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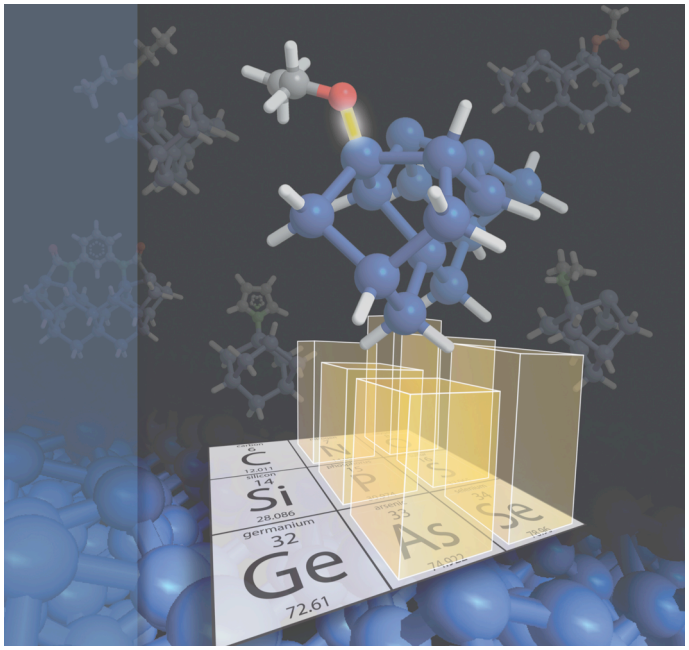
MASTERQO

MÁSTER UNIVERSITARIO EN QUÍMICA ORGÁNICA

XIV Simposio

Máster Interuniversitario en Química Orgánica



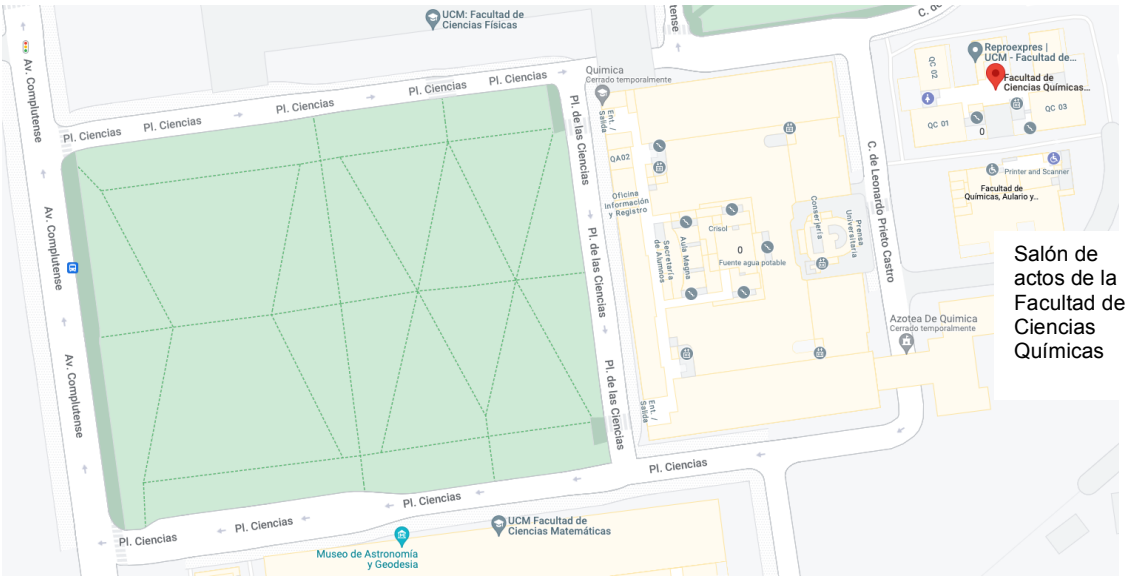
Universidad Complutense de Madrid

15-17 de Junio de 2022

INFORMACIÓN GENERAL

XIV Simposio del Máster Interuniversitario en Química Orgánica

El Simposio tendrá lugar en la Facultad de Ciencias Químicas y en el Aulario de la Facultad de Farmacia de la Universidad Complutense de Madrid.



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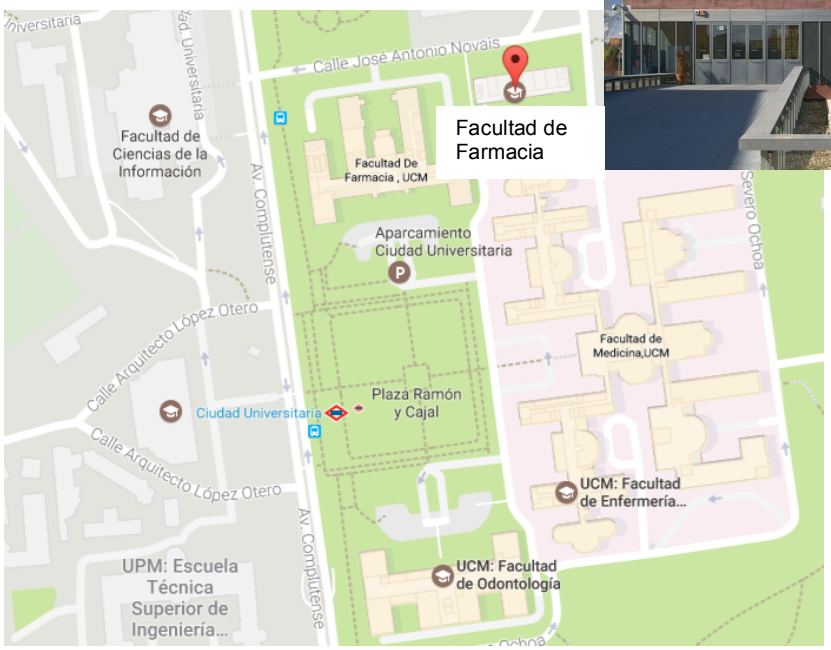

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PROGRAMA

XIV Simposio del Máster Interuniversitario en Química Orgánica

Universidad Complutense de Madrid
Facultad de Ciencias Químicas y Aulario de la Facultad de Farmacia

15 de Junio de 2022
12:15 Apertura

12:30 Conferencia: “Luces y sombras de la genética y la genómica forenses en el siglo XXI”.
Dr. Antonio Alonso (Instituto Nacional de Toxicología y Ciencias Forenses)
Salón de Actos de la Facultad de CC. Químicas

16:00 Sesión de Pósteres I (P1-P28) (Sótano Aulario Facultad de Farmacia)

16 de Junio de 2022
9:30 Sesión de Pósteres II (P29-P48) (Sótano Aulario Facultad de Farmacia)

12:30 Conferencia: “Astroquímica y origen de la vida” Dr. José A. Martín Gago (ICM, CSIC)

16:00 Sesión de Pósteres III (P49-P66)

17 de Junio de 2022
10:00 Visualización de vídeos (Aula QC-13, Fac. de CC. Químicas)

12:00 Encuestas (Aula QC-13, Fac. de CC. Químicas)

13:30 Entrega de premios y Clausura (Aula QC-13, Fac. de CC. Químicas)

ORGANIZACIÓN

Comité Organizador Local

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Mar Gómez Gallego (UCM)
Silvia Ortega Gutiérrez (UCM)

Departamento de Química Orgánica I, Facultad de Ciencias Químicas,
Universidad Complutense de Madrid

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Ramón Gómez (UAM)
Pablo Mauleón (UAM)
Mercedes Rodríguez (UAM)
Gabriel Tojo (USC)
Mercedes Torneiro (USC)

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Vizuete, Marta	UCM	P65

ABSTRACTS

Synthesis of benzylic sulfinic acid via decatunstage photocatalysis: methodology evaluation, and diversification into a rage of medicinal chemistry relevant functional groups

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Keywords: *Photocatalytic hydrogen atom transfer (HAT), Tetra-butylammonium decatugnstate (TBADT)*

Photochemical organic chemistry is at the center of the most current breakthroughs in synthetic chemistry. The huge interest and possibilities are due to its ability to perform and/or simplify challenging transformations that otherwise would be impossible or would take more steps. The number of new transformations and the variety of new catalytic systems is growing rapidly transforming this methodology in one of the most powerfull medicinal chemistry synthetic tools[1].

However, one of the limitations is the inconsistencies observing while transferring the reaction conditions described in the literature and their application as efficient processes for drug discovery efforts. This is because there is still much to learn in the effects of increasing scales and light sources.

To demonstrate the broad potential of this methodology for the divergent synthesis of pharmaceutically relevant molecules, here we evaluate the direct conversion of strong aliphatic C(sp^3)-H bonds into the corresponding benzylic sulfinic acids via TBADT photocatalysis[2], as well as representative diversification reactions of the sulfinic acid products into a range of medicinally relevant functional groups.

The investigation demonstrates the reproducibility of this approach from initial batch conditions, which was extended to supply on demand different substrates using a flow chemistry reactor, as well as their transformation in sulfonamides, sulfones, and sulfides broadly found in modern materials, agrochemicals, and pharmaceuticals[3].

References:

[1] Noël, T. and Zysman-Colman, E. The promise and pitfalls of photocatalysis for organic synthesis. *Chem Catalysis* **2022**, *2* (3), 468-476

[2] (a) Wan, T.; Capaldo, L.; Laudadio, G.; Nyuchev, A.; Rincon, J.; Garcia-Losada, P.; Mateos Gutierrez, C.; O. Frederick, M.; Nuno, M. and Noël, T. Decatungstate-Mediated C(sp^3)–H Heteroarylation via Radical-Polar Crossover in Batch and Flow. *Angewandte Chemie International Edition* **2021**, *60* (33), 17893–17897. (b) Patrick J. Sarver, Noah B. Bissonnette, and David W. C. MacMillan. Decatungstate-Catalyzed C(sp^3)–H Sulfinylation: Rapid Access to Diverse Organosulfur Functionality. *Journal of the American Chemical Society* **2021** *143* (26), 9737-9743

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Polymorphism in supramolecular polymerization of N-annulated PBIs

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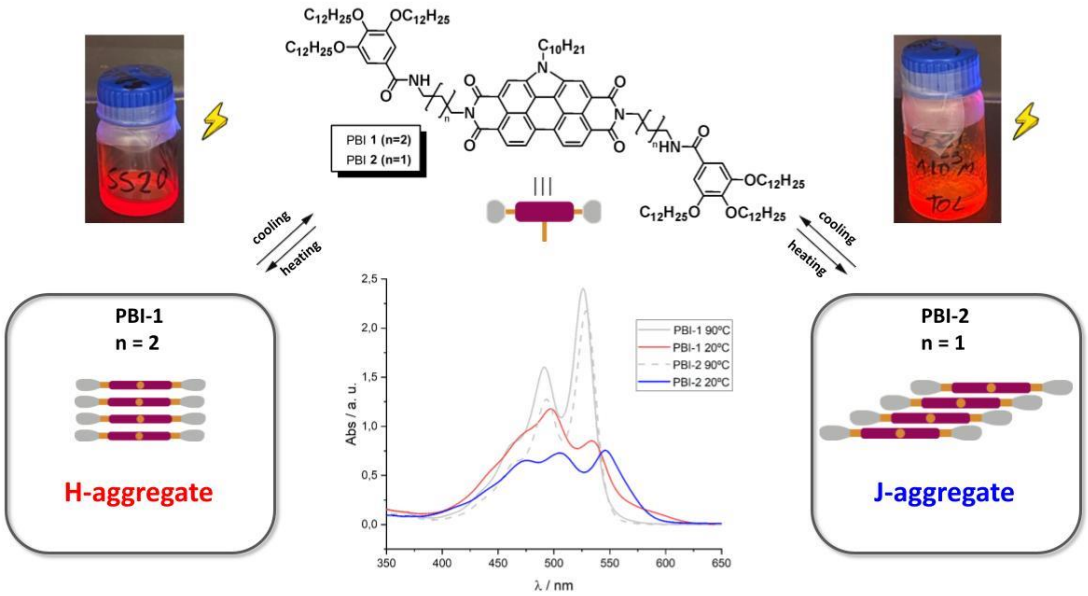
Keywords: *(NPBI, supramolecular polymers, self-assembly)*

In this project, the synthesis of two N-annulated perylenebisimide derivatives (NPBIs, **1** and **2**) has been carried out by following a multistep protocol in good analogy to that previously described in our research group. The chemical structure of these derivatives allows an efficient self-assembly, resulting in the formation of supramolecular polymers via hydrogen bonding, π-stacking of the aromatic units and Van der Waals interactions between the peripheral chains.[1] These self-assembling features for both derivatives **1** and **2** have been studied by different spectroscopic techniques such as FTIR, ^{1}H-RMN and UV-Vis. ^{1}H-RMN experiments at variable concentration show the displacement of the resonances corresponding to the aromatic and amide protons, indicating the self-assembly for both PBI derivatives in these experimental conditions.

Variable temperature UV-Vis (VT-UV-Vis) studies demonstrate the strong impact of the length of the central linker connecting the central aromatic unit and the peripheral trialkoxybenzamide units in good agreement to referable self-assembling systems.[2] Thus, whilst **1** forms H-type aggregate, the formation of a J- type aggregate is observed for **2**.



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[1] (a) de Greef, T. F. A.; Smulders, M. M. J.; Wolffs, M.; Scheening, A. P. H. J.; Sijbesma, R. P.; Meijer, E. W. *Chem. Rev.* **2009**, 109, 5687–5754; (b) Aida, T.; Meijer, E. W.; Stupp, S. I. *Science* **2012**, 335, 813–817.

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Chiral Poly(disubstitutedacetylene)s with Potential AIEgens as Pendant Groups

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Keywords: *Helical Polymers, AIEgen, Circular Dichroism*

Helical structures are a fundamental part of the molecular organization of biomacromolecules such as proteins, DNA or polysaccharides.[1] The relation between the helical organizations of these molecules and their functions has inspired the scientific community to develop non-natural helical structures such as foldamers, supramolecular helices or synthetic helical polymers.[2]
Poly(diphenylacetylene)s are helical polymers useful in the creation of smart materials with applications in sensing or chiral recognition.[3] In this project, we explored the possibility of replace one of the aromatic rings of the diphenylacetylene m.r.u. by a molecule that presents aggregation-induced emission (AIEgen) and to study its properties with different techniques such as circular dichroism (CD) and ultraviolet (UV) spectra as shown in Figure 1.
Aggregation-induced emission (AIE) is a photophysical phenomenon in which non-emissive luminogens are induced to emit by the formation of aggregates.[4] The possibility of incorporate these fragments in helical polymers open the opportunity to access to new materials with interesting properties for optoelectronic applications.

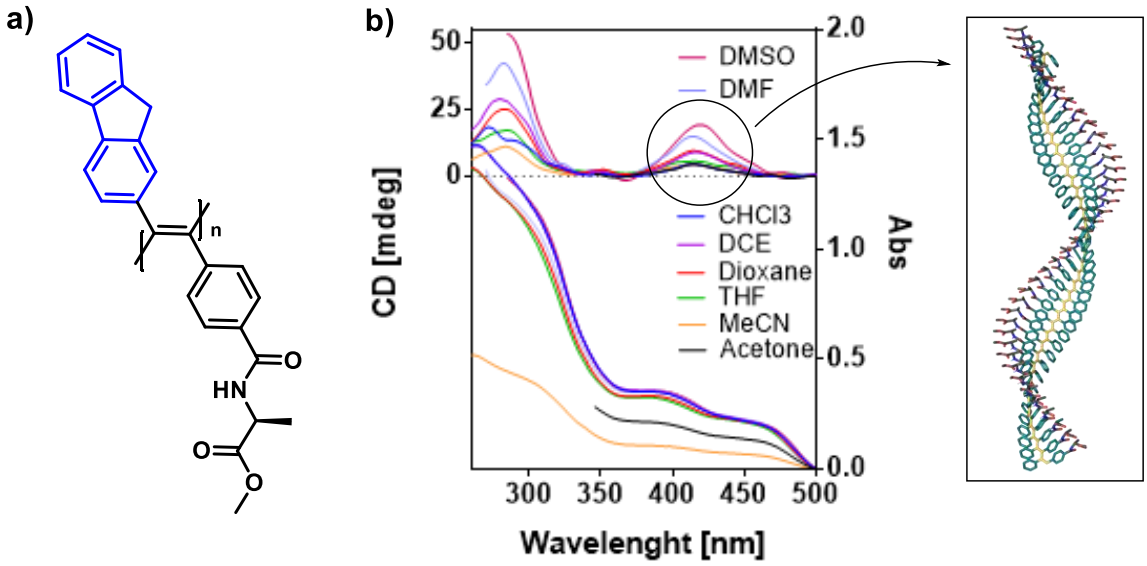

Figure 1. a) Schematic structure of Poly-(*S*)-1 and b) CD and UV spectra of poly-(*S*)-1 in different solvents and schematic helical structure of the corresponding PDPA.

References:

[1] (a) Pauling, L.; Corey, R. B.; Branson, H. R. *Proc. Natl. Acad. Sci. U.S.A*. **1951**, *37*, 205). (b) Watson, J. D.; Crick, F. H. *Nature* **1953**, *171*, 737. (c) Hinrichs, W.; Büttner, G.; Steifa, M.; Betzel, CH.; Zabel, V.; Pfannemüller, B.; Saenger, W. *Science* **1987**, *238*, 205.
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Towards polycyclic scaffolds via sequential Aryl palladation of alkynes/Pd 1,4-migration

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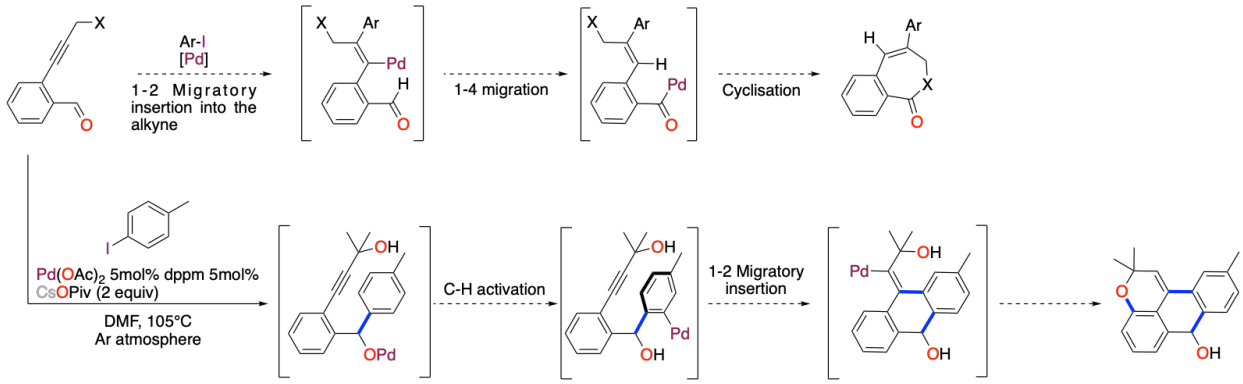
Keywords: *C-H activation, Pd 1-4 migration, Pd-catalysed hydroarylation*

This project aims to build benzo[c]oxepin-1(3H)-one- and benzo[c]azepin-1(3H)-one-type scaffolds via a strategic 1-4 “through space” palladium migration to an aldehyde from a strategic vinyl palladium species formed by the migratory insertion of an aryl-palladium species to an alkyne.



Scheme 1: Graphical abstract

Instead, employing conditions found in the literature,[1] we discovered a process in which a tetracyclic system is formed. The proposed mechanism for this transformation involves an initial aryl-palladium 1-2 migratory insertion into the aldehyde (Barbier-type reaction) instead of the alkyne, followed by an OH-coordination directed C-H activation of the inserted ring forming an aryl-palladium species which is able to suffer an intramolecular insertion into the alkyne, followed by protodepalladation and another OH-coordination directed CH-activation and cyclisation or a migration of the palladium and a final cyclisation.

Although this reaction differs from the aimed reactivity; it represents a rare example of a palladium mediated intermolecular Barbier reaction which might open new routes in the cascade reactions field.

References:

[1] Tanay Kesharwani, Akhilesh K. Verma, Daniel Emrich, Jeffrey A. Ward, and Richard C. Larock. Organic Letters **2009** 11 (12), 2591-2593

Synthesis of new entry inhibitors for SARS-CoV-2 based on multivalent derivatives of tryptophan

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Keywords: *entry inhibitors, SARS-CoV-2, tryptophan*

SARS-CoV-2 is the etiological agent of COVID-19, a pandemic that have impacted the world in the last three years. Despite the quick development and commercialization of different vaccines against this pathogen, there is a clear need for effective antivirals to be used in a combination therapy.[1]

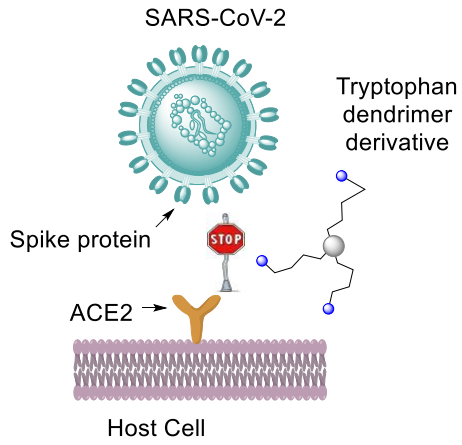

Figure 1. Multivalent derivatives of tryptophan as entry inhibitor.

Based on the identified hits, **new multivalent compounds** tryptophan derivatives have been synthesized. In particular, the **N1 position of the indol** of the Trp units has been functionalized with a **substituted phenyl group** through different chemistry strategies to determine how the **conformational freedom** of this substituent could affect their **antiviral activity** (**Figure 2**).

Our research group has been involved in the design and synthesis of entry inhibitors against HIV-1 and Enterovirus-A71 based on **multivalent derivatives of tryptophan**.[2] Selected members from our own collection of Trp derivatives have been tested in a HTS system settled up to identify compounds able to **block the interaction** between the viral SARS-Cov-2 **spike protein** and the host cellular **receptor ACE2** (**Figure 1**).

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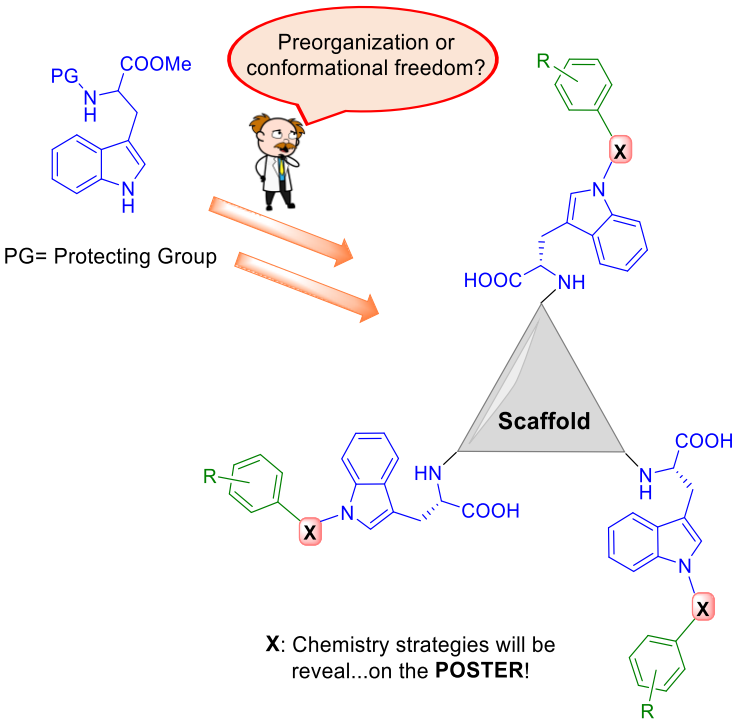

Figure 2. General strategy to synthesize multivalent tryptophan derivatives.

References:

[1] Kozlov, M. *Nature.* **2022,** 601, 496. DOI: 10.1038/d41586-022-00112-8

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Impact on the Catalytic Efficacy of Class D β-Lactamase Enzymes of Modifications on its Amino Acid Sequence

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Keywords: *antibiotic bacterial resistance, β-lactamase enzymes, in silico studies*

The utility of β-lactam antibiotics, which compromise 70% of all antibacterial drugs in clinical use, is being threatened by the ever-increasing production and dissemination worldwide of β-lactamases. These enzymes confer resistance to β-lactam antibiotics through hydrolysis of the β-lactam ring to afford inactive products, thus preventing the inhibition of their therapeutic target [1]. This inactivation process is one of the most relevant resistance mechanisms in Gram-negative bacteria, including the multidrug-resistant pathogens highlighted by the World Health Organization (WHO), namely *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacteriaceae.*

Antibiotic resistance evolves rapidly, often on the course of a long-term therapy (weeks). This is caused by bacteria exchanging resistance-conferring genes with each other, or by an individual bacterium becoming resistant through mutations in its own genes. Resistant bacteria are more likely to survive antimicrobial treatments and spread the infection to other individuals. Recently, we have described examples of patients hospitalized in the ICU who underwent intensive treatment with the latest generation combination therapy for the treatment of infections caused by *P. aeruginosa or A. baumannii* (ceftolozane@tazobactam) that evolve resistance to the antibiotic during treatment by rapidly producing more efficient β-lactamases [2]. We demonstrated that this is due to modifications on the amino acid sequence in remote positions, globally imperceptible in the enzyme architecture, resulting in significant improvement of the hydrolytic capacity of the enzyme (up to 17-fold). This project is directed to know if there is a « *evolution pattern* », as well as the « *hot spot regions in these high-risk β-lactamase enzymes* » to develop a platform for predicting the « *evolution pattern to antibiotics of these enzymes*». This would facilitate earlier diagnosis and successful selection of the suitable therapy.

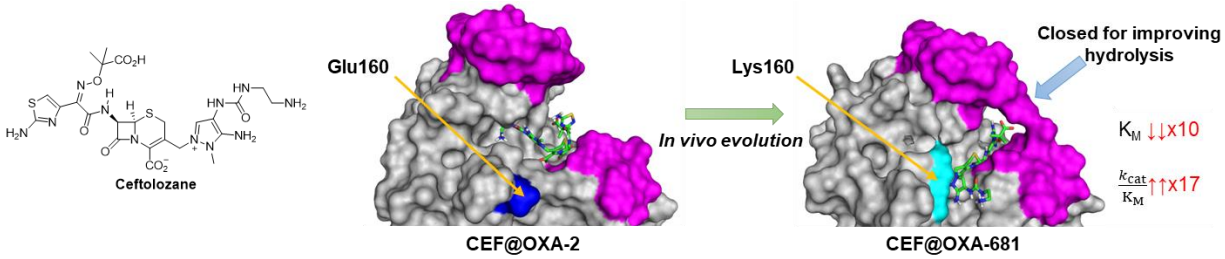

Figure 1. Example of the impact on the catalytic efficiency of the modification of Glu160 by Lys160 in the OXA-2 enzyme. The new variant OXA-681 enzyme improves its hydrolytic capacity of ceftolozane by 17-fold. Note how this change causes the closing of the active site to enhance substrate recognition.

References:

[1] (a) González-Bello, C.; Rodríguez, D.; Pernas, M.; Rodríguez, A.; Colchón, E. *J. Med. Chem.* **2020**, *63*, 1859. (b) Ben, Z.; Hanen, S. *Chem. Rev.* **2017**, *99*, 3181. (b) Lence, E.; González-Bello, C. *Adv. Therap.* **2021**, *4*, 2000246. (c) Lence, E.; González-Bello, C. *Front. Microbiol.* **2021**, *12,* 721826.

[2] Arca-Suárez, J.; Vázquez-Ucha, J. C.; Fraile-Ribot, P. A.; Lence, E.; Cabot, G.; Martínez-Guitián, M.; Lasarte-Monterrubio, C.; Rodríguez-Iglesias, M.; Beceiro, A.; González-Bello, C.; Galán-Sánchez, F.; Oliver, A.; Bou, G. *J. Antimicrob. Chemother.* **2020**, *75*, 3209.

Synthesis of carbohydrate-BODIPY hybrids for bioimaging applications

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Keywords: *BODIPY, carbohydrate*

The increasing use of bioimaging techniques for in vivo studies has triggered, among others, the development of fluorescent tags for carbohydrates.[1] In this context, **bo**ron**dipy**rromethene (BODIPY) dyes have enjoyed ample recent recognition. BODIPYs display high thermal, chemical, and photochemical stability, along with elevated molar absorptivity and fluorescence quantum yields. In addition, subtle structural modifications of the BODIPY core produce interesting variations in their photophysical properties.[2] However, despite being zwitterionic species, BODIPYs are still highly hydrophobic compounds, and their solubility in aqueous or physiological media might become an issue in certain applications. In this regard, carbohydrates could play an important role in designing water-soluble or amphiphilic BODIPY-based dyes. Furthermore, the covalent attachment of a carbohydrate to a BODIPY fluorophore could significantly improve the selectivity of the dye toward a specific biological target and even reduce its toxicity.[3]

Along these lines, we have focused on the preparation of two families of water-soluble fluorescent dyes by a chemoselective ligation reaction between racemic BODIPY-methoxyamine derivative **1,** and suitable reducing carbohydrate derivatives. This coupling reaction provided fluorescent products **2,** that displayed good water solubility. These derivatives, which exist as diastereomeric pairs because of the axial chirality of BODIPY **1**, could not be separated at this stage. However, to our delight, the incorporation of an additional disaccharide unit (through a CuAAC click reaction) in its structure, as in **3**, permitted their separation as diasterereomerically pure compounds.

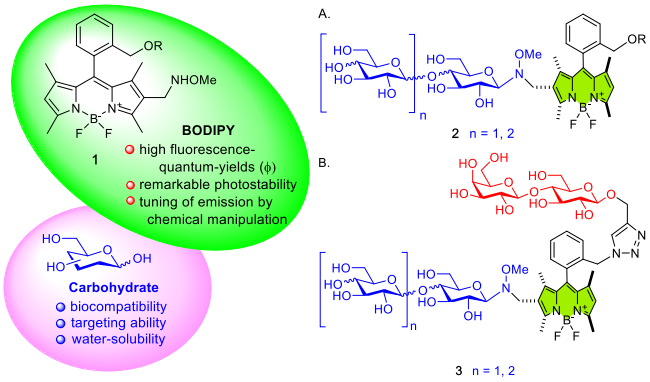

Figure 1. Main advantages of carbohydrates and BODIPYs (left), and general structures of families **2** and **3** (right).

References:

[1] a) X.-P. He, Y. Zang, T. D. James, J. Li, G.-R. Chen and J. Xie, *Chem. Commun.*, **2017**, *53*,82–90; b) B. Thomas, K.-C. Yan, X.-L. Hu, M. Donnier-Maréchal, G.-R. Chen, X.-P. He and S. Vidal, *Chem. Soc. Rev.*, **2020**, *49*, 593–641; c) A. M. Gomez and J. C. Lopez, *Chem. Rec.*, **2021**, *21*, 3112– 3130.

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SMART POLYMERIC MATERIALS: A NON-TOXIC ALTERNATIVE TO CHEMOTHERAPY

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Keywords: *Cancer, Heparanase Inhibitors, Heparin Derivatives*

An enzyme closely related to cancer is heparanase, which through its endoglycosidase activity has the capacity to remodel the extracellular matrix by degrading the heparan sulphates that form part of it, causing the release of angiogenic factors that favour tumour proliferation.[1, 2] The aim of this project has been to develop inhibitors of heparanase activity and the modification of a non-natural substrate of the enzyme, heparin, as it is closely related structurally to heparan sulphates, since both contain variably sulphonated repeating disaccharide units, thus avoiding the need to use heparan sulphates, which are difficult to isolate, as a substrate.[3, 4]

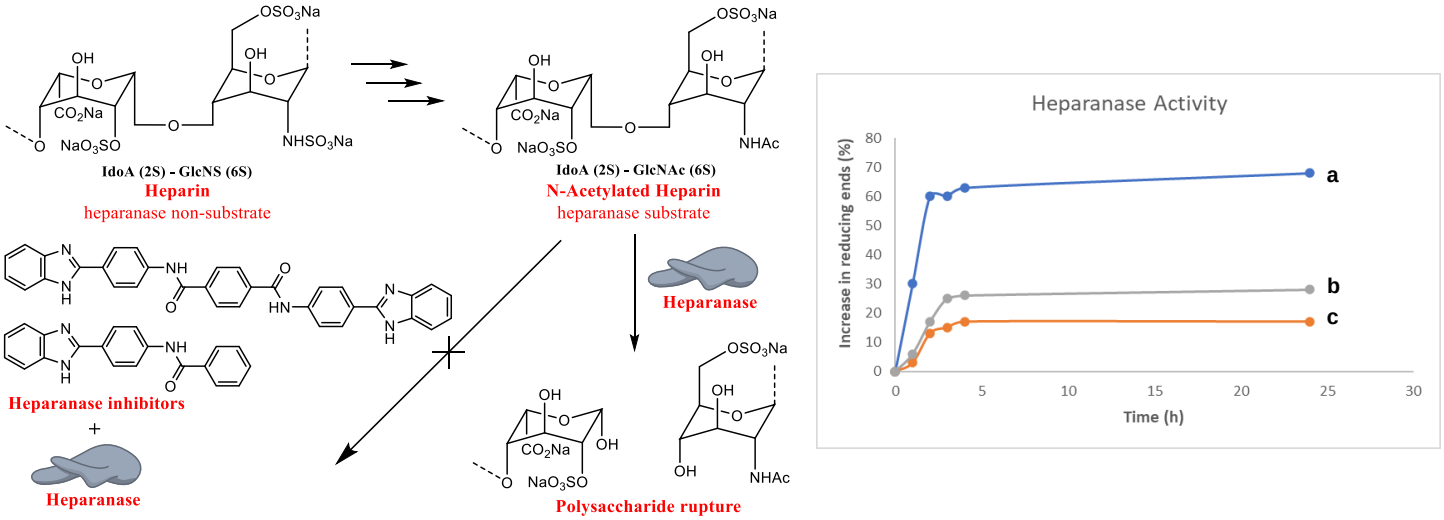

Figure 1. Difference in heparanase activity on substrate in the presence of enzyme inhibitors; **a)** Control, **b)** *N*-(4-(1H-benzo[d]imidazol-2-yl)phenyl)benzamide, **c)** N^1,N^4-bis(4-(1H-benzo[d]imidazol-2-yl)phenyl)terephthalamide

References:

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Novel Reactions of Alkylidenecyclopropanes Promoted by Gold(III): From New Gold(III)-Complexes to Catalytic Applications

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Keywords: *Catalysis, Gold (III), alkylidenecyclopropanes.*

Organic synthesis is a fundamental tool for the progress of many branches of science.[1] Progress in recent years has been impressive and the search continues for an ideal scenario wherein molecules could be synthesized in few steps, using cheap, environmentally friendly and sustainable materials.[2,3] One of the most attractive ways to advance in this direction consists of developing highly efficient catalytic reactions. In particular, organometallic catalysts are very appealing, as they allow to obtain complex molecules from simple, low-functionalized precursors.

Among the different types of metal catalysts, gold(I) complexes have been proven extremely efficient to unveil novel reactions with C-C unsaturated partners. Curiously, the development of related high-valent Au(III) catalysts clearly lagged behind.[4] Indeed, most Au(III) catalysts reported so far are still restricted to Au(III) halide salts that are unstable and many other Au(III) complexes are catalytically inefficient. In this context, our group, in collaboration with Nevado's lab developed in 2021 new types of [C^N]-gold(III) complexes (**2**), by proximal ring opening of 2-pyridil-alkylidenecyclopropanes (**1**, Figure 1).[5] More recently, alternative gold(III) complexes derived from o-pyridyldiphenyl alkylidenecyclopropanes were also obtained.[6]

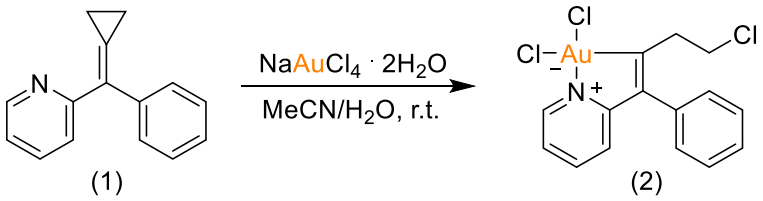

Figure 1. Synthesis of new gold complexes (III)[4].

Based on these precedents, in this project we will optimize the preparation of this latter Au(III) complexes and we will compare their catalytic performance with that of complexes of type **2**. Moreover, we will design and develop new routes aimed to prepare similar gold(III) complexes from related alkylidenecyclopropane precursors. Finally, analysis of the reactivity of these ACP's with Au(III) salts led as to discover a new functionalization reaction of ACPs, based on the proximal ring opening of the cycloprapanic ring.

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SELF-ASSEMBLED NANOTUBES BASED ON AMIDINIUM-CARBOXYLATE INTERACTIONS IN WATER

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Keywords: *amidinium-carboxylate salt bridge, supramolecular nanotubes, self-assembly*

Nature has shown its own capacity to facilitate self-assembly reactions such as the tube forming proteins like tubulin or even sequence-controlled polymerization, for example natural DNA strands, all with specific functions. Our group Nanostructured Molecular Systems and Materials (MSMn) has taken inspiration from said systems and tried to recreate these non-covalent interactions with organic molecules to form discrete tubular systems [1]. This project specifically focuses on the synthesis and study of supramolecular nanotubes which are made water-soluble due to various groups of tetra ethylene glycol. The monomers are synthesised with a "main-block" with lateral components amidine (A) and carboxylate (C) which can form hydrogen bonds and therefore will hold the cyclic structure together [2]. These cyclic dimers are formed due to the high complementarity and association strengths of these functional groups through the amidinium-carboxylate "salt-bridge" [3]. The dimers also have a rigid π-system that will allow the monomers to preform π- π stacking which promotes the polymeric self-assembly of the water-soluble nanotubes. These compounds will be analysed with spectroscopic techniques such as UV-vis and fluorescence. Further characterisation will be determined by microscopy techniques (SEM).

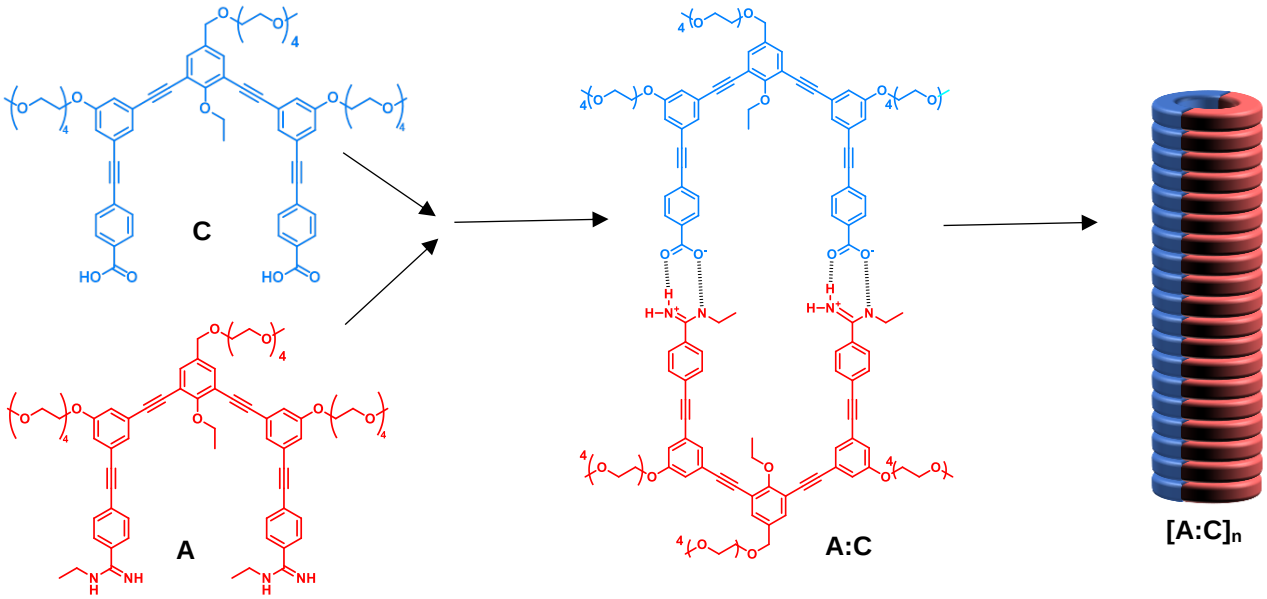

Figure 1. Showing the H-bonding interactions between the carboxylate and amidinium to form the dimer. These complementary monomers then self-assemble to form the water-soluble nanotube.

References:

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Synthesis and phenotypic study of small molecules inspired by human microbiota metabolites

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Keywords: *microbiota, leukemia, nucleophosmin-1 (NPM-1)*

Microbiota plays a major role in the maintenance of human health, in part through the secretion of metabolites that can regulate human proteins. Indeed, several metabolites have demostrated to have a key role in tumor protection.[1] In this context, our research group is involved in a project based on the hypothesis that microbiota metabolites represent an unexplored chemical space that could lead to the identification of new drug candidates for the treatment of cancer. A library of compounds containing privileged structures present in different microbiota metabolites was designed and synthesized using asymmetric organocatalytic reaction as key synthetic step. In a cancer phenotypic screening, compound UCM13369 was capable to promote the differentiation or death of cancer stem cells.[2] Differential proteomic studies revealed that UCM13369 reduces the expression of nucleophosmin-1 (NPM-1), a nuclear protein deregulated in various hematological cancers, which represents the most common mutation in acute myeloid leukemia (AML).[3] The interaction of NPM-1 with UCM13369 was confirmed by NMR experiments, confocal microscopy using a fluorescent probe, and in vitro activity in OCL-AML3 and MOLM13 cell lines, expressing the mutated and wild type protein, respectively. Importantly, UCM13369 induced cell death in hematopoietic stem cells in blood samples from AML patients, and has shown in vivo efficacy in a preliminary xenograft model of AML. The number of small molecules that interfere with NPM-1 is scarce and none of them has reached the clinic for AML.[4] Therefore, UCM13369 has entered a medicinal chemistry program for optimization towards a drug candidate for AML treatment. The present Master project, as a part of this program, is focused on the synthesis of new structural analogues of UCM13369, including the optimization of the organocatalytic Diels-Alder reaction employed for their preparation. Synthesized compounds will be assayed in AML cell lines, fibroblasts and renal cells for the assessment of in vitro efficacy and toxicity.

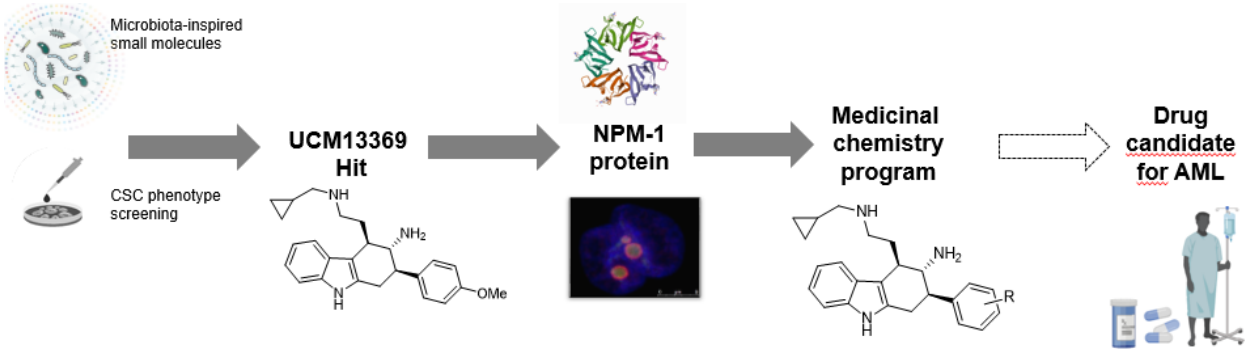

Figure 1. Medicinal chemistry program outline for the identification of NPM-1 inhibitors for AML treatment.

References:

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Synthesis of advanced catalytic materials based on chitosan-cyclodextrin: Development of a glucose detector

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Keywords: *Glucose detector, chitosan, cyclodextrin*

Chitosan is a biopolymer composed of β-(1-4) D-glucosamine and N-acetyl-D-glucosamine units. It is obtained commercially by the alkaline deacetylation of chitin, this being a structural element of the exoskeleton of crustaceans [1]. In this project, chitosan is used as the main axis for the immobilization of β-cyclodextrin (β-CD) molecules; for this union, different linkers were used and compared. The chitosan beads functionalized with the β-CD by means of the different linkers were characterized by infrared spectroscopy, fluorescence spectroscopy and elemental analysis.

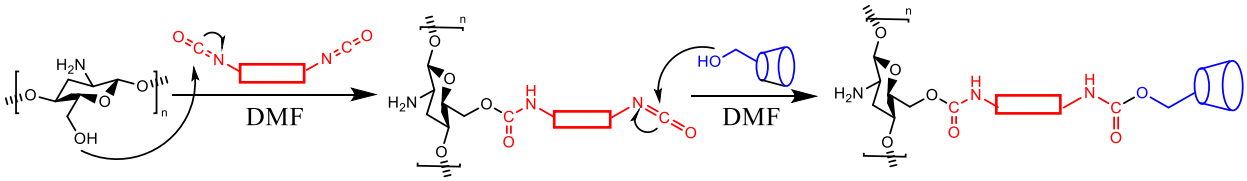

Figure 1. Direct conjugation between chitosan and β-cyclodextrin using a diisocyanate linker type.

The β-CD is capable of encapsulating molecules within it. One of the most used moieties for this purpose is the adamantyl molecule, the union between both is a host-guest interaction [2].

The ultimate aim of the project is to be able to immobilize enzymes in such system, for this purpose the enzymes are going to be functionalized with an adamantyl group, thus allowing the formation of the non-covalent β-CD - adamantyl complex. The enzymes that were immobilized were glucose oxidase and peroxidase, in order to be able to detect glucose.

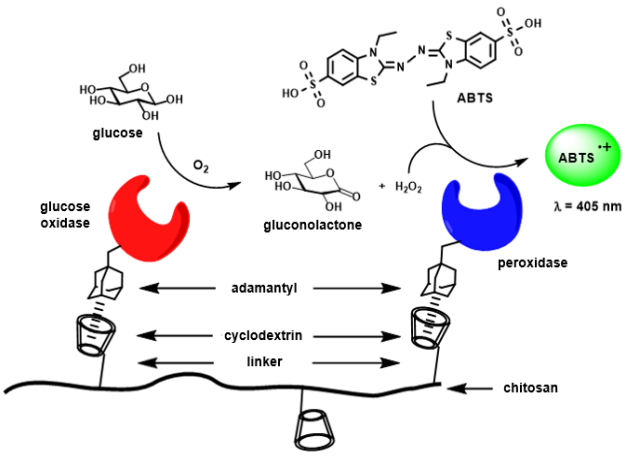

Figure 2. Glucose detector mechanism.

References:

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Gas-liquid microscale continuous Ozone Flow Platform validation: safe, robust, and efficient methodology for medicinal chemistry scaffold diversification

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Keywords: *Ozone, Microreactor, Flow Chemistry*

Discovered in 1839 by Friedrich Schönbein who named it after the Greek verb for smell (ozein), Ozone is a natural component present in the atmosphere with strong oxidant properties. Numerous applications were reported in organic synthesis particularly to take advantage of the high atom efficiency and the environmentally friendly behavior[1].

However, their wide use was limited due to safety issues because the low molecular weight ozonide and peroxides produced are unstable intermediates with potential to form an explosive hazard[2]. In addition, inconsistencies when transferring reaction conditions described in the literature and their application on medicinal chemsitry work, keep this transformation in the group of ´´forgotten chemistries´´.

One of the key features of flow chemistry is his ability to be combined with different methodologies, that allows to enable safer, robust, and efficient processes. In general, reactions in a confined space can achieve rapid mixing of reagents and heat transfer, which provide ideal chemical transformation environment.

To demonstrate the broad potential of the combination of ozone methodology and flow chemistry for the divergent synthesis of pharmaceutically relevant molecules, here we validate a flow microreactor prototype by testing the direct transformation of a variety of alkenes and alkynes, as representative diversification reaction to provide access to a range of medicinally relevant functional groups. The investigation demonstrates the reproducibility of this approach, which was extended to supply on demand different substrates, as well as their transformation in ketones, aldehydes, alcohol, acids, etc… broadly used by organic and medicinal chemist[3].

References:

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Engineering carbon nanostructures for the detection of physiological cations

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Keywords: *C_{60}, carbon dots, 18-crown-6*

The serendipitous discovery of buckminsterfullerene (C_{60})[1] by Kroto, Smalley and Curl brought about a new class of carbon based compounds that allowed the development of new structures with applications in many scientific areas, including biomedicine.[2] In this regard, the family of carbon nanostructures recently expanded with carbon dots (CDs), nanoparticles with a characteristic size of < 10 nm and exhibiting photoluminescence, which have stimulated intensive research for optical and electrochemical (bio)sensing.[3]

This work has focused in the synthesis of functionalized CDs and C_{60} derivatives to be used as biosensors for recognition of physiological cations. To obtain the CDs we applied a bottom-up strategy using urea and citric acid as precursors under hydrothermal and microwave conditions.[4] For C_{60} it was necessary to obtain a mono-adduct through a Bingel reaction. The desired materials containing an alkyne will be obtained from these structures to be coupled to an azido crown ether in a copper catalyzed “click” reaction.

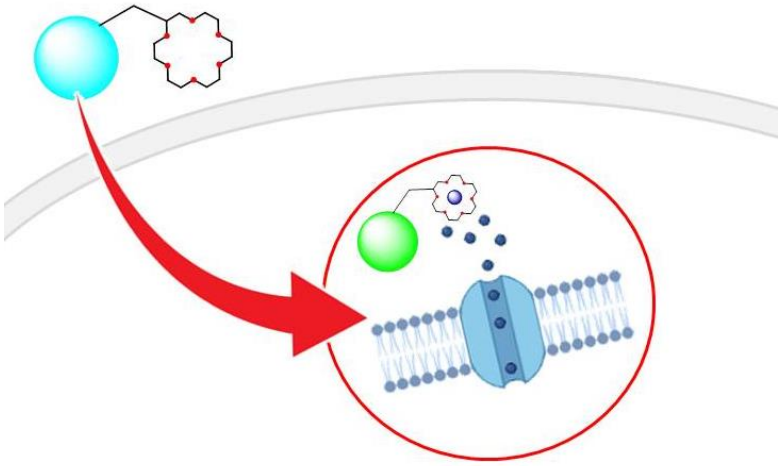

Figure 1. Idealized representation of 18-crown-6 derivatives of C_{60} or CDs working as biosensors for physiological cation recognition.

References:

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A Polyhydroxy/Alkyl Amphiphic Amides. Synthesis and IRI Activty

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Keywords: *Amides, Amphiphilic, Ice Recrystallization Inhibition (IRI)*

Body low molecular weight molecules capable of inhibiting the recrystallisation of ice are one of the most important synthetic targets for the scientific community, due to the enormous interest in their important applications (preservation of cells, organs, food, etc.).
Within the group of these molecules, *n*-butylamide of D-glucuronolactone **1b** (Figure 1), described some years ago by Prof. R. Ben[1] stands out for its excelent IRI activity. However, the modifications made to this molecule, preparing amides with monosaccharides with different stereochemistry in the hydroxyl groups than the D-glucose, such as D-galactose[1], L-Idose or L-Gulose[2] have resulted in molecules with very little or none IRI activity.
As a result of this, in this work we address the study of other modifications of amide **1b**, making changes in one of its two structural units:

- The alkyl chain (changing its length) to give amides **1a**,**1c** and **1d**.
- The hydroxylated chain (changing the number of hydroxyl groups) to give amides **2**, **3** and **4.**

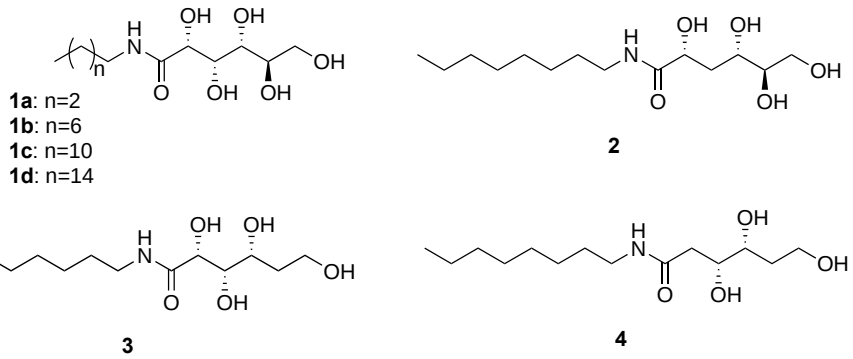

Figure 1

Studies on the IRI activity properties of this set of amides were also performed.

References:
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Nitrone condensation as an alternative in the assembly of porous organic materials: Synthesis and photocatalytic properties.

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Keywords: *(Material, Nitrone, Photocatalyst)*

From a general perspective, covalent organic polymers (COP's) constitute an emerging class of materials with a variety of relevant applications such as energy conversion and storage, gas storage and separation, sensing and catalysis. These materials are assembled through covalent bonding between organic building blocks usually via condensation or cross coupling reactions.[1] The nature of linkage groups determines the physical and chemical properties of the materials. The most common class of covalent linkages employed are boroxine, boronate ester, imine, β-ketoenamine, hydrazine, and cyanovinylene bonds.[2] However the organic chemistry toolkit offers many other possibilities to explore, opening the doors towards a next generation of materials with predesigned features. Following this idea, in this work we use a condensation reaction applied for the first time in the construction of an organic framework. In particular, herein we describe a material based on the generation of nitrone linkages from condensation of a tri-hydroxylamine and a di-aldehyde precursors. The obtained material is chemically robust and resistant to hydrolysis. It was fully characterized by solid ^{13}C RMN, infrared spectroscopy, UV-Vis absorption, light emission measured in solid state, powder X-ray diffraction, thermogravimetric analysis, gas absorption and scanning electron microscopy. In addition, we tested this material as a new heterogeneous photocatalyst in oxidation organic sulfides as a model reaction.[3] Interestingly, nitrone-based material shows better photocatalytic activities than its imine-based analogous material, pointing to the beneficial effect of nitrone moiety.

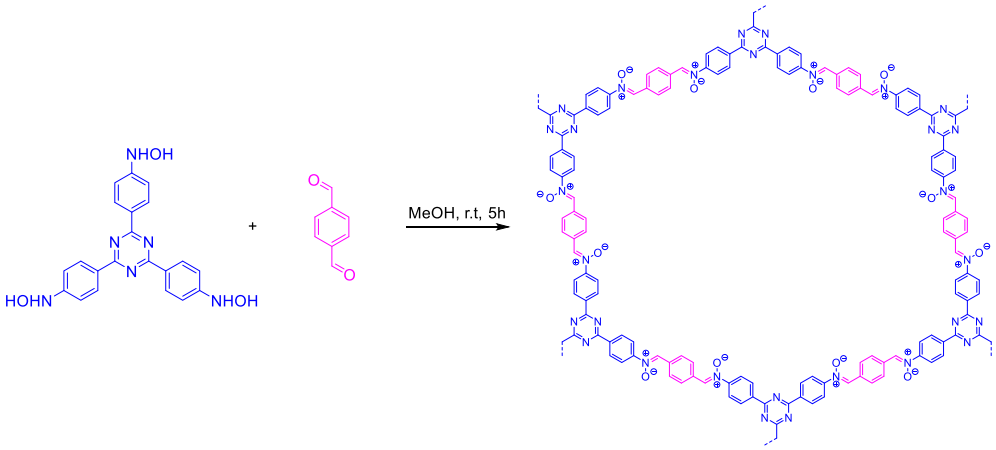

Figure 1. Material formation.

References

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Synthesis and validation of calcium-sensitive chemical probes for their application in new cellular diagnostic tools

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Keywords: *Ca^{2+}, Fluorescent probe, Calcium Detection.*

Ca^{2+} is an intracellular divalent cation involved in many biological phenomena and often acts as a second messenger in signaling pathways. Changes in subcellular free Ca^{2+} concentration serve as important cell signaling elements, regulating processes as diverse as neuronal excitability, enzyme activation and deactivation, cell apoptosis, and gene expression.[1] Abnormalities in Ca^{2+} signaling have severe pathological consequences and can result in neurodegeneration [2,3], disorders of the central nervous system, skeletal muscle defects, heart disease, and skin disorders among others.[4]

Therefore, the development of probes for specific Ca^{2+} detection is of great importance, as these probes exhibit altered fluorescent properties when bound with that cation. The focus of this work will be based on the synthesis of a novel fluorescent probe for the detection of Ca^{2+} which will be also functionalized for their covalent linking to microchip (**Figure 1**). This project has been developed in collaboration with the company *Arrays for Cell Nanodevices, SL*. [5]

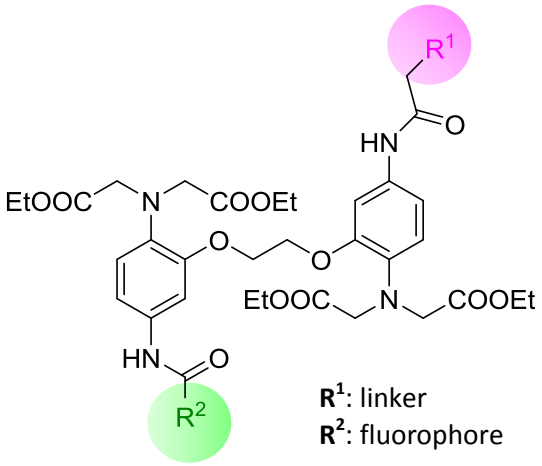

Figure 1. Generic scheme of the probe to be synthesized

References:

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Helical Polymers as Dynamic Chiral Catalyst in Asymmetric Synthesis

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Keywords: *Polymers, chirality, catalyst.*

In nature, the polymeric structure that plays a crucial role is helical conformation. This structural motif is part of many macromolecules such as coiled-coil helix bundle proteins, DNA superhelices or protein-DNA hybrid superstructures. Also, this type of conformation is inherently chiral, thus right- and left-handed scaffolds cannot be overlapped.

In organometallic catalysis the use of chiral ligands is very important, because it determines the enantioselective of the reaction. In this sense, we propose to combine these two ideas to develop a polymeric chiral ligand. In this field, some examples of enantioselective reactions using a helical polymer as ligand have been reported which led to pretty good enantiomeric excesses. Their promising results are due to the asymmetry induced on the periphery of the polymer where the reaction takes place.[1] However, the chiral effect could be improved if they were placed close to the helical backbone. Thus, in this work we propose poly(phenylacetylene)s (PPA)s derivatives as chiral ligand bearing phosphines groups at the monomers as catalytic active positions. PPAs are dynamic helical polymers, so this property makes them very interesting for asymmetric synthesis.[2] In addition, this type of polymers has a chiral pocket near the backbone polymer that could increase enantioselectivity.

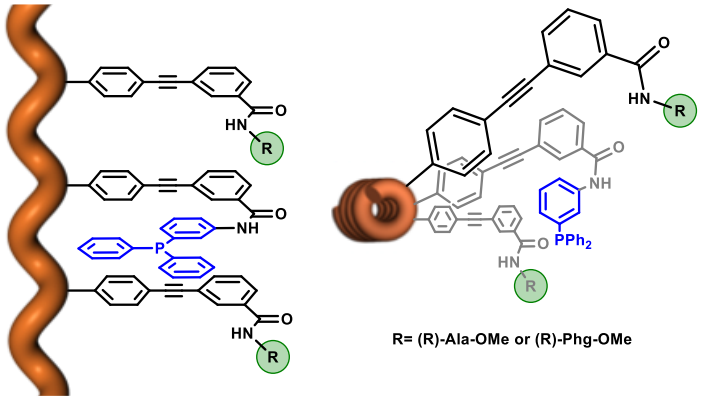

Figure 1. Side view (left) and top view (right) of our helical polymeric ligand.

References:

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Heterocyclic cores from cascade reactions between internal alkynes and gem-diborylalkanes

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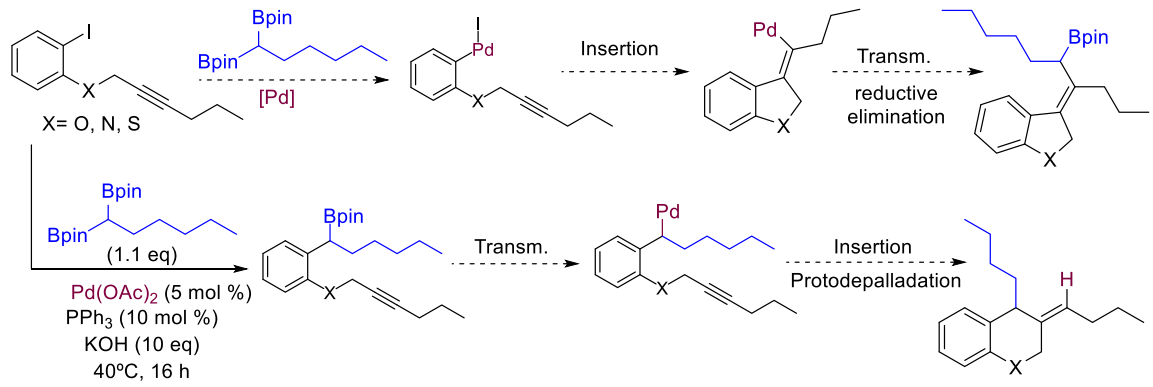
Keywords: *cascade reactions, gem-diborylalkanes, Palladium*

The versatility of C-B bonds has been demonstrated over the years in the formation of complex molecules due to their high versatility. Different methodologies have been developed in which their catalytic efficiency has been demonstrated with metals (Cu or Pd), such as the Suzuki reaction.[1] Recently, gem-diborylalkane species have been introduced as versatile intermediates in organic synthesis due to a particular reactive that stems from the presence of two boron atoms in their structure, a useful feature in cascade coupling reactions.[2]

Initially, this project aimed at developing a method to synthesize heterocyclic structures such as benzofuran, benzothiophene and indoline in which two C-C bonds are formed in a single reaction step by using gem-diborylalkanes in a Pd-catalyzed process with internal triple bonds (Scheme 1, above). Instead, using the reaction conditions described in Scheme 1 (below), we have observed the formation of heterocyclic structures like chromane, thiochromane and quinoline, which arise from a chemo- and regioselective sequence that involves the stereoselective formation of a trisubstituted exocyclic double bond and with two C-C bonds.



Scheme 1. Catalytic scheme for the proposed reaction and the product obtained

References:

[1] (a) Wu, Y.; Wu, L.; Zhang, Z.; Xu, B.; Liu, Y.; Zhang, J. *Chem. Sci. Ed*. **2022**, *13*, 2021 (b) Whyte, A.; Burton, K.; Zhang, J.; Lautens, M. *Angew. Chem. Int. Ed*. **2018**, *57*, 13927 (c) Yu, H.; N. Richey, R.; W. Carson, M.; J. Coghlan, M. *Org. Lett.* **2006**, *8*, 1685

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COVID-19: Searching solutions from medical chemistry.

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Keyword: *4C UGI reaction, SARS-CoV-2, Structure-activity relationships.*

In 2019, the virus SARS-CoV-2 emerged and spread to cause the COVID-19 global pandemic. Initially, broad-spectrum antivirals were used to treat compromised patients[1], and then, different vaccines were developed to protect people from severe disease[2]. Despite recently, specific SARS-Cov-2 approved drugs, the synthesis of new active substances for different targets is still being pursued. Screening studies with structurally diverse compounds form the group, discovered hit 1, coming from a Ugi multicomponent reaction (4C)[3]. This molecule was a phenylglycine derivative, prepared by using benzaldehyde as the carbonyl component, and was obtained as a mixture of two inseparable diastereoisomers. To solve this isomery problem, benzaldehyde was changed to cyclohexanone (Compound **2a**, R^1 = H, R^2 = Cy), which slightly improved the antiviral activity. The aim of this work is the preparation of a small combinatorial library around the second hit, combining the incorporation of different functional groups in *para* position of the N-Ph ring (H, F, OMe, NO_2) and three isocyanide (CyNC, BnNC, and *p*-OMePhNC) components.

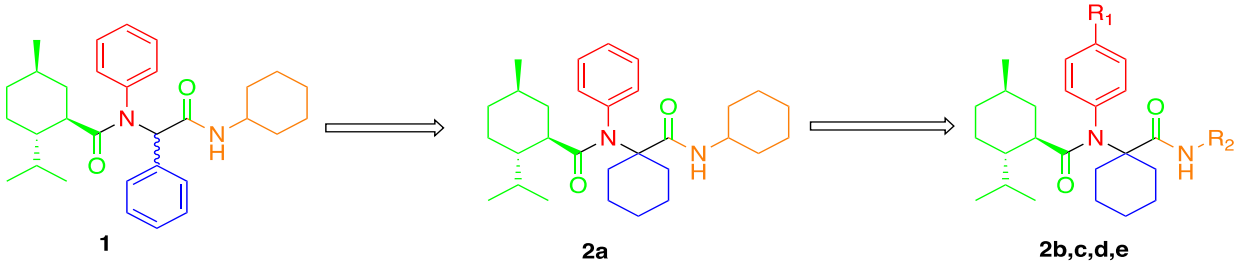

Figure1: Compound **2a** and the combination of different functional groups R^1 (H, F, OMe, OH, NO_2), R^2 (Cy, Bn, *p*-MeOPh)

Since the reaction with *p*-NO_2 Ph-NH2 did not work, the corresponding *m*-NO_2 aniline was used to explore the importance on the activity of an electron-withdrawing group. Difficulties in the preparation of OH derivatives from OMe-substituted analogues, due to an unexpected C-terminal amide hydrolysis, will be explained. Compounds are being assayed for their SARS-CoV-2 antiviral activity at the CNB collaborating group.

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^{1}H and ^{11}B NMR study of the interactions between Wulff-type boronic acids and 1,2 diols and their application to the formation of micelles for DDS

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Keywords: *Boronic acid, catechol, block copolymer.*

The high versatility of boronic acids has led to their implementation in the development of numerous drug delivery systems (DDS).[1] Recently, our research group has developed the synthesis of a novel dendritic block copolymer functionalized with Wulff-type boronic acids (PEG-[G3]-BO_2H_2) that in the presence of 1,2 and 1,3 diols is able to aggregate in an ordered way, leading to the formation of nanometric micelles with promising applications in nanomedicine.[2]

In this presentation, we will describe a systematic study by ^{1}H and ^{11}B NMR about the chemical properties in solution (pKa) of the Wulff-type boronic acids used in the functionalization of our block copolymer, and their interactions with catechol.[3] This study will help us to better understand the nature of these interactions, laying the groundwork for the development of improved DDS.

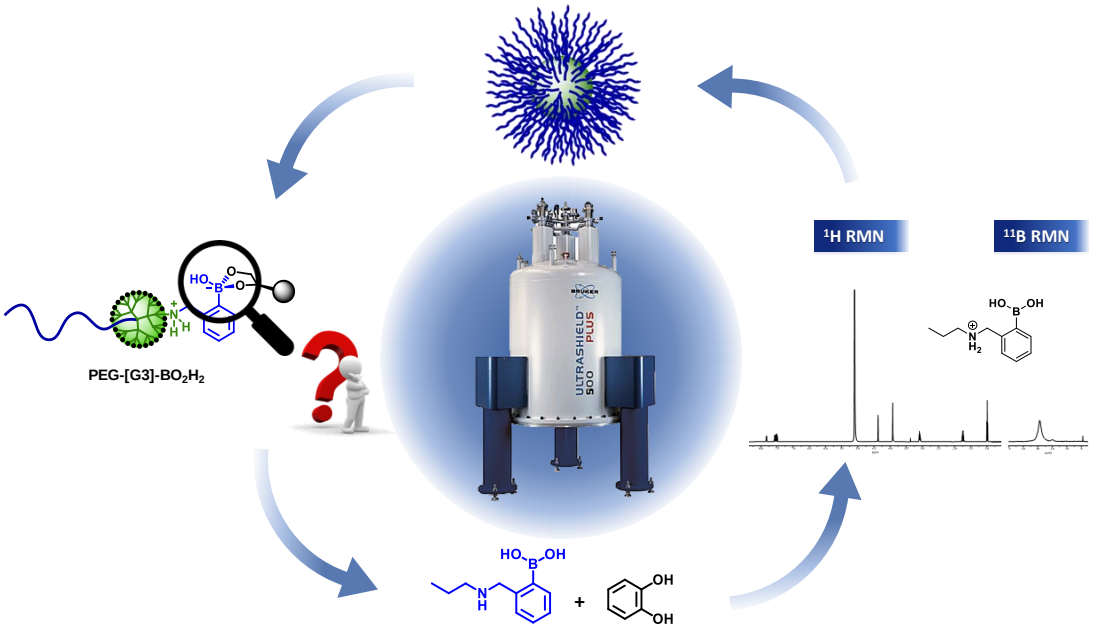

Figure 1. Schematic process of the study of the interaction of Wulff-type boronic acids with 1,2-diols.

References:

[1] Brooks, W. L. A.; Sumerlin, B. S. *Chem. Rev.* **2016**, *116*, 1375-1397.
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Novel catalytic methods for the selective cleavage of carbon-nitrogen bonds

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Keywords: *amines, radicals, photoredox*

Amines are ubiquitous molecules, abundant, and commercially available in a wide variety from simple to complex compounds. Therefore, they are an attractive feedstock as potential building blocks for the formation of more complex molecules. However, the selective catalytic cleavage of C-N bonds in amines is a difficult challenge, mainly due to the high dissociation energy of this bond compared to other carbon-heteroatom bonds. Pyridinium salts are an example of a simple amine derivative recently used in a photocatalyzed single-electron reduction process,[1] forming a carbon-centered radical capable of engaging in different bond-forming events.

Inspired by the early work reported by Barton, [2] we have envisioned that amine derivatives such as α-iminoacids and isonitriles, could serve as carbon-centered radical precursors under oxidative conditions in the presence of a photocatalyst and visible light irradiation.

Using isonitriles as a precursor, silicon derivatives as radical initiators, and an organic photocatalyst, we have been able to optimize the homolytic cleavage of the C-N bond to generate primary, secondary, and tertiary alkyl radicals. These intermediates have undergone conjugate addition with electron-poor alkenes, forming $C(sp^3)$-$C(sp^3)$ cross-coupled products.

Alternatively, α-iminoacids have proven to be more challenging substrates to be synthesized and the activation of the C-N bond has yet to be studied.

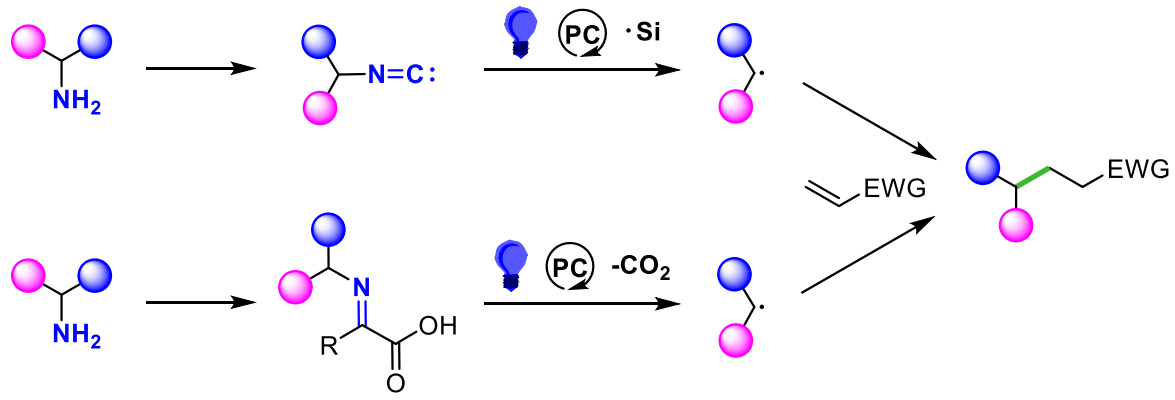

Figure 1. Activation of amines through isonitriles and α-iminoacids, and capture of the radical with an electron-poor alkene.

References:

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Synthesis and purification of new cyano-selenoesters compounds as new antibacterial and antitumor agents

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Keywords: *Selenium; Multidrug Resistance; Cyano-selenoesters.*

Selenium, as well as the organic and inorganic compounds that contain this element, are essential in various biological processes. Selenium deficiency is known to be related with specific diseases and it increases the risk of cancer [1]. Alternatively, epidemiological studies report that selenium dietary supplements may reduce the incidence of certain types of cancer. These early works on selenium supplementation led to reports of multiple organic and inorganic compounds with ability to prevent cancer development or with antiproliferative and cytotoxic activities against cancer cells [2]. Finally, last decades have witnessed a very significant increase in the number of selenium-related works [3].

Considering these lines of evidence, the aim of this work is first to synthesize and characterize selenium-containing anticancer agents with a selenoester functional group and secondly to determine their biological activities. These compounds have been synthetized following a synthetic procedure with three one-pot reactions to obtain cyano-selenoesters (Figure 1):

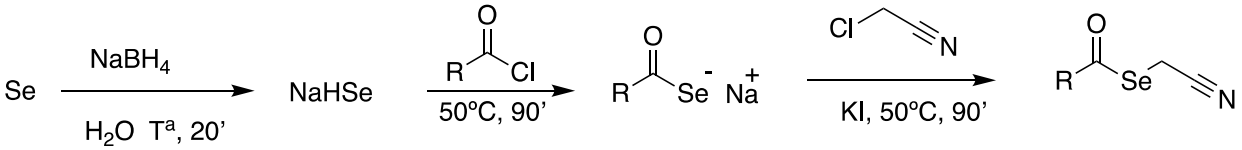

Figure 1. Scheme of the synthetic route of cyanoselenoesters, departing from elemental selenium.

After the synthetic procedure, these compounds have been purified and later characterized by NMR (Nuclear Magnetic Resonance) spectra: NMR-^{1}H, NMR-^{13}C, HPLC-MS and Melting Point. When necessary, also bidimensional COSY (Correlation spectroscopy), HSQC (Heteronuclear Single-Quantum Correlation Spectroscopy) and HMBC (Heteronuclear Multiple-Bond Correlation Spectroscopy) experiments have been performed. In addition, a computational study has been carried out in which it has been confirmed that all the synthesized compounds accomplish with the Lipinski's Rule of Five. Finally, the pharmacological activity of the compounds will be evaluated in Hungary. According to previous results of the group [4], these derivatives are hypothesized to have a good activity, but this hypothesis need to be proved experimentally.

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Allenes and alkynes in the efficient synthesis of novel potential bioactive heterocycles

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Keywords: *allenes, epoxides, sulfones*

Allenes are a class of organic compounds with a characteristic cumulated C–C double bond. They exhibit high reactivity and selectivity and are versatile intermediates in Organic Synthesis.[1] On the other hand, sulfonyl derivatives are very important compounds as they can be found in sulfones and sulfonamides, two classes of compounds with prominent biological and pharmacological activities.[2] In relation to the metal-catalyzed oxycyclization reactions undergone by α-allenols, most of the previous reports consist of the typical 5-*endo* cyclization to afford 2,5-dihydrofurans with different substituents.[3] Noticeable, in this work we present a new diastereoselective synthesis of trisubstituted epoxides via a copper-catalyzed 3-*exo* cyclization/sulfonylation cascade (Figure 1). These epoxides are obtained by the reaction between allenols and aromatic sodium sulfinates. This reaction is carried out at 100 ºC in a sealed tube, and copper acetate (II) is employed as the catalyst and silver nitrate as the oxidant. Both electron-donating and electron-withdrawing groups are tolerated on the aromatic rings of the α-allenols and sodium sulfinates.

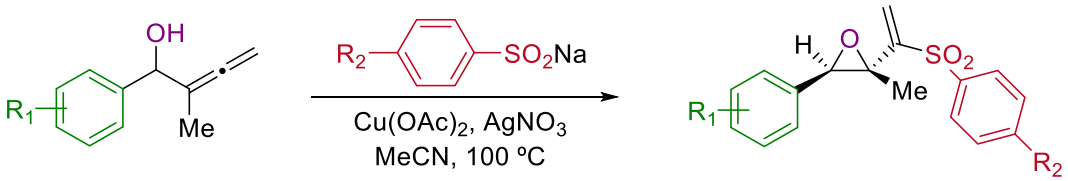

Figure 1. Copper-catalyzed 3-*exo* cyclization/sulfonylation cascade to obtain epoxides

References:

[1] (a) Alonso, J. M.; Almendros, P. *Chem. Rev.* **2021**, *121*, 4913. (b) Lu, L.; Ward, R. M.; Schomaker, J. M. *Chem. Rev.* **2019**, *119*, 12422. (c) Mascareñas, J. L.; Varela, I.; López, F. *Acc. Chem. Res.* **2019**, *52*, 465.

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Conformational control of porphyrin molecular capsules

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Keywords: *Porous organic cages, porphyrins, supramolecular chemistry.*

Organic molecular cages based on porphyrins have been widely studied due to their exceptional ability to host molecules into their inner cavities as well as their interesting (photo)catalytic properties. These molecular cages may be assembled via covalent, dynamic covalent, metal and hydrogen bonds.[1,2]

In the *Nanostructured Molecular Materials and Systems* group, an active research line aims to develop self-assembled (2D and 3D) materials based on porphyrins, with (photo)catalytic nanocavities. Currently, the research group is focused on prepare and understand the behavior of the unit cell of these materials, a porphyrin molecular cage. Specifically, previous studies have demonstrated the feasiblity of the synthesis of cages by means of the connection of two cofacial porphyrins via four linkers forming **dynamic imine bonds**. In order to form the imine bonds, the aldehyde and amine groups may be present in the porphyrin and linker, respectively or the other way round. Conformational analysis of these cages revealed that they adopt an elongated conformation which is thermodynamically favored with respect to the compact one.

The aim of this project is directed towards the obtention of the compact conformation by means of three strategies: **silver coordination** with nitrogen atoms of imines, introducing **steric hindrance** through methyl group in the spacers and finally, the formation of **hydrogen bonds** between hydroxyl group of linkers and the imines.

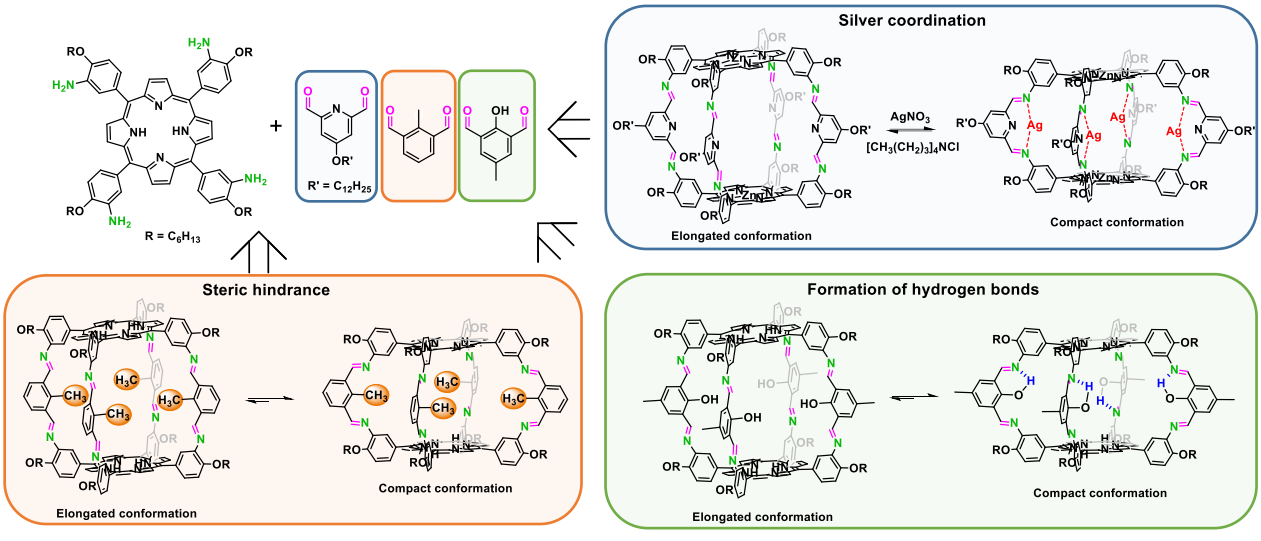

Figure 1. Different strategies to control the porphyrin cage conformation.

References:

[1] Durot, S., Taesch, J., Heitz, V., *Chem. Rev*. **2014**, *114*, 17.
[2] Mukhopadhyay, R., Kim, Y., Koo, J., Kim K., *Acc. Chem. Res*. **2018**, *51*,11.

SYNTHESIS OF POLYMETALLIC HYDROGENASE MIMETIC SYSTEMS FOR EFFICIENT HYDROGEN PRODUCTION

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Keywords: *(Hydrogen, hydrogenase, metathesis)*

Power to hydrogen is a likely way of solving the storage of variable renewable energy to achieve a whole balanced and sustainable hydrogen economy.[1] To achieve this goal, hydrogenases have been studied in recent years, since they are metalloenzymes present in living bodies (such as bacteria, prokaryotic and eukaryotic cells) responsible for hydrogen production. Hydrogenases catalyze the reversible oxidation of molecular hydrogen and play a central role in microbial energy metabolism.[2]

It seems crucial for the development of this area to examine the behaviour of these molecules. In order to investigate them, our goal is to synthesize some mimetic systems of these natural structures, trying to replicate their biological functions, looking for a more sustainable, cleaner and safer future.

In this case, we present a molecule which contains our mimetic system[3] containing two iron atoms attached to different linkers or spacers which will bind to the rest of the molecule via cross-metathesis. The iridium complex acts as photosensitizer and is also connected to an electron donating structure.

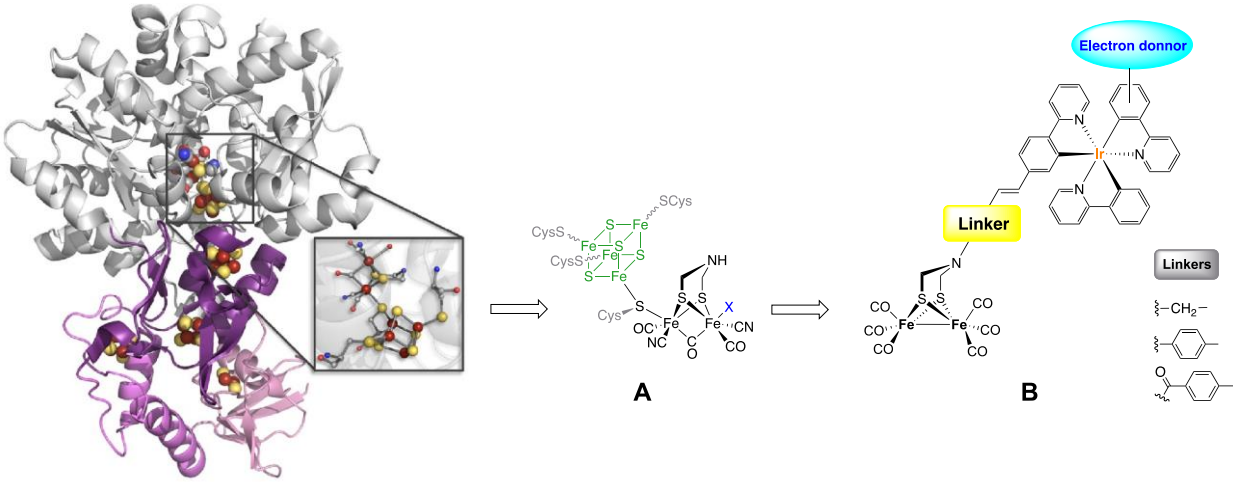

Figure 1. Structures of the active site of natural [FeFe]-hydrogenase (A) and the artificial mimetic cluster synthesized with different linkers (B). X represents a vacant which is needed for the catalytic cycle to proceed.

References:

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Unexpected reactivity of 4,4-dichloro-2-butenoates brings access to a novel synthetically versatile building block

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Keywords: *catalysis, copper, alkyl 4,4-dichloro-2-butenoates.*

During the last years, our group has been working on a research line based on the development of catalytic carboboration processes of unsaturated hydrocarbons.[1] Within this program, we recently reported the first asymmetric copper-catalyzed allylboration of alkynes using allylic *gem*-dichlorides. In this reaction, by using a chiral NHC-Cu catalyst we can generate in a single step chiral skipped dienes bearing a *Z*-alkenyl chloride, a trisubstituted *E*-alkenyl boronate and a bisallylic stereocenter with excellent levels of chemo-, regio- enantio- and diastereoselectivity (Figure 1). [2]

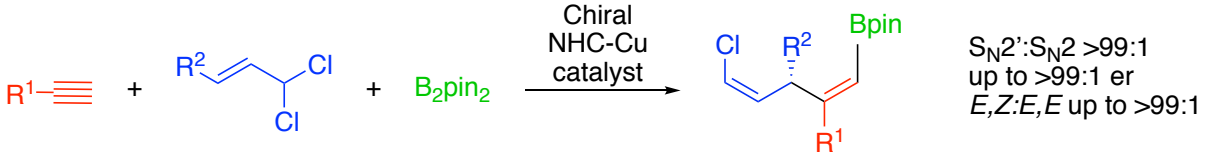

Figure 1. General scheme of copper-catalyzed enantioselective allylboration of alkynes using allylic *gem*-dichlorides.

Surprisingly, when we performed this reaction using an alkyl 4,4-dichloro-2-butenoate **1** as substrate, we observed a completely different reactivity. Instead of the expected tricomponent product, we observed the formation of a dialkyl 3-(dichloromethyl)-2-(2,2-dichlorovinyl)pentanedioate **2** with total diastereoselectivity.

Given the novelty of the reaction, and as the main objective of this Master Project, we proceeded to study the scope of the reaction, as well as the reactivity of this new compound to obtain novel highly functionalized cyclopropanes **3** (Figure 2).

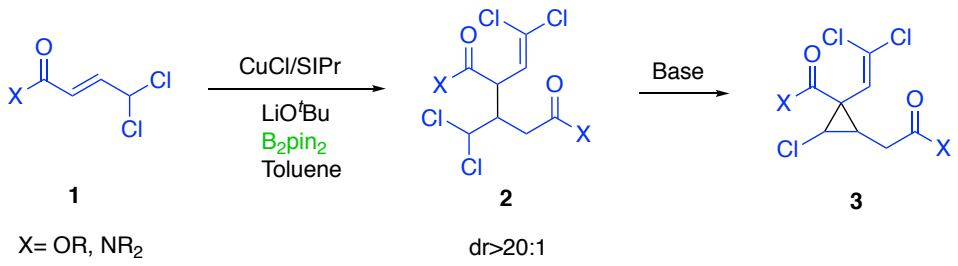

Figure 2. General reaction scheme of 4,4-dichloro-2-butenoates to give new functionalized products.

References:

[1] a) Rivera-Chao, E.; Fañanás-Mastral, M. *Angew. Chem. Int. Ed.* **2018**, 57, 9945-9949. b) Rivera-Chao, E.; Mitxelena, M.; Varela, J. A.; Fañanás-Mastral, M. *Angew. Chem. Int. Ed.* **2019**, *58*, 18230-18234.

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Preparation of Hypoxia Sensors Based on Azobenzenes

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Keywords: *azobenzene, BODIPY, chirality.*

Azobenzenes are a well-known family of organic dyes, with outstanding photophysical properties that have found applications in the field of molecular switches, and more recently as fluorescent quenchers for biosensing and bioimaging studies. The fluorescence of the azo-based fluorophores can be turned-on by a chemical or biological reductant, such as azoreductases, promoting the cleavage of the N=N azo moiety, liberating the fluorescent probe, and allowing the easy-tracking of biological processes by fluorescence microscopy.[1] This type of azo-based fluorescent quenchers have emerged as promising biosensors of hypoxia-like conditions.

Recently, our group has reported a new type of OFF/ON fluorescent biosensors based on 3-azo-conjugated BODIPYs dyes for hypoxia like conditions.[2] In this work, we have incorporated a chiral sulfoxide unit to the azo-based BODIPY structure. To the best of our knowledge, there are no examples reported in the literature related to chiral azo-based fluorescence quenchers. This type of chiral sensors will provide new chiroptical properties which can be used for an exclusive read out of reductive events, such as circular dichroism (CD) and circular polarized luminescence (CPL).

Herein, a 5-chloro-3-arylazo-BODIPY was prepared and the sulfoxide chiral unit has been attached to the azo-BODIPY structure by cross-coupling or nucleophilic additions reactions to the 5-chloro-BODIPY. Details of the reductive cleavage the azo N=N double bond, to obtain the corresponding chiral amino-BODIPYs, together with the photophysical and chiroptical properties will be detailed.

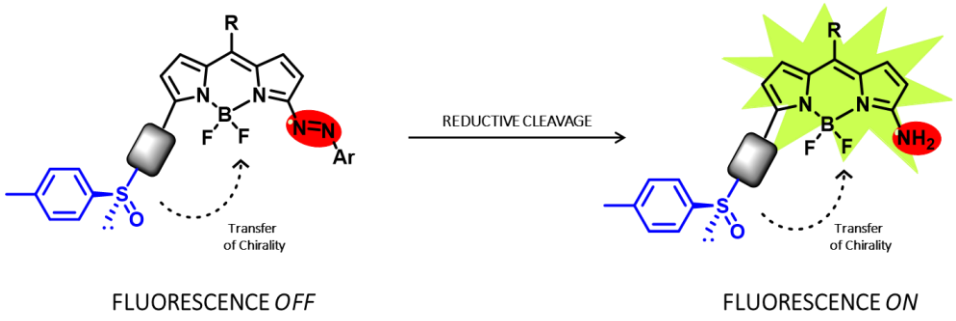

Figure 1. Reductive cleavage of the azo-BODIPY to the amino-BODIPY turning on the fluorescence.

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Study of aromatic compounds with potential applications in biomedicine and materials science

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Keywords: *Aromatic compounds, fluorenones, peptides.*

The Peptides and Aromatic Compounds (PEPARO) research group directed by Bernardo Herradón has focused its efforts on the investigation of peptide-arene hybrids. These compounds are made up of an amino acid or peptide fragment linked to an arene through an amide bond. The arenes endow the molecule with conformational rigidity, while the peptide or amino acid fragment adds aditional functionality, thus giving the possibility of generating a wide molecular diversity. This chemicals have been found to be biologically active both as inhibitors of calpain —a cysteine protease— as well as antiviral agents against coronavirus.[1]

In parallel, the group has a line of research in material science focused on developing new organic electrolytes for sodium ion batteries. [2] The structural characteristics of peptide-arene hybrids and their ability to complex metal cations suggest that they may have applications as electrode materials.

In connection with these interests of our group, we have now focused on the synthesis and structural study of a variety of hybrids using 9-oxo-4-fluorenocarbonyl moiety as the arene component with the aim to futher evaluate their biological activity as well as electrochemical properties. This type of compounds was previously obtained as by-products in the synthesis of peptide-biphenyl hybrids, one of the most studied kind of compunds in our group, and they were found to be potent calpain inhibitors.[1,3] Various amines have been used for the synthesis of a variety of fluorenone derivatives, so that it is possible to study the influence of this structural features on the conformation of the molules as well as on their properties. In order to evaluate the influence of experimental conditions on the outcome of the reaction, several solvents have been used, showing that acetonitrile is a good solvent for this type of reactions. A collection of compounds with a wide functional variety has been obtained with good yields and in many cases high purities directly from the reaction.

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Degradation study of dalbavancin hydrochloride in the medicine Xydalba

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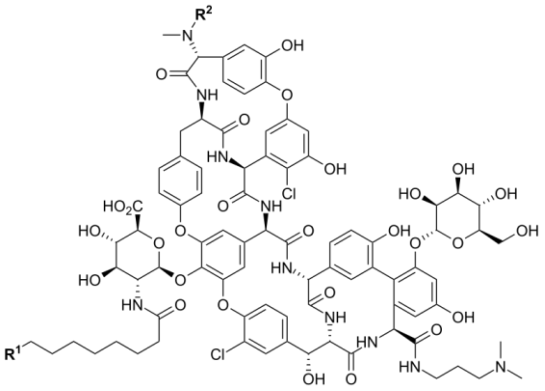
Keywords: *xydalba, dalbavancin, impurities.*

Xydalba is a freeze-dried medicine. This product is presented as a concentrate powder for solution for infusion containing dalbavancin hydrochloride as active substance equivalent to 500mg of dalbavancin. The other components of xydalba are: lactose monohydrate, hydrochlorid acid, mannitol and sodium hydroxide.[1]

Dalbavancin is a glycopeptide antibiotic semisynthetic, a derivate of teicoplanin analogous A40926. The action mechanism is similar than vancomycin and teicoplanin, it inhibits the cellular wall biosynthesis of Gram-Positive cells, ant it is using like drug for skin infection and soft tissue treatment. Dalbavancin is making up of five components: A_0, A_1, B_0, B_1 and B_2, with similar structures, where the principal component is B_0. These components have the same central structure, like we can see in Figure 1.[2]



Homolog	Alkyl sidechain of *N-acylaminoglucuronic* (R1)	Amino terminal substituent (R2)
A_0	$CH(CH_3)_2$	H
A_1	$CH_2CH_2CH_3$	H
B_0	$CH_2CH(CH_3)_2$	H
B_1	$CH_2CH_2CH_2CH_3$	H
B_2	$CH_2CH(CH_3)_2$	CH_3

Figure 1: *Dalbavancin structures.*

Dalbavancin have different impurities: due to degradation and for by process. Different analytical method are being optimized to indentify and quantify the drug substance and its impurities, to undergo extreme conditions, thus being able to study its degradation.

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New sustainable synthetic routes to azulenic heteroaromatic PAHs

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Keywords: *(Azulenes, C-H activation, PAHs)*

The polycyclic aromatic hydrocarbons (PAHs) containing non-benzenoid aromatic rings, e.g. azulene, feature curved nanographenic systems that can noticeably change its electronic and optical properties, which makes them suitable for the construction of semiconductors (Figure 1).[1] Consequently, the development of synthetically efficient and sustainable methods for non-benzenoid (azulenic) PAHs is highly relevant and very demanded.[2]

Azulene-embedded nanographenes

Azulene-fused heteroaromatic PAHs

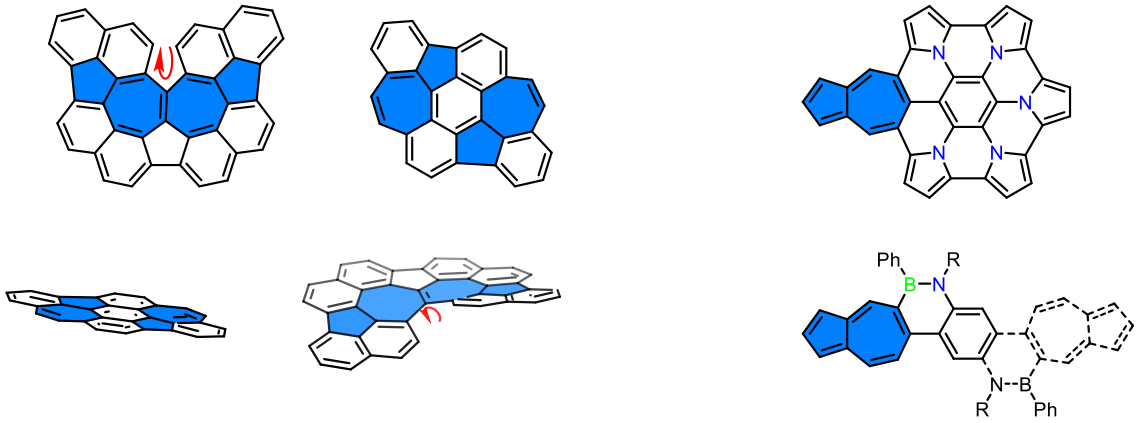
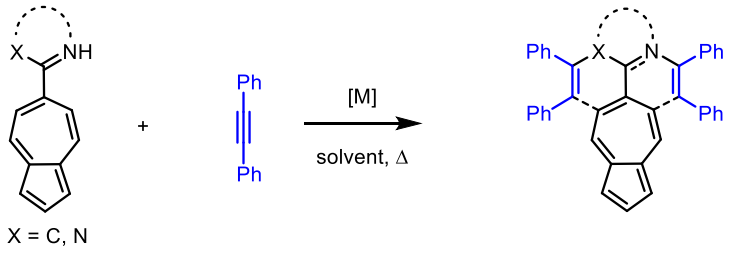


Figure 1. Schematic representation of azulene-based systems.

The main objective of this TFM work is the development of a synthetic route to linear azulene-[*f,g*]-fused heteroaromatic PAHs by metal-catalyzed [4+2] oxidative annulation of 2-heteroaryl substituted azulenes with alkynes (Scheme 1).[1]



Scheme 1. Proposed transformation for accessing azulene-[f,g]-fused non-benzenoid PAHs.

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Synthesis of a folic acid–DNA minor groove binding drug conjugate as antileishmanial agent

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Keywords: *total synthesis; medicinal chemistry; ligand-targeted drug delivery*

Leishmaniasis is a vector-borne parasitic disease caused by *Leishmania* subspecies. Amastigote forms of *Leishmania* infect macrophages of the mammalian host where they replicate, and later spread and infect new cells. Infected macrophages overexpress the folate receptor that recognizes folic acid (FA). A ligand-targeted drug delivery approach was used to allow a better efficacy and a lower toxicity of the antileishmanial lead compound **1**. In this project, the folic acid ligand, which is recognized by the FA receptors of macrophages, is linked to a self-destructive linker that will release the therapeutic agent **1** once the conjugate has been taken up by the infected cells.
This work is based on the previous work of the team who studied the therapeutic agent [1] and different drug-ligand synthetic strategies [2]. The aim of this project was to continue the synthesis of the target conjugate molecule in order to study its antileishmanial activity *in vitro*.

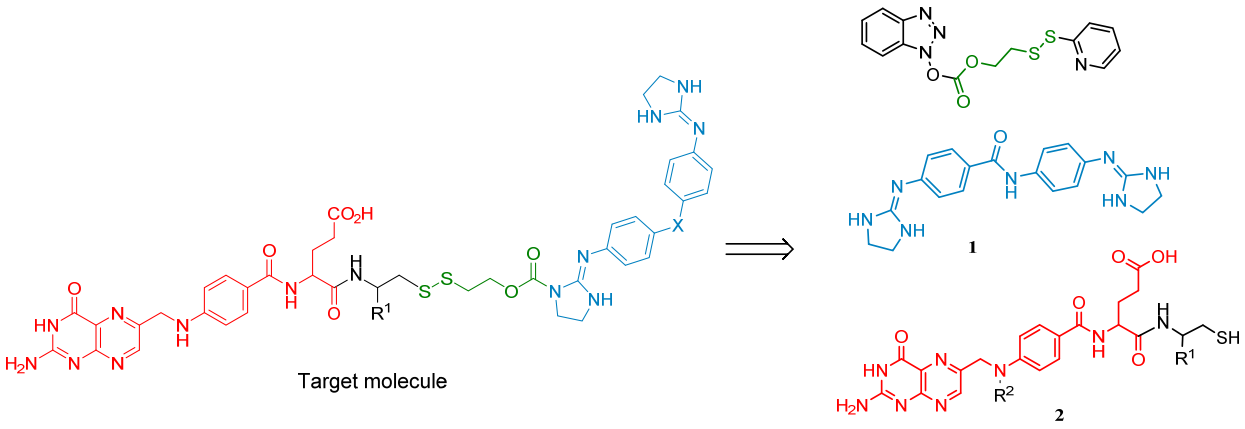

Figure 1. Proposed retrosynthesis of the target molecule.

During this project, two major advances were achieved, the conjugation of compound **1** with the auto-destructive linker and the synthesis of folic acid derivative **2**. For the functionalization of compound **1**, which holds several possible *N*-substitution sites, the problematic was turned around the control of the reaction. The synthesis of the folic acid derivative was a complicated step which required the protection of the NH group with the 2,2,2-trifluoroacetyl group (Figure 1, $R^2 = COCF_3$). This step allowed to obtain the compound **2** and to continue the synthesis of the target molecule.

References:

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Applications of NMR in the study of glycoprotein recognition

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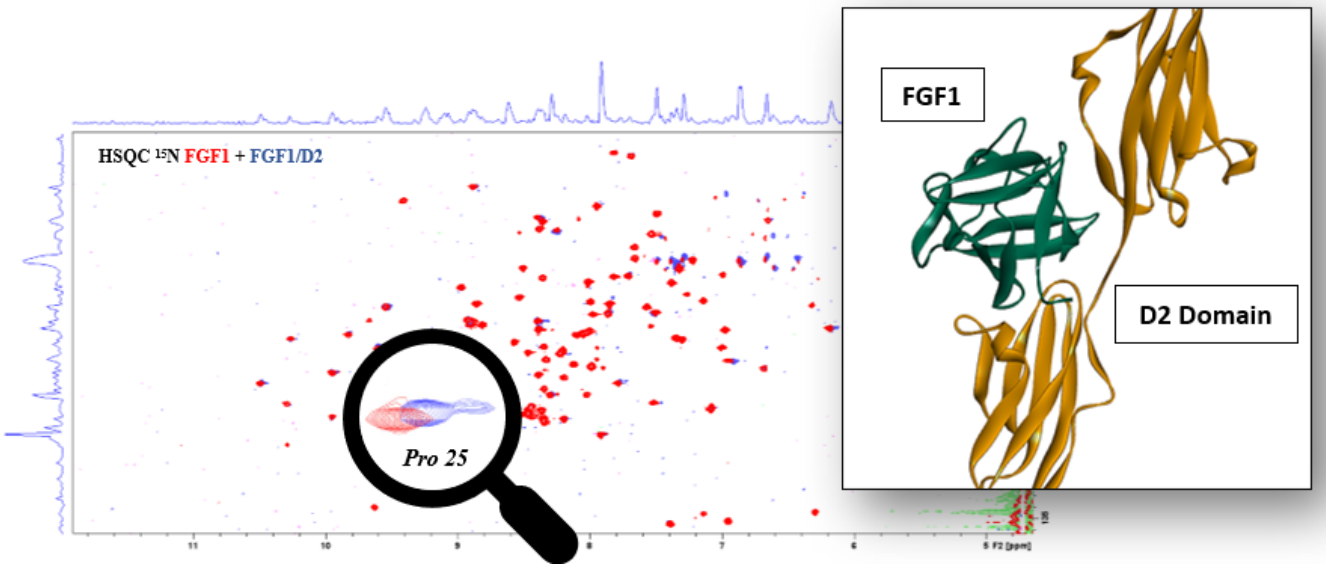
***Keywords**: NMR, Fibroblast Growth Factor 1, D2 domain*

Glycosylation of proteins is one of the most fundamental post-translational modification in eukaryotic cells.[1] There are two types of glycosylation, depending on the linkage connecting the glycan and the protein: N-linked glycans[2], involve asparagine residue and O-linked glycans[3], involve serine or threonine residues. Protein glycosylation modulates protein folding, stability function and location. However, despite the importance of glycosylation there is a lack of structural information about glycoproteins mainly due to the flexibility and heterogeneity of the glycan part.

Fibroblast Growth Factors (FGFs)[4], belong to a family of secreted proteins, which have important roles in metabolic, cell-cell communication and neuropathic diseases. FGF exerts its biological function by interacting with FGF receptors (FGFR). [5] FGFR is glycosylated in vivo and it has been described that the glycosylation of this receptor modulates the interaction with their activators. However, there are no structural studies focus on charactering FGFR glycoprotein recognition.

In this work, we study the interaction of glycosylated FGFR1 with FGF1 by using NMR spectroscopy. The recognition process is monitored from the FGF perspective by using ^{15}N labelled FGF1 (produced in *Escherichia coli*) and from the FGFR1 perspective by using ^{13}C labelled FGFR (produced in HEK293 mammalian cells).



References:

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Synthesis of axially-chiral O-N and N-N ligands for the development of new asymmetric reactions

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Keywords: *axial chirality, asymmetric catalysis, C-H functionalization*

Today's organic synthetic chemistry highly demands new reactions that allow the construction of relevant and complex scaffolds in a quick, efficient and environmentally friendly manner, being the most attractive those that proceed in an enantioselective way. The most common approaches for synthesizing enantiopure compounds are the use of chiral ligands in transition metal catalysis, the use of organocatalysts and the employment of easy-removable chiral auxiliaries. 2'-amino-[1,1'-binaphthalen]-2-ol (NOBIN) and its derivates have been used as chirality inductors in a bast and diverse number of asymmetric reactions among these three approaches[1]. With this in hand, some NOBIN analogs were synthesized by reported methods[2] for the development of new asymmetric reactions.

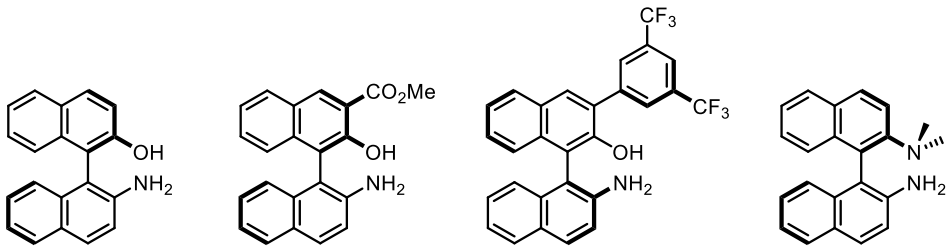

Figure 1. Structure of the synthesized ligands.

Due to the inefficiency of most methods described in the literature, in this work was proposed to synthesized enantioenriched NOBIN by a kinetic resolution of protected 1,1´-binaphthalene-2-amine through palladium-catalyzed C-H γ-acetoxylation. Until now, only the bases of the racemic transformation were stablished, pretending to start now with the kinetic resolution viability studies.

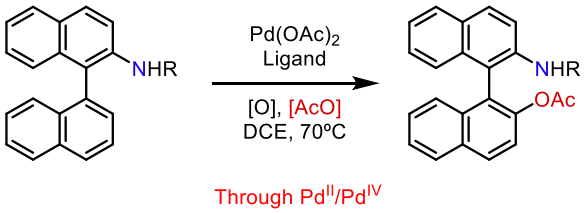

Figure 2. Racemic Pd-catalyzed C-H γ-acetoxylation of protected 1,1´-binaphthalene-2-amine.

References:

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Enantioselective desymmetrization of 1,2-diboryl cyclopropanes

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Keywords: *diboration, Suzuki coupling, desymmetrization*

An interesting way to generate nucleophilic boron species is the activation of diboron compounds with Lewis bases. This strategy has been sucessfully used to promote the transition metal-free borylation of unactivated alkenes.[1] Surprisingly, the use of these conditions to promote the borylation of strained alkenes, such as cyclopropenes, has not been explored to date. The products are interesting diborylated cyclopropanes that have not been prepared before and, therefore, their reactivity remains unexplored.

Following our work on the diboration of spirocyclobutenes[2], we have achieved the first metal-free diboration of cyclopropenes (Figure 1). By exploring the reactivity of the diborylated product, we have found that, under previously reported conditions,[3] the mono-cross-coupling reaction with several electrophiles could be performed. In addition, the enantioselective desymmetrization of the diboronyl products through a Suzuki-Miyaura[4] reaction was possible with the help of a chiral ligand (Figure 2).

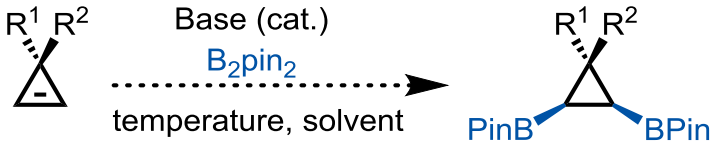

Figure 1. Diboration of cyclopropenes.

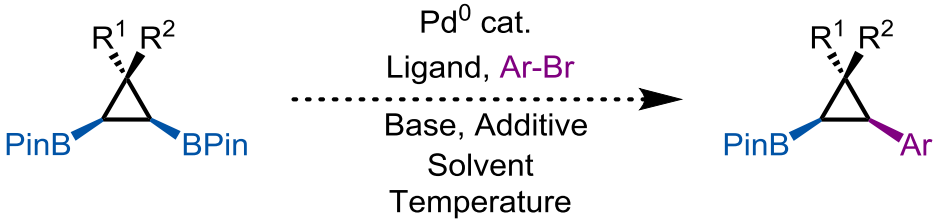

Figure 2. Suzuki-Miyaura cross-coupling reaction of the dyborilated cyclopropane.

References:

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Synthesis of Multivalent Fullerenes with Potential Applications in Nanomedicine

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Keywords: *DC-SIGN, fullerenes, carbohydrates.*

DC-SIGN is a C-type lectin receptor present in plasmatic membranes of some cells that interacts with carbohydrates like those on the surface of viruses such as Zika, Dengue or Ebola. Therefore, this receptor is an interesting therapeutic target for the design of vaccines or treatments.[1]

Because DC-SIGN binds to Ebola virus via a special *N*-linked glycosylation pattern on the Ebola virus envelope glycoprotein, we have developed some glycoconjugates to block the carbohydrate recognition domain of DC-SIGN.[1] In particular, we have worked with fucose-type glycoconjugates bound to C_{60} fullerene forming a symmetrical hexa-adduct structure, which was synthesized using a strain-promoted alkyne-azide cycloaddition (SPAAC), a reaction that avoids the use of copper as a catalyst.[2]

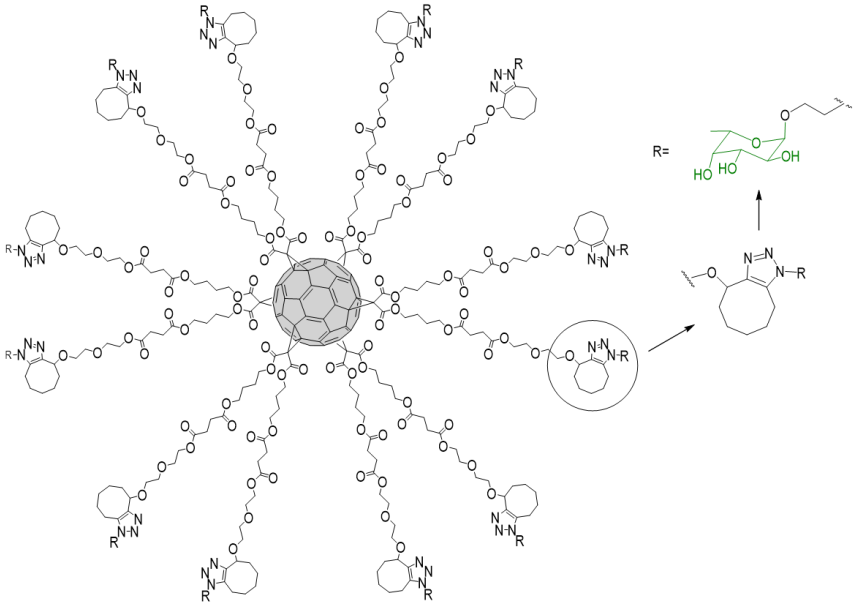

Figure 1. Example of glycoconjugate derivative used in the project.[2]

References:

[1] Ramos-Soriano, J.; Reina, J. J.; Illescas, B. M.; De La Cruz, N.; Rodríguez-Pérez, L.; Lasala, F.; Rojo, J.; Delgado, R.; Martín, N. Synthesis of Highly Efficient Multivalent Disaccharide/[60]Fullerene Nanoballs for Emergent Viruses. *J. Am. Chem. Soc.* **2019**, *141*, 15403-15412.

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Towards antikekulene: synthesis of aryne precursors derived from angular [3]phenylene

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Keywords: *cycloarenes, [N]phenylenes, arynes, cycloadditions.*

Cycloarenes constitute a unique family of polycyclic aromatic hydrocarbons (PAHs) that have attracted the interest of chemists for decades, being ideal platforms to address unresolved scientific problems surrounding the fundamental concept of aromaticity.[1] Our group has recently reported the synthesis and single molecule imaging of the paradigmatic cycloarene kekulene.[2] Related to this work, a current goal in our group focuses in the synthesis of antikekulene, a cyclic [*N*]phenylene[3] that has never been prepared, constituted by the alternation of ortho-fused benzene and cyclobutadiene rings. The presence of two 4n π-electron circuits could confer global antiaromatic character to this system.

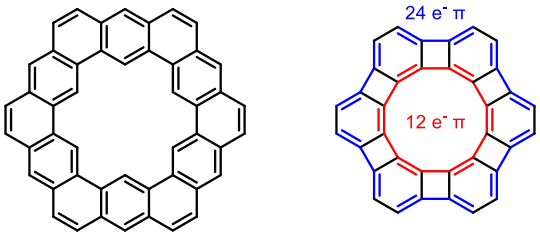

Figure 1. Structures of kekulene (left) and antikekulene (right).

In this context, the present project proposes an approach to the synthesis of antikekulene based on aryne chemistry. In particular, the specific objective is to obtain suitable precursor(s) of an aryne **1,** derived from angular [3]phenylene, and to study their application to the synthesis of advanced polycyclic intermediates towards antikekulene. Key steps in our approach will involve selective Sonogashira coupling reactions to get triyne **4**, and subsequent cobalt-catalyzed [2+2+2] cycloaddition to build the [3]phenylene core.

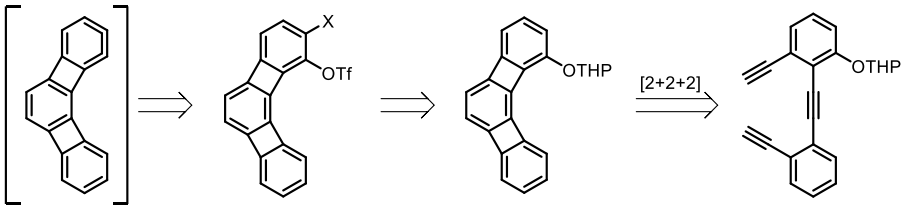

Figure 2. Approach to the generation of aryne **1**

References:

[1] Buttrick, J.; King, B. *Chem. Soc. Rev.,* **2017**, *46*, 7-20.

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Stereoselective Synthesis of Molecules Containing Boronic Esters

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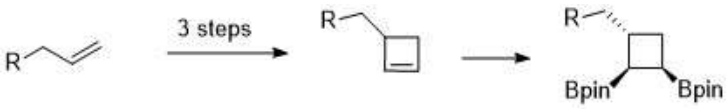
***Keywords**: cyclobutenes, cyclobutanes, bisborylation*

Cyclobutanes, are a paramount class of compounds in a large number of biologically active natural products and drugs[1]. As an example, the use of carboplatin as cell death inducer has been profoundly studied in recent years[2]. In addition, cyclobutanes are important synthetic intermediates due to their rich chemistry, which is due to its inherent ring strain[3-5]. In the last years, the regio- and enantioselective[6,7] synthesis of cyclobutylboronates, have gained increasing attention, due to their use as useful building blocks for the synthesis of functionalized cyclobutanes.

Starting from commercial available alkenes, in this work we synthesized cyclobutenes that after some optimization, were submitted to steroselective transition-metal-free diboration.[8] The resulting cyclobutylbisboronates have been submitted to different boron transformations, seeking for regioselective functionalizations on the vicinal C-B bonds, which could make the new cyclobutanes suitable building blocks for the development of more complex and biologically active molecules.



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Synthesis of functional organic materials based on electroactive units.

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Keywords: *Non-fullerene acceptors, Y6-derivatives, rylenimides.*

The conversion efficiencies above 16% obtained for organic solar cells based on the non-fullerene acceptor Y6 have stimulated the attention of many researchers for the development of novel non-fullerene acceptors. The structure of Y6 involves the introduction of an electron-withdrawing segment (A_1) in the centre of a conjugated electron-donating π-system (D-A_1-D), to generate a final structural block A_2-D-A_1-D-A_2.[1] In this work, we have slightly modified the structure of Y6 by tuning the nature of the A_1 moiety while keeping unaltered the rest of the structure of the molecule. Thus, the central benzothiazole ring of the π-conjugated skeleton of Y6 is used to generate a reactive diamine derivative that allows the linkage of ryleneimides[2] to the Y6 skeleton through pyrazine connectors. The UV-vis and electrochemical properties of these novel non-fullerene acceptors with the general structure A_2-D-A_x-D-A_2 are investigated showing significant improvement in the molar extinction coefficients in comparison with pristine Y6.[3,4]

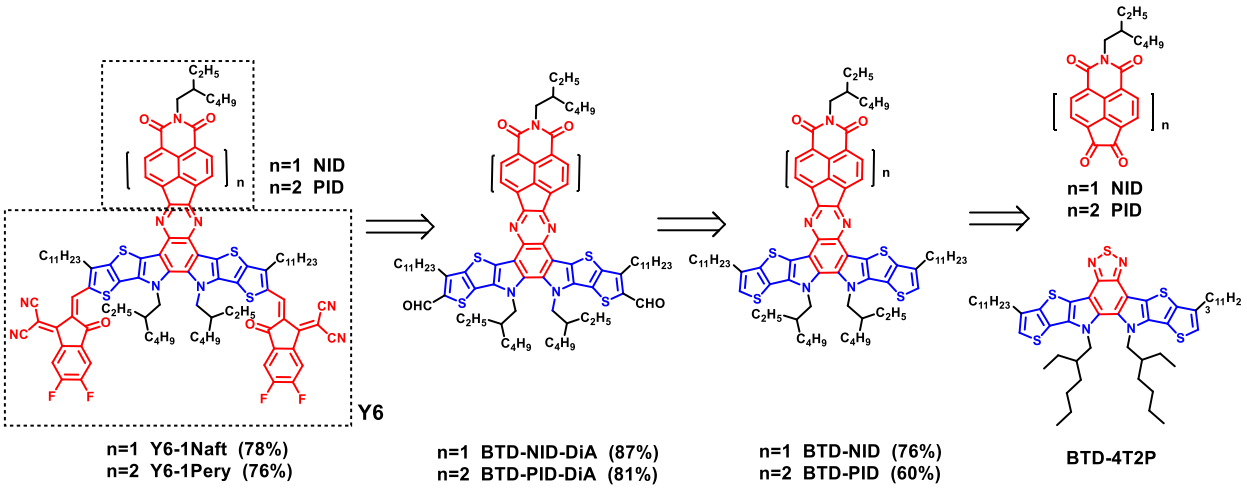

Figure 1. Chemical structures of synthesized systems. Acceptors moieties in red and donor fragment in blue.

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Síntesis y Caracterización de Nuevos Colorantes Orgánicos para Aplicaciones Biofotónicas

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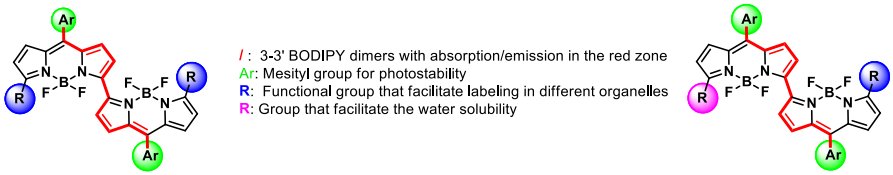
Keywords: *3-3' BODIPY dimers, Bioimaging, Photodynamic therapy, Photo-theragnosis.*

Boron dipyrromethenes (4-bora-3a,4a-diaza-*s*-indacene; abbreviated as BODIPY) constitute a family of organic dyes widely used in photonics due to their excellent physical and chemical properties, such as high fluorescence quantum yield, significant solubility in a wide range of organic solvents, and a great chemical versatility.[1] An interesting modification that can be obtained through this chemistry of BODIPYs is the extension of the π-conjugation of the chromophoric core, thereby causing a bathochromic shift of the absorption and emission wavelengths towards the red edge of the visible spectrum.[2] Red-to-NIR BODIPYs are interesting due to the advantages of the red-to-NIR region (specifically, the biological window region) for biological and medical applications.[3] Thus, these BODIPYs type have been successfully developed as fluorescent bioprobes and ROS (reactive oxygen species) photosensitizers for photodynamic therapy (PDT).[4] Interesting PDT photosensitizers can be also tuned for conducting photo-theragnosis, which consists in performing PDT and diagnosis (by luminescence-based bioimaging) by using a single fluorescent-enough photosensitizer[5]. In this context, our research group has recently demonstrated that some highly fluorescent BODIPY dyes (poor ROS photosensitizers) are able to trigger an efficient PDT action when efficiently accumulated into “sensible-to-PDT” cell organelles, such a lipid droplets[6] or mitochondria.[7]

In the present work, we carried out the synthesis of new 3-3’ BODIPY dimers with absorption and emission in the red zone that have: 1) a mesityl group in the *meso* position for photostability, 2) a functional group in 5 and/or 5’ positions that facilitate membrane penetration and specific labeling to different organelles, 3) a group that facilitate the water solubility. Photophysical and biological studies will allow to validate the synthetic design of these systems as probes, PDTagents, or even as teragnostic agents.



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N-SO_2Py-assisted Pd-catalysed ε-C(sp^2)–H intramolecular alkenylation on linear peptides

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Keywords: *ε-C(sp^2)–H alkenylation, palladium catalysis, peptides*

Peptide post-synthetic modification methods present enormous potential for drug discovery and for the pharmaceutical industry.[1] Among the various tactical strategies available for this purpose, direct C–H bond functionalization processes allow introducing diversity and complexity into the peptide structure by adjusting the processes to the principles of atom economy.[2]
Within this line, we have developed a methodology for the *N*–SO_2Py-assisted Pd-catalysed ε-C(sp^2)–H intramolecular alkenylation on linear peptides that allows to efficiently access macrocyclic peptide structures.[3] Preliminary results show that the protocol seems suitable for the macrocyclisation regardless of the substitution pattern in the γ-aryl amino acid at the *N*-terminus position. Moreover, it is possible to have diverse AAs in the peptide skeleton, as well as to modify the size of the macrocycle formed depending on the length of the peptide chain. In any case, macrocyclisation occurs with high yields and excellent *E*-diastereoselectivity.

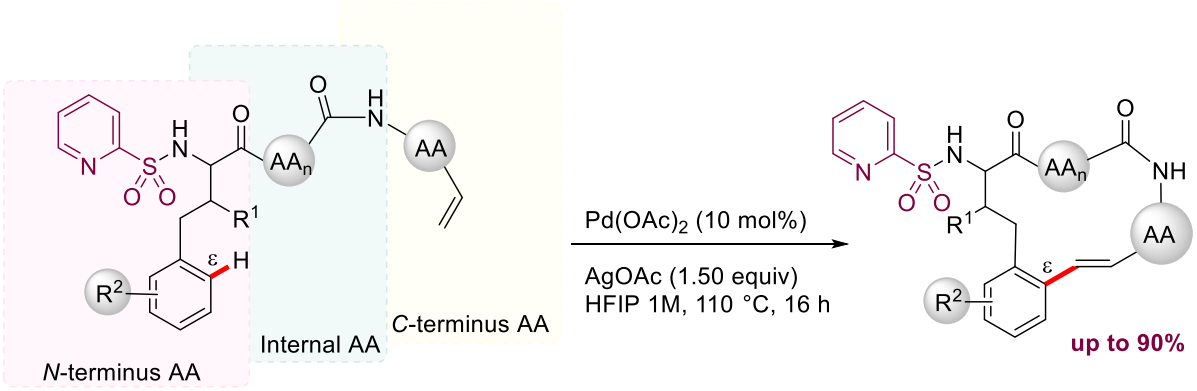

Figure 1. *N*-SO_2Py-assisted Pd-catalysed macrocyclisation.

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Expanding the chemistry of tetracyanobuta-1,3-diene (TCBD): Synthesis and study of novel TCBD derivatives fused to anthryl moieties

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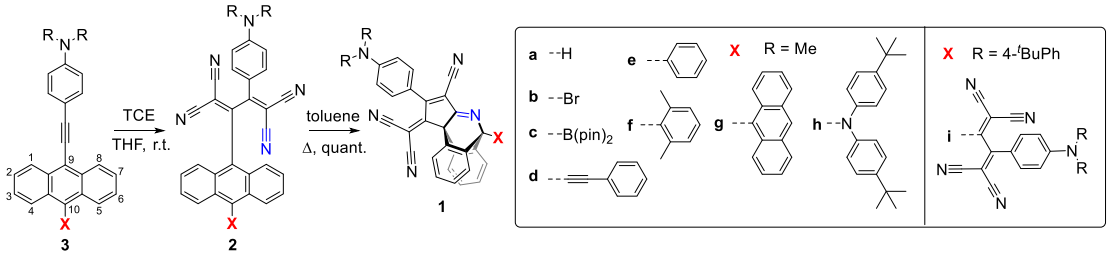
Keywords: *Tetracyanobutadiene, Cyano-Diels-Alder, Electron-acceptor*

The preparation and study of electron donor-acceptor systems (D-A) is a research topic with important implications in relevant technologically fields such as light-to-energy conversion schemes and organic electronics.[1a] In this context, while the family of electron donors is large and diverse, the one of electron acceptors is significantly more limited and mostly centered around fullerenes, perylene diimides, and multicyano fragments. Within the latter, tetracyanobuta-1,3-diene (TCBD), a unit which can be easily integrated in molecules bearing activated alkynes via [2+2] cycloaddition−retroelectrocyclization (CA-RE) reaction with tetracyanoethylene (TCE),[1b] stands out as an interesting moiety for the preparation of D-A conjugates.[1c]

During our research on the preparation and study of TCBD-based derivatives, we discovered a rare example of high-yielding, intramolecular cyano-Diels-Alder (CDA) reaction taking place in an anthryl derivative functionalized at its 9 position with a TCBD moiety (**2a**→**1a** in Scheme 1).[1d] Based on these premises, we decided here to explore the reaction scope of such CDA reaction. With this goal in mind, we prepared an assortment of derivatives bearing a 4-ethynyl-*N*,*N*-disubstituted aniline and different molecular fragments at the anthryl 9 and 10 position (**3b-i**). The latter species were reacted with TCE to afford the corresponding TCBD-functionalized derivatives **2b-i** in high to moderate yields (59-87%). Finally, compounds **2b-i** were subjected to a thermal treatment which triggers, in some cases, the intramolecular CDA leading to the corresponding anthryl-fused TCBD species **1**. The "opened" (*i.e.*, **2**) and "closed" (*i.e.*, **1**) TCBD derivatives were characterized by a wide range of spectrometric and spectroscopic techniques. Moreover, a possible rationale behind the successful activation of the CDA reaction as a function of the nature of the X fragment in **2** was put forward.



Scheme 1. Synthesis of anthryl-fused-TCBD derivatives **1** by intramolecular CDA reaction of the respective conjugates **2**, the latter obtained by CA-RE reaction of 4-ethynyl-*N*,*N*-dimethylaniline-based conjugates **3** with TCE.

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Functional Organic Materials Based on Covalent Organic Frameworks

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Keywords: *COF, crystallinity, porosity.*

Covalent Organic Frameworks (COFs) are porous and crystalline polymers which present great features like predesignability of the network, functionality tailoring, and modulation of its properties via pre or post synthetic methods.[1,2] Introduction of redox units, for example, gives rise to an electroactive polymer which can be used in batteries, capacitors, fuel-cells or electrocatalysis.[2,3] In this work, $Azide_{0,17}$-COF was synthesized for the first time and then modified by introduction of electroactive dimiide units into the framework, specifically, *via* "click" chemistry by the Hüisgen's cycloaddition in the COF pores. The final products were characterized and delaminated *via* liquid phase exfoliation to obtain colloidal covalent organic nanosheets (CONs) to achieve electrode modification by drop-casting. Finally, the electrochemical behavior towards the electrocatalysis of oxygen reduction reaction is currently being studied.

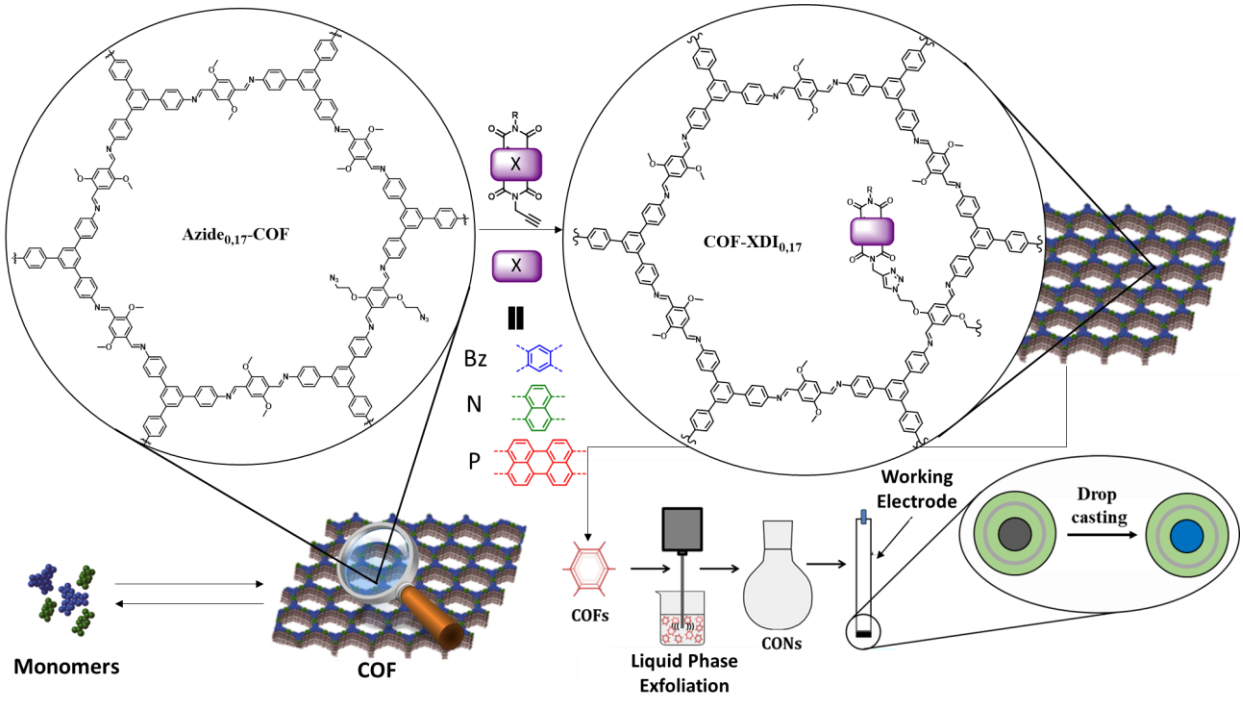

Figure 1. General scheme of our research.

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TOWARDS THE SYNTHESIS OF NEW CYCLOARENES THROUGH ARYNE CYCLOADDITION REACTIONS

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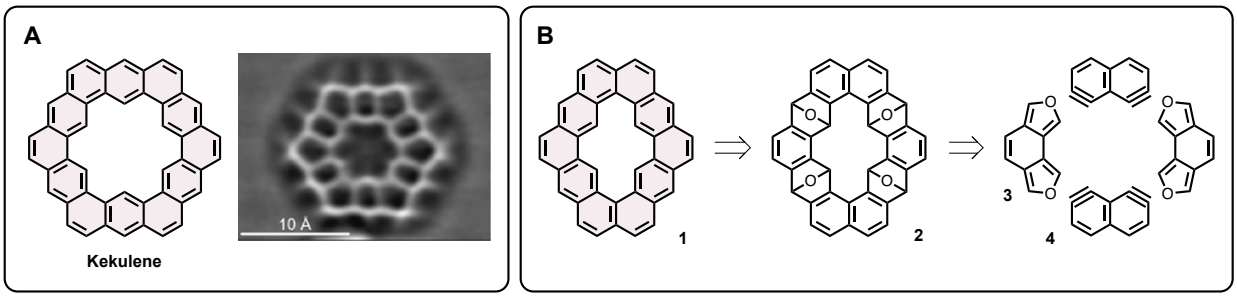
Keywords: *arynes, cycloarenes, nanoporous graphenes.*

Cycloarenes are polycyclic aromatic hydrocarbons characterized by the circular arrangement of *cata*-fused benzene rings.[1] This family of compounds have attracted the attention of the scientific community for decades due to their electronic properties and, more recently, because of their structural relationship with nanoporous graphenes.[2] One iconic example of cycloarene is Kekulene (Figure A), which was synthesized for the first time in 1978.[3] Recently, our research group has reported an improved methodology for the synthesis of this molecule. Also, in collaboration with IBM Research, we have characterized individual Kekulene molecules on surface using atomic force microscopy (AFM).[4]

Some of the most effective strategies for accessing new polycyclic aromatic systems are based on aryne cycloaddition reactions. In this project, we proposed a new approach towards the synthesis of other cycloarenes based on aryne chemistry, as well as the development of new methodologies for the synthesis of the corresponding bisaryne precursors.

In particular, in this communication we describe our efforts to optimize the synthesis of cycloarene **1**, which was reported for the first time in 1986,[5] through a sequence of [4+2] cycloaddition reactions between bisarynes (i.e. **4**) and bisbenzofurans (i.e. **2**) (Figure B).



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Synthesis of cysteine-azobenzene derivatives bearing nucleobases and study of their thiol-disulfide oxidation processes

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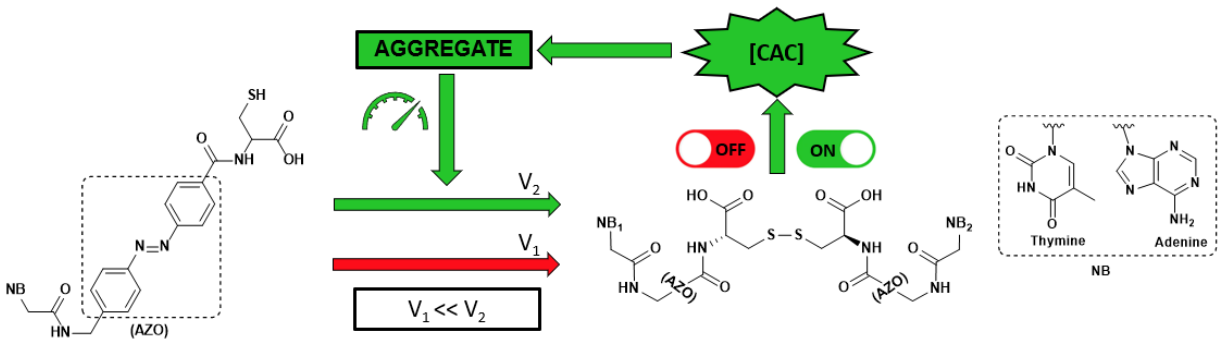
Keywords: *cysteine-azobenzene derivatives, nucleobases, systems chemistry.*

From a holistic perspective, Systems Chemistry [1] tries to explain how life could have arisen, as well as the implicit mechanisms that sustain it. The study of emergent properties is of utmost importance in this discipline, and to investigate it, a very common and at the same time very versatile reaction that takes place in living organisms was taken as reference: the oxidation of thiols to disulfide compounds.

Moreover, disulfide bonds are dynamic and, as long as free thiol remains in the medium, a thiol-disulfide exchange takes place simultaneously. Cysteine is a proteinogenic amino acid present in living beings and for which both processes have been described. Therefore, it was taken as a building block to couple nucleobase moieties, generating adenine (A) or thymine (T) containing hybrids [2]. The nucleobase is a minimal motif responsible for intermolecular recognition, and its effect on the rate of thiol to disulfide oxidation was studied. The oxidation kinetics of these hybrids were studied separately and in mixtures, as they can give rise to three different dimers: AA, TT and AT. All three experiments showed kinetics characteristic of autocatalysis, due to the aggregation of products into supramolecular structures, which act as templates accelerating the reaction.

With these results, it was considered interesting to insert an azobenzene unit between both building blocks with a double intention (see the Figure below). The first one is to favor the formation of aggregates by additional π-π stacking interactions. The second and main one is trying to regulate the oxidation kinetics with light. This motif is mainly used as a molecular switch [3], so that, aggregation can be modulated by playing with its photoisomerization, thus influencing the rate at which the autocatalytic oxidation process takes place.



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Toward the enantioselective synthesis of nanographenes

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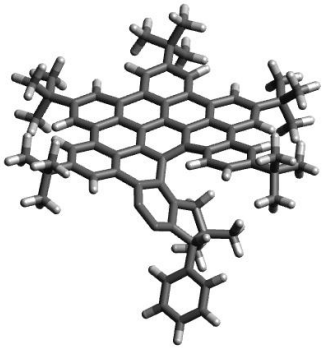
Keywords: *nanographene, enantioselective, chiroptical*

Bottom-up synthesis of nanographene represents a very important approach to control the size, shape and therefore the fundamental optoelectronic properties of nanographenes[1]. Among them, chiroptical properties depend on the ability to escape from the flatland and to introduce chiral elements into the planar structure of the nanographene, such as either planar, helical, or axial stereogenic units.
To date, racemic syntheses followed by chromatographic separations have been the usual route,[2] chiral starting reagents have rarely been used,[3] while an enantioselective synthesis route to optically active nanographenes is lacking.
In this communication, we present the synthesis of a nanographene with a helical substructure consisting of six fused rings. In addition, some general approaches to control the stereochemical outcome will be outlined.



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Tetraphenylmethane-based porous materials and its interaction with fullerenes.

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Keywords: *Porous material, tetraphenylmethane, fullerene*

Research in the field of porous organic polymers (POPs) has experienced rapid expansion over the past decade, being notorious the development of porous aromatic frameworks (PAFs), porous materials based on aromatic building blocks, whose main applications are related to adsorption and storage processes.[1] On the other side, fullerenes comprise a wide family of carbon allotropes with interesting electronic properties arising from their delocalized pi surface, and the inclusion of atoms or clusters inside their molecular cage structure, but unfortunately a lack of efficient purification methods in fullerene chemistry puts a curb on its development. Supramolecular chemistry has attracted the attention of researchers to solve this problem.[3]

In our research group, we are interested in porous materials based in tetraphenylmethane building blocks, particularly PAFs and their soluble shape-persistent dendrimer counterparts.[2] Both kinds of materials present well-defined cavities with numerous arene motifs in their walls, which can serve as molecular recognition elements for interaction with aromatic compounds. We envisaged that the porous materials could be doped with fullerenes for the development of hybrid materials with new electronic properties, or serve as a framework for selective adsorption of fullerene molecules allowing the separation of mixtures of fullerenes and/or endohedral fullerenes (see model example in Fig. 1). As a proof of concept, preliminary studies to probe the viability of these materials to store fullerenes and their level of selectivity in this task will be presented. In addition, we will discuss our advances towards a new synthesis of PAF materials.

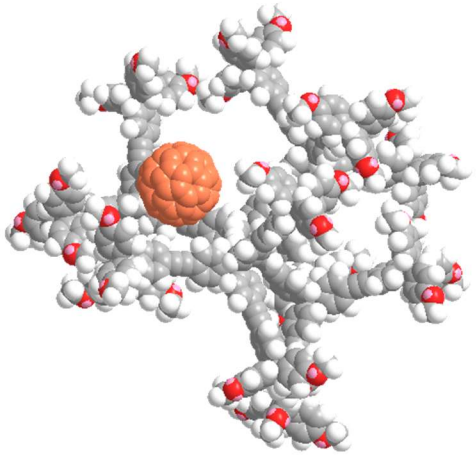

Figure 1. Model for the inclusion of a C_{60} fullerene molecule inside a 2G tetraphenylmethane-based dendrimer. C: grey (dendrimer) / orange (fullerene), O: red, H: white.

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Visible light driven alkylation of cyclic enolates in remote positions

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Keywords: *Photocatalysis, Alkylation, Halide reduction*

Visible light photocatalysis is a tool in synthetic chemistry that has been increasing in popularity in recent times. It allows new reaction pathways by accessing to the excited state of colored molecules employed as photocatalysts that harvest the energy coming from visible light and transfer it to the reagents, generating reactive species of reactants to perform the desired transformation. [1]

One of the advantages of photocatalysis compared to traditional polar chemistry is the ability to perform the alkylation of electrophiles with sterically hindered alkyl halides [2], which is a reaction that may not happen through an S_N2 mechanism.

A suitable way of producing the alkylation of the enolate is to generate an alkyl radical by reducing the corresponding alkyl halide. One of the drawbacks of the classic generation of these radicals from the halides is the use of toxic tin hydrides. Photocatalysis has been able to overcome this drawback, affording much greener processes. [3] In this work we have studied the alkylation of cyclic carbaldehyde derivatives under photocatalytic conditions.

Benzothiophene, benzofuran and indene derivatives were selected as substrates because they are common moieties in medicinal chemistry [4], and an aldehyde could be easily introduced in the structure to form conjugated systems.

When we tried to perform the alkylation we discovered that with this methodology, the indene based carbaldehyde had better reactivity than the other two moieties, Therefore, different indenes carbaldehydes were synthesised with different substituyents in the arene group in β-position to the carbonyl, and in the aromatic ring, and the reaction was also studied with different alkyl bromides.

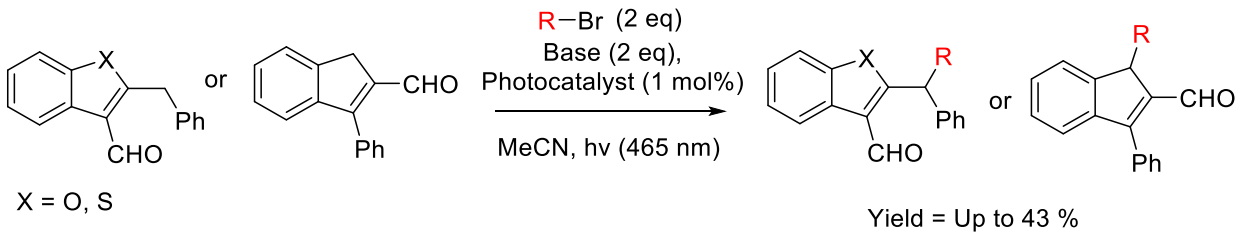

Figure 1. Reaction scheme of the alkylation of cyclic carbaldehydes.

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Novel synthetic methodologies based in allenes, alkynes and bioactive heterocycles

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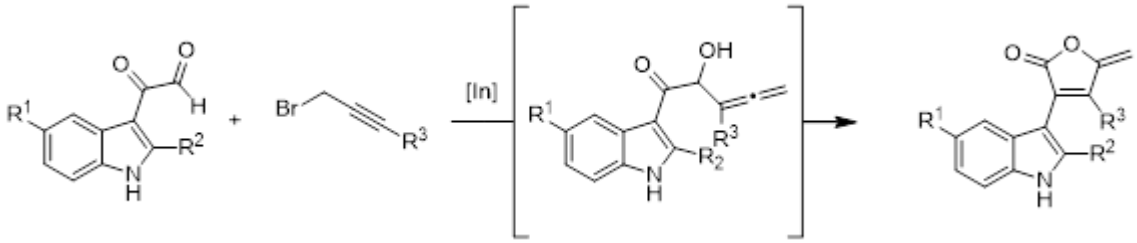
Keywords: *allenol, γ-butenolides, indium*

Allenes are the simplest type of cumullenes. The allene functionality has been of great interest during the last decades because of its unique and special reactivity. Allenes can undergo transformations such as carbometalation, electrophilic, nucleophilic, and radical addition, and, in contrast to alkenes and alkynes, allenes can transfer axial-to-central chirality. For this reason, allenes are considered synthetically versatile starting materials in organic chemistry.[1] On the other hand, γ-butenolides are structural cores of a wide variety of natural and bioactive compounds. Considering the broad spectrum of biological activities that molecules containing a γ-butenolide moiety display, it is not surprising to find a large range of studies that try to develop novel synthetic strategies which improve traditional methods in terms of synthetic efficiency, feasibility, and green chemistry.[2]

In this project a novel strategy for the synthesis of structurally complex γ-butenolides in aqueous media was accomplished using indium as metallic reaction promoter under mild conditions (Scheme 1). This one-pot reaction proceeds through an allene-like intermediate.



Scheme 1. Synthesis of γ-butenolides.

References:

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Cyclopeptides for the formation of self-sorted nanotubes

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Keywords: *cyclic peptides, self-sorting, nanotubes*

Supramolecular hierarchical process allows the formation of different type of materials through a sequential step process based on programmed weak interactions.[1] At this respect self-assembling cyclic peptides (SCPNs) are a practical biomaterial made by the stacking of small cyclic peptides.[2] In the recent years it has been shown that this type of materials can be easily tunned to carry out different applications.

The fidelity in the assembling process between a group of different type of cyclic peptides was evaluated to search for new fibrillar chemical systems.[3] Among the use of different type of weak interaction between each residue of the cyclic peptides, the chirality (enantiomers) was also evaluated in other to explore their amplification in the nanotube formation.

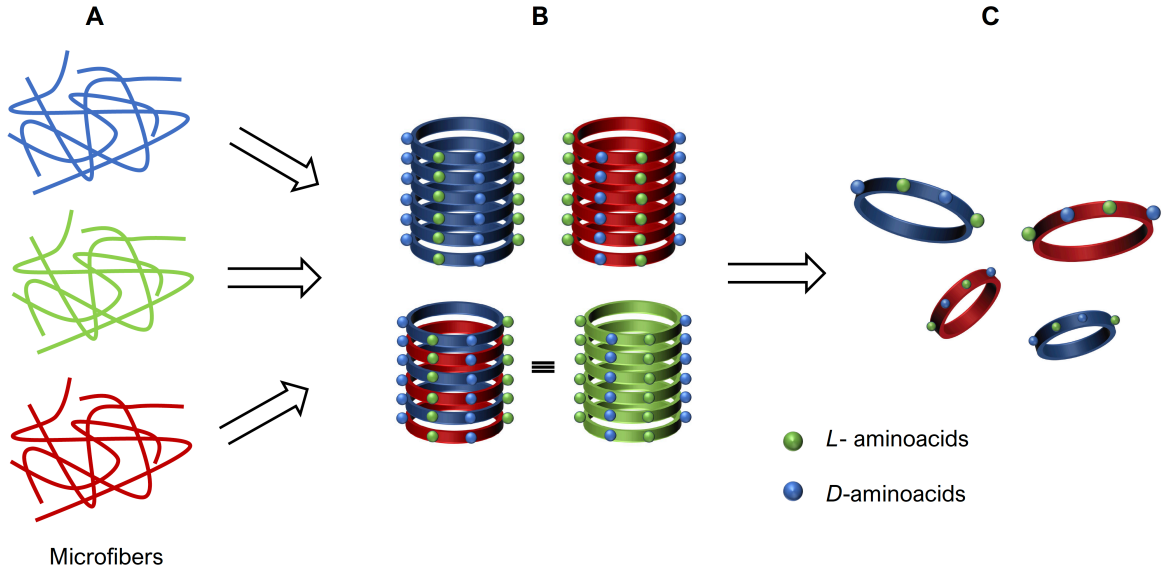

Figure 1. Retrosynthesis of hierarchical system process: (A) Microfibers formed by nanotubes (NT) strictly with themselves except green; (B) Representation of NT (blue), its enantiomer (red) and a mix of both cyclic peptides inside the nanotube (green); and (C) Monomeric state of CPs with inverse quirality.

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Autoorganized π-conjugated systems for organic solar cell developement

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Keywords: *organic solar cells, supramolecular chemistry, cyclic voltammetry*

This project focuses on the study of different organic π-conjugated building blocks and their influence on photovoltaic performance in Organic solar cells. The need to develop new and efficient energy sources has sparked interest in organic molecules as alternatives to silicon in the formation of solar cells. These molecules possess a π-conjugated system to allow obtain energy from the absorption of the sunlight, the generation of charge carriers and subsequent transport to the electrodes [1] but, although these processes are possible, they are hampered by easy recombination of the exciton and the difficulty in separating the charges [2]. To ease these phenomena, we have synthetized two donor-acceptor couples of molecules (Fig 1). In this work, we study the capacity to promote the generation of current in organic solar cells these target molecules.

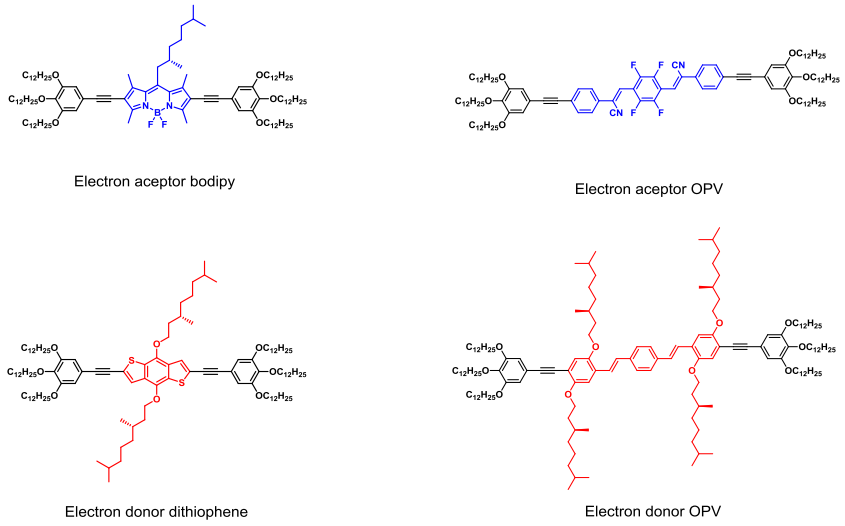

Figure 1 Complementary pairs of donor-aceptor molecules

To carry out the present study and determine the suitability of each couple of molecules, several experiments were performed to calculate the oxidation and reduction potentials, like cyclic voltammetry measurements. Finally, to prove the ability to form supramolecular aggregates via π– π interaction, we used spectroscopic techniques, such as Uv-vis, Fluorescence and Circular Dichroism[3].

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Synthesis of amphiphilic phthalocyanines for application in photodynamic therapy against cancer

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Keywords: *Nanodrugs, Phthalocyanines, Photodynamic therapy.*

Photodynamic therapy (PDT) has emerged as a promising and non-invasive modality for the treatment of several diseases including cancer and microbial infections.[1] It utilizes the combined action of three individual components, namely, photosensitizer (PS), light, and molecular oxygen, to cause cellular damage through the formation of reactive oxygen species (ROS). Unfortunately, the full potential of PDT has not been achieved thus far, mainly due to the lack of efficient delivery process of the PS.[2] A novel strategy, noted by some authors as "one-in-all", relies on the self-assembly of amphiphilic PS to form nanostructures with enhanced cellular uptake and tumor targeting due to the Enhanced Permeation and Retention (EPR) effect.[3]

In this regard, the present study is focused on the preparation of amphiphilic zinc(II) phthalocyanines (ZnPcs) as units for building self-assembled nanoparticles. Particularly, we describe a novel archetype of Pc-based PS that relies on a binaphthyloxy-linked AABB ZnPc, which has been functionalized by Sonogashira coupling with two different polycationic chains at the binaphthyl unit (Figure 1). These molecules, with a strongly marked amphiphilic character, are programmed to: i) self-assemble in aqueous media forming nanodrugs with cancelled photophysical activity but with improved transport properties; and ii) once internalized, disassemble inside the cell due to the larger hydrophobicity of the cellular media, recovering their photophysical activity, responsible of ROS generation. In addition, due to the presence of positive charges, both ZnPcs could localize in mitochondria, thus increasing the overall PDT efficiency.[2]

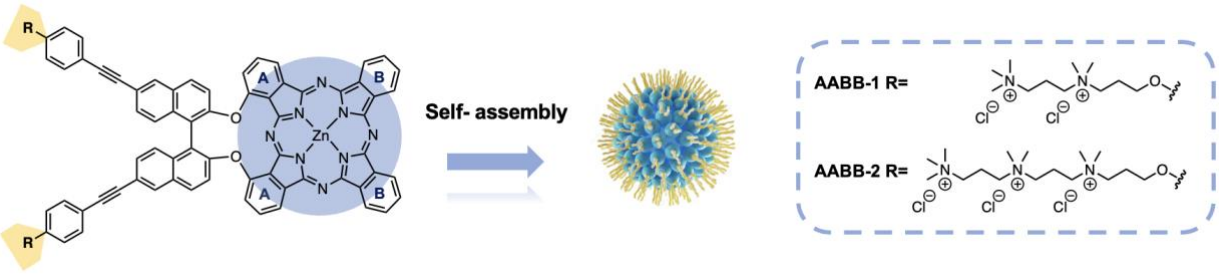

Figure 1. Schematic diagram showing the molecular structure and self-assemble of both AABB ZnPcs.

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Propeller molecular nanographene with a triply benzylic carbon atom

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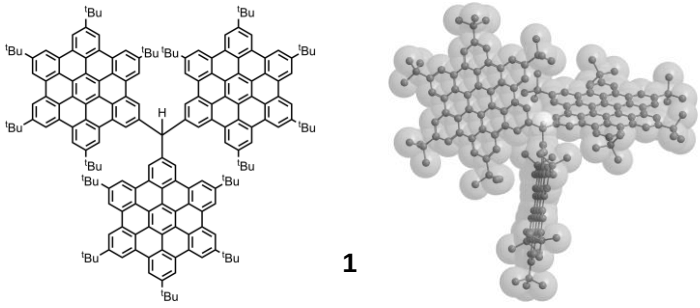
Keywords: *molecular nanographenes, bottom-up synthesis, propeller*

With the discovery of graphene in 2004 by A. Geim and K. Novoselov, new frontiers for the physical, chemical, and material sciences were opened. However, graphene is a zero-bandgap material, which limits its applications in the semiconductor industry.[1] One of the most elegant strategies to open its bandgap is by synthesizing graphene's nanometer-sized structures: nanographenes (NGs). Consequently, different applications arise in the fields of energy storage, biosensing, and photovoltaics, among others.

In order to obtain the desired NGs, the top-down approach grants chemists with a straightforward procedure, which consists in "cutting" graphene into nanoscale pieces. The main drawback of this methodology, though, is the poor control of the shape homogeneity and the size of the obtained NGs. On the other hand, the bottom-up approach is based on conventional organic synthesis, using well-defined reaction steps to afford the final molecular NGs. Despite being a rather complex process, it guarantees an atomically precise control of their edge structure and, therefore, of their chemical, optical, and electronic properties.[2]

Herein, the bottom-up synthesis of the molecular nanographene **1** is presented (Figure 1). The synthetic route, based on a stepwise methodology, includes a Sonogashira cross-coupling, a Diels-Alder cycloaddition, and a Scholl cyclodehydrogenation.



1

Figure 1. Molecular NG **1**: molecular structure (left) and 3D modeling (right).

This molecule adopts a propeller structure,[3] and presents a central carbon atom with sp^3 hybridization, which is endowed with a highly acidic hydrogen atom. Being a triply benzylic position, this hydrogen atom can be removed to stabilize three different intermediates: an anion, a cation, and a radical. The corresponding anion may react with electrophiles, whereas the cationic form would undergo addition reactions of nucleophiles. This allows the further functionalization of **1**. The radical form, on the other hand, would yield an open-shell molecular NG, and therefore present intriguing magnetic properties.[4] These studies are in course.

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Luminescent Platinum (N^C^N) complexes derived from purine nucleobases

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Keywords: *Platinum complexes, Nucleobases*

The tridentate Pt (II) complexes with structure [Pt(N^C^N)L] (L = anionic or neutral ligand) have attracted great interest in the last years due to their luminescent properties and applications in other fields (biological labels, catalysts, anticancer agents)[1-4]. Related to our ongoing research in the development of methodologies that allow the incorporation of transition metals in nucleobases through M-C bonds,[5] we describe in this work the synthesis of two types of non-symmetric (N^C^N) ligands, built on 6-phenyl purine derivatives, the preparation of several types of tridentate Pt(II) complexes that incorporate both Cl and alkynyl ligands and the study of their photophysical properties.

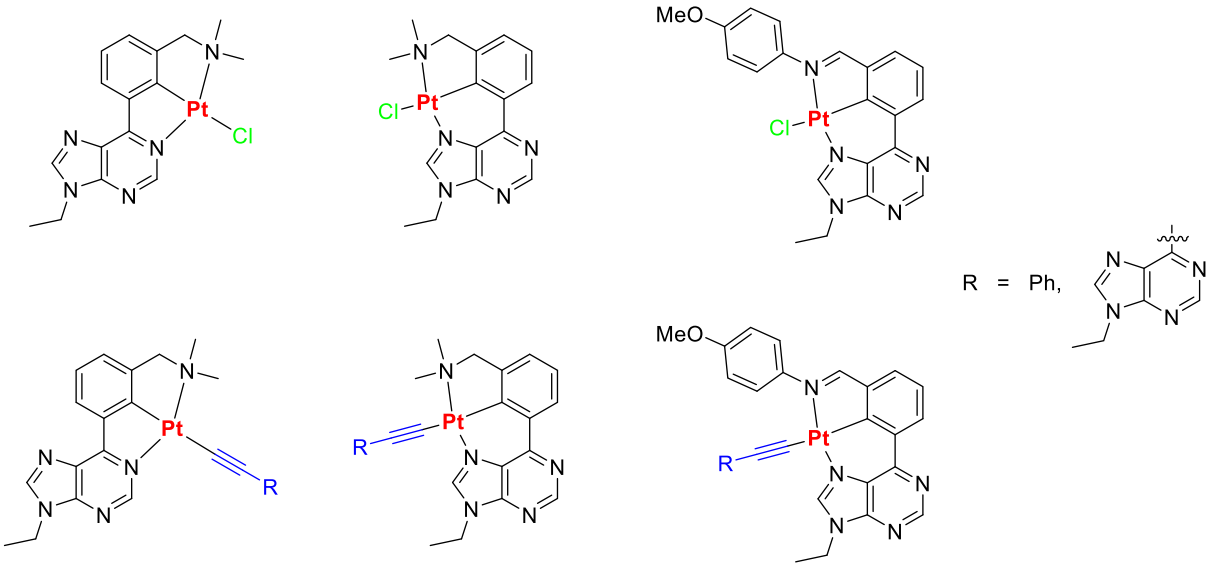

Figure 1. Complexes studied in this work.

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ADAPTATIVE CHEMISTRY APPLIED TO DRUG DISCOVERY

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Keywords: *Dynamic combinatorial chemistry, building block, Lysozyme.*

Dynamic combinatorial chemistry (DCC) is a useful strategy for the identification of new ligands with great affinity for a specific protein target. A Dynamic combinatorial library (DCL) consists of mixing different building blocks which will reversibly react through covalent or non-covalent bonds under thermodynamic control. The library composition changes when a protein template is added to the library shifting the library composition, according to Le Châtelier principle, to the formation of the best binder of the protein target (Protein-directed DCLs).[1, 2]

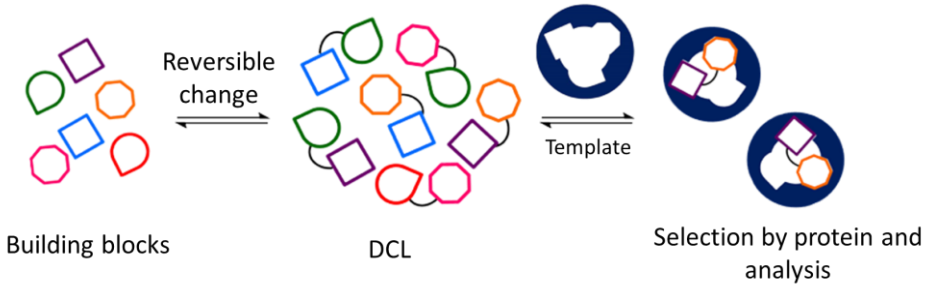

Figure 1. General scheme of a protein-directed DCL.

Here we present the discovery of a new ligand to hen white Lysozyme (HEW Lys) and human lysozyme (hLYS), a glycoside hydrolase that catalyzes the hydrolysis of 1,4-beta-linkages between *N*-acetylmuramic acid and *N*-acetyl-D-glucosamine residues in peptidoglycan, which is the major component of gram-positive bacterial cell wall.[3, 4]

References:

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N–SO_2Py-assisted Pd-catalyzed δ-C(sp^3)–H thiolation of α-amino acids

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***Keywords**: Palladium catalysis, direct thiolation, α-amino acids*

Sulfur-based functionalities are ubiquitous in numerous biologically active compounds, medicinal agents, functional materials, chiral auxiliaries and ligands.[1] Their preparation has always attracted the interest of the scientific community, with important achievements in the metal-catalyzed thiolation of C(sp^2)–H bonds.[2] However, these methods are not as effective when it comes to the functionalization of unactivated C(sp^3)–H bonds.[3] This difference in reactivity may be justified in part by the inherent low reactivity of aliphatic C–H bonds and the competitive coordination of sulfur species interfering with the C–H functionalization reaction.

Overcoming these obstacles, we herein present the development of a methodology for the Pd-catalyzed δ-C(sp^3)–H thiolation process on α-amino acid (αAA) derivatives using disulfides as thiolating agents (Figure 1). Using the removable *N*-(2-pyridyl)sulfonyl (*N*–SO_2Py) group as temporal coordinating auxiliar, the method is suitable for the derivatization of α,α-disubstituted AAs, obtaining monofunctionalized products with moderate diastereoselectivity. DFT studies of the reaction mechanism seem to indicate that the δ-C(sp^3)–H thiolation would proceed through a Pd(II)/Pd(IV) catalytic cycle, with the activation of the C–H bond being the rate-determining step.

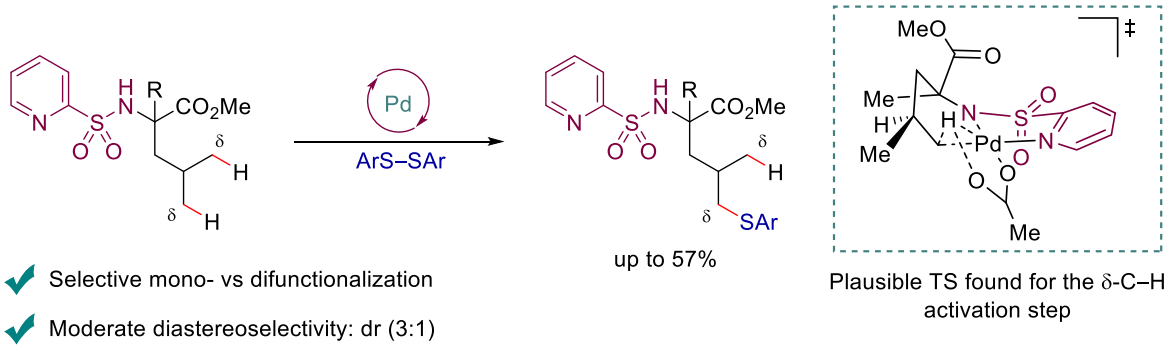

Figure 1. *N*-SO_2Py-assisted Pd-catalyzed δ-C(sp^3)–H thiolation

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Synthesis of new heterogeneous porous catalysts for the conversion of CO_2 into cyclic carbonates

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Keywords: *Porous Organic Polymers, Heterogeneous Catalysts, CO_2 conversion*

Carbon dioxide (CO_2), is a greenhouse gas whose excessive accumulation in the atmosphere causes global warming. To mitigate this problem, recent investigations are focused on the use of this gas as chemical and on its conversion to useful chemicals with the aid of novel catalysts. For such porous heterogeneous catalysts has been considered in the last years due to their great thermal stability, larger contact surface and high versatility in terms of polymer design [1]. The existence of pores implies that there are active sites capable of capturing and modifying CO_2 together with a substrate to obtain high added value products. The aim of this work is the development of heterogeneous catalysts based on porous organic polymers synthesized (both via solvothermal and microwave methods), from 2,6-pyridinedicarxyaldehide and two type of amines where different metal salts [2] are fixed in the polymeric structure (Figure 1):

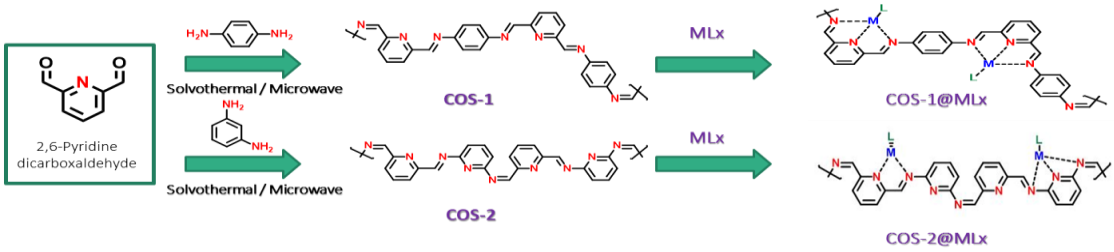

Figure 1. Scheme of the reaction process. From the chosen aldehide, on the left, to the catalyst on the right passing through the synthesis of the polymer at the center.

After characterization by FTIR, NMR and XRD to evaluate their physical-chemical properties, SEM, BET and BJH techniques to determine the porosity, and analysis by TGA and ICP to identify the metal content and purity, the prepared catalysts were tested in the model carbonation reaction between CO2 and small epoxides to yield cyclic carbonates from those substrates. Some results are displayed on Figure 2:

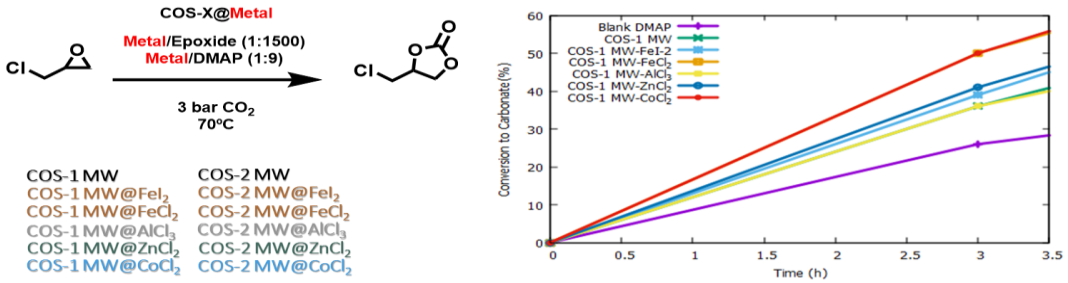

Figure 2. Scheme of the catalysis process with epiclorhidrine as a substrate, the list of the metallic salts used and a graphic where some conversion results to carbonate are shown.

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A One Pot Metal-Free Approach to Highly Substituted Isocoumarins

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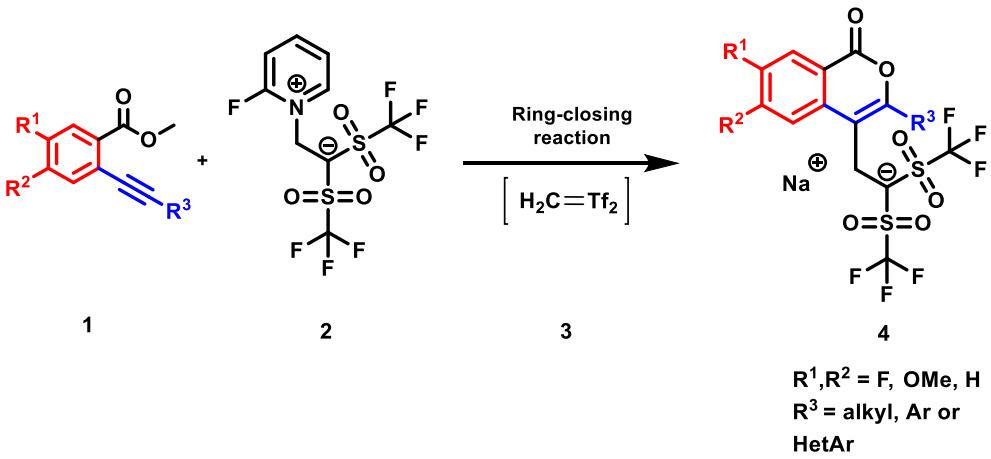
Keywords: *isocoumarin, Yanai´s reagent*

The isocoumarin skeleton is present in numerous natural products derived from plants, insects or microbes and is also present in many synthetic compounds with diverse pharmacological activity, such as antimicrobial, antiallergic, cytotoxic, antifungal or anti-inflammatory.[1] In our research group, we are looking for greener alternatives for the synthesis of heterocyclic molecules with potential biological activity.[2] In this regard, we propose a metal-free route for the synthesis of fluorine-decorated isocoumarins **4**. Thus, reaction of alkynyl esters **1** with bis(triflyl)ethene **3**, in situ generated from spontaneous decomposition of 2-fluoropyridinium salt **2**, provides the expected isocoumarin skeleton as sodium salts. The high reactivity of **3** allows the ring cyclization under mild reaction conditions (between 25 and 60 ºC, short reaction times) and in the absence of any metal or Lewis acid catalyst. Both electron-donating and electron-withdrawing groups are well tolerated on the aromatic ring of **1** and both alkyl and aryl groups can be accommodated at the terminus of the alkyne moiety (Scheme 1).



1 2 3 4

Scheme 1. Synthesis of highly substituted isocoumarins

References:

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Synthesis and autocatalysis of molecular chimeras composed of amino acids and nucleobases

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Keywords: *system chemistry, autocatalysis, kinetic.*

Systems chemistry studies the dynamic interactions and reactions that occur in complex chemical mixtures, both in and out of equilibrium, in search of emergent behaviors [1]. In this context, hybrid molecules that combine in their structure a fragment capable of interacting supramolecularly in various ways, such as a nucleobase, and a reversible bond that provides a dynamic character, like the disulfide bond of cystine, are potential candidates to form an attractive system (Figure 1). In addition, autocatalytic processes can occur in these systems, which have been observed in previous studies using hybrids of adenine and thymine [2]. Considering the above, this work aims to broaden the knowledge that exists about these systems by extending the scope to hybrids of guanine (G) and cytosine (C), whose synthesis has been achieved by combining the conventional methodology in liquid phase with SPS (solid phase synthesis). The behavior of monomers G and C in solution will be studied by different techniques such as UV-Visible spectroscopy and transmission electron microscopy (TEM). Also, kinetic studies of the oxidation process in aqueous medium of the cysteine thiol, which leads to the formation of dimers (CC, GG or GC), will be carried out. The results are expected to show an autocatalytic behavior, which will open the door to continue exploring these systems in search of new properties, and to study in the future how a mixture that combines monomers with the four nucleobases would behave.

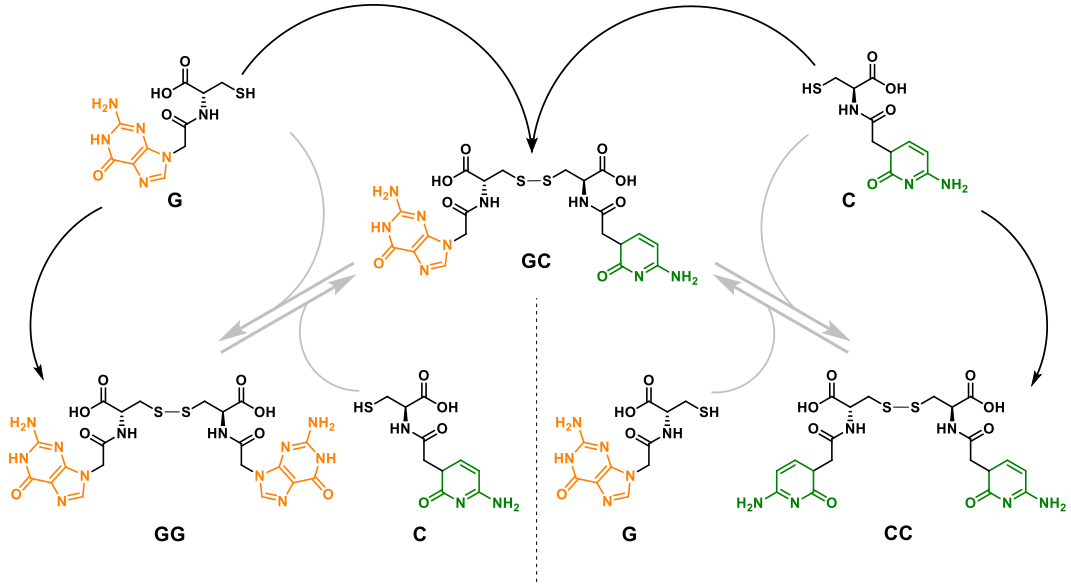

Figure 1. Scheme of the replication network that could be formed with the cysteine monomers G (containing guanine) and C (containing cytosine).

References:

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Diboron reagents activated by Lewis bases in N-N bond cleavage

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Keywords: *Diboron-compound, Pyridine, Reduction*

In the 70's decade silanes were known as good deoxygenating agents in the reduction of amine N-oxides, aryl nitrocompounds and phosphine sulfides and oxides due to the silicon oxophilia. The use of this element was extended to the deoxygenation of nitrones.[1] This method requires relatively mild conditions, but it is limited by harsh and side reactions and low selectivity.[2] It is also described in the literature that diboron compounds can deoxygenate amine[3] and pyridine N-oxides and nitroarenes[4] in presence of bases[5] and pyridines[6] as additives.
Given the interest of developing methods for the selective preparation of nitrogen containing compounds, our group started to evaluate the possibilities offered by boryl-pyridine complexes for the reduction of nitrones. They found that these compounds react with diboron reagents to form the corresponding imines in high yields. The aim of this project is to evaluate the denitrogenating power of diboron derivative. For that we have chosen three different nitrogenous compounds: (a) hydrazines, (b) azides and (c) nitrosamines. The first type was chosen for conceptual as well as mechanistic interest, the second for the description of a method with mild conditions to reduce azides and finally, it is worth highlighting the interest of nitrosamines for being not only potential carcinogenic agents but also contaminants.

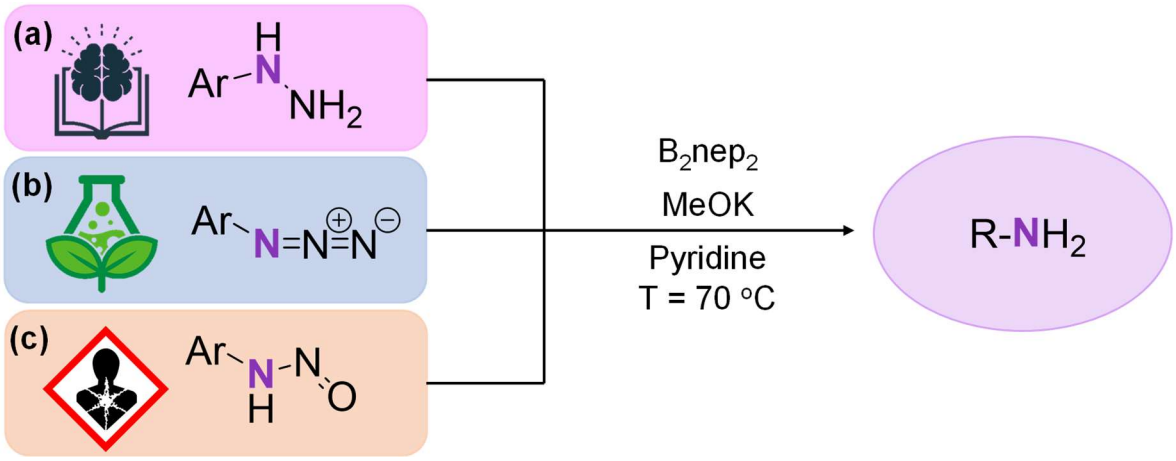

Figure 1. General conditions and applications of the reduction.

Using pyridine and/or MeOK amines are obtained in moderate-high yields. It is also noteworthy the mild conditions, the short reaction times, the absence of transition metals and the mechanistic interest.

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New Compounds for Alzheimer's Disease Therapy

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Keywords*: Alzheimer`s disease, Contilisant analogues, Synthesis*

Alzheimer's disease (AD) is a neurodegenerative disease that affects millions of the elderly around the world, and whose etiology has not yet been determined, with no efficient therapeutic treatment.[1]

AD is a complex disease that entails a wide range of diverse biological events, such as the deficit of biogenic amines (acetylcholine, dopamine, serotonine, etc.), the key neurotransmitters in the cognitive and learning processes, oxidative stress, accumulation and aggregation of misfolded proteins (tau, beta-amyloid), or bio-metal (Fe, Zn, Cu) deposition. This is why a therapeutic strategy based on the design of multitarget drugs able to act simultaneously on the diverse biological events involved in the progress of the disease, should be considered to get more effective drugs for the therapy of AD.[1]

In this context, ***Contilisant***[2] (Figure 1) has been identified as a multitarget-small molecule for the potential therapy of AD. ***Contilisant*** inhibits cholinesterase and monoamine oxidase enzymes, and modulates potent and selectively histamine 3, and sigma 1 receptors, enhancing the levels of the neurotransmitters.

Recently, we have started a project targeted to the optimization of the biological profile of ***Contilisant*** by designing new analogues able to inhibit, in addition to the biological targets shown above, new ones, such as histone deacetylase (HDAC) enzymes,[3] and serotonine 6 receptor (5-HT6R),[4] whose modulation is known to add positive and superior biological effects to the molecules bearing the pharmacophore groups (GP) responsible for their biological activities.

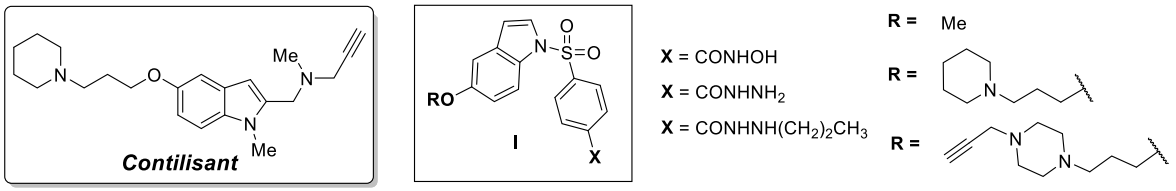

Figure 1. Structure of ***Contilisant*** and the synthesized compounds in this project.

Based on these precedents, in the present project new ***Contilisant*** analogues of type **I** (Figure 1) have been designed bearing GPs, such as the *N*(1)-arylsulfonyl motif for the modulation of 5-HT6R, and hydroxamate, and hydrazide groups for the inhibition of HDACs. The main goal being the synthesis and bio-evaluation of new ligands analogues of ***Contilisant*** for a more effective AD therapy.

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Advancing BOPIDY-based molecular emitters of circularly polarized light

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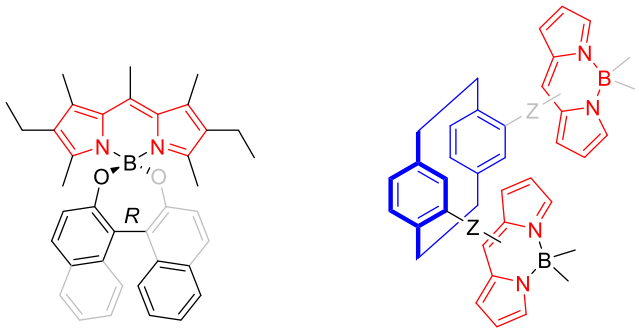
Keywords: *BODIPY, CPL, [2.2]Paracyclophane*

Circularly polarized luminescence (CPL), which is the differential emission of right- and left-handed circularly polarized light by chiral luminescent systems, plays a fundamental role in the development and improvement of multiple photonic tools such as 3D optical displays, spintronic-based devices, biological probes, chemical sensors, OLEDs or security inks, as well as to advancing sophisticated asymmetric photosynthetic processes.[1] Among all the chiral CPL-enabling systems, those based on Simple Organic Molecule (CPL-SOMs) stand out owing to intrinsic advantages coming from their organic nature.[2] One of the most successful organic fluorophores is the BODIPY (BOron DIPYrromethene) one (see in red in Figure 1), due to its excellent photophysical properties, easy access and possibility of tuning key properties by the well-known BODIPY chemistry.[3] All these facts have promoted the BODIPYs as one of the most valuable dyes to develop CPL-SOMs.[2b] However, CPL efficiency in BODIPY CPL-SOMs still needs to be improved by exploring new chiral designs. In this context, the compact [2.2]paracyclophane scaffold has recently arisen as specially interesting for the development of efficient CPL-SOMs,[4] and it could be also used for advancing those based on BODIPY. This communication shows preliminary results on the development of BODIPY-based planar chiral [2.2]paracyclophanes (*e.g.*, **2** in Figure 1) as new molecular emitters of circularly polarized light.



1 **2**

Figure 1. Example of a BODIPY-based CPL-SOM (**1**) and envisaged CPL-SOM design based on BODIPY chromophores (red) and chiral [2.2]paracyclophane (blue). Z denotes a linker (**2**)

References:

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Bottom-up Synthesis of CPL active chiral COF films

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Keywords: *Covalent Organic Frameworks, Chiral Films, Chiroptical materials*

Covalent organic frameworks (COFs) represent an interest class of 2D or 3D network nanomaterials with well-defined topology, periodic lattice and tunable pore size, that can be ingeniously formed through strong covalent bonds. Compared to metal-organic frameworks and zeolitic, COFs have the features of low mass density, totally organic backbone, , permanent porosity, structural diversity, high surface area,and high stability in both wáter an organic solvents.[1] As a result, COFs have gained notewothy attention for potential aplications in gas adsorption, water purification, drug delivery, catalysis...

In this project, the development of chiral COF films with circularly polarized luminescence (CPL) will be carried out using botton-up synthetic strategies by interfacial polymerization of the bulding blocks, cyclen and chiral binol derivative (Figure 1). CPL active chiral COFs have been scarcely reported to date,[2] but surely, we will play an important role in the development of advanced chiroptical materials.

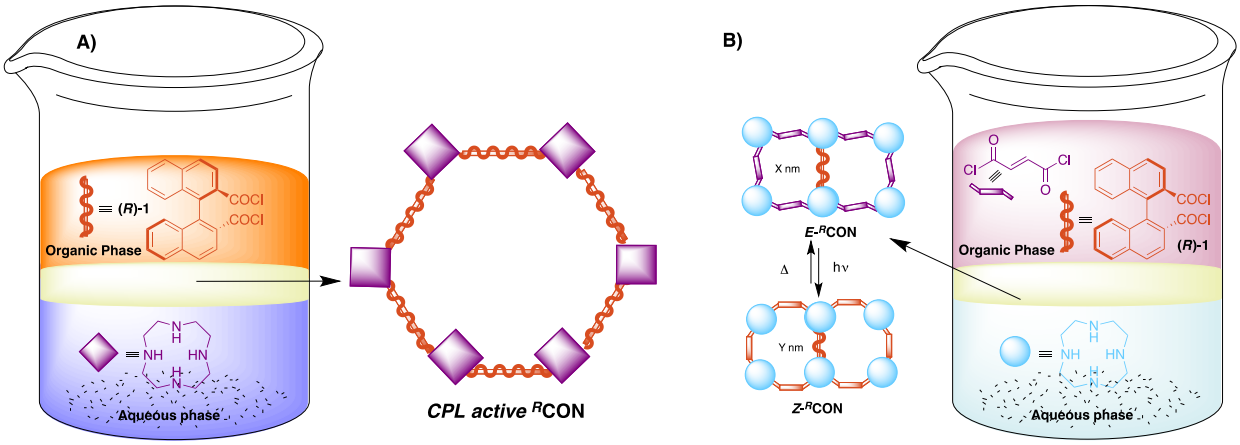

Figure 1. Interfacial polymerization of CPL active **CON films.** A) A CPL active film based on a chiral COF. B) *A CPL active "Smart" COF films with a light-switchable pores.*

References:

[1] Feng, X.; Ding, X.; Jiang, D. *Chem. Soc. Rev.,* **2012**, *41*, 6010–6022.

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Encapsulation of Biomolecules in Self-Assembled Nanotubes

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Keywords: *nanotubes, self-assembled, encapsulation*

Self-assembled nanotubes are one of the most important supramolecular tubular structures as they mimic structures found in nature and their properties can be modified in an easier manner than the ones of covalent nanotubes which results in a higher degree of applicability, especially in the field of encapsulation and transport because the cavity size can be easily modified. However, there are only a few examples on which pore functionality is used.[1] In our research group, self-assembled nanotubes based on hydrogen bonding between complementary nucleobases derivatives (mainly cytosine and guanine) and π-π stacking have been thoroughly studied.[2] Also, extraction processes of dyes in water have been documented.[3] On this project, nanotubes showing different functionalization will be prepared and tested to explore their encapsulation capabilities of hydrophilic molecules in organic media such as DNA, RNA, proteins, and more.

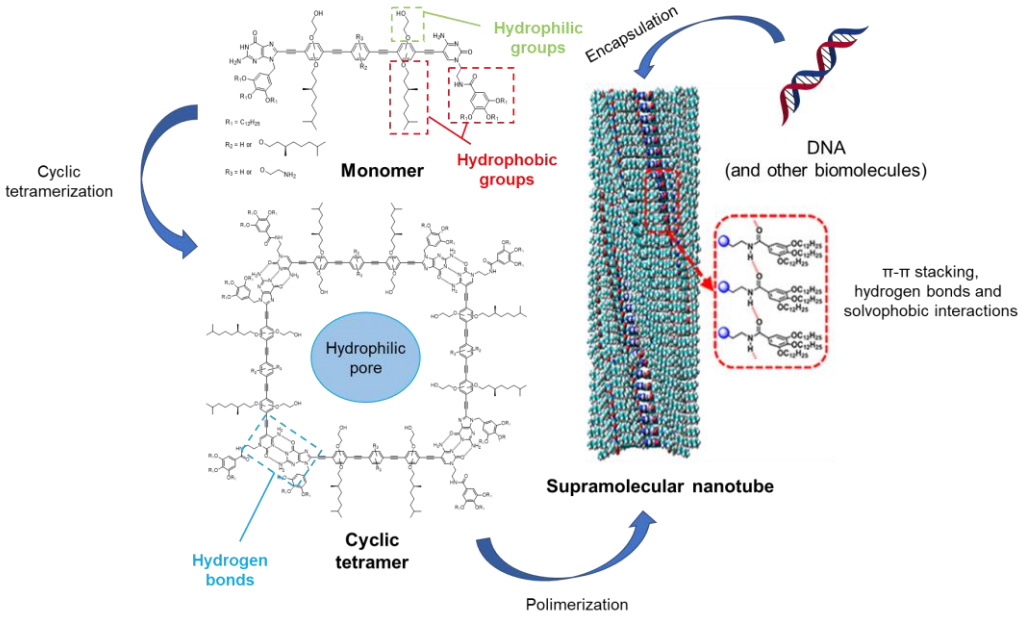

Figure 1. Formation of the self-assembled nanotube and summary of its properties

References:

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Identification of new progerin ligands for the treatment of progeria

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***Keywords**: Progeria, proteolysis targeting chimeras (PROTACs), progerin ligands.*

Hutchinson-Gilford progeria syndrome (HGPS) or progeria is a rare disease that affects around 1 in 4 million new births causing their death at 14-15 years resulting from heart failure. Some of its characteristic symptoms are accelerated aging, alopecia, abnormal skin pigmentation and hearing loss. Progeria is caused by a mutation in the LMNA gene that leads to the biosynthesis of a mutant lamin A protein, known as progerin, which accumulates in the nuclear membrane.[1] Recent studies have shown that the reduction of progerin levels in the nuclear membrane improves the phenotype of this disease.[2] Considering these results, our research group has started a project aimed at the direct reduction of these mutant protein levels using proteolysis targeting chimeras (PROTACs). A PROTAC molecule contains three moieties: (i) A ligand that binds to the protein of interest, (ii) a subunit responsible for the recognition of the E3 ligase that labels the protein of interest for degradation and (iii) a linker that binds both moieties.[3]

Whereas different E3 ligase recognition substrates are known,[4] only one ligand for progerin (based on the natural product decursinol) has been described.[5] Hence, finding new progerin ligands is a current need and also the first step to develop new PROTACs. With this objective in mind, our research group has identified compound UCM-91 as a new ligand for this protein. In this project, we have carried out a systematic exploration around this hit aimed at studying the influence of the different structural moieties of the compound (Figure 1) on the affinity for progerin. The affinity of the synthesized compounds for this mutant protein is being evaluated by cellular thermal shift assays, experiments that are ongoing in our laboratory.

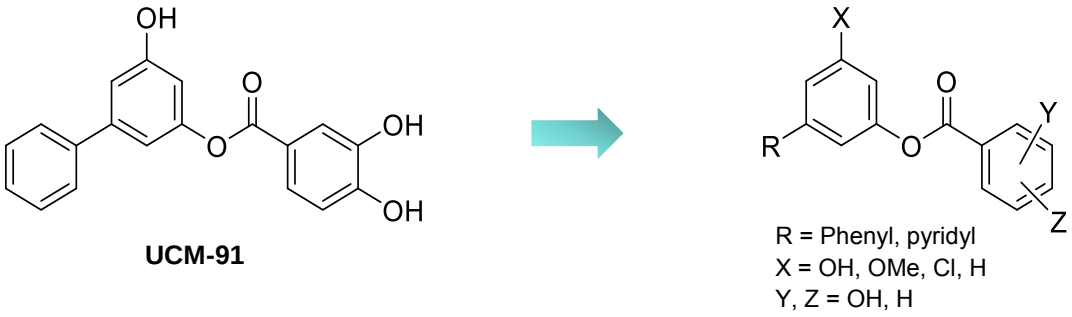

Figure 1. Structural exploration around hit UCM-91

References:

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Extended conjugation in Subphthalocyanines for solar cell applications

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Keywords: *Subphthalocyanines, organic photovoltaic devices, polycyclic aromatic hydrocarbons*

Subphthalocyanines (SubPcs) are aromatic macrocycles with a unique concave structure, because of the tetrahedral coordination of the boron atom located in their central cavity to the nitrogens of the three diiminoisoindole units that constitute them. These molecules are of great interest for different technological applications, among which organic photovoltaic devices are of particular interest. For this purpose, it is important that they have an absorption as red-shifted as possible (around 650-700 nm).

The introduction of peripheral π-extended conjugated substituents has proven to be the most successful method to shift the Q band absorption of SubPc towards the near-IR region.[1] Peripheral annulation represents a less explored approach to modify SubPc structure, permitting the extension of its π-conjugated system and, therefore, the modulation of the macrocycle properties. Among the few examples, Subnaphthalocyanines (SubNcs) are the best known benzoannulated SubPc derivatives that have found a relevant role in photovoltaic devices, due to their red-shifted absorption.[2]

In most cases, these SubPcs have been prepared by conventional cyclotrimerization of the corresponding annulated-phthalotriles, leading to different synthetic problems and low reaction yields. Considering the high impact of merging SubPcs and polycyclic aromatic hydrocarbons (PAHs), the development of new efficient synthetic approaches for the preparation of π-extended PAH-fused SubPc derivatives, based on the post-functionalization of easily prepared preformed SubPcs, is important. We are presenting here our efforts in this direction.[3]

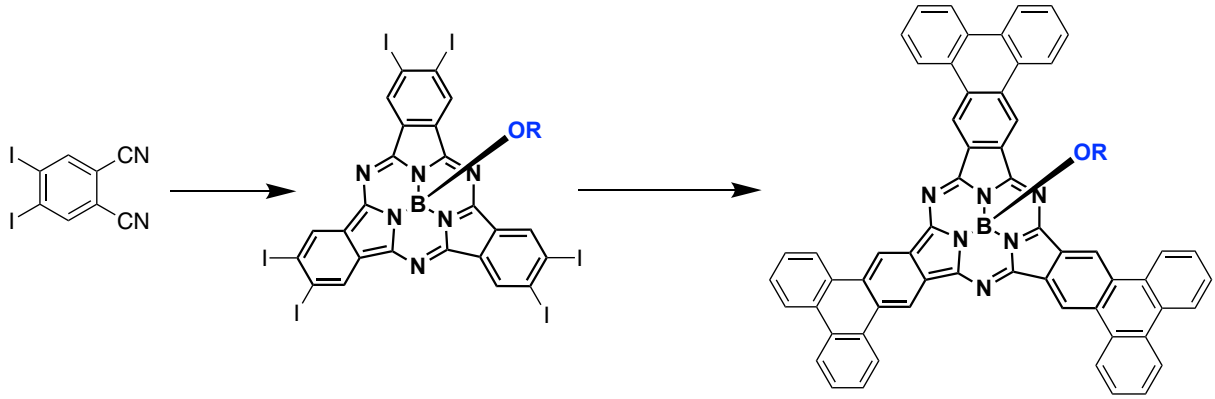

Figure 1. Synthetic route followed to increase the π-system of the SubPcs.

References:

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