - Figure 1. This communication illustrates the use of several microelectrochemical techniques in the characterization of important cases of localised corrosion.

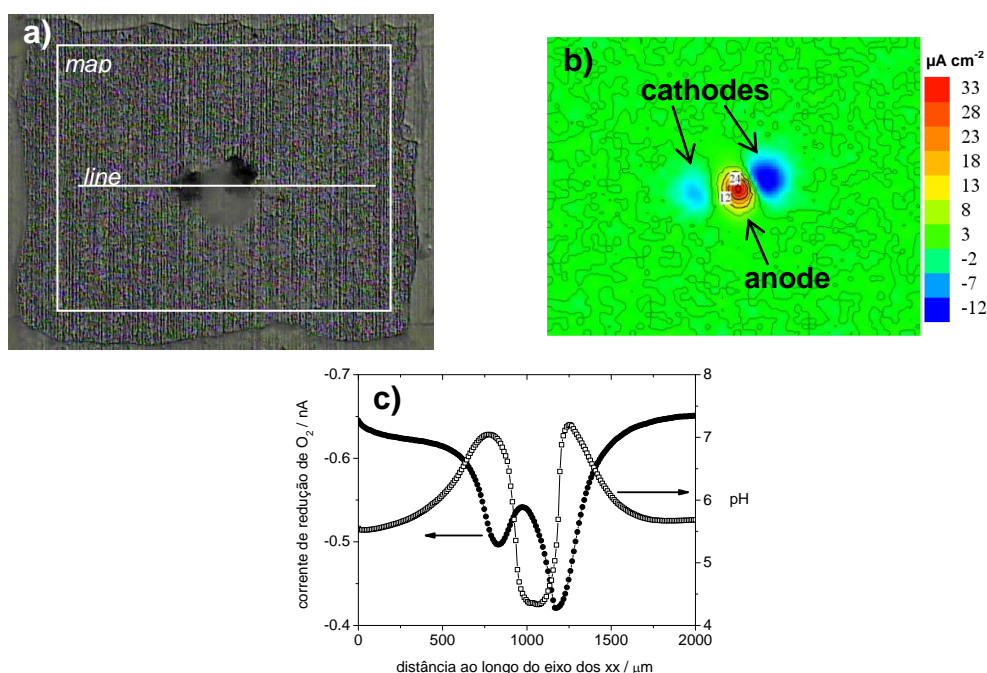


Figure 1. Sample of aluminum alloy 2024-T3 coated with sol-gel film with two artificial defects after 30 hours of immersion in 0.05M NaCl (a), ionic current density map measured by SVET (b) and pH and reduction current of dissolved oxygen in solution both obtained in a line 50 μm above the surface.

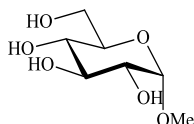
Acknowledgements: The authors acknowledge funding from FCT and the European project AtCorAS.

Approach to the synthesis of nucleoside inhibitors of butyrylcholinesterase

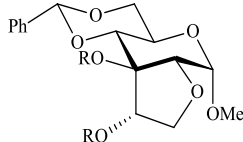
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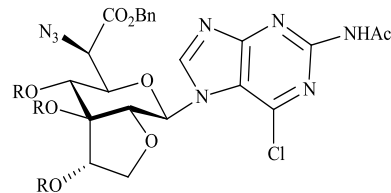
Alzheimer's disease (AD) is clinically characterized by a progressive memory loss and other cognitive impairments. Although the etiology of AD is not completely known, the current therapeutic options are acetylcholinesterase inhibitors (AChEIs), which increase neurotransmission at cholinergic synapses in the brain and reduce temporarily the cognitive deficit [1]. Butyrylcholinesterase (BuChE) is an enzyme also involved in cholinergic neurotransmission, which has received an increasing attention in the past years. With AD progression, the activity of AChE decreases while that of BuChE rises in an attempt to modulate ACh levels in cholinergic neurons. Recently it was reported that BuChE is present in AD beta-amyloid plaques but its role is still unknown [2]. This discovery also encouraged the search for new and selective inhibitors of this enzyme. We present herein a simple, efficient and non-expensive approach to synthesize the sugar moiety of nucleosides type **3**, which are selective inhibitors of butyrylcholinesterase [3]. The sugar bicycle **2** is built starting from methyl α -D-glucopyranoside (**1**) through regioselective protection, oxidation, Wittig reaction, cyclization and reduction.



1



2



3

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A green integrated biocatalytic system for the conversion of CO₂ and vegetable oils into biodiesel

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The global demand for alternative fuels has increased on the last two decades. This fact is directly related with the increasing of the public awareness for the fossil fuel scarcity and also for the negative environmental consequences of fossil fuels consumption. One of the best examples is biodiesel, which is a green alternative for conventional diesel and that can be produced by the transesterification of common cooking oil and methanol [1].

Here we present a green integrated production design that is able to produce simultaneously methanol and biodiesel using two different biocatalytic systems and an ionic liquid/supercritical carbon dioxide media (scCO₂) (Figure 1). The methanol was produced from the reduction of scCO₂ using three different dehydrogenases: Formate (FDH), Formaldehyde (FaldDH) and Alcohol (ADH) which uses NADH to catalyse the CO₂ reduction. In order to continually produce methanol we have added to this biocatalytic system glutamate dehydrogenase (GDH) that converts glutamate to α -ketoglutarate and regenerates the NAD⁺ produced by the three dehydrogenases system mention before [2]. The integration of all these enzymes was achieved through their immobilization in a sol-gel matrix. This reaction as conducted in [emim][etSO₄] which is an ionic liquid that exhibit a good solubility of CO₂.

The methanol was then used to obtain biodiesel by enzymatic transesterification of triglycerides, using Novozyme 435 [1]. We have evaluated different operational parameters. Our results show that the higher production of methanol and consequently of biodiesel was achieved using a pressure of 80 bar, a flow of 1,5ml/min and a temperature of 35°C. These preliminary results shown that is possible to produce biodiesel using a green integrated approach from CO₂ and vegetable oils.

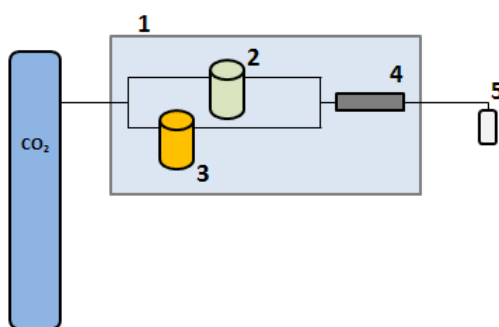


Figure 1. Schematic diagram of the experimental apparatus (1-Water heating bath; 2-Enzymatic reactor for the production of methanol; 3-Vegetable oil; 4-Enzymatic reactor with Novozyme 435; 5-Biodiesel collector)

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Development of ionic liquids based on biological compounds

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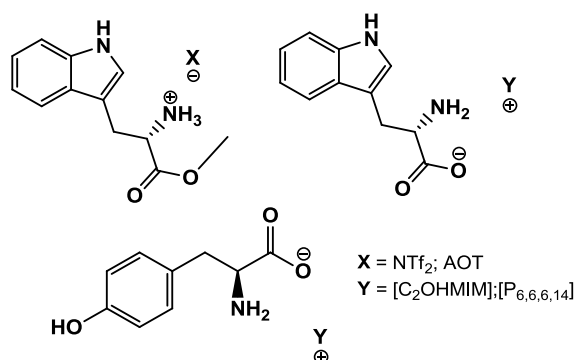
The objective of this study is related with the development of Ionic Liquids (ILs) based on L-tryptophan and L-tyrosine as biological units. These aminoacids were combined with different anions and/or cations in order to tune some of their final physical, chemical and thermal properties. Amino acids are normally used in the food, medical and chemical industry. These building blocks, obtained from the hydrolysis of proteins, are the main components in the synthesis of different drugs and biodegradable polymers [1]. The amino acids differ in the side chains which vary in structure, size, electric charge, and influence the solubility of these precursor blocks in water [2].

Taking advantage to the dual functional groups (amine and carboxylic acid units) from aminoacids, we have developed novel ILs using L-tryptophan methyl ester as organic cation and L-tryptophan and L-tyrosine as organic anions. The appropriate counter ions were selected according their toxicity as well as hydrophobicity behavior (as described on the Figure).

All novel ILs were completely characterized by NMR, FTIR and elemental analysis in order to check their expected structure and purity. Some physical (density, viscosity and solubility) and thermal (melting point, glass transition temperature T_g and decomposition temperature) properties will be evaluated.

In addition different partition studies using water-octanol systems have been performed through UV/Vis and fluorescence spectroscopy measurements for the ILs. The partition coefficients can be relevant to understand the tendency of these novels ILs to cross biological membranes [3].

Tryptophan and Tyrosine ILs



Acknowledgements: The authors would like to thanks to FCT-MCTES (PTDC/CTM/103664/2008 and PTDC/QUI/70902/2006 projects).

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Topical drug delivery of lidocaine and diclofenac gels: viscoelastic properties and *in vitro* skin distribution studies

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This study examined the mechanical and viscoelastic properties of a range of aqueous gels of lidocaine and diclofenac composed of either hydroxymethyl propyl cellulose (HPMC), xanthan gum (XG) and carbopol 940 (C940) and six absorption enhancers with different partition coefficient (diethylene glycol, tetraethylene glycol, dimethyl sulfoxide, azone, oleic acid and linoleic acid). For each formulation those properties were determined using texture profile analysis (TPA) and rheology [1].

Additionally *in vitro* distribution studies of these gels were done using Franz Cells with quantification with HPLC.

The mechanical properties and the lidocaine and diclofenac amount permeated allow us to select the best vehicles for topical drug delivery and personal care agents of skin.

Acknowledgements: The author wishes to thank the project “LaserLeap” of RedEmprendia for financial support.

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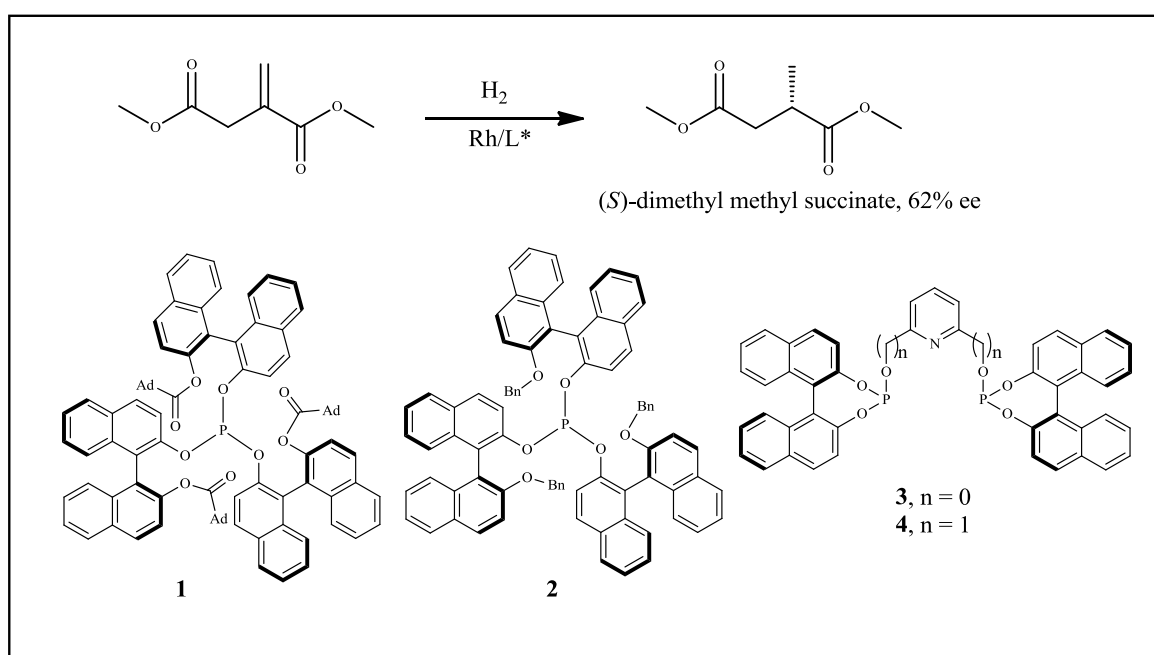
Computational studies of Binol based phosphites and respective metal complexes at PM6 and DFT levels. Application in asymmetric hydrogenation of olefins.

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BINOL based mono and di-phosphite ligands have been largely used as excellent inductors of chirality in several catalytic systems [1]. In order to predict the activity and selectivity of some of these ligands in asymmetric catalysis, computational studies has been a powerful tool. The PM6 semiempirical Hamiltonian [2] and DFT (*Density Functional Theory*) methods were used to determine the lowest energy structure of BINOL-based C_3 -symmetric monophosphite, of pyridine-*bis*-BINOL-phosphite ditopic ligands and some of their rhodium complexes, to rationalize/interpret experimental data obtained in the asymmetric hydrogenation of dymethyl itaconate, Scheme 1.



Scheme 1

Acknowledgements: Financial support from QREN/FEDER/FCT (PTDC/QUI-QUI/112913/2009).

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Gamma irradiation protects oleic acid from oxidation: an experiment in *Lactarius deliciosus* wild mushroom

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The short shelf-life of mushrooms is an obstacle to the distribution and marketing of the fresh product. Thus, prolonging postharvest storage, while preserving their quality, would benefit the mushroom industry as well as consumers [1]. There has been extensive research on finding the most appropriate technology for mushrooms preservation and a particular interest arises for wild species. Treatment by irradiation emerges as a possible conservation technique that has been tested successfully in several food products and is regulated in the European Union by the Directive 1999/2/EC.

In the present work, the influence of gamma irradiation dose (0.5 and 1 kGy) over the fatty acids profile of *Lactarius deliciosus* L. wild mushroom, collected in the Northeast of Portugal (November 2011), was evaluated by gas-chromatography coupled to flame ionization detection (GC-FID). The analyses were performed after 0, 4 and 8 days of storage at 4 °C in irradiated and non-irradiated samples (control). The control and the irradiated samples revealed an identical profile, with C18:0 (stearic acid), C18:2n6c (linoleic acid), C18:1n9c (oleic acid) and C16:0 (palmitic acid) as main fatty acids. These results are in agreement to the reported by our research group in a previous study with nutritional characterization of this species [2]. Nevertheless, some differences were found in the percentage of some fatty acids in the different samples, mainly in oleic acid. Control sample (non-irradiated) after 8 days of storage, showed a lower C18:1n9c percentage (decreased from 8 to 4.4%) contributing to a decrease in monounsaturated fatty acids (MUFA) levels. Otherwise, in the sample irradiated with 0.5 kGy the percentage of the mentioned fatty acid did not changed until day 8.

Overall, irradiation could be an alternative to ensure the quality and extend the life of mushrooms, protecting their fatty acids from oxidation, as is was demonstrated herein for oleic acid. In fact, food irradiation is now being commonly used in many countries, as people are becoming more aware of the role of food irradiation in regards to food safety and product shelf-life extension.

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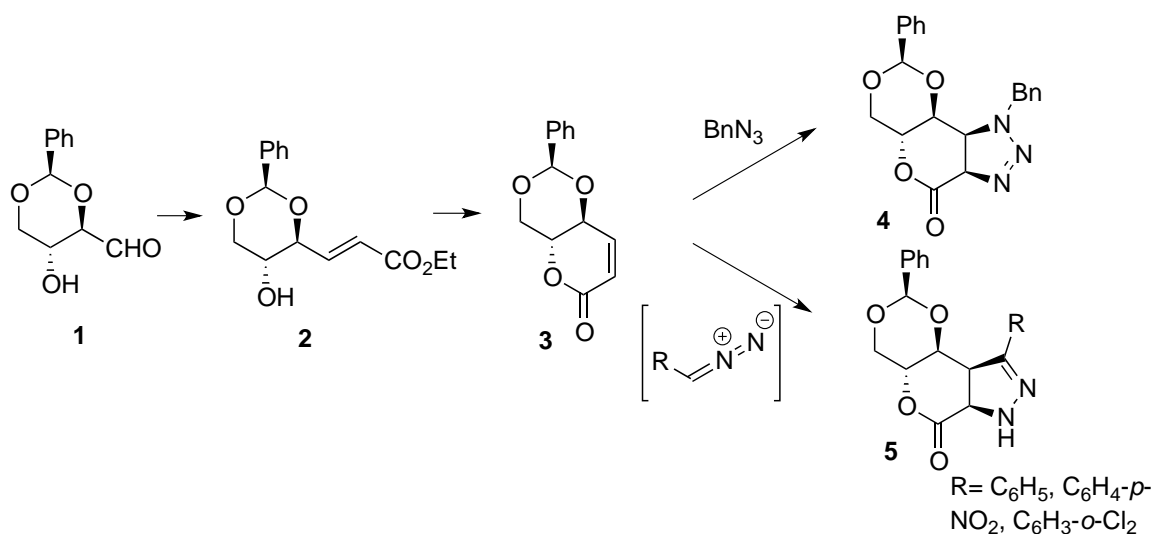
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1,3-Dipolar cycloaddition of (2*R*,4*aR*,8*aS*)-2-phenyl-4,4*a*-dihydropyrano[3,2-*d*][1,3]dioxin-6(8*aH*)-one with aromatic diazomethyl compounds

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Small chiral synthons are being more and more appealing to synthetic chemists to build up target molecules possessing multi-stereogenic centres. We have been looking at the usefulness of D-erythrose derivatives obtained from D-glucose. The aldehyde **1** [1] was reacted with phosphorane to give α,β -unsaturated compound **2** which was cyclized to lactone **3** in 63.4 % overall yield from **1**. The open chain compound **2** resisted to 1,3-dipolar cycloaddition with benzyl azide, but lactone **3** reacted smoothly with benzylazide to afford triazole **4** in 81.3 % yield, with total *regio*- and *stereo*-selectivity. Diazomethyl compounds have also shown the same trend of excellent selectivities and good yields. All compounds **5** were fully characterized and the stereochemistry studied by n.O.e. experiments.



Scheme 1

Acknowledgements: We thanks to FCT (Project PTDC/QUI/67407/2006) QREN, COMPETE and POPH for financial support and to the Portuguese NMR Network (Bruker Avance II 400).

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An efficient synthetic approach to 6-triazolopurines

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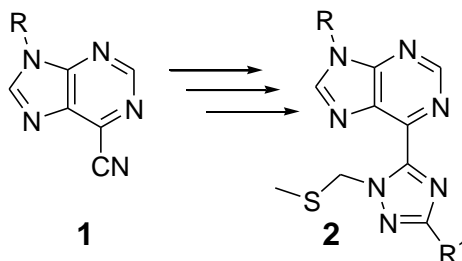
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Tuberculosis is an air-borne infectious disease that has been scouring humanity for thousands of years. The World Health Organization (WHO) has estimated that at least 2 billion people are infected with a latent form of *M. tuberculosis* and about 10% will develop the active form of the disease during their lifetime [1]. Upon the discovery of efficient antibiotics the fatal disease was sought as defeatable. However, in the last decade, tuberculosis has resurfaced as a significant threat to public health as the microorganism accountable for this disease has gained resistance to the antibiotics that have been previously used in treatment [2]. This resistance is commonly referenced as multi-drug resistant tuberculosis (MDR-TB) and extreme-drug resistant tuberculosis (XDR-TB). To avoid a future epidemic the development of new TB drugs is imperative.

Recently, in our research group, a new class of compounds active against the microorganism was discovered, the 6-substituted-arylurines [3]. These results prompted us to synthesize novel purine derivatives having new substituents on C6 of the purine core.

In this work we report the synthesis of 6-triazolopurine derivatives, compounds of structure **2**. These compounds were obtained in three sequential steps from 6-cyanopurines **1**. The reaction conditions and the mechanism of the reaction will be presented.



Acknowledgements: Thanks are due to University of Minho and *Fundação para a Ciência e Tecnologia* for financial support (project n°F-COMP-01-0124-FEDER-022716 (ref. FCT PEst-/QUI/UI0686/2011) FEDER-COMPETE, FCT-Portugal. The NMR spectrometer (Bruker 400 Avance III) is part of the National NMR Network supported with funds from FCT.

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A left-handed helical 3D metal-organic chiral framework derived from the decomposition of 3-amino-1H-1,2,4-triazole-5-carboxylic acid

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The rational design novel metal-organic frameworks (MOFs) by self-assembly has received remarkable interest due to their fascinating structural features and potential to be applied as novel functional materials. The final assembly can be influenced by numerous factors, such as geometric requirements of metal centers, shape and nature of ligands, reaction routes, solvents, templates, pH of solution and counter-ions. The N-donor 1,2,4-triazoles have been extensively utilized in the construction of coordination complexes due to their various applications in materials, supramolecular chemistry and crystal engineering [1]. It is also used to fabricate “simple, high-symmetry” structures to study new topological nets [2].

In this work we report a novel 3D metal-organic chiral framework containing left-handed helices, [Cu(atr)(OH)]·3H₂O (Hatr = 3-Amino-1H-1,2,4-triazole), which is derived from the decarboxylation of 3-Amino-1H-1,2,4-triazole-5-carboxylic acid. The skeleton of the left-handed helix in the present compound is based on foundational repeating neutral unit [Cu(atr)(OH)]. With the topology analysis using TOPOS 4.0 program package [3], and A. F. Wells' topology definition [4], Cu center and atr[−] moiety could be both regarded as 3-connected nodes. The overall structure can be simplified to a uninodal 5-connected topology with a Schläfli symbol of (3³.4.6³.7³).

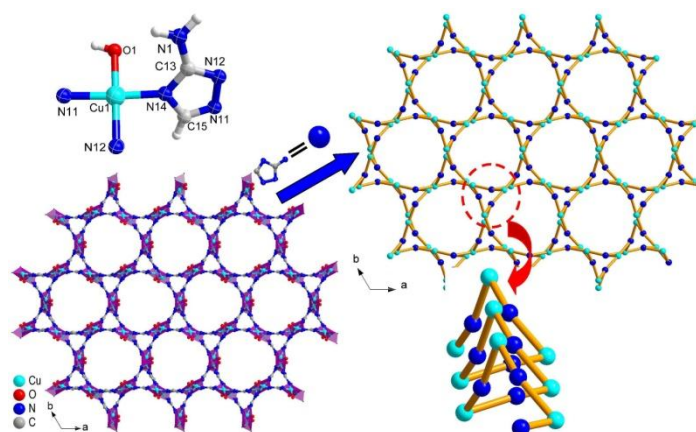


Figure 1. Coordination of Cu(II) center, the 3D framework and its topology based on the left-hand helices.

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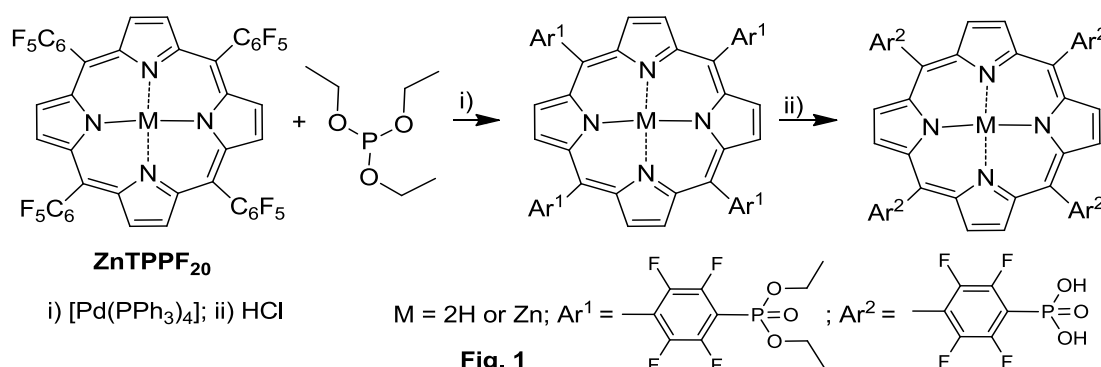
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Synthesis of new porphyrin-phosphonate derivatives for MOFs construction

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Porphyrins (Pors) possess unique physico-chemical properties which make them valuable compounds in different scientific fields, namely in medicine, catalysis, solar energy converters, etc. [1]. The possibility of using Pors as primary building blocks of multidimensional coordination polymers, which combine a myriad of metallic centers with ligands having multiple binding sites, prompted us to prepare porphyrin macrocycles with multi-phosphonate groups at the periphery of their core (Fig. 1). Following our research interest in the use phosphonate-based organic ligands for the construction of coordination polymers [2] and on Por chemistry we start preparing new Por-phosphonate ligands to build new MOF materials [3]. Having several coordination capable groups may allow a fine tuning of the framework topology and functionality. In this communication we will be presented the synthesis and structural characterization of some of these new molecules.



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Application of an optimized ELISA assay in the assessment of 17 β -estradiol levels in surface and waste waters from the Aveiro region (Portugal)

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The estrogen 17 β -estradiol (E2) is considered an endocrine disruptor as it may interfere with the normal function of the endocrine system of humans and wildlife. This steroid hormone, being excreted by humans, as well as animals, enters in the environment mainly through discharge of domestic sewage effluents and disposal of animal waste [1].

The methods used to quantify steroids are based mainly in solid-phase extraction or micro-extraction (SPE or SPME, respectively) followed by gas chromatography-mass spectrometry (GC-MS; GC-MS/MS) or high-performance liquid chromatography-mass spectrometry (HPLC-MS; HPLC-MS/MS). However, rapid, simple and cost-effective methods are needed for quantitative analysis of estrogenic hormones. Enzyme linked immunosorbent assay (ELISA) offers these characteristics with detection limits in the ng L⁻¹ range. Also, a large number of samples may be analysed simultaneously and, usually, sample pre-treatment is not required.

In this study, first, an ELISA procedure was optimized in order to overcome difficulties related to the analysis of real samples, such as the presence of organic matter and/or salinity. Matrix effects were overpassed and a quantification limit of 30 ng L⁻¹ was achieved. Then, real samples – wastewater samples and surface samples from an estuarine system – were analysed in order to assess the presence and levels of this estrogen in waters from the Aveiro region (Portugal). It must be highlighted that all the analysis were performed in the absence of sample pre-treatments.

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Computational studies of Cu-catalyzed addition of azides to iodoalkynes

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Click reactions are easily performed, fast, highly selective, insensitive to oxygen and water, and regio- and stereospecific. One of the most popular click-reactions is the copper-catalyzed generation of a variety of five-membered heterocycles from the reaction of organic azides with terminal alkynes (Cu-azide-alkyne-coupling, CuAAC) [1,2]. CuAAC can be observed in the presence of many functional groups and under demanding reactions conditions. Traditional CuAAC is however limited to terminal acetylenes and yields only 1,4-disubstituted triazoles. A recent development of CuAAC allows the generation of 1,4,5-trissubstituted triazoles by reacting organic azides with iodoalkynes [3]. We have thoroughly explored this improved CuAAC *via* density functional calculations. We first compared the performance of several density-functionals (B3LYP, PBE0, PBEPW91, BHHLYP, PBE1PW91, B3PW91, X3LYP) to higher-level MP2 computations in a simple prototypical reaction. The selected functionals (B3LYP, PBE0 and PBEPW91) were then used to study a large number of possible reaction pathways in several substituted iodoalkynes and organic azides. These computations clearly identify the reaction mechanism, and greatly improve the current understanding of substituent effects in these interesting reactions.

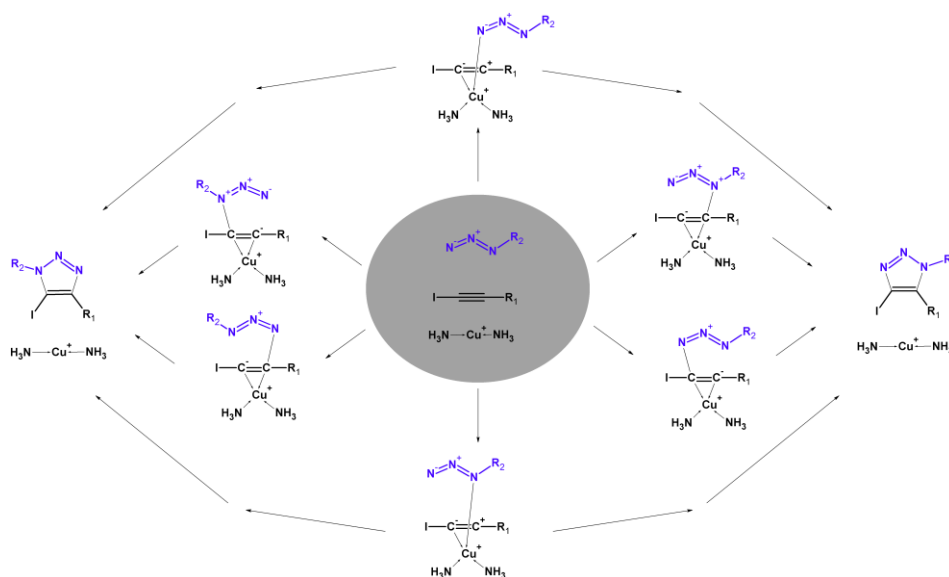


Figure 1. General representation of the tested mechanisms.

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Screening of single-walled carbon nanotubes by optical fiber sensing

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Single walled carbon nanotubes (SWCNT) are allotropes of carbon commonly used in energy and environmental applications, as well as in biology and medicine research, with several scientific interests [1,2]; however, due to the high manufacturing rate, consequent accidental discharges of SWCNT to aquatic ecosystems have been occurred [3], and then their actual detection in aqueous solutions has become an important issue. The main objective of this work is to apply an optical fibre (OF) sensor as a tool to screen SWCNT, in order to monitor the variation of optical power in various SWCNT samples. Experimental conditions for the dispersion of SWCNT in aqueous solutions of surfactant were previously optimized by an experimental design, i.e., a full factorial design, and different periods of sonication (60 and 100 minutes), and centrifugation (5 and 10 minutes), as well as different values of relative centrifugal force (2000 $\times g$ and 10000 $\times g$) were used in order to compare the influence of such conditions on absorbance intensities recorded at 500 nm. It was found that the centrifugation time was the main factor responsible to such dispersion, as well as that the SWCNT sample obtained from 60 minutes of sonication, and centrifuged 5 minutes at 2000 $\times g$ was the most statistically significant at 500 nm. Such sample was then diluted to obtain different subsamples (with concentrations of 0.01, 0.05, 0.1, 0.15, 0.2 and 0.25 mg/mL), and a linear regression was obtained between the absorbance intensities at 500 nm and concentration of SWCNT ($R^2 = 0.9985$). The same series of subsamples were applied to the OF sensor, and a nonlinear calibration was observed on the analytical response (variation of optical power). The results obtained by the OF sensor were encouraging in what concerns a new approach for detection and quantification of SWCNT in solutions due to its compact design, less expensive materials and equipment as well as a requirement of low volume of sample (0.2 mL). Additionally, it was verified that the nonlinear calibration model observed for the analytical response with the OF probe follows the general cumulative symmetric double sigmoidal (SDS) model ($R^2 = 0.9999$), as an adequate alternative to classical calibration models.

Acknowledgements: This work was funded by FEDER under the Operational Program for Competitiveness Factors – COMPETE and by national funds via FCT (Fundação para a Ciência e a Tecnologia, Portugal) within the framework of research project CARDIOSENSOR (references FCOMP-01-0124-FEDER-010902 and PTDC/SAU-BEB/099042/2008). This work was also funded through scholarships - references SFRH/BD/60429/2009, SFRH/BPD/65410/2009, and SFRH/BPD/73781/2010 under QREN-POPH funds, co-financed by the European Social Fund and Portuguese National Funds from MCTES.

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Breath analysis by optical fiber sensor for the diagnosis of human health

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Breath analysis has been used as a non-invasive clinical practice for diagnostics of metabolic disorders as well as for the monitoring of therapeutic progress [1]. The measurement of exhaled breath is clinically employed due to its safe, rapid, and simple sampling, and its quantitative analysis allows the monitoring of compounds produced by cellular metabolic processes; for example, different classes of volatile organic compounds (VOCs) such as saturated and unsaturated hydrocarbons, oxygen-containing, sulfur-containing, and nitrogen-containing compounds [2] are present. Then, the monitoring of breath composition changes on levels of VOCs in subjects can lead to diagnosis diabetes, hepatic dysfunctions, and lung diseases [1,3]. Although the analytical techniques commonly used in laboratory are sensitive and selective, such as methods based on gas chromatography coupled to mass spectrometry (GC-MS), and on laser-absorption spectroscopy [3], they require expensive instrumentation, and complex procedures for analysis preparation.

This work proposes a sensing system based on optical fiber (OF) transducer for clinical diagnosis for the determination of various VOCs, i.e., alkanes (ethane, pentane, heptane, octane, and decane), and aromatic compounds (benzene, toluene, and styrene) from human breath. The developed methodology provides near real-time analytical responses, rapid analysis, and low instrumentation costs; it also exhibits an adequate analytical performance for breath analysis, in terms of the analytical signal stability, linear range, accuracy, and detection limits (ranging from 0.8 pM for heptane, and to 9.5 pM for decane). Furthermore, the developed OF sensor was found to be comparable with GC-MS as a reference method, since linear correlations were obtained between the two methodologies for the eight tested analytes (with R^2 between 0.9925 and 0.9999, and $p < 1.40 \times 10^{-20}$ and $p < 5.91 \times 10^{-36}$, for heptane and decane, respectively); the OF system also provides narrow intervals at 95% confidence level, suggesting low dispersion levels of the results obtained by referred methodologies. Then, the developed OF analyzer can constitute a useful and inexpensive clinical device for the monitoring of various VOCs, promoting the diagnosis of human health.

Acknowledgements: This work was funded by FEDER under the Operational Program for Competitiveness Factors – COMPETE and by national funds via FCT (Fundação para a Ciência e a Tecnologia, Portugal) within the framework of research project CARDIOSENSOR (references FCOMP-01-0124-FEDER-010902 and PTDC/SAU-BEB/099042/2008). This work was also funded through scholarships - references SFRH/BD/60429/2009, SFRH/BPD/65410/2009, and SFRH/BPD/73781/2010 under QREN-POPH funds, co-financed by the European Social Fund and Portuguese National Funds from MCTES.

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Determination of α -dicarbonyl compounds in foodstuff by HPLC-UV using gas-diffusion microextraction

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α -diketones, such as diacetyl (2,3-butanedione) and 2,3-pentanedione, play an important role in the aroma of many fermented foods and beverages. In some cases due to the intense butter like aroma, the presence of vicinal diketones in beverages can become unpleasant [1]. Methylglyoxal, a smaller α -dicarbonyl compound, also known as pyruvaldehyde or 2-oxopropanal is a highly reactive and toxic compound that disrupts DNA, kills bacteria and inhibits protein synthesis [2]. The aroma of methylglyoxal in foodstuff belongs to the same family of odours as the α -diketones, being lactic and butter-like [3].

Gas-diffusion microextraction (GDME) was used to extract α -dicarbonyl compounds from the samples. The process is based on gas-diffusion of semi-volatile and volatile compounds through a superhydrophobic membrane to an acceptor solution. This acceptor solution is composed by *o*-phenylenediamine (OPDA) in order to derivatize the compounds [4]. The extractions were made at 55°C, for 10 minutes, with stirring. The collected quinoxalines were analyzed by high performance liquid chromatography with UV-Vis detection, which allows the determination of the dicarbonyl compounds - methylglyoxal, diacetyl and 2,3-pentanedione - in different samples. These compounds were detected and quantified in different Port wines, black tea, cacao, cola drink and soy sauce (methylglyoxal – 0.24 to 1.86 mg/L, diacetyl – 0.10 to 1.85 mg/L and 2,3-pentanedione 24.1 to 145.8 μ g/L).

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Synthesis of *N*-ethyl β,β -diaryldehydroalanine and *N*-ethylindole derivatives

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Non-proteinogenic amino acids are an important class of organic compounds that can have intrinsic biological activity or can be found in peptides with antiviral, antitumor, anti-inflammatory or immunosuppressive activities. Among non-proteinogenic amino acids are the *N*-alkylamino acids and dehydroamino acids, which can be found in many biologically important peptides [1]. *N*-Alkylation of the peptide bond causes changes in the volume and conformation of peptides. *N*-Alkylation results in reduced flexibility, increase of permeability for the membrane (increased lipophilicity) and prevention of cleavage by proteolytic enzymes [2].

Recently, Liguori *et al.* proposed the ethylation of several 4-nitrobenzenesulfonyl (Nosyl) protected amino acids using triethyloxonium tetrafluoroborate (Et_3OBF_4) as alkylating agent and *N,N*-diisopropylethylamine (DIPEA) as base to give *N*-ethylamino acid derivatives in high yields [3]. Monteiro *et al.* used a combination of this alkylation procedure and dehydration methodologies previously developed to obtain new non-proteinogenic amino acids namely, *N*-(4-nitrophenylsulfonyl), *N*-ethyl- α,β -dehydroamino acids [4]. The application of this *N*-alkylation procedure to several methyl esters of β,β -dibromo and β -bromo, β -substituted dehydroamino acids protected with standard amine protecting groups gave *N*-ethyl, β -bromo dehydroamino acid derivatives in fair to high yields [5]. By substituting DIPEA for potassium *tert*-butoxide the method was applied to obtain in high yields *N*-ethyl β -halogenated dehydroamino acid derivatives and also non-halogenated *N*-ethyl dehydroamino acid derivatives [6].

In this work, two strategies for the synthesis of *N*-ethyl indole derivatives from a phenylserine derivative are presented. The first route consists of *N*-alkylation of the methyl esters of 2-(*tert*-butoxycarbonylamino)-3,3-diarylacrylates by treatment with triethyloxonium tetrafluoroborate, followed by a metal-assisted C-N intramolecular cyclization. However, this procedure was unsuccessful. The second strategy applied the same procedures but in inverse order: metal-assisted C-N intramolecular cyclization followed by alkylation and allowed the preparation of *N*-ethyl indole derivative in good yields. This method constitutes in a valuable procedure for high yielding synthesis of *N*-ethylated indole derivatives, which can be further applied in peptide synthesis.

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Magnetic core-shell nanoparticles as catalyst supports

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Nanochemistry is an exponentially growing research field in modern science that involves the synthesis and application of nanoparticles of different sizes and shapes. Nanoparticles are different from their bulk counterparts and exhibit unique properties [1]. Due to the high external surface of non-porous nanoparticles a high loading of catalytically active sites is guaranteed and diffusion will no longer limit the kinetics. Hence nanocatalysis may effectively bridge homogeneous and heterogeneous catalysis [2]. Fabrication of core-shell magnetic nanoparticles has been recently subject to extensive research, since such materials combine the unique magnetic properties of the core together with the possibility to further functionalize the surface. This has motivated research to develop designed applications in different fields like bioseparation, drug delivery, catalysis, and others [2]. In the present work we used magnetic nanoparticles of approximately 30 nm diameter which were prepared by a co-precipitation method. The particles were subsequently coated with a dense silica layer yielding binding sites (Si-OH units) for the heterogenization of molecular catalysts [2]. Then nanoparticles were coated with bifunctional molecules containing functional groups with *N*, *O*, or *S* donor atoms, such as derivatives of pyridine, amines or phosphines. Such ligands react with $\text{MoI}_2(\text{CO})_3(\text{NCMe})_2$ precursor complex, giving rise to nanocatalysts. All synthesized materials are characterized by means of adequate spectroscopic (such as NMR and FTIR) or other (XRD and SEM/TEM) techniques. The nanoparticles were tested in oxidation catalysis, namely, epoxidation of olefins and allylic alcohols, with *t*-butylhydroperoxide because selective oxidation is fundamentally important in many food processing, pharmaceutical and fine chemical processes [3]. Cyclooctene, styrene, geraniol and other allylic alcohols were tested as substrates.

Results demonstrated that magnetic nanoparticle supported molybdenum species are efficient, easily recoverable and recyclable catalysts for selective olefin epoxidation. Results show that the systems are completely selective for the epoxidation of cyclo-octene.

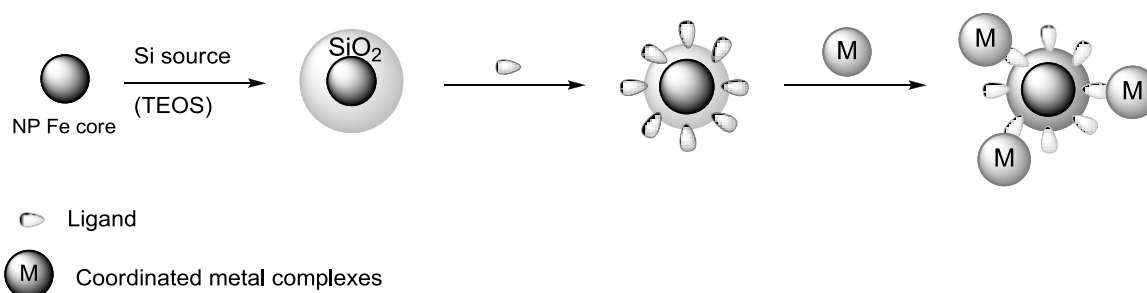


Figure 1. Schematic representation of the catalysts.

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Influence of different malt varieties on xanthohumol isomerization in pale and dark beers

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Xanthohumol (XN) is a prenylflavonoid of hops and has been found to have anti-inflammatory, antioxidant and antilipoperoxidative activities, as well as antiangiogenic, antiproliferative and apoptotic effects [1]. The important health benefits of XN lead to a special attention of the brewing industry concerning the production of XN enriched beers [2]. However, during the wort boiling XN is largely isomerized to isoxanthohumol (IXN) [3]. The aim of this work is to study the influence of different types of malt (pilsner, caramel and roasted malts) in the XN thermal isomerization during wort boiling.

Worts were prepared using a EBC Congress mash and analyzed according to analytical-EBC methods (moisture, wort apparent extract, color and pH). The worts were heated at 70 and 100 °C, during 100 min., with a previous addition of 20 mg/L of XN at the beginning of boiling. The determination of XN and IXN was carried out by RP-HPLC. In addition, the total polyphenol content, flavan-2-ols and proanthocyanidins, reducing power (FRP) and the melanoidin content were also determined.

The results showed that approximately 90% of XN was converted into IXN during *pale* malt wort heating at 100 °C. In the caramel malts, approximately 85% of XN was converted into IXN on *melanoidin* malt varieties, whereas only 65% in the *carared* variety. The *roasted* varieties showed a different behavior, with about 50% of the initial XN after wort cooling. Roasted malt has an inhibiting effect on XN isomerization, resulting in remarkably high levels of XN in the final wort (approx. 10 mg/L), as already described by Magalhães and co-workers [4]. Comparing the temperatures of boiling, a reduction on the temperature leads to significant reduction of XN isomerization, an important factor accounting for higher final XN content. XN is probably bound to roasted substances present in colored malts, preventing its isomerization by changing its chemical properties. In fact, the melanoidin content in roasted malts (approx. 6100 mg/L) are much higher than in pale malts (approx. 330 mg/L). A correlation between color of worts and some chemical properties was also observed. Roasted malts have higher total phenolic content (5-fold higher) as well as flavan-3-ols and proanthocyanidins, due to partial degradation of larger phenolic compounds by roasting.

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The PROFILES project as a way to provide continuous professional development of the science teachers

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Nowadays, we have been witnessing an interesting phenomenon, however, worrying: there are indicators that suggest that students do not like science, as it is taught in European schools [1]. Of course, the reason for this phenomenon is not from the responsibility of a single entity. Effective science learning is a challenge that all teachers must face in modern times. Therefore, it is essential that teachers develop a self-critical spirit on his school activity – in order to achieve the ultimate goal of teacher ownership [2].

Thus, from this inherent problem in science teaching has emerged a project promoted by the European Commission (through the Seventh Framework Programme – FP7) which aims to provide professional, methodological and self-reflexivity competences to science teachers: the PROFILES project. The PROFILES acronym means Professional Reflection-Oriented Focus on Inquiry Learning and Education through Science, and this project arises from the need to invest in continuing training for teachers as a way to a better educational future.

Portugal is one of the various participating countries in PROFILES and is represented by the Faculty of Science, University of Porto. A significant component of the project was implemented through an action of teacher training which was attended by about 30 chemistry teachers. The project promotes a formal learning through creativity, problem solving and socio-scientific decision-making procedures. Therefore, it is possible and important to establish a link between society and science, influencing the ways of teaching and educating through science [2]. So far, we have some interesting themes for research with students: “Do you need chemistry in order to be a good bone surgeon?”, “How can we avoid energy losses in our school?”, “Ways into the Microscopic World ‘What happens with the ice-blocks in my soft drink?’”, among others. All participants in the project are extremely excited about the opportunity to take part in this european project. The poster will develop the basic precepts of PROFILES and discuss how this project contributes to an improvement in the self-critical spirit and continuous professional development in several chemistry teachers from Portugal.

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Chemical composition and antimicrobial activity of *Salvia sclareoides* Brot. extracts

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Salvia is one of the largest genera of the Lamiaceae family that is widespread in the Mediterranean region, South-East Asia and Central America. *Salvia* species are reputed for their medicinal properties and they have been used in folk medicine to treat colds, wounds and skin infections, headache, cerebral ischaemia and memory disorders [1]. *Salvia sclareoides* is an aromatic herb native to Portugal that was reported for its high potential in the inhibition of acetyl- and butyrylcholinesterase, two enzymes involved in the Alzheimer disease [2]. Prion binding properties and strong antioxidant activity of its extracts were also recently reported [3]. The phytochemical study of this plant revealed a high content of terpenoid type compounds, mainly ursolic and sumaresinolic acids, lupenediol and a new triterpenetriol, as well as phenolic compounds [3].

In this work we present the antimicrobial activity of six *S. sclareoides* extracts. Seven pathogenic bacteria (*Bacillus cereus*, *Enterococcus faecalis*, *Escherichia coli*, *Listeria monocytogenes*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *Staphylococcus aureus*), and five pathogenic fungi (*Aspergillus brasiliensis*, *Botrytis cinerea*, *Candida albicans*, *Penicillium aurantiogriseum*, *Fusarium culmorum*), were used in the tests and evaluated by the paper disk diffusion method.

Some inhibition on the growth of the bacteria *Enterococcus faecalis* and the fungus *Botrytis cinerea* was observed with the dichloromethane extract, while the acetone and methanol extracts only inhibited the growth of the pathogenic bacteria *Enterococcus faecalis* and *Listeria monocytogenes*. The relationship between the antimicrobial activity and the chemical composition of the extracts will be discussed.

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Functionalized Fe₃O₄/SiO₂ core/shell particles: new sorbents for the magnetic removal of aqueous Hg(II)

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Mercury and its compounds are one of the most dangerous contaminants in the environment, threatening the human health and natural ecosystems. They are included in the list of priority hazardous substances [1] and consequently, the removal of Hg and its compounds, from aquatic systems is a major goal of wastewater treatment and cleanup technologies.

Conventional techniques for Hg removal from aqueous solutions include sulphate or hydrazine precipitation, ion-exchange, liquid-liquid extraction, adsorption and solid phase extraction via activated carbon sorption [2].

In the last few years, we have carried out several studies envisaging the development of a new class of sorbents based on dithiocarbamate functionalized Fe₃O₄/SiO₂ core/shell particles [3,4]. These materials not only take advantage of the high affinity between Hg(II) and sulphur donor ligands, but also allows the magnetic removal of the particles with the contaminants. The effectiveness of these sorbents was investigated, and its potential as cleanup agent for contaminated waters was assessed. Therefore batch stirred tank experiments have been performed by contacting a volume of solution with known amounts of functionalized Fe₃O₄ particles. Several aspects of the water treatment process will be presented in this communication, such as: effect of sorbent dose, effect of natural waters constituents (*e.g.* seawater and river water), the kinetics of the removal process and the equilibrium. In this context, the performance of these materials will be discussed in light of their surface chemistry and morphological characteristics.

The results obtained from this study allow us to conclude that the dithiocarbamate functionalized Fe₃O₄/SiO₂ are effective sorbents for water treatment, presenting several advantages. These include the need of just a few milligrams of material per liter to decrease Hg(II) concentration to values lower than the guideline values for drinking water; easy separation from solution under an external magnetic field; and ability to be used in complex matrices such as seawater and river water, without compromising their performance. Additionally, it must be highlighted that the sorption capacity of these sorbents as predicted by well-known equilibrium models, such as Langmuir or Sips (*ca.* 200 mg/g), surmount the majority of the values found in literature for other type of sorbents.

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Application of ESI-MS/MS to the structural characterization of *Genista tenera* flavonoids and flavonoid glycosides

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Mass spectrometry has evolved into a strong analytical tool for the structural characterization of natural products. The development of soft ionization techniques, e.g. electrospray, and the low detection limits made this technique extremely useful when only small amounts of sample are available [1,2], which is a common occurrence in analytical studies of natural products.

In this work we present a putative identification of compounds present in the lyophilized aqueous extract of *Genista tenera* (Leguminosae), a medicinal plant used in folk medicine to control diabetes. A preliminary phytochemical study of extracts obtained from plant's aerial parts, by using several solvents, showed the presence of alkaloids [3] and flavonoids [4-6]. Pursuing our studies on the research of new bioactive compounds for diabetes prevention and treatment, we hereby present a more detailed overview of the phytochemical composition of the aqueous extract. The samples were analysed by electrospray tandem mass spectrometry (ESI-MS/MS) in the negative and positive ion modes. The flavonoids apigenin/genistein (m/z 269), biochanin A (m/z 283), vitexin/isovitexin, genistein 7-*O*-glucoside (m/z 431), orobol 7-*O*-glucoside/8-glucosylorobol/luteolin 7-*O*-glucoside (m/z 447) and the glucosylluteolin-*O*-glucoside (m/z 609) were tentatively identified in negative ion mode on an ion trap mass spectrometer, while chrysoeriol identification (m/z 301) was accomplished in positive mode, on a triple quadrupole spectrometer.

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ELISA application on EE2 water monitoring

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Recently, has been a growing concern about the harmful effects of endocrine disrupting chemicals (EDCs) on the reproduction and development of animals and humans, becoming important the study of their persistence in the environment [1]. 17 α -ethinylestradiol (EE2) is a manufactured pharmaceutical chemical used for birth control and medical treatments of cancer, hormonal imbalance, osteoporosis, and other ailments [2]. All humans and animals can excrete hormone steroids from their bodies that will end up in the environment through sewage discharge and animal waste disposal [3]. The women daily excretion of EE2 was estimated as being 35 μ g day⁻¹ [3]. Sewage treatment plants are not designed to remove estrogens or other micropollutants, thus estrogens that are not degraded during wastewater treatment processes are released into the environment in the effluent [4].

The methods used to quantify steroids are based mainly in SPE (solid-phase extraction) or SPME (micro-extraction) combined with GC-MS or LC-MS-MS. However, there is a strong need for rapid, simple, and cost-effective methods for quantitative analysis of estrogenic hormones, such as the enzyme linked immunosorbent assay (ELISA). In this study, the development of an ELISA procedure for EE2, was performed in order to evaluate problems such as interference of organic matter and high salinity present on real samples. ELISA method performance was also evaluated and ground, surface and waste water samples were analyzed.

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Photochemical properties of rigidified and non-rigidified heptamethine cyanine NIR dyes in solution and adsorbed onto polymers

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Organic Near Infrared (NIR) fluorescent dyes, more precisely heptamethine cyanines, are very attractive candidates for imaging due to the strong absorption from 600nm to 1000nm, high molar absorption coefficients and fluorescence quantum yields [1]. Aiming to further improve the properties of these molecules, a rigid cyclohexenyl can be introduced in the middle of polymethine chain. This rigidification may increase the photostability and the fluorescence quantum yield [2].

In the present work, we intend to compare a serie of non-rigidified heptamethine cyanine dyes with the respective rigidified compounds in terms of absorption properties (figure 1), fluorescence quantum yields, fluorescence lifetimes and singlet oxygen quantum yield of formation. We also studied these dyes adsorbed onto microcrystalline cellulose and chitosan in order to understand their behavior in rigid environments. Laser-induced room temperature luminescence and the use of a lifetime analysis (lifetime distribution analysis for the powdered solid samples) revealed in most cases the existence of good fluorescence quantum yields and lifetimes [3]. Singlet oxygen studies of the solution samples were also performed.

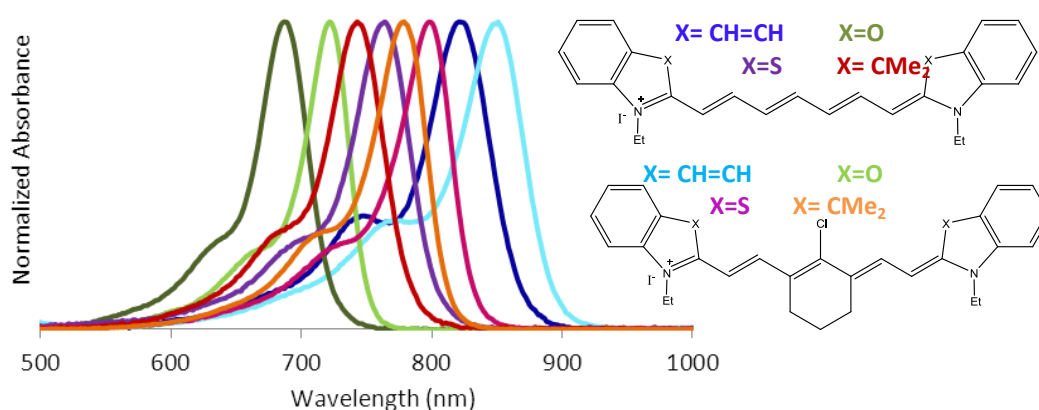


Figure 1. Structures and normalized absorption spectra of the heptamethine cyanine dyes.

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Unveiling the catalytic mechanism of L-asparaginase II using computational methods

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Recent studies have shown that certain types of cancer are associated with the high blood serum concentration of some amino acids. When the tumor is extracted, the concentration of these amino acids returns to its normal levels in the body. These findings show that the disturbance in the amino acids catabolism is a direct consequence of the fast growth of cancer cells, due to their high need of certain amino acids. Therefore, if we could in some way reduce the concentration of these amino acids in the organism, the tumor would be unable to grow [1].

L-asparaginase II is an enzyme present in a large number of organisms, except primates and humans [2], that catalysis the hydrolysis of L-asparagine to L-aspartate, with the release of ammonia (NH₃). It is currently used as a chemotherapeutic drug against several types of cancer, including acute lymphoblastic leukemia and other lymphoid malignancies. L-asparaginase exploits the fact that some types of tumor cells lack the enzyme asparagine synthase, which is usually expressed in normal cells [3]. The administration of L-asparaginase results in the decrease of asparagine levels in the organism, and, as a consequence, in the starvation of cancer cells, with little effect on normal cells. L-asparaginase is also currently used in food industry, as a mean of reducing the formation of acrylamide in starchy foods. Despite all these applications, the catalytic mechanism of L-asparaginase is still unknown.

The aim of this study was to investigate the catalytic mechanism of L-asparaginase II using QM/QM hybrid methodologies (ONIOM). We found that the hydrolysis of asparagine to aspartic acid comprises three steps, with the first one being the rate-limiting step. The catalytic residues are Thr89 and Lys162, though a water molecule is also needed for the reaction to occur. The activation barrier amounts to 20.2 kcal/mol and the reaction energy to -9.0 kcal/mol. We also found that the acyl-enzyme intermediate is not energetically favorable and was not obtained in our mechanism (contrarily to what is hypothesized in the literature). We propose that such intermediate is an artifact of the mutated protein.

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Preparation of multifunctional fluorophore-doped silica nanoparticles for genetic detection applications

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Recent works on the use of fluorescent nanoparticles for the detection of specific gene sequences have shown their potential for the design of novel biosensors with increased sensitivity and ease of use. In this context, the use of fluorophore-doped silica nanoparticles can confer several advantages such as water solubility, biocompatibility, and chemical stability coupled with a well-established chemistry that allows a wide range of linking methodologies [1].

In the present work we report the synthesis of rhodamine-B isothiocyanate-doped silica nanoparticles (RITC-SiNPs) with bound ssDNA oligomers by using an organosilane as a linker *via* a thioether linkage. Furthermore, we also report the synthesis of a new composite nanoparticle (Au-RITC-SiNPs) consisting of a gold decorated version of RITC-SiNPs. The synthesis of Au-RITC-SiNPs was carried using a deposition-precipitation methodology [2] that comprises the modification of the surface of RITC-doped silica nanoparticles with the organosilane APTES before the addition of a HAuCl₄/NaOH solution, resulting in the formation of gold hydroxide clusters, followed by reduction to metallic gold. The nanoparticles were characterized by UV-Vis spectroscopy, fluorimetry, TEM, ¹H NMR and light scattering-based zeta potential and size measurements.

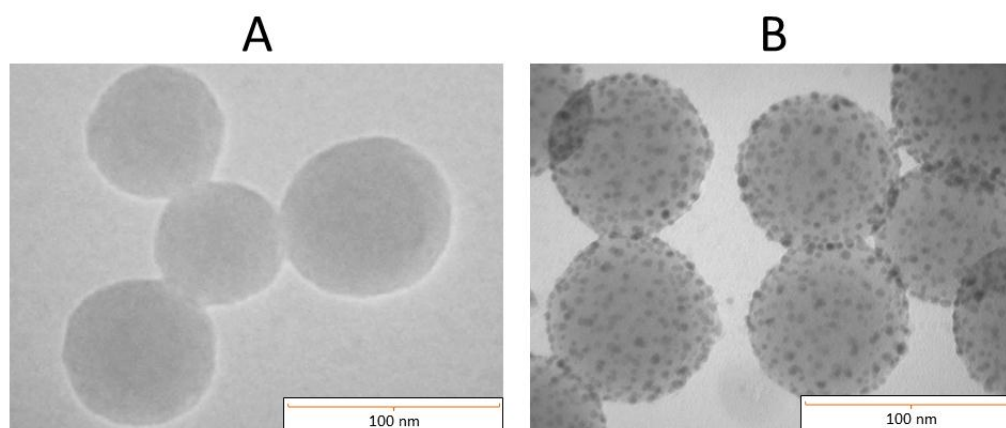


Figure 1. TEM images of RITC-doped silica nanoparticles, RITC-SiNPs (A) and gold-decorated RITC-doped silica nanoparticles, Au-RITC-SiNPs (B)

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Pyridinium porphyrins and their host-guest interactions with cucurbituril macrocycles

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The attempt to create new porphyrin derivatives has been a challenge area for many synthetic chemists in view of their many applications [1]. Following our research in the preparation of new porphyrin derivatives, we have been using *meso*-tetrakis(pentafluorophenyl)porphyrin (TPPF₂₀, **1**) as template [2]. Recently, we reported that the aromatic nucleophilic substitution reaction of the *para*-fluorine atoms of TPPF₂₀ with 4-mercaptopyridine gives the corresponding porphyrin **2a** with four pyridyl groups in about 90% yield [3]. This compound was also methylated with methyl iodide, obtaining quantitatively the tetra-pyridinium porphyrin **2b** (Scheme 1). Taking into account these results we decided to use the same reaction conditions with other pyridine derivatives, such as 4-hydroxypyridine expecting to obtain a similar product, the *O*-pyridyl derivative. Surprisingly we obtained a more polar product than in the case of thio-pyridyl **2a**. The characterization by ¹H, ¹⁹F and ¹³C NMR spectroscopy revealed the porphyrin pyridinone derivative **3a** as product (Scheme 1). In this communication the synthesis and characterization details of the new compounds will be presented along with some preliminary studies on host-guest interactions with cucurbituril macrocycles.

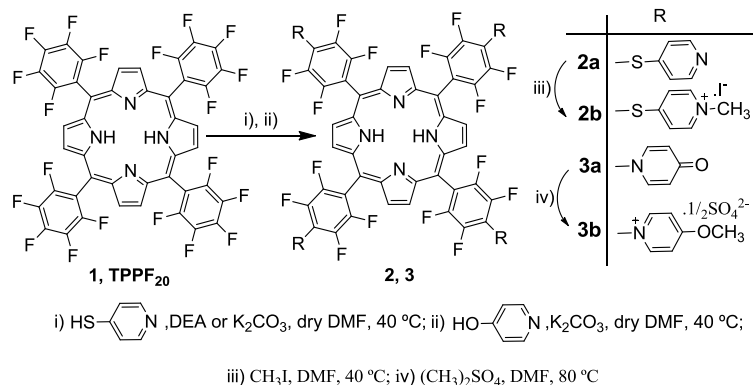


Figure 1. Synthesis of compound **2a**, **2b**, **3a** and **3b**.

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The reaction of anthranilonitrile with carbonyl compounds: a convenient synthesis of fused quinazolines

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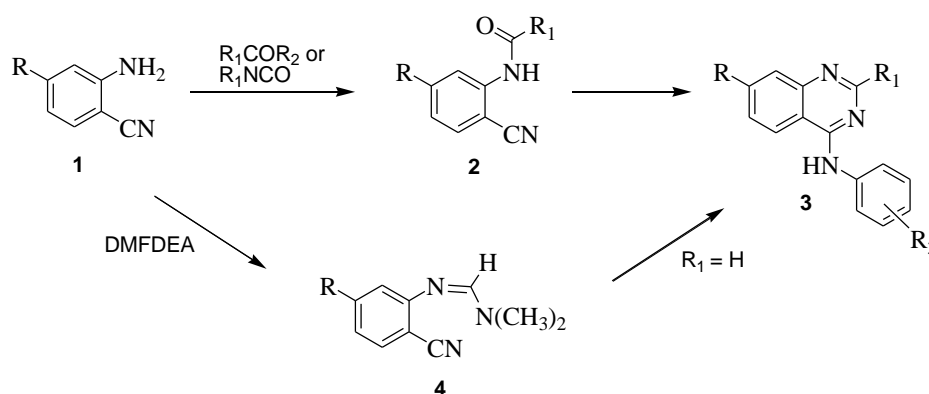
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A wide range of biologically active compounds contains the quinazoline ring system [1]. Compounds incorporating this scaffold present, among others, antimicrobial, anti-inflammatory, antifungal, anticonvulsant, antibacterial, antihypertensive and anticancer activity [2].

Many methods for the synthesis of quinazolines derivatives have been developed. Most of them use anthranilonitrile derivatives as starting materials that are converted into the corresponding formamidine by reaction with dimethylformamide diethylacetal (DMFDEA) under reflux conditions [3].

This work reports the formation of compound **3** from the reaction of anthranilonitrile **1** with different anhydrides, isocyanates or ethyl chloroformate at room temperature. The reaction is initiated with the formation of compound **2**, that evolves to the fused quinazoline **3** upon heating in the presence of a selection of aromatic primary amines with acid catalysis.

All the compounds were fully characterized by IR, EA and NMR (^1H , ^{13}C , HMQC and HMBC) techniques.



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Synthesis of dihydroquinazolines by microwave irradiation

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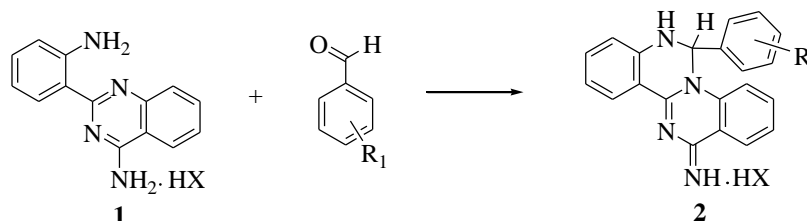
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Compounds of the quinazoline family have attracted much attention either concerning their synthetic approach or the variety of biological activities they present [1]. Molecules incorporating this core structure proved to be useful as antimicrobial, antihypertensive, fungicides, anti-inflammatory, anticancer and antibacterial agents and inhibitors of tyrosine kinase [2]. Most of the synthetic methods, reported in the literature are time consuming and lead to low yields of the product.

The use of clean and more efficient technologies, such as microwave assisted synthesis, have already demonstrated to be widely successful in the organic chemistry field. This method allows to obtain good yields, while reducing the reaction time and the amount of solvent.

The synthesis of 2-(2-aminophenyl)quinazolin-4-amine **1** was previously reported from the reaction of anthranilonitrile with triethylorthoformate, followed by treatment with acid [3].

In the present work, the tetracyclic compound **2** was prepared from compound **1** upon reaction with aromatic aldehydes using a polar protic solvent. The reaction was performed under microwave irradiation and under conventional heating conditions. The results of a comparative analysis as well as the product yields will be presented. Compounds **2** were fully characterized by elemental analysis and spectroscopic techniques: ^1H and ^{13}C NMR, including two-dimensional correlation techniques (HMQC and HMBC) and IR spectroscopy.



Acknowledgements: The authors gratefully acknowledge the financial support by the University of Minho and Fundação para a Ciência e a Tecnologia through the Portuguese NMR network (RNRMN), the Project F-COMP-01-0124-FEDER-022716 (ref. FCT PEst-C/UI0686/2011) FEDER-COMPETE and a PhD grant awarded to Elina Marinho (SFRH/BD/73659/2010).

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Mimicking bleaching reactions in cellulosic pulp: oxidation of xylo-oligosaccharides by alkaline hydrogen peroxide

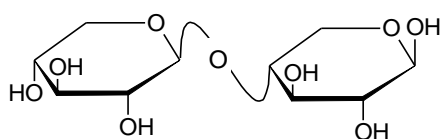
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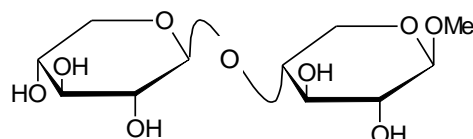
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Brightness reversion (yellowing) is an undesirable phenomenon affecting consumer properties of paper products. During industrial process, eucalyptus kraft pulp is bleached to high brightness by oxidising reagents such as ClO_2 , O_2 and H_2O_2 . However, this bleached pulp reveals insufficiently brightness stability (yellowing). The yellowing of kraft pulp is usually associated with hydrothermal degradation of oxidised polysaccharides in pulp (POS), including xylans, after bleaching stages, with formation of new chromophores/chromogens. Only a scarce knowledge is available about the oxidative reactions of xylans under bleaching conditions leading to the formation of chromogenic structures. To fill this gap, further understanding of the underlying fundamental chemistry in oxygen and hydrogen peroxide bleaching of POS is required. The main goal of this work was to study the oxidation of xylo-oligosaccharides (XOS) models (Xyl_2 and MeXyl_2) by hydrogen peroxide under alkaline conditions, thus mimicking xylans oxidation during bleaching of kraft pulps. The oxidised structures, potentially responsible for the brightness reversion, were analysed by GC-MS, and LEX-SEC coupled with ESI-MS and MS/MS. The results showed that Xyl_2 under $\text{H}_2\text{O}_2/\text{NaOH}$ is almost completely degraded affording the main oxidative products 2,3,4-trihydroxybutanoic, 2,4-dihydroxypentanedioic, 2,3-dihydroxy-4-oxopentanedioic and 2,3,4-dihydroxypentanedioic acids (glutaric acids) and short chain acids as glycolic and hydroxy-propanoic acids, identified by GC-MS. LEX-SEC with ESI-MS allowed the identification of polymerization as well as oxidation products from Xyl_2 , Xyl_3 and Xyl_4 . These oxidation products were formed mainly by consecutive decarboxylations from the reducing end unit. The MeXyl_2 was more resistant to oxidation, thus allowing the conclusion that the methyl group at the reducing ends effectively protects the XOS against radical oxidation. New structural information on oxidized structures will provide better understanding of brightness reversion phenomena in pulp and paper manufacturing and will provide ideas to overcome this undesirable phenomenon.



Xyl_2 : β -(1 \rightarrow 4)-D-xylobiose



Me Xyl_2 : β -(1 \rightarrow 4)-D-methyl xylobiose

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Analysis of pesticides in wine by coupled chromatographic techniques

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The generalized use of fungicides in wine has resulted in the detection of residues of these products in wine consumption [1-3]. For these compounds present harmful health effects, their levels in wine should be checked regularly. Therefore, it is essential to development of analytical methods of determining fungicide to be reliable and have detection limits of protection. The objective of this study is the development and validation of methodologies for the analyses of pesticides in “vinho verde”. Four pesticides *i.e* metalaxyl, benalaxyl, cyprodinil and iprovalicarbe were studied for the validation of analytical techniques. These pesticides are widely used in vineyards in the northern region of Portugal for the production of “vinho verde”. The analyses of the samples were performed by SPME-GC-MS and LC-MS techniques in Full scan, SIM and MS-MS modes. The calibration curves of the standards were carried out in ethanol (12%)/water mixtures. Calibration curves gave linear responses for all the pesticides and the found detection limits were lower than LMR values. Four commercial wine samples were analyzed and the concentrations of the studied pesticides in these samples were determined.

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Composition of the volatile oil of *Eryngium dilatatum* Lam.

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Eryngium L. is probably the most extensive and taxonomically complex genus of the Apiaceae family, including about 250 species distributed all around the world.

One of its species, *E. dilatatum* is a perennial herbaceous plant occurring wild in dry and stony fields of the Iberian Peninsula and North Africa. Unlikely as for other *Eryngium* species growing wild in Portugal, as *E. duriaei* subsp. *juresianum* [1], there are no phytochemical studies on *E. dilatatum*.

We report now on the essential oil isolated by hydrodistillation from the aerial parts of *E. dilatatum*. The composition was established by processing chromatographic data (GC retention indices on columns with different stationary phases) and mass spectra acquired by GC-MS according a methodology previously reported [2].

Thirty-eight components were identified. Sesquiterpenes are dominant, representing 57.5% of the whole composition; monoterpenes attain only 23.0%. *Z*-Chrysantenyl acetate (11.1%), germacrene D (10.3%), bicyclogermacrene (8.1%), α -Pinene (9.2%), spathulenol (5.9%) and α -cadinol (5.7%) are the major constituents.

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The solid - liquid phase diagram for BINOL enantiomer mixtures

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1,1'-Binaphthalene-2,2'-diol (BINOL) has been widely used as the starting material for the synthesis of a great variety of molecular sensors, chiral selectors and enantioselective catalysts [1].

Thermodynamic data on binary mixtures of enantiomers are useful in a large number of cases, for instance for checking the purity of chiral compounds, and for obtaining information concerning a particular technique to be used for achieving enantiomeric resolution. Although racemic BINOL is known to crystallize as a racemic compound, the complete binary solid – liquid phase diagram is not available [2,3].

In this work the solid - liquid binary phase diagram of BINOL enantiomer mixtures, at atmospheric pressure, was determined. Enantiomer mixtures were prepared by ball milling, and analyzed using differential scanning calorimetry and infrared spectroscopy. The solid - liquid phase diagram (melting temperature against composition) obtained for this system confirms the formation of a racemic compound.

Acknowledgements: FCT-PTDC/QUI/QUI/112913/2009; Scholarship from CAPES - Case: 4709/10-1.

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Regioselective modification of natural polyphenols and their glycosides through enzyme catalyzed reactions

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Polyphenols and their glycosyl derivatives are widely used in pharmaceutic, cosmetic and food preparations. They exert several biological activities and some of them are lead compounds for drug discovery and development [1, 2].

Being polyfunctionalized molecules, the modification of one functional group among others is a challenging task in organic chemistry.

Enzymatic acylation of these molecules as well as the enzymatic alcoholysis of the corresponding per-acyl derivatives provide a simple strategy to achieve monoacyl or monoalcohol derivatives with exquisite regioselectivity [3-5].

Indeed, lipases have been increasingly accepted by organic chemists as effective catalysts for stereo- and regioselective reactions, being able to operate in organic media and to accept non natural substrates.

In this communication, we report our results on the regioselective modification of polyphenolic compounds and their glycosides (Figure 1), using lipases as catalysts. The influence of the type of enzyme, the nature of the reaction (transesterification of alcoholysis), the solvent and the structure of the substrates on regioselectivity is discussed.

Diverse monoacyl and monoalcohol derivatives were isolated in high yields. Further synthetic modification of these compounds by chemical synthesis is under investigation aiming to obtain novel bioactive compounds.

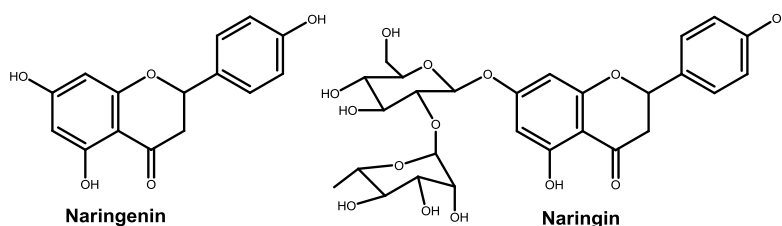


Figure 1. Examples of substrates.

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Prenylated xanthonic derivatives: an inspiration for synthesis of new inhibitors of growth of human tumor cell lines

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Xanthone derivatives, namely prenylated xanthones (PXs), have prompted a great deal of interest due to their wide range of biological activities, particularly antitumor [1]. The presence of prenyl groups becomes an important structural factor for the interaction of these molecules with biological targets, taking into account the influence on the overall stereochemistry as well as the possibility of additional interactions [1]. Therefore, PXs could represent an excellent model for the development of new and more effective anticancer drugs, and for this reason the introduction of prenyl groups in "hit" compounds has been one of the strategies used in CEQUIMED-UP [2].

The central aim of this work is to carry out some molecular modifications by introduction of prenyl groups on the xanthonic scaffold, in order to improve their antitumor potential. The synthetic approach to obtain these compounds involves the application of classical and "non-classical" synthetic methodologies, namely microwave-assisted organic synthesis and heterogeneous catalysis. In this communication, we reported the synthesis of 1,3-dihydroxy-5-methoxyxanthone (**1**) through the Grover, Shah and Shah (GSS) method (**A**) [3] and also applying Eaton's reagent (P_2O_5/CH_3SO_3H) (**B**) as the condensation agent [4] (**Figure 1**). Subsequently the synthesized compounds will be tested for their effect on the *in vitro* growth of some human tumor cell lines. From the results of the biological evaluation, we expect to obtain new compounds with improved antitumor activity. We also report the synthesis of PXs **2** and **3**, by the reaction of 1,3-dihydroxy-5-methoxyxanthone (**1**) with prenyl bromide under microwave irradiation (MW) (**Figure 2**).

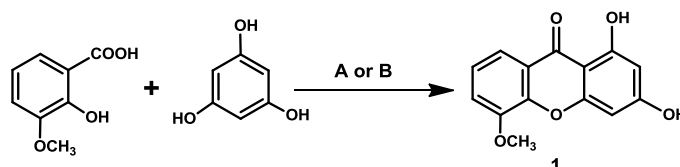


Figure 1. Synthesis of 1,3-dihydroxy-5-methoxyxanthone through methodologies **A** or **B**.

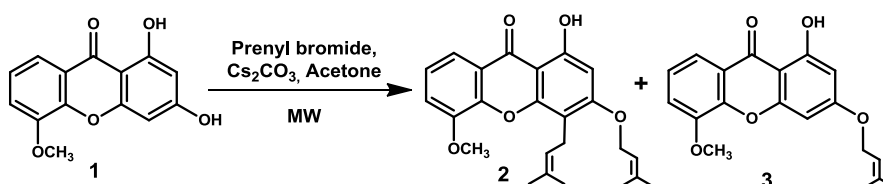


Figure 2. General procedure for the synthesis of PXs **2** and **3** by MW irradiation.

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Synthesis of prenylated (*E*)-2-styrylchromones

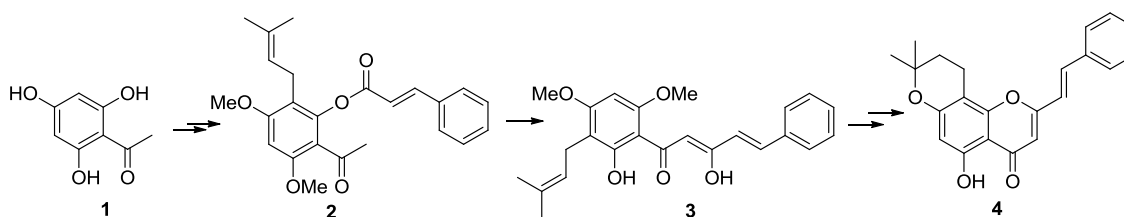
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2-Styrylchromones are a small group of naturally occurring chromones, only four naturally occurring 2-styrylchromones were reported, two isolated from the marine algae *Chrysophaeum taylori* [1], one from *Imperata cylindrical* [2] and, more recently, another was isolated from the Chinese eaglewood from the tree *Aquilaria sinensis* (Lour.) [3]. Nevertheless, both natural and synthetic 2-styrylchromone derivatives are associated with a wide variety of biological properties such as antioxidant and anti-inflammatory activities [1,4]. Prenylflavones are important naturally occurring compounds and their biological activities are well documented, for instance we can point out the antioxidant and anti-inflammatory activities [5]. As far as we know, there are no reports on the synthesis of prenyl-2-styrylchromones, although synthetic routes of 2-styrylchromones are well known and reported in literature [6].

In this communication we describe our studies on the synthesis of novel hydroxylated prenyl-2-styrylchromones starting from 2,4,6-trihydroxyacetophenone **1**. The strategy involves the C-prenylation of this acetophenone **1** [7] and then the synthesis of the (*E*)-2-styrylchromone **4** using our efficient methodologies [8].



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Solid-phase peptide synthesis of bombesin analogs bearing unnatural amino acids with fluorescent and metal-chelating properties

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Unnatural amino acids, bearing fluorescent heterocyclic moieties, have been described as fluorescent and/or colorimetric chemosensors for anions and metal cations and biomarkers [1]. Also, radionuclide-chelating moieties have been linked to tumor-specific peptides for nuclear medicine applications, such as *in vivo* imaging by single photon emission computed tomography (SPECT) or positron emission tomography (PET), or radiotherapy [2]. Known examples are those of somatostatin or bombesin analogues targeted at, respectively, neuroendocrine tumours or breast/prostate cancer [3], among many other tumor-seeking peptides [4]. In addition to SPECT/PET techniques, fluorescence resonance energy transfer (FRET) techniques are gaining relevance for *in vivo* imaging, as a safer alternative to radioactive labels; however, FRET-based imaging is still hampered by the low variety of adequate fluorescent probes [5].

Classical approaches to the development of peptide-fluorescent/chelating probes usually involve stepwise assembly of the bioactive peptide followed by its conjugation to a non-peptidic probe [6]. The conjugation is often a low yield step that requires fine-tuning of synthetic conditions to ensure that amino acid side chains involved in peptide-receptor recognition are not modified. Also, many of the classical probes lower peptide solubility in aqueous media and are not biofriendly. So, it is expectable that the more a probe resembles a natural amino acid, the best it will perform *in vivo*.

In the present communication, we will report the solid phase synthesis and characterization of two bombesin analogues with unnatural amino-acids with both fluorescent and metal chelating properties.

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Synthetic unnatural amino acids as fluorimetric probes for metallic cations

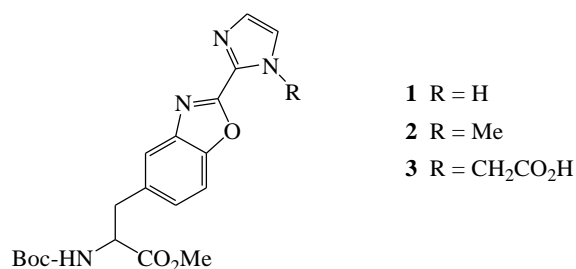
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Molecular recognition is the basis for most biological functions and in recent years the research on compounds capable of recognizing and binding organic and inorganic molecules involved in biological pathways has evolved to mimic as much as possible the natural mechanisms of organization [1]. The design of peptides that coordinate metals, by incorporation of modified amino acids, has potential for applications as varied as the study on protein-protein interactions mediated by metals, protein binding to nanoparticles and metal surfaces, and the development of selective chemosensors for metals for use *in vivo* and *in vitro* [2]. For the synthesis of peptide based chemosensors, fluorescent ligands which are mostly heteroaromatic ring systems often substituted by potentially chelating groups which act as both the recognition and signalling site can be used, as reported recently for ligands capable to chelate various metal ions and whose complexes possess diversified photophysical properties [3].

Bearing these facts in mind and following our research interests that include the synthesis and application of fluorimetric probes for metallic cations based on heterocycles and amino acids, namely benzoxazolyl-alanines, thiadiazolyl-, benzothiazolyl- and benzimidazolyl-asparagines [4], we now report the evaluation of unnatural alanine derivatives as fluorimetric chemosensors for the recognition of metallic cations with analytical, biological, and medicinal relevance, through the introduction of oxygen and nitrogen heterocycles as coordinating/reporting units in an alanine core in order to obtain new chemosensors. Benzoxazolyl-alanines **1-3** with an imidazolyl moiety with different substituents were synthesised and evaluated for their ability to respond, *via* changes in the fluorescence spectra, in the presence of biologically important alkaline, alkaline-earth and transition metallic cations through spectrofluorometric titrations and also by ¹H NMR titrations.



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Rhodium-phosphite catalyzed hydroformylation of natural products

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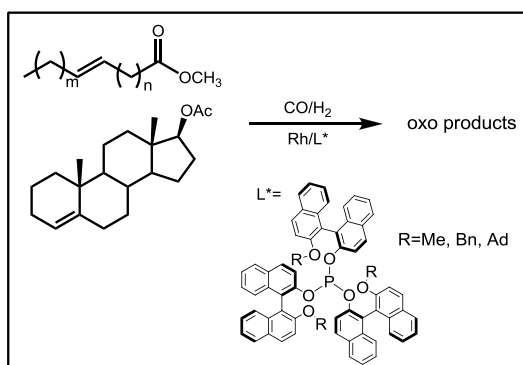
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Vegetable oils consist in triglycerides of fatty esters with internal double bonds. The hydroformylation of this type of compounds represents an excellent synthetic alternative for the preparation of aldehydes, which are precursors for added value products, like adhesives, lubricants, biodiesel, etc [1]. Steroid molecules constitute another type of relevant natural products that have been recently reported in hydroformylation reactions, due to their potential as anti-inflammatory and as therapeutic agents for cancer preventing and treatment [2].

In this context, the design and synthesis of phosphorous ligands, like bulky phosphites has significantly contributed to the extensive application of this reaction to hindered olefins. Recently, we have reported the synthesis of tris-binaphthyl chiral monophosphite ligands [3].

In the present work, the rhodium/phosphite catalytic systems were evaluated in the hydroformylation of methyl-3-nonenoate, methyl oleate and also methyl esters obtained from the transesterification of Champalo oil (*Calophyllum inophyllum* Linn.).

Studies on the effect of the ligand structure in terms of activity, chemoselectivity and regioselectivity performed. The usefulness of this reaction for the functionalization of natural oils will be discussed.



Acknowledgements: The authors thank financial support from Portuguese FCT through the project PTDC/QUI-QUI/112913/2009. G. N. Costa thanks Coimbra Chemistry Center for a research grant. R.M.B. Carrilho thanks FCT for the PhD grant SFRH/BD/60499/2009.

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Cytotoxic oxysterols: synthesis and biological evaluation of ketal derivatives

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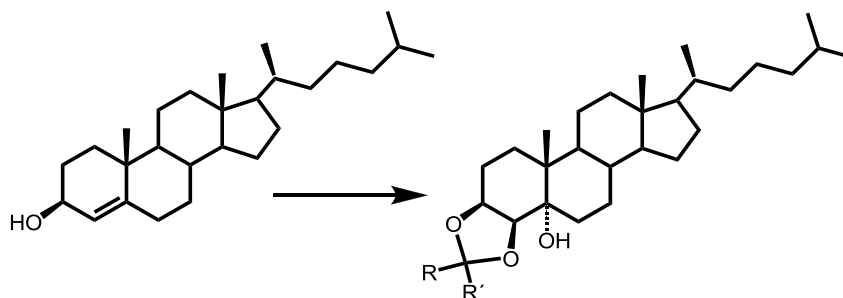
Oxygenated derivatives of cholesterol, known as oxysterols, have gained increased attention in medicinal chemistry, due to their wide range of biological effects [1,2]. Natural and synthetic oxysterols have shown cytotoxic activity against cancer cell lines [3-5].

Therefore, these are interesting starting molecules for drug discovery and development.

In this communication, we have synthesised several polyhydroxylated derivatives of cholesterol and their ketal counterparts aiming to evaluate the effect of these structural modifications on selective cytotoxicity, by in vitro studies in cancer and non cancer cell lines.

A method to synthesize ketals from allylic alcohols is reported and a library of 3,4-ketals (Scheme 1) and 6,7-ketals was prepared.

The compounds synthesized exhibited antiproliferative activity in a low micromolar range and SAR studies have shown key structural features for cytotoxic activity and selectivity.



Scheme 1

R= H, R'= H

R= CH₃, R'= CH₃

R= CH₂CH₃, R'= CH₂CH₃

R, R'= cyclopentyl

R, R'= cyclohexyl

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3(5)-(2-Hydroxyphenyl)-5(3)-styryl-1*H*-pyrazoles: synthesis and reactivity studies on Diels-Alder transformations

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Pyrazoles have been extensively studied and several methods have been developed for their synthesis due to their widespread application in the fields of agriculture, industry and medicine [1]. The use of *C*- and/or *N*-(2-hydroxyphenyl)pyrazoles as ultraviolet stabilizers, analytical reagents in the complexation of transition metal ions, analgesic agents, platelet aggregation inhibitors, and also potent inhibitors of Hsp90 ATP-ase highlight these compounds as targets for the preparation of new derivatives or/and to develop new strategies for their synthesis [2]. As part of our continuing work on the synthesis and transformation of 3(5)-(2-hydroxyphenyl)-5-styryl-1*H*-pyrazoles, we are interested in studying their reactivity as dienes in cycloaddition reactions with electron rich and electron poor dienophiles, thus developing a method for the synthesis of fused 1*H*-indazoles. However, vinylpyrazoles are very reluctant to participate as dienes in cycloaddition reactions due to the loss of their aromaticity, thus cycloaddition reactions of these compounds require very reactive dienophiles, high temperatures and pressures and are usually slow reactions giving rise to adducts in moderate to low yields [3,4]. In spite of vinylpyrazoles being very unreactive we decided to study the reactivities of styrylpyrazoles as dienes under classical heating or microwave irradiation conditions, following our previous work with this type of compounds [5]. In this communication we will present and discuss our first results on the Diels Alder transformations of styrylpyrazoles and the structural characterization of the newly prepared compounds.

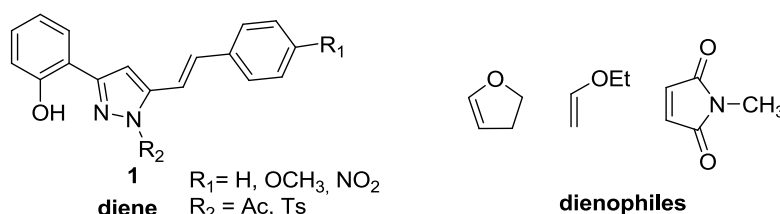


Figure 1. Structure of the diene 3(5)-(2-hydroxyphenyl)-5-styryl-1*H*-pyrazole and selected dienophiles.

Acknowledgements: Thanks are due to the University of Aveiro, “Fundação para a Ciência e a Tecnologia” (FCT) and FEDER for funding the Organic Chemistry Research Unit (project PEst-C/UI0062/2011) and the project PTDC/QUI-QUI/102454/2008 and to the Portuguese National NMR network also funded by FCT.

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Gold nanoparticles functionalized with Gd³⁺ chelates as high relaxivity contrast agents for Magnetic Resonance Imaging

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Magnetic Resonance Imaging (MRI) is the most useful imaging modality in clinical diagnosis and in biomedical research: superb spatial resolution, non invasive nature and use of non-ionizing radiation. 3D anatomical images are generated in MRI by processing the signals originated by the relaxation processes of the water protons of tissues. Paramagnetic relaxers (Gd³⁺ chelates, Mn³⁺ chelates and Fe₂O₃ nanoparticles) enhance selectively the relaxation rates of the water protons in their vicinity - Contrast Agents (CAs) [1]. The enhancement of the relaxation rates brought about by a 1 mM concentration of paramagnetic centers, relaxivity (mM⁻¹.s⁻¹), measures the efficacy of CAs. We have reported recently the preparation of a new chelator -DO3A-*N*- α -aminopropionate. The Gd(DO3A-*N*- α -aminopropionate) chelate displays high stability, fast water exchange, and potential for conjugation [2]. We have since, demonstrated that Gd³⁺ chelates of amide conjugates of the DO3A-*N*- α -aminopropionate chelator retain the stability and fast water exchange properties of its parent complex [3]. Au NPs functionalized with Gd³⁺ chelates are promising platforms for developing efficacious CAs for MRI. Clustering a high number of efficient Gd³⁺ chelates on nanoparticles can create (nano) objects displaying high density of relaxivity, ideal for molecular imaging applications. We have disclosed recently the preparation and relaxometric characterization of Au NPs functionalized with Gd³⁺ chelates of cystein conjugates of the DO3A-*N*- α -aminopropionate chelator[4]. Despite the unprecedented high relaxivity per Gd³⁺ chelate obtained (29 mM⁻¹.s⁻¹, 25 °C, 30 MHz) and superb stability, the relaxivity still is limited by chelate flexibility. The (fast) water exchange is not limiting the relaxivity, suggesting that rigidifying further the chelate monolayer on the NPs surface should lead to higher relaxivities.

In this communication we report the synthesis and characterization of a new ω -thiol functionalized chelator, DO3A-*N*-(α -11-mercaptoundecanamido)propionate (**1**). The synthesis and characterization (TEM, DLS, Zeta potential, ICP, pH and transmetallation stability and ¹H NMRD studies) of gold nanoparticles functionalized with Gd(DO3A-*N*-(α -11-mercaptoundecanamido)propionate) chelates as a new CA for MRI will be described and discussed in detail.

Acknowledgements: We thank the support from the F.C.T. Portugal (project PTDC/QUI/70063/2006 "Targeted Nanoconstructs for Multimodal Medical Molecular Imaging". J.Gonçalves thank the support from the I.N.AB.E, Angola.

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Synthesis of new titanocene(IV) carboxylate complexes: An alternative chemotherapeutic treatment against cancer

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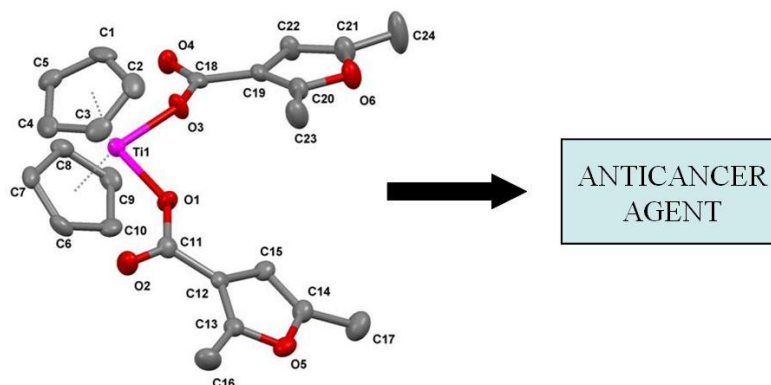
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Currently, cancer is the principal cause of death in developed countries, ahead of even cardiovascular diseases. For this reason, research on different transition metal complexes with cytotoxic activity is a very important and active field in medicinal inorganic chemistry [1].

Titanium complexes are a class of important compounds tested in the preclinical treatment of several tumours. The history of these compounds as anticancer agents began with the discovery of the antitumour properties of metallocene complexes by Köpf-Maier and Köpf with the subsequent phase I clinical trials carried out for titanocene dichloride in 1993 [2].

In this communication, the synthesis of several titanocene compounds with different carboxylato ligands is presented. These ligands have been previously used successfully by our research group for the study of the cytotoxic properties of tin(IV) and gallium(III) complexes [3]. Taking into account that water solubility is an important pharmacokinetic aspect to consider in the action mechanism of anticancer drugs in biological organisms, we show an improvement in the cytotoxic activity with an increase of the polarity of the titanocene complexes.



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Synthesis of new flavon-3-ols with potential antioxidant activity

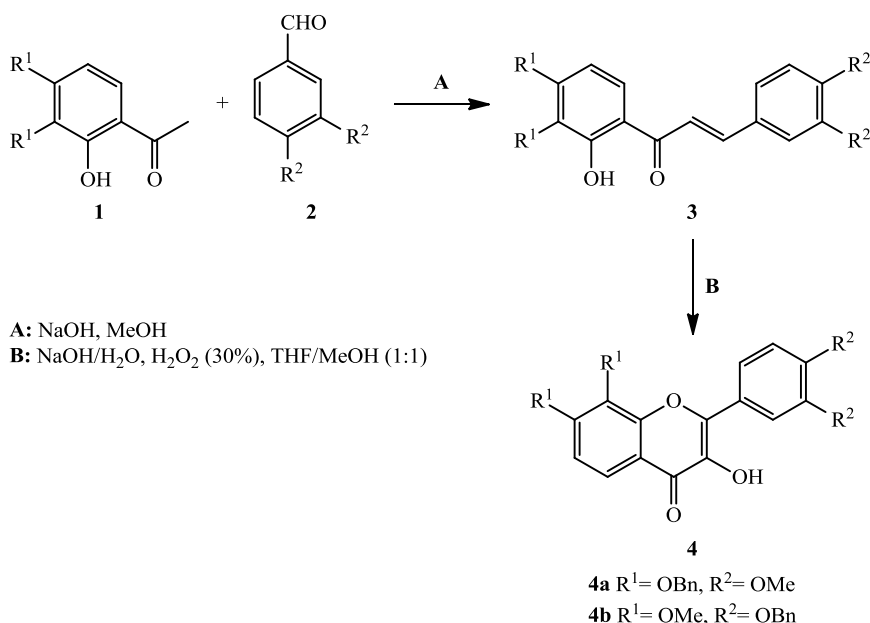
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The flavonoids are prominent components of citrus fruits, seeds, olive oil, tea, red wine and other food sources. They are consumed regularly in the human diet and can show important beneficial effects on human health. The flavonols are a subclass of this family of low molecular weight compounds, which have a 3-hydroxyflavone backbone. The presence of a 4-keto group, a double bond between carbon atoms 2 and 3 (C2=C3), and a 3-hydroxyl group on the C ring make them desirable compounds to present good biological properties, especially the antioxidant activity [1]. Examples of some well-known naturally-occurring flavonols are quercetin, kaempferol, myricetin, among others.

In the present work, 3-hydroxyflavones **4** were prepared through a two-step synthetic route (Scheme 1), namely an aldol condensation of appropriately substituted 2'-hydroxyacetophenones **1** and benzaldehydes **2** (A) [2] and an Algar-Flynn-Oyamada (AFO) reaction (B) [3], ending with the cleavage of the protecting groups. All experimental details and results of this study will be presented and discussed in this communication.



Scheme 1

Acknowledgements: Thanks are due to the University of Aveiro, FCT and FEDER for funding the Organic Chemistry Research Unit (project PEst-C/QUI/UI0062/2011) and the Portuguese National NMR Network (RNRMN). J. L. C. Sousa is also grateful to FCT for her PhD grant (SFRH/BD/76407/2011).

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Development of a new library of novel and reversible MAO-B inhibitors based on the benzopyranic nucleus: an overview

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Monoamine oxidase is an enzyme present in many living organisms that is present in two isoforms, MAO-A and MAO-B, precisely located in the outer membrane of the mitochondria. These two isoforms are involved in the oxidative deamination of exogenous and endogenous amines, including neurotransmitters, which modulates their concentrations in the brain and peripheral tissues. MAO-B isoform has a crucial role in neurotransmitters metabolism by representing an attractive drug target for neurodegenerative diseases therapy, such as Parkinson's [1]. The first line of PD treatment is dopamine replacement therapy with Levodopa though at present monoamine oxidase inhibitors (IMAO), specifically of MAO-B type, are considered also to be beneficial therapeutic drugs [2]. The inadequacy of the current pharmacotherapy and the lack of drugs that can be effective in PD, mainly declined by side-effects, are the reasons why the discovery of novel chemical entities (NCE) is still a demand.

During our project on drug discovery and development of novel chemical entities for the treatment of neurodegenerative diseases, efforts were done on finding an innovative drug candidate for IMAO B. The project is connected with the development of versatile libraries incorporating privileged structures with benzo- γ -pyrone substructure, namely sustained on chromone scaffold ((4H)-1-benzopyran-4-one). The SAR study performed allow concluding that chromones that have substituents in position-3 of γ -pyrone nucleus act preferably as MAO-B inhibitors with IC₅₀ values in the micromolar to nanomolar range. Our findings, supported by theoretical and docking studies, pointed out a crucial and undisclosed role of the presence of a carboxylate/amide group in C3 of the pyrone ring able to establish hydrogen bond interactions with active site residue, in order to obtain highly potent and selective MAO-B inhibitors [3]. Additional studies are warranted for a systematic lead optimization, modulated by appropriate modifications of length, size, and chemical nature of the substituents, process that can lead in a next future to a novel drug candidate.

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Confinement effects over the energetic profile of a Menshutkin S_N2 reaction, a computational study

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It is widely known that a medium confinement can exert great effects over the energetic profile and reaction path of a reaction. These new confinement structures can prove to be very useful in the development of more sustainable and less costing chemical reactions, with implications in pharmaceutical, industrial and scientific fields.

In this computational study we aimed to examine the effects of the confinement of a S_N2 Menshutkin reaction inside different carbon nanotubes, varying in length, diameter and type. This particular well known reaction yields formally charged products from uncharged ammonia and chloromethane, making it highly sensitive to medium confinement changes and important for our study.

Following previous work done [1,2], we developed an alternative ONIOM methodology [3] for reaction steps simulations using different CNT lengths, diameters and types. This allowed us not only to better understand the reaction path changes caused by the confinement medium as well as to understand the effects slight variations in CNT morphology and structure have over the reaction energetic profile.

The results show that the computational approach devised is able to accurately predict unconfined reaction path steps and electronic energies as well as CNT confined reaction path steps and energies. Structural differences in carbon nanotubes [4] are observed as having different influences over the reaction path steps in accordance to the expected results. Further studies are projected, particularly as to test different carbon nanostructures effects such as multi-walled nanotubes.

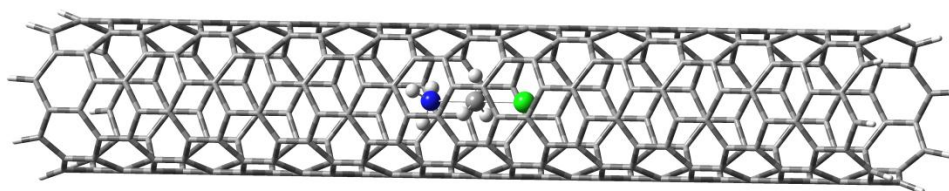


Figure 1. Confined Menshutkin transition state inside a 38 Å carbon nanotube.

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Environmental and pharmaceutical applications of cyclodextrin-assisted molecular encapsulation

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Cyclodextrins (CDs) are natural cyclic oligosaccharides that are formed through enzymatic degradation of starch. The most common of these naturally occurring, ring-shaped molecules are the α - (alpha), β - (beta) and γ - (gamma) CDs formed by six, seven and eight glucose units, respectively, and which enclose cavities of approximately 0.6, 0.8 and 1.0 nm in diameter.

Due to their hydrophilic outer surface and hydrophobic inner cavity they are able to form inclusion complexes with a large variety of predominantly hydrophobic guest molecules. This makes CDs useful for many applications, especially within environmental, pharmaceutical and food sciences.

An inclusion compound is a unique form of chemical complex in which one molecule is enclosed within another molecule or aggregation of molecules. When the guests have a similar molecular dimension, the more hydrophobic molecule or residue has the higher affinity for the CD cavity in aqueous solution, because the cavity provides a microheterogeneous hydrophobic matrix in such polar solvents; the cavity is more hydrophobic than water.

Molecular encapsulation by CDs often advantageously modifies various physicochemical properties of the encapsulated molecules such as aqueous solubility and stability. It is also simpler and cheaper than most other methods of encapsulation. As a result of molecular complexation phenomena CDs are widely used in many industrial products and technologies. The negligible cytotoxic effects of CDs are an important attribute in applications such as drug carriers, agriculture and in environment protection.

In this communication, an overview of our latest research in this field will be presented. A special focus will be given to the most recent application in pharmaceutical and environmental area.

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Thermodynamic study of two 9-substituted fluorene derivatives

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Polycyclic aromatic hydrocarbons (PAHs) are considered one of the major interests of the modern electronic industry, being successfully used as active organic components in a new generation of electronic devices, like organic light-emitting diodes (OLEDs), organic photovoltaic cells (OPCs), organic field effect transistors (OFETs), etc.

The successful application of these materials depends greatly on the volatility of their solid phases, amongst other thermodynamic properties. The lack of a reliable energetic data base for PAHs and their derivatives has lead us to the study of thermodynamic properties of some fluorene and fluorenone derivatives [1,2], in order to determine key values not available in the literature and to correlate molecular energetic data with structural characteristics of the molecules, through experimental and computational studies.

As part of this project, we have performed the energetic study of the compounds fluorene-9-methanol and fluorene-9-carboxylic acid (Fig. 1). These compounds were studied by static bomb calorimetry, from which the energy of combustion and the standard molar enthalpy of formation in the crystalline phase were derived.

In addition, the sublimation vapour pressures of these compounds were measured as function of the temperature, by means of a static apparatus and a Knudsen effusion apparatus. The results enabled the determination of the standard molar enthalpies of sublimation, at $T = 298.15$ K.

The combination of these thermodynamic parameters yielded the standard ($p^\circ = 0.1$ MPa) molar enthalpies of formation, in the gaseous phase, at $T = 298.15$ K.

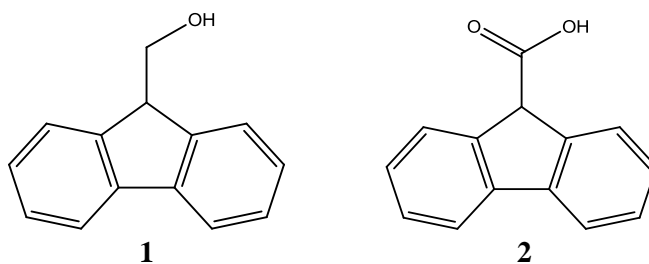


Figure 1. Chemical structures of the fluorene-9-methanol (**1**) and fluorene-9-carboxylic acid (**2**).

Acknowledgements: Thanks are due to Fundação para a Ciência e Tecnologia (FCT), Lisbon, Portugal, for granting the financial support to Centro de Investigação em Química – UP, for financing the research project PTDC/QUI-QUI/102814/2008, and for the Ph. D. research grant (SFRH/BD/80372/2011) awarded to JASAO.

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Incorporation of polyfluorenes into poly(lactic acid) films for sensor and optoelectronics applications

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Films of neat and plasticized biodegradable poly(lactic acid) (PLA) matrices containing anionic conjugated polyelectrolytes, poly[9,9-bis(4-phenoxybutylsulfonate)]fluorene-2,7-diyl-*alt*-arylenes, with 1,4-phenylene and 4,4''-*p*-terphenylene, respectively, as arylene groups or a neutral poly(9,9-dialkylfluorene) for comparison were prepared by solution casting. These films were characterized using differential scanning calorimetry, thermogravimetry, scanning electronmicroscopy and fluorescence spectroscopy. In addition, the effects of plasticizer on the thermal properties and the oxygen permeability of the PLA films were measured through the oxygen transmission rate.

Results show that it is possible to obtain thin, optically transparent and luminescent films with potential in oxygen sensing, exhibiting good thermal and photochemical stability. At high polyelectrolyte content, evidence is found for phase separation and aggregate formation and it is no longer possible to obtain completely homogeneous films.

The possibility of incorporating the cationic metal complex tris(2,2-bipyridyl)ruthenium(II) into plasticized PLA films containing conjugated polyelectrolytes for dual-wavelength ratiometric luminescence sensing is also discussed (Figure 1).

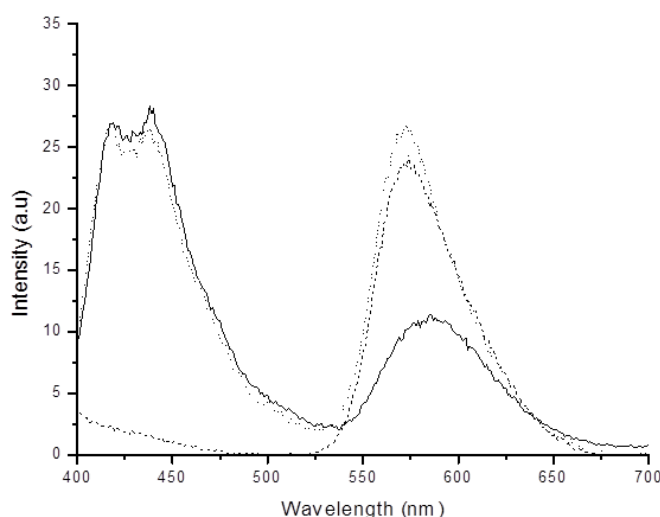


Figure 1. Fluorescence spectra of PLA + 10 wt % of C207/6 + 1089 ppm of PBS-PFP in relation between the $\text{Ru}(\text{bpy})_3^{2+}$ of: 1:0.75 (solid line), 1:1 (dashed line) and 1:1.25 (dotted line).

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In situ oxalate formation from imidazole 4,5-dicarboxylic acid in ionothermal reactions

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Ionothermal synthesis is an emerging method for the preparation of new materials due to intriguing physicochemical properties of ionic liquids (ILs), such as high ionic conductivity, non-flammability and negligible vapor pressure [1]. In this project, we are interested in the utilization of functionalized ILs in the design and preparation of novel Metal-Organic Framework materials

In the present work, several ILs based in 1-alkyl-3-methylimidazolium bromides were employed as solvents in the reactions of Zn(II) salts with imidazole 4,5-dicarboxylic acid (H₂ImDC). Remarkable, a phenomenon of in situ formation of oxalate anions unexpectedly appeared in the various reactions, leading to the formation of the same 1D crystalline product of Zn(Ox)·2H₂O (Ox²⁻ = C₂O₄²⁻), as revealed by single-crystal X-ray diffraction analysis. A cautious search in the literature and in the CCDC database reveal various examples of metal-ImDC complexes obtained in hydro/solvothermal conditions with temperature up to 180°C [2] however, no report concerns the decomposition of H₂ImDC were found. In fact, we are reporting the first observation of the decomposition of H₂ImDC under ionothermal conditions. The in situ formation of Ox²⁻ is possibly affected by the IL environment, whose decomposition may occur according to the route in Figure 1 [3]. More systematic investigations are being carried on in our lab.

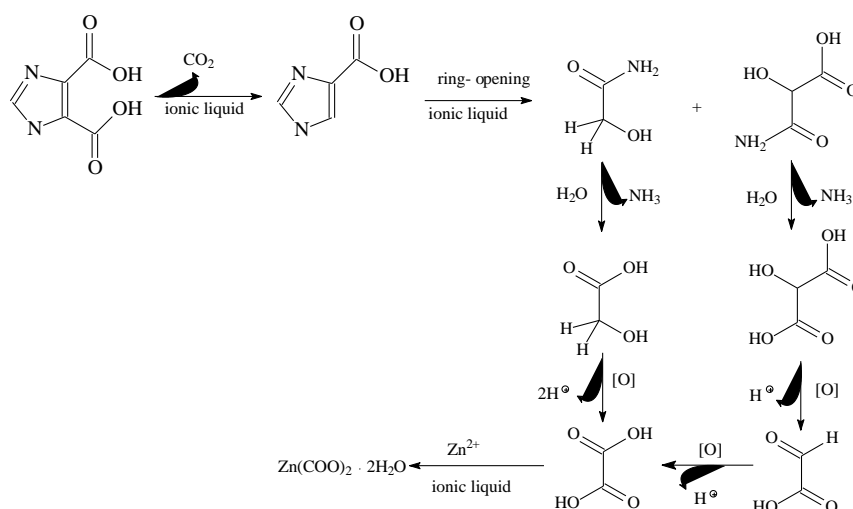


Figure 1. Probable route of the decomposition of H₂ImDC in ILs.

Acknowledgements: Thanks are due to Fundação para a Ciência e a Tecnologia (FCT, MEC, Portugal) through the post-doctoral grant SFRH/BPD/73415/2010 (to LX), the strategic project no. Pest C/EQB/LA0006/2011 (to Associated Laboratory REQUIMTE), and the R&D project PTDC/CTM/100357/2008.

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Monitoring the production of biodiesel with real-time laser spectroscopy

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To meet the demands of Resolution of the Assembly of the Republic No. 33/2010 [1] that aim to reduce by 2020 the nation's dependence on fossil fuels is important to raise the energy efficiency of processes related to production of fuels. In this scenario also fits the production of biodiesel conducted by the transesterification reaction. Monitor this reaction by laser spectroscopy helps to determine when it reached the chemical equilibrium [2,3], avoiding unnecessary energy input to the reaction and consequently raising the nation's sovereignty against external sources of energy.

This monitoring technique is computer assisted. It consists in the use of an optronic sensor that can be inserted into the reaction and it is able to measure the change of light as a function of the reaction development. As the reaction tends to chemical equilibrium, the change in the light captured by the sensor becomes nearly constant. At this time interval it is possible to arbitrate that the reaction reached the chemical equilibrium, so it is possible to separate the glycerin from the biodiesel to continue the fuel refining operations.

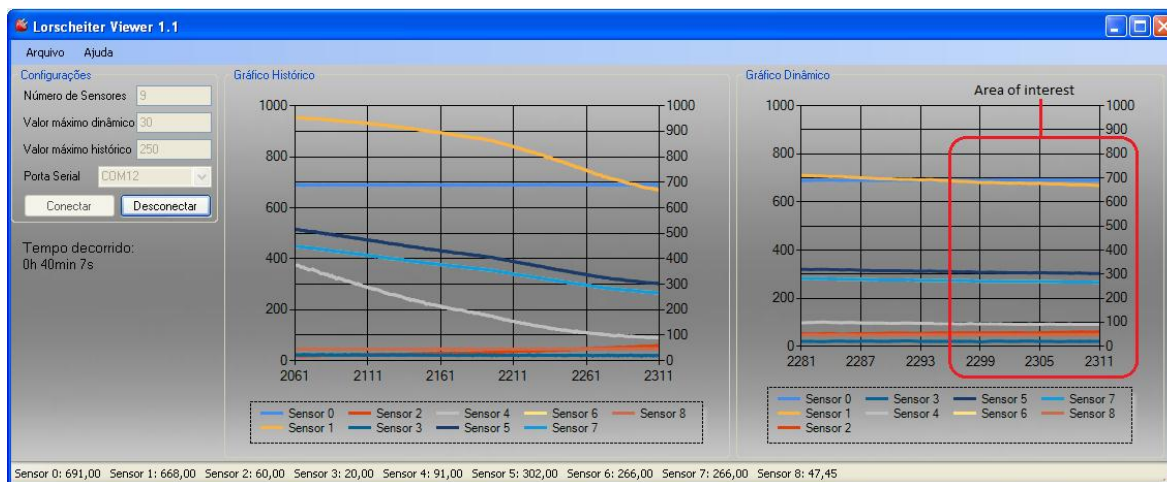


Figure 1. Screen of the monitoring system software pointing the area of interest.

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New insights about malvidin-3-glucoside-catechin dimeric compound

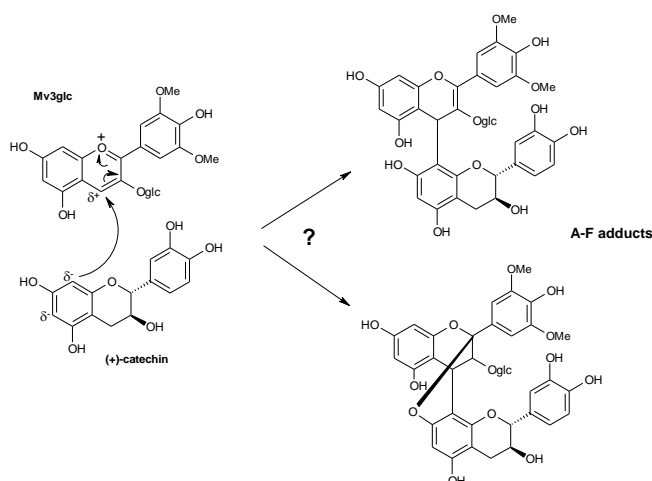
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Anthocyanins and flavanols are the main flavonoid compounds present in red wine. Chemical reactions between these two types of compounds can occur directly or mediated by small molecules like aldehydes during wine processing and ageing. These reactions lead to the formation of a broad range of compounds which gives an important contribution to the alteration of the organoleptic properties of red wines (flavor and color).

Direct reactions between anthocyanins and flavanols originate the dimeric-type flavanol-(4,8)-anthocyanin (F-A) and anthocyanin-(4,8)-flavanol (A-F) adducts. The characterization and formation pathway of F-A adducts in wines is well documented in the literature while the A-F pigments formation mechanisms are not totally elucidated. In fact, the A-F adducts formation in wines is described in literature through a mechanism in which occurs a nucleophilic attack of flavanols (C-6/C-8) to the electropositive C-4 of anthocyanin giving rise to a colorless product (flavene structure). This adduct could further evolve to the colorless bicyclic form (supplementary interflavanolic linkage type-A, A-(O)-F) or undergo oxidation to give the red pigment A⁺-F which could dehydrate to the orange-yellow xanthylium salt [1-5]. In summary, the reaction pathway of A-F adducts and their structures characterization remain somehow unclear. Besides, this kind of adducts were never isolated in sufficient quantities from wines or model solutions to proceed to full structural elucidation and follow their evolution. Bearing this, this work aimed to bring new insights about the reaction between malvidin-3-glucoside and (+)-catechin in order to clarify the dimeric A-F flavene structure and follow its evolution.



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Electrochemical mineralization of oxalic acid at metallic catalyst based on carbon nanotubes

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Water contaminated by organic compounds remains a serious problem concerning public and environmental health. In this context, monitoring and removal of the organic pollutants in wastewater is of high importance. Catalysis employing nanostructured materials is one of the methodologies proposed to reach this objective [1]. Actually, the use of carbon nanotubes (CNT) as catalysts have attracted increasing attention for environmental applications, including the oxidation of organic compounds present in polluted waters by catalytic wet oxidation, ozonation or electro-oxidation. The CNTs peculiar characteristics qualify them as potential electrode materials for the oxidative degradation of organic pollutants in wastewater [2].

In this work, the electrocatalytic oxidation of acid oxalic was studied on metallic and bimetallic electrocatalysts based on platinum or ruthenium /copper supported on carbon nanotubes, having in mind the total transformation of these compounds into carbon dioxide and water. The modified electrode, based on the commercial multiwalled carbon nanotube sample Nanocyl-3100 (CNT) [3], was prepared and dispersed onto Toray carbon (CT) (used as supporting electrode) with a Nafion/water solution. Oxalic acid was transformed to carbon dioxide with good yields.

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Young chemists at IJUP: opportunities for research training at U. Porto

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IJUP means “Investigação Jovem na U.Porto” and this was the designation chosen to identify all initiatives for promoting the participation of young researchers (undergraduate and Master students) in research activities at U.Porto. Since 2008, IJUP meetings have been held yearly, where research projects from all U.Porto are presented to the scientific community. The 5th IJUP edition took place last February and it had about 1000 participants and more than 500 presentations.

One of the objectives of the present communication is to analyze the contributions presented at IJUP meetings that were originated from research projects related to Chemistry. The second objective is to provide insights about the areas and topics in Chemistry focused upon early training of young researchers at U.Porto. Moreover, it is intended to bring out current research opportunities for young chemists and undergraduate students of Chemistry within U.Porto Faculties and Research Centers.

Preliminary data analysis showed that communications from chemical sciences research projects represented 9.9 to 24.4% of oral contributions and 20.4 to 46.7% of poster contributions in the period 2008-2012 (percentage values reporting to each meeting [1]). Data concerning the young chemists' participation at IJUP will be also presented, regarding the disciplinary area (Physical-Chemistry, Organic Chemistry, Analytical Chemistry, Computational Chemistry, Medicinal Chemistry, Chemical Engineering) and application areas (food, health, industry, pharmaceuticals, environment, among others) along each of its five editions. Special, emerging research topics will also be highlighted (nanotechnology, for instance) in order to indicate trends upon chemical research at U.Porto.

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Characterisation of phenolic compounds from *Acacia melanoxylon* biomass extracts by capillary electrophoresis

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The genus *Acacia* belongs to the family Mimosaceae and there are almost 1380 species, mostly in Australia. Nowadays, the species *Acacia dealbata*, *Acacia melanoxylon* and *Acacia longifolia* are the most prolific invaders in France, Italy, Spain and Portugal, especially in conservation areas, leading to the progressive disappearance of native biodiversity and consequent disruption of ecosystemc[1]. Although the biomass of these species is considered a waste, it is possible to attribute added value to it in terms of chemical composition, particularly in what concerns phenolics compounds. In fact, there have been efforts to isolate and identify a few compounds like quinones [2] and flavonols [3] from *Acacia melanoxylon*. Thus, the aim of the present study was to gather detailed information on the phenolic composition of *Acacia melanoxylon* biomass in order to identify bioactive phenolic compounds, valuing the initial waste. Primarily, the use of ultrasound for the extraction of phenolics from *Acacia melanoxylon* dried aerial parts with one solvent system was investigated, followed by liquid-liquid extraction using two different solvents. The extracts thus obtained were purified by CC using Sephadex LH-20 and phenolics profile of the different fractions were performed by Capillary electrophoresis (CE), revealing some important bioactive phenolics, namely quercitrin. The findings of this work assess the importance of *Acacia melanoxylon* biomass as a cheap, renewable and abundant source of natural bioactive polyphenols with potential applications in the pharmaceutical and food industries.

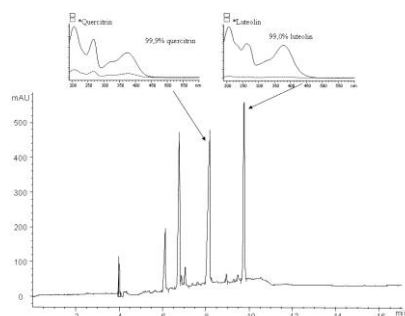


Figure 1. CE phenolic profile of a diethyl ether extract fraction from *A. melanoxylon* biomass.

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Interaction of 4-chromanone with double stranded DNA: a UV spectroscopy study

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Biologically important natural products contain the chromanone ring system as a basic structural unit. These compounds are known to exhibit interesting pharmacological properties such as antioxidant, antibacterial and anti-HIV. Chromanone is also one of the important building blocks for the synthesis of chromones, chromanes, chromenes and different tricyclic biologically active compounds.

4-Chromanone is featured in a large number of pharmacologically active compounds, as well as natural products, as the core component. For this reason 4-chromanone and 4-chromanone derivatives have received considerable attention among chemists in recent years.

Studies of the binding of small molecules to DNA are helpful for better understanding the molecular basis of their bioactivities as well as providing useful guidance for further design of more efficient drugs. In this context, the binding of small molecules to nucleic acid structures has been recognized as one important mechanism of their actions. Therefore nucleic acids represent a major target in drug development strategies designed to produce new therapeutics. For this reason, characterization of the interaction of small molecular ligands with DNA has been the subject of numerous studies.

The present study aims to investigate the interaction of 4-chromanone with double stranded DNA, occurring in aqueous solution. UV spectroscopy has been used to study the effect of this compound on the structure and stability of the DNA molecule. The characteristics of DNA thermal denaturation have been used as a measure of the effect of 4-chromanone on the stability of the double helix.

Absorption spectra, as well as UV melting curves, were recorded for solutions with constant DNA concentration and different concentrations of 4-chromanone. DNA melting experiments were carried out by recording the change in absorbance at 260 nm for DNA in the absence and presence of 4-chromanone.

The values of DNA denaturation temperature (T_m) have been obtained, from the curves of fraction of melted base pairs (θ) as a function of temperature, for each concentration of 4-chromanone. The hyperchromicity at 260 nm (H_{260}) has also been obtained for each concentration of 4-chromanone, at the denaturation temperature and at a higher temperature, at which it is assumed that the strands of DNA have been totally separated.

The results obtained by UV spectroscopy evidence a noteworthy interaction of 4-chromanone with DNA, affecting the stability of the double helix. The concentration of 4-chromanone has a pronounced effect on the characteristics of DNA thermal denaturation.

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2D NMR Studies of sesquiterpene lactones with potential antitumoral activity

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The isolation and structural elucidation of grosshemin 2,3-dihydroxyisobutyrate and dehydrogrosshemin-2,3-dihydroxyisobutyrate were performed [1].

These substances belong to the sesquiterpene lactone (STL) group of secondary metabolites that exert a broad spectrum of biological activities [2]. The STL have shown to exhibit cytotoxic and antitumoral activities (some are in cancer clinical trials), anti-microbial, insecticide and anti-inflammatory activities among others [1].

The presence of different moieties is duly studied with a great number of publications concerning Quantitative Structure-Activity Relationships (QSAR) studies that correlate the presence of several functional groups with a certain biological activity [3]. In that sense, the structural elucidation of these two compounds is paramount for further activity studies.

Since the first NMR studies didn't guarantee an unambiguous elucidation, further ¹³C NMR Broad Band (BB) and ¹³C NMR Distortionless Enhanced Polarization Transfer (DEPT) studies were performed in order to identify the carbon skeleton [1]. Homonuclear Correlation Spectroscopy (COSY) and Heteronuclear Correlation Spectroscopy (HMQC and HMBC) were also performed, guaranteeing an elucidation on the carbon-hydrogen correlation and confirming that the sesquiterpenic nucleus of these substances belonged to the guaianolide series [1].

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High-resolution solid-state MAS NMR methods applied to structural studies of mammalian end-binding protein 3

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Solid-state nuclear magnetic resonance (NMR) spectroscopy still needs the development of procedures and protocols in order to become a generally applicable tool for 3D high-resolution protein structure determination. Crystalline model proteins play an important role in this context, as they allow further developing and optimizing the different approaches including for spectral assignments, the measurement of restraints and structure calculation.

Here, we use the end binding protein 3 (EB3), a small dimeric protein, containing both an N-terminal calponin homology domain, responsible for the interaction with microtubules (MTs), and a C-terminal coiled-coil domain extending into a four-helix bundle, essential for dimer formation. [1] EB3 belongs to a family of proteins that associate specifically with the plus ends of growing MTs (plus end tracking proteins, +TIPs). +TIPs form clusters at the end of growing MTs and this specific sub-cellular position makes them ideally suited for regulating MT dynamics. [2]

Our work focuses on the analysis of the N-terminal globular part of the EB3 protein (132 residues, 15 kDa, PDB reference 3CO1 [1]) employing high-resolution solid-state MAS NMR methods. The initial steps for solid-state NMR 3D structure determination will be presented, namely sample preparation and experimental 2D/3D ¹³C-¹⁵N correlation spectra for assignment purposes.

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Electrocatalytic reduction of nitrate in water with mono and bimetallic catalysts supported on carbon nanotubes

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The increasing level of nitrate concentration in water becomes an important problem for health and environment. Nitrate ions at high concentration could cause human health problems because they can be converted into nitrites in the human body and may cause various diseases: blue baby syndrome, cancer or hypertension. The main sources of nitrate in water include fertilizers, industrial effluents and human wastes [1]. Therefore, monitoring and elimination of this pollutant gains renewed attention. Diverse technologies have been used to reduce the contents of nitrate in water; among them the catalytic reduction is one of the most promising alternatives due to its convenience, environmental respectability, and low cost in-use, without the drawbacks of the conventional methods [2]. This method consists of the reduction of nitrate to nitrogen in the presence of an appropriate catalyst, while nitrite and ammonia appears as by-products [3].

Electrochemical oxidation may constitute an alternative route which allows the reduction of nitrate in mild conditions, *i.e.* ambient temperature and atmospheric pressure. In this work, the electrocatalytic reduction of nitrate in aqueous medium was investigated at mono and bimetallic electrocatalysts based on palladium, platinum, palladium/copper, platinum/copper and ruthenium/copper supported on carbon nanotubes (CNT). The modified electrodes were prepared by deposition of the Metals/CNT on Toray Carbon surface using a Nafion/water solution [4]. The electro-reactivity of nitrate in aqueous medium on modified electrodes was investigated by cyclic voltammetry. Long term electrolyses of nitrate in aqueous media were carried out. Analyses of the products were performed using ionic chromatography (IC) and an ammonia selective electrode, in order to determine conversion and selectivity.

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Polycyclic aromatic hydrocarbons extraction from digestive glands by microwave-assisted and solid phase extraction

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Cephalopod species are territorial in nature and are particularly enjoyed by coastal communities such as Portugal, Italy, Spain and Greece. They can be an important source of several nutritionally essential elements for consumers [1] but, on the other hand, can constitute a potential source of inorganic and organic contaminants. The most known and studied cephalopod species is the octopus that exists in several habitats being exposed to different pollution sources. Polycyclic aromatic hydrocarbons (PAHs) are one of the priority environmental pollutants due to their extremely hazardous properties to human health. Many of the individual PAHs are cytotoxic and mutagenic to both lower and higher organisms, and some of them being considered as carcinogens (probable, possible) to humans [2,3]. The collective characteristics of being persistent and lipophilic make biomagnification and bioaccumulation a major concern. It is well known that PAHs can accumulate in the fatty tissues of animals and people.

In this work, a previously developed and validated methodology for microwave-assisted extraction (MAE) of PAHs from fish [4] was adapted and optimized to quantify PAHs in octopus digestive glands by liquid chromatography (LC) with fluorescence (FLD) and photodiode array (PAD) detection. A step of solid phase extraction was introduced after MAE due to the complexity of the matrix and the high content of lipids of digestive glands. Since low weight samples generally contain small amounts of analyte, it is essential not only to reduce as much as possible the number of pre-treatment steps to reduce the level of blank contamination, but also to avoid the use of large solvent volumes which require subsequent high pre-concentration, hence increasing the risk of losing analytes by evaporation in the concentration steps. Validation was performed by spiking assays at different levels and the overall recoveries obtained were acceptable. The optimal operational parameters were found to be for MAE: 20 minutes at 110 °C with 20 mL of acetonitrile, 1 g of sample and medium stirring speed, and for SPE the application of a Sep-Pak® Plus Silica cartridge 55-105 µm with a pore size of 125 Å.

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Electrochemical techniques applied to the study of pesticide's photodegradation

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Pesticides (herbicides, fungicides, insecticides) are widely used in the agriculture and industry around the world due to their high insecticidal activity. The presence of pesticide residues and metabolites in food, water and soil currently represents one of the major issues for environmental chemistry. Pesticides are, in fact, among the most important environmental pollutants because of their increasing use in agriculture.

Photochemical reactions are one of the most often transformations of pesticides in the environment. Therefore, investigations of photodegradation processes can provide better knowledge on transformations and degradation processes of pesticides and about their oxidation/degradation pattern.

Electroanalytical techniques has been shown to be very useful in the study of toxic substances such pesticides used for disease and pest control. Most of the electroanalytical studies of pesticides are focused on the analysis of the parent substances and on the identification of products formed on the electrode surface by the electrochemical reaction. There are few information about the electroactivity of degradation products of pesticides generated by chemical, photochemical and biological processes, that in some circumstances can be even more toxic and dangerous than the parent products [1].

The presence of electroactive by-products can interfere in the determination of the parent pesticide if the redox potentials are close or it can be an advantage if both electroactives compounds (parent and by-products) present very different redox potentials, allowing the determination of such compounds simultaneously.

The present work aim is related with the use and development of electrochemical methodologies to the study of the photodegradation of pesticides. The results gathered along this work, will be presented in this communication.

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Impact of antioxidants on the oxidation stability of biodiesel

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Biodiesel has been over the years one of the biofuels that is in great development featuring a promising growth potential in worldwide. Biodiesel, which is derived from vegetable oils or animal fats through transesterification to produce monoalkyl esters, exhibits fuel properties comparable with conventional petroleum diesel. Biodiesel provides enhanced lubricity properties and produces low exhaust emissions, such as particulate matter, polycyclic aromatic hydrocarbons, sulfur dioxide and smoke.

One of the environmental advantages of biodiesel is that it degrades more quickly than petrodiesel, and so does not pose a long-term harm to the environment. However, this can also be a disadvantage if the fuel degrades before it can be used.

Biodiesel degrades due to oxidation, contact with water, and/or microbial activity. The oxidation of biodiesel can produce various acids or polymers, which, if in high enough concentration, can cause fuel system corrosion and deposits which in turn can lead to filter clogging and fuel system malfunctions.

Most raw vegetable oils contain vitamin E (tocopherols), a naturally occurring antioxidant. However, vitamin E can be destroyed during the oil refining process. To avoid oxidation and extend the shelf life of biodiesel, commercial antioxidants can be added. The antioxidants used for improvement of the fuel chemical stability are inhibitors of hydrocarbons radical-chain oxidation.

Phenolic antioxidants have been described as one of the most effective additives to improve chemical stability. Phenolic acids are derivatives of benzoic and cinnamic acids and are present in all cereals.

Based on already existing knowledge on the influence of antioxidants on the oxidation stability of biodiesel, the aim of the present study was to investigate the potential of new synthetic phenolic antioxidants concerning improvement of biodiesel stability. The results gathered along this work, will be presented in this communication.

Mo(II) catalysts in the epoxidation of cy8: the effect of temperature, solvent and oxidants

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The complex $[\text{MoBr}(\eta^3\text{-C}_3\text{H}_5)(\text{CO})_2(8\text{-aminoquinoline})]$ was synthesized substituting the acetonitriles ligands in the precursor complex $[\text{MoBr}(\eta^3\text{-C}_3\text{H}_5)(\text{CO})_2(\text{CH}_3\text{CN})_2]$ by the dinitrogen bidentated ligand 8-aminoquinoline. The complex was characterized through FTIR, ^1H and ^{13}C NMR and elemental analysis.

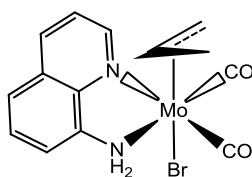


Figure 1. Complex $[\text{MoBr}(\eta^3\text{-C}_3\text{H}_5)(\text{CO})_2(8\text{-aminoquinoline})]$

This complex was tested as catalyst in the epoxidation of cis-cyclooctene. It converted 74% of the substrate after 24h of reaction, at 55 °C, using dichloromethane as solvent, dibutyl ether as the internal standard and 200% *tert*-butyl hydroperoxide as the oxidant, for 1% of catalyst and 100% of substrate. Different conditions were tested to screen the best conditions for the epoxidation of cis-cyclooctene, and optimize the behavior of the Mo(II) complex as catalyst.

The first factor studied was the solvent. Acetonitrile and toluene were used at their respective boiling temperatures (85 °C and 120 °C respectively). The same reactions were also tested without any solvent at 55 °C, 85 °C and 120 °C. The conversions observed without solvent were the same or (in some cases) better than in the presence of solvents. We observed also that higher temperature leads to better conversion.

In order to check the effect of the relative load of oxidant used, 100%, 125%, 150% and 175% of *tert*-butyl hydroperoxide were used in different catalytic runs. Different oxidants, such as cumene hydroperoxide and hydrogen peroxide were also tested. The best conditions were obtained with 150% of cumene hydroperoxide.

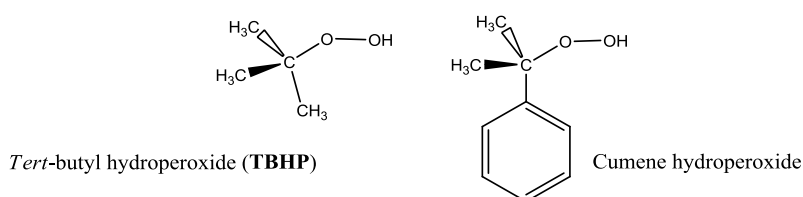


Figure 2. The oxidants *tert*-butyl hydroperoxide (TBHP) and cumene hydroperoxide.

Acknowledgements: We thank FCT (PEst-OE/QUI/UI0612/2011 and PTDC/QUI/71576/2006) for financial support and MSS for a research grant (SFRH/BD/48640/2008).

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Assessment of endpoint antioxidant capacity of red wines using a novel kinetic matching approach

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Antioxidant capacity of food samples is usually assessed by different analytical methods, however the results attained even for the same method are strongly dependent on the selected reaction time and also on the standard compound used [1, 2]. To tackle this problem, we propose here a kinetic matching approach, associated to the conversion of results into equivalents of a common standard compound, as a universal way for expression of results. The methodology proposed was applied to methods based on different chemistries (Folin-Ciocalteu (F-C), CUPRAC, DPPH[•] and ABTS^{•+} assays) and red wines ($n = 40$) were chosen as a model of complex food sample. Results showed that, for all methods, there was no statistical difference between results attained by the kinetic matching approach (after <10 min of reaction) and those at endpoint conditions (after 60 to 300 min of reaction). The repeatability and the reproducibility of the kinetic matching approach was <4.5%, for all antioxidant assays. The sample throughput increases from <18 (endpoint measurements) to >108 h⁻¹ using the proposed kinetic approach. Moreover, we have established here a way of converting results to equivalents of a single standard, providing values independent of its kinetic profile, by using the ratio between calibration sensitivities performed at endpoint conditions.

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A novel and efficient approach to 2-amino-6-cyanopurines

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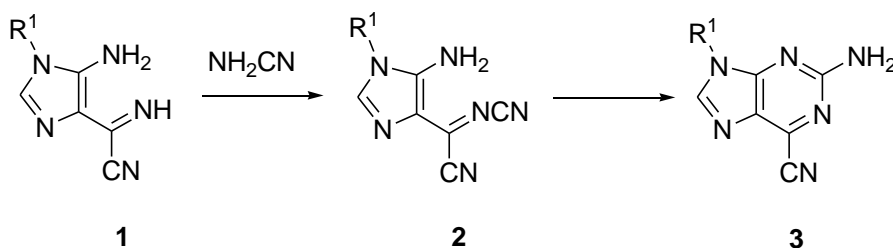
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Despite decades of research, tuberculosis (TB) remains a deadly disease and claims approximately 2 million lives annually, being the greatest single infection worldwide. It is estimated that one third of the world population is infected with *Mycobacterium Tuberculosis*, which persists in a slow-growing or non-growing state. Internationally, efforts are being made to develop new anti-tubercular agents due to the lack of new drugs in the market and also due to the advent of multidrug resistant strains. Recent advances in the search or new drug candidates to treat TB show compounds containing the purine ring as a new class of promising antimicrobacteril agents [1,2].

In a previous work, the activity exhibited on the *Mycobacterium Tuberculosis* strain H37Rv by some of new 2-oxo-6-cyanopurines prepared on our research group, prompted us to investigate more versatile methods to generate several analogs **3**, bearing the amino group on the 2-position of the purine ring.

Imidazoles **1** proved to be important tools for inexpensive synthesis of a number of substituted purines and can be easily obtained from commercially available reagents [3]. Here we report a novel and efficient synthetic approach to obtain 2-amino-6-cyanopurines **3** from 5-amino-4-cyanoformimidoyl imidazoles **1**, involving imidazoles **2** as intermediates.

All the purine derivatives **3** and intermediates **2** were isolated in good-excellent yields, and their structure was assigned on the basis of elemental analysis, IR and NMR spectroscopy, including ^{13}C and 2D techniques.



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A new and efficient synthesis of 3-amino[1,2,4]-triazoles

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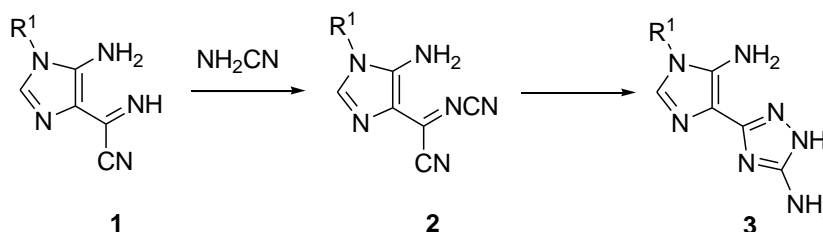
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Azole heterocycles are present in a wide range of biologically active molecules. The growing number of patents describing 1,2,4-triazole derivatives with biological properties reveals the importance of this heterocycle [1]. The biological activities displayed by 1,2,4-triazoles and 1,2,4-triazolones include antibacterial, antifungal, antitumor, anti-inflammatory, and adenosine receptor antagonistic effects [2].

In our research group 5-amino-4-cyanoformimidoyl imidazoles **1** have been used as versatile precursors for nitrogen heterocycles linked or fused with the imidazole ring.

In a previous work, new 3-imidazolyl 1,2,4-triazoles and 1,2,4-oxadiazoles were prepared from 1-substituted imidazoles **1**, which can be easily obtained from commercially available reagents. As an extension of this work, we present now the synthesis of 1,2,4-triazole analogs of type **3**, bearing an amino group on the 3-position of the triazole ring. The synthetic method to obtain the triazoles **3** involved the reaction of cyanamide with imidazoles **1** to generate intermediates **2**. The reaction of compounds **2** with hydrazine led to the synthesis of 3-amino[1,2,4]-triazoles **3** in a one-pot two steps reaction. The triazoles **3** were isolated in excellent yield after 5-10 min. under mild conditions. The structure of the new molecules was assigned on the base of IR, Elemental Analysis and NMR spectroscopy (including 2D techniques).

These new molecules will be submitted to biological assays.



Acknowledgements: The authors gratefully acknowledge the financial support by the University of Minho and Fundação para a Ciência e Tecnologia through the Portuguese NMR network (RNRMN), the Project F-COMP-01-0124-FEDER-COMPETE and a PhD grant awarded to Nádia Senhorães (SFRH/BD/73721/2010).

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The effect of conformational preorganization on the micellization of calixarene-based surfactants

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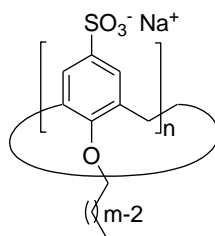
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Structural preorganization is a well known effect in the field of molecular recognition. One illustrative example of this effect is observed in the complexation of cations by polyethers: generally, preorganized macrocyclic analogues form more stable complexes than their open-chain counterparts. Preorganization was defined by D. J. Cram as follow: *the more highly hosts and guests are organized for binding and low solvation prior to their complexation, the more stable will be their complexes* [1]. While the observation of preorganization effects is common and readily identified in host-guest chemistry, in the case of more complex self-assembly processes such as micellization these effects are more subtle and difficult to identify.

In this work the micellization of five amphiphilic *p*-sulfonatocalix[n]arenes (Figure 1) was studied in detail by several techniques (Conductivity, NMR and ITC) and the results were correlated with both the alkyl chain length and the number of monomeric units present in the calix[n]arene structure (i.e. the ring size). The conformations adopted by the calix[n]arenes were identified both below and above the critical micelle concentration (cmc) and their tendency to aggregate was found to be related with their conformational properties. Because all calix[n]arenes studied here adopt the cone conformation in the micelles, those preorganized in this conformation prior to self-assembly show a higher tendency to micellize. The thermodynamic parameters of micellization allowed us to find that both enthalpic and entropic components are involved in preorganization.



SC4TB $n = 4$, $m = 4$
 SC4TH $n = 4$, $m = 6$
 SC4TO $n = 4$, $m = 8$
 SC6HH $n = 6$, $m = 6$
 SC8OH $n = 8$, $m = 6$

Figure 1. Calixarene-based surfactants used in this study.

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Primaquine peptidomimetic and organometallic derivatives against *Leishmania infantum*

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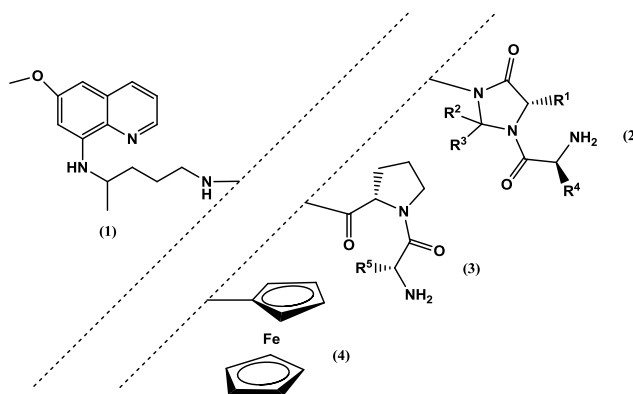
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The treatment of visceral leishmaniasis is intricate by the low efficacy and high toxicity of available drugs. Primaquine (**1**), an anti-malarial 8-aminoquinoline, displays activity against *Leishmania* spp. and several derivatives have been developed as potential anti-leishmanial drugs [1]. However, primaquine exhibits hemotoxicity and low oral bioavailability due to oxidative deamination of its aliphatic chain. We have previously developed peptidomimetic (**2** and **3**) and organometallic (**4**) derivatives of primaquine with higher resistance to proteolytic degradation and oxidative deamination, which presented significant activity against primaquine-sensitive pathogens like *Plasmodium* or *Pneumocystis* [2,3]. At the light of these relevant findings, we decided to evaluate these compounds against *Leishmania infantum*. Results herein reported show that some derivatives have an interesting anti-leishmanial profile with very low toxicity for host cells [4].



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New oxysterol derivatives on *Opisthorchis viverrini*

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The International Agency for Research on Cancer has summarized animal, human and epidemiological studies and recognizes *Opisthorchis viverrini* (*Ov*), a metazoan parasite that can induce carcinogenesis in humans, as a class I carcinogen. *Ov* can develop mitogenic substances into excretory/secretory products that may play an important role in promoting the genesis of cholangiocarcinoma [1]. Elevation of bile acids has also been reported in opisthorchiasis [2] and oxidative and nitrative DNA damage, as 8-oxo-7-8-dihydro-2'-deoxyguanine (8-oxodG) and 8-nitroguanine was found to be involved in inflammation-related carcinogenesis [3]. Certain oxysterols, which are metabolic oxidation products of cholesterol, have been shown to be mutagenic and genotoxic; oxysterols possess pro-oxidative and pro-inflammatory properties which can contribute to carcinogenesis [4]. Therefore, it is possible that oxysterols play an important role in *Ov*-induced carcinogenesis. We have recently developed a liquid chromatography with tandem mass spectrometry (LC-MS/MS) method to identify oxysterols in *Opisthorchis viverrini* samples. Results obtained allowed detecting bile acid conjugates with guanine which possibly underlie *Ov*-promoted DNA damage. Therefore, LC-MS/MS emerges as an important tool to address eventual correlations between oxysterols and various types of *Ov*-associated cancer (Figure 1).

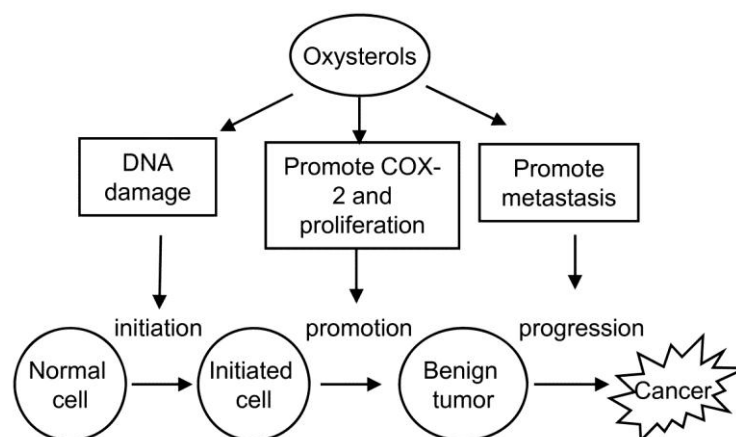


Figure 1. Effects of oxysterols on carcinogenesis. Adapted from reference [4].

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Photophysics study of complexation between β -lapachone-3-sulfonic acid with bovine serum albumin (BSA)

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Lapachol and its isomers, α - and β -lapachone are naphthoquinones of pharmacological importance. These substances and their derivatives have some application against tropical parasitic diseases, such as *Chagas' disease* [1]. The Bovine Serum Albumin (BSA) is the most abundant protein in blood plasma and therefore is the most studied between the proteins. Among its function are: maintenance of osmotic pressure, control of pH, carrier, distributor and metabolizing of multiple ligands, as the drugs [2].

This work aims to perform the photophysical study of the interaction of β -lapachone-3-sulfonic acid (BL3SA) with a solution of BSA buffered with PBS, pH=7.4, by UV-Visible, fluorescence and circular dichroism spectroscopies. This study is important to understand the pharmacodynamics and pharmacokinetics in the distribution and elimination of the drug in the body.

The spectra of UV-Visible show a maximum of absorption at 280 nm, corresponding to the tryptophan residue [3]. The spectra of fluorescence ($\lambda_{exc} = 280$ nm) show that the increase in the concentration of BL3SA cause a suppression of the fluorescence of the albumin in the region of the tryptophan.

The mathematical treatment of the experimental data lead to Stern-Volmer dynamic quenching constant ($K_{sv} = 2,20 \times 10^5$ L.mol⁻¹) and the rate constant of fluorescence quenching ($K_q = 2,20 \times 10^{13}$ L.mol⁻¹.s⁻¹). These values indicate some interaction between BL3SA and the tryptophan of BSA. The process of fluorescence quenching of the BSA is static due to the high value of K_q [3].

The values of some thermodynamic constants (ΔH° , ΔS° and ΔG°) were obtained using the plot of Van't Hoff Stern-Volmer modified. The negative value of ΔG° shows the spontaneity of the interaction, the positive value to ΔH° shows that the interaction between MnTPPS and BSA is endothermic and the positive value of ΔS° shows that the interaction is hydrophobic [4].

The circular dichroism spectra indicate that the addition of the acid influence the ellipticity of albumin, showing a decrease of two bands, 208 nm and 222 nm. This proves complex formation between BL3SA and BSA [5].

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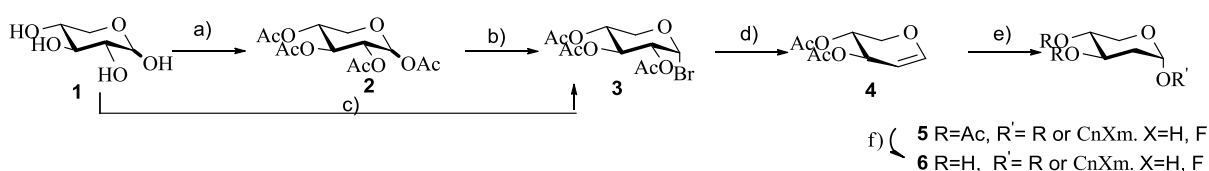
Synthesis of alkyl glycosides with potential application as antimicrobial agents

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Nowadays, our society concerns are related to public health and to find new drugs for diseases that cannot be cured. Concerning pathogenic infections, the main obstacle is related with the ongoing spread of multidrug-resistance. Other important issue is the biohazard security matters and the lack of treatment [1]. These facts demand a continuous research on new antibacterial agents more effective and with new mechanisms of action. Our investigation led to the introduction of a new family of compounds structurally related to alkyl deoxy glycosides, which exhibited a potent activity against *Bacillus cereus* [2,3], a pathogenic bacteria responsible for severe foodborne diseases, among others, which eradication is of great importance for health purposes and also for the food industry.

The first target is the protected glycal **4**, a suitable precursor for the preparation of antimicrobial alkyl 2-deoxy glycosides. Regarding the molecular diversity associated to derivatives synthesised from glycals, new strategies for their synthesis have the major importance. The bioactivity exhibited by the above mentioned glycosides encouraged the search for cleaner and less expensive methods for their preparation. Glycosylation with **4** of a variety of alcohols led to compounds type **5** (scheme 1), which were submitted to the Zémlen deacetylation to give **6** in good yields [4]. The structure of the isolated compounds was confirmed by spectroscopic analysis using NMR as a prime tool. The 2-deoxy glycosides were subjected to surface activity studies and the results will be discussed.



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Pt and Ru complexes and porphyrins as sensitizers for dye-sensitized solar cells

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The conversion of sunlight to electricity using dye sensitized solar cells (DSSC) represents one of the most promising alternatives to energy production by fossil fuels [1]. Although thousands of dyes have been synthesized for DSSC with the aim of improving device efficiency the ruthenium-bipyridyl family of dyes has dominated high-efficiency DSSC devices for many years. Therefore the synthesis of new tailor made dyes and the understanding of the fundamental electron transfer processes in DSSC is still an challenging area of research. In recent years Pt(II) coordination complexes have been studied for their potential use in the area of dye-sensitized solar cells (DSSCs) and in solar to chemical energy conversion [2]. Porphyrins are also viewed as an important alternative class of dyes owing to their photostability, potentially high light-harvesting capabilities and low cost [3].

In this work we compare the performance of Ru and Pt complexes and porphyrins as sensitizers for DSSC and relate the observed efficiencies with the structural, photophysical and electrochemical characteristics of the dyes. 1 cm² DSSCs devices were prepared with the sensitizer anchored to the TiO₂ semiconductor. The adsorption kinetics of these dyes on TiO₂ surface was studied and related with the number, nature and position of anchor groups. The DSSC performance was accessed by measuring the IPCE profiles and I-V curves, yielding their IPCE spectrum, VOC, JSC and η values. We also applied time-resolved photoacoustic calorimetry [4] to evaluate the potential of the photosensitizers anchored to the semiconductor surface in thin films for reductive photocatalysis through measurements of electron injection efficiencies and electron transfer energies.

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Multi-residue method for the analysis of veterinary pharmaceutical compounds in sludge

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Pharmaceutical compounds are currently labeled as emerging contaminants in the environment due to their bioactivity, wide usage, and potential health and ecological risks. Inadequate/non-efficient wastewater treatment processes, as well as, usage of treated sludge's and manure applications (biosolids) as fertilizers are considered the major sources of these pollutants. Veterinary drugs, despite their high usage and possible endpoint in biosolids, are still poorly studied in terms of pathways, release rates and effects into the environment. The large variety of drugs and the matrices where they are found pose difficult challenges to the detection and analysis of these compounds.

A variety of techniques have been used for the analysis of broad therapeutic classes of drugs, worldwide consumed, in environmental samples. Methods described for the analysis of pharmaceutical compounds, mainly for human usage, in environmental matrix use high performance liquid chromatography (HPLC), gas chromatography or capillary electrophoresis allowing a multi-compound analysis approach. In case of solid matrices a previous extraction method such as Soxhlet extraction, microwave assisted extraction (MAE), ultrasonic solvent extraction (USE), pressurized liquid extraction (PLE) or even Vortex agitation (VA), followed by a pre-concentration and clean up procedure, is required.

The determination of veterinary drugs in a complex matrix such as sludge requires the optimization of an adequate process. A methodology for the simultaneous determination of minocycline, oxytetracycline, tetracycline (tetracycline family), enrofloxacin (a fluoroquinolone) and ceftiofur (cephalosporin type), commonly used veterinary pharmaceuticals, in sludge samples is being developed. An optimization of the drugs extraction using three different techniques (MAE, USE and VA) and five different extraction solvents (methanol alone or combined with formic or chloridric acid, acetonitrile and water) was applied. The final methodology includes USE followed by solid-phase extraction (SPE) and analysis by HPLC with a diode array detector. In this communication, the optimization steps and the method characteristics will be presented.

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Synthesis and characterization of novel alkaline and lanthanide metal alkoxides

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The synthesis of metal alkoxides has been the object of interest since they are very useful compounds with applications in synthesis and catalysis. They are important precursors for the deposition of metal oxides (with several applications in the electronics field) and for the obtainment of new compounds [1-3]. Also in the pharmaceutical, agrochemical and food industries they had a wide application.

Despite the relevance of these compounds, their thermal and energetic characterizations are still rare [4], since these types of compounds are difficult to analyze using the most common methods due to their properties.

This communication presents the synthesis of alkaline metal (sodium and potassium) and rare earth–ytterbium alkoxides with 1,2 ethanediol and 1,4 butanediol. For their characterization, there were used thermo gravimetric analysis (TGA), differential scanning calorimetry (DSC), elemental analysis, x-ray (XR) and infrared (IR) spectroscopy methods.

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Synthesis of 2-*N*-benzyl carboxamide derivatives of 1-azafagomine

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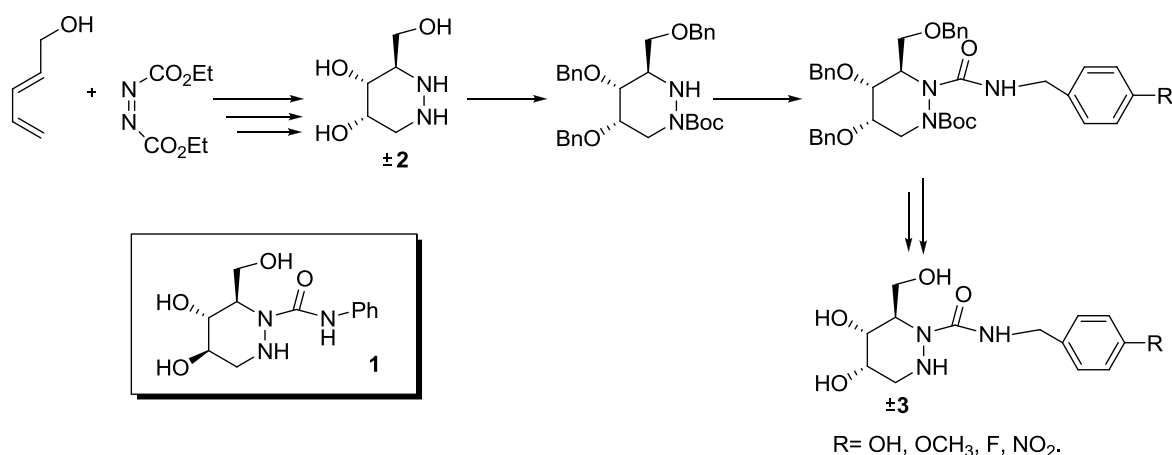
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Imino sugars, also known as azasugars, are a group of compounds that have received a lot of attention in recent years because they typically exhibit excellent inhibitory properties over a range of enzymes involved in carbohydrate recognizing receptors, widely found in living organisms [1]. The inhibition of α - and β -glucosidases by 1-*N*-phenyl carboxamide derivatives of 1-azafagomine **1** was studied in our laboratory indicating that they are new leads for the synthesis of glycosidase inhibitors [2].

Our objective now is to synthesise new 1-*N*-phenyl carboxamide derivatives of 1-azafagomine **1** bearing groups at the *p*- position of the aromatic ring with ability to form extra hydrogen bonds. The interest of this structural modification is based on molecular modelling studies, which predicted a higher inhibitory activity for the final products.

The synthesis of the 1-*N*-benzyl carboxamide derivatives **4** can be achieved from 1-azafagomine **2**, which can be converted into the partially protected compound **3** [3]. The introduction of benzyl carboxamide groups at position 1 have been achieved by reaction of compound **3** with different isocyanates to afford compounds **4** to be tested against a panel of glycosidases.



Scheme 1. Synthetic strategy for compound 4.

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One-pot method in the synthesis of diphosphonic-based lanthanide metal-organic frameworks

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Metal Organic Framework (MOF) is a term used to specify a class of coordination polymers, which are crystalline compounds consisting of metal ions or clusters coordinated to often rigid organic molecules to form one-, two-, or three-dimensional structures. Many of these frameworks exhibit permanent porosity. In order to promote functionality, these compounds should have some specific properties: (1) strong metal-to-ligand binding so to increase mechanical robustness; (2) the linking units should allow chemical modification by way of organic synthesis; (3) well defined geometrical structures of the building blocks; (4) self-assembly should occur so to produce highly crystalline frameworks [1-3]. We note that the majority of the reported MOFs have been produced using the building-block approach in which cationic metal centers are interlinked by organic ligands, the reason which ultimately led to the vast number of MOFs with different structures and morphologies reported to date [4]. Many of these materials may find direct applications in various areas, ranging from catalysis to ionic change, gas storage and, more recently, even as contrast agents and in drug delivery.

This communication reports on the synthesis of a novel system based on the self-assembly of lanthanum with a diphosphonic acid, 1,4-phenylenebis(methylene)diphosphonic acid. We adopted a simple and rapid synthetic approach, based on a one-pot synthesis that consists in the addition of the metallic solution to a second solution containing the organic linker. Reaction occurs at a fixed temperature during a pre-determined reaction period. This method allows, only by fine-tuning the experimental conditions, the isolation of a novel family of MOF structures, showing several different phases and crystal morphologies. We summarize herein the reaction conditions (temperature, reaction period and composition of the reactive mixture) which can lead to the formation of up to four distinct phases. Materials were characterized by using vibrational spectroscopy (FT-IR and FT-Raman), powder X-ray diffraction and electron microscopy (SEM and EDS). The present work is already being used in the preparation of an article to be submitted in Crystal Growth and Design journal.

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Stability of simvastatin under different atmospheric humidities

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Simvastatin (SIM, C₂₅H₃₈O₅, CAS number [79902-63-9], Figure 1) is an antilipidemic drug used in the treatment of high plasma cholesterol concentrations, and thus, in the prevention of cardiovascular diseases.

Information on the influence of different conditions on the stability of a drug is often required during the design and production phases. Indeed polymorphism, crystallinity, moisture content, or other factors may affect the properties of the final product. Water is normally used during the process of production of medicines and present in the environment where the medicine is stored. Stability studies of SIM at different relative humidities are, therefore, important for the pharmaceutical industry.

The purpose of the present work was to evaluate the stability of SIM when stored at different atmospheric humidities. Samples of pure SIM were placed in desiccators with different relative humidities (11%, 52%, and 93%) and studied by differential scanning calorimetry (DSC) after pre-defined residence periods (1, 2, 5, 7, 15, 30, and 60 days). The temperatures and enthalpies obtained from the observed peaks were analyzed as a function of storage time.

The results showed no phase changes, water absorption, or significant variations of peak positions and enthalpies indicating that differences in relative humidity do not seem to significantly affect the physical and chemical properties of SIM.

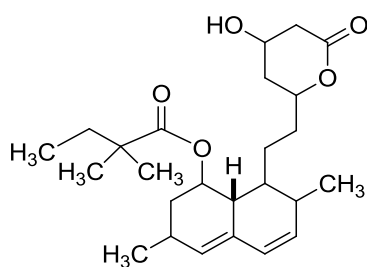


Figure 1. Molecular structure of simvastatin.

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Enzymatic conversion of CO₂ to methanol: a spectroscopic approach

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Conversion of atmospheric CO₂ to methanol is a new and promising alternative for the recycling of the CO₂, which can have significant impact in the greenhouse effect. This conversion can also be used in the efficient production of fuel alternatives [1], since methanol has an important value as a raw material for the production of clean fuels like biodiesel. A known and proved method of conversion of CO₂ to Methanol was used [2], through consecutive reduction reactions, catalyzed by three dehydrogenases encapsulated in silica matrices prepared via sol-gel process.

The reaction consists in the reduction of CO₂ to formate catalyzed by formate dehydrogenase (FateDH), followed by the reduction of formate to formaldehyde catalyzed by formaldehyde dehydrogenase (FaldDH), and finally the reduction of formaldehyde to methanol catalyzed by alcohol dehydrogenase (ADH). All these reactions are NADH dependent that acts as a terminal electron donor. Reactions were performed in the presence of supercritical CO₂ (ScCO₂), using both water and ionic liquid [EMIM][EtSO₄], so these were also object of the study.

Spectroscopic techniques, namely fluorescence and 2D NMR, were used to investigate the interactions between enzymes, the silica sol-gel matrix and the solvent. This will help to understand and improve the solubilization of CO₂, in order to enhance the methanol conversion.

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Setting a new biomolecular force-field: parameterizing manganese first coordination spheres from metalloproteins

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Manganese enzymes have been targeted as important components in biological systems, namely the photosystem II, manganese catalase, manganese deoxygenase... [1,2], and present several regular characteristics due to their varied oxidation states. We highlight the high spin states of their biologic complexes, frequent dative covalent bonding with aspartates, glutamates, histidines or waters, or their 5- and 6-coordination geometries [1,2].

The parameterization of metallic enzymes is of high importance in current Computational Chemistry, since the current biomolecular force fields that are specialized in the treatment of proteins do not contain accurate parameters for the treatment of the metal coordination spheres that are critical for the structure/activity of such systems. This weakness greatly limits the application of Molecular Dynamics simulations and related methodologies to metalloproteins.

In the current work, a library of parameters has been developed for single-metallic manganese coordination spheres in biologically relevant metalloenzymes, based in the AMBER force-field, and ultimately transferable to any of the existent protein-related force-fields.

Among the manganese enzymes defined in the literature [2,3], twelve have already been parameterized using Density Functional Theory, with the B3LYP hybrid functional.

Each of these systems has been described within a bonded model approach [4], with bond and angle force constants, as well as atomic charges having been calculated already. Molecular dynamics was run to validate the obtained parameters.

As future prospects, the group intends to continue developing this database, applying a consistent methodology, which is still under development, to the rows of known transition metals, in order to set a new biomolecular force-field based on a high theoretical level parameterization.

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Ionic liquids containing nitro and cyano groups

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The main objective of this work is focused on the development of novel energetic materials based on ionic liquids (ILs), taking advantage of some peculiar ILs properties such as low vapour pressure, an adjustable physical properties (e.g. viscosity and density) as well as their high chemical and thermal stability [1].

Energetic salts offer many advantages over conventional energetic molecular compounds, in particular due the presence of nitrogen rich salts which can contribute to high heats of formation, and high densities. These materials combine other several advantages such as their high propulsive power, high specific impulse and flame temperatures [1,2].

In this context, different energetic ILs or molten salts based on as tetramethylguanidinium [TMG], cetylpyridinium [C16pyr] and methylimidazolium [MIM] as nitrogen-rich organic cations combined with thiocyanate [SCN], nitrate [NO₃], dicyanamide [DCA] and tricyanomethanide [TCM] as anions. Some functionalized TMG cations were also developed by the reaction with an adequate halo-alkyl compound [3]. All new energetic salts containing nitro and cyano units have been characterized by ¹H and ¹³C NMR; FTIR and elemental analysis. Complementary calorimetric (determination of melting point and glass transition temperatures) and solubility studies have been also performed.

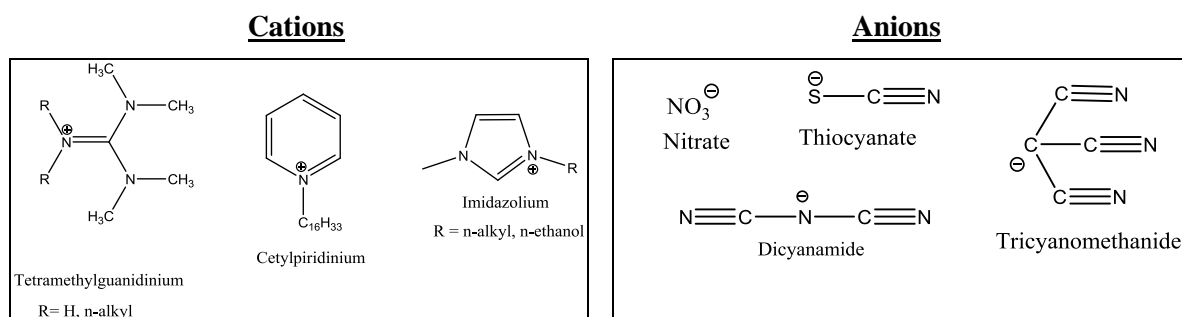


Figure 1. Structures of cations and anions.

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Molecular fluorescence spectroscopy as a technique for the assessment of secondary organic aerosol formation during sampling of atmospheric particles

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Secondary organic aerosol (SOA) formation is considered to be a major source of water-soluble organic carbon (WSOC) in atmospheric aerosols. Currently, it is also recognized that during sampling of atmospheric particles, SOA can be formed on the filters substrate by chemical reactions and gas-to-particle conversion of volatile organic compounds. This situation significantly contributes to the uncertainties on the determination of aerosol mass and WSOC concentrations in atmospheric aerosols. For the assessment of such phenomenon, high-volume fine atmospheric aerosols (PM_{2.5}) samples were collected using a tandem quartz fiber filters methodology (front and back filters). The sampling was conducted in an urban North Western European coastal region (Aveiro, Portugal, (40°38'N, 8°39'W)) between June 2008 and June 2009. Besides a global carbon balance, the WSOC components were further analysed using excitation-emission matrix (EEM) and synchronous fluorescence spectroscopy. The results show that the back filter-to-front filter ratio of WSOC in Summer 2008 can reach values up to 39%, while in Spring of 2009 those ratios increase up to values of 60%. The EEM contour profile of the aqueous extracts of the back filters exhibited two different fluorophores at different excitation/emission wavelengths ($\lambda_{Exc}/\lambda_{Em}$): 310/418 nm and 249/420 nm. These results suggest the likely occurrence of SOA formation during the quartz filter sampling procedure of atmospheric particles. These results also emphasize the need for a correction method when measuring aerosol WSOC in urban environments.

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Interaction of 3,4-dihydroxyxanthone with double stranded DNA in water/ethanol solutions

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Xanthenes comprise an important class of oxygenated heterocycles, which have been found to possess interesting biological and pharmacological activities. The biological activities of this class of compounds are associated with their tricyclic scaffold and depend on the nature and/or position of the different substituents [1].

The aim of the present work is to evaluate the interaction mode of 3,4-dihydroxyxanthone with DNA. UV spectroscopy has been used to determine the effect of 3,4-dihydroxyxanthone on the process of thermal denaturation of double stranded DNA.

UV spectra and melting curves have been recorded for solutions with constant DNA concentration and different concentrations of 3,4-dihydroxyxanthone. Due to the low solubility of 3,4-dihydroxyxanthone in water, all the experiments have been carried out in water/ethanol solutions and the results are compared with previous results obtained by us in aqueous solution.

The values of DNA denaturation temperature (T_m) have been obtained for each concentration of 3,4-dihydroxyxanthone, from the curves of fraction of melted base pairs (θ) as a function of temperature. The hyperchromicity at 260 nm (H_{260}) has also been obtained for each concentration of 3,4-dihydroxyxanthone, at the denaturation temperature and at a higher temperature, at which it is assumed that the strands of DNA have been totally separated.

The results indicate a strong binding affinity of 3,4-dihydroxyxanthone with DNA, showing that 3,4-dihydroxyxanthone interacts with DNA, affecting the stability of the double helix. The concentration of 3,4-dihydroxyxanthone has also a noteworthy effect on the characteristics of DNA thermal denaturation

The results suggest that 3,4-dihydroxyxanthone can intercalate into the base pairs of DNA, taking into account the planar geometry of the molecule.

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Pedagogical material for the teaching of Organic Chemistry in the primary level

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Organic Chemistry is one of the most up-to-date scientific areas. In spite of the current scientific interest in Organic Chemistry, the Portuguese curricula of pre-university education doesn't give the due importance to it [1]. In fact, its basic concepts only arise at the ninth year of twelve.

It is aimed to develop and validate educational materials to teach/learn basic Organic Chemistry at the ninth grade level (theme 'Living Best on Earth' – Portuguese curricula), with a positive impact on students' learning. Also students and teachers seem not motivated about this subject [2].

The use of such educational material is expected to lead to a change in teachers' methods of sciences, in particular Organic Chemistry, and to an increase in the motivation and interest to learn Science.

Previous studies suggest that one of the best ways to increase students' scientific knowledge is expanding the use of technologies and experimental work in teaching methods [1].

The next step will be the production of additional pedagogical materials using new technologies of communication and information as online virtual laboratories, virtual learning environments, e-learning projects and experiences, computer software education, videos for learning, digital libraries or repositories and e-portfolios. A strong point to increase students motivation and interest in science, could be relating the scientific knowledge with everyday life since primary school.

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Novel lanthanide phosphonate MOFs: synthesis, crystal structures, photoluminescent and catalytic properties

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The last two decades have been marked with the emergence of a new class of crystalline and multidimensional compounds, usually known as coordination polymers or Metal-Organic Frameworks (MOFs). The preparation of these materials is based on the self-assembly of multipodal organic linkers and metallic centers. Because MOFs may possess interesting architectures and unique properties, they may also find applicability in distinct areas such as gas storage and separation, ion exchange, catalysis, magnetism, as optical sensors, among others [1].

Recently, we have been interested in the preparation of multidimensional MOFs combining lanthanide centers with phosphonate organic linkers [2-4]. In this communication we report the synthesis, structural characterization and the study of some properties of new family of three-dimensional lanthanide-organic frameworks. The tripodal (benzene-1,3,5-triyltris(methylene))triphosphonic acid (H_6bmt) was self-assembled with several lanthanide cations, under typical hydrothermal conditions, yielding crystalline and phase-pure $[Ln_2(H_3bmt)_2(H_2O)_2 \cdot H_2O]$ materials [where $Ln^{3+} = La^{3+}$ (**1**), Ce^{3+} (**2**), Pr^{3+} (**3**), Nd^{3+} (**4**), $(La_{0.95}Eu_{0.05})^{3+}$ (**5**) and $(La_{0.95}Tb_{0.05})^{3+}$ (**6**)].

Materials were fully studied and characterized by standard solid-state techniques and their crystalline structures unveiled by single-crystal X-ray diffraction. The catalytic behavior of **1** was investigated in the ring opening of styrene oxide and the photoluminescent properties of **5**, its dehydrated form **5-dehyd**, and **6** were studied.

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The influence of microwave irradiation in the outcome of solid phase peptide synthesis

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Since 1986, with the demonstration of the efficiency of microwave irradiation for promoting difficult organic reactions, a considerable amount of articles have been published in the area of microwave-assisted organic synthesis (MW-OS). Although most of the first described experiments were performed in domestic kitchen microwave ovens, nowadays chemistry-dedicated microwave instruments are commercially available. MW-OS has revolutionized organic chemistry. Molecules can be built in a fraction of the time required by classical thermal methods, and microwave-assisted methods can be applied to a large number of organic reactions in solution or in solid phase [1,2]. As a result, this technique has rapidly gained acceptance as a valuable tool for accelerating drug discovery and development processes.

Solid phase peptide synthesis (SPPS) has come a long way since its introduction by Bruce R. Merrifield in 1963. During the last decades, attempts to improve SPPS yields and minimize side reactions were dependent on discovery of new and more effective types of solid supports, protecting groups or coupling reagents, or use of distinct synthetic strategies. The outcome of the peptide synthesis is determined by the efficiency of each coupling and deprotection steps and the competition of undesired side reactions. Recently, it has been shown that microwave-assisted SPPS (MW-SPPS) benefits from the fact that MW irradiation significantly improves coupling and deprotection efficiencies, namely through disruption of non-covalent peptide aggregates that tend to form during chain elongation and which hamper successful synthesis; also, MW-SPPS allows peptides to be produced at much higher rates than traditional SPPS [3-5].

In this work, we have been investigating the influence of MW irradiation on the outcome of the solid-phase synthesis of a well-known antimicrobial peptide, human lactoferrin (1-11), hLF(1-11), (GRRRRSVQWCA) [6]. To this end, we have synthesized the same peptide by conventional and MW-assisted SPPS, using a classic Fmoc/tBu SPPS orthogonal protection scheme [7] and a Fmoc-Rink-amide resin as solid support [8]. Conveniently protected amino acids were sequentially coupled in the $C \rightarrow N$ direction and, once the peptide chain was assembled, acidolytic cleavage of peptide-resin support was carried out by standard methods [9]. After cleavage, the crude peptides were analyzed and compared in terms of yield and purity degree. It was concluded that MW-SPPS not only yielded higher amounts of purer peptide, but also allowed its synthesis in 9 hours whereas 4 days were needed to complete the synthesis by a conventional approach.

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Bisphenol-A adsorption onto activated carbon. Langmuir and Freundlich isotherms and kinetics.

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Bisphenol-A (BPA) is one of the highest volume produced chemicals worldwide in the plastic industry. It is an endocrine disruptor classified as an emerging pollutant.

In this work we studied the adsorption of BPA from aqueous solutions onto walnutshell-based activated carbon.

For activated carbon preparation, walnut shell was soaked with ZnCl_2 (1:2 m/m) during 9h at 105°C. It was then activated and carbonized in a muffle under N_2 atmosphere: room temperature to 500°C at 5°C/min; 1h at 500°C; natural cooling to 140°C. Kinetics and equilibrium studies were investigated at initial BPA concentrations ranging from 5 to 60 ppm.

Three adsorption kinetic models - first, second and pseudo-second order - were used to fit the experimental data. The first order model gave the best description of the adsorption process ($R^2 = 0,9888\text{--}0,9990$) with k_1 values ranging from $0,0521\text{ h}^{-1}$ to $0,0394\text{ h}^{-1}$ for all initial concentrations studied. The experimental data fits better to a Langmuir isotherm ($R^2 = 0,9986$) than to a Freundlich isotherm ($R^2 = 0,9483$), which suggests that the adsorption occurs in a homogeneous surface, with formation of a monolayer and without interaction between adsorbed particles. The equilibrium constant of Langmuir, K_L , is 1,5 L/mg and the maximum adsorption capacity, q_{max} , is 277,8 mg/g (1,22 mmol/g).

The fit of experimental data to diffusion models reveals that, during the first 9h, the adsorption process is preferentially controlled through intra-particle diffusion.

When comparing the results with those reported in the literature, the value of q_{max} obtained in this work, 1,22 mmol/g, is similar to q_{max} when a mesoporous carbon was used, 1,30 mmol/g [1], but significantly higher than that of a hydrophobic zeolite, q_{max} 0,49 mmol/g [2]. The results indicate that walnutshell-based activated carbon may represent a useful tool in biotechnological processes of environmental remediation of BPA. Since it is an abundant and affordable byproduct, its application in the removal of BPA and similar contaminants from urban and industrial effluents, or even from drinking water, seems to be an advantage.

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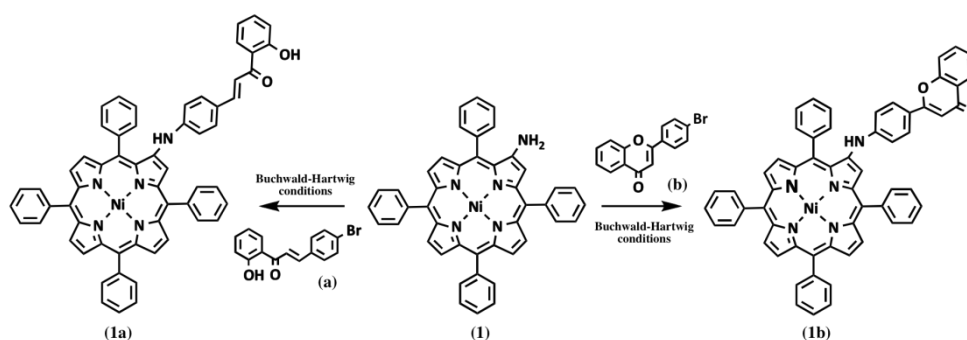
Synthesis and evaluation of the biological activity of new flavonoid-porphyrin dyads

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Flavonoids are polyphenolic compounds widely spread in the plant kingdom. These compounds are becoming the subject of medical research due to a wide variety of biological properties such as anti-inflammatory, antimicrobial, antioxidant and anticarcinogenic activities [1]. Porphyrins are tetrapyrrolic macrocycles known to be involved in many important biological processes and have also proven to be versatile in numerous areas such as catalysis, supermolecular chemistry and in medicine [2].

A recent strategy for the discovery of new drugs or the improvement to already known drug entities, consist in the synthesis of molecules with dual functions [3]. In this context and considering the important biological activities exhibited by flavonoids and porphyrins, we set up a program aiming the synthesis of new flavonoid-porphyrin dyads, believing that the combination of these compounds may induce an increase in the biological activity. In the present communication we will present and describe the synthesis of new flavonoid-porphyrin dyads **1a** and **1b** using the Buchwald-Hartwig amination for the coupling of porphyrin and flavonoid unities. We will also describe the evaluation of its DNA intercalating activity using fluorescence methods, aiming to evaluate their use as potential anti-carcinogenic agents.



Scheme 1. Synthesis of chalcone-porphyrin **1a** and flavone-porphyrin **1b** dyads.

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Application of scientific computation in the chemistry education

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The utilization of computational softwares, as MAPLE, MATHEMATICA and MATLAB for the solving of mathematical problems in the chemistry student routine makes that the same have a differential formation. It was then developed one application of the MAPLE software for the construction of atomic orbitals surfaces and their wave functions, radial and angular. Thus, it's expected to present an alternative to the academic development of the student, especially in theoretical and experimental disciplines that presents complex calculations. The software in question allows the student to obtain a full and interactive analysis of the generated orbitals, manipulating them in the most comfortable way in accordance with the program tools.

The wave functions of the hydrogen-like atoms are from the multiplication between the radial and angular wave functions [1]. The radial wave function is responsible for the size of the surface, while the angular is responsible for the shape and orientation of it. Will be also generated the radial distribution function, which shows more clearly the nodal regions of the orbitals.

An advantage of the MAPLE is that the radial eigenfunctions (related with the associated Laguerre polynomials) and the angular eigenfunctions (related with the associated Legendre polynomials), are already part of the original internal library of the software. Based on that, a simple command, which can be made quickly in the classroom, can represent generally the radial and angular wave functions.

Thus, is computed the Ψ function and, by specific commands from the MAPLE, we reach in the desired atomic orbitals surfaces. Another effect that occurs in the orbitals, the shielding, can be also analysed through the overlap of the radial distribution function with close energy.

The results of this stage of the project, along with those who will be developed, present an encouragement to the chemistry student in the study of atomic orbitals. It is still possible to expand the routine to many degrees of the undergraduate and even develop new for the other areas of chemistry.

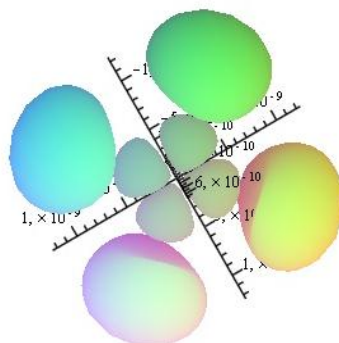


Figure 1. Surface of a d-orbital, generated from MAPLE. Compared with the references [2] and [3].

Acknowledgements: MAPLE, quantum chemistry, wave function, atomic orbitals, 3D surfaces.

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Biocompatible fluorescence based temperature sensor

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Optical sensors based on fluorescence and exploiting the temperature dependence of either intensity or lifetime have been widely explored [1]. The use of temperature fluorescence based sensors in real applications is very simple because they can work with cheap excitation sources such as LEDs, and the signal can be collected in intensity, time or phase modes. Additionally, they exhibit a very fast response and reversibility.

Stimuli-responsive polymers are particularly interesting materials, giving the possibility to control the polymer expanded/collapsed state in water by using an external stimuli, such as temperature [2]. Water-soluble biocompatible copolymers of 2-(2-methoxyethoxy)ethyl methacrylate and oligo(ethylene oxide)methacrylate exhibit a lower critical solution temperature (LCST) that can be accurately tuned by adjusting the ratio of the two monomers [3]. Herein we present the preparation of these thermoresponsive co-polymers labeled with different pyrene derivatives using atom transfer radical polymerization (ATRP), and the LCST tuned to ca. around 37°C. The collapse/expansion of the polymer chains changes the pyrene excimer-to-monomer intensity ratio, providing a very sensitive remote temperature sensing platform. Additionally, the intensity of the monomer is temperature independent, allowing the internal calibration of the sensor system.

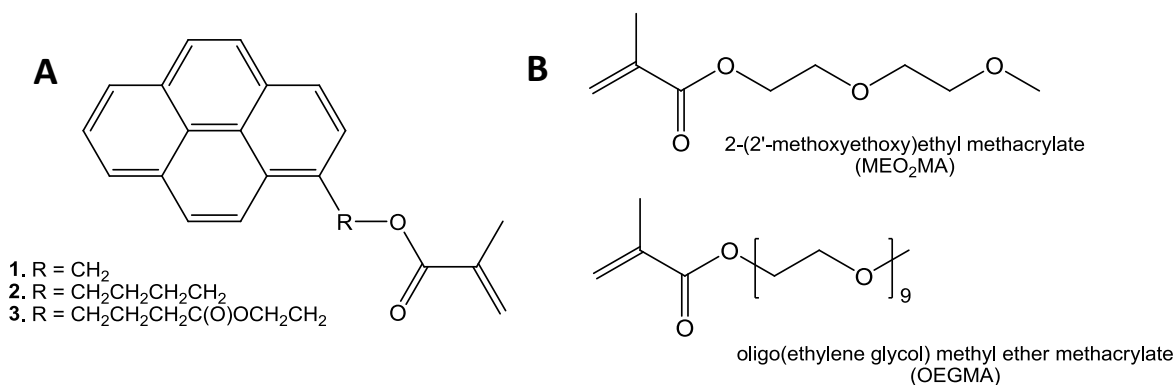


Figure. Pyrene derivatives (**A**) and monomers (**B**) used in the preparation of biocompatible responsive polymers.

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Palladium/carbon catalyzed hydrogenolysis and hydrogenation of xanthene type fluorophores: a study by NMR

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In the past few decades, there has been a remarkable growth in the use of fluorescent probes for biological and environmental sciences [1]. The xanthene type fluorophores, such as rhodamine and fluorescein derivatives, are particularly attractive, either as fluorophores or fluorescent probes, because of their excellent photophysical properties namely, high molar absorptivity, intense fluorescent spectrum in the visible region and high quantum yield.

In the present work we report the synthesis and characterization of a range of novel xanthene derivatives containing a 3-hydroxy-4-pyridinone or a catechol chelating unit, which were designed to act as chemosensors and iron (III) chelators (Figure 1). The synthesis of these ligands involves the coupling reaction of the xanthene fluorescent platform with the chelating unit, followed by the removal of the protecting groups. This deprotection step is been performed by dissolution of the protected ligand in a mixture of methanol/HCl and placed under a hydrogen atmosphere over 10% Pd/C [2]. This method has been also highly used as an efficient protocol for the selective removal of the benzyl protecting groups of other fluorescent systems including naphthalenes [3], 1,8-naphthalimides [4] and porphyrins [5]. The process is also found to be suitable when we think about green chemistry as a more ecofriendly deprotection methodology when compared with the Lewis-acid mediated debenzylation employing the boron trichloride in dichloromethane.

NMR spectroscopy revealed that sing hydrogen over 10% Pd/C conditions the protecting groups are successfully removed but in some cases, it was also observed the reduction of the double bond at position 9 of the xanthene ring. The results showed that depending on substituent groups introduced in the periphery of the xanthene ring, the reduction in the double bond at position 9 is more or less favoured and yields fluorescent chelators with different photophysical properties.

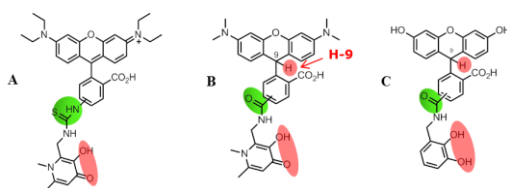


Figure 1. Novel xanthene ligands containing a 3-hydroxy-4-pyridinone (A, B) or catechol (C) chelating unit.

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Synthesis and anticancer activity of a selection of quercetin analogues and their precursors

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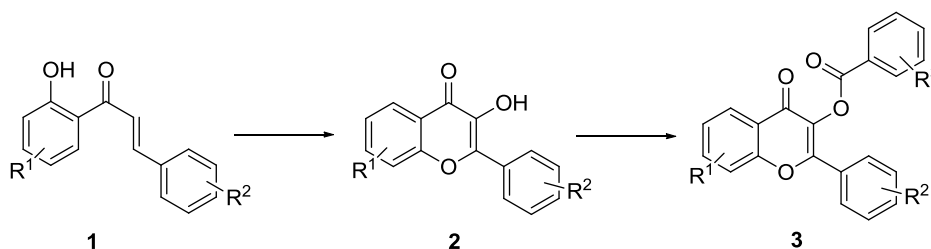
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Compounds incorporating the flavonoid moiety and its structural derivatives are present in a multiplicity of naturally occurring molecules. They were identified in many fruits and vegetables.

Quercetin, a polyphenolic plant secondary metabolite, is one of the most studied flavonols. In the last years, a considerable number of biological studies involving this structure and its analogs have been reported. A broad range of biological activities were discussed, namely antioxidant, anticancer, antithrombotic, antimicrobial and antiviral. Consequently, quercetin represents a remarkable lead compound for further pharmaceutical development, acting as a scavenger of reactive oxygen species [1]. Its biological action, related to inhibition of signaling pathways has also been argued and confers to this molecule and other flavonoids, the prospective for being active on anticancer therapy [2,3].

In the present work, simple synthetic approaches were developed to prepare quercetin analogues to be tested on cancer cell lines. Previous work on the synthesis α,β -unsaturated carbonyl compounds, carried out in our research group, was applied to the synthesis of chalcones **1**. Intramolecular cyclization to generate flavonols **2** was performed in a single step, under appropriate experimental conditions. Later, a simple condensation reaction led to product **3**. Structural modifications were performed by changing the substituents in the pyran moiety, in the aromatic rings, or in both.

All compounds were fully characterized by ¹H and ¹³C NMR, IR and EA. The potential anticancer activity of these compounds was evaluated in the colorectal carcinoma cell line HCT116 by the MTT assay.



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Synthesis of new molecules with the 4*H*-chromen-4-ylidene scaffold

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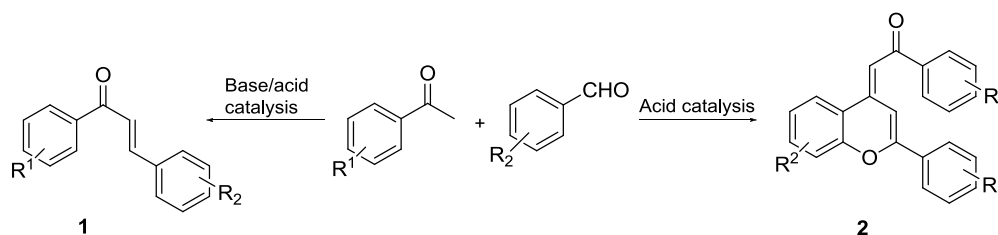
The chromene scaffold is present in a wide variety of compounds including natural products that usually display important pharmacological properties [1]. 4*H*-Chromen-4-ylidenamines can also be identified in the literature, but only a few reports are known on the association of the chromene moiety to a 4-methylene substituent [2,3].

α,β -Unsaturated carbonyl compounds are often used as starting materials for the synthesis of the chromene ring system. They can be obtained from the reaction of ketones and aldehydes in an Aldol condensation, commonly performed in aqueous basic media. Acid catalysis was also reported to lead to the desired product, although usually with lower yields, but only a small number of publications refer this process [4].

Previous experimental work on the synthesis of α,β -unsaturated carbonyl compounds, made in our research group, revealed that extensive degradation and complex reaction mixtures are often a consequence of the presence of base catalysis, in the reaction of acetophenone and polyphenolic aldehydes.

For the synthesis of chalcones **1**, the reaction of polyphenolic aldehydes and acetophenone performed with acid catalysis proved to be a cleaner and simpler synthetic approach. When salicylaldehydes were used, the 4-methylene substituted flavone derivative **2** was also isolated. A straightforward synthetic process was developed for the formation of the 4-methylene substituted derivative that represents a new chromene derivative, to the best of our knowledge.

Several experimental conditions were tested in order to select the synthetic approach that favors the formation of chromene **2**. The reaction mechanism will be discussed, together with the full structural characterization of the products.



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Nutritional value of Senegalese sole (*Solea senegalensis* Kaup, 1858) fed with sustainable diets

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Sustainable development of intensive production is a challenge facing the aquaculture industry and scientific community in order to avoid remarkable changes on the nutritional value of the fillet. Senegalese sole (*Solea senegalensis* Kaup, 1858) is a highly appreciated fish and a strong candidate for intensive aquaculture in Mediterranean countries. Recent studies demonstrated that fishmeal can be successfully replaced up to 75% by a mixture of plant protein sources [1], but total fishmeal replacement has never been evaluated.

A fishmeal based diet (FM) was compared to diets containing increasing levels of plant protein (PP) sources, (50, 75 and 100% PP) during 140 days.) By the end of the trial, total lipids in muscle and skin tissues were similar among the different diets while in liver fat content was significantly higher ($P < 0.05$) in PP50 (25.59%) and PP100 (28.57%) groups. Fatty acid profiles, achieved by GC-FID technique, were significantly affected by the different levels of PP sources, mainly in liver: PP50 showed higher levels of Saturated Fatty Acids (34.77%), Monounsaturated Fatty Acids (46.35%), DHA/EPA ratio (15.62) and reduced contents of Polyunsaturated Fatty Acids (16.40%). Despite some significant differences, no major alterations were found in muscle fatty acid profile, which means that the main edible portion of the fish preserves its lipid constitution, remaining as a very important source of PUFA, such as the long chain *n*-3 fatty acids, EPA (20:5 *n*-3) (3.24-4.35%) and DHA (22:6 *n*-3) (17.14-20.93%), which play an advantageous role on human health, as the prevention of coronary heart disease (CHD) and neural disorders.

In conclusion, senegalese sole can reach the market size with blends of plant protein up to 75% incorporation level without compromising muscle lipid content and fatty acid profile.

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Biosensor development for pirimicarb pesticide determination

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Vegetables and fruits are an essential component of our diet due to their nutritional value. For better yield and quality, insecticides are repeatedly applied during the entire period of growth and sometimes even at the fruiting stage. Serious public concern has risen regarding food safety and environmental health. Pirimicarb (2-dimethylamino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate) is a systemic insecticide from the carbamate family. It is a cholinesterase inhibitor widely applied in cereals, fruit, ornamentals, strawberries, potatoes, sugar beet, cotton, and glasshouse crops [1].

A biosensor is defined by IUPAC as a self-contained integrated device that is capable of providing specific quantitative or semi-quantitative analytical information using a biological recognition element [2]. User advantages include low price, reliability, no or little sample preparation, disposability and clean technology. Hence, biosensors show the potential to complement both laboratory-based and field analytical methods for environmental and foodstuff monitoring [3].

This project aims to develop an enzymatic biosensor for pirimicarb quantification in fruits and vegetables. The selected sensing element of the developed biosensor is laccase, a copper oxidoreductase enzyme which is a highly specific bioreceptor for phenolic compounds. A carbon paste electrode was used as the working electrode. Experimental variables such as, enzyme immobilization, substrate, pH, time of incubation, frequency, step and amplitude were optimized. Analytical data concerning pirimicarb quantification is obtained by square-wave voltammetry based on the inhibition of the catalysis reaction performed by laccase.

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Transition metal substituted polyoxometalates: potentialities in oxidation by hydrogen peroxide

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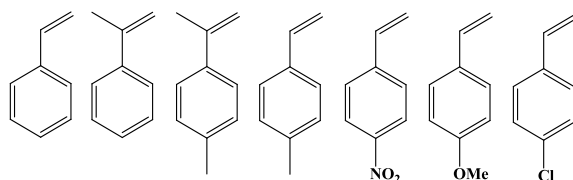
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Throughout the last few decades, polyoxometalates (POMs) have received great attention [1-5], since this compounds present an easily and economic synthesis, having structural versatility and properties that can be straightforwardly tuned. All these factors led to its use in several applications, ranging from materials science to catalysis and medicine [2-4]. Particularly, their use as catalysts for oxidation reactions has been an important research goal, given that POMs may be viewed as possessing reactive low valent transition metal centres complexed by inorganic oxometalate ligands [5-6].

The use of H₂O₂ in the oxidation of organic substrates is very attractive from the point of view of industrial technology and synthetic organic chemistry, since dilute aqueous H₂O₂ is cheap, environmentally clean and easy to handle [7].

We will present the results obtained in the oxidation of different styrenes (Scheme 1) with H₂O₂, in the presence of the tetrabutylammonium salts of [XW₁₁M(H₂O)O₃₉]ⁿ⁻, X = P, Si or B; M = Fe^{III}, Mn^{III} or Co^{II}. The oxidation of the different substrates always occurs at the vinyl substituent, and gives rise to the carbon-carbon double bond cleavage as the main oxidation pathway. The efficiency and the selectivity associated with the different catalysts tested will be presented and discussed. The influence of the different derivative groups at the styrene will also be discussed.



Scheme 1. Substrates used in the present homogeneous catalysis studies

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From 2-hydroxypyridine to 4(3*H*)-pyrimidinone: the role of aromaticity, hydrogen bonds and substituent effects in tautomeric equilibrium

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The question of why the entrance of a nitrogen atom in the ring of *cis*-2-hydroxypyridine and 2-pyridinone, to give *cis*-4-hydroxypyrimidine and 4(3*H*)-pyrimidinone, respectively, shifts the tautomeric equilibrium from the hydroxyl form, in the pyridine derivative [1], to the ketonic form, in pyrimidine derivative [2,3], is addressed in the present work.

The influence of aromaticity, intramolecular hydrogen bonds and electrostatics were evaluated using NICS, Quantum Theory of Atoms in Molecules, Natural Bond Orbital Analysis, Atomic Charges and several computational methods for calculating the thermodynamic changes of appropriate reactions.

The conclusions obtained for these model systems allow to understand how to control the gaseous-phase keto-enol tautomeric equilibrium in nitrogen rings and justify the tautomeric preference in pyrimidine nucleobases.

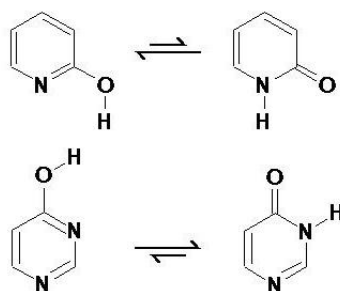


Figure 1. Tautomeric equilibrium between *cis*-2-hydroxypyridine (I) and 2-pyridinone (II), and between *cis*-4-hydroxypyrimidine (III) and 4(3*H*)-pyrimidinone (IV).

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Fate of the antiepileptic drug carbamazepine at the water/soil interface

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Pharmaceuticals are important organic pollutants which occur ubiquitously in the environment. These compounds are continuously being introduced in the environment mainly due to the inadequacy of the treatment methods applied in waste water treatment plants (WWTPs) [1,2]. Apart from WWTP's effluent release in surface waters, which highly contributes to aquatic contamination, the application of sludge in agricultural fields and the use of effluents for irrigation constitute important sources of soil contamination [3]. Consequently, the assessment of the interaction between pharmaceuticals and soils is of crucial importance to understand their fate in the environment.

In this study, the adsorption behavior of carbamazepine (one of the most frequently detected pharmaceuticals in the environment) onto agricultural soils was investigated. For this purpose, batch equilibrium experiments were performed using soils subjected to distinct long-term fertilizations. The adsorption experiments were followed by UV spectral deconvolution (UVSD) and by micellar electrokinetic chromatography (MEKC) allowing to compare the performance of both methods. The adsorption of carbamazepine onto the studied soils was satisfactorily described by the Freundlich model. Overall, the obtained results indicate that the adsorption behavior of carbamazepine is dependent on the type of fertilization. Also, it is not extensively adsorbed, highlighting that carbamazepine present in soils can be a potential source of contamination of surface and ground waters through run-off and infiltration. This study points out the environmental risks involved in the application of treated effluents and sludge for agricultural purposes, taking into account that the presence of carbamazepine in these matrices is generalized worldwide.

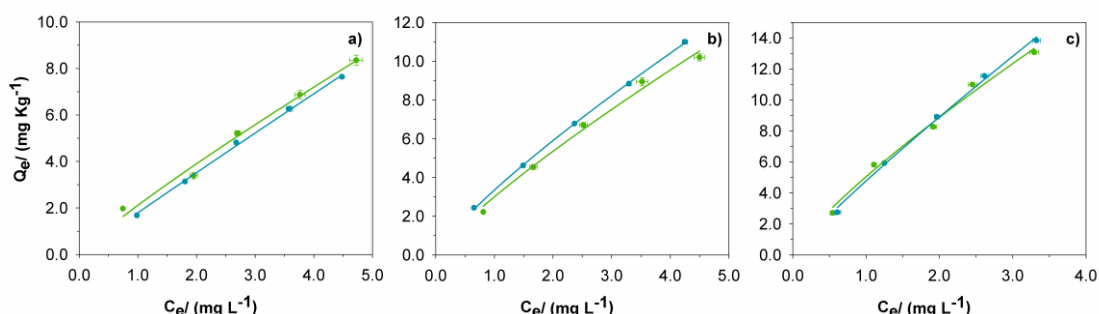


Figure 1. Adsorption isotherms of carbamazepine considering the soils subjected to a) mineral fertilization, b) sewage sludge fertilization and c) compost organic fertilization. Results obtained by MEKC and UVSD are shown in green and blue, respectively.

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Structural and thermophysical studies of 9-acridanone and 10-methyl-9-acridanone

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Acridanone is a heteropolycyclic compound with two benzene rings fused to a hexagonal central ring containing the amino and the keto groups in *para* position. The presence of these two substituents lends to this compound and to its derivatives a wide spectrum of properties, like considerable biological activity, strong absorption and emission in the UV-Vis region, among others. For these reasons acridanones are used as suitable models for the characterization of entities being simultaneously aromatic amines and ketones.

The present work presents computational and experimental studies of 9-acridanone (**a**) and one derivative with a methyl group linked to the nitrogen, the 10-methyl-9-acridanone (**b**), whose structures are presented in Figure 1.

The experimental work corresponds to a thermophysical study using the Calvet microcalorimetry technique, allowing the determination of the standard molar enthalpy of sublimation, at $T = 298.15$ K, of the two compounds. Some thermophysical data for 9-acridanone are already available in the literature [1], however the accuracy of the results is crucial for the basis of predicting schemes, and that is the reason for the redetermination of those parameters.

In the computational study the effect of the bonding of the methyl group on the nitrogen was analyzed comparing the structures of acridanones, optimized by the B3LYP/6-31G(*d*) method, and the electrostatic potential map, from total self consisting field density, of the 9-acridanone (**c**) and 10-methyl-9-acridanone (**d**) molecules (in Figure 1), determined by studies based on Natural Bond Orbital (NBO) theory.

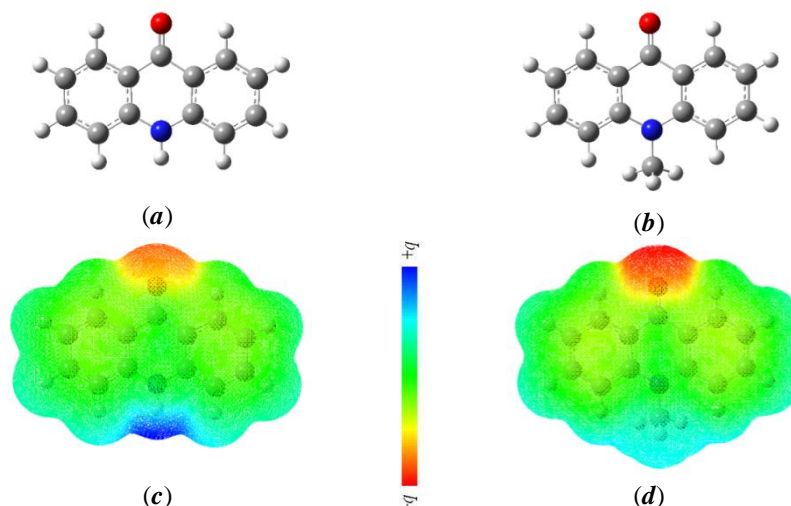


Figure 1. Structures optimized at the B3LYP/6-31G(*d*) level of theory and electrostatic potential map (isovalues 0.001 a_0^{-3}) for the gaseous molecules 9-acridanone (**a**, **c**) and 10-methyl-9-acridanone (**b**, **d**), respectively.

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Host:guest binding constant influenced by the host counterion

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Calixarenes are host frameworks that belong to the most versatile building blocks in supramolecular chemistry. When they are functionalized at upper rim with sulfonate groups, these calixarene became water soluble, which combined with a preorganized framework and biological compatibility [1], allow that these calixarenes have a variety of applications in the field of molecular recognition/sensing [2].

Recently we have confirmed by ^{23}Na relaxation NMR measurements and self-diffusion coefficients that the counterion of *p*-sulfonatocalix[4]arene (SC4) is complexed by the host[3]. This is, in the absence of added salts and at neutral pH, the cavity of *p*-sulfonatocalix[4]arene (SC4) fully binds an Na^+ counterion. Our hypothesis is that if Na^+ binds to the SC4, then a competition between the guest and the counterions should be considered. As a result, the binding constants should be affected by the SC4 concentration.

Calorimetric titration experiments have been done to measure the binding constant between SC4 and a quaternary ammonium ion, benzyltrimethylammonium bromide (BTA). In the experiments, the SC4 concentration was kept constant and without adding buffer to thereby maintain constant the concentration of Na^+ . These two aspects were not taken into account in the complexation of guests by SC4 and therefore comparison of literature data must be made with great care. Changing the SC4 concentration or adding buffers changes the Na^+ concentration in solution and therefore the fraction of cation-free calixarene. Our results show that the binding constant depend on the calixarene concentration.

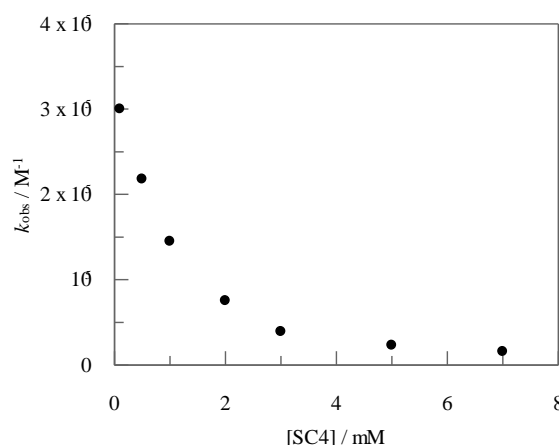


Figure 1. Influence of SC4 concentration on K_{obs} for the complex formation between BTA and SC4 at 25°C. The K_{obs} values were obtained by microcalorimetric titrations and fitted to the “one set of binding sites” model.

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The mathematical description for the electrochemical synthesis of heterocyclic compounds in galvanostatic mode

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Conducting polymers have been one of the most investigated compounds for the last decades. They have been already gained different application, beginning from the corrosion-protecting coatings and ending with biosensors, because they are capable to combine the characteristics of plastics (light weight, tough, resiliency in shaping and corrosion resistance) with the metal conductivity and also the facility to be modified.

One can gain conducting polymers either by chemical synthesis, or by electrochemical and the last one nowadays is recognized as more advantaged, because the conducting polymers obtained electrochemically (by electropolymerization) are better conductors because of the presence of the dopant and also because of better complanarity of polymeric chain.

The electropolymerization of heterocyclic compounds can be realized in three modes – potentiostatically, galvanostatically and potentiodynamically. The potentiostatic electropolymerization is most used, because the polymer that synthesizes itself in those conditions is better conductor and has less defects. Also, the working potential is easy to be found by cyclic voltamperometry. The galvanostatic electropolymerization is used to get thin films, but the value of current density, applied to the system is difficult to be determined and the electrosynthesis may be accompanied by overoxidation, giving origin to the phenomena, relative to the “polythiophene paradox”.

Either in galvanostatic mode, or in potentiostatic and potentiodynamic modes the electropolymerization is accompanied by electrochemical instabilities. For example, the potential oscillations in galvanostatic mode were observed during the electropolymerization of thiophene and pyrrole and the current oscillation in potentiostatic mode were observed during the electropolymerization of indole and thiophene.

Although the phenomenological explanation for this phenomena can be accepted, it won't have exact aprobaton, gained by development of mathematical model, capable to describe adequately the processes in this system. The three-dimensioned mathematical model that describes the behavior in this system can be represented as

$$\begin{cases} \frac{dc}{dt} = \frac{2}{\delta} \left(v_{-1} - v_1 + \frac{D}{\delta} (c_s - c) \right) \\ \frac{d\Theta}{dt} = \tilde{A}_{t,max} (v_1 - v_{-1} - v_2) \\ \frac{dq}{dt} = i - i_F \end{cases}$$

In which c is the monomer concentration in the pre-surface layer, θ – the coverage degree of the anode surface by monomer, q – electrode charge v_1 , v_{-1} and v_2 are adsorption, desorption and electropolymerization rates, $\Gamma_{t,max}$ is the maximal surfacial concentration of the monomer, D is the diffusion coefficient, δ is the diffusion layer thickness, i is the anodic current density and i_F is the Faraday current.

The steady-state stability conditions were found by analysis of the equation system. The oscillatory instability has to be caused by attraction between adsorbed particles and by influences of the electropolymerization process to the double electric layer (DEL).