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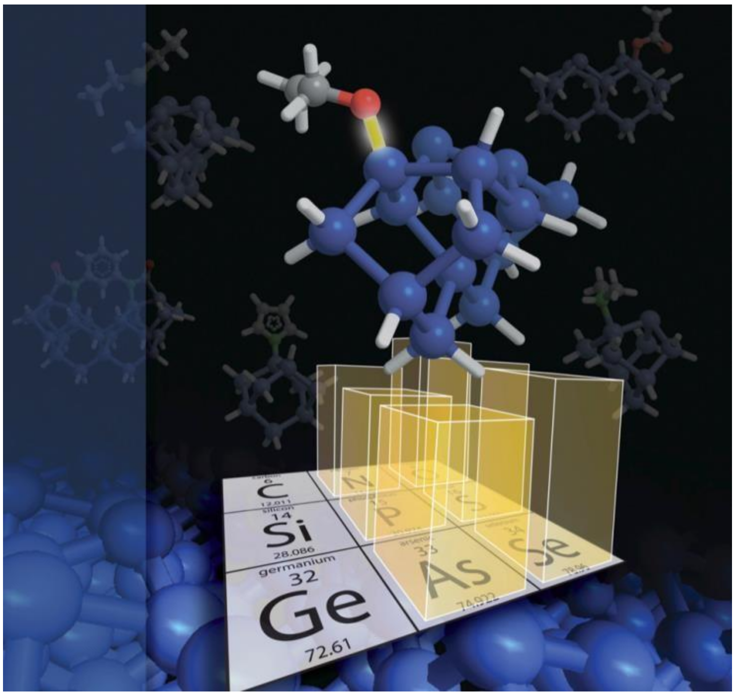
XVII Simposio del MQO Universidad Autónoma de Madrid

11-13 de junio de 2025



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Cursos 2023/24 - 2027/28

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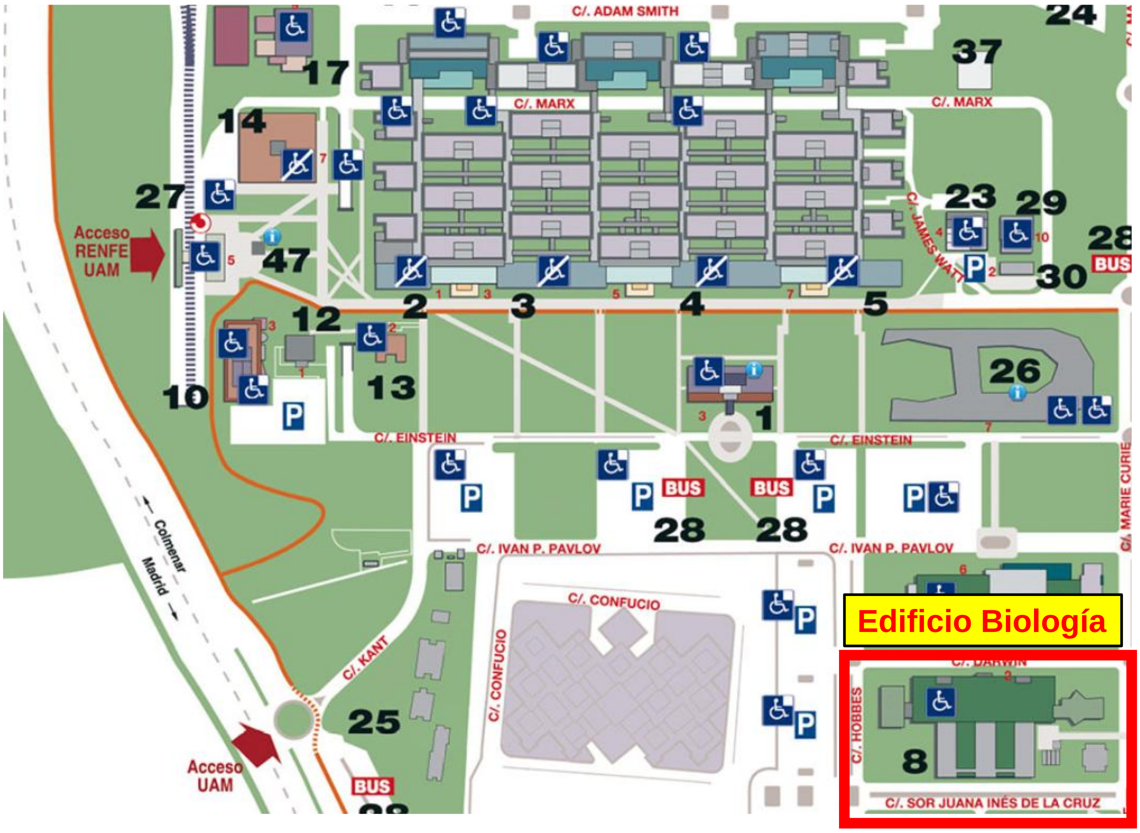
El XVII Simposio del Máster en Química Orgánica se celebrará en el Edificio de Biología de la Universidad Autónoma de Madrid, Campus de Cantoblanco, 28049, Madrid.



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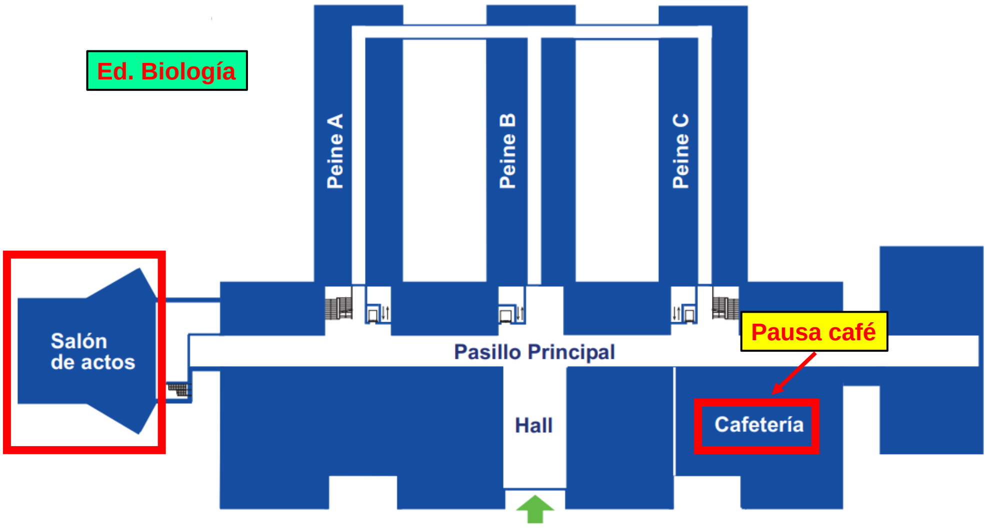
Las sesiones de pósteres se realizarán en la Plata Baja del **Edificio de Biología**.



PROGRAMA

Miercoles 11 de junio

15:30 Apertura (Salón de actos, Ed. Biología)

16:00 Sesión de pósteres I (P1-P23) (Planta baja, Ed. Biología)

Jueves 12 de junio

9:30 Sesión de pósteres II (P24-P45) (Planta baja, Ed. Biología)

11:30 Pausa café (Cafetería, Ed. Biología)

12:00 Conferencia Dra. Carmen González Espínola (BioNTech SE) "Techos de Cristal", (Salón de actos, Ed. Biología)

14:00 Comida (Cafetería, Ed. Biología)

16:00 Actividades de networking dirigido (Ed. Biología, UAM)

> **16:15 a 17:30 -** Escape Room (Grupo 1, Aula 001, Ed. Biología) y Actividad sobre liderazgo (Grupo 2, Aula 102, Ed. Biología)
>
> **17:45 a 19:00 -** Escape Room (Grupo 2, Aula 001, Ed. Biología) y Actividad sobre liderazgo (Grupo 1, Aula 102, Ed. Biología)

Viernes 13 de junio

9:30 Sesión de pósteres III (P46-65) (Planta baja, Ed. Biología)

11:30 Pausa café (Cafetería, Ed. Biología)

12:00 Conferencia Dra. María Ángeles Fernández-Ibáñez (UvA) "S,O-Ligand Promoted Pd-catalyzed non-Directed C-H Functionalization of Arenes". (Salón de actos, Ed. Biología)

13:30 Encuestas (Salón de actos, Ed. Biología)

13:45 Entrega de premios y Clausura (Salón de actos, Ed. Biología)

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64. Vera Guijarro, Alejandro (UCM)	**P63**
65. Vidal Sánchez, Micaela (UAM)	**P65**

ABSTRACTS DE LOS PÓSTERES

Precision Therapy for *Pseudomonas aeruginosa* Infections *via* Inhibition of the LasB Enzyme

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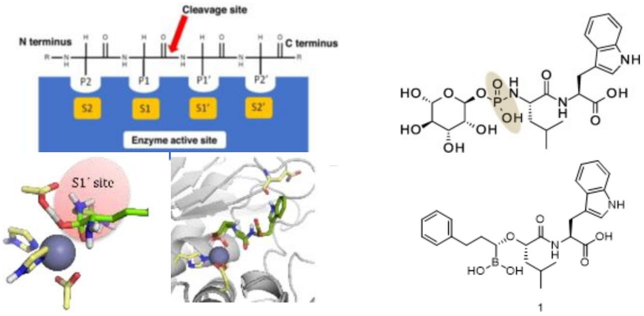
Keywords: *Pseudomonas aeruginosa, LasB enzyme, Boron-based inhibitors.*

The ability of antibiotics to cure these diseases is now at serious risk due to the consequences of broad-spectrum antibiotic use on microbiome stability and pathogen resistance. The disappointing returns from this approach and noting the huge success of precision medicine in oncology, have triggered a big shift in the antibiotic discovery perspective in recent years to turn the attention on narrow-spectrum antibiotics. Precision antibiotics with focused and well-defined activities are emerging as a means of addressing infections without damaging microbiomes or incentivizing resistance*. Pseudomonas aeruginosa* is one of the most worrisome pathogens recently highlighted by the World Health Organization (WHO), because it is responsible of ~8% of all healthcare-associated infections and ~13% of severe healthcare-associated infections due to this bacterium are multi-drug resistant. It is therefore urgent to search for new anti-pseudomonas drugs with a new mechanism of action by selectively disabling clinically unexploited bacterial targets without microbiome damaging. An innovative antibacterial approach that is increasingly being explored comprises inhibition of the bacterial capacity to produce the infection (pathogenesis).

This project seeks for the discovery of novel inhibitors of LasB (Pseudomonas elastase B, pseudolysin, encoded by *lasB* gene, EC 3.4.24.26), the most abundant protein within the *P. aeruginosa* secretome and the main virulence factor of this pathogen.[1] The proposed inhibitor focuses to improve selectivity by incorporating a boronate group, which mimicks the tetrahedral transition state (addition-elimination mechanism) involved in LasB catalysis by changing the hybridization from sp2 to sp3. Phosphoramidon is the most relevant LasB inhibitor but lacks selectivity. This project seeks to overcome this limitation with compound **1** that contain boronic acid group.



1

Figure 1. Tetrahedral intermediate formed in the reaction catalyzed by LasB by coordination with the Zn site at SN1´, chemical structure of phosphoramidon and the phosphoramidon derivative **1** containing a boronic acid.

References:

[1] (a) M.J. Everett, D.T. Davies, *Drug Discov.* **2021**, *26*, 2108. (b) A.M. Kany et al., *ACS Infect. Dis.* **2018**, *4*, 988. (c) C.M. Galdino et al., *Curr. Protein Pept. Sci.* **2019**, *20*, 471. (d) A.M. Kany et al., *ACS Chem. Biol.* **2018**,*13*, 2449. (e) C. Kaya et al., *Angew. Chem. Int. Ed.* **2022**, *61*, e202112295.

Developing an unconventional methodology for labeling nucleophiles with BODIPYs

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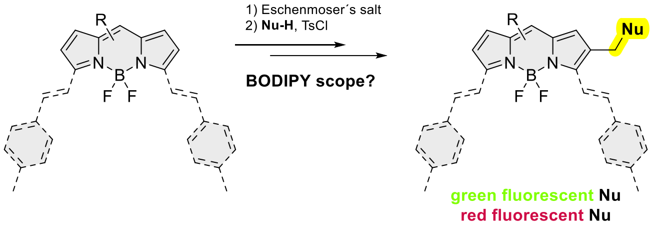
***Keywords**: BODIPYs, Fluorescent labeling, Post-functionalization*

Boron dipyrromethene (4-bora-3a,4a-diaza-*s*-indacene) dyes, nowadays referred to as BODIPYs, are complexes of dipyrromethenes with a disubstituted boron atom, typically BF$_2$, in its structure. These fluorophores have been getting more recognition due to their excellent photophysical properties and easy synthetic accessibility. Consequently, they are widely used in numerous applications, achieving great success and demand in the photonics field.[1] For example, many efficient fluorescent probes for bioimaging techniques have BODIPY as the fluorescent chromophore.[2] However, most of these probes require multistep specific synthesis, involving *ad-hoc* pre-functionalized BODIPYs for the attachment of the probing functionality.[2] Therefore, there is a great interest in the development of methods for the direct functionalization of BODIPYs.[3] This interest has prompted Prof. de la Moya's research group to develop a new methodology for the post-functionalization of BODIPYs in order to label molecules having a nucleophilic site. This methodology consists of obtaining a common intermediate by S$_E$Ar reaction with commercial *N*-methyl-*N*-methylenmethanaminium iodide (Eschenmoser´s salt), and then carrying out a S$_N$ reaction with the nucleophile, activated by tosyl chloride. This has proven a versatile methodology that allows the introduction of nucleophiles of different nature (*O*-, *N*-, *S*- and *C*-nucleophiles). This work explores the scope of the new methodology relative to the starting BODIPYs, including 3,5-π-extended ones (Scheme 1). These BODIPYs have a huge interest, for example in biological applications due to their emission in the red/NIR biologically-interesting region.[4] However, functionalizing them with nucleophiles by known methods is not straightforward.[3c] We demonstrate that our methodology can be successfully applied to these red BODIPYs, aiming to provide nucleophiles with red fluorescence (Scheme 1).



Scheme 1. Exploration of the new methodology for labeling nucleophiles with green and red fluorescent BODIPYs.

References:

[1] (a) Loudet, A.; Burgess, K. *Chem. Rev.*, **2007**, *107*, 4891. (b) Bañuelos, *J. Chem. Rec.*, **2016**, *16*, 335.
[2] Abramchuk, D.; Voskresenskaya, A.; Kuzmichev, I.; Erofeev, A.; Gorelkin, P.; Abakumov, M.; Beloglazkina, E.; Krasnovskaya, O. *Eur. J. Med. Chem.*, **2024**, *276*, 116682.
[3] (a) Clarke, R. G.; Hall, M. J. *Adv. Heterocycl. Chem.*, **2019**, *128*, 181. (b) Boens, N.; Verbelen, B.; Ortiz, M. J.; Jiao, L.; Dehaen, W. *Coord. Chem. Rev.*, **2019**, *399*, 213024. (c) Blázquez-Moraleja, A.; Maierhofer, L.; Mann, E.; Prieto-Montero, R.; Oliden-Sánchez, A.; Celada, L.; Martínez-Martínez, V.; Chiara, M.-D-; Chiara, J.L. *Org. Chem. Front.*, **2022**, *9*, 5774.
[4] Lu, H.; Mack, J.; Yang, Y.; Shen, Z. *Chem. Soc. Rev.*, **2014**, *43*, 4778.

Design of new photoactivatable probes based on diazaxanthilidenes

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***Keywords**: photoconvertible fluorescent probes, diazaxanthilidenes, chiroptical properties.*

Photoactivatable fluorescent probes are powerful tools for studying biological systems at cellular level, as they enable spatial and temporal control in fluorescence microscopy imaging. These dyes can be broadly classified into two categories: the first undergoes an off/on transition from a non-emissive (dark) state to a fluorescent state, while the second involves on/on photoconversion between two distinct fluorescent states. Chenoweth et al.[1] have recently reported a family of photoconvertible fluorescent probes based on diazaxanthilidenes (DXT) scaffolds, capable of photoswitching from a *pre*-activated form to a more conjugated *post*-activated, resulting in markedly red-shifted emission properties. Recently, our group has initiated a collaboration with Prof. Chenoweth to design new functionalized photoconvertible derivatives with chiroptical properties. Chirality plays a fundamental role in biological systems, affecting processes such as enzymatic activity or drug biodistribution.[2] In this context, the development of chiral fluorescent sensors capable of exhibiting chiroptical phenomena, such as circular polarized luminescence (CPL), is of significant interest for advanced bioimaging applications.[3]

This work presents the design and ongoing progress toward the synthesis of a novel photoconvertible fluorophore featuring a DXT scaffold functionalized with a chiral moiety (Figure 1). The incorporation of this chiral unit is expected to extend the π-conjugation system, which is particularly advantageous for cellular imaging. Furthermore, the chiral unit will enable the evaluation of the chiroptical properties, such as in circular dichroism (CD) or CPL, which will be carried out in collaboration with J. M. Cueva's research group at the Universidad de Granada.

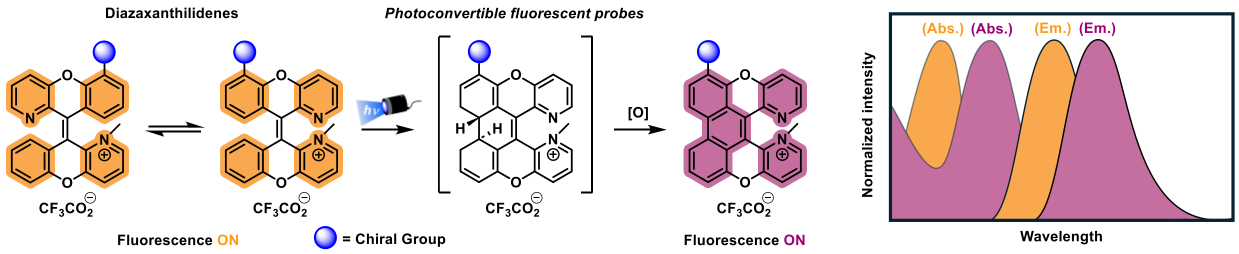

Figure 1. Photoconvertible fluorescent on/on chiroptical probes based on diazaxanthilidene structures.

References:

[1] Tran, M. N.; Rarig, R.-A. F.; Chenoweth, D. M. *Chem. Sci.* **2015**, *6*, 4508-4512.

[2] Stachelek, P.; MacKenzie, L.; Parker, D.; Pal, R. *Nat Commun* **2022**, *13*, 553.

[3] Uceda, R. G.; Míguez-Lago, S.; Cruz, C. M.; Morcillo, S. P.; Álvarez de Cienfuegos, L.; Blanco, V.; Campaña, A. G.; Ribagorda, M.; Miguel, D.; Cuerva, J. M.; *ChemRxiv*. **2025**; doi:10.26434/chemrxiv-2025-tqz5g-v2.

Donor-Acceptor Polar Columnar Materials

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Keywords: *optoelectronic, subphthalocyanines, polarization.*

Organic photovoltaic technologies represent nowadays a promising pathway toward clean and sustainable energy production, owing to the intrinsic advantages of organic materials, such as low weight, mechanical flexibility, and cost-effective processing.[1] A widely adopted strategy in the development of optoelectronic materials is the design of donor–acceptor (D–A) systems inspired by natural photosynthesis. In parallel, columnar liquid crystals (CLCs) based on π-conjugated discotic molecules exhibit significant potential in optoelectronic applications due to their ability to self-assemble into columnar stacks via π–π interactions,[2] enabling alignment under external electric fields and the generation of materials with net polarization.[3] Subphthalocyanines (SubPcs) are a notable example of such molecules; their conical π-conjugated geometry endow them with unique electronic and structural properties, including the formation of non-centrosymmetric columns with permanent[4] or switchable[5] polarization. In this work, we aim to develop a next generation of nano-structured OPV devices using self-assembled donor-acceptor conjugates, consisting in this case of a fluorinated SubPc core functionalized at its periphery with naphthalenediimide (NDI) units via acetylenic linkers (**Figure 1**). With this design, we aim to develop non-centrosymmetric CLC materials exhibiting both permanent polarization and photoinduced charge-transfer properties.

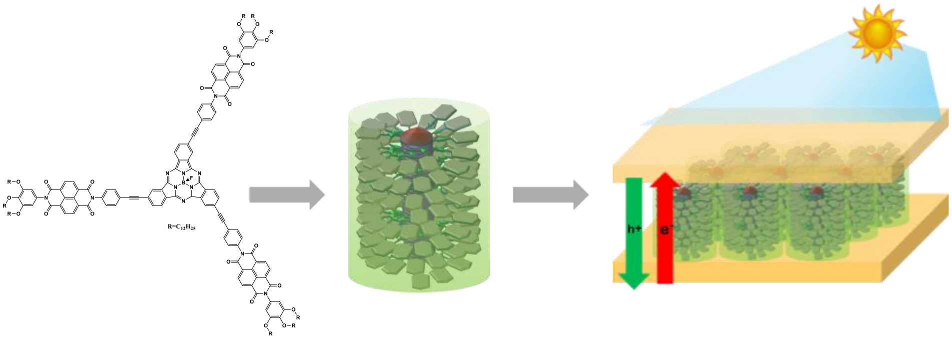

Figure 1. Non-centrosymmetric columnar stacking of cone-shaped SubPc semiconductors and columnar polar alignment in photovoltaic architectures.

References:

[1] (a) Mazzio, K. A.; Luscombe, C. K. *Chem. Soc. Rev.* **2015**, *44*, 78–90.

[2] (a) Wöhrle, T.; Wurzbach, I.; Kirres, J.; Kostidou, A.; Kapernaum, N.; Litterscheidt, J.; Haenle, J. C.; Staffeld, P.; Baro, A.; Giesselmann, F.; Laschat, S. *Chem. Rev.* **2016**, *116*, 1139–1241.

[3] (a) Miyajima, D.; Araoka, F.; Takezoe, H.; Kim, J.; Kato, K.; Takata, M.; Aida, T. *J. Am. Chem. Soc.* **2010**, *132*, 8530–8531.

[4] (a) Guilleme, J.; Aragó, J.; Ortí, E.; Cavero, E.; Sierra, T.; Ortega, J.; Folcia, C. L.; Etxebarria, J.; González-Rodríguez, D.; Torres, T. *J. Mater. Chem. C.* **2015**, 3, 985–989. (b) Zhang, C.; Nakano, K.; Nakamura, M.; Araoka, F.; Tajima, K.; Miyajima, D. *J. Am. Chem. Soc.* **2020**, *142*, 3326–3330.

[5] (a) Guilleme, J.; Cavero, E.; Sierra, T.; Ortega, J.; Folcia, C. L.; Etxebarria, J.; Torres, T.; González-Rodríguez, D. *Adv. Mater.* **2015**, *27*, 4280–4284. (b) Gorbunov, A. V.; Iglesias, M. G.; Guilleme, J.; Cornelissen, T. D.; Roelofs, W. S. C.; Torres, T.; González-Rodríguez, D.; Meijer, E. W.; Kemerink, M. *Sci. Adv.* **2017**, 3, eaao0172.

Towards the enantioselective synthesis of chiral nanographenes

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***Keywords**: arynes, [2+2+2] cycloaddition, asymmetric catalysis.*

The chirality in helicenes and other chiral nanographenes make them of high interest due to their optoelectronic properties for the development of chiroptical materials, specially those related with circular polarized luminescence (CPL).[1] The present project aims to study the asymmetric synthesis of distorted nanographenes through [2+2+2] cycloaddition of sterically hindered arynes[2] with an electron-deficient alkyne, employing a palladium catalyst provided with a chiral ligand (Figure 1). As a proof of concept of this approach, the synthesis of aryne precursor **1** and the preliminary study of its reactivity will be described.

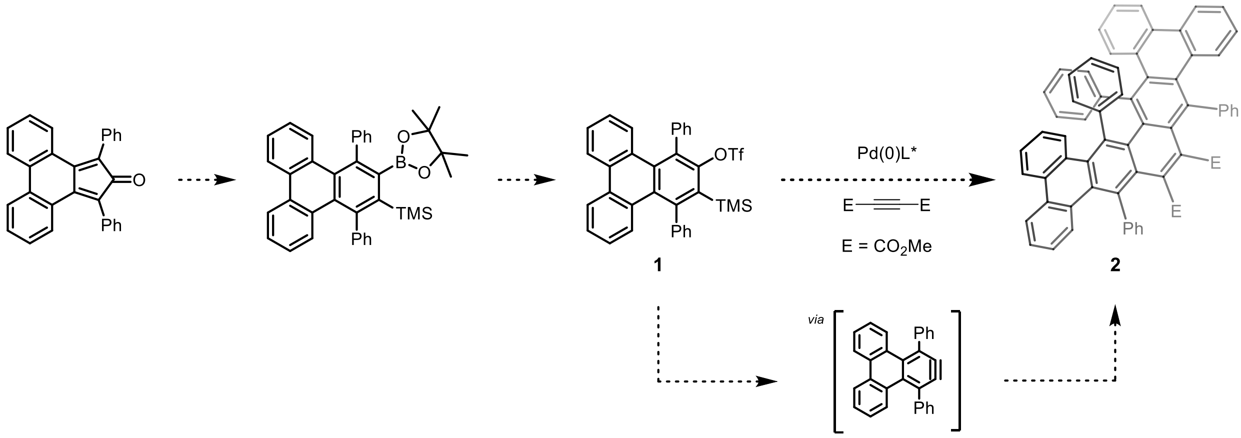

Figure 1. Proposed pathway to synthetize the twisted polyarene **2**.

The project also includes the evaluation of other arynes as potential building blocks for the synthesis of helically twisted nanographenes with different topology.

References:

[1] Anderson,H. V.; Gois, N. D.; Chalifoux, W. A. *Org. Chem. Front*. **2023,** *10,* 4167-4197.
[2] Caeiro, J.; Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. Adv. Synth. Catal. **2006**, *348*, 2466-2474.

Luminescent materials for hyperfluorescent OLED devices

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Keywords: *Photoluminiscence, TADF, OLED.*

Thermally activated delayed fluorescence (TADF) has enabled the design of purely organic emitters capable of harvesting both singlet and triplet excitons in OLEDs, allowing the devices to achieve internal quantum efficiencies of 100%. Conventional TADF materials are based on donor–acceptor (DA) architectures, which promote charge-transfer excited states and reduce the singlet–triplet energy gap (ΔE_{ST}), facilitating reverse intersystem crossing (RISC) from triplet to singlet at room temperature.[1] Multiresonant TADF (MR-TADF) materials provide an alternative by localizing frontier orbitals through rigid, fused polycyclic frameworks containing strategically placed heteroatoms (i.e. nitrogen, boron, oxygen). These induce a resonant distribution of frontier states, where HOMO and LUMO are segregated in an atomically alternating layout, that enables narrowband emission via second-order spin–vibronic coupling.[2] Hyperfluorescent OLEDs synergically exploit both types of emitters, where a DA-TADF molecule efficiently transfers excitonic energy via Förster resonance to an MR-TADF fluorophore, combining efficient triplet harvesting with high colour purity.[3]

In this work, we present two new emitters (**PC8**, **PC16**) that combine electron-poor dibenzo[*a*,*c*]phenazine (DBP) with electron-rich carbazole in a fashion that may facilitate the apparition of TADF. Both systems show strong emissions, which remarkably redshift from **PC16** to **PC8** by modifying the insertion position of the carbazoles into the DBP core (Figure 1). Singlet oxygen generation experiments suggest the accessibility to the triplet manifold which in turn is a precondition for enabling delayed fluorescence. Further experiments are still ongoing to evaluate the delayed fluorescence.

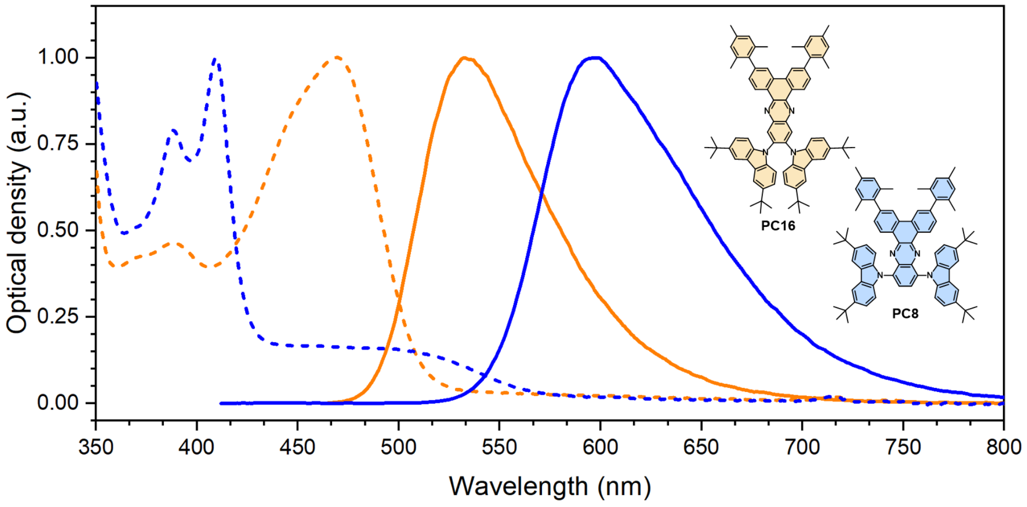

Figure 1. Normalized fluorescence (solid line) and absorption (dashed line) spectra of PC8 and PC16 in toluene.

References:
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New synthetic methodologies of bis(triflyl)ethenylation of dialkynes. Preparation of highly functionalized cyclobutenes

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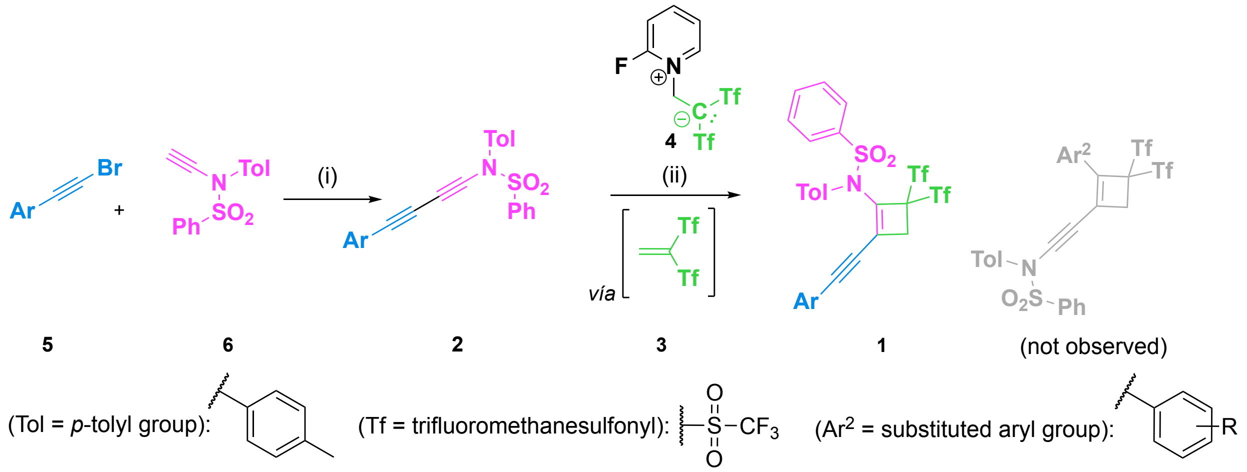
***Keywords**: cycloaddition, cyclobutene, zwitterion*

Cyclobutenes are four-membered carbocycles exhibiting a significant ring strain. Their value as synthetic intermediates has driven the development of new methodologies for their efficient and selective construction.[1] Building upon previous work in the group,[2] we report the synthesis of aminocyclobutenes **1** via a metal-free, regioselective formal [2+2] cycloaddition [3] between amino-substituted diynes **2** and bis(triflyl)ethene **(3)**. The latter is generated *in situ* from the decomposition of the 2-fluoropyridinium salt **(4)** (Yanai's reagent) in solution.[4] The reaction proceeds under mild conditions and shows high selectivity, with the most electron-rich alkyne in the diyne preferentially undergoing cycloaddition. The resulting aminocyclobutene scaffolds feature strongly electron-withdrawing triflyl groups, which serve as useful synthetic handles for further derivatization.[5] This strategy expands the synthetic utility of Koshar-type zwitterions and provides access to densely functionalized, strained carbocycles without the need for transition-metal catalysis (Scheme 1).



Scheme 1. Synthetic route for the preparation of the cyclobutenes. (i) Cadiot–Chodkiewicz coupling. (ii) [2+2] Regioselective cycloaddition.

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The missing regioisomer: Regioselectivity control in Cu/Pd catalyzed borylative allyl-allyl coupling

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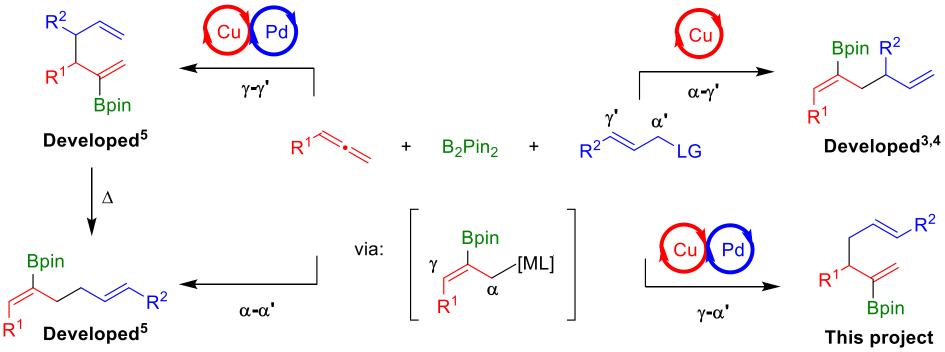
***Keywords**: allylboration, synergistic catalysis, regioselectivity.*

One of the most important challenges in today's chemistry is the development of multicomponent reactions that give efficient and selective access to molecules with high functionalization and that are able to undergo different chemical transformations.

In our research group, we are studying multicomponent catalytic processes which allow the assembly of simple starting materials to form complex molecules. In this line, we have recently developed different allylboration reactions of unsaturated hydrocarbons that lead to the selective formation of different borylated dienes. [1,2]

Within this field, the borylative coupling between allenes and allylic electrophiles represents a significant challenge, especially in terms of regioselectivity control. The catalytic allyl nucleophile, generated in-situ by allene borylcupration, can couple either at the α- or γ-position with the α'- or γ'-position of the allylic electrophile (Scheme 1). Therefore, the formation of up to four different regioisomers is possible. On this point, Hoveyda[3] and Tsuji[4] reported different copper-catalyzed allylboration of allenes to access the α,γ' coupling product. Recently, our group found that using synergistic Cu/Pd-catalysis could be used as a platform to switch the selectivity towards the γ,γ' coupling product.[5] It was also demonstrated that this product can be converted into the α,α' product by means of a Cope rearrangement. However, a route that selectively affords the γ,α' isomer was still missing.

We here report how by fine tuning of both copper and palladium catalysts the regioselectivity of the reaction can be further switched towards the missing isomer. The new conditions provide the γ,α' products in good yield and excellent control over the regioselectivity.



Scheme 1. Borylative allyl-allyl cross-couplings.

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Synthesis of flavonoid glycosides of food interest by enzyme-catalyzed reactions

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Keywords: *Enzyme, glucosylation, acylation*

Polyphenols are a family of natural compounds widely present in plant sources. These compounds have antioxidant activity and their consumption provides benefits to human health, such as the prevention of cancer and degenerative diseases related to oxidative damage. However, these compounds have low solubility and bioavailability **[1]**. Therefore, enzymatic reactions such as glucosylation and acylation have been studied to modify their structure and improve their properties. In the present work, the glucosylation of a battery of polyphenols (**Figure 1**) has been addressed to improve their solubility and stability, using the enzyme sucrose phosphorylase from *T. thermosaccharolyticum* as a catalyst **[2]**. Through computational analysis of induced-fit docking, it has been studied why the glycosidic residue of rutin or hesperidin prevents enzymatic transglycosylation.

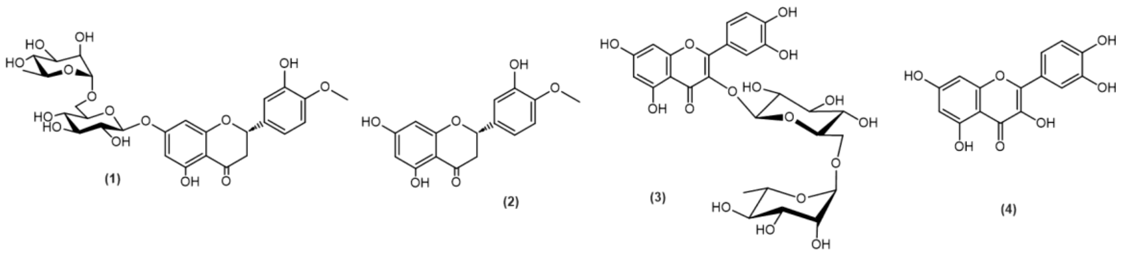

Figure 1. Structures of the studied flavonoids. Hesperidin (**1**), hesperetin (**2**), rutin (**3**), and quercetin (**4**).

In addition, a scale-up of the glucosylation of epigallocatechin gallate (EGCG), previously obtained in the group, was carried out to obtain new acylated derivatives with different vinyl esters, specifically esters of octanoic acid and palmitic acid (**Figure 2**). For the acylation, immobilized lipase from *T. lanuginosus* on granulated silica was used as a catalyst. The derivatives were characterized by NMR and mass spectrometry.

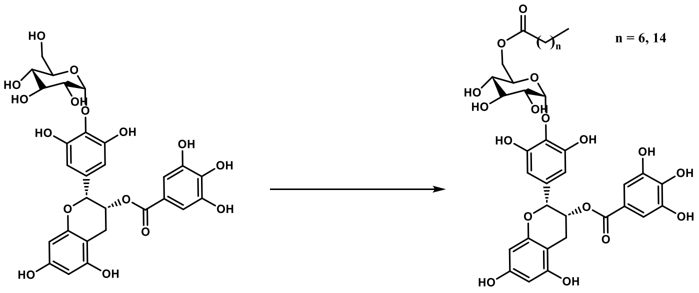

Figure 2. Acylation of glucosylated EGCG by an enzyme-catalyzed reaction.

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Z-shaped Perylenediimides: Transamidation for the Preparation of Chiral Supramolecular Polymers

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***Keywords**: Supramolecular polymers, perylenbisimide, chirality amplification*

Supramolecular polymers are materials with great versatility, mainly due to two factors: the ability to control their self-assembly through different parameters such as pH, temperature, or concentration; and the ease of functionalizing their structures, allowing for their use in various applications (photovoltaic panels, dyes, pigments, etc.). Linear supramolecular polymers derived from perylene bisimide (PBIs) have been widely studied; however, their Z-shaped PBI analogues have been poorly explored. Therefore, the aim of this work is to carry out the synthesis, purification, and study of three chiral Z-PBI derivatives (PBI-1, PBI-2, PBI-3).

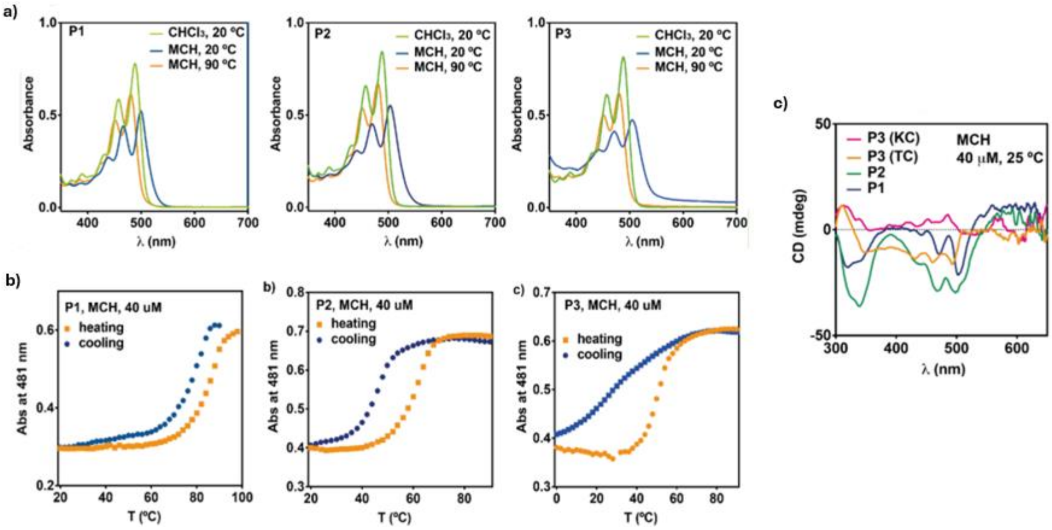

Figure 1: a) Espectros UV-Vis de los derivados. b) Curvas calentamiento-enfriamiento. c) Espectros CD

Based on UV-Vis measurements at high and low temperatures, it can first be confirmed that in all cases, null-type aggregates are formed.[1] This is due to the similarity between the absorption spectra of the aggregates and those of the starting monomers an aggregate type that has been very rarely described in the literature. Secondly, the heating-cooling curves reveal the presence of hysteresis phenomena in all derivatives, associated with the *in situ* formation of metastable species during the aggregation process. This effect is particularly pronounced in the case of the PBI-3 derivative, and when combined with the UV-Vis data, it provides a basis for conducting kinetic studies. Moreover, circular dichroism (CD) studies reveal a chirality amplification process: the point chirality present in the initial monomers extends to the final aggregate, resulting in an enantiomerically enriched helical supramolecular polymer.

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Functionalization with amino acids of metal-organic frameworks for environmental applications

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Keywords: *metal-organic frameworks, amino acids, CO2 capture.*

This study investigates the functionalization of two Zr-based metal-organic frameworks (MOFs), MIP-206 and MIP-206-OH,[1] with amino acids as a strategy to enhance CO_2 adsorption properties (Figure 1). The aim was to evaluate how the size and chemical nature of the amino acids influence adsorption capacity and the interaction strength between CO_2 molecules and the functional groups.[2] A total of ten materials were synthesized: the two pristine MOFs and their respective derivatives functionalized with glycine, L-proline, L-tryptophan, and p-aminobenzoic acid. For all materials, optimal functionalization processes were developed for high-purity, reproducible synthesis, and their identity was verified by several spectroscopic and diffraction techniques.

Preliminary CO_2 adsorption results confirm that, although functionalization with bulkier amino acids leads to a reduction in uptake due to steric hindrance, glycine-functionalized materials exhibit an increase in adsorption capacity. Moreover, the presence of additional hydroxyl groups in the MIP-206-OH analogues leads to a reverse trend in CO_2 uptake compared to MIP-206-based derivatives. The findings highlight amino acid functionalization in MOFs as a promising approach for designing improved materials for CO_2 capture, indicating the role of steric and electronic effects in the resulting performance.

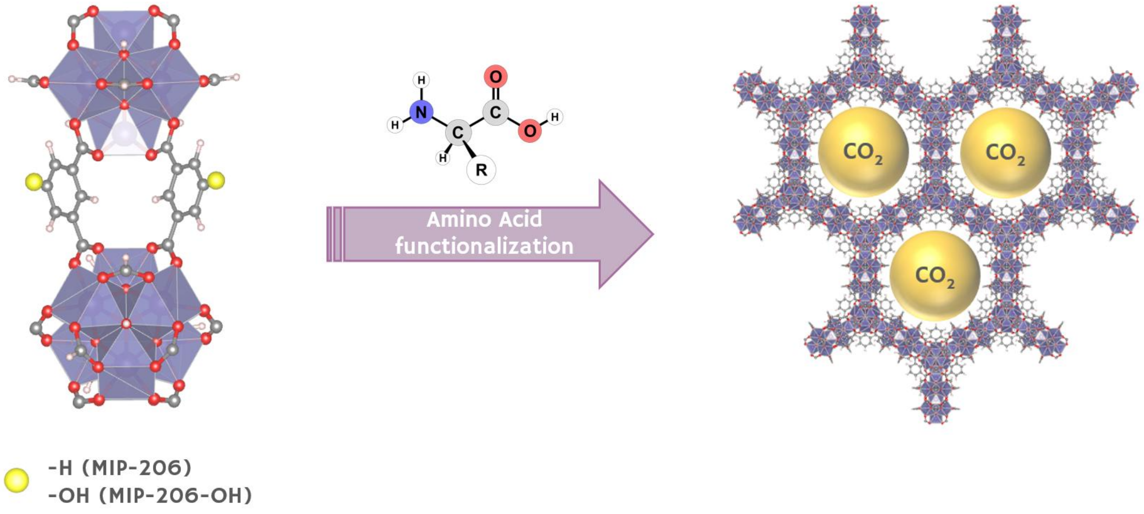

Figure 1. Graphical abstract. Strategy to enhance CO_2 adsorption properties

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Tuning Peptide Conformation through Compositionally Designed Deep Eutectic Solvents

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***Keywords**: peptide, conformation, Deep Eutectic Solvent.*

Peptides show a great potential as chemical tools, so their behaviour and folding is crucial to understanding the expand of their use beyond life frontiers. Deep Eutectic Solvents (DES) are alternative solvents that act as green media,[1] where peptides can be solubilised. Notably, the "design" character of DES can be exploited to tailor the conformational landscape of proteins.[2] However, nowadays is not possible to easily predict DES effects on peptide structure, so it is becoming a key theme in supramolecular chemistry.[3] In this research line, we try to stablish correlations between the system composition and the topology of model peptides. We synthesized a series of peptides by solid-phase peptide synthesis with different overall charge. We reveal that peptides undergo conformational changes from a fully random coil structure in pH 7 phosphate buffer to ordered secondary structures once solved in DES with pre-designed properties. Moreover, this topology is different depending on the charge and composition of the DES and peptides. These observations can lead to the precise design of solvents capable of precisely controlling the conformation of proteins and peptides in order to enhance their enzymatic, structural and other properties.

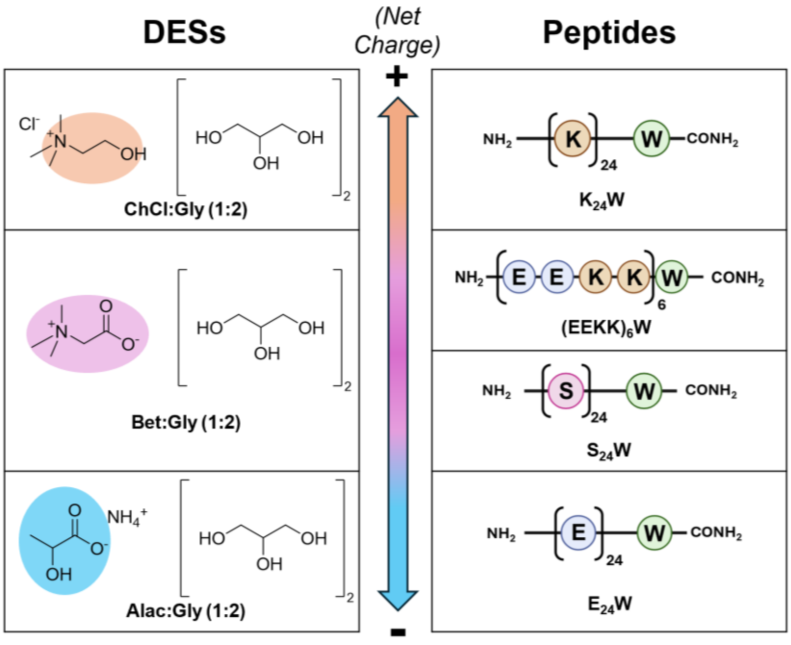

Figure 1. DESs components and peptides ordered by charge.

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Synthesis of new PROTACs for progerin degradation

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Keywords: *Progeria, Progerin ligands, Proteolysis targeting chimeras (PROTACs)*

Hutchinson–Gilford progeria syndrome (HGPS) is a rare laminopathy caused by a mutation in the lamin A gene, leading to the accumulation of an abnormal protein called progerin, which disrupts nuclear, cellular, and tissue function. These disruptions cause a systemic disorder that severely impacts the heart, bones, skin, and growth, leading to early death around the age of 14.5.[1]

To improve the disease phenotype, our laboratory has initiated a project focused on reducing progerin levels using proteolysis-targeting chimeras (PROTACs). A PROTAC molecule consists of three key components: a ligand that binds to the target protein, a moiety that interacts with the E3 ligase to mark the protein for degradation, and a linker that connects both moieties.[2] While many E3 ligase substrates are known,[3] few ligands exist for progerin, mostly derived from the natural product decursinol.[4] Thus, finding new progerin ligands is essential and the first step in developing new PROTACs. With this objective in mind, our group identified compound UCM-91 as a new progerin ligand. In this work, we have initiated a structure-activity relationship study focused on UCM-91 (Figure 1) to investigate the impact of different structural modifications on the affinity for progerin. The evaluation of the affinity of the synthesized compounds for this protein has been conducted through cellular thermal shift assays. Besides, the progerin ligand that has shown the highest affinity has been used to synthesize a new PROTAC, whose efficacy is currently being studied in our laboratory.

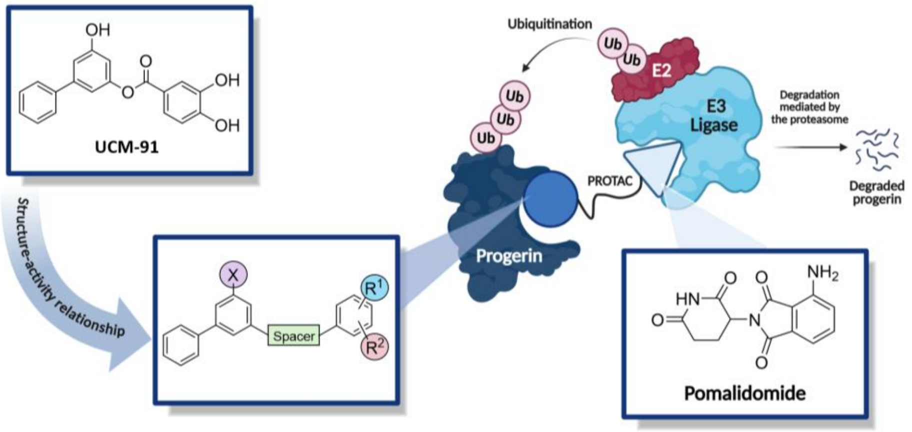

Figure 1. Structural modifications around hit compound UCM-91

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Synthesis and study of autocatalytic systems based on cysteine and thymine/adenine

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Keywords: *systems chemistry, autocatalysis, replicator network.*

The origin of life remains one of the most intriguing questions in science. Life at the cellular level arises from the interaction of three key subsystems: the ability to replicate and transmit genetic information, the possession of a metabolic machinery that allows it to stay away from equilibrium and a compartment that separates it from the environment. Systems chemistry, which focuses on dynamic interactions and reactions within complex chemical mixtures, plays a crucial role in this investigation.[1] By studying how molecular networks emerge and evolve, systems chemistry offers understanding into the complex processes that could have contributed to the emergence of life. Until now, a family of replicators based on adenine and thymine nucleobases linked to cysteine via amide bonds has been reported.[2] Oxidation of the cysteine thiol allowed disulfide-linked sequences, which controlled self-assembly and, consequently, replication efficiency. To improve the self-assembly of the dimers involved, this project is focused on synthesizing a replicator network analogous to the existing one, incorporating a chromophore spacer group. This modification is expected to promote aggregation and, therefore, magnify autocatalytic behaviour (Figure 1).

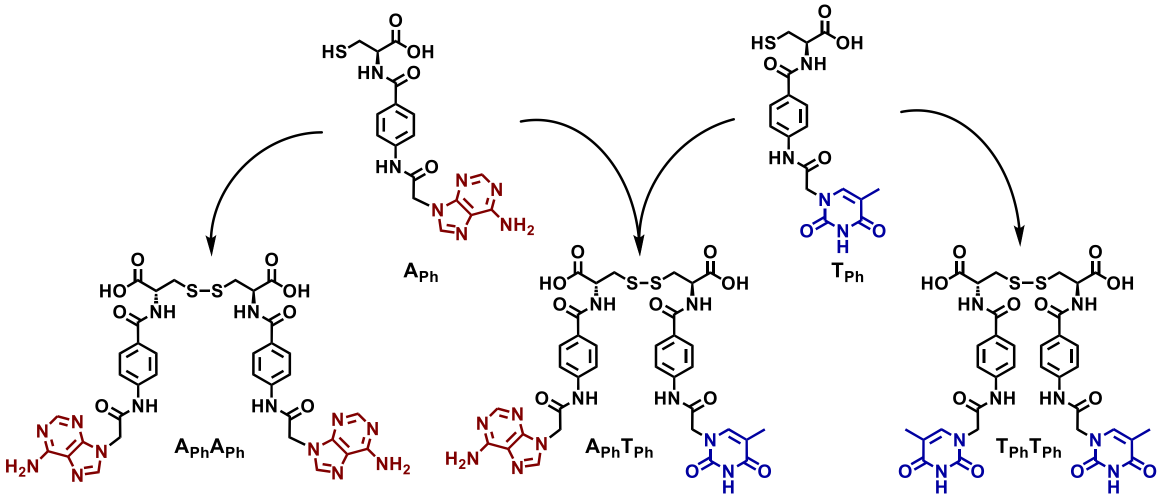

Figure 1. Reaction network of a set of cysteine-based minimal nucleobase sequences.

The aim of this study is to verify the autocatalysis of A_{Ph} and T_{Ph}, using $A_{Ph}A_{Ph}$ and $T_{Ph}T_{Ph}$ as initiators and to investigate for amplification processes that may occur to the dimers $A_{Ph}A_{Ph}$, $T_{Ph}T_{Ph}$ and $A_{Ph}T_{Ph}$ via kinetics studies.

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Photocatalytic Cascade Cyclizations using Isobutane: Unveiling a Regioselective Disparity

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Keywords: *cascade cyclization, gaseous alkanes, photocatalysis.*

With a production of 4 trillion m^3 per year, gaseous alkanes (natural gas) represent one of the most abundant and underutilized carbon-based feedstocks on the planet. Typically, they are burned off as fuel or used in processes such as steam cracking or reforming. These processes have raised global concerns from both environmental and economic points of views for being highly energy-intensive and leading to substantial greenhouse gas emissions. As a result, it is highly important to develop protocols which could allow the use of gaseous alkanes as viable alkylating agents in organic synthesis. However, due to the extreme inertness of gaseous alkanes reports on their use as reagents in organic synthesis are still rare.

Cascade cyclization protocols that provide access to complex cyclic architectures from relatively simple linear ones have been reported in several ways.[1] Radical cyclization via thermal initiation usually requires the use of peroxides as radical precursors and high temperatures, which compromises their industrial application.[2] Generation of C(sp^3) centered radicals via a photo-induced pathway is an alternative way to achieve a radical cyclization.[3-4] However, most of these protocols rely on the use of prefunctionalized substrates, compromising the atom efficiency of these transformations. Indeed, the use of simple alkanes as radical precursors in this type of cyclization reaction remains elusive.

In this regard, we hereby report a photocatalytic cascade cyclization of *N*-acrylamides using isobutane gas. The transformation provides the corresponding indolinone products in good yields with high regioselectivities. Notably, the reaction conditions favor the functionalization of the primary C-H bond, which is in sharp contrast with the previously reported methods for the functionalization of isobutane, that typically feature preference towards the tertiary C-H bond.[5]

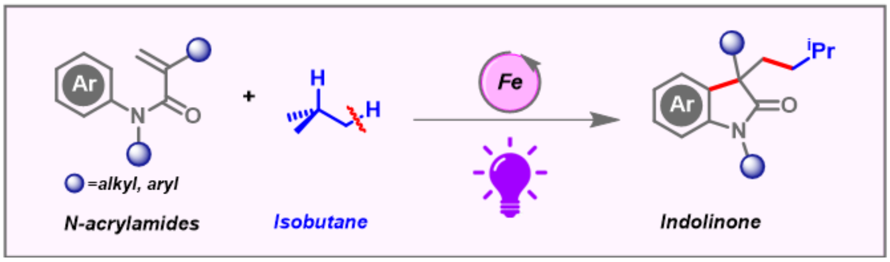

Figure 1. Reaction scheme.

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Synthesis of Substituted Quinolines by Direct Electrochemical Reduction of Nitro Arenes

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***Keywords**: Electrochemistry, quinoline, sustainable.*

Nitrogen heterocycles are common structural motifs in biologically active compounds and natural products. Notably, approximately 59% of FDA-approved small-molecule drugs feature nitrogen-containing heterocycles.[1] While various methods exist for their synthesis, the development of environmentally benign synthetic methodologies has become a central goal in modern chemical research, driven by growing societal demand for sustainable practices.[2] Electrochemical methods have emerged as a promising alternative for minimizing chemical waste, as they eliminate the need for stoichiometric amounts of external oxidants or reductants agents.[3] In this context, we report a sustainable approach for the selective cathodic reduction of an easily accessible nitro compound, followed by an intramolecular cyclization to afford a range of substituted quinolines. The method proceeds under mild, reagent-free conditions in a simple undivided cell utilizing inexpensive and readily available electrodes, and operates under constant current electrolysis, affording efficient conversion and high atom economy. The mechanism underlying quinoline formation was elucidated through the trapping and isolation of key intermediates, supported by previous studies on the electrochemical reduction of nitro groups N-Oxide formation.[4]

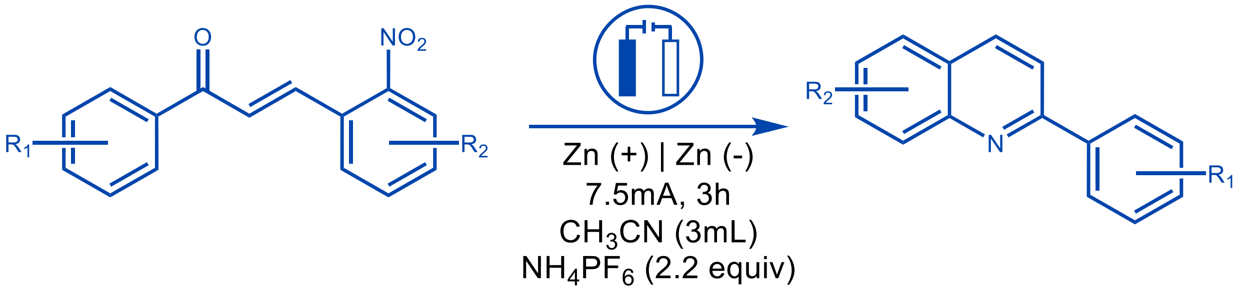

Figure 1. Electrochemical synthesis of quinoline derivates from nitrochalcones.

References:

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Synthesis and Characterization of Carbon Nanoparticles for Advanced Applications

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***Keywords**: carbon nanostructure, fluorescence, nanomaterials.*

Carbon nanoparticles (CNPs) are a type of fluorescent zero-dimensional carbon nanostructures whose size is typically less than 10 nm, and its structure is mostly composed of Csp^2 and Csp^3 atoms. CNPs have quasi-spherical shapes, strong absorption in the UV with a band entering the visible region and, commonly, excitation wavelength-dependent fluorescence emission with moderate quantum yields. Other properties like biocompatibility, high thermal and photochemical stability and ease of preparation following simple synthetic routes starting from widely available organic molecular precursors, make them interesting nanomaterials for the development of novel applications such as optoelectronics, bioimaging or catalysis.[1]

This work focuses on the pulsed laser synthesis and the structural and photophysical characterization of new types of CNPs doped with transition metals (Fe(III) or Ni(II)). The synthesis was carried out by nanosecond pulsed laser irradiation,[2] following a bottom-up approach that employs liquid/molten organic precursors such as aniline, triphenylamine, resorcinol or *trans*-stilbene as the starting materials. Irradiation of precursors was performed with 532 nm light (1 W, 6 ns·pulse^{-1}) for 6 hours. FTIR spectra evidence the presence of surface functional groups. Figure 1A shows a TEM image of the nanosized particles. Figure 1B shows the UV-vis absorption and excitation spectra, and Figure 1C displays the corresponding fluorescence spectra. Fluorescence lifetime measurements show multiexponential decays, with an average value (τ_{INT}) of 4.1 ns in air-equilibrated 2-propanol. DLS measurements show important solvent-dependent aggregation, displaying aggregate sizes as big as 334 nm.

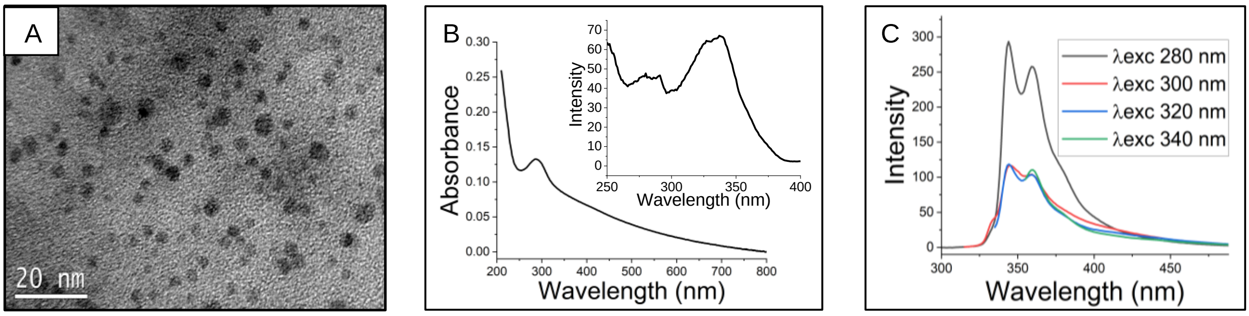

Figure 1. A) TEM images of carbon nanoparticles prepared from triphenylamine, B) UV-vis absortion and excitation (insert, λ_{em} = 425 nm) spectra of the carbon nanoparticles, C) fluorescence spectra at different excitation wavelenghts.

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Synthesis of Ru(II)-BODIPY and Ir(III)-BODIPY Metallomacrocycles for Application in Photodynamic Therapy

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***Keywords**: photodynamic therapy, BODIPYs, metallo-organic cages.*

Photodynamic therapy (PDT) is a non-invasive therapeutic strategy that has gained considerable attention in the treatment of various diseases, particularly in oncology. This modality is based on the use of photosensitizers (PS) that, when activated by an appropriate light source, generate singlet oxygen ($^1O_2$) or reactive oxygen species (ROS), which induce cellular damage.[1]

BODIPYs have emerged as excellent candidates for PDT due to their ability to absorb light in strategic spectral ranges, the high efficiency in generating ROS and $^1O_2$, their high photostability and low dark toxicity. Furthermore, their structural versatility allows for easy chemical modifications that shift their absorption within the therapeutic window and improve their solubility in aqueous media, facilitating their integration into biological systems.[2]

Meanwhile, Ru(II) and Ir(III) metal complexes have been explored as PS in PDT due to their ability to participate in electron transfer processes, promoting efficient ROS generation—especially advantageous in hypoxic tumor environments, where limited oxygen compromises traditional PS efficacy. Additionally, their optical and electronic properties can be tuned by ligand modification, optimizing photophysical performance.[3]

This work proposes the design and synthesis of two-dimensional metal-organic structures that incorporate BODIPY-type chromophores, functionalized with biologically relevant substituents, with Ru(II) and Ir(III) metal complexes, aiming to develop new multifunctional PS for PDT. This strategy seeks to: i) exploit the complementarity of both systems to enhance ROS generation; ii) improve efficacy under hypoxic conditions; and iii) increase therapeutic selectivity, thereby overcoming the limitations of conventional systems.

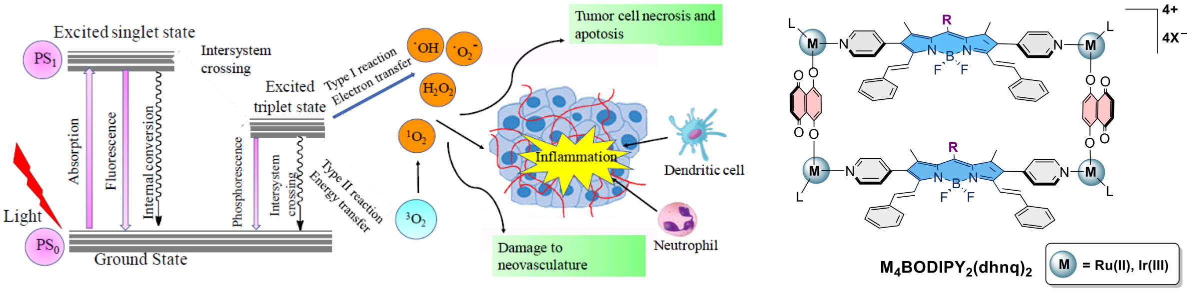

Figure 1. a) Modified Jablonski scheme illustrating the principles of PDT.[1] b) Target metallo–organic structure.

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Developing new chiral ligands for asymmetric catalysis with Rh

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***Keywords**: Asymmetric catalysis, C–H functionalization, Group IX metals.*

Cyclopentadienyl (Cp) ligands and their corresponding group IX metal complexes (Co, Rh, Ir) are highly relevant in the field of organometallic catalysis—for example, in the development of C–H functionalization reactions that directly transform inert C–H bonds into specific functional groups through the formation of new C–O, C–N, or C–C bonds[1].

Unfortunately, the synthetic methods for preparing chiral Cp ligands are complex and not very versatile[2]. As a result, the development of enantioselective C–H functionalization reactions using such catalysts remains very limited, with no reported examples involving electron-deficient Cp ligands.

Recently, we discovered a cobalt-catalyzed cycloaddition that enables the one-step construction of cyclopentadienyl ligands bearing a wide variety of substituents, allowing fine-tuning of their steric and electronic properties[3]. In addition, we have found that the resulting Cp–rhodium and Cp–iridium complexes are highly catalytically active.

Our methodology is particularly effective for preparing these "Cp–metal" complexes with planar chirality, opening the door to their use as chiral catalysts in various C–H functionalization reactions.

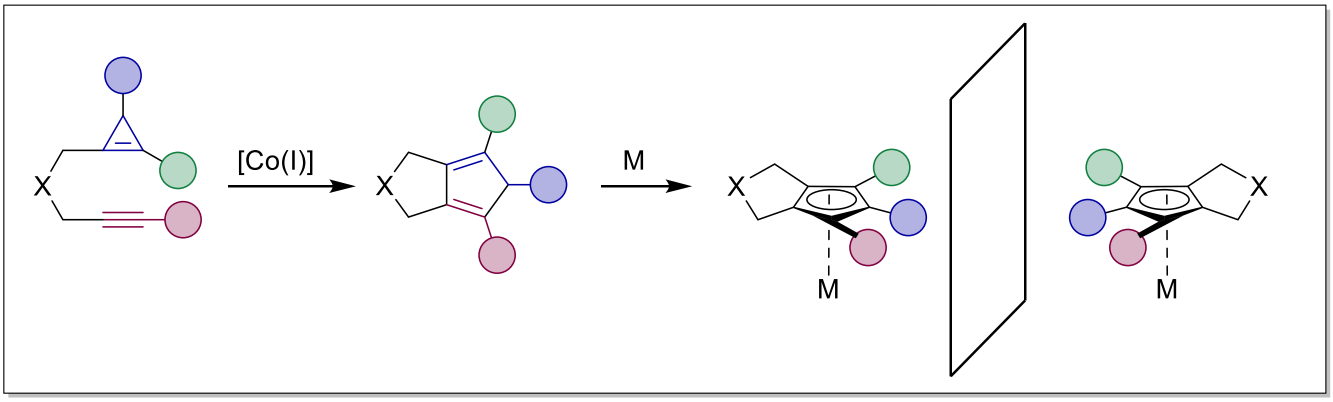

Figure 1 Scheme of our novel methodology to prepare these "Cp–metal" complexes with planar chirality

Based on this background, our objective will be to use our methodology to prepare a series of enantiopure Cp–rhodium and Cp–iridium complexes and to evaluate their catalytic properties in relevant asymmetric C–H functionalization reactions[4].

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Electroactive Glycofullerene Derivatives for Biological Applications

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Keywords: *biosensing, glycofullerene, multivalency.*

Multivalent interactions between lectins and carbohydrates play a significant role in many biological processes as in the infection mechanisms exploited by numerous viruses.[1] In this context, [60]fullerene hexa-adducts functionalized with peripheral carbohydrates have emerged as promising platforms designed to mimic the multivalent binding strategies found in nature. These nanostructures, known as glycofullerenes, have been reported to interact with lectins and effectively inhibit different viral infection pathways.[2]

Over the course of this project, a synthetic route was developed to obtain asymmetric mannose-functionalized glycofullerenes, and to chemically anchor them to different redox-active cores. These two new molecules demonstrate a redox-based biosensing strategy suitable for the detailed study of lectin-carbohydrate interactions.

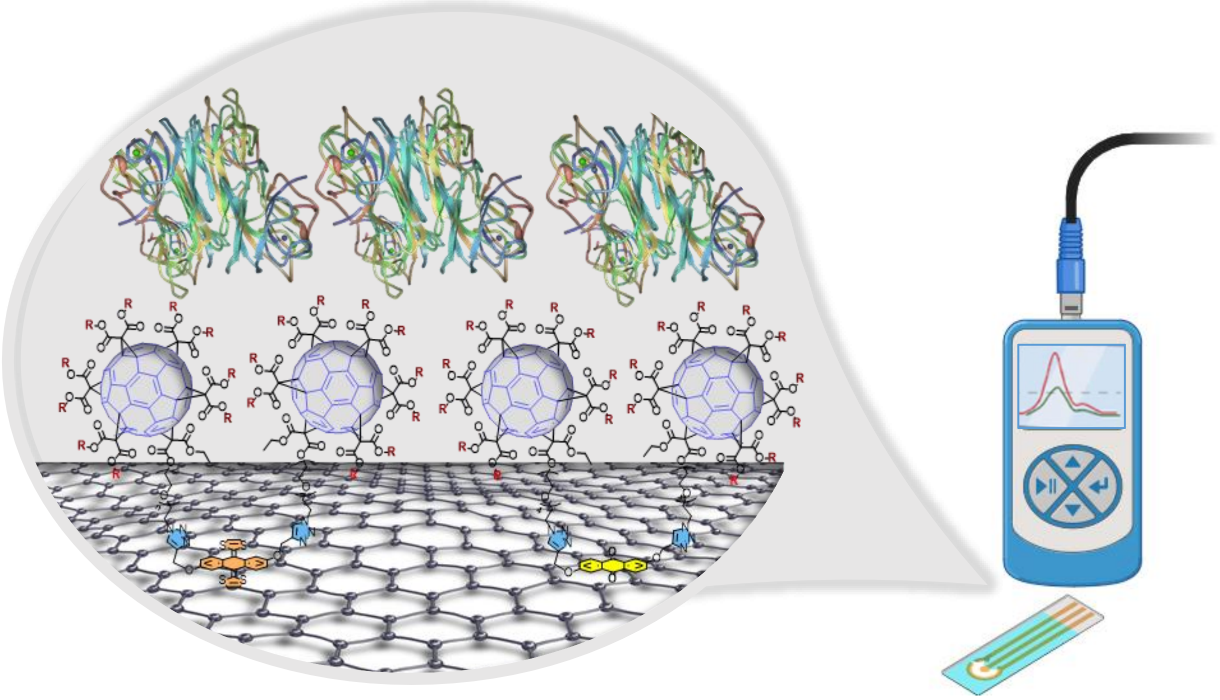

Figure 1. Biosensor based on glycofullerenes as bioreceptors coupled to different central redox-active cores.

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Crystallization of Covalent Organic Frameworks (COFs) for Use as Nanoreactors

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***Keywords**: Covalent Organic Frameworks, Crystal Structure, Diffraction.*

Covalent Organic Frameworks (COFs) are crystalline and porous materials formed through the condensation of purely organic building blocks, which assemble into networks with a defined topology. These materials have demonstrated their utility in various applications such as gas storage and separation, catalysis, and optoelectronics.[1] However, their atomic-level structural characterization remains a challenge due to the small crystalline domains typically obtained through conventional synthetic routes. A general methodology has been proposed to obtain crystals with sufficiently large domains for single-crystal X-ray diffraction analysis, applicable across a variety of topologies. By controlling the concentration of monomers, through slow diffusion, varying stoichiometries, and the use of crystal growth modulators, samples of COF-300, a prototypical imine-based COF,[2] have been obtained with dimensions suitable for single-crystal structural resolution (Figure 1). This methodology is being further extended to the synthesis of mechanically interlocked COFs[3] such as COF-112 and COF-505.

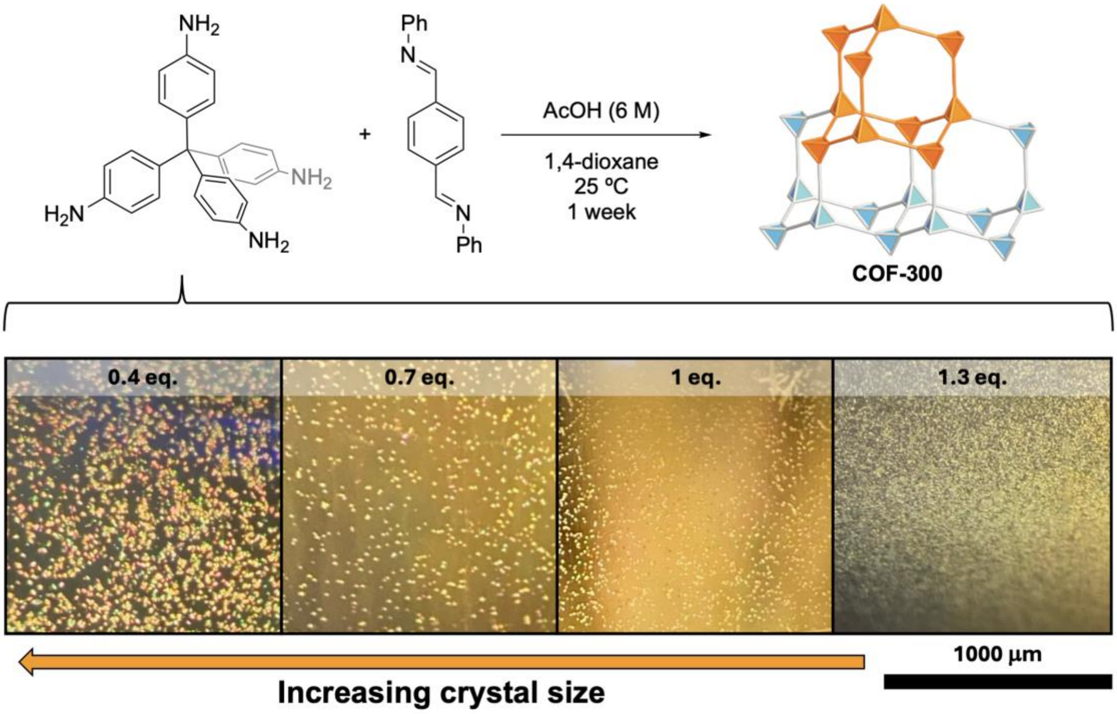

Figure 1. Crystalline domain modulation in COF-300 crystals with equivalents of tetrakis-(4-aminophenyl)-methane.

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Synthesis of Nanowires from Self-Assembled Helical Peptides

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Keywords: *Self-assembly, spectroscopy, peptide synthesis.*

Conductive proteins are a group of electrically conductive protein filaments first isolated from the bacterium *Geobacter sulfureducens*, which exhibit metal-like conductivity.[1] In recent years, here has been growing interest in the development of synthetic proteins and peptides designed to enhance this conductivity for application in electronic devices with low production cost and toxicity, and ecologically friendlier.[2] These peptide nanowires transmit electric current through charge delocalization facilitated by π-π stacking interactions between the side chains of aromatic amino acids.[3]

In 2004, M. Lu *et al*., discovered a protein structure in which five α-helix self-assembled to form a pentamer, with stacked tryptophan residues located at the centre and stabilized by N/C-H···π y π-π interactions.[4] These aromatic residues are close enough to allow electron transfer along the fiber. We optimized this sequence to make it shorter and increase its thermodynamic stability. In this study, the describe a second generation sequence that replaces the Tryptophan residues with the commercially available non-natural amino acid (L)-3-Benzothienylalanine, a structural analogue of tryptophan in which the indole group replaced by a benzo[b]thiophen-3-*yl* side chain, which, given the wide application of thiophenes in conductive materials, might display enhanced electron transport properties.

The peptide sequence was assembled via solid-phase peptide synthesis, purified and its identity confirmed by High-Performance Liquid Chromatography–Mass Spectrometry (HPLC-MS), and the supramolecular assembly of the oligomers was characterized using a variety o techniques: Circular Dichroism (CD), Ultraviolet-Visible (UV-Vis) Spectroscopy, Atomic Force (AFM), and Transmission Electron Microscopy (TEM), and Matrix-Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-TOF).

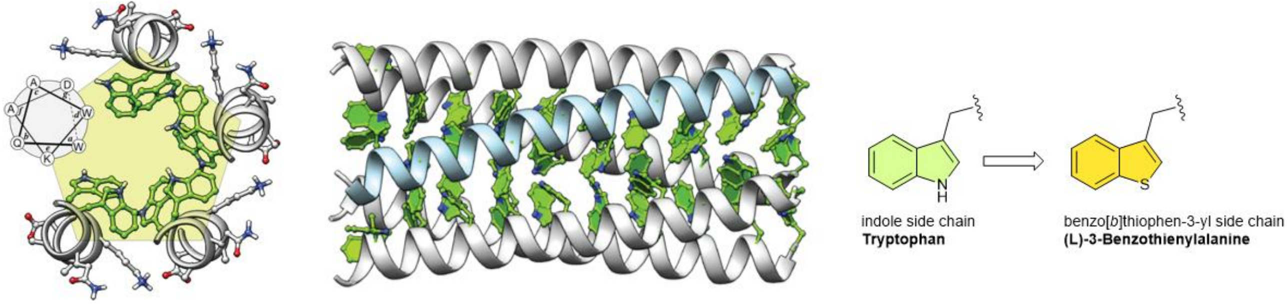

Figure 1. On the left, top and side view of the tryptophan-derived pentamer, with the benzothiophene side chain stacked in the core. On the right, the structure of the Trp and Trp-derived side chain.

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Selective [2+2] formal cycloadditions of aminodiynes and Koshar-type zwitterions. Synthesis of densely-functionalized cyclobutenes.

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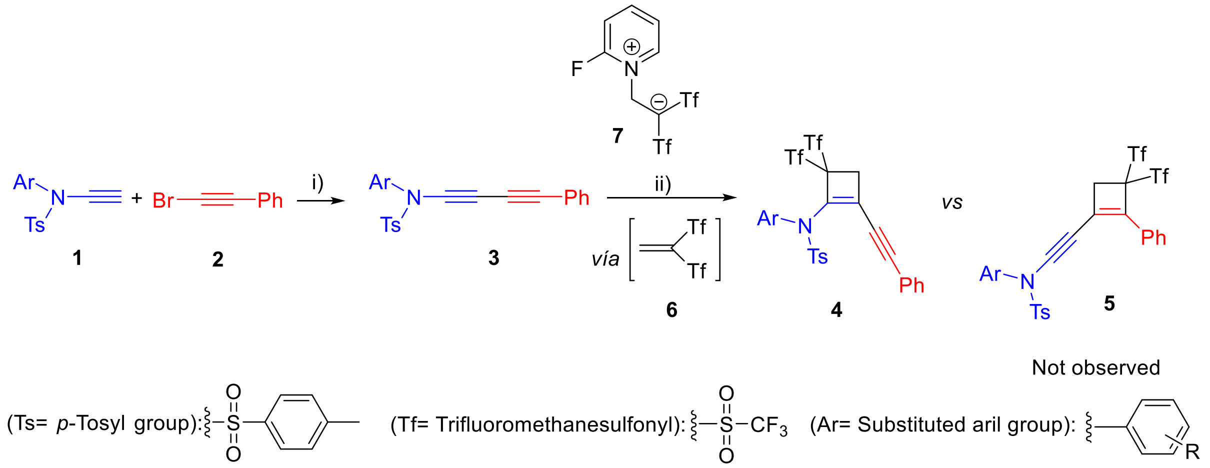
***Keywords**: [2+2] cycloaddition, cyclobutene, diyne.*

Cyclobutenes are unsaturated four-membered cyclic compounds that stand out for their high ring strain. In recent years, progress has been made in their synthesis, mainly due to the fact that these structures are present in bioactive natural products and in small molecules of pharmaceutical interest.[1] Considering the background of our research group,[2] we report the synthesis of aminocyclobutenes via a metal-free and regioselective [2+2] formal cycloaddition between amino-substituted diynes **3** and bis(triflyl)ethene (**6**). Compounds **6** are generated *in situ* from the decomposition of the 2-fluoropyridinium salt (**7**) (Yanai's reagent) in solution.[3] The reaction takes place under mild conditions and exhibits high selectivity, with the most electron-rich alkyne in the diyne preferentially undergoing cycloaddition (Scheme 1). The resulting aminocyclobutene scaffolds feature strongly electron-withdrawing triflyl groups in a highly conjugated skeleton. Both the electronic properties and the good leaving group nature of Tf substituents could be use in further derivatization reactions.[4]



Scheme 1. Synthetic route for the preparation of cyclobutenes. (i) Cadiot–Chodkiewicz coupling. (ii) [2+2] Regioselective cycloaddition.

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Copper-Catalized Enantioselective Synthesis of 1,2-disubstituted Bicyclo[2.1.1]hexanes as *ortho*-Phenyl Bioisosteres

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***Keywords**: bioisosteres, enantioselective catalysis, hydroboration.*

Bicyclo[2.1.1]hexanes are bridged scaffolds with well-defined exit vectors that attracted interest among the medicinal chemists since they represent saturated bioisosteres of disubstituted phenyl rings.[1a,b] Nevertheless, the stereocontrolled construction of such bicyclic skeletons remains a difficult task and only few seminal examples have been reported so far.[1c] In this context, the development of enantioselective strategies that enable the obtainment of chiral bioisostere scaffolds with control of the tridimensionality would be highly desirable since enantiomers often display a completely different behaviour in biological systems.[2] Herein we disclose the development of an enantioselective catalytic strategy to obtain 1,2-disubstituted bicyclo[2.1.1]hexanes as suitable *ortho*-phenyl bioisosteres.[3] This was achieved through an asymmetric copper hydride-catalyzed hydroboration of unactivated exocyclic alkenes (Figure 1),[4] which were obtained by a key intramolecular [2+2] photocycloaddition under triplet energy transfer catalysis. The development of this reaction provided a straightforward access to versatile building blocks containing the bicyclo[2.1.1]hexane core and, upon appropiate derivatization, the absolute configuration of the products was determined by X-ray analysis. Overall, this preliminary study provides an efficient tool for the stereocontrolled synthesis of 1,2-bicyclo[2.1.1]hexanes, anticipating a possible application for the construction of saturated analogues of real drugs with a direct impact in the fields of organic and medicinal chemistry.

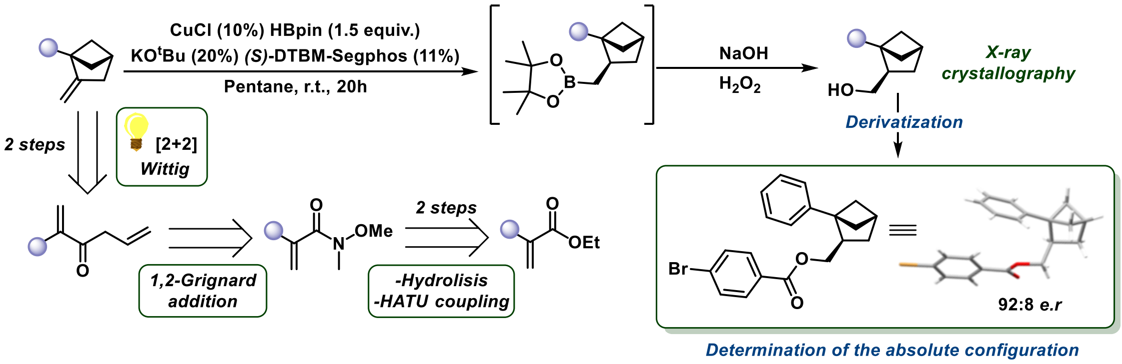

Figure 1. Enantioselective copper hydride-catalyzed hydroboration and preparation of starting materials.

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Preparation of new mechanoluminescent compounds

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Keywords: *mechanoluminescence, organic synthesis, chromism.*

Mechanoluminescence (ML) is a fascinating photophysical phenomenon where mechanical stress induces light emission in a material.[1] Although it has been widely studied in inorganic systems, its occurrence in organic compounds remains rare and underexplored. However, this unique property has gained considerable attention for potential applications in smart sensors, optomechanical devices, and responsive materials.

In our recent work, we have developed a new class of organic materials exhibiting both mechanoluminescent and thermochromic responses in the solid state. These compounds were designed to promote aggregation-induced emission (AIE)[2] and enhance non-covalent interactions, enabling efficient light emission upon mechanical stimulation. Their photophysical behavior revealed a dual chromic behavior[3]: (i) a reversible mechanochromism, with visible color changes associated with a crystalline-to-amorphous phase transition, and (ii) a reversible thermochromism, triggered by moderate heating, attributed to dynamic structural rearrangements.

Importantly, no chromic behavior was observed in solution, confirming the crucial role of solid-state organization. These materials were successfully embedded into biodegradable polymeric matrices and processed using additive manufacturing techniques. The integration of these stimuli-responsive systems into soft materials highlights their potential for the development of visually readable, printable mechano-optical sensors[4], with promising applications in flexible electronics, packaging, or structural monitoring.

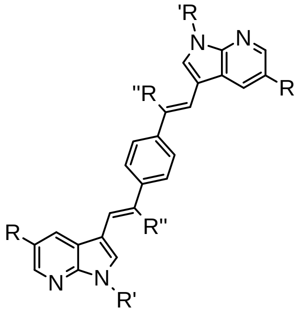

Figure 1. Generic structure of the synthesized compounds

References:

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Synthesis of Cyclic Peptides for the Formation of Nanoreactors

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Supramolecular chemistry is centered on the study of complex molecular assemblies stabilized by non-covalent interactions. This discipline has progressed significantly from its early focus on molecular recognition to the design of sophisticated systems capable of performing specific functions at the nanoscale, with catalysis emerging as a prominent application.[1] Our research group investigates a range of supramolecular assemblies derived from cyclopeptides. These macrocycles, composed of an even number of alternating chiral α- and γ-amino acids, orient their amide and carbonyl groups perpendicularly to the plane of the ring, enabling the formation of higher-order structures through directional hydrogen bonding.[2]

Recent advances have allowed us to strategically methylate selected amide groups within the peptide sequence, yielding discrete dimers characterized by rigid and well-defined internal cavities. The modularity of these systems permits extensive functionalization of the peptide backbone, offering a versatile platform for catalysis within confined environments. The properties of these molecular capsules can be finely tuned by altering the nature of the functional groups displayed within the cavity.[2]

In this work, we present our preliminary results toward the synthesis of a dimeric capsule functionalized with two cofacial zinc-porphyrin moieties. These porphyrin caps enable the selective recognition of various bipyridine derivatives within the cavity, laying the foundation for the development of catalytic systems capable of promoting a range of chemical transformations in a spatially constrained setting.[3]

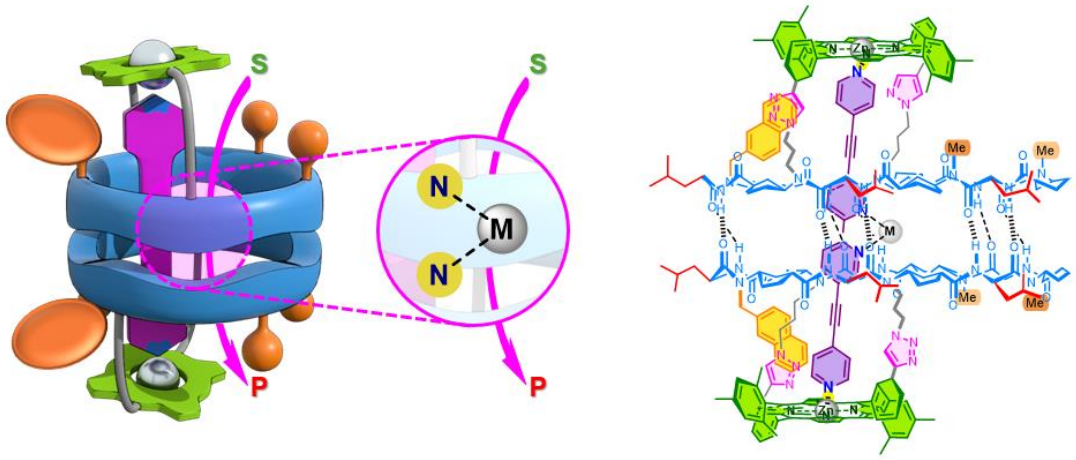

Figure 1. 3D model of the peptidic Capsule for bipyridine recognition and catalysis

References:

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Synthesis and functionalization of 1,3-oxazin-2-ones with 1,1-bis(triflyl)ethylene for the preparation of carbon superacids

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***Keywords**: allenes, 1,3-oxazin-2-ones, triflyl.*

Allenes are a special functional group in organic chemistry due to its characteristic cumulated C-C double bond. This provides them with a high reactivity and selectivity, leading to a high versatility in Organic Synthesis.[1] Our research group is interested in the design of new fluorinated heterocycles because of the incorporation of fluorine atom(s) into organic compounds often increases their lipophilicity and metabolic stability, enhancing their bioavailability and affinity for target proteins.[2] The present work is focused on the functionalization of 1,3-oxazin-2-ones (prepared from accessible allenic carbamates) with 1,1-bis(triflyl)ethylene generated *in situ* from the decomposition of a 2-fluoropyridinium salt. The functionalization with bis(triflyl)ethylene offers a valuable entry point to strongly electron-withdrawing and mildly lipophilic triflyl-containing motifs, which are useful in catalysis and further synthetic elaborations. In this context, our study has two possible outcomes, a chemoselective Alder−ene or a [2+2] cycloaddition reaction.[3] Herein we present an Alder–ene type reaction and this efficient and atom economic methodology allows the synthesis of new fluorinated oxazinones bearing aromatic and heteroaromatic substituents under mild conditions and good functional group tolerance.

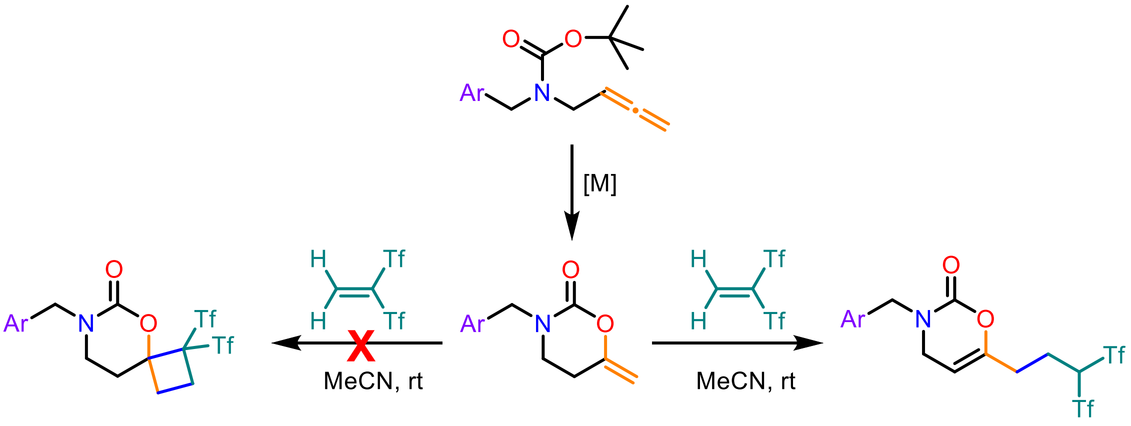

Figure 1. Scheme illustrating the possible pathways of the reaction**.**

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Synthesis of a Porous Organic Polymer with photocatalytic activity via thiol-ene photochemistry

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***Keywords**: Photopolymerization, Thiol-ene reaction, Photocatalysis*

Porous organic polymers (POPs) are an emerging class of materials that are attracting significant attention due to their properties, *e.g.* low density, porosity, or high chemical and thermal stability. Conventionally, the synthesis of these materials relies on polar-thermal reactions under harsh conditions.[1] Therefore, the development of alternative strategies that employ milder and more sustainable protocols, such as photochemical methodologies which use light as clean energy source and operate in ambient conditions, is highly desirable.

In this context, the thiol-ene reaction is a light-induced radical addition between a thiol and an alkene. Thiol-ene reactions planned across polytopic substrates may proceed via step-growth polymerization pathways, affording crosslinked networks with uniform structure, low shrinkage stress, and good mechanical properties.[2] Despite its versatility, thiol-ene application in the direct synthesis of POPs employing rigid aromatic monomers remains underexplored.

Herein, we report the synthesis of a novel POP via photochemical polymerization based on thiol-ene chemistry. The use of a pyrene-based monomer acting as built-in photoinitiator enabled efficient polymerization under visible light, avoiding the need for high-energy UV irradiation or additional photoinitiators, *e.g.* benzophenone,[2] which are commonly required in similar thiol-ene systems.[3] Comprehensive characterization of the resulting materials included FTIR, solid-state NMR, XRD, SEM-EDX, TGA, elemental analysis, N_2 adsorption isotherm and UV-Vis DRS. The obtained results confirm successful polymer formation through the anticipated thiol-ene chemistry. Furthermore, the material retained visible light absorption after polymerization and was able to promote the reductive photocatalytic hydrodehalogenation of aromatic bromides and even chlorides, therefore acting as a heterogeneous photocatalyst.

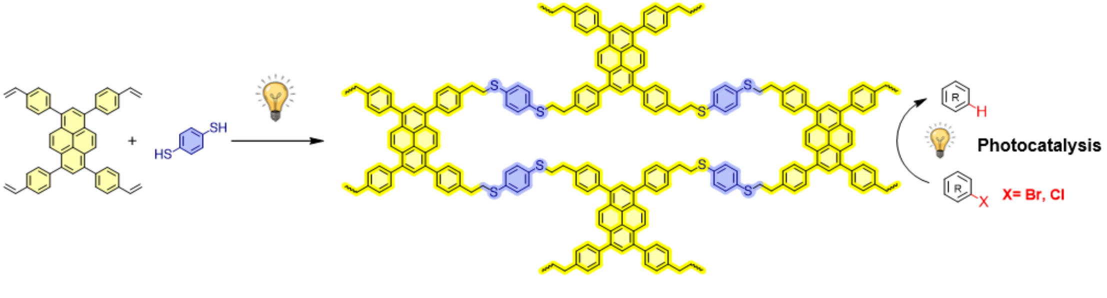

Figure 1. Photochemical thiol-ene material synthesis and photocatalytic activity.

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Novel Sulfonopenicillin-Siderophore Conjugates to Restore β-Lactam Antibiotic Efficacy

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***Keywords**: antibiotic bacterial resistance, β-lactamase inhibitors, sulfonopenicillins*

The ability of antibiotics to cure bacterial infectious diseases is now at serious risk due to the emergence and spread worldwide of multi-drug resistant bacteria. The impact that this situation has on the older population, healthcare-associated patients or those with a compromised immune system is a cause of great concern since treatment options are not available in certain cases. Of particular concern is the increasing incidence of the priority pathogens highlighted by the World Health Organization (WHO): carbapenem-resistant *Acinetobacter baumanii, Pseudomonas aeruginosa,* and *Enterobacterales*.[1] Today the treatment of infections caused by these pathogens is one of the most challenging problems in clinical settings, due to its adaptability and intrinsic evolutionary character to develop highly efficient resistance mechanisms to escape the action of antibiotics.

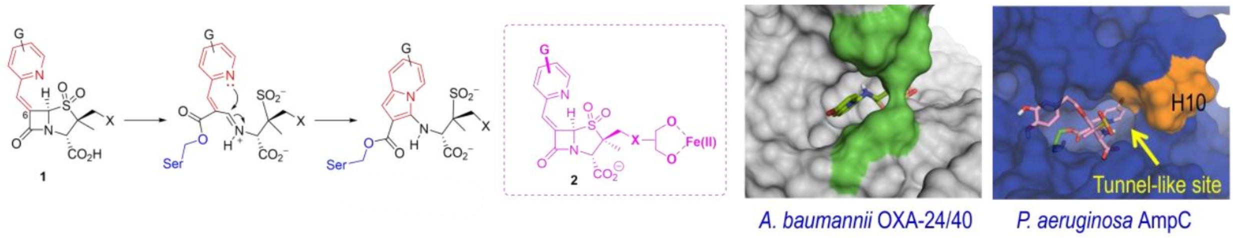

Figure 1. Inhibition mechanism of sulfonopenicillin-siderophore conjugates **1** (left) and 3D structure of some *β*-lactamases inactivated by them (right).

In recent years, great success has been achieved with combined therapy approaches (antibiotic + inhibitor of resistance) that block the most relevant mechanism of bacterial resistance, the enzymatic inactivation of the most widely used antibiotics (β-lactams) by β-lactamases.[2] These enzymes represent the most prevalent cause of antibiotic resistance in Gram-negative bacteria. In our research group, highly efficient inhibitors have been developed against the most challenging β-lactamase enzymes. These compounds can react with the enzyme, generating an indolizine adduct, which is stable against hydrolysis thus permanently blocking the target.[3] This project aims to develop new sulfonopenicillin-siderophore conjugates to facilitate its internalization, to identify inhibitors with broad-spectrum activity against the most challenging β-lactamases produced by the life-threatening pathogens highlighted by WHO.

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Tetrahedral nanographenes: Studies on aggregation-induced emission

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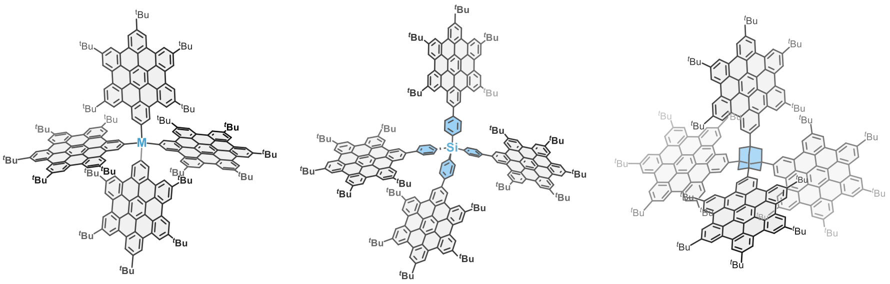
***Keywords**: molecular nanographenes, photophysical properties, aggregation-induced emission.*

Graphene emerged in 2004 as groundbreaking material with the potential to revolutionize the future of nano-electronics. It exhibits exceptional mechanical strength, remarkably flexibility and high carrier mobility at room temperature. However, as it is a zero-gap semiconductor, devices made of large area graphene are not suitable for conventional transistors. Among the strategies proposed to open a bandgap between the conduction and the valence bands, quantum confinement of the electrons in smaller fragments such as nanographenes has gained significant attention in the scientific community.

The bottom-up benchtop synthesis by stepwise organic chemical transformations leads to monodisperse molecular nanographenes with a precise control on the size and shape and, therefore, on their properties. Following this approach, our research group has recently developed the synthesis of tetrakis(penta-*tert*-butyl-hexa-*peri*-hexabenzocoronenyl)methane, "tetrahedraphene" **1a** (Figure 1), a molecule composed of a central sp^3 carbon atom linked to four hexa-*peri*-hexabenzocoronenes (HBCs). This molecule, showed aggregation-induced emission (AIE), observed as a fluorescence color change occurred between the solution and the solid state [1].



1a= C
1b=Si

2

3

Figure 1. Tetrahedral nanographenes with a central atom **1** (M= C or Si), with a benzene spacer **2** and with a central adamantane moiety **3**.

Encouraged by this result, we proceeded to design and synthesize a new series of tetrahedral nanographenes to gain deeper insight into the relationship between molecular structure and the photophysical properties. Our efforts focused on three key structural modifications to investigate the change in the AIE. Firstly, by the variation of the central atom to Si, **1b** (Figure 1)**.** Then, by. the introduction of rotational and vibrational freedom using a spacer between the HBC fragments and the central atom **2**. Finally, by the modification of the central core employing molecular fragments such as adamantane **3**, instead single atoms.

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Study of the acylation of alkyl halides under photochemical conditions

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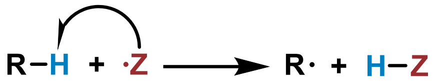
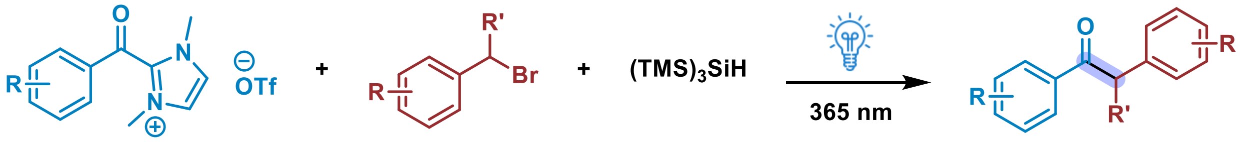
***Keywords**: photochemistry, N-heterocyclic carbenes, cross-coupling*

Photochemistry is a technique of great importance in green chemistry, due to the use of light as a source of clean energy to carry out chemical transformations, thus fulfilling one of the main Sustainable Development Goals.[1] Carbonyl compounds, especially ketones, are one of the most studied species, as they are used in numerous photochemical reactions. One of the most characteristic photochemical transformations of ketones is the hydrogen atom transfer reaction (HAT) (Scheme 1).[2] Acyl azolium intermediates are diaryl ketones with reactivity analogous to benzophenone, that has been widely used in photochemistry.[3]



Scheme 1. Hydrogen atom transfer reaction (HAT).

In this work, taking advantage of the reactivity of these intermediates, a new methodology for the acylation of alkyl halides is described, obtaining aryl alkyl ketones through a HAT/XAT process (Scheme 2). For this purpose, different acyl azolium salts have been prepared, including two natural product derivatives, with which the photochemical reaction has been studied, achieving the best results in the presence of electron-withdrawing groups in the *para* position of the aromatic ring. It has also been studied with different alkyl halides, such as primary and secondary bromides, highlighting the reactivity of secondary alkyl bromides. Finally, a reaction mechanism is proposed based on the reactivity of the triplet excited state, through the formation of a biradical. This species promotes a hydrogen atom transfer (HAT), followed by a halogen atom transfer (XAT) from the alkyl halide and the process ends with a radical cross-coupling, resulting in the formation of a new C-C bond.



Scheme 2. Proposed photochemical acylation reaction.

References:

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Gold-promoted cascade reactions in biological media

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***Keywords**: catalysis, bioorthogonal chemistry, gold.*

The development of abiotic reactions within living systems represents a promising strategy for the design of new therapies. Accordingly, bioorthogonal chemistry has established itself as a key discipline, studying highly selective chemical transformations in complex biological environments without disrupting their intrinsic biochemical processes.[1] In this context, the use of catalytic transition metal complexes, aimed at the development of new biocompatible reactivities, has emerged as a tool of great interest.[2]

In this project we explore the use of gold – a traditionally considered inert metal – as a catalyst able to promote multiple cyclization processes through cascade mechanisms within biological environments, upon the activation of C-C multiple bonds for a nucleophile attack.[3] This approach aims to achieve high chemical complexity in a straightforward, efficient and biocompatible manner, by mimicking natural processes such as steroid biosynthesis. To this end, we have optimized a cascade process that involves a double cyclization in biologically relevant conditions, including high dilution and compatibility with air and water, and we have evaluated its tolerance in complex media. Besides, the expansion of the π-system enables to afford fluorescent products through three consecutive gold-promoted cyclizations. Finally, this reactivity is being explored in A549 living mammalian cells.

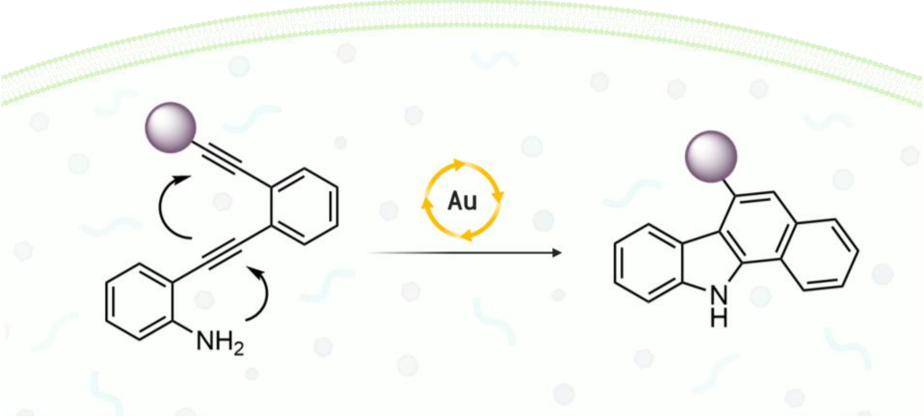

Figure 1. Gold-promoted cascade reaction within a complex biological system**.**

References:

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Heparanase-Sensitive Modified Heparin Gels as a Strategy Against Tumorigenic Processes

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Keywords: *heparin, heparanase, drug-delivery*

Chemotherapy remains one of the most widely used cancer treatments, despite its significant side effects on patients. To address this issue, this project investigates the development of responsive polymeric systems designed to act as controlled release systems for anticancer drugs in response to tumor biomarkers. Specifically, the study focuses on modified heparin gels sensitive to heparanase (Figure 1), an enzyme overexpressed in tumor tissues that degrades glycosaminoglycans in the extracellular matrix.[1]

To this end, chemically modified heparins were synthesized and evaluated as potential heparanase substrates. In order to do so, a bacterial heparanase was cloned. A modified version of the colorimetric Park–Johnson assay was employed to assess heparanase activity and thereby evaluate the substrate suitability of the tested compounds.[2] In parallel, the heparanase activity present in HeLa cell cultures was measured (Table 1).

This work enabled the exploration of structural modifications in the hydrogels to improve their responsiveness. The results obtained are promising and pave the way for further development of these systems, with the aim of enhancing their applicability in cancer therapy.

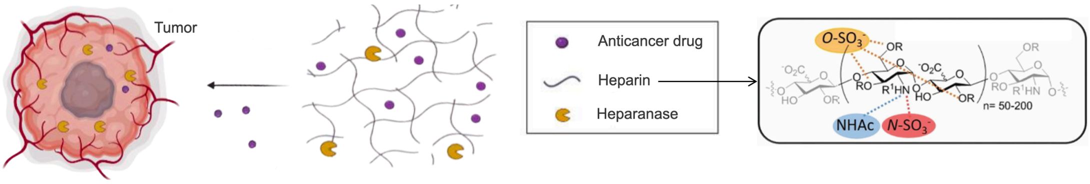

Figure 1. Schematic representation of the main objective of the project based on the synthesis of heparin hydrogels to encapsulate and release anticancer drugs in a specific area.

Table 1. Evaluation of Heparanase Activity in HeLa Cell Cultures.

	Reaction	**Without substrate**	**Thermal inactivated CFE[1]**	**Heparanase control**
Time (h)	**Reducing Ends (μg/mL)**			
0	8,7803	8,3180	8,2910	7,6430
3	8,8208	8,3450	8,2640	7,7240
24	9,0503	8,3855	8,2505	8,0210
Heparanase Activity in HeLa Cell Cultures (ng.h^{-1}.10^{6}.cells^{-1})	3,7105	0,82895	-0,43421	5,0526

[1] CFE stands for Cell Free Extract.

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Metabolite identification in biological samples by NMR spectroscopy

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***Keywords**: NMR, metabolomics, mixture analysis.*

The identification of metabolites in biological samples plays a crucial role in advancing personalized medicine, particularly in the early diagnosis and therapeutic monitoring of diseases.[1] Nuclear Magnetic Resonance (NMR) spectroscopy is a powerful tool for the analysis of such samples due to its non-destructive nature and the wealth of structural information it provides. The use of common and advanced 1D and 2D NMR characterization experiments enables the acquisition of high-quality spectral data, aiding in the identification and structural elucidation of metabolites.[2,3] Furthermore, when combined with bioinformatic databanks (e.g. the Human Metabolome Database)[4] and spectral deconvolution software (e.g. CHENOMX),[5] the accuracy and reliability of metabolite identification is significantly enhanced.

This study demonstrates the effectiveness of integrating NMR and bioinformatic tools for metabolite identification in human serum (Figure 1) and cellular extracts. It also highlights the untapped potential for further development of advanced NMR methods aimed at achieving comprehensive metabolomic profiles, which could lead to the identification of previously uncategorized biomarkers.

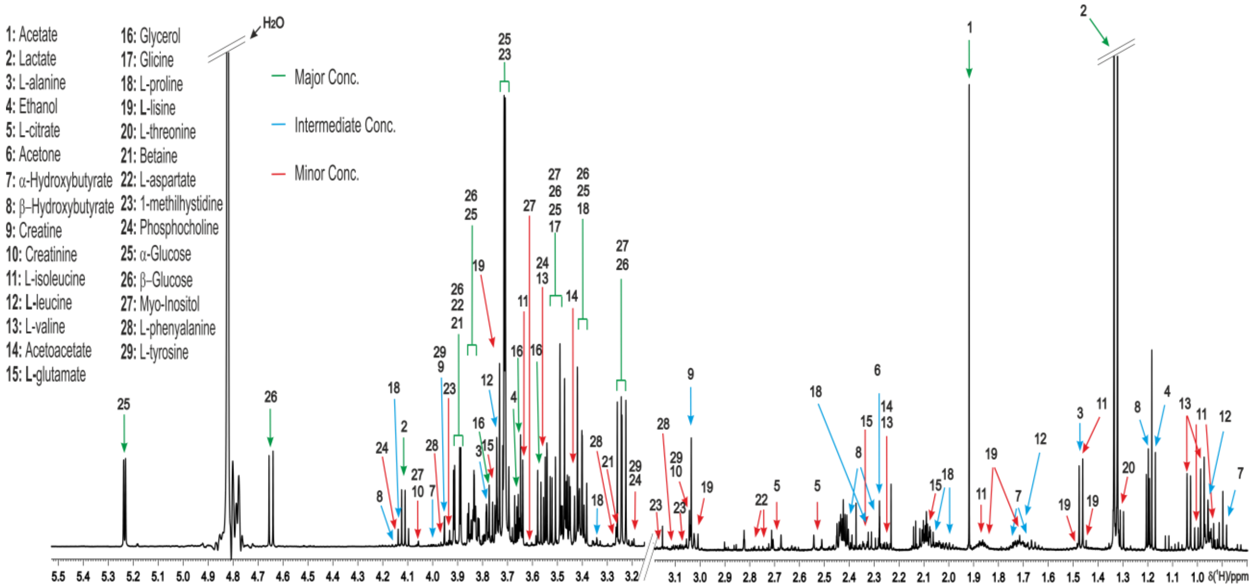

Figure 1. 500 MHz ^{1}H NMR spectrum of a human serum sample from a patient with cerebral hemorrhage.

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Activation of diboron reagents for the generation of reactive intermediates in organic synthesis

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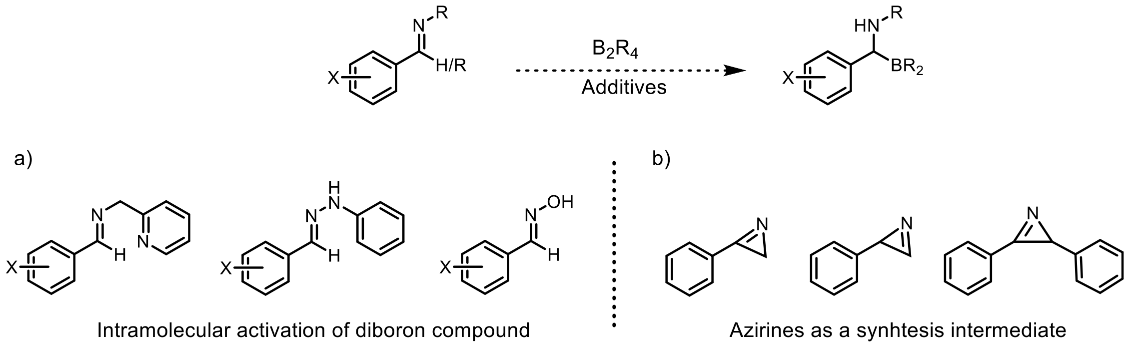
Keywords: *Diboron compound, pseudo-intramolecular, azirines*

α-Aminoboronic compounds are highly relevant in various organic synthetic pathways and represent a key functional group in biologically significant molecules such as Bortezomib and Vaborbactam.[1]

This study is divided into two main parts. The first focuses on exploring the reactivity of different diboron compounds with suitably functionalized C=N bond-containing substrates—such as imines, hydrazones, and oximes—designed to promote pseudointramolecular activation of the diboron reagent under transition-metal-free conditions (Scheme 1a). Various strategies were investigated to achieve this activation.

The second part examines the reactivity of azirines in the presence of diboron reagents, with a dual objective: to understand their reactivity toward diboron species and to access synthetically useful compounds with potential biological activity (Scheme 1b).



Scheme 1: (a): Pseudointramolecular activation of diboron reagents with C=N bond-containing compounds; Part (b): Reactivity of azirines with diboron reagents.[3]

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Synthesis of Nanographenes: Aryne-Involving Cycloaddition Reactions

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Keywords: *synthesis, arynes, polycyclic aromatic hydrocarbons (PAHs)*

The synthesis of large polycyclic aromatic hydrocarbons (PAHs) and nanographenes (fragments exceeding one nanometer) is challenging due to the absence of functional groups in their chemical structures and their typically poor solubility. Our research group is pioneer in the synthesis in solution-phase and on-surface of these compounds. Here, we summarize some of the most used reactions in their preparation by means of aryne chemistry.

The participation of arynes in cycloaddition reactions allows to increase the molecular complexity in a single step, providing straight-forward access to a wide variety of PAHs. For example, arynes demonstrated high performance in Diels-Alder reactions with dienes such as furan and cyclopentadienones.[1] In 1998, our research group discovered that arynes can undergo Pd-catalyzed [2+2+2] cycloaddition reactions, facilitating the synthesis of compounds with trigonal geometry, such as starphenes and cloverphenes.[2,3] In many examples, aryne cycloaddition reactions are combined with a cyclodehydrogenation step to access large and flat nanographenes by a Scholl reaction[4] or alternative methods, such as those reported on-surface.[5]

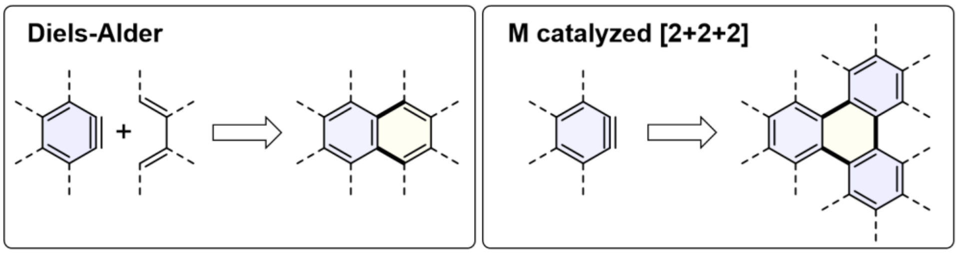

Figure 1. Aryne cycloaddition reactions used in the synthesis of PAHs.

The limited information presented here is related to the protection process we have initiated, in accordance with the guidelines provided by the USC valorization and transfer office.

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New catalytic approaches to the functionalization of C−H bonds in organic compounds of interest

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Keywords: *C−H activation, photocatalysis, cobalt*

Transition metal catalysis provides an effective solution for the synthesis of complex molecules by simple transformations. Among these catalytic strategies, C−H bond activation has gained significant attention during the last decade as it eliminates the need for pre-functionalized substrates, which traditionally results in lengthy procedures and excessive waste. This method not only streamlines synthetic processes but also aligns with principles of Green Chemistry by reducing the use of hazardous reagents and minimizing the generation of by-products. Moreover, the use of 1st row metals as catalysts, such as cobalt, in contrast to methodologies based on noble metals, offers a more accessible, cost-effective, and biocompatible approach. However, the use of metal oxidants is sometimes required to accommodate changes in metal´s oxidation state. In this way, visible-light photocatalysis has emerged as a sustainable alternative due to its ability to perform organic reactions under mild conditions. Its high selectivity and efficiency enable the formation of valuable compounds with broad functional group tolerance, which, together with its photoredox properties, makes it highly compatible with C−H activation strategies.[1]

Furthermore, allenes are of great interest in synthetic transformations due to their high reactivity and chemical diversity. Their reactivity is strongly influenced by the steric and electronic nature of their substituents, which renders the control of regio- and chemoselectivity particularly challenging. As a result, allenes represent attractive coupling partners in C−H activation reactions.[2]

This work demonstrates the successful control of regioselectivity in allene insertion by combining photocatalysis with cobalt-catalyzed C−H activation, yielding isoquinolones with a diene moiety in their structure (Figure 1).[3] This cobaltophotoredox strategy enables the functionalization of various aromatic and heteroaromatic rings, including biologically relevant molecules. Additionally, diverse allenes react efficiently, providing a broad range of isoquinolones that can be further modified, showcasing the method's potential for integration into complex synthetic pathways.

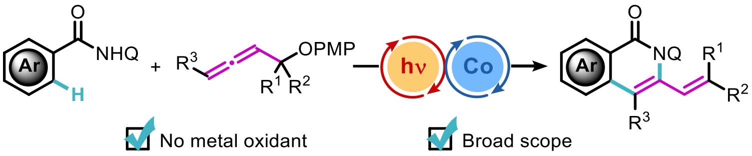

Figure 1. Regioselective synthesis of isoquinolones with a diene unit via dual cobaltophotoredox-catalyzed C−H activation.

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New molecules for Alzheimer's disease

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Keywords: *Alzheimer's disease (AD), Synthesis, Contilisant.*

Alzheimer's disease (AD) is a multifactorial and complex neurodegenerative disorder that primarily affects the elderly and currently has no effective treatment, due to its complex mechanism. AD is characterized, among other factors, by the accumulation of senile plaques and intracellular neurofibrillary tangles in the brain, together with loss of synapses and progressive degeneration of neurons in the hippocampus, leading to memory loss and dementia.[1] Over the past few years, researching has increasingly focused on multitarget compounds, capable of simultaneously interacting with various biological targets in effort to discover more effective therapeutic agents for AD.[2]

The multitarget compound in which this work has been based on is called ***Contilisant***, a molecule designed and developed by our research group. ***Contilisant*** stands out for its pharmacological profile: it inhibits monoamine oxidase enzymes (MAO), cholinesterase enzymes (ChEs) and modulates histamine 3 receptor (H3R) and sigma 1 receptor (S1R). Moreover, it is also capable of crossing the blood-brain barrier and it has demonstrated neuroprotective and antioxidant properties.[3]

Nowadays, we are working on the pharmacological optimization of ***Contilisant*** aiming to identify new analogs with enhanced activity and pharmacological diversity.[4] This includes incorporating new pharmacophores capable of inhibiting histone deacetylase enzymes (HDACs) and modulating dopamine receptors (DRs), two biological targets strongly implicated in the progression and development of AD.

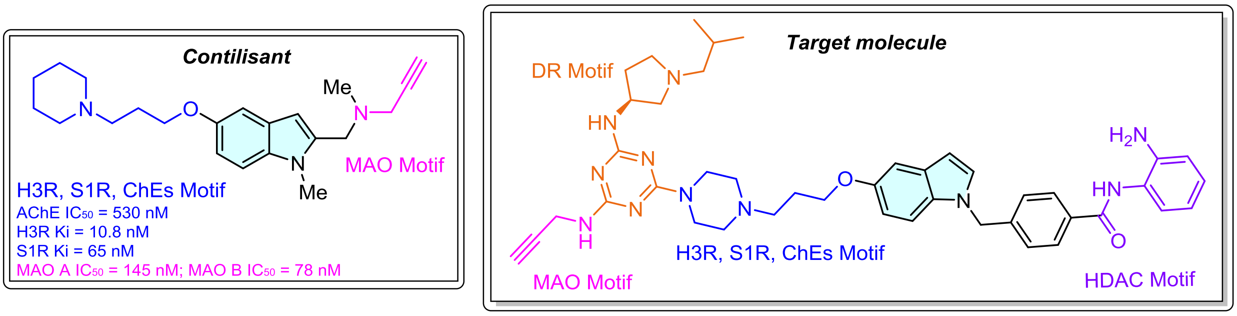

Figure 1. Chemical structure of ***Contilisant*** (left) and target molecule (right)

In this context, the synthesis, isolation and characterization of all intermediates to reach the target ligand has been done in 11 synthetic steps. Finally, the ligand obtained will be analyzed by *in vitro* assays in order to study its pharmacological profile and assess its effectiveness against AD.

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SYNTHESIS OF VITAMIND D ANALOGS WITH M-CARBORANE UNIT IN THE SIDE CHAIN

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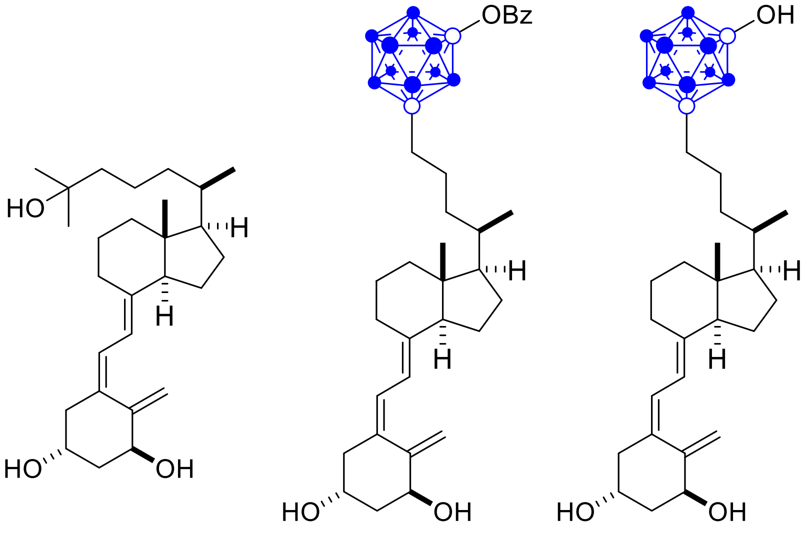
***Keywords**: 1,25D$_3$, carborane, VDR.*

Vitamin D$_3$ carries out its biological functions through its active form, the hormone 1α,25-dihydroxyvitamin D3 (1,25D$_3$, **1**), which is essential for maintaining calcium and phosphorus homeostasis. It is important for cell differentiation and the inhibition of cell proliferation, as well as for the regulation of the immune system. Unfortunately, the pharmacological doses required for treatment hyperproliferative diseases lead to hypercalcemia[1,2].

The vitamin D receptor (VDR) is considered a promising target in cancer therapy, as it is present in many types of tumors and its ligand has shown anticancer effects. Moreover, biological assays demonstrate that carborane analogs are as active as the native hormone but less calcemic[3]. To combine these properties with boron neutron capture therapy (BNCT), this project aims to synthesize two 1,25D3 analogs (**2** and **3**) with m-carborane units added into their side chain. Additionally, molecular docking studies will be performed to analyze how these compounds interact with the VDR.



1 **2** **3**

Figure 1. 1,25D$_3$ and analogs with carborane units in the side chain.

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Assembly and applications of porous nanomaterials functionalized with molecular gates

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Keywords: *nanomachines, drug delivery, molecular gates.*

One of the most active areas of research in the field of biomedicine is the development of controlled drug-release devices. Among these, nanomachines and nanorobots based on mesoporous silica nanoparticles stand out as they can be easily modified on their surface, allowing the design of systems that selectively release their cargo content in response to specific stimuli[1]. Here, the construction of L-lactate sensitive enzyme-controlled nanomachines for controlled drug release is described. As a previous proof of concept, two model dye-loaded nanomachines of increasing complexity capable of reacting to the presence of hydrogen peroxide (S_2) or L-Lactate (S_{3R}) were prepared. The silica nanoparticles were functionalized with a hydrogen peroxide-sensitive organic ligand such as 1-(4-aminophenyl)-2-phenylethane-1,2-dione[2], loaded with tris(bipyridine)ruthenium(II) chloride or doxorubicin and capped with a supramolecular complex formed between the ligand and the neoglycoenzyme lactate oxidase-β-cyclodextrin[3,4]. These nanomachines specifically recognize L-lactate as natural substrate of the controlling enzyme, and upon catalytic transformation, yield H_2O_2 able to trigger the disruption of the gating mechanism, leading to the release of the encapsulated cargo. Since high levels of L-lactate have been related to metastasis and tumor growth, it is expected the nanomachine to recognize the presence of cancer cells and combat their proliferation through this assembly[5].

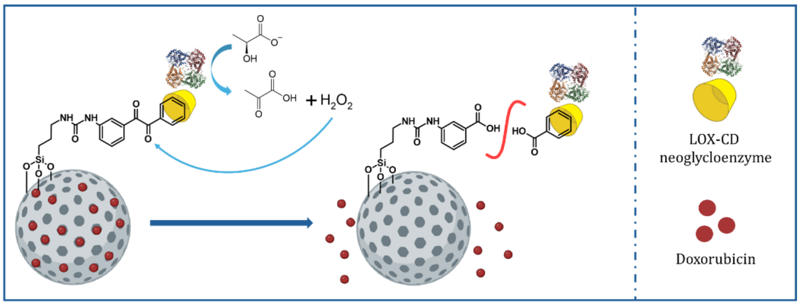

Figure 1. Release mechanism of the enzyme-controlled nanomachine S_{3D}

The suitability of the proposed nanomachines for autonomous and specific delivery was evaluated through kinetics release and selectivity experiments. Finally, to demonstrate the on-command release of the cargo, *in vitro* cell viability and confocal microscopy assays were conducted incubating HeLa cancer cells with the doxorubicin-loaded nanocarrier (S_{3D}).

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Photoactive molecules for advanced biomedical applications

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Keywords: *POSS, BODIPY, multichromophoric systems.*

Polyhedral oligomeric silsesquioxanes (POSS) are a class of inorganic-organic hybrid materials with well-defined three-dimensional cage-like nanostructures. These nanomaterials are based on an inorganic silicon-oxygen framework, where the silicon atoms at the vertices are covalently bonded to organic functional groups.[1] POSS exhibits exceptional properties, including structural rigidity and high stability, attributed to its inorganic core. Additionally, the organic substituents provide chemical versatility and functional tunability, and play a key role in modulating properties such as solubility, thermal stability or photophysical behavior.[2]

BODIPYs are fluorescent dyes with remarkable properties, such as high fluorescence quantum yields and absorption coefficients, and a wide range of applications, particularly in biomedical fields such as biolabeling, bioimaging, and photodynamic therapy (PDT).[3]

The aim of this project is the design and synthesis of photoactive BODIPYs–POSS systems in which the chromophoric units are spatially organized to minimize conformational mobility and intramolecular stacking. To achieve this, both a highly rigid and symmetric multichromophoric system, T_8–POSS, and a simpler monochromophoric system, T_1–POSS, have been synthesized.

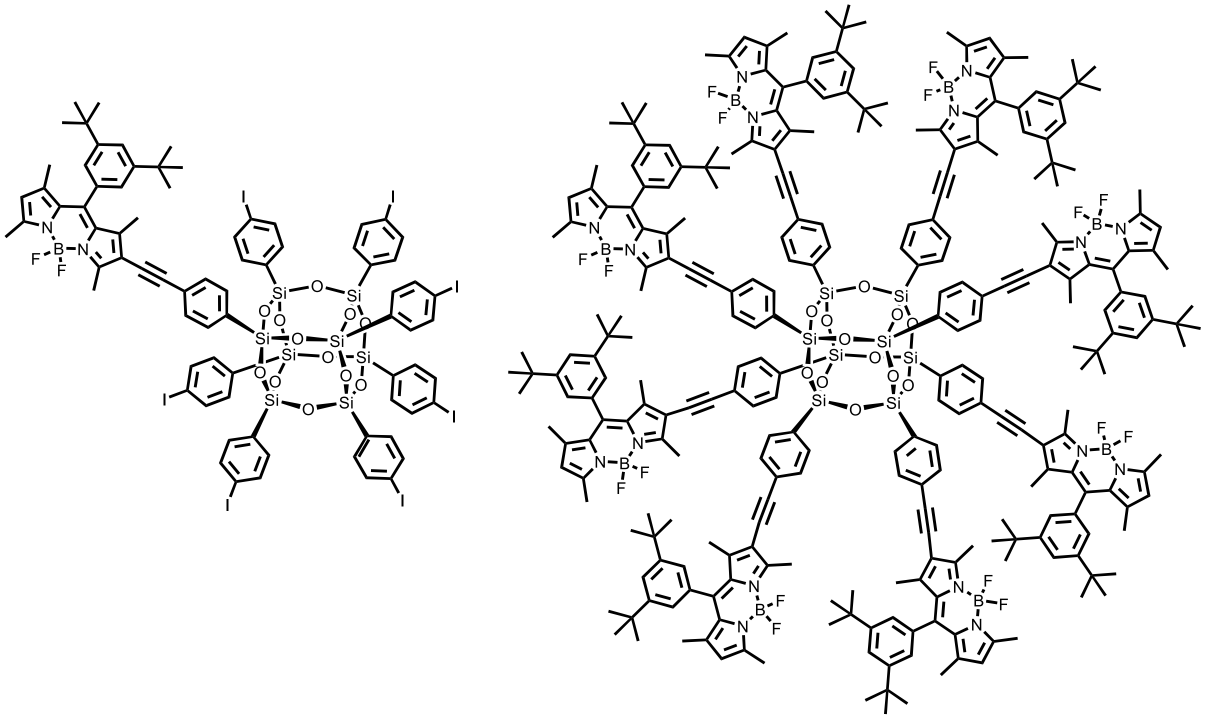

Figure 1. Hybrid nanostructures mono- and octa-POSS functionalized with BODIPYs prepared in this work.

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Synthesis, self-assembly and photophysical studies of a novel “cyanostar” derivative

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***Keywords**: macrocycles, cyanostars, supramolecular aggregates.*

Firstly reported in 2012 by the group of Flood, *cyanostars* (CSs) are a class of star-shaped macrocycles obtained by Knoevenagel self-condensation of a benzaldehyde derivative *meta* substituted with a cyanomethylene unit in the presence of a base.[1] A key feature of CSs is the presence in their structure of five covalently-linked cyanostilbene units which gives rise to an electron-deficient cavity suited for the complexation of anions, particularly large, weakly coordinated ones like PF_6^-, ClO_4^-, or BF_4^- through a combination of electrostatic, hydrogen-bonding, and CH···anion interactions. Such binding is often accompanied by a change in the fluorescence, thus enabling anion sensing. Recently, the group of Flood reported a triphenylamine (TPA)-based CS (**1**, Figure 1a) showing a zero overlap between its absorption and emission spectra leading to concentration-independent fluorescence band maxima (Figure 1b), a remarkable finding which allows to study chemical processes at high concentrations using fluorescence spectroscopy.[2] Based on this study, and in order to evaluate how the presence of multiple TPA units would affect the emission features of the CS, our group engaged in the preparation and study of a CS analogue of **1** featuring five ethynyl-TPA moieties (**2**, Figure 1a). Interestingly, this CS showed some solvent-dependent emission (Figure 1c) and aggregation features (i.e., very broad ^{1}H-NMR) not observed for CS **1** nor in any previously reported CS. To nail the origin of such distinctive behaviour of **2**, in this TFM we prepared and studied two new CS derivatives, namely CS **3** (an analogue of **1** featuring five instead of one TPA unit) and CS **4** (an analogue of **2** featuring one instead of five ethynyl-TPA moieties) with the aim of understanding how i) the presence of the ethynyl linker connecting the TPA to the CS, and ii) the number of electron-donating TPA units attached to the CS would influence the physicochemical properties of the macrocycle.

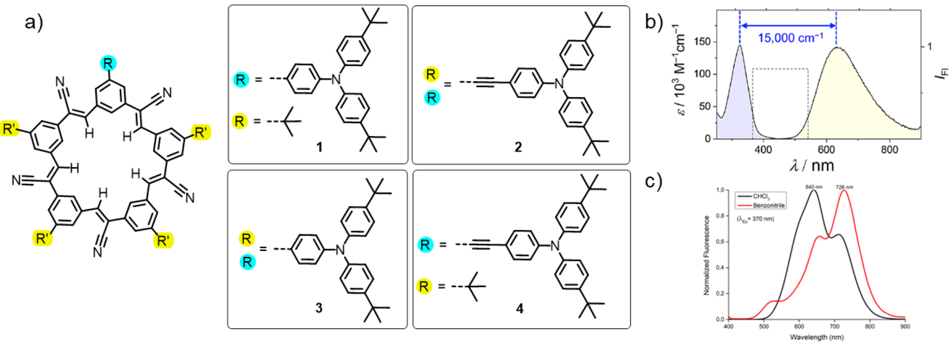

Figure 1. a) Molecular structure of cyanostars **1-4**. b) Absorption and emission spectra of CS **1**. c) Emission spectra of CS **2** in $CHCl_3$ (black line) and benzonitrile (red line) at 250 μM.

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Synthesis of peripherally restricted compounds based on the cannabinoid ligand WIN55,212-2 and study in the immune system

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***Keywords**: WIN55,212-2, peripherally restricted, immune system*

The synthetic cannabinoid ligand WIN55,212-2 (WIN) is receiving growing attention because of its recently reported immunomodulatory capacity, promoting Treg cell production and reducing anaphylaxis.[1] However, WIN may produce adverse psychotropic effects due to its agonist activity at the CB_1 receptor in the brain.[2]

In this context, the main objective of this project is the synthesis of new WIN-based compounds that cannot cross the blood-brain barrier while maintaining effects on the immune system. For the design of these peripherally restricted compounds, we have introduced polar moieties in the WIN scaffold, with the aim of increasing the polarity (tPSA) and decreasing the lipophilicity (clogP) (Figure 1). In this work, we have set up the synthetic route for the new compounds **1-5** that will be assayed for NF-κB inhibition in THP1 cells and for cytokines (IL-6 and IL-10) production in dendritic cells from human donors. Subsequent determination of the ADME properties and the brain/plasma distribution of the active compounds will identify peripherally restricted compounds with immunomodulatory activity that will be assessed for in vivo efficacy in animal models of allergy.

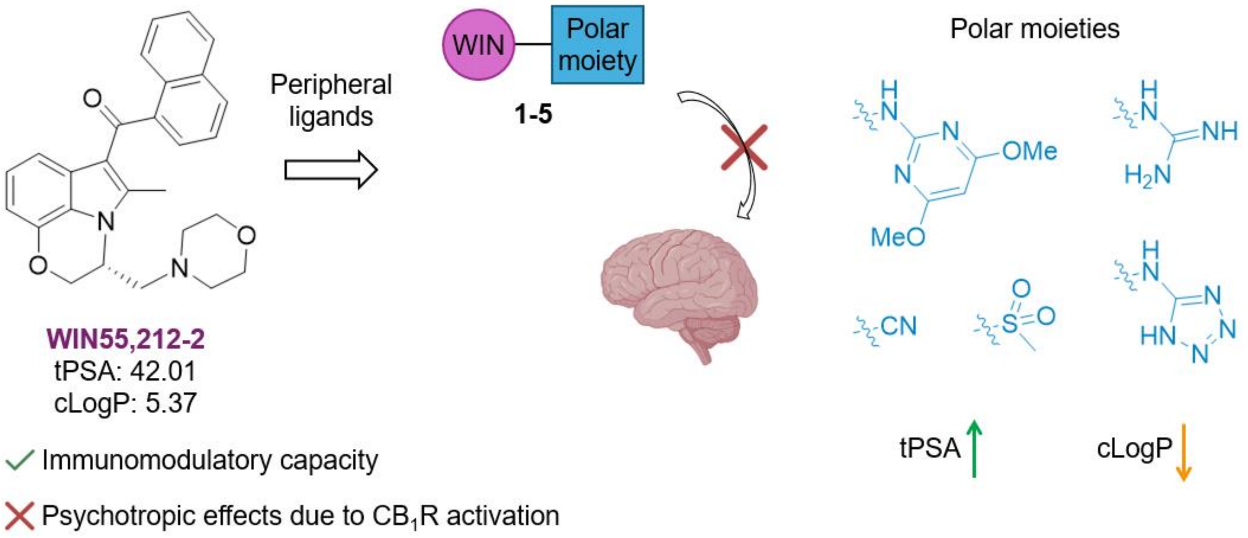

Figure 1. Design of peripherally restricted WIN-based compounds for the treatment of immune system diseases.

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BODIPY-Tagged Nitrogen Heterocycles via Catalytic Asymmetric 1,3-Dipolar Cycloaddition

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***Keywords**: BODIPY, enantioselective 1.3-dipolar cycloaddition, bioimagine*

Boron-dipyrromethenes (BODIPYs) represent a versatile class of fluorescent probes widely employed in bioimaging studies via fluorescence microscopy.[1] Mainly due to their photostability, high values of molar extinction (ε), high fluorescence quantum yields (Φ), narrow emission bandwidths, and structural versatility, which allows fine-tuning of their photophysical and biocompatibility profiles through chemical modification. Moreover, these compounds are stable to physiologic medium and have a very low cytotoxicity. In recent decades, the development of BODIPYs with chiroptical properties has advanced significantly, driven by their potential applications in areas such as optoelectronics or chiral sensing. Most synthetic strategies rely on the introduction of carbon stereocenters or axial/helical chirality into the fluorophore core, and chirality at the boron atom.[2]

Building on our group's interest in the development of BODIPY-based biological sensors,[3] we report here the enantioselective synthesis of BODIPY derivatives via an asymmetric catalytic 1,3-dipolar cycloaddition of azomethine ylides.[4] This strategy affords enantioenriched BODIPY–pyrrolidine conjugates in moderate to good yields and with high enantiomeric excess. Preliminary biological evaluations in HeLa cells, including assays of dark cytotoxicity, subcellular localization, and light-induced phototoxicity, are also presented.

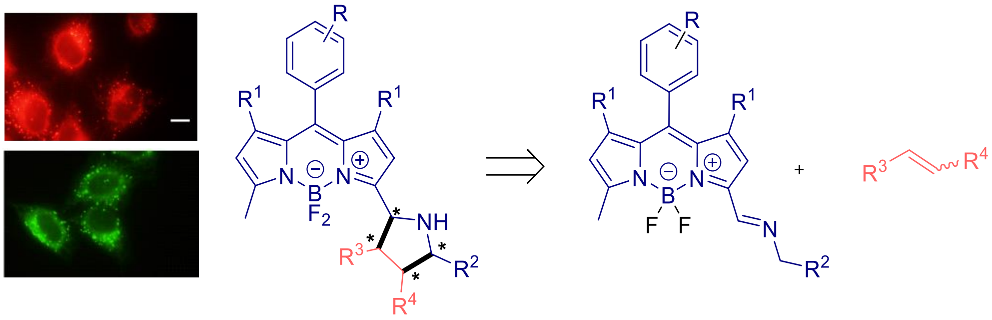

Figure 1. Image of subcellular localization of BODIPY (left) and 1,3-dipolar cycloaddition retrosynthesis (right).

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Molecular Nanographenes: a Journey Through Antiaromaticity

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Keywords: *nanographene, antiaromaticity, Sholl reaction.*

Molecular nanographenes are precisely defined graphene fragments whose size and shape can be controlled through organic synthetic methods. This bottom-up approach enables atomic-level control in structure design, making it possible to tailor their electronic and optical properties. Strategies such as tuning the π-extension or introducing non-hexagonal rings have been widely used to modulate those features.[1]

In this work, we explore a less common strategy: the incorporation of antiaromatic units into nanographenes. These substructures are expected to significantly influence the electronic behaviour by narrowing the energy gap between the conduction and valence bands, with direct consequences on the optoelectronic response.[2]

We report the synthesis of molecular nanographene **1** (Figure 1), which features a central pentalene-based antiaromatic core (highlighted in yellow) fused to two hexa-*peri*-hexabenzocoronene units (in green). The synthetic route involves four key transformations. First, nucleophilic addition of methylmagnesium bromide to the diketone precursor **2** yields the antiaromatic compound **3**, a dibromodimethyldibenzopentalene. The subsequent two-fold Sonogashira coupling between compound **3** and 4-*tert*-butylphenylacetylene provides the bis(arylethynyl) derivative **4**. This intermediate reacts with tetraarylcyclopentadienone **5** in a double Diels–Alder reaction with extrusion of CO, leading to compound **6**, a bis(pentaryl)dibenzopentalene framework. In the final step, Scholl cyclodehydrogenation induces the formation of 12 new C–C bonds around the antiaromatic core, completing the graphitization process. We are currently investigating the optoelectronic properties of nanographene **1** via UV–vis absorption, fluorescence spectroscopy, and cyclic voltammetry.

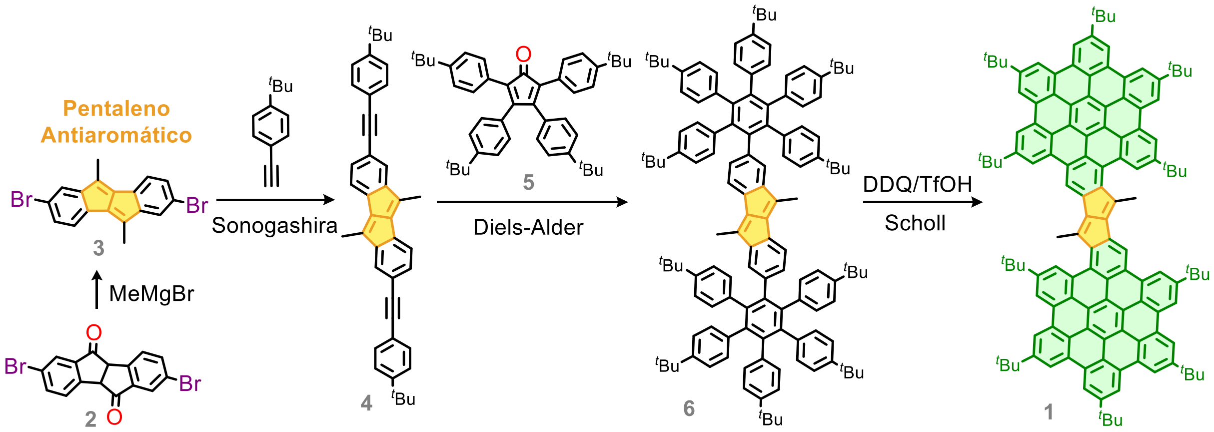

Figure 1. Stepwise synthesis of nanographene **1** incorporating a central antiaromatic pentalene unit.

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Pd-catalyzed regiodivergent access to Indenes and Benzocyclobutenes

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***Keywords**: Regiodivergent, Indene, Benzocyclobutene.*

Regiodivergent processes are transformations where it is possible to form two different regioisomers from the same starting material. This phenomenon follows the guidelines of green chemistry as a key factor in the concept of efficiency and atom economy proving its value. Obtain complete control over the regioselectivity in a reaction is challenging and, in many cases, inaccessible. Regioselectivity can be achieved by using different catalysts, ligands or manipulating the reaction conditions.[1] Over the last 20 years, a variety of catalytic regiodivergent reactions have been reported, including addition reactions to unsaturated C-C bonds[2a] C-H activation reactions[2b] and cross-couplings[2c]. The possibility of switching between two modes of reactivity in the same system changing the catalyst or adding additives make the proccess a powerful tool to reach molecule complexity starting from the same substrate.

Based on our wide experience in the regioselective functionalization of conjugated dienes using HFIP[3] and our extensive knowledge about palladium-catalyzed reactions with olefins[4] we envisioned the possibility of a regiodivergent process starting from allyl *ortho*-bromobenzenes **1** (Figure 1).

Herein, we report a complete regiodivergent process to obtain indenes **2** or benzocyclobutenes (BCBs) **3** tuning the reaction conditions, to give the respective products with absolute control of the regioselectivity (Figure 1).

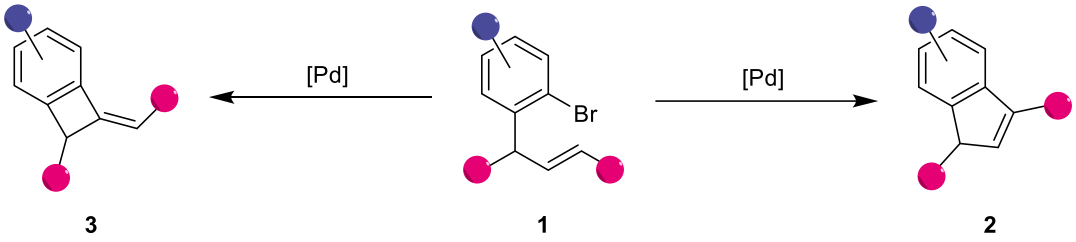

Figure 1. Regiodivergent synthesis of indenes **2** and benzocyclobutenes **3**.

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Evaluation of sulfinamides in the Petasis reaction as chiral auxiliaries

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Keywords: *Petasis, amino acids, sulfinimines.*

The Petasis reaction, also known as the Petasis borono-Manich reaction, is a multicomponent transformation that enables the synthesis of functionalized amines through the condensation of an amine, an aldehyde and boronic acid. Since its discovery in 1993,[1] this reaction has been widely used in medicinal chemistry due to its synthetic versatility.[2]

In 2019, Molander and co-workers described the Photoredox version of Petasis reaction by introducing an iridium-based photocatalysts and potassium trifluoroborates as source of radicals,[3] opening a new scope for this transformation.

In a different work, Baran's group reported a new asymetric synthesis of non-natural amino acids by the use of sulfinimines as chiral auxiliaries in combination with activated carboxylic acids.[4]

Building on these precedents, in this work, we aim to investigate the feasibility of a Photocatalytic Petasis reaction employing sulfinimines to induce chiral selectivity in combination with aromatic aldehydes and alkyltrifluoroborates as a source of radicals.

Additionally, we investigate the use of oxalate derivatives as an alternative to aromatic aldehydes, with the goal of synthesizing non-natural amino acid precursors.

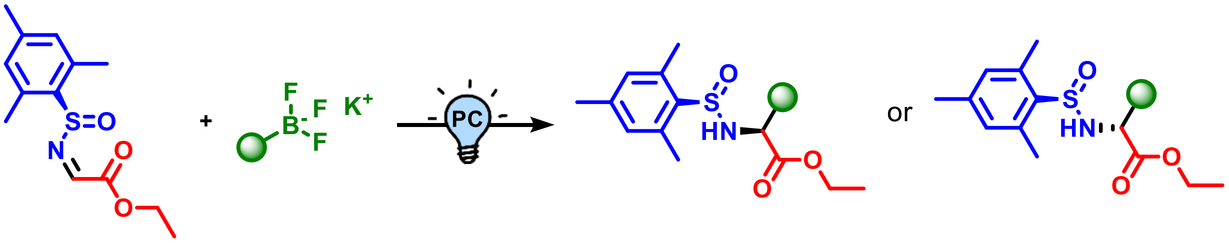

Figure 1. Representative transformation using Chiral sulfinimines at Petasis reaction

This poster summarizes the validation work carried out using aromatic aldehydes and oxalate derivatives, in combination with chiral sulfinimines, including insights of reaction kinetics, scope and limitations when alkyl trifluoroborates were used as radical source.

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Pt (II) (N,C,NX) pincer complexes with [FeFe]-H$_2$ase Mimics: Synthesis and Electrocatalytic Behavior

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Keywords: *Hydrogenase mimics, Pt (II) (N,C,N) pincer complexes*

The use of molecular hydrogen as a clean energy source, has driven the scientific community to search for new hydrogen sources. Hydrogenases are metalloenzymes capable of catalysing the conversion of protons into molecular hydrogen. In recent years, most of the attention has been focused on the development of [FeFe]-hydrogenase mimics as surrogates for the natural enzymes.[1,2]

Our research group is interested in the study of [FeFe]-hydrogenase mimics anchored to surfaces or solid supports (SiO2, metal-nanoparticles). In this regard, the planarity and the rigid structure of platinum pincer complexes can be an advantage to study the catalytic activity of hydrogenase mimics assembled through π-stacking interactions.[3]

The objectives of this work focus on the synthesis and functionalization of [FeFe]-hydrogenase mimics with platinum pincer ligands, which can serve as electron reservoirs, potentially enhancing catalytic performance. Additionally, their structural features offer potential anchoring sites for immobilization on solid supports, enabling future applications in heterogeneous catalysis and hydrogen production technologies.

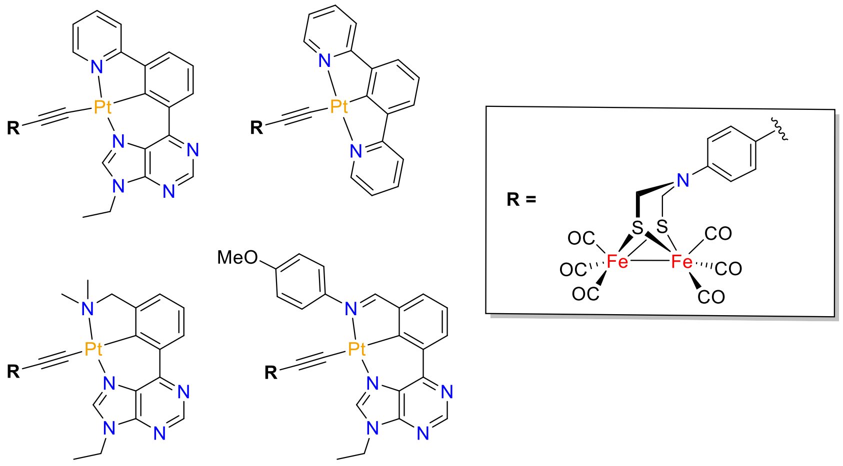

Figure 1. Examples of [FeFe] complexes bearing Pt (II) (N,C,N) pincer moieties.

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β-to-β Singly Linked Subphthalocyanine Oligomers with Effective π-Conjugation

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***Keywords**: Porphyrinoids, π-Conjugated Systems, Chromophores.*

π-Conjugated porphyrin arrays have garnered significant attention as models for light-harvesting antenna complexes and for the study of electron excitation and charge transport. Owing to their highly delocalized electronic networks, they exhibit unique optical and redox properties that can be exploited in cutting-edge technologies. Such properties can be fine-tuned through precise control over the π-layout.[1] In this context, breaking the planarity of porphyrin arrays represents a new design avenue, as it imparts intriguing electronic features and opens the door to curved π-systems with novel topologies and supramolecular characteristics.

For this purpose, Subphthalocyanines (SubPcs), with their distinctive bowl-shaped, 14π-electron aromatic skeleton, emerge as prime candidates due to their rich functional landscape.[2] To date, very few π-conjugated SubPc arrays have been reported. Recently, it has been demonstrated that simple π-bridges such as alkene, alkyne, or thiophene units can enable effective electronic communication between two SubPc units.[3] Building on this, and with the aim of exploring π-electron communication in more complex systems, herein we present a series of π-conjugated SubPcs oligomers (Figure 1) assembled *via* simple alkyne bridges. Despite being singly linked, these readily accessible arrays exhibit excellent π-electron communication, significantly perturbing the orbital distribution of conventional SubPcs and inducing notable alterations in their optical properties.

The findings presented here demonstrate the potential of SubPcs for constructing curved porphyrin arrays with well-conjugated skeletons and intriguing functionalities.

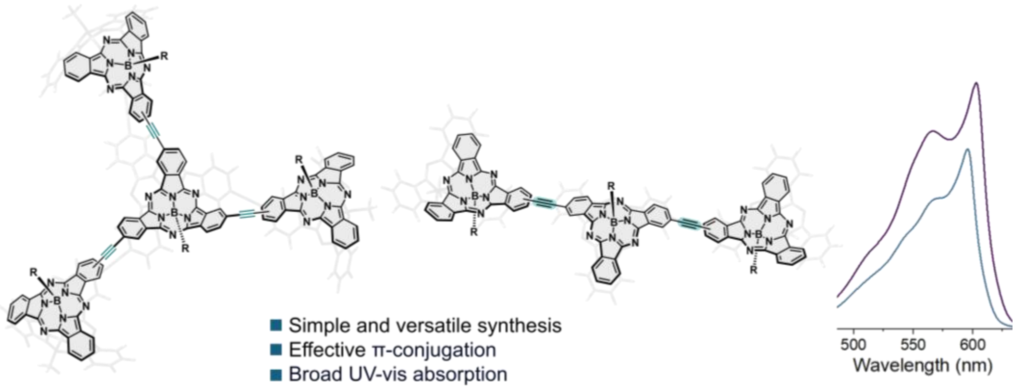

Figure 1. Models of SubPc oligomers studied and their absorption spectra.

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Synthesis of Radiotracers for Positron Emission Tomography.

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***Keywords**: radiotracers, cyclooxygenases, PET.*

Positron Emission Tomography (PET) is a molecular imaging technique that utilizes radiotracers labelled with positron-emitting radioisotopes, allowing in vivo molecular study of biological and pathological processes.[1] The emission of these β^+ particles (positrons) typically occurs in the radioactive nuclei of light elements, such as fluorine-18 (^{18}F). Due to its short half-life (109.8 minutes), it is necessary to design a rapid and efficient radiosynthesis process for its incorporation at molecular level. For this reason, the presence of a nitroso group is required, as it facilitates a faster reaction.

There is a group of key enzymes involved in the synthesis of thromboxanes and prostaglandins known as cyclooxygenases. Currently, two isoforms are known; COX-1, which is involved in cellular homeostasis and is present in most tissues of the body, and COX-2, an essential enzyme due to its role in inflammatory processes. COX-2 is crucial for understanding various types of cancer as well as diseases like Parkinson's and Alzheimer's, as it is overexpressed in cancerous cells.[2,3]

In order to locate these malignant cells, a radiotracer designed to detect COX-2 will be synthesized. To achieve this, and in collaboration with a research group from Germany, the radiosynthesis of various fenamates -known inhibitors of this cyclooxygenase isoform- will be carried out. The critical stage of the project involves a previously designed synthetic route for a sydnone with a nitroso group, to which the positron-emitting ^{18}F atom will be attached. Additionally, an alternative pathway for the fluorination reaction is proposed, involving the use of different arenes substituted with both hydroxyl and nitroso groups.

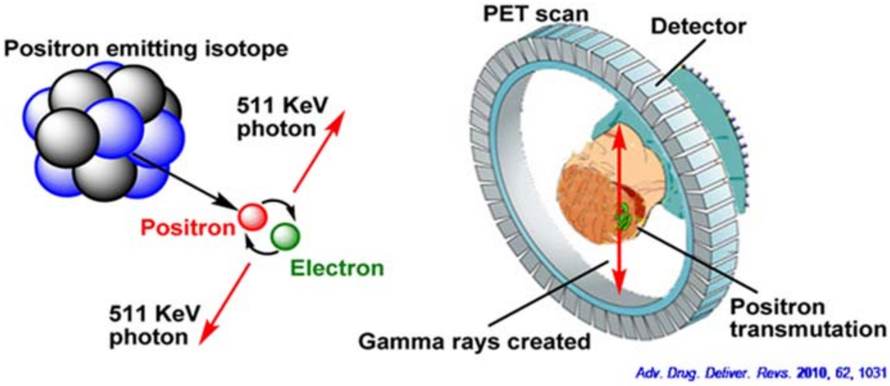

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Figure 1. Gamma ray generation from positrons and PET scanner.

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Lipopeptides as tools in supramolecular chemistry and catalysis.

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Keywords: *lipopeptide, self-assembly, catalysis.*

Lipopeptides are an excellent example of amphiphilic molecules.[1] Their structure is the result of combining a polar peptidic head and a nonpolar lipidic chain which confers the ability to self-assemble into supramolecular structures. The morphology can be tuned depending on the external conditions (solvent, pH, Temp…). [2]

There are particular peptide sequences, known as ATCUN (Amino Terminal Cu(II)- and Ni(II)-binding motif) rich in histidine, glycine and cysteine amino acids, that coordinate to transition metals such as Cu, Zn and Ni, allowing them to catalyze certain reactions. [3]

In this work, a library of tripeptides and their dodecanoyl lipopeptides, based on ATCUN motifs, has been obtained using solid-phase peptide synthesis (SPPS). In order to study their activity as minimal artificial metalloenzymes, Suzuki-Miyaura cross-coupling reaction catalyzed by Ni(II) was chosen.[4] Lipopeptide C_{12}-GGH was selected as a model to optimize the reaction conditions.

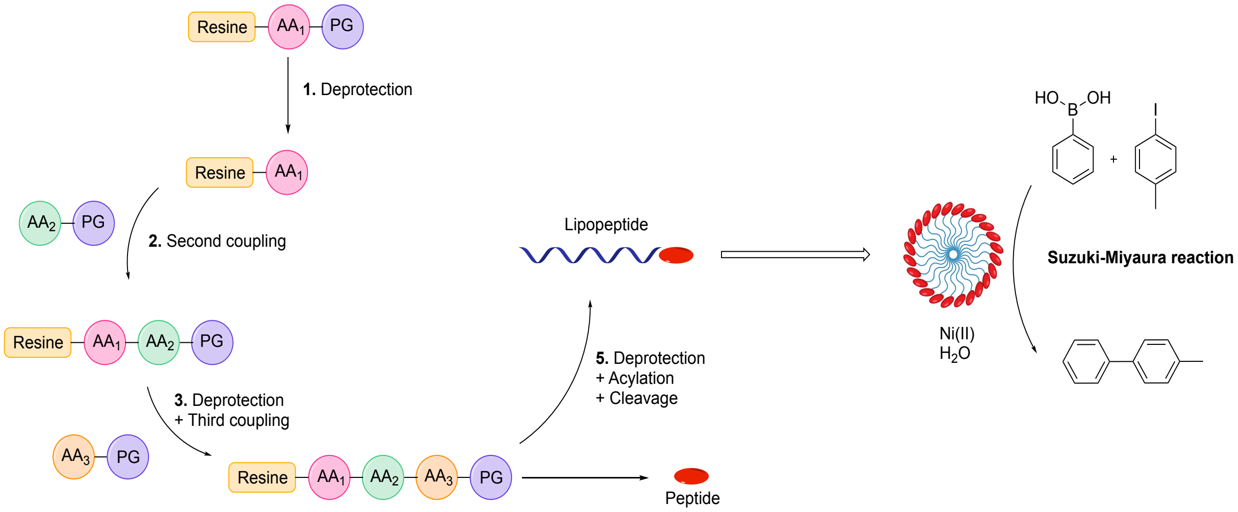

Figure 1. Synthesis of peptides and lipopeptides using SPPS and proposed Suzuki-Miyaura reaction catalyzed by self-assembly Niquel-Lipopeptide complex.

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Organic porous materials as heterogeneous photocatalysts and pollutant sensors.

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Keywords: *photocatalysis, nitroaromatics sensing, porous polymers.*

Porous organic polymers (POPs) are a broad field that encompasses many porous materials classified by their structural properties[1]. Two types of POPs are covalent triazine frameworks (CTFs)[2] and hyper-crosslinked polymers (HCPs)[3]. These amorphous materials are characterized by their excellent chemical and thermal stability, as well as large specific surface areas[1,2]. We obtained and characterized two novel organic polymers using Attenuated Total Reflectance (ATR), UV-Vis, fluorescence, and ^{13}C NMR spectroscopies; thermogravimetric analysis (TGA); etc. One of the polymers, **1,6-Pyr-3Ph-CTF**, was obtained as a fluorescent solid in a good yield via a Suzuki-Miyaura cross-coupling reaction between 1,6-dibromopyrene and ((1,3,5-triazine-2,4,6-triyl)*tris*-(benzene-4,1-diyl))triboronic acid.

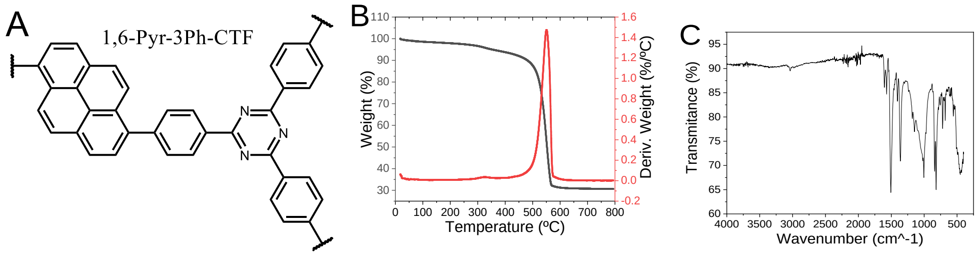

Figure 1. A. Idealized structure **1,6-Pyr-3Ph-CTF**, B. TGA and C. ATR Infrared Spectroscopy.

The other polymer, **HCP-TANC**, was effectively prepared from 5,6,11,12-tetraazanaphthacene (TANC) as monomer and dimethoxymethane as co-monomer by a Friedel-Crafts reaction catalyzed by $FeCl_3$ (knitting strategy).

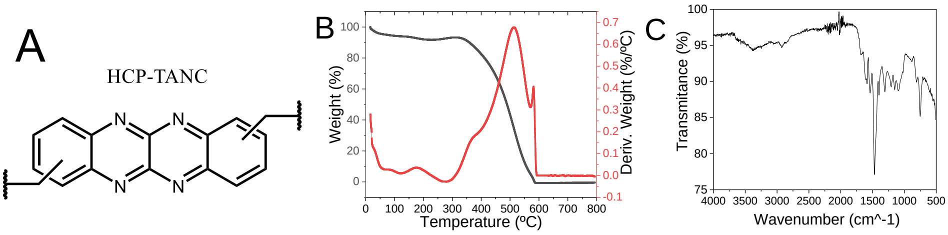

Figure 2. A: Idealized structure of **HCP-TANC**, B. TGA and C. ATR Infrared Spectroscopy.

Our objective is to tackle the critical issues posed by water and air contamination with adaptable porous materials. For instance, **1,6-Pyr-3Ph-CTF** displays excellent capabilities for nitroaromatics sensing in water. **HCP-TANC**, on the other hand, has proven to be an effective photocatalyst for the aerobic oxidation of organic sulfides, such as stimulant mustard gas.

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Strategies for the stabilization and assembly of colloidal metallic nanocrystals

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***Keywords**: Functional polymers, Metal Nanoparticles (NPs), Colloidal Nanocrystals (NCs)*

Catalysis plays a central role in both organic synthesis and industrial chemistry. One of the most recent advances is the use of metallic nanoparticles (NPs), which have gained increasing attention due to their high efficiency, surface-to-volume ratio and atom economy compared to conventional metal catalysts [1]. However, stabilizing these nanoparticles in organic solvents remains challenging, as aggregation can compromise their catalytic properties [2].

This research focuses on synthesizing functional polymers that are tailored to stabilize colloidal metal nanocrystals (NCs) in organic solvents. These polymers have dual-segment architecture comprising reactive blocks that anchor to the NP surface and non-reactive chains that ensure colloidal stability through steric hindrance. Inspired by LEGO-like modular strategies [3], the polymers are based on polystyrene backbones that are functionalized to enable tunable grafting onto nanoparticle surfaces.

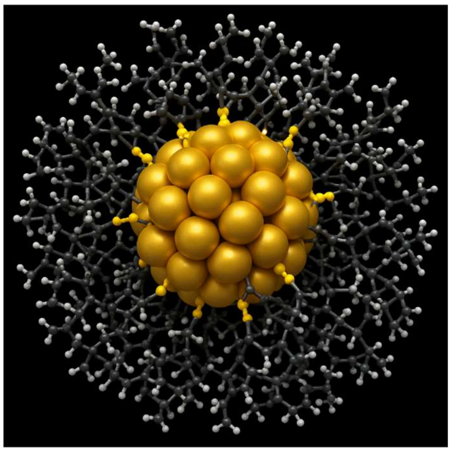

Figure 1. Schematic 3D representation of a gold nanoparticle stabilized by cysteine functionalized polystyrene ligands.

A diverse polymer library is being synthesized and characterized using spectroscopic and microscopic techniques, including ^{1}H and ^{19}F NMR, FTIR, elemental microanalysis and TEM. The resulting polymer-stabilized nanoparticles will be tested for stability and catalytic potential in model reactions. The aim of this strategy is to create a versatile nanoplatform for future applications in recyclable and selective nanocatalysis.

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POTASSIUM SALTS OF AROMATIC AMIDES: SYNTHESIS, STRUCTURE AND ELECTROCHEMICAL PROPERTIES

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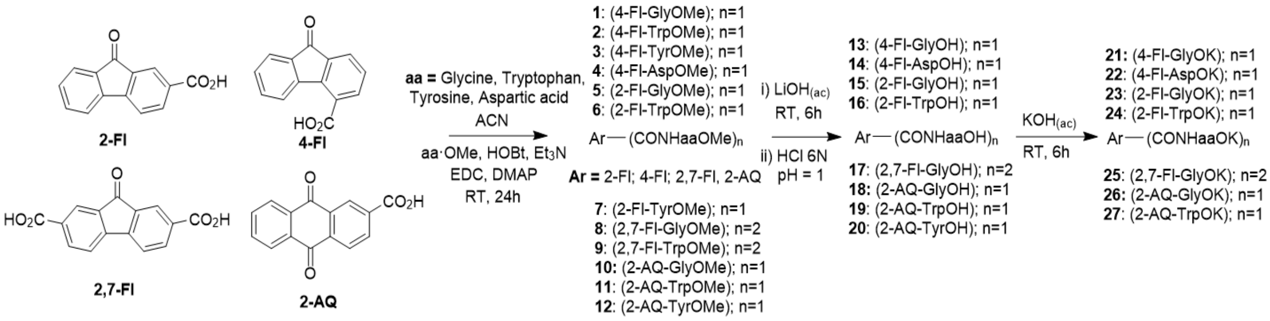
Nowadays, renewable energy sources are surpassing fossil fuel combustion as society drives to a greener energy production structure. This generates an energy storage problem, as green energy sources peak production hours do not match the peak consumption hours.

For the past 35 years, lithium-ion batteries (LIBs) have been the standard for energy storage, but the scarcity of lithium, the high toxicity of some of its materials (mainly nickel and cadmium) and its zero biodegradability pushes us to search for alternatives that allow the development of massive energy storage devices, ideally made from abundant compounds with a low price, low toxicity and zero environmental impact. The most viable alternative is the substitution of lithium for other alkali metal, such as sodium or potassium (NaIBs, KIBs), which are much more abundant in earth's crust and to replace the highly polluting inorganic materials with organic compounds[1,2].

Because of these reasons, we present the preparation of potassium salts of amides via the coupling of some selected carbonyl protected amino acids with various electrochemically interesting aromatic acids, as seen in ***Scheme 1***[3,4].



Scheme 1. Synthetic route for the obtention of potassium salts of aromatic amides.

For all the prepared compounds spectroscopy characterization (NMR-^{1}H, NMR-^{13}C, IR, MS), powder X-ray diffraction, polarimetry and melting point was conducted. Electrochemical properties were measured via galvanostatic charge-discharge. With the data obtained we discussed the usage of these compounds as electrodes for KIBs.

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Studying a new organometallic reaction

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***Keywords**: Huisgen reaction, alkyne-pyridoazide coupling, triazole to iridium complex.*

In a recent work from the group about metal quiral Iridium-triazole complexes and the formation of mesoionic carbene intermediates we found a new organometallic reaction.[1,2] Following the standard methodology developed by us, we carried out a Huisgen *CuAAC* reaction between a pyridoazide and an alkynyl sulfoxide to get the corresponding triazole. Subsequent iridation using the iridium dimer $[IrCl_2Cp^*]_2$ in boiling dichloroethane afforded a new complex.

The structure of this complex was not the expected bimetallic complex according to the ^{1}H-RMN spectrum. Further X-Ray analysis revealed that the structure of the new complex was the depicted in **Fig. 1 (A)**. So far, we have synthetized and characterized complexes **C**, **D**.

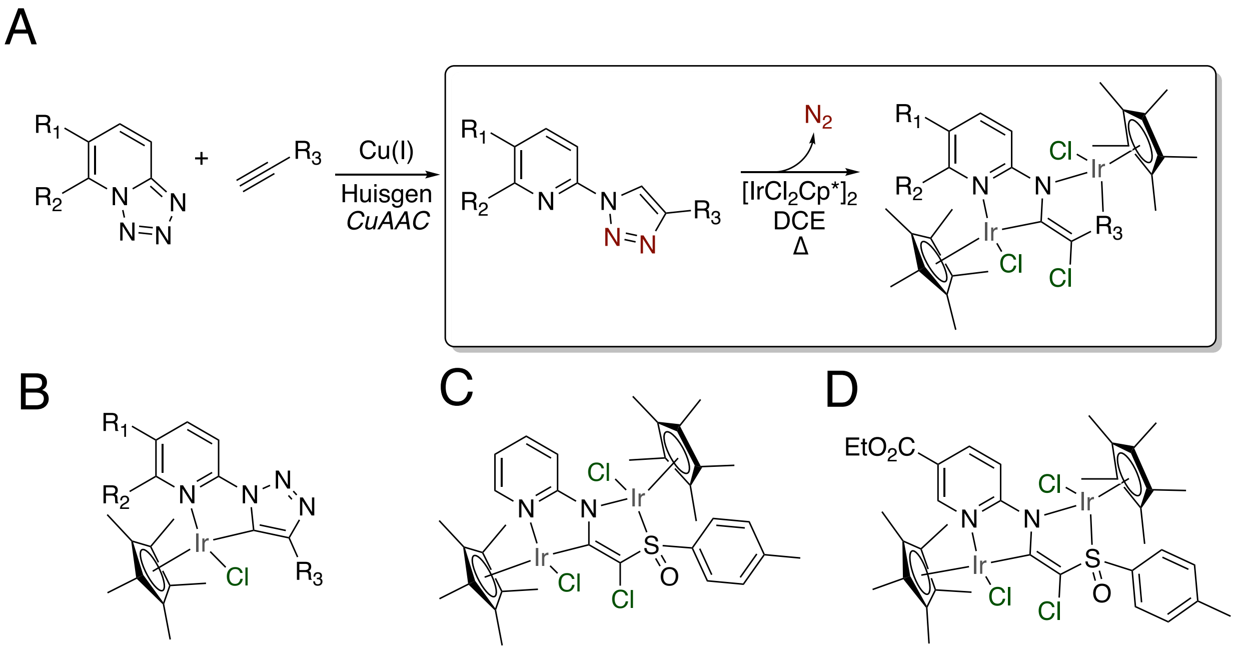

Figure 1. A: General reaction of study; **B:** Iridium complex first formed; **B, C**: characterized products so far.

We are studying the mechanism of the reaction. Our preliminary computational data show that the initially formed iridium complex **B** extrudes nitrogen to form a diazo derivative that upon the attack of a chlorine ion and coordination of a second iridium moiety affords the isolated product.

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N-thioimides as a novel and unexplored class of antiviral agents

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Keywords: *Thioimides, antiviral agents, SARS-CoV-2*

Despite the official end of the COVID-19 public health emergency [1], the continued spread of the causative agent of the disease, the SARS-CoV-2 virus, remains a significant threat to global health. Viral entry into host cells is initiated by the interaction of the Spike S glycoprotein (S-Prot) located on the surface of the pathogen with the angiotensin-converting enzyme 2 (ACE2) receptor of the host cells. Due to its crucial role and its surface exposure, S-Prot has been identified as the primary immunological target for most COVID-19 vaccines, which elicit a robust immune response that block infection. However, vaccines immunization is hampered by the high mutation rate of the S-Prot, which facilitates the emergence of new variants which evade immune protection. These circumstances emphasize the interest of identifying and developing new chemotherapeutics, including small molecules, targeting S-prot and adapted to the dominant variants [2] as complementary source of antiviral treatments.

In this context, high-throughput screening (HTS) assays employing pseudotyped vesicular stomatitis viruses expressing the up-to-date dominant SARS-CoV-2 S-Prot (VSV-S) represent simple and reliable tools for the rapid identification of novel entry inhibitors [3]. This project builds upon the evaluation of an in-house collection of synthetic small molecules on VSV-based pseudoparticles displaying the XBB.1.5 variant of the S-Prot. This screening campaign allowed to identify thioaryl imides as compounds with significant ability to inhibit viral entry in this model system, showing IC_{50} values ranging from 0.2 to 7.0 µM and a safety profile (selectivity indexes above 10). Noticeably, thioaryl imides have been used exclusively as synthetic intermediates, specifically as sulfenylating agents, without any attention having been paid to their biological activity, which remains unexplored so far. These findings position thioaryl imides as a promising class of compounds for further investigation as SARS-CoV-2 entry inhibitors and support the interest of extending biological evaluation to other viral pathogens.

Based on these findings, we herein present a project focused on structural modifications of the most active thioaryl imides identified. A new series of derivatives was synthesized, incorporating functional groups aimed at improving their pharmacological properties. Furthermore, due to structural similarities observed between some of the synthesized compounds and Tecovirimat -—an antiviral drug approved for the treatment of orthopoxvirus infections such as smallpox and monkeypox—future efforts will also be devoted to exploring their potential activity against these viral pathogens, complementing ongoing research on SARS-CoV-2.

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New synthetic methodologies based on unsaturated systems for accessing relevant organic molecules.

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Keywords: *bis-allenols, cyclization, cyclic peroxides.*

Allenols represent a specific subclass of allenes characterized by their high synthetic versatility.[1] These compounds feature a nucleophilic center, typically a hydroxyl group, within their molecular framework.[2] Recently, our research group has described the regio- and diasteroselective Barbier-type allenylation reaction of glyoxals mediated by indium to furnish highly valuable *syn*-bis(α-hydroxyallenes) and *syn*-α,α'-dihydroxyallenynes (Figure 1).[3]

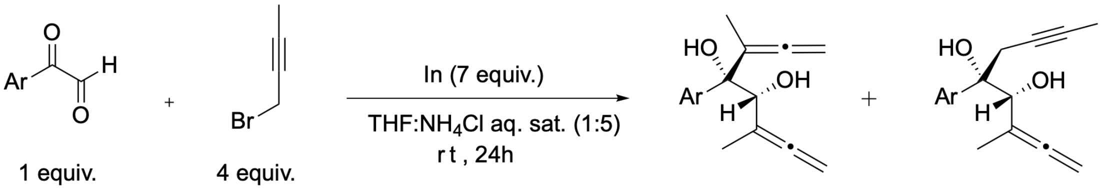

Figure 1. Barbier-type allenylation reaction of glyoxals mediated by indium.

These *syn*-bis(α-hydroxyallenes) are idoneous starting materials for the study of cyclization and functionalization reactions with a wide range of reagents and transition metals, enabling the formation of rings of various sizes with a good regio- and stereoselectivity.[4]

Continuing our interest in allenol functionalization chemistry, this work presents the study of the $Zn(OTf)_2$-promoted cyclization reaction of *syn*-bis(α-hydroxyallenes) with a dual objective: to control the cyclization pathway and to access structurally interesting compounds with potential biological relevance.

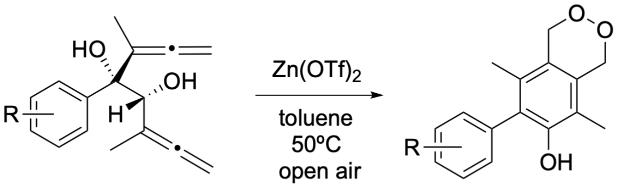

Figure 2. $Zn(OTf)_2$-promoted cyclization reaction of *syn*-bis(α-hydroxyallenes).

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Synthesis of Hemilabile P-Stereogenic Ligands and Their Application in Gold-Catalyzed Asymmetric C–C Bond Formation

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Phosphines are among the most versatile donor ligands in homogeneous catalysis, owing to their tunable electronic and steric properties and excellent compatibility with a wide variety of transition-metal centres[1]. In particular, P-stereogenic phosphines—in which the phosphorus atom itself constitutes the stereocentre—afford rigid, well-defined chiral environments that translate into high enantioselectivities in C–C and C–X bond-forming processes[2,4].

On the other hand, hemilabile ligands, which incorporate a permanently bound donor (e.g. P) alongside a more labile site (e.g. N, O), enable dynamic modulation of the metal's coordination sphere[3]. The reversible binding of the labile arm can stabilize key intermediates or vacate coordination sites on demand, thereby accelerating elementary steps such as oxidative addition, reductive elimination or migratory insertion under mild conditions[5].

In this project, we propose the design, synthesis and application of a new family of chiral hemilabile P-stereogenic ligands for Au(I)-mediated catalysis. By appending an N-based hemilabile donor adjacent to the stereogenic phosphorus centre (Figure 1c), we aim to fine-tune the first coordination sphere of Au(I) and exploit cooperative P–N binding events to drive asymmetric C–C bond-forming and –cleaving transformations with enhanced activity and enantioselectivity. Stoichiometric studies of elementary steps (nucleophilic addition, oxidative addition, reductive elimination) and catalytic assays in hydroarylation, aminoarylation and oxyarylation will establish structure–reactivity–selectivity relationships and reveal new mechanistic paradigms in Au(I) chemistry[3,4,5].

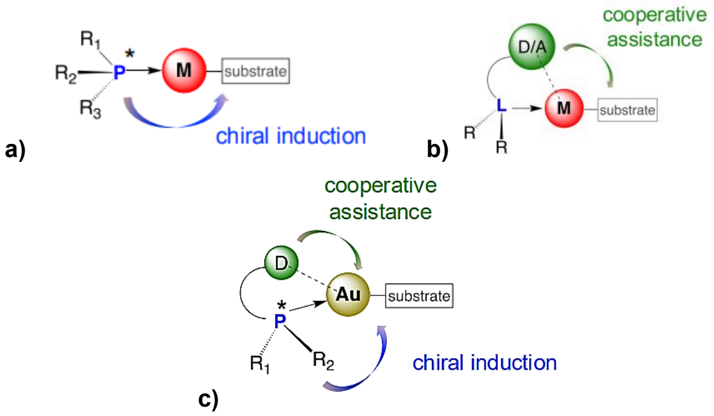

Figure 1. State of the art (a), b)) and objective of the project (c)).

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Cationic *N*-Doped Nanographene

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***Keywords**: Nanographenes, Organic Electrochemistry, Luminescence.*

Molecular nanographenes are well-defined polycyclic aromatic hydrocarbons, typically 1–5 nm in size, that bridge the gap between small fused arenes and larger graphene sheets. Their π-conjugated structures offer tunable optical and electronic properties, making them promising materials for applications in electronics, photonics, and sensing.[1]

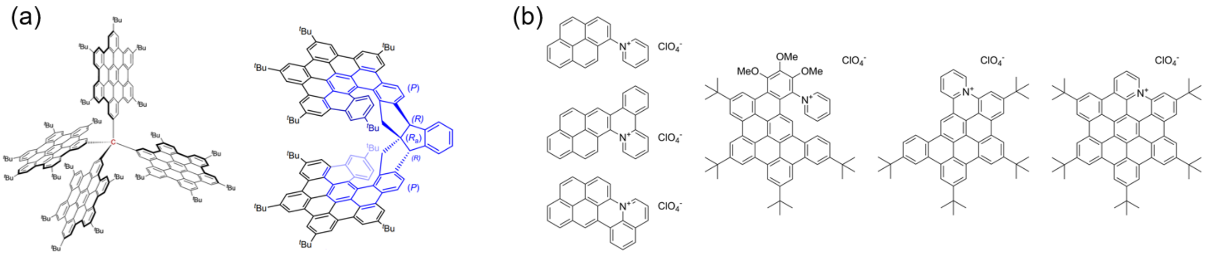

Figure 1. (a) Examples of diverse molecular nanographenes obtained in a bottom-up approach.[2] (b) Cationic nitrogen-containing compounds synthesized in this work, including the first cationic nitrogen-containing HBC.

In recent years, a diverse group of molecular nanographenes has been synthesized, achieving remarkable control over their three-dimensional, often chiral structures.[2,3]

However, due to the challenges involved in their preparation, the synthesis and study of heteroatom- or metal-doped nanographenes remain less explored, despite their potential to significantly enhance optical and electronic properties.

In this work, diverse poly-heteroaromatic compounds featuring a quaternary nitrogen atom embedded in their π-extended structure have been prepared. The synthesis of poly-heteroaromatic structures —ranging from simple pyridinium salts to *N*-doped cationic hexabenzocoronene (HBC)— using electrochemical and photochemical methods will be presented.

The properties of all these compounds were investigated by electrochemical and photophysical characterization.

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Development and optimization of Iridium mediated Petasis reaction with boronic esters as the radical source

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***Keywords**: Photochemistry, Petasis reaction.*

A multi-component chemical reaction refers to a process where three or more compounds are added simultaneously to yield a combined product that contains the majority of the atoms of the starting materials improving reaction time and atom economy. Among them, the Petasis reaction [1] (where boronic acids with adjacent heteroatoms are combined with amines and aldehydes) is particularly efficient in the generation of substituted amines and aminoacids derivatives.

Developed in 2019, the Iridium photocatalyzed Petasis reaction [2] was described as an alternative approach to access these compounds via a redox neutral single electron transfer mechanism with alkyl trifluoroborates as the radical source. This process combines the great impact of photochemistry in direct functionalization of molecules using mild reaction conditions with the reduction in synthetic steps offered by multi-component reactions. This transformation is specially promising in the context of the pharmaceutical industry given the high variability of transformations it could enable access to.

In this work the photocatalyzed Petasis reaction is studied with boronic esters as the radical source. The use of boronic esters could offer a pool of cheaper and more diverse set of molecules with motifs widely present in active pharmaceutical ingredients and intermediates. Given the model reaction shown in Figure 1, exhaustive reaction optimization is performed using batch and high throughput experimentation photochemsitry platforms such as Pennoc or Lumidox photoreactors. Additives, solvents, and photo-physical parameters are optimized to achieve good-moderate conversions, minimize impurities, and ensure compatibility with future transfer to a flow chemistry platform.

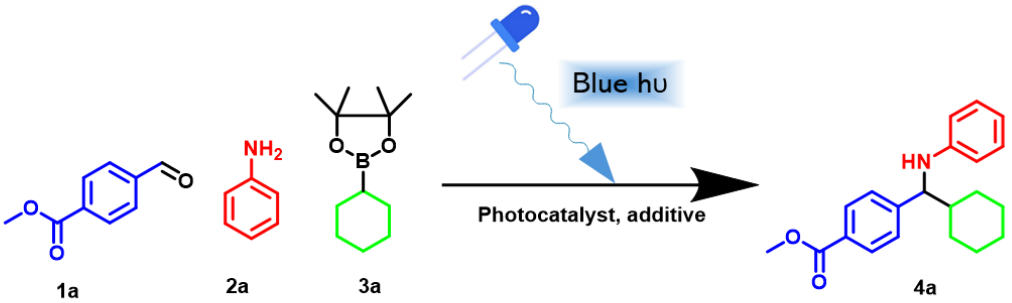

Figure 1. Model photocatalyzed Petasis reaction with boronic esters

The optimized reaction conditions are tested with various boronic esters to exemplify with a wide scope. Finally, the transformation was optimized in Vapourtec flow platform to check the reproducibility of the reaction and its scalability.

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Development of new fluorescent biomarkers based on BOPHY chromophore modification

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***Keywords**: Fluorescent dyes, Nicholas reaction, "Click" chemistry.*

Fluorescent dyes based on boron complexes, such as BODIPYs and BOPHYs, have attracted considerable interest in fields like bioimaging and optoelectronics due to their excellent photostability, high quantum yields, and finely tunable photophysical properties.[1] Among them, BOPHYs stand out for their strong solid-state fluorescence and bathochromic shifts compared to their BODIPY counterparts.[2] In this work, we report the synthesis of alkyne-functionalized BODIPY and BOPHY derivatives via the Nicholas reaction, which allows for regioselective incorporation of propargylic substituents.[3] These alkyne groups were subsequently used in copper(I)-catalyzed azide–alkyne cycloaddition (CuAAC) "click" reactions to attach a benzyl-type spacer [Figure 1].[4] This spacer is designed to serve as a versatile platform for conjugation with various functional molecules, such as carbohydrates, and is expected to facilitate the formation of J-aggregates, enhancing their potential utility in high-resolution biomedical imaging.[5]

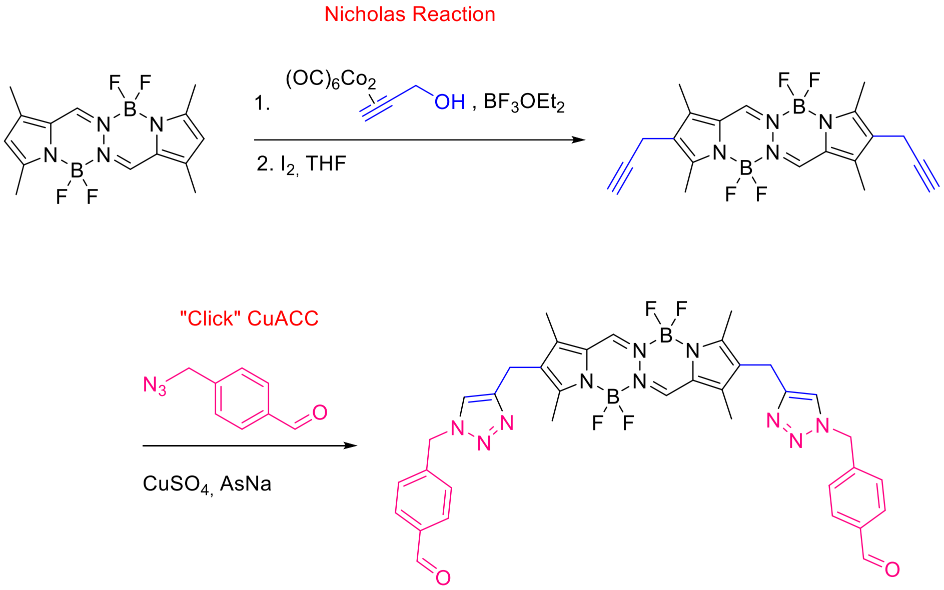

Figure 1. Synthesis of Alkyne-Functionalized BOPHY via the Nicholas Reaction and Subsequent CuAAC Conjugation

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Synthesis of polar lipids with increased stability properties: evaluation of their incorporation into lipid nanoparticles for drug delivery

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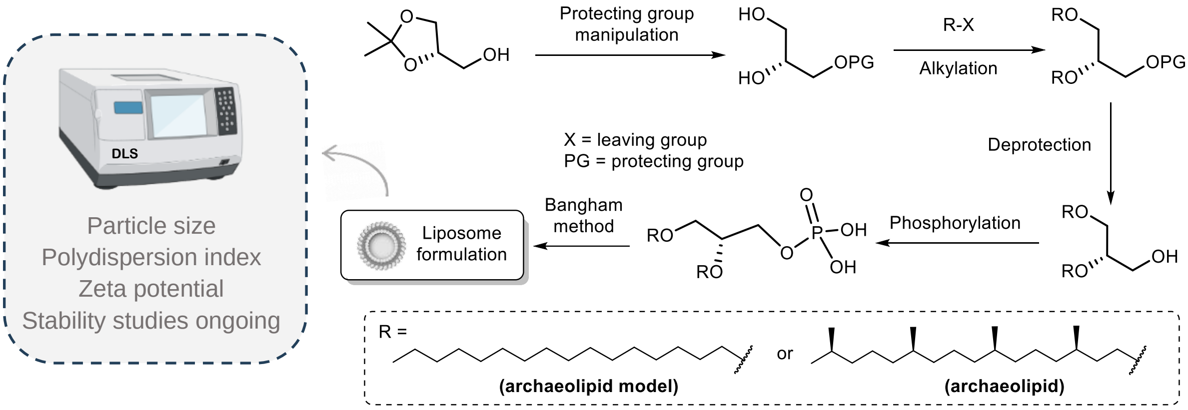
Keywords: *Archaeosomes ● Synthetic lipid analigues ● Drug delivery systems ●*

The development of stable and effective drug delivery systems is essential to enhance the therapeutic efficacy and bioavailability of pharmaceutical compounds. Liposomes have been widely studied due to their biocompatibility and ability to encapsulate both hydrophilic and lipophilic drugs. However, conventional liposomes present important limitations, including low physical and chemical stability, enzymatic degradation, and uncontrolled drug release, which restrict their use in demanding biological environments such as the gastrointestinal tract or transdermal applications.[1]

Archaeosomes, liposomes composed of archaeal lipids (characterized by ether bonds and branched isoprenoid chains), represent a promising alternative due to their exceptional resistance to extreme pH, oxidation, and high temperatures. Nevertheless, the extraction and purification of natural archaeal lipids remains complex, costly, and poorly scalable process.

To overcome these limitations, this work focuses on the design and synthesis of simplified lipid analogues that mimic the essential properties of archaeal membranes.[2]



Scheme 1. Synthetic route of the model archaeosome and physicochemical characterization[3-4]

One synthetic analogue has been successfully obtained and used to form vesicles, which are currently being evaluated under different temperature conditions to assess their stability and potential as drug delivery systems. In parallel, two additional analogues are being synthesized to improve performance and better understand the influence of structural variations. This model system offers an accessible platform to investigate archaeosome-like behavior and supports the development of more robust drug delivery strategies.[5]

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Synthesis of Adrenergic Drugs

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Keywords: *β2-Adrenergic receptor antagonists, Aminophosphonation, β-Naphthols.*

β^2-Adrenergic receptors play a central role in physiological processes such as bronchodilation, vascular regulation, and inflammatory response. Their involvement in various pathologies, including respiratory, cardiovascular diseases, and certain types of cancer, has driven the search for selective antagonists that modulate their activity with high specificity.[1] In this context, compounds like ICI-118,551,[2] which exhibit high selectivity for β^2 receptors, have proven valuable as pharmacological tools and as starting points for the development of new therapeutic candidates.[3] This work focuses on the design and synthesis of structural analogs of ICI-118,551 via the aminophosphonation of β-naphthols (Figure 1), a strategy that enables the simultaneous introduction of amino and phosphonate groups onto the aromatic core. These functional groups are key to replicating the configuration and interaction properties of ICI-118,551 with the β^2 receptor, making the resulting products relevant candidates for the development of new selective modulators. Using 1-nitroso-2-naphthol as a model substrate, the aminophosphonation reaction was optimized. This methodology, based on sustainable and metal-free conditions, provides regioselective access to functionalized naphtholic derivatives that will serve as key intermediates in the synthesis of new bioactive oxiranes with selective affinity toward β^2-adrenergic receptors.

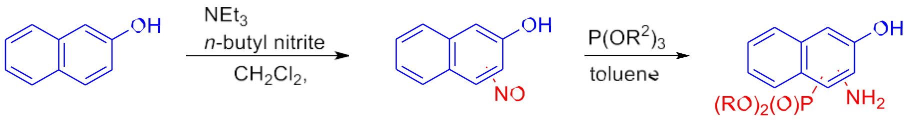

Figure 1. Synthesis of aminophosphonylated naphthols as precursors of (2R,3R)-2-methyl-3-(naphthyloxymethyl)oxirane derivatives (analogs of ICI-118,551).

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Evaluation of different methodologies for the Minisci-type Methylation of N-heterocycles

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***Keywords**: Minisci, Methylation, Photocatalysis.*

Methodologies targeting the methylation of organic structures have great interest in the modification of biologically active compounds in the pharmaceutical industry. The introduction of a methyl group in a molecule can lead to significant changes in their physical and/or chemical properties, modulating their solubility, lipophilicity and reactivity.[1] In the case of N-heteroarenes, a structural motif highly present in biologically active compounds, the most common methylation strategy is the addition of a C-centred radical through a Minisci-type reaction.[2] Even though the reaction with different alkyl radicals for this goal has successfully been explored, the generation and introduction of a methyl radical remains challenging due its low stability.[3] Dialkyl peroxides have proved to be useful reagents in the generation of small alkyl radicals, although their use has traditionally been accompanied with high temperatures. Recently, different methodologies have been developed that explore their activation under photochemical conditions.[4]

In this work, we have explored the use of di-*tert*-butyl peroxide (DTBP) as methyl source for the methylation of N-heteroarenes in a photocatalyzed Minisci-type reaction. DTBP is activated through energy transfer catalysis and plays various roles in the reaction, generating only *tert*-butanol and acetone as by-products. In our studies, we observed the introduction of a methyl group from methanol when it is used as solvent. We have explored the mechanistic insights of both radical sources, to evaluate their use in more complex biologically active compounds.

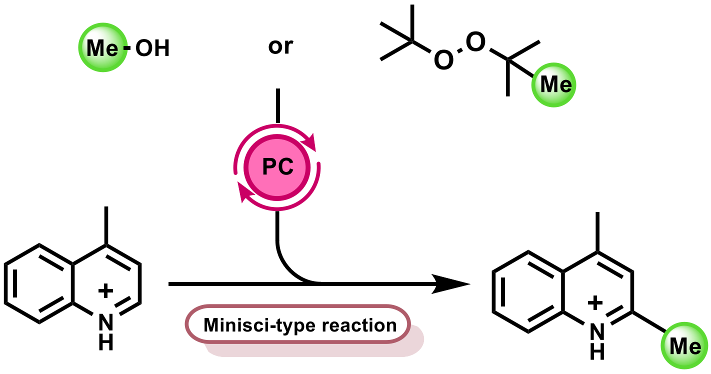

Figure 1. Two different methodologies for the Minisci reaction depending on the source of methyl radicals

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Development of Catalytic Processes guided by Artificial Intelligence

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Keywords: *Site-Selectivity, Artificial Intelligence, Suzuki-Miyaura.*

Pd and Ni-catalysed cross-coupling reactions have transformed organic synthesis, with the Suzuki-Miyaura reaction being the second most widely used in medicinal chemistry.[1] A major challenge in these types of reactions is achieving site-selectivity-promoting reactivity at a specific site when multiple sites are available. The use of artificial intelligence (AI) and machine learning (ML) offers a powerful solution by developing predictive models that could not only predict, but also optimize, site-selectivity.[2] Focusing on the oxidative addition stage — often considered the rate- and selectivity- determining step — as a foundation, we combine computational data (DFT and semiempirical calculations, XTB-GFN2) alongside experimental validation to obtain molecular descriptors and develop a model suitable for different ligand environments (Figure 1a). Expanding beyond previous research focused on single ligands, we aim to study well-known oxidative addition reactions involving numerous reagents and phosphine ligands to improve predictive accuracy and incorporate site selectivity optimization in cross-coupling reactions.

To demonstrate its applicability, we have tackled the synthesis of the anti-inflammatory drug Etoricoxib (Figure 1b). Previously reported synthetic routes involve multiple derivatization steps and selective oxidation using different halide or pseudo-halide groups.[3] We propose a cost-effective, simplified alternative route that reduces the number of steps by selectively activating either one of two halides (bromine or chlorine) in a commercially available substrate. Ideally, our AI- predictive model will address the challenge of discriminating between both reactive sites.

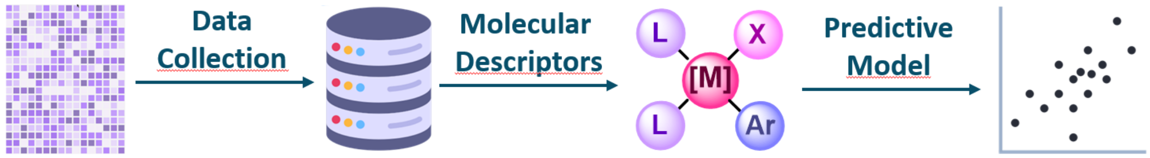

Figure 1a. Workflow for data collection, descriptor generation, and predictive modeling based on Pd/Ni structure.

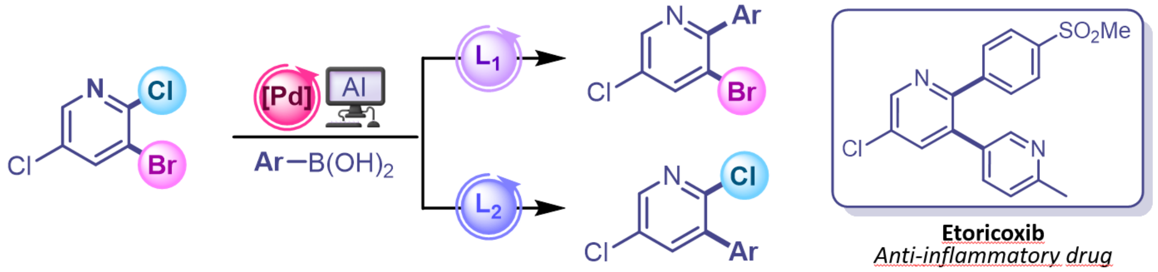

Figure 1b. *Etoricoxib* synthesis optimized through AI-predicted site selectivity.

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