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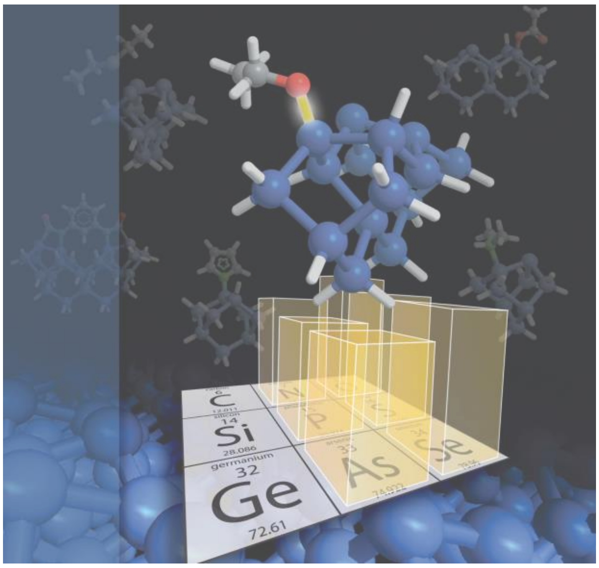
MASTERQO
MÁSTER UNIVERSITARIO EN QUÍMICA ORGÁNICA

XVIII Simposio

Máster Interuniversitario en Química Orgánica

En memoria del Profesor Ramón J. Estévez Cabanas, Catedrático de Química Orgánica en la Universidad de Santiago de Compostela (USC). Como impulsor clave y coordinador del Máster Universitario de Química Orgánica desde su fundación en 2008 hasta el año 2022.

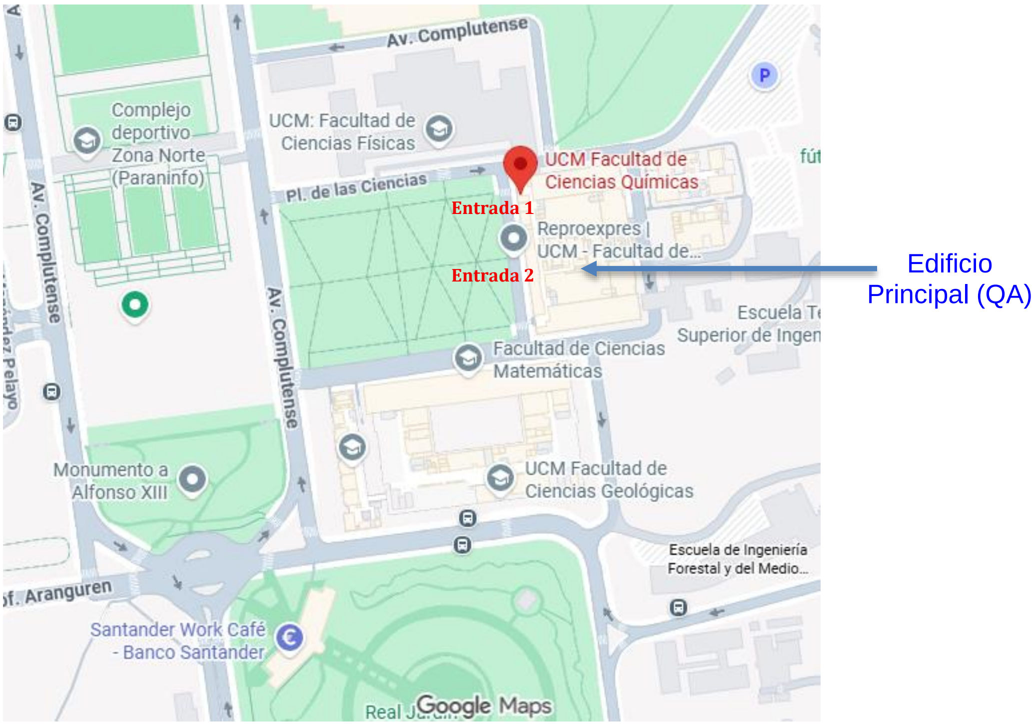


Universidad Complutense de Madrid
27-29 de Mayo de 2026

INFORMACIÓN GENERAL

XVIII Simposio del Máster Interuniversitario en Química Orgánica

El Simposio tendrá lugar en el Salón de Actos para la ceremonia de apertura y en el Aula Ana Mª LaJusticia de la Facultad de Ciencias Químicas (Edificio A).



Atravesando la Plaza de Ciencias se llega al Edificio Principal (QA) que dispone de dos entradas: una de ellas cercana a la Facultad de Físicas y la otra cercana a la Facultad de Matemáticas.

Facultad de Ciencias Químicas

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Desde la estación de metro de Ciudad Universitaria, caminar siguiendo la Avenida de la Complutense, girar ligeramente a la derecha a la altura del Jardín Botánico y atravesar la Plaza de Ciencias hasta llegar al Edificio Principal de la Facultad.

Autobús
Línea 82 (Desde Moncloa)
Línea 132 (Desde Moncloa)
Línea G (Desde Moncloa)
Línea F (Desde Cuatro Caminos)
Línea U
Los autobuses tienen parada en la Plaza de Ciencias (Parada Paraninfo-Matemáticas), salvo el 132 que tiene parada en el Jardín Botánico.

Las sesiones de pósteres se realizarán en 3 zonas diferentes de la Facultad de Ciencias Químicas.

1.- **Aulario I y Aulario II**. Entrada del Aulario

2.- **Aulario exterior I y Aulario exterior II**. Exterior de la entrada del Aulario

3.- **Aula Ana Mª LaJusticia** de la Facultad de Ciencias Químicas (Edificio A).

PROGRAMA
XVIII Simposio del Máster Interuniversitario en Química Orgánica

Universidad Complutense de Madrid
Facultad de Ciencias Químicas y Edificio Multiusos de la UCM

27 de mayo de 2026

15:00 Apertura (Salón de Actos)

15:30 Sesión de Pósteres I (P1-P28) (Aula Ana Ma LaJusticia y Hall aulario)

28 de mayo de 2026

9:30 Sesión de Pósteres II (P29-P56) (Aula Ana Ma LaJusticia y Hall aulario)

11:30 Descanso

12:00 Sesión de Pósteres III (P57-P77) (Aula Ana Ma LaJusticia y Hall aulario)

14:00 Almuerzo

16:00 Actividades de Team building

16:00-17:15 – Escape Room (Grupos 1A y 1B, aula Ana Mª LaJusticia)
– Synthetic Challenge: Build the Molecule
Grupo 2A, aula QC-22; Grupo 2B, aula QC-25

17:30-18:45 – Escape Room (Grupos 2A y 2B, aula Ana Mª LaJusticia)
– Synthetic Challenge: Build the Molecule
Grupo 1A, aula QC-22; Grupo 1B, aula QC-25

29 de mayo de 2026

9:30 Conferencia (Aula Miguel de Guzmán, Fac. de CC. Matemáticas)

“Un viaje químico de la física de partículas a la quimioterapia del cáncer: nuevos heterociclos capaces de unirse a metales”
Prof. Fernando Cossío, Facultad de Química (UPV/EUH)

11:30 Encuestas (Aula Miguel de Guzmán, Fac. de CC. Matemáticas)

12:00 Descanso

12:30 Conferencia (Aula Miguel de Guzmán, Fac. de CC. Matemáticas)

“Divulgar, ¿por qué y para qué?”
Manuel Seara Valero, Dir. Programa “A hombros de gigantes” (RTVE)

13:45 Entrega de premios y Clausura

ORGANIZACIÓN

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

Departamento de Química Orgánica, Facultad de Ciencias Químicas,
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Gómez Utrilla, Pablo	UCM	**P39**
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González Martínez, Beatriz	UCM	**P42**
González-Calero Hernández, Raquel	UAM	**P25**
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Jiménez Álvarez, Claudia	UCM	**P54**
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Morales Herradón, David	UAM	**P52**
Morales Vazquez, Luis	USC	**P47**
Ortiz Rovira, Sandra	UCM	**P63**
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Pan Pabon, Ricardo Antonio	USC	**P50**
Paz Montoya, Miriam	UCM	**P66**
Pedruelo Dopico, Antía	USC	**P53**
Pinilla Molero, Jorge	UCM	**P68**
Pinto Martínez, Noa	UCM	**P70**
Pomares Alemañ, Antonio	USC	**P56**
Reinlein García, Lucas	USC	**P59**
Rodríguez Ospina, Carlos Andrés	UAM	**P58**
Roldán Esgueva, David	UAM	**P61**
Rovira Díaz, Yaiza	UCM	**P72**
Rubia Gutiérrez-Cañas, Paula De La	UAM	**P64**
Rubio Ramírez, Alejandro	UCM	**P74**
Sánchez De Lope, Daniel	UAM	**P67**
Sánchez-Mateos Calcerrada, Lucía	UAM	**P69**
Serrano Pacheco, Daniel	UCM	**P75**
Siguero Hernanz, Marina	UAM	**P71**
Tenorio García, Aitana	UCM	**P57**
Teruel Blein, Patricia	UAM	**P73**
Vázquez Carballo, Marina	USC	**P62**
Villariño Cal, Bruno	USC	**P65**

ABSTRACTS

Synthesis of luminescent cyanostilbene derivatives. Study of their self-assembly behavior and optical properties

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***Keywords**: supramolecular, bipyridine, self-assembly, mechanism*

Supramolecular polymers based on π-conjugated systems constitute a versatile platform for the development of functional materials with tuneable optoelectronic properties. Their formation relies on a delicate balance of non-covalent interactions, where subtle structure variations can significantly influence both self-assembly and optical behavior.[1] Herein, the design, synthesis and study of the self-assembling features of a bipyridine-based π-conjugated system is presented. The incorporation of the bipyridine moiety, in contrast to previously reported aromatic cores within the group, introduces a distinct electronic distribution that may influence intermolecular interactions.[2] The supramolecular polymerization of this bipyridine-based luminophore has been investigated by using a number of spectroscopic techniques (UV-Vis, emission, FTIR and variable temperature and concentration ^{1}H-NMR experiments) in $CHCl_3$ and MCH as good and poor solvents, respectively. Solvent dependent studies reveal a clear transition from monomeric species to the aggregated state, driven by a combination of π-π stacking and intermolecular hydrogen bonding, as supported by the downfield shift of the amide protons in ^{1}H-NMR and characteristic changes in the IR spectra. Unlike previously reported and referable cyanostilbenes,[2] the aggregated species of this bipyridine derivative does not display enhanced emission intensity upon self-assembly most probably due to the planar geometry of the bipyridine moiety.[3] Unfolding experiments display a sigmoidal profile (Figure 1 c), evidencing a cooperative nucleation-elongation mechanism.[4] Overall, these results demonstrate that the bipyridine-based system undergoes cooperative supramolecular polymerization driven by non-covalent interactions, highlighting the influence of the core structure on the aggregation behavior.

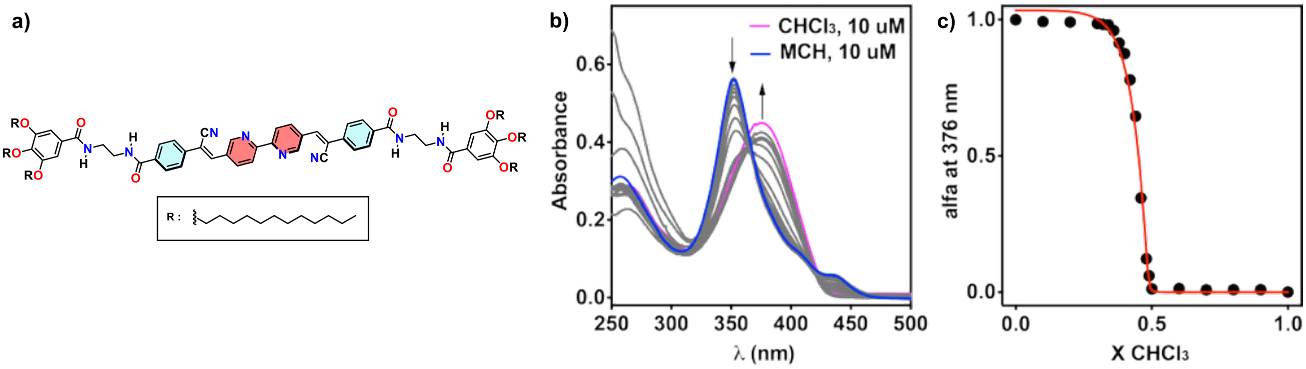

Figure 1. a) Structure of **1**. b) Solvent-dependent UV-Vis absorption spectra (10 μM). c) Plot of the degree of aggregation (α) vs. $CHCl_3$ mole fraction.

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Catalytic asymmetric synthesis of planar-chiral cyclophanes via 1,3-dipolar macrocyclization of azomethine ylides

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***Keywords**: 1,3-Dipolar cycloaddition, planar chirality, macrocyclization*

Planar-chiral cyclophanes are a unique class of chiral molecules where a molecular plane is bridged by a chain (*ansa* bridge) that is sterically restricted from flipping, resulting in configurationally stable chirality. These structures are found in a wide range of compounds with applications in natural products, asymmetric catalysis, drug discovery and supramolecular chemistry.[1] Consequently, the development of efficient new methodologies for their synthesis has attracted considerable attention, with numerous research groups invested in the expansion of the chemical space of these compounds.[2]

In this context, this work describes a novel strategy for the synthesis of planar-chiral cyclophanes through a Cu-catalyzed intramolecular 1,3-dipolar cycloaddition of azomethine ylides.[3] A series of linear precursors bearing α-iminoesters as dipoles and activated alkenes as dipolarophiles were prepared through a multistep synthetic sequence.[4] In this new methodology, the 1,3-dipolar cycloaddition reaction takes place with simultaneous installation of central and planar chirality, affording the desired cyclophanes in good yields and diastereoselectivities, with high levels of enantioselectivity.

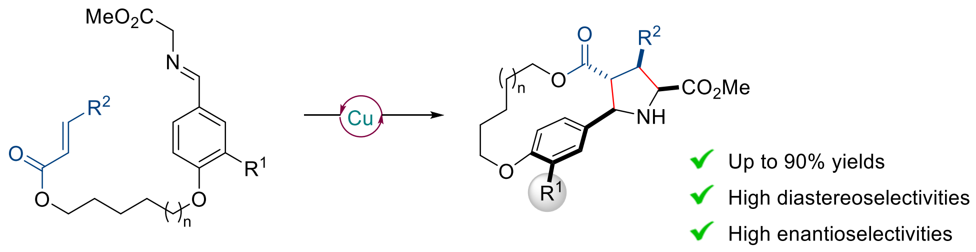

Figure 1. Stereoselective synthesis of planar-chiral cyclophanes via 1,3-dipolar macrocyclization.

References:

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PHOTOCHEMICAL METAL-FREE OXYBORATION OF ALKENES

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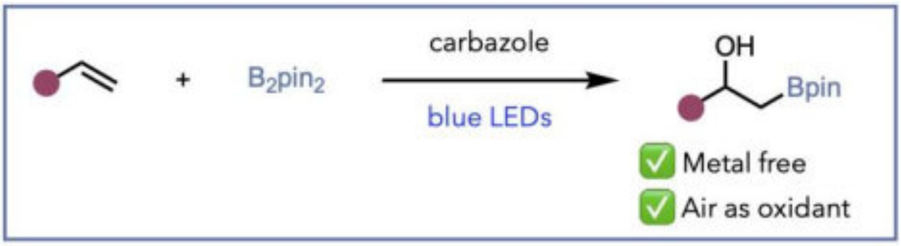
***Keywords**: photochemical, metal-free, oxyboration.*

Organoboron compounds are highly important motifs in organic chemistry. In addition to their well-established versatile reactivity –exemplified by the extensively used Suzuki-Miyaura cross-coupling– advances in boron-containing pharmaceuticals have also emerged as an important area in medicinal chemistry.[1-2]

In particular, β-hydroxyboronate esters have been proven to be valuable precursors of 1,2-aminoalcohols and bioisosteres of β-hydroxycarboxilic acids, prevalent motif in natural products and pharmaceuticals.[3-4]

There has been intensive research on new methods to synthetize organoboron compounds, being difuntionalization of unsaturated bonds a powerful tool due to the wide avaibility of alkenes and alkynes and the concomitant formation of two new bonds. Difuntionalization of alkenes to form of a C-B bond and a C-H, C-C or C-N has been deeply explored, mainly by metal catalyzed approaches.[5-7] By far, oxyboration methods to afford β-hydroxyboronate esters derivatives remain underdeveloped.[8-9]

In this communication, we report a novel photochemical metal-free oxyboration of alkenes. This transformation proceeds under mild conditions using substoichiometric amounts of carbazole, B_2pin_2 and the alkene under air and blue light irradiation. Key to achieve the reaction is the activation of B_2pin_2 by carbazole, which generates a series of reactives intermediates that ultimately engage with de alkene.



Scheme 1. Oxyboration reaction.

References:
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Advanced NMR methods for decoding fluorinated glycans as key organic molecules in biology

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***Keywords**: NMR spectroscopy, Structure assignment, Molecular interactions.*

Glycans constitute one of the most diverse and essential classes of biomolecules in nature. They are involved in critical biological processes ranging from cell signaling and protein folding to immune response modulation. Among these, the oligomannoside $Man_9GlcNAc_2$ (Man_9) is of extraordinary biological relevance, as it is the primary component that covers the gp120 spike of the HIV-1.[1] This shield acts as an evasion mechanism against the host's immune system, yet it also serves as the specific target for broadly neutralizing antibodies like 2G12. Despite its critical role, the complete structure characterization and interaction studies in solution of Man_9 presents a formidable challenge. The use of conventional NMR spectroscopy for its determination is severely hampered by the inherent structural complexity of the glycan. The presence of multiple branched mannose residues leads to severe signal overlap in the 3.5–5.0 ppm region of the convention 1D ^{1}H NMR spectrum, making it extremely difficult to unambiguously assign all proton signals and obtain site-specific interaction information.

To circumvent this limitation in the assignment process, this research follows an established strategy by employing the fluorinated analogue ^{19}F-Man_9. Fluorine-19 (^{19}F) acts as a true bioisostere for the hydroxyl group.[2] A key advantage is the absence of endogenous fluorine nuclei in biological systems. Despite this benefit, the ^{19}F NMR spectrum alone provides limited structural information about the glycan. Therefore, in assignment studies, fluorine signals are used as a strategic starting point for conventional heteronuclear 2D NMR methods and advance 1D NMR methods such as ^{1}H-^{19}F FESTA NMR.[3]

The core of this work involves a comprehensive suite of conventional and advanced NMR experiments for the structural characterization and interaction studies of fluorinated glycans, with particular focus on ^{19}F-Man_9. Beyond standard 2D ^{1}H-^{13}C HSQC, ^{1}H-^{1}H COSY and ^{1}H-^{13}C HMBC experiments, we use the novel 1D ^{1}H-^{19}F FESTA NMR experiment, which provides simplified ^{1}H NMR subspectra containing only the signals within the fluorinated ring of interest. We also apply advanced 1D ^{1}H pure shift experiments,[4,5] which collapse multiplets into singlets. Finally, the interaction between ^{19}F-Man_9 and the 2G12 antibody is investigated using STD NMR experiments together with NMR relaxation measurements.

References:
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***N*-thioimides and analogues as a novel and unexplored class of antiviral agents**

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***Keywords**: thioimides, antiviral agentes, mpox*

The global health emergency caused by the SARS-CoV-2 pandemic emphasized the urgent need for broad-spectrum antiviral small molecules as a complement to traditional vaccination. In this context, previous research by our group identified a novel family of thioaryl imides through high-throughput screening (HTS) using pseudotyped vesicular stomatitis viruses. These compounds demonstrated significant entry inhibition of SARS-CoV-2 by targeting the Spike (S) glycoprotein, exhibiting EC_{50} values in the low micromolar range and favorable safety profiles.[1] This discovery established thioaryl imides as a versatile scaffold for antiviral drug development, in addition to being a completely unexplored chemical family in terms of biological activity.

During the structural optimization of these lead compounds, the introduction of a carbonyl group between the sulfur atom and the phenyl ring was explored. This strategic modification led to a structural core that closely resembles tecovirimat, the only FDA-approved antiviral for the treatment of orthopoxvirus infections, including smallpox and mpox (TPOXX).[2,3] Tecovirimat exerts its antiviral activity by targeting the highly conserved Viral P37 protein (encoded by the F13L gene in vaccinia), thereby inhibiting the formation and release of extracellular enveloped virions. Given the recent global outbreaks of mpox and the potential emergence of resistant strains due to the high mutability of the virus, expanding the availability of orthopoxvirus inhibitors is of critical importance.[4]

Building upon the initial synthesis of this new series, the present work focuses on completing the development of a comprehensive library of thioaryl imide analogs. This project involves the systematic modification of the imide scaffold and the introduction of diverse electron-donating and electron-withdrawing substituents on the phenyl ring. These targeted variations are designed to establish a preliminary structure-activity relationship to enhance both pharmacological properties and antiviral potency. The synthesized compounds are purified and fully characterized using standard analytical techniques, including NMR spectroscopy and mass spectrometry. Once the chemical library is complete, the derivatives will undergo stability studies and biological evaluation. Initial screenings will assess in vitro cytotoxicity to ensure a favorable safety profile, followed by efficacy assays primarily against orthopoxvirus models, to evaluate their potential as mpox antiviral agents, but also against a wide panel of pathogens, including bacteria.

By pivoting the focus from the original COVID-19 background toward emerging orthopoxviruses and other targets, this research aims to identify potent small-molecule inhibitors. These novel derivatives could serve as alternatives, back-up compounds, or synergistic treatments in the fight against mpox, ultimately contributing to global pandemic preparedness.

References:

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Enantioselective Iridium-Catalyzed Intramolecular Hydrocarbonation of Alkene-Tethered Prochiral Diketones

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***Keywords**: Iridium; C–H activation; hydrocarbonations.*

Over the past two decades, the transition metal-catalyzed direct addition of inert C-H bonds across unsaturated moieties has emerged as a powerful carbon-carbon bond-forming tool that enables a substantial increase of molecular complexity in an atom-economical manner.[1] The group has previously reported an enantioselective desymmetrizing cyclization that entails carbonyls, providing direct access to architecturally complex polycyclic frameworks bearing a tertiary alcohol and an adjacent all-carbon quaternary stereocenter at their ring junctions. To date, this methodology was limited to the activation of (hetero)aromatic C-H bonds.

We now report the extension of this hydroarylation to alkene hydrocarbonations by using precursors in which the C-H activation occurs in an alkene.

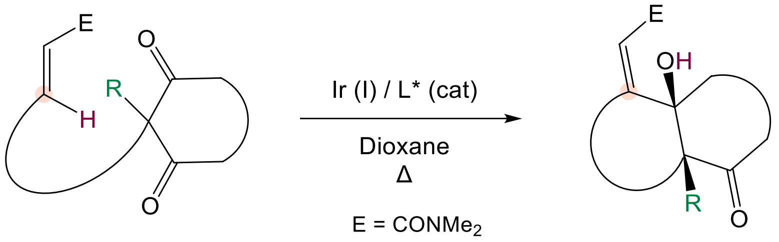

Figure 1. Desymmetrization of prochiral diketones via iridium catalysis obtaining two adjacent tetrasubstitued stereocenters.

The use of an Ir (I) complex generated *in situ* from $[Ir(cod)_2]BAr^F_4$ and chiral phosphines, under optimal reaction conditions, led to high yields and enantiomeric ratios. The scope of the process was also preliminary explored with substrates structurally related to the model, providing equally satisfying results.

Finally, to explore the reactivity of the product, a hydrogenation reaction was carried out. While preserving the previously obtained stereoselectivity, the saturated product was obtained in good yield and very high diastereomeric ratio.

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Functionalization of ketyl radical for the synteshis of aliphatic alcohols

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***Keywords**: umpolung, alcohols, photolysis.*

The umpolung reaction of carbonyls and unsaturated systems is a powerful emerging strategy for the synteshis of aliphatic alcohols. Although the significant adavances in this field, the coupling between apliphatic carbonyl compounds and unsaturated molecules is very challenging. Herein, we present how a novel catalytic activation mode for aliphatic carbonyl compounds enables the development of a platform for reductive couplings. An important part of this process is the formation of a hemiaminal intermediate with a nucleophilic phenothiazine catalyst, which generates the ketyl radical via photolysis due to the absorption of visible light. Our protocol is distinguished by its mild reaction conditions and wide substrate scope.

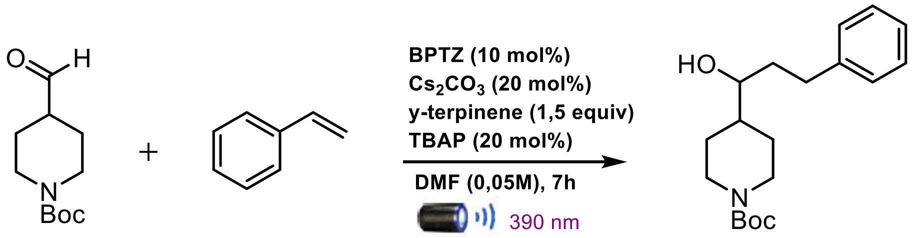

Figure 1. Reaction conditions of our new photocatalytic system for the synthesis of aliphatic alcohols

Nanomotors as Vehicle of smart Drug Delivery Systems

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***Keywords**: Nanomotor, Mesoporous Silica nanoparticles, Drug Delivery systems.*

Ensuring the efficacy and safety of drugs is one of the greatest challenges in modern medicine, advances in nanotechnology in recent decades have enabled the development of controlled-release systems based on nanomaterials. Among these materials, mesoporous silica nanoparticles (MSNs) have gained significant popularity due to their advantageous properties, such as their high surface area, large pore volume, and versatility in terms of functionalization.[1] However, these systems face a major limitation. Their passive transport *via* the blood plasma causes them to have a poor abilityto reach target tissues.[2]

To overcome this problem, we designed and prepared enzyme-controlled release systems equipped with nanomotors, termed "nanoships". These nanoships consist of two main modules: a propulsion module composed of gold and nickel nanomotors, which grant the system magnetic properties and enable self-propulsion using ultrasonic waves,[3] and a Drug Delivery System (DDS) based on Janus mesoporous silica nanoparticles (MCM-41 type). The nanoparticles are functionalized with thiolated PEG groups on one face and contain a dye encapsulated within the silica through pH-sensitive supramolecular gates formed by GOx-modified cyclodextrins (CD-GOx) on the opposite face, this enzyme in presence of glucose generates gluconic acid, which triggers the release of the cargo. The assembly of both modules is completed using the Au-SH bond, as shown in Figure 1.

Finally, we characterized these systems using techniques such as TEM, SEM, FT-IR, dynamic light scattering (DLS), and BET nitrogen gas adsorption/desorption isotherms. To evaluate proper system function, tracking was performed under an inverted optical microscope, along with cargo release assays, selectivity tests, and enzyme kinetics studies.

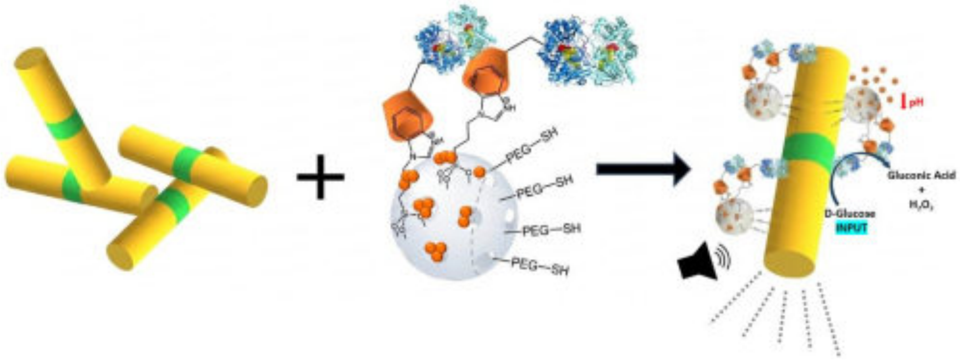

Figure 1. Scheme of nanoships assembly.

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Design and Initiation of the Synthesis of C18-Functionalized Vitamin D Derivatives for Metabolite Determination and Cancer Therapies

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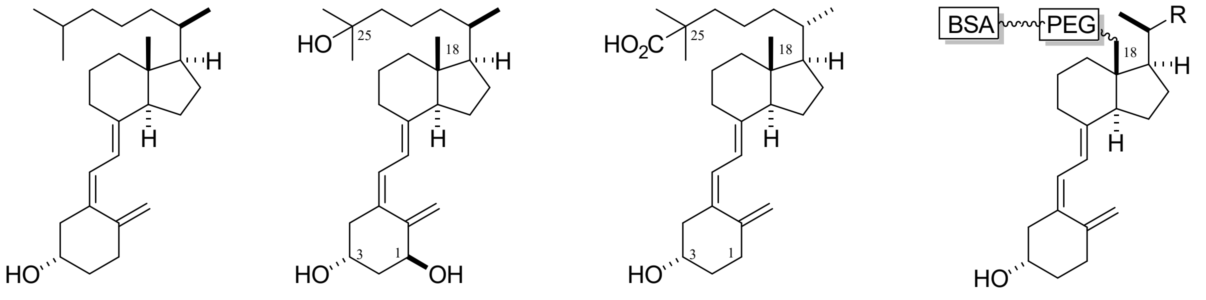
***Keywords**: 1,25D$_3$, haptens, C18-Functionalized derivates.*

1α,25-dihydroxyvitamin D$_3$, [**2**, 1,25D$_3$, calcitriol, Fig. 1], the hormonally active form of vitamin D$_3$, plays a crucial role in mineral homeostasis, promotes cell differentiation and inhibits cell proliferation in various tumor cells, suggesting its potential use in cancer treatment.[1, 2] Regrettably, the therapeutic potential of 1,25D$_3$ as an antitumor agent is severely limited due to its intense calcium-related side effects. Recent interest in the development of highly active, non-calcemic 1,25D$_3$ analogs for the treatment of cancer and dermatological diseases has led to increased activity in the field of vitamin D, with some of these analogs already undergoing clinical trials for the treatment of cancer and psoriasis.[3] In addition to its therapeutic potential, the quantification of vitamin D$_3$ [**1**, Fig. 1] metabolites using immunoassays is essential in clinical practice. These methods employ specific conjugated antibodies generated from antigens synthesized from haptens, the specificity of which depends on the starting hapten and, in particular on the site of functionalization of the molecule. Currently, the conjugated antibodies used exhibit cross-reactivity and a lack of precision, as they do not distinguish between the metabolites of vitamins D$_3$ and D$_2$. To improve selectivity, it is preferable to functionalize positions distant from the key hydroxyl groups (C1, C3, C25), like **3** in Figure 1; so we describe the design and synthetic approach to new vitamin D derivatives functionalized at the strategic C18 position of the corner methyl group [**4**, Fig. 1], thereby reducing cross-reactivity in hapten-based immunodiagnostic methods.



1
Vitamin D$_3$

2
1,25D$_3$

3
25-Carboxi-D$_3$

4
R = side chain of vitamins D$_2$ and D$_3$ metabolites

Figure 1. Structures of vitamin D$_3$ (**1**), 1,25D$_3$ (**2**), an hapten's example used to generate antibodies against the metabolites 1,25D$_3$ (**3**), and C18-Functionalized vitamin D derivate (**4**).

References:

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Synthesis of azulenes through C-H activation methodologies employing Rh(III) complexes.

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***Keywords**: C-H activation, Rh(III), Azulenes.*

Azulene derivatives are of special interest to materials science due to their singular electric properties, significantly differing from that of naphthalenes, their structural isomers, and a large majority of aromatic compounds. They remarkably show dipolar moment and interesting physical properties when inserted into graphene moieties, acting as a topological defect that confers novel optoelectronic characteristics as calculated by Oleg V. Yazyev and Steven G. Louie[1].

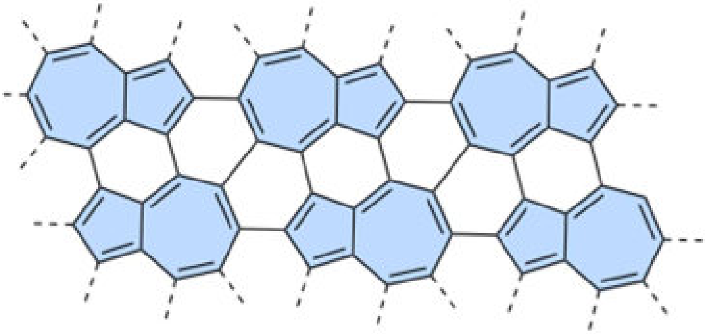

Figure 1. A non-alternant, azulene doped PAH. Non-alterant implying the existence of non six membered rings on the structure.

Their synthesis is complicated by the fact that very few practical strategies have been developed. Most graphene structures incorporating azulenes are the product of on-surface chemistry, such as the ones performed by Professor Diego Peña[3] or suffer from very low yields. Thus, in this work we present a cascade reaction involving Rh(III) catalysed C-H activation, dearomatization and ring expansion of phenol-derivated molecules developed by our group[2] to prepare azulenes, which will then be transformed into the non-alternant graphene nanoribbons in order to further study their optoelectronic properties, which are not sufficiently described in many publications, according to Bartłomiej Pigulski's overview of the field.[4] In particular, fluorescence characteristics and TD-DFT calculations of S_0 -> S_1 transitions go unreported on most publications.

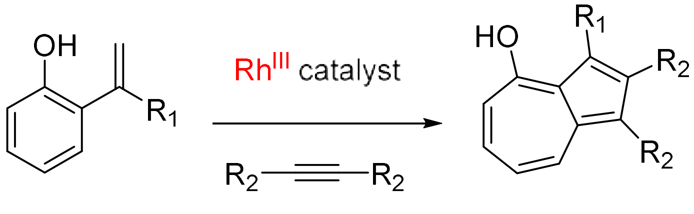

Figure 2. A summarised version of our relevant transformation proposal featuring Rh (III).

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Innovative synthethic methods based on unsaturated systems for accesing novel organic compounds

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Keywords: *bis-allenols, cyclization, Au (III) catalyst.*

Allenes are organic compounds that exhibit great synthetic versatility. Allenols are notable among the allene family due to their notable synthetic utility.[1] Allenols are a group of interest due to their reactivity depending on where the hydroxyl group is located relative to the allene, especially in the α-position.[2] Our research group has discovered a regio- and diasteroselective Barbier-type allenylation reaction of glyoxals using indium, to obtain highly valuable *syn*-bis(α-hydroxyallenes) and *syn*-α,α'-dihydroxyallenynes (Figure 1).[3]

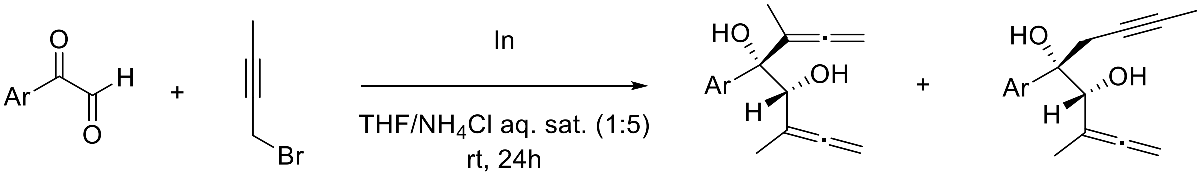

Figure 1. Barbier-type allenylation reaction of glyoxals using indium.

These compounds have proven to be suitable systems for the study of cyclization and functionalization reactions, enabling the formation of rings of different sizes with a good regio- and stereoselectivity.[4] Following our study on the functionalization of *syn*-bis(α-hydroxyallenes),[3] this work presents a novel Au(III)-catalyzed cyclization reaction with the main objectives to guide the cyclization process toward selective formation of the desired product and to assemble the central scaffold of compounds with possible biological properties.

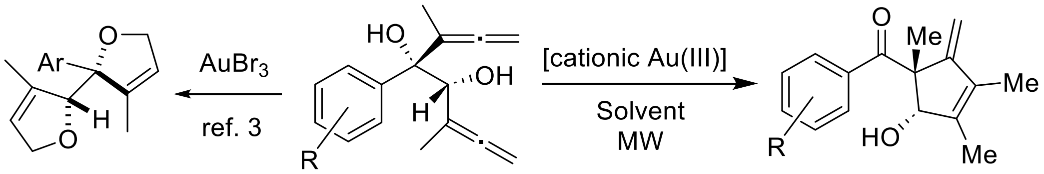

Figure 2. [Au(III)]-catalyzed cyclization reaction of *syn*-bis(α-hydroxyallenes).

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Development of molecular assemblies for the preparation of controlled release-based systems based on mesoporous nanomaterials

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***Keywords**: pH-responsive drug delivery, Mesoporous silica, Janus nanoparticles.*

The field of drug delivery has seen a surge in the utilization of mesoporous silica nanoparticles (MSNs), primarily attributed to their high porosity and structural architecture. Current research highlights their effectiveness in managing various release profiles, including both controlled-release mechanisms and site-specific targeting.[1]

Thus, this work presents the synthesis of anisotropic Janus nanomaterials based on MCM-41 silica, chosen for its large surface area and tunable pores.[2] These particles, prepared via masking, feature an asymmetric design where one face is functionalized with a biocompatible polymer-enzyme complex, while the other serves as a cargo reservoir protected by a stimuli-responsive molecular gate.[1]

Two Janus prototypes were synthesized via Pickering emulsion: in the first one, the enzyme is anchored to a gold nanoparticle via a PEG-SH linker; in the second one, the enzyme binds directly to the carboxyl end of a PEG-COOH chain. To regulate release, a pH-responsive gate of silanized benzimidazole and β-cyclodextrin was anchored to the other face of the silica as a cap. This gate opens upon acidification driven by glucose oxidase, which generates gluconic acid and H_2O_2 in the presence of glucose.[3]

The functionality was verified through release assays using tris(2,2-bipyridyl)ruthenium(II) chloride hexahydrate, a complex that exhibits an intense red color. Finally, therapeutic efficacy was evaluated in HeLa cells using doxorubicin, a colored antibiotic, to evaluate cell viability.

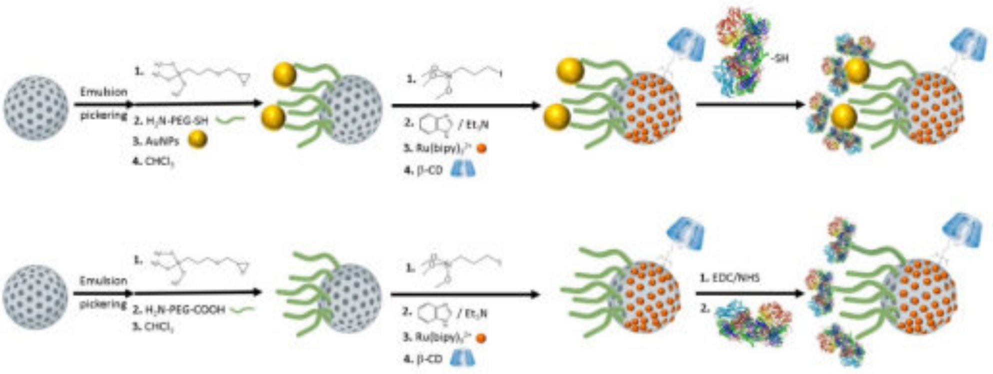

Figure 1 Scheme showing the preparation of PEG-SH and PEG-COOH derived Janus silica nanoparticles

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Synthesis and Functionalization of Covalent Organic Frameworks (COFs): New Materials for Sustainable Applications

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***Keywords**: Covalent organic frameworks, post-synthetic modification, amine.*

Covalent organic frameworks (COFs) are organic porous materials with many potential applications, which very often depend on the presence of chemical functionality within their structure. The organic backbones of these materials can be functionalized after being synthesized, a process known as a post-synthetic modification (PSM) strategy. In this work, we have performed two different modifications in one step: (i) the functional group interconversion of pendant groups and (ii) the chemical conversion on linkages.[1] Specifically, a series of imine-linked multivariate COFs (MTV-COFs) were synthesized by the condensation of 1,3,5-tris(4-aminophenyl)benzene (TAPB) with varying ratios of 2,5-dimethoxyterephtaldehyde (DMTA) and the azide-functionalized monomer 2,5-bis(2-azidoethoxy)terephtaldehyde (BAETA).[2] Subsequently, the post-synthetic modification was carried out via a reductive treatment using PPh_3 and $NaBH_4$. The chemical transformations were monitored through various characterization techniques, most notably by FT-IR spectroscopy, which confirmed the successful reduction of the material. This was clearly evidenced by the complete disappearance of the characteristic azide stretching band at ~2100cm^{-1} (**Figure 1**), alongside the targeted chemical conversion of the framework's imine linkages into amine bonds. These results demonstrate the viability of this post-synthetic approach to effectively tailor both the pore surface functionality and the backbone structure of COFs.

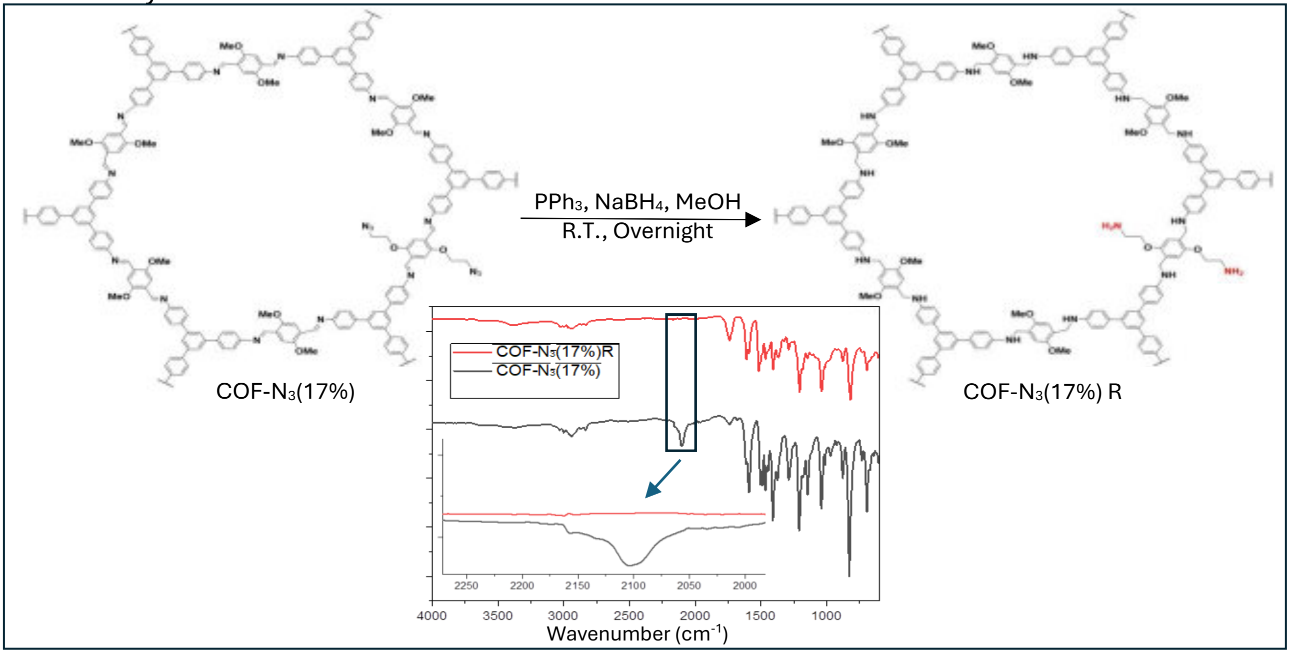

Figure 1. Post-synthetic reduction of the MTV-COF and its monitoring by FT-IR spectroscopy, showing the disappearance of the azide stretching band.

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Synthesis of nanostructurated polymers for photocatalysis and luminescent solar concentrator.

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Keywords: *polymers, fluorescence, photocatalysis.*

While traditional photocatalytic research has historically focused on inorganic semiconductors like metal oxides and chalcogenides, the scientific community is currently witnessing a renaissance of organic-based semiconductors, such as Covalent Organic Frameworks (COFs), and Conjugated Porous Polymers (CPPs).[1] By modulating these organic building blocks through synthetic control, it is possible to design targeted frameworks with optimized electronic structures that enhance light harvesting and facilitate superior charge carrier mobility through extended π-conjugated systems. Nevertheless, these polymers have been synthesized as bulk, a process which has large particle size and a poor processability.[2]

With High-Performance Microfluidic Techniques (HPMT) the "ultra-nanostructuration" of CPPs (UN_CPPs) can be achieved, what can produce polymer nanoparticles with significantly smaller particle sizes and narrower dispersions than those obtained through standard miniemulsion methods.[1] These nanostructured organic semiconductors are coupled with TiO^2 to form synergetic *p−n* hybrid heterojunctions, increasing its hydrogen production.[2]

Nonetheless, as these UN_CPPs materials has also enhanced fluorescence properties, they can be applied for luminescent solar concentrator (LSC) . LSCs consist of a light-guiding polymer coating (epoxy resin for example) loaded with fluorescence entities, which can redirect sun radiation.[3] This new technology is perfect for the use in new architecture based on zero-energy consumption.

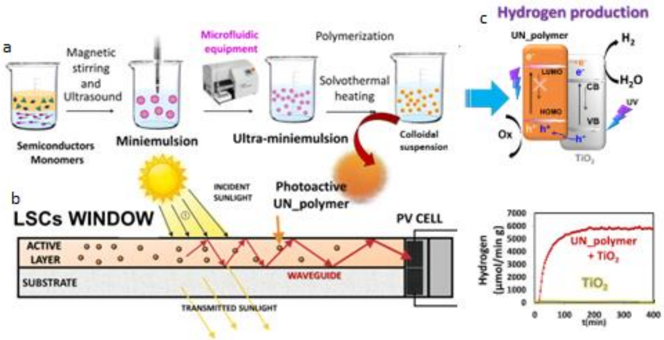

Figure 1. a. Synthesis of UN_CPPs. b. Application of UN_CPPs for LSCs. c. Photocatalytic application of UN_CPPs for hydrogen production.

In this communication, we are going to synthesize new nano-structured polymers based on their luminescence truxenes and BODIPY moieties for their application both in photocatalysis and in LSCs.

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Development of Amphiphilic Supramolecular Nanotubes for Lipid Bilayer Insertion

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***Keywords**: supramolecular nanotubes, self-assembly, artificial transmembrane channel.*

In recent years, there has been an increasing scientific interest in constructing complex nanometric systems from discrete molecules. This has led to the development of complex structures or molecular machines based on molecular self-assembly via specific and directional non-covalent interactions. Taking advantage of this, researchers have succeeded in designing self-assembled tubes capable of inserting themselves into lipid bilayers to function as artificial transmembrane channels.[1] A widely used approach to build these supramolecular tubes involves the stacking of individual cyclic units.[2] The present work aims at establishing a strategy to prepare tubular nanostructures based on complementary monomers featuring an amphiphilic central block, which can self-assemble through hydrogen bonds to produce a non-covalent cycle.[3] In a second step, these cycles could stack through additional non-covalent forces, such as π-π stacking, to yield the desired nanotubes. These architectures have been designed to possess a hydrophilic interior and a hydrophobic exterior, thus favouring their insertion into lipid bilayers and enabling them to act as artificial channels (Figure 1).

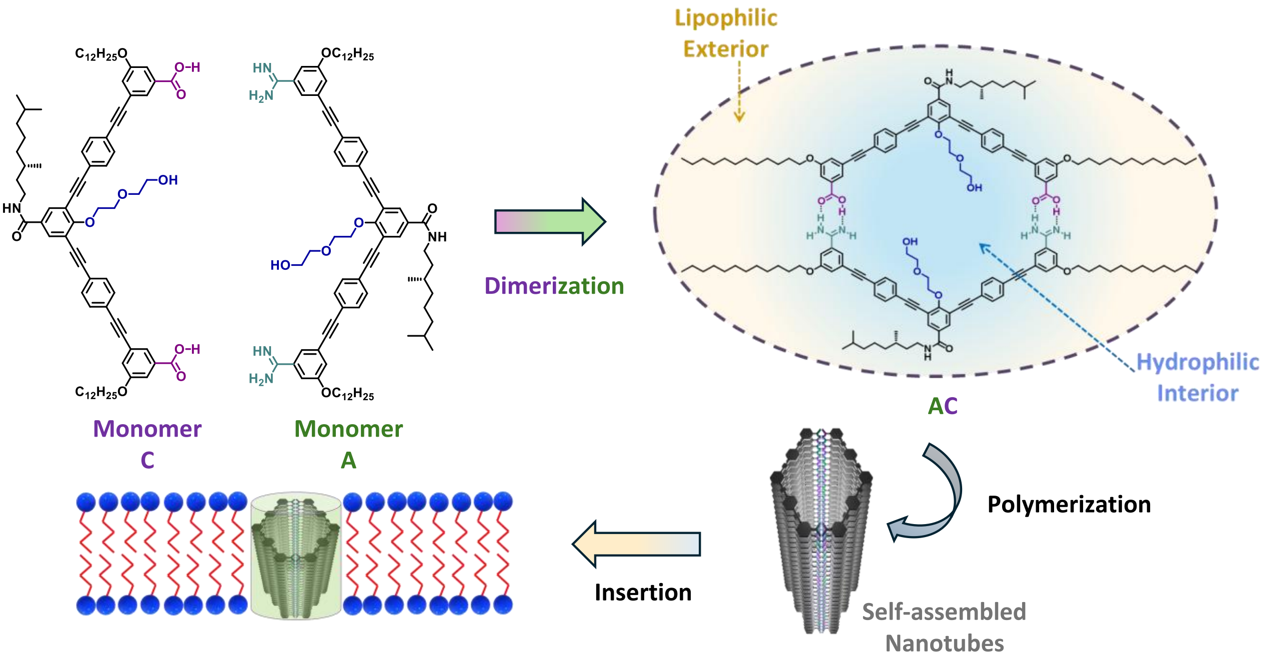

Figure 1: Target monomers and illustration of the dimerization and supramolecular polymerization processes.

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Pyrrolopyridopyrimidine-based allosteric inhibitors for the development of precision antibiotics

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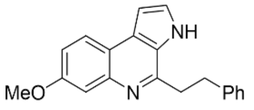
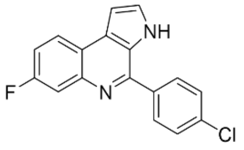
***Keywords**: allosteric inhibition, tuberculosis, precision medicine*

According to the World Health Organization, tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remained the leading global cause of death from a single infectious agent and ranked among the top ten causes of mortality world. The emergence of multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB) strains of *M. tuberculosis* is particularly worrisome, especially among immuno-compromised patients, representing a significant global health security threat. Therefore, the development of new drugs with innovative mechanisms of action that specifically target this challenging pathogen is urgently needed.[1] In this context, our research group has recently explored the therapeutic potential of 3*H*-pyrrolo[2,3-*c*]quinolines for the development of novel anti-tuberculosis (anti-TB) agents.[2] Chemical modification of various structural positions led to the identification of two pyrroloquinoline derivatives exhibiting excellent *in vitro* activity against virulent strains of *M. tuberculosis* (H37Rv, MIC = 4.2 μM and 4.1 μM), operating through a novel mechanism of action. Both derivatives act as inhibitors of glutamate-5-kinase (G5K), an enzyme essential to the pathogen that catalyzes the first step of the proline biosynthetic pathway. *In silico* studies revealed that enzymatic inhibition stems from the allosteric interaction of these compounds at the interface between enzymatic domains, targeting two distinct pockets with different recognition patterns. The present work aims to further optimize the activity of the 3*H*-pyrrolo[2,3-*c*]quinoline scaffold by introducing additional contacts with the side-chain residues of the binding pocket. Specifically, this study seeks to enhance cation-π and hydrogen-bonding interactions with the arginine residues located within the pocket through the incorporation of additional nitrogen atoms into the scaffold. To this end, the synthesis of target pyrrolopyridopyrimidine derivatives was explored.



MIC (H37Rv) = 4.1 μM



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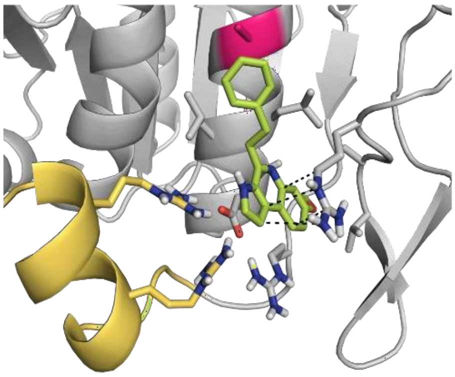

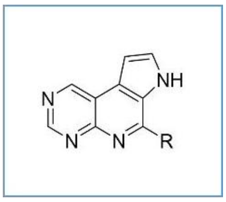

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Synthesis of Nitrogen-Doped Nanographenes via Cyclopentadienones

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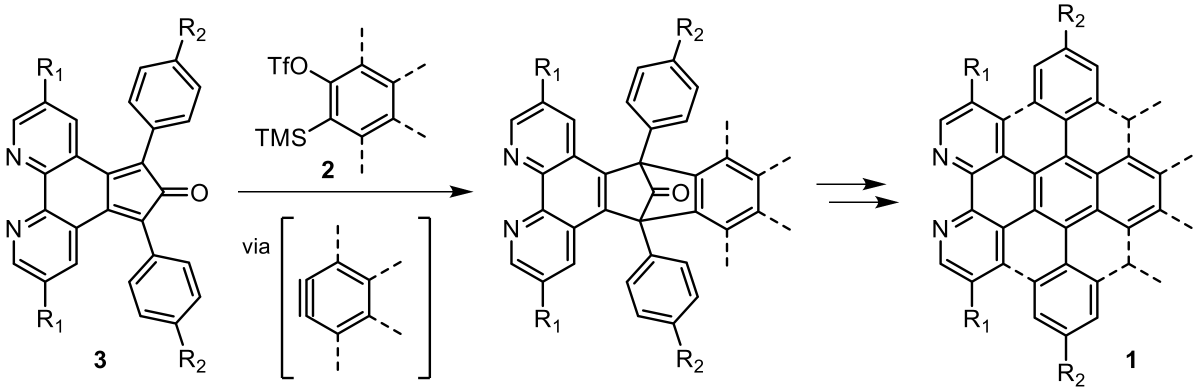
***Keywords**: aryne, nanographene, cyclopentadienone*

The synthesis of polycyclic conjugated hydrocarbons (PCHs) and nanographenes represents a major scientific challenge. These compounds are very appealing due to their unique optoelectronic properties that arise prospects over their potential use as electroactive components in devices such as organic field-effect transistors (OFETs) and organic light-emitting diodes (OLEDs).

The incorporation of nitrogen atoms into carbon-based nanostructures offers a versatile strategy to modulate their physical properties.[1] Nitrogen, as an electron-donating element with a lone pair, can either participate in the π-conjugated system or remain orthogonal to it. In heterocyclic systems derived from pyridine, its higher electronegativity relative to carbon results in electron-deficient polycyclic frameworks compared to purely carbon-based analogues.

This work focuses on the synthesis of nitrogen-containing nanographenes (type **1**) using a synthetic methodology based on the Diels-Alder reaction between arynes and cyclopentadienones. Arynes are generated from Kobayashi-type precursors (**2**) by fluoride treatment under mild reaction conditions. Concretely, the most relevant approaches are focused on the preparation of 1,10-phenanthroline-cyclopentadienone derivates (**3**),[2,3] as a very promising synthetic platform.



R_1 = H, (3,5-di-*tert*-butyl)phenyl
R_2 = H, *tert*-butyl, (3,5-di-*tert*-butyl)phenyl

Figure 1. Synthesis of nitrogen-doped nanographene (**3**).

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Graphene quantum dot networks: Synthesis and physicochemical properties

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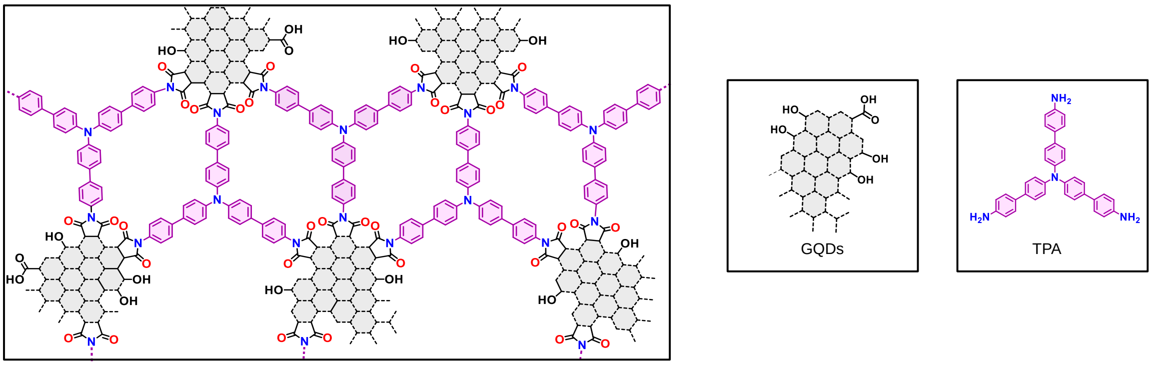
***Keywords**: graphene quantum dots, two-dimensional networks, triphenylamines.*

Graphene has attracted considerable attention due to its exceptional charge-carrier mobility, high specific surface area, and outstanding physicochemical properties. However, its lack of an intrinsic bandgap limits its application in semiconductor technologies.[1] In this context, graphene quantum dots (GQDs) have emerged as an attractive alternative due to quantum confinement and edge effects, which generate discrete energy levels and overcome the limitations of pristine graphene. Furthermore, their optical and electronic properties can be effectively tailored through surface functionalization and heteroatom doping, enabling modulation of their physicochemical behavior. In addition, GQDs present advantageous characteristics such as high aqueous solubility, chemical stability, and low toxicity, making them promising candidates for applications in sensing, bioimaging, photocatalysis, and energy conversion devices.[2]

Recent studies have demonstrated how the photophysical properties of GQDs systems can be tuned by covalent functionalization with organic fluorophores. In particular, Arimura *et al.* reported that the incorporation of different triphenylamine (TPA) derivatives, using GQDs as a platform, leads to dual emission, resulting in intermediate colors.[3] Building on this strategy, the present work explores the design of two-dimensional networks based on functionalized GQDs to investigate how the integration of organic fluorophores influences their optical and physicochemical properties.

Herein, we report the synthesis of GQDs covalently functionalized with TPA derivatives, following a strategy analogous to that described by Arimura *et al.*[3] These systems were employed as model compounds to evaluate the effect of fluorophore incorporation on their photophysical properties. Furthermore, this approach was extended to two-dimensional networks (Figure 1), allowing us to compare the behavior of isolated functionalized GQDs with that of their corresponding networks.



GQDs
TPA

Figure 1. Idealized representation of two-dimensional GQDs networks.

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Rapid construction of novel heterocyclic scaffolds from allenyl carbamates

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***Keywords**: allenes, 1,3-oxazin-2-ones, carbamates*

Allenes are a class of compounds with two cumulated carbon-carbon double bonds, which are versatile synthetic intermediates in organic synthesis. They have shown an interesting reactivity and selectivity affording complex structures in a limited number of steps using a wide variety of transition metals.[1] Moreover, 1,3-oxazin-2-ones are highly interesting heterocyclic compounds due to their presence in a wide range of natural and non-natural products with relevant biological activity, making them valuable scaffolds in medicinal chemistry[2] and organic synthesis.[3] For this reason, in this work, we describe a gold-catalyzed synthetic route for preparing a variety of oxazinones from allenic carbamates. The cyclization reaction proceeds with excellent regioselectivity and good yields. It is important to note that the nature of the cyclization pathway, 6-*exo* or 6-*endo*, is determined by the reaction temperature. On the other hand, the preparation of the heteroatom-decorated 1,3-oxazin-2-one nucleus was carried out at 70 ºC, where *N*-bromosuccinimide (NBS) smoothly promotes a bromoheterocyclization reaction. These processes are compatible with both electron-donating and electron-withdrawing groups in the aromatic rings of the carbamate substituents.

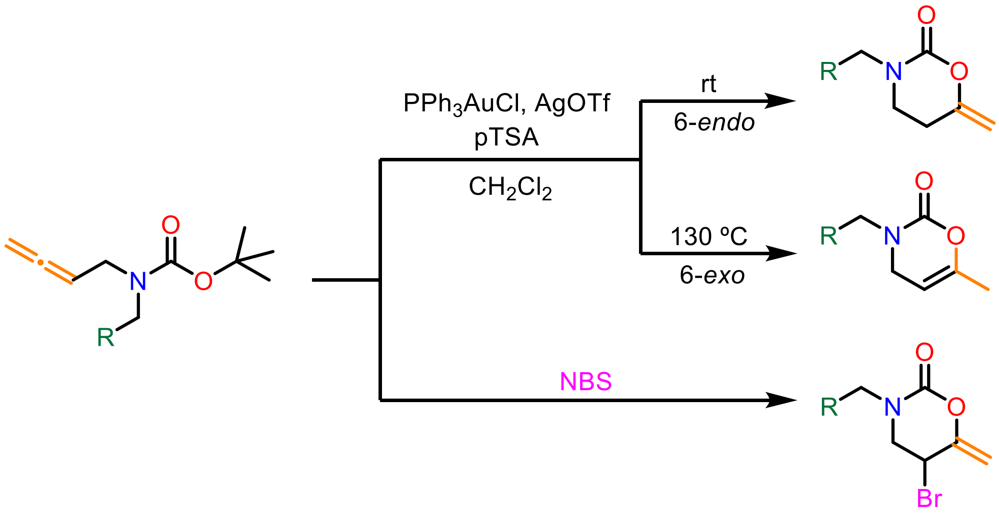

Figure 1. Synthesis of 1,3-oxazin-2-ones from easily accessible allenyl carbamates.

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Three-Dimensional PAH $C_{60}H_{36}$ (TTBA): Redox Properties and Complexation Studies

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Keywords: *Cyclotrimerization, Non-planar PAHs, COTynes, alkali metals (K, Na)*

Non-planar polycyclic aromatic hydrocarbons (PAHs) are attracting significant research attention due to their unique properties arising from their three-dimensional geometry. The cyclooctatetraene moiety (COT) is an ideal scaffold for constructing this type of PAHs. COT-embedded PAHs can act as cavitands or, in their reduced forms, as counterions in the presence of various metal cations.
Among the common synthetic approaches to planar PAHs, metal-catalyzed [2+2+2] cycloadditions of arynes (cyclotrimerizations) stand out. However, this strategy remains largely unexplored for eight-membered ring analogues such as COTynes and benzoCOTyne derivatives.
In this TFM project, the cyclotrimerization of tribenzoCOTyne to benzofused (α, α, α) *tris*(tribenzo[8]annulene) (TTBA), previously described by the research group, has been scaled up and optimized.[1] The reduction of TTBA with alkali metals (K, Na) was investigated to evaluate the electron-uptake capacity of the system, as well as the feasibility of planarizing the COT rings.
Considering the reactivity of the reduced species and the difficulty of crystallizing them, trapping experiments with several electrophiles (B, Si) were performed to rationalize the results.[2,3] These studies will likely help to elucidate the charge distribution and structural changes in the functionalized products.

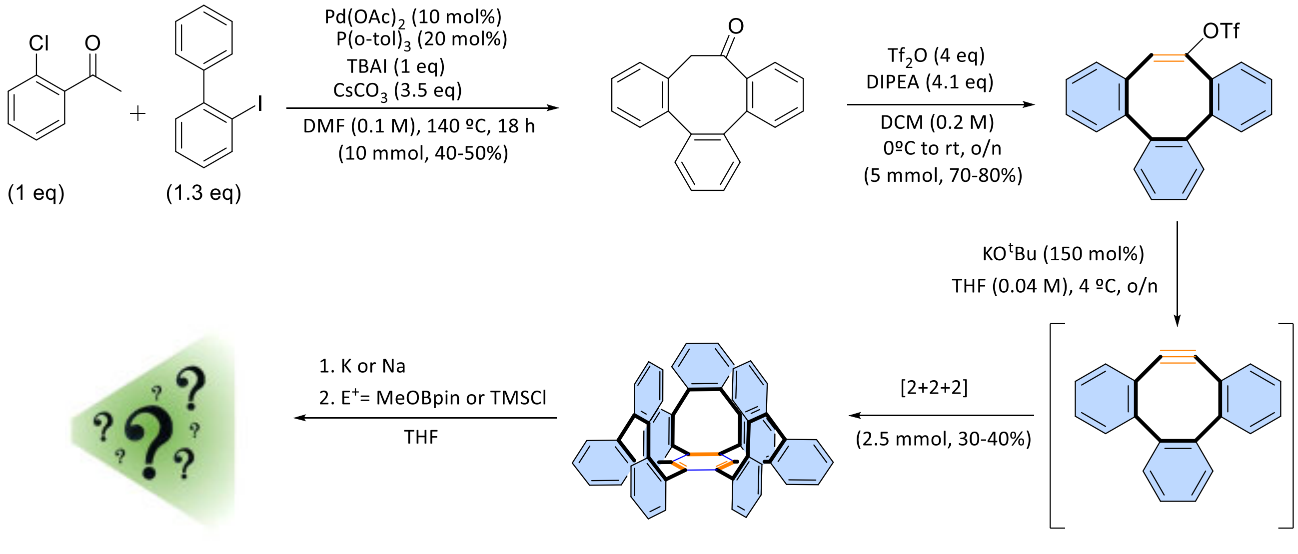

Figure 1. Synthetic route to (α, α, α)-TTBA by K$^+$-mediated cyclotrimerization of tribenzoCOTyne and its alkali metal-mediated (K, Na) functionalization.

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Dendritic Coacervates as a Platform for Interaction Between Synthetic and Natural Cells and the Construction of Synthetic Tissues

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Keywords: *dendrimers, coacervates, synthetic tissues.*

Bottom-up synthetic biology seeks to construct artificial cells with biomimetic or novel functionalities to uncover the fundamental principles of cellular evolution and drive advances in medicine and bioengineering. Among them, membranized coacervate microdroplets (MCM) uniquely combine a molecularly crowded aqueous interior with a surrounding membrane, both hallmarks of eukaryotic cells. By leveraging the globular and rigid architecture of dendrimers, herein we report the obtention of MCM, composed of oppositely charged small dendrimers and polypeptides, further stabilized by a charged PEG-dendritic copolymer assembled at the periphery.[1] Dendritic MCM display cellular behaviors ranging from engaging in signal transduction pathways within synthetic-natural cell consortia to the formation of tissue-like assemblies,[2] bringing them closer to lifelike matter.

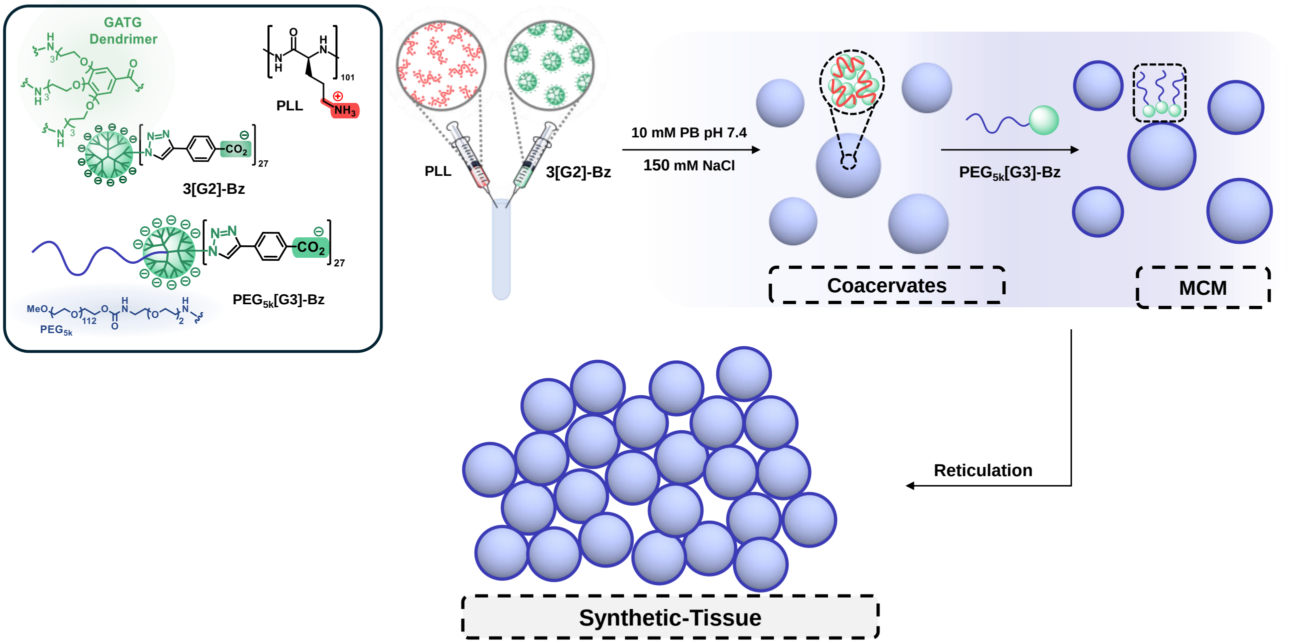

Figure 1. Schematic representation of the complex coacervation of 3[G2]-Bz and PLL, the subsequent interfacial stabilization with PEG$_{5k}$[G3]-Bz, and the preparation of synthetic tissues.

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Synthesis and study of molecular cages based on cyanostar-type macrocycles

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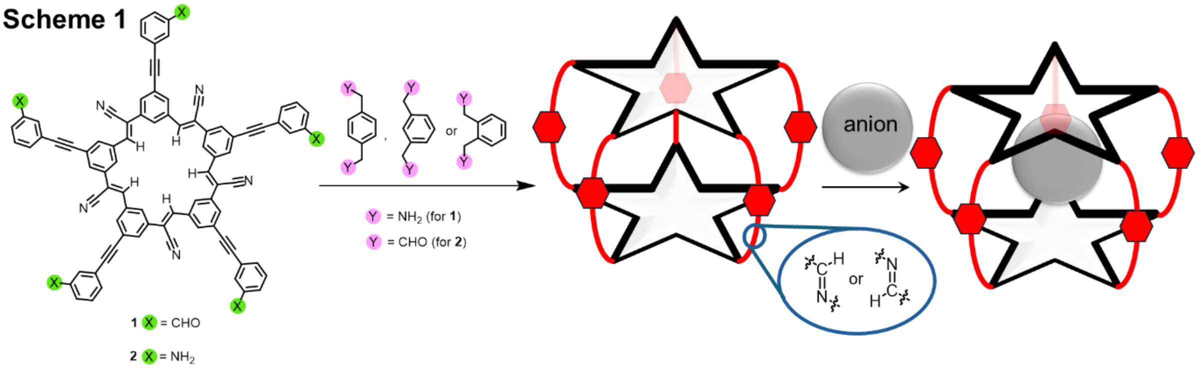
***Keywords**: cyanostar, molecular cages, Knoevenagel condensation*

Cyanostars (CSs) are star-shaped, C_5-symmetric molecules obtained by Knoevenagel condensation of five 3-formylphenyl acetonitrile derivatives leading to the formation of a rigid, cyano-stilbene-based macrocyclic framework.[1] In the CSs, the five radially oriented nitrile groups impart a pronounced electron-deficient character to the macrocycle central cavity.[2] This feature endows these molecules with an excellent affinity for monovalent anions in solution, typically yielding 2:1 host:guest complexes where the anion is "sandwiched" between two macrocyclic units. Supramolecular complexes with a 2:2 stoichiometry can also be obtained by using phosphate or phosphonate as anions.[3] Furthermore, bidentate diphosphate or diphosphonate anions have been shown to promote the formation of CS-based supramolecular copolymers which, upon processing, exhibit adhesive properties comparable to those of commercial covalent polymeric glues.[4]

However, while the anion complexation capability of monomeric CSs is well-established, the incorporation of these macrocycles into dimeric, cage-like architectures has been overlooked. In this TFM, we aimed to prepare CS-based cages by covalently linking two CSs using imine-based dynamic combinatorial chemistry. To reach this goal, we focused on the synthesis of CSs functionalized at their peripheral position with five aldehyde (*i.e.*, **1**) or amino (*i.e.*, **2**) moieties (Scheme 1). We are currently in the process of obtaining pure samples of these two CS derivatives which once obtained will be separately reacted with different ditopic diamine (in the case of **1**) or dialdehyde (in the case of **2**) derivatives to obtain the corresponding imine-based CS cages. Once obtained the CS-based cages, their complexation capability towards anions as well as the formation of supramolecular polymers will be explored.

Scheme 1



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Asymmetric synthesis of 1,3-disubstituted bicyclo[2.1.1]hexanes as *meta*-benzene bioisosteres

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Keywords: *bioisosteres, asymmetric synthesis, bicyclo[2.1.1]hexanes.*

In recent years, bioisosterism has emerged as a key area of research in medicinal chemistry, gaining importance in the development of new drug candidates. This concept involves replacing molecular moieties (e.g., functional groups) with others possessing different chemical structures, but similar or enhanced pharmacological properties. Benzene rings are of particular interest, as they can be substituted with a range of sp^3-rich bicyclic frameworks.[1] This increases molecular three-dimensionality and enables the formation of new stereocenters. While racemic syntheses are widely explored, examples providing products with controlled stereochemistry remain limited. Therefore, the asymmetric synthesis of these bicyclic skeletons represents an important challenge.

Our research group has previously reported the enantioselective synthesis of *ortho-* and *meta-* benzene bioisosteres via a Lewis acid-catalyzed [2+2] photocycloaddition or through a copper-catalyzed protoborylation, obtaining 1,2- and 1,3-bicyclo[2.1.1]hexanes (BCHs), respectively.[2,3] Building on these works, we now describe a straightforward asymmetric strategy for the synthesis of 1,3-BCHs starting from commercially available enantiopure epoxides. The proposed pathway relies on a homoallylation reaction previously developed by our group that proceeds through a Negishi cross-coupling.[4] The obtained 1,5-dienes present defined stereochemistry and can undergo a subsequent [2+2] photocycloaddition under triplet energy transfer catalysis to afford the desired bicyclic products. The final objective is to introduce this scaffold into the structure of known drugs, demonstrating the utility of them for drug discovery programs.

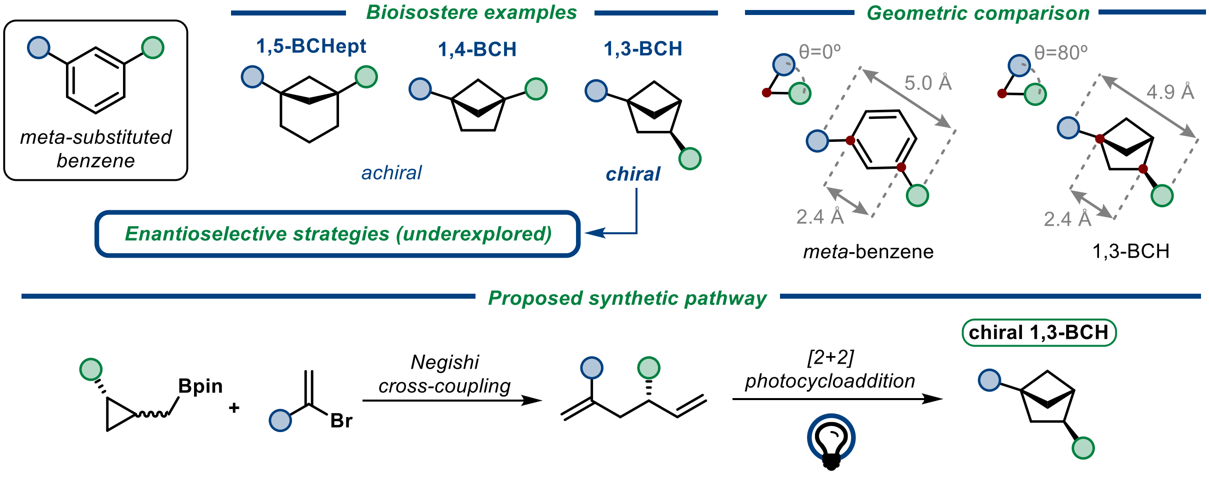

Figure 1. Characteristics and proposed synthesis of 1,3-BCHs as *meta*-benzene bioisosteres.

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Exploration of New Methodologies for the Tailored Functionalization of BODIPYs

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***Keywords**: BODIPYs, BODIPY Functionalization, Phosphorous-containing Dyes*

Boron-dipyrromethenes (BODIPY) are highly versatile fluorescent dyes whose structural adaptability enables an extensive range of applications.[1] To expand their use in advanced fields, the ability to functionalize these fluorophores in a precise and controlled manner is essential. In this context, incorporating phosphorus-containing groups into these fluorophores further enhances their tunability allowing control over photophysical properties and expanding their potential in advanced fields such as bioimaging or sensing.[2] While traditional BODIPY derivatizations focus on the dipyrrin core, functionalization at the boron center has emerged as a complementary strategy to achieve additional properties, such as solubility or stability, without significantly altering the photophysical properties.[3] However, substitution of fluorine atoms remains challenging due to the strength and stability of the B-F bonds. Previous strategies for the nucleophilic substitution of fluorine have relied on Lewis acid activation, leading to *C*-, *O*-, *COO*- and *N*-BODIPYs (defined by the nature of the substituents at the boron center).[3] In this work, we present a general methodology for accessing BODIPYs bearing phosphate substituents at the boron atom (*PO*-BODIPYs, Figure 1). This strategy is based on the procedure reported by our group for the synthesis of *COO*-BODIPYs and relies on activation with BCl_3, in the presence of Et_3N.[4] The scope is evaluated regarding both the BODIPY substrates and the phosphate nucleophiles. Furthermore, we explore the methodology towards the incorporation of diverse groups tailored to the specific requirements of a given application, such as CPL emitters and fluorescent probes for bioimaging.

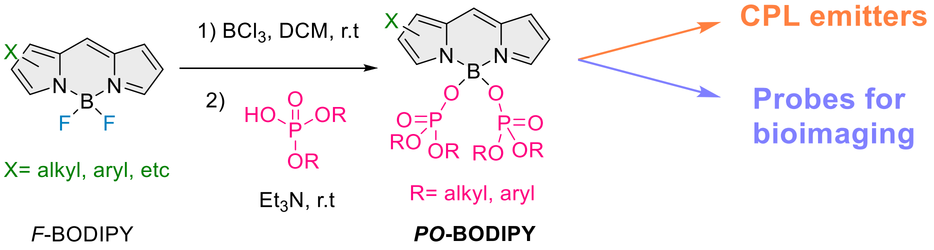

Figure 1. General synthesis for unprecedented BODIPYs having phosphate groups at boron (*PO*-BODIPYs).

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Synthesis of new molecules with therapeutic applications in the immune system

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Keywords: *WIN55,212-2, immune system, bioconjugated allergen vaccines.*

Allergic diseases have become a global health problem due to their alarming prevalence constituting an economic burden for healthcare systems.[1] Allergen-specific immunotherapy (AIT) is the only treatment with long-term disease-modifying capacity for these disorders. However, conventional AIT based on allergen extracts presents important drawbacks such as limited efficacy and high risk of anaphylactic reactions. Therefore, new approaches to overcome these limitations are highly demanded. Bioconjugated allergen vaccines are an innovative AIT strategy based on the chemical conjugation of an allergen with an immunomodulatory adjuvant that enhances immune tolerance to the allergen while minimizing the risk of severe allergic reactions.[2]

In this context, the MedChemLab at Complutense University is carrying out a project based on the development of bioconjugates of a peanut allergen covalently coupled to the synthetic cannabinoid ligand WIN55,212-2 (WIN) as an adjuvant due to the described ability of this cannabinoid to reduce anaphylaxis in peanut-allergic models.[3] In this work, WIN scaffold has been attached to different amide linkers bearing a maleimide for further conjugation with *N*-acetylcysteine via thiol-Michael addition. The new synthesized derivatives will be assessed for their immunomodulatory capacity in the NF-κB activation assay prior to the bioconjugation with the peanut allergen.

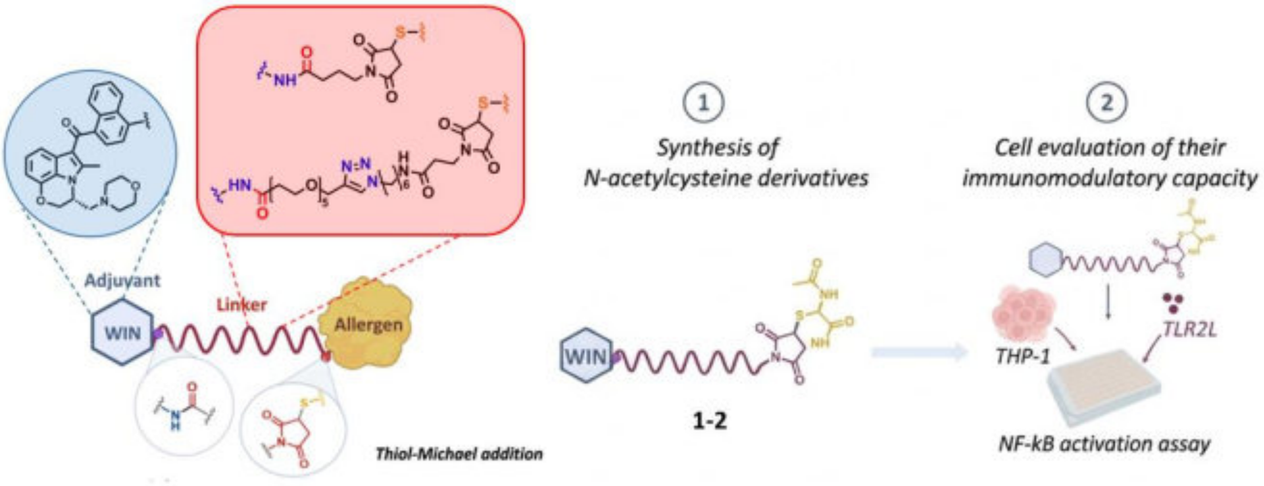

Figure 1. Development of WIN-allergen conjugates for AIT.

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Long-wavelength fluorescence in HER2-binding affibody variants

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***Keywords**: Non-aromatic fluorescence, electron transfer, excitation-emission matrices.*

Non-aromatic fluorescence (NAF) has been reported in peptides lacking aromatic chromophores, where emission arises from cooperative side-chain interactions[1]. Motivated by these precedents, we investigated a long-wavelength emission band (λ_{em}= 545-555 nm) detected in a HER2 binding affibody containing histidine in the 33rd position. Structural inspection suggested that this added amino acid could stabilize a hydrogen bond network enabling electron transfer through two tyrosines and a tryptophan located along the structure; all of them shown in Figure 1.

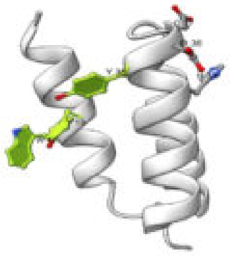
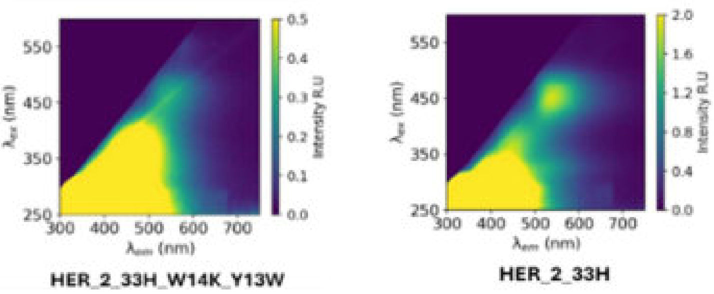


Figure 1. Structural representation of the HER2 binding scaffold highlighting the region proposed to support the long wavelength emission.

The variant with histidine in the 33rd position displayed a clear emission band in the 545-555 nm range, while introducing a tryptophan at position 13 produced a weaker but detectable signal; both shown in Figure 2. In contrast, mutants lacking Trp14 or the whole Tyr35-Tyr13-Trp14 chain, as well as the R32Q variant, showed no emission in this wavelength, indicating that both the electron transfer route and the His33/Arg32 environment are required for this NAF phenomenon. Circular dichroism confirmed that all variants retained the α-helical fold, demonstrating that these fluorescence differences are not caused by structural effects.



HER_2_33H_W14K_Y13W

HER_2_33H

Figure 2. Excitation-emission maps comparing the long wavelength fluorescence of the reference variant and the only mutant that remains with that emission.

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Recovery and purification of glycols from polyestrer production streams for reuse in polyester synthesis.

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***Keywords**: Purification, glycols, polyester.*

In the present study, the recovery and purification of glycols from one or more polyester synthesis streams production was investigated, with special focus on obtaining odorless glycols with minimal by-product content for reuse as raw material in polyester formulations. To achieve this goal, a comprehensive characterization of both, the recovery products and the generated by-products was carried out[1] in order to design a laboratory-scale purification process with potential industrial-scale implementation. In addition, an interdisciplinary approach was adopted, taking into account plant-relevant parameters as well as regulatory and economic considerations.

The purification process was successfully developed through a controlled distillation strategy involving precise management of temperature and vacuum ramps. Under the optimized conditions, a glycol purity of 99.95% and a recovery yield of 61% were achieved. Process efficiency was significant enhance by adding an inexpensive and widely available additive that effectively mitigated chemo- and physisorption phenomena associated with odorous cyclic ethers and others volatile compounds.

The recovery glycols were subsequently employed in the synthesis of a commercial polyester used in flexible packaging (B product), demonstrating their suitability as alternative feedstocks. Polymer characterization by DSC, IR and HPLC-GPC revealed no significant deviations compared with the reference material produced through the standard synthesis route (A product). Furthermore, GC-FID and GC-MS and other complementary techniques confirmed that the incorporation of recovery glycols did not promote the formation of additional by-products during the synthesis.

Table 1. Characterizations results.

Product	Mw	PD	Tg	GC-MS[1]	IR	QC and AT[2]
Polyester A	18932	3.43	-4.13	Pending	99.70%	Conform
Polyester B	23036	3.42	-3.76	Pending	99.70%	Conform

[1]Using GC-MS we´ll see if the amount of oligomer is the same as MORCHEM standards in synthesis of polyester B. [2]Quality and technical application standard requirements

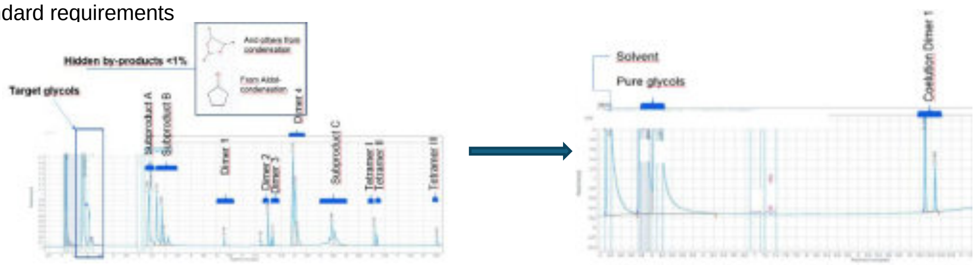

Figure 1. Example of Figure showing the purification glycols by GC-FID analysis. Sample before purification process designed (left) and after (right).

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Nuevas metodologías de carbo- y heterociclación con incorporación de halógeno para la síntesis de estructuras policíclicas

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***Keywords**: Cyclobutenes, Cyclobutenones, Zwitterion.*

Koshar-type zwitterions **1** are organic compounds constituted by a pyridine unit and a bis(triflyl)ethane moiety (Figure 1). When Koshar zwitterions are in solution, they slowly dissociate providing the corresponding pyridine **2** and a molecule of bis(triflil)ethane **3**.[1] This olefin is so reactive that it cannot be stored or isolated. Nevertheless, it can be trapped in the reaction medium by nucleophiles, leading to a wide variety of different molecules.

Recently, our research group has reported the synthesis of iodocyclobutenes **5** through a formal [2+2] cycloaddition in the presence of iodoalkynes **4**. Further transformation under Suzuki conditions allows the generation of substituted cyclobutenones **6**,[2] versatile building blocks that often exhibit multi-step synthetic routes and harsh reaction conditions.[3]

Herein is reported the two-step synthesis of cyclobutenones **6** involving a formal [2+2] cycloaddition of zwitterion **1** and alkynes **4**, and preliminary reactivity investigation, including dehydrogenation reactions, allylation and allenylation processes.

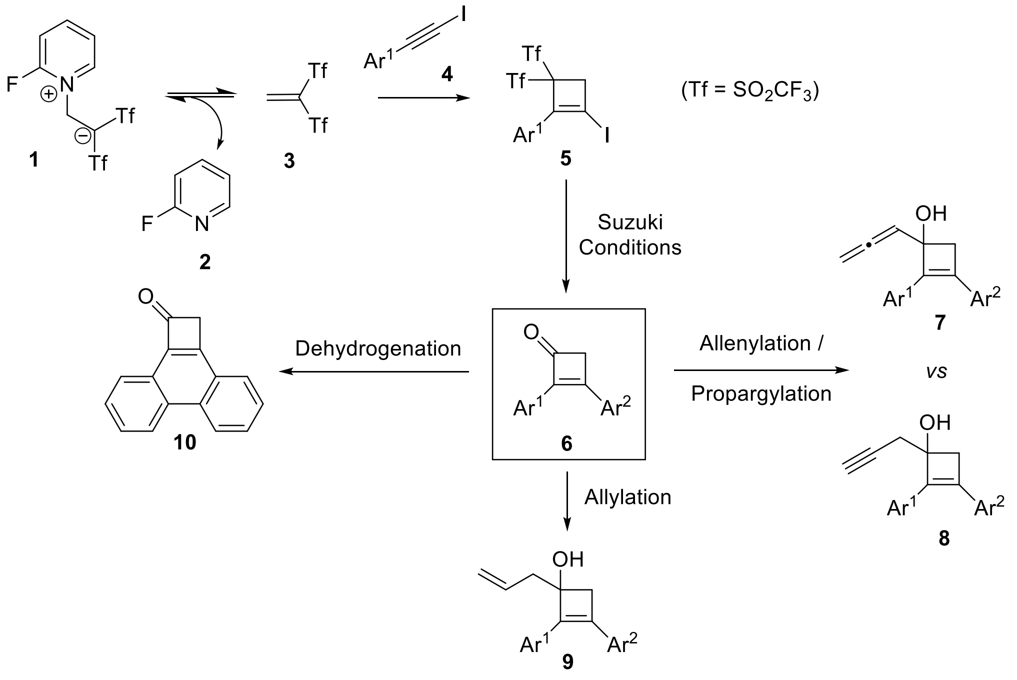

Figure 1. Synthesis of cyclobutenones and reactivity investigation.

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Reshaping lactonization: accessing γ-butenolides through efficient Pd-catalysis

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Keywords: *Pd-catalysis, γ-butenolides, lactones*

γ-Lactones are a ubiquitous structural core present in over 13.000 natural products. Their unsaturated derivatives, γ-butenolides, have become a valuable building block not only for the preparation of different lactone moieties, but also as versatile synthetic precursors for the preparation of other heterocyclic compounds with biological activity (Figure 1A).[1] Despite their importance in modern organic synthesis, current methodologies suffer from lack of sustainability, normally through inefficient condensation reactions or through challenging synthetic routes.[2]

Palladium catalysis has emerged as a powerful approach to build complex structures. However, to achieve good levels of regioselectivity most of these methodologies require the installation and subsequent removal of an exogenous directing group or the use of a prefunctionalized halogenated substrate, thereby reducing overall synthetic efficiency. In this context, the use of native or endogenous directing groups that not only coordinate with the metal center but also actively participate in the functionalization has arisen as a less time-consuming and more efficient alternative. Among them, carboxylic acids have demonstrated to be considerably effective for the functionalization of $C(sp^3)$–H and $C(sp^2)$–H bonds. Nonetheless, the functionalization of β,γ-unsaturated acids remains largely unexplored and further research needs to be conducted.[3]

Herein, we report a novel and efficient Pd catalyzed lactonization method to access γ–butenolides from β,γ-unsaturated carboxylic acids, providing a straightforward and sustainable pathway to these essential chemical scaffolds (Figure 1B).

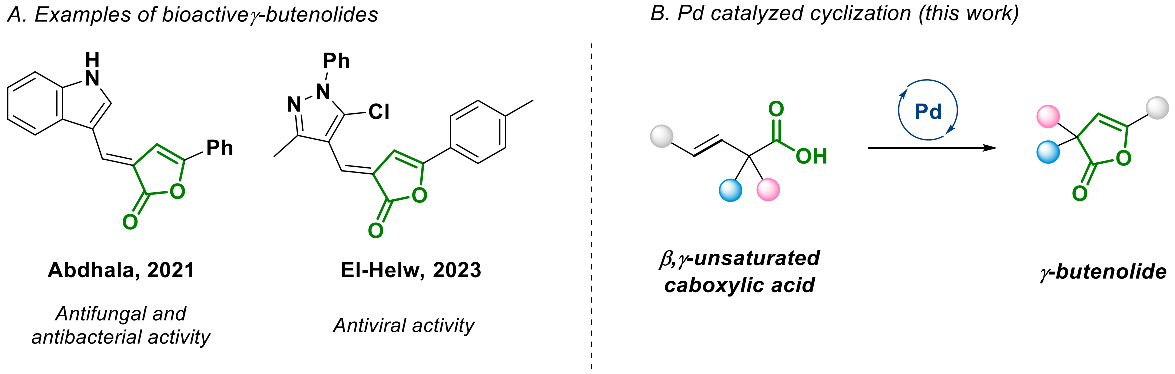

Figure 1. A) Butenolide-containing drugs. B) γ–Butenolides via Pd-catalyzed cyclization of β,γ-unsaturated acids.

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Photochemical [3+2] functionalization of carbon nanotubes

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***Keywords**: carbon nanotubes, aziridine, photochemical*

Carbon nanotubes (CNTs) are materials composed solely of carbon atoms and are one of the carbon allotropes. Their *sp*^{2} hybridization offers an aromatic honeycomb network rolled into cylinders with nanometric diameter, variable lengths and a different reactivity depending on the CNT employed, such as single-walled carbon nanotube (SWCNT) or multi-walled carbon nanotube (MWCNT).[1] Although CNTs exhibit remarkable potential for applications in advanced materials and other fields due to their exceptional mechanical strength and electrical and thermal conductivity, their low solubility, poor wettability and limited dispersibility in common solvents have restricted their processing and applications.[2] To solve this problem, the chemistry of CNTs has also been extensively studied over the past decade, especially for thermal reactivity with aggressive conditions. However, CNT's photochemistry is not a field widely studied but has a lot of advantages such as mild conditions and avoiding the classical methods.

Herein, a new approach for the functionalization of carbon nanotubes through photocatalytic processes is described, using aziridines 1 as a principal substrate. Among other available strategies, reported methodologies were used to reach the main product.[3] Then, 1 undergoes a photocatalyzed oxidative ring opening to react with the nanotube wall. Under the best reaction conditions, including the appropriate photocatalyst, blue light-emitting diode and 24 hours, a general cycloaddition process via azomethine ylide achieve a functionalization degree of 21.2%. This degree of functionalization was determined through characterization techniques such as Raman spectroscopy, which revealed an increase in defects associated with the change in hybridization from *sp*^{2} to a *sp*^{3} providing evidence of successful functionalization. In addition, the functionalization's percentage was found to be proportional to nitrogen and sulfur content derived from the starting aziridine. In conclusion, a general photochemical process for CNTs is presented through azomethine ylide and the electronic characteristics of aziridines may play an important role in the evolution into the cycloadducts.

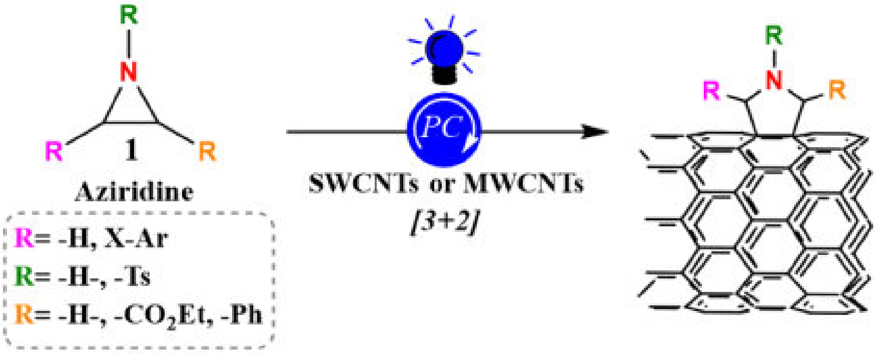

Figure 1. General reaction scheme for photochemical [3+2] cycloaddition and information about aromatic substituents.

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Advanced Catalytic Strategies for the Functionalization of Relevant Organic Compounds

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***Keywords**: manganese catalysis, C-H activation, hydroarylation*

Manganese presents the unique advantage of being non-toxic and environmentally benign, which together with its low cost and natural abundance, makes it an ideal candidate for catalysis, both as a replacement for precious metals and as a platform for developing new methodologies. However, its potential has remained largely unexploited until recent years. While manganese plays a well-established role in radical chemistry, it also exhibits rich organometallic reactivity, including C-H activation and hydrogen transference processes.[1]

More recently, novel manganese-catalyzed methodologies based on transmetalation processes have emerged, including both cross-coupling and hydroarylation reactions of unsaturated compounds. With regard to cross-coupling transformations, manganese has shown promising potential as an alternative to traditional palladium catalysts in Stille-type reactions, enabling aryl-aryl bonds, although generally under relatively harsh conditions. In contrast, hydroarylation methodologies of unsaturated compounds remain largely underdeveloped, with only a few examples reported under highly specific conditions that strongly depend on the functional group present in the starting materials, while the corresponding mechanisms are not yet fully understood.[2]

In this context, our research group has focused on studying manganese-catalyzed hydroarylation reactions in greater depth. When combined with a C-H activation process,[3] this approach has enabled the development of a simple, efficient, and environmentally sustainable methodology for the synthesis of 1,1-diarylated compounds, a class of molecules of considerable interest in medicinal chemistry. This method allows the selective installation of two aromatic rings onto the same carbon centre from an activated alkyne, which had not been utilized before in this type of reaction. Notably, the process does not require inert conditions or unusual solvents and exhibits broad substrate scope (Figure 1).

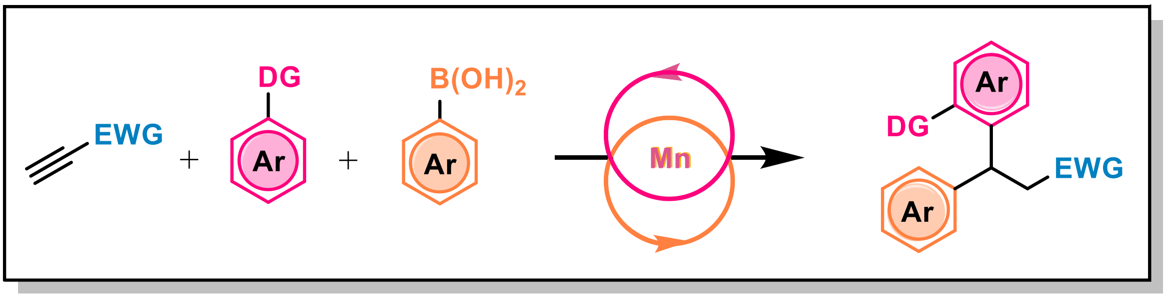

Figure 1. Three-component direct 1,1-diarylation via Mn(I) catalysis.

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Nitroreductase-catalyzed reduction of nitroarenes to heterocyclic amines: kinetic characterization, reaction optimization, and substrate scope as a sustainable alternative to metal-catalyzed hydrogenation

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***Keywords**: nitroreductases, biocatalysis, green chemistry.*

Nitroreductases (NRs) are flavin-dependent enzymes that catalyze the selective reduction of aromatic nitro groups to the corresponding amines,[1] offering a sustainable and chemically orthogonal alternative to traditional metal-catalyzed hydrogenation methods, which typically require pressurized H_2 or stoichiometric reductants under harsh conditions.[2] The biocatalytic system employed here integrates a synergistic NR/metal cofactor strategy to drive complete nitro reduction, coupled with an NAD(P)H recycling loop to ensure continuous enzymatic turnover, a design that enables mild, scalable, and operationally safe reaction conditions.[3] Kinetic parameters of the transformation were first determined and validated using a model substrate, establishing a mechanistic framework that guided subsequent optimization. A systematic study of key reaction variables (including enzyme loading, cofactor concentration, and reaction time) was then performed to maximize conversion efficiency. The optimized protocol was applied to a structurally diverse panel of nitroarene substrates of varying electronic and steric demand, to evaluate the substrate scope and functional group tolerance, with conversions of [59-97 %] and chemoselectivity for the nitro group in the presence of halogens, carboxylic acids, esters and heterocycles.

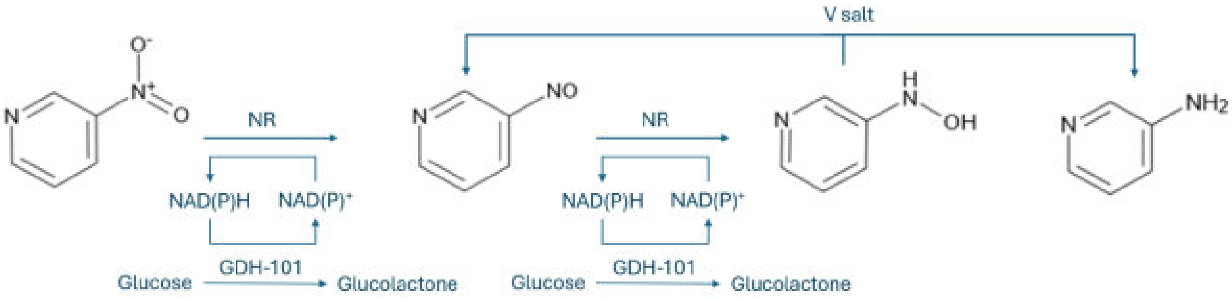

Figure 1. Reaction scheme for nitroreductases in an NAD(P)H recycling system in the presence of metal cofactor.

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Panchromatic Polar Supramolecular Polymers

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***Keywords**: Optoelectronics, subphthalocyanines, polarization.*

The study of renewable energy sources, particularly those based on solar radiation, has gained significant attention in a society still heavily reliant on fossil fuels. A common approach is the synthesis of π-conjugated molecules with electron-donating and electron-accepting characteristics[1], designed to incorporate supramolecular features through the coupling of functional groups promoting non-covalent interactions. Moreover, 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]In this context, subphthalocyanines have a special interest due to their ability to form non-centrosymmetric polar columnar materials, which can be aligned under an external electric field as a result of their intrinsic axial dipole moment.[4] Accordingly, the target molecule is a fluorinated SubPc core functionalized at its periphery with porphyrin units via acetylenic linkers, where the subphthalocyanine unit acts as the electron acceptor, while the porphyrin units as electron donor and can provide complementary light-harvesting properties.[1,5] (**Figure 1**).

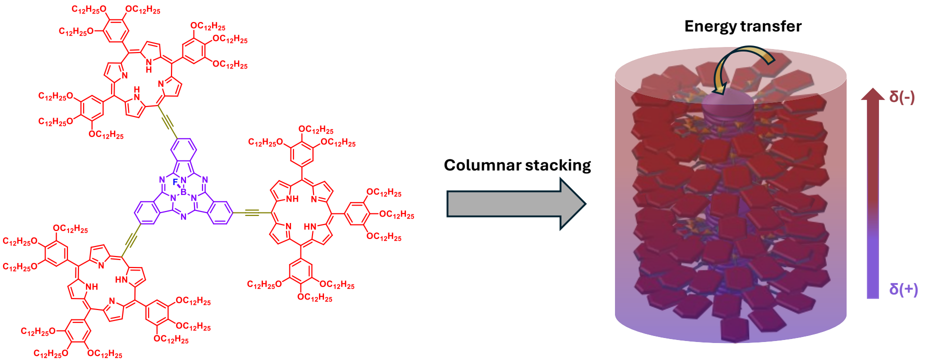

Figure 1. Structure of SubPc(Porph)$_3$, designed to stack into non-centrosymmetric columnar assemblies that simultaneously exhibit net polarization and photophysical phenomena.

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Luminiscent materials for OLED devices

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Keywords: *TADF, OLED, TSCT.*

Thermally activated delayed fluorescence (TADF) organic materials have been extensively investigated for organic light-emitting diodes (OLEDs) applications due to their ability to efficiently upconvert triplet excitons into singlets through reverse intersystem crossing (RISC).[1,2] Efficient RISC requires a narrow singlet-triplet energy gap ($\Delta E_{ST} < 0.2$ eV) to occur. Originally this has been achieved by through-bond charge transfer (TBCT) in highly twisted donor-acceptor (D-A) structures.[3] Alternatively, systems where donor and acceptor are sterically forced to intramolecularly stack have demonstrated the ability to present strong TADF. In these molecules where steric congestion produces rigid conformations that effectively supress non-radiative relaxation, the emission is mediated by through space charge transfer (TSCT).[4]

In this work, we designed a series of D-A molecules, where two donors and two acceptors are forced into an extremely cluttered space to promote their intramolecular association. The strategy consists of linking two triphenyl triazine acceptors and two carbazole based donors to a single phenyl ring. All molecules show strong fluorescence that ranges from sky blue to yellow as more conjugated and stronger donors are employed.

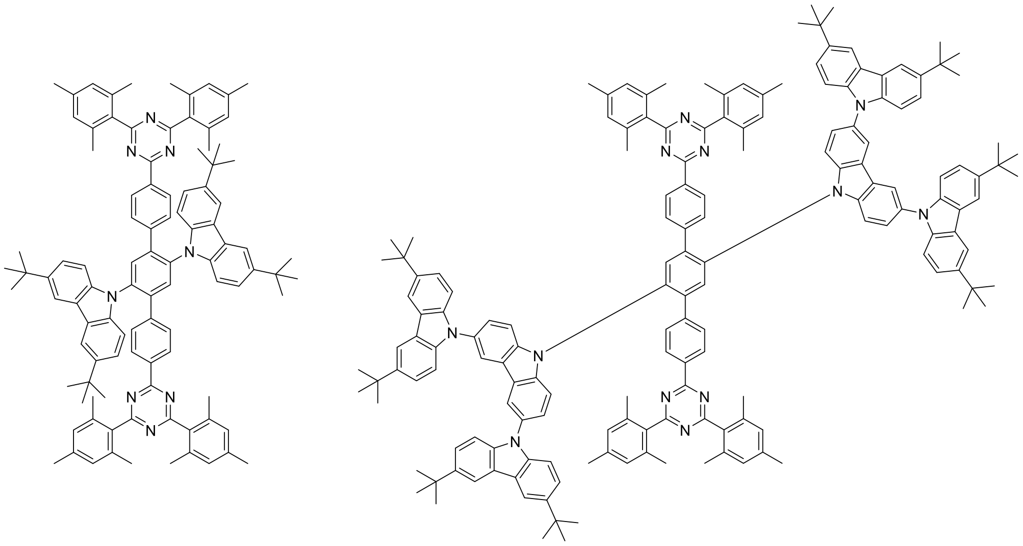

Figure 1. Chemical structures of the two molecules synthesized in this work.

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Synthesis of an Alkoxylated Three-Dimensional PAH via the Scholl Reaction

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***Keywords**: Non-planar PAHs, Scholl reaction, Suzuki cross-coupling*

Planar polycyclic aromatic hydrocarbons (PAHs) are typically present in nanomaterials with a wide range of technical applications.[1] Recently, it was discovered that incorporating distorted regions (e.g. eight-membered saddle-shaped rings) can further tune PAH properties for use in advanced applications. Therefore, efficient synthetic approaches to these non-planar polycycles are highly in demand.[2] In our group, a remarkably stereodivergent K^+-mediated cyclotrimerization of tribenzoCOTyne to a three-dimensional PAH, (α,α,α)-TTBA **1a**, has been developed (Figure 1).[3] Unfortunately, access to functionalized derivatives via this synthetic route remains as a challenge.

In this TFM project, an alternative synthetic route to a functionalized TTBA **1b** based on the Scholl reaction of a convenient alkoxy-substituted *hexa*-phenylbenzene derivative **2** is explored.[4] Access to this compound via Suzuki-type cross-coupling reactions from 1,3,5-tribromo-2,4,6-triiodobenzene **3** will be discussed.

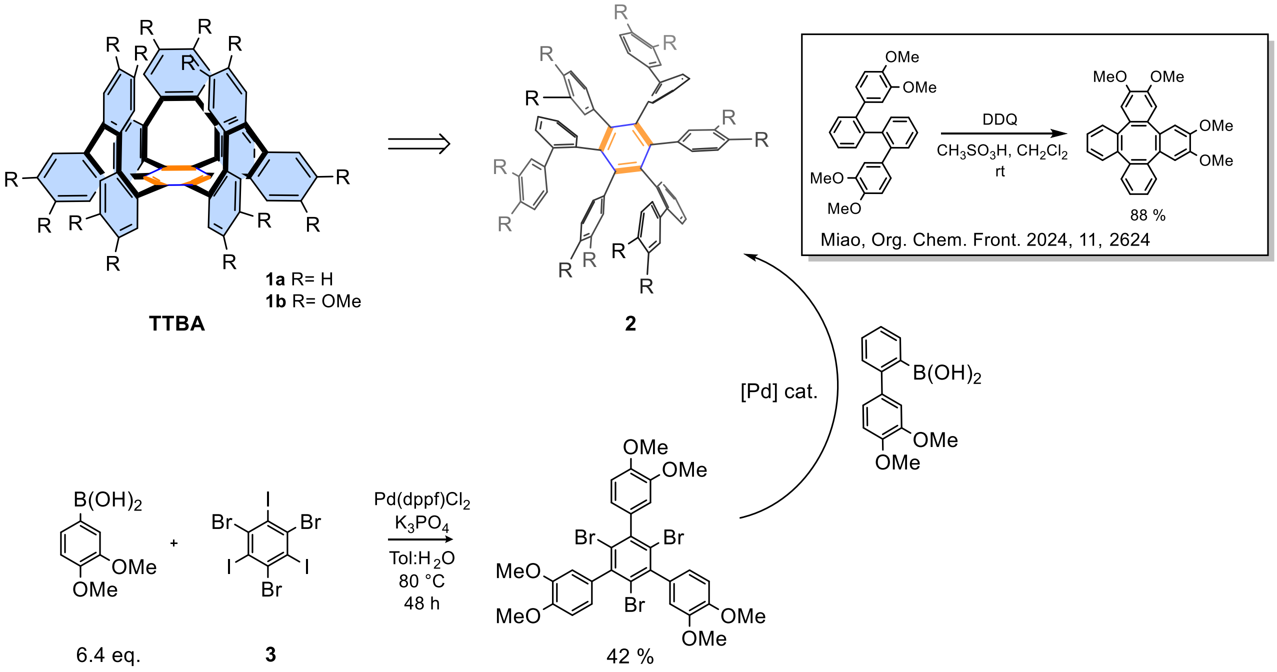

Figure 1. Retrosysnthetic analysis of TTBA **1b** and synthetic route to the *hexa*-phenylbenzene derivative **2**.

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Fluorescent Molecularly Imprinted Polymers for Fusaric Acid Detection

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Keywords: *fluorophores, mycotoxins, molecularly imprinted polymers (MIPs).*

Mycotoxins are toxic secondary metabolites produced by fungi that represent a relevant concern in food safety and environmental monitoring. Among them, fusaric acid, produced by several *Fusarium* species,[1] is a key target for the development of selective optical sensing platforms. In this context, molecularly imprinted polymers (MIPs) offer a robust and cost-effective alternative to biological receptors for analyte recognition. MIPs are capable of selectively recognizing a target molecule through preorganized binding cavities.[2] This binding can be optically monitored if the polymer is functionalized with photoactive molecules. Here, we describe the synthesis of fluorescent MIPs, by using phenazine or phenoxazinone fluorophores (Figure 1, compounds **1** and **2**)[3] derivatized with acrylate groups for co-polymerization within the MIP matrix. The dyes also incorporate urea groups, which can establish directional hydrogen-bonding interactions with the carboxylate moiety of the target analyte (the fusarate anion). Such urea-fusarate binding is expected to modulate the photophysical properties of the chromophore, enabling the use of the MIPs as optical probes.[4]

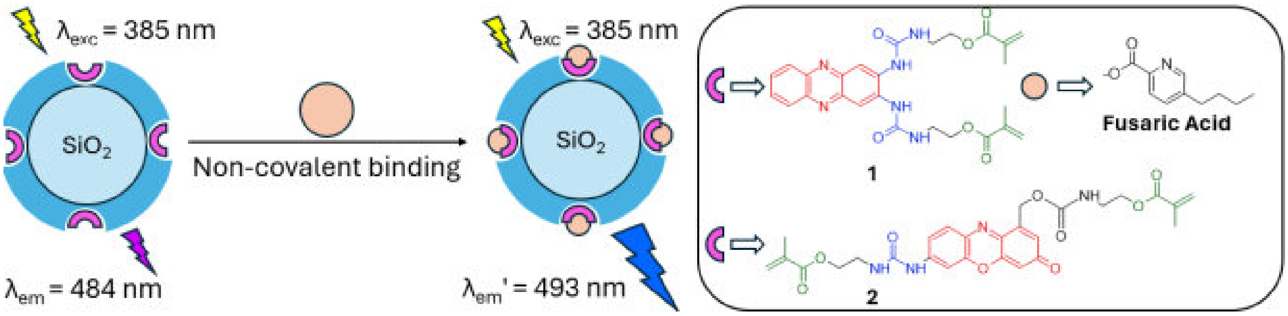

Figure 1. Scheme illustrating the selective recognition of fusaric acid (in the form of its conjugated base, fusarate) by fluorescent MIPs, showing the fluorescence change upon non-covalent binding to the MIP. The caption shows the chemical structure of the fusarate anion (analyte) and the fluorescent monomers **1** and **2:** the fluorescent core is indicated in red, the bonding binding groups in blue and the polymerizable subunits in green.

The synthesis of MIPs was carried out over silica nanoparticles surface-derivatized with acrylate groups. The fluorescent monomers **1** or **2** are mixed with the target analyte (acting as a molecular template), crosslinkers, additional functional monomers and the acrylate-silica cores.[2,3] After addition of a radical initiator (azobisisobutyronitrile, AIBN) and heating, a fluorescent MIP nanolayer is grown onto the silica cores, that contains selective cavities for fusaric acid recognition.

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Controlled Post-Synthetic Modification of Covalent Organic Frameworks-Gels

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***Keywords**: COFs, gels, post-synthetic modifications.*

Porous materials play a key role in applications involving adsorption and molecular transport due to their high surface area and ability to host guest species. In this context, Covalent Organic Frameworks (COFs) have emerged as highly attractive platforms for the rational design of crystalline porous materials through the directed assembly of organic building blocks via dynamic covalent chemistry [1a]. The strategic selection of the precursors enables precise tuning not only of the geometry, connectivity and porosity of the resulting framework, but also of its chemical functionalization [1b]. In this regard, post-synthetic modification (PSM) strategies provide access to additional functionalities that are difficult or impossible to incorporate through direct synthesis [2].

To date, post-synthetic modification strategies in COFs have been largely limited to conventional powder materials. Recent advances in sol-gel methodologies, however, have enabled the formation of macroscopic, continuous COF monoliths with hierarchical porosity [3]. In contrast to conventional COFs obtained as powders, this structural organization enhances mass transport while simultaneously introducing diffusion-controlled reactivity across the material. As a result, these systems offer new opportunities to study functionalization gradients and spatial control of reactivity, aspects that have not yet been explored.

In this work, the post-synthetic modification of hydroxyl groups in DHTA-TAPB (DHTA = 2,5-dihydroxyterephthaldehyde; TAPB = 1,3,5-tris(4-aminophenyl)benzene) COF gels was investigated with the aim of obtaining gels with unidirectional chemical gradients (Figure 1). Functionalization was achieved through the diffusion of 1,3-propanesultone or succinic anhydride across the gel, enabling the incorporation of sulfonate and carboxylic acid functionalities, respectively, as confirmed by FTIR spectroscopy. In the case of the sulfonate-functionalized COF gel, ^{1}H-NMR spectra after acid digestion allowed quantitative assessment, revealing a functionalization gradient across the monolith with conversion values ranging from 50% to 32%. These results demonstrate the feasibility of generating controlled chemical gradients within COF gels through post-synthetic modification. Such spatial control over functionality enables the modulation of local properties including hydrophilicity, ionic character, and acidity, opening new possibilities for selective ion transport, with potential applications in osmotic energy generation.

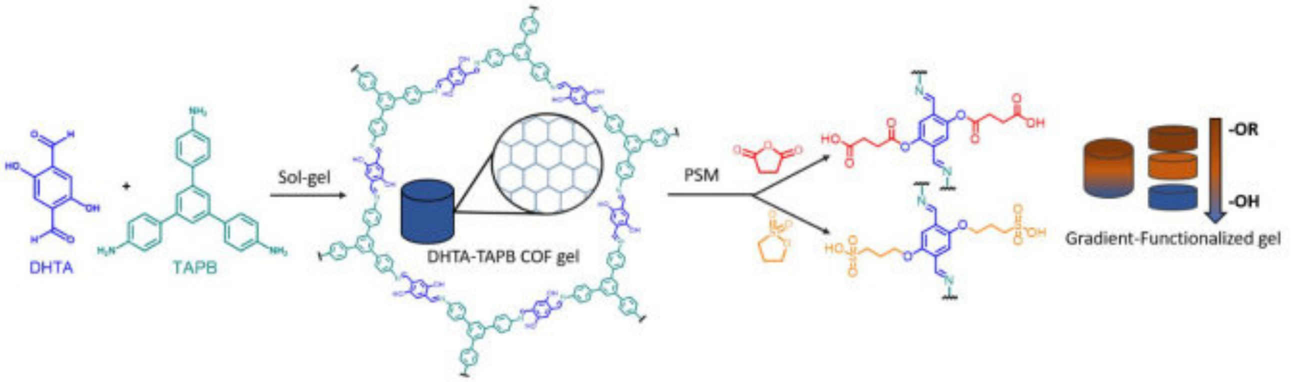

Figure 1. Synthesis of DHTA-TAPB COF gels and PSM-driven functionalization gradients.

References:

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IONIC PAIR OF BILAYER NANOGRAPHENES

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Keywords: *nanographene, ionic pair, bilayer.*

Nanographenes are nanometric molecules based on polycyclic aromatic hydrocarbons (PAHs) which share some characteristics with the graphene. Unlike graphene, nanographenes exhibit non-zero band gaps due to quantum confinement. Their properties are strongly governed by topology and confinement effects, making them promising materials for applications in organic electronics, quantum computing, bioimaging, and other emerging technologies.[1,2]

Molecular nanographenes can take advantage of their bottom-up synthesis to precisely control different fundamental aspects of their structure and properties. Chirality is one of these features and has recently been achieved in our group through the enantioselective synthesis of multilayer chiral nanographenes.[3,4] On the other hand, controlling doping together with exploiting bilayer effects is highly desirable for tuning their optoelectronic properties, since the stacking of two nanographene layers extends the π-system and promotes through-space electronic communication.[5]

In this communication, we present the preparation of a nanographene bilayer formed by an ionic pair of two nanographenes: a cationic layer featuring a quaternary nitrogen atom in its structure, and an anionic layer bearing a carboxylate group responsible for the negative charge.

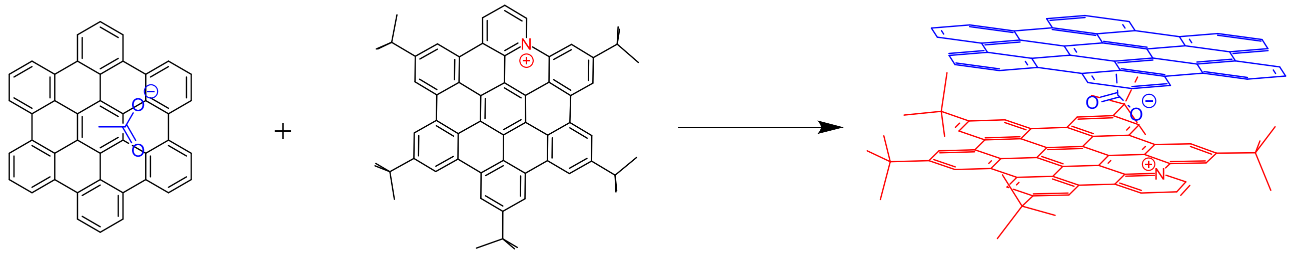

Figure 1. Schematic representation of the ionic pair bilayer nanographenes.

References:

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[2] Martín, N. Nanographenes: Synthesis, Properties, and Applications. In Molecular Nanographenes, 1st ed.; Wiley-VCH, Vol. 1; Wiley Publications, **2025**, pp 1-24.
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[5] Izquierdo-García, P.; Lión-Villar, J.; Fernández-García, J. M.; Martín, N. *Chem. Soc. Rev.* **2025**, *54*, 11089.

Luminescent supramolecular polymers based on donor-acceptor systems.

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Keywords: *supramolecular polymers, chiral, self-assembly.*

In this work, the design, synthesis and self-assembly of the chiral luminogen **1** is reported (Figure 1a). This system is based on a donor-acceptor (D-A) carbazole-phthalimide scaffolds functionalized with peripheral tris((*R*)-3,7-dimethyloctyloxy)benzamide groups to facilitate the aggregation through hydrogen bonds and π-stacking. Supramolecular D-A systems have attracted increasing interest due to their applications in relevant photophysical processes upon aggregation.[1] The self-assembling features of **1** have been investigated by a number of spectroscopic techniques (^{1}H NMR; FTIR and UV-Vis) which corroborates the supramolecular polymerization through H-bonding interactions between the amide functional groups and the π-stacking of the aromatic backbones. The presence of point chirality in the peripheral chains provokes an efficient chirality transfer from the monomer to the supramolecular polymer by the formation of chiral aggregates in heptane solution (CD; Figure 1b). Moreover, an increase in the emission intensity is obtained upon supramolecular polymerization through an aggregation induced emission process[2,3] together with a hypsochromic shift of the emission (Figure 1c). The results presented herein demonstrate the formation of chiral supramolecular polymers with promising chiroptical properties.

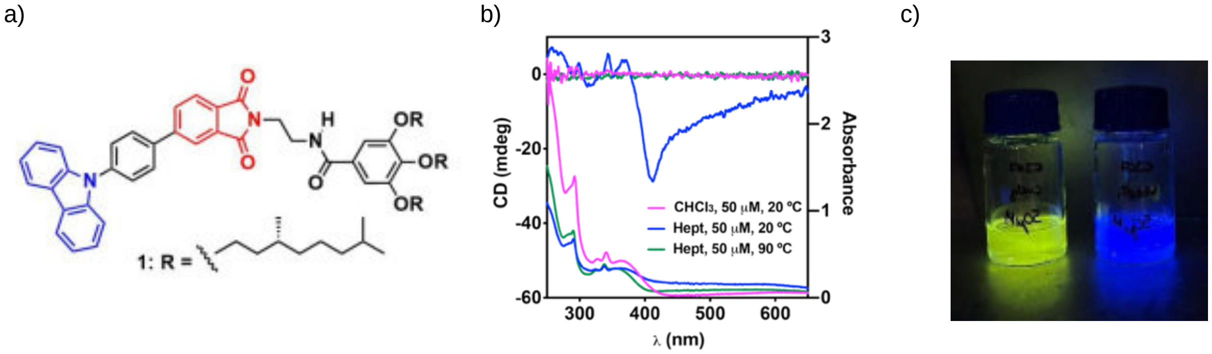

Figure 1. a) Chemical structure of **1**. b) CD and UVs spectra of **1** in 50 mM solution in heptane and $CHCl_3$. c) Pictures of heptane (blue) and $CHCl_3$ (yellow) solution under UV-irradiation (365 nm).

References:

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Development of a chemical library of glycosidase inhibitors from (-)-shikimic acid

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***Keywords**: (-)-shikimic acid, glycosidase inhibitors, octahydro-1H-isoindoles.*

The synthesis of enantiomerically pure polyhydroxylated molecules with potential therapeutic applications, particularly in enzymology, remains a cornerstone of asymmetric organic chemistry. Traditionally, carbohydrates have predominantly served as the primary chiral pool for synthesizing these complex scaffolds.[1] However, (-)-shikimic acid (**1**) (Figure 1) offers a unique and highly versatile alternative.[2] This natural building block possesses a multifaceted structure characterized by a preformed cyclohexane ring incorporating an α,β-unsaturated carboxylic acid moiety, along with a stereodefined trihydroxyl system. Building upon our research group's extensive experience with both monosaccharides and (-)-shikimic acid,[3] this work focuses on the generation of a structurally diverse library of potential glycosidase inhibitors (**3**) based on an octahydro-1*H*-isoindole core.[4]

The synthetic strategy follows a retrosynthetic analysis where the target bicyclic mimetics (**3**) are derived from **1** through a key protected octahydro-1*H*-isoindole intermediate (**2**). The design of the compound library is based on the structural diversification of the resulting amine group in **2**, through *N*-alkylation with a variety of substituents. This diversification strategy aims to investigate the structure-activity relationship (SAR) requirements for the inhibition of various glycosidases. These novel bicyclic compounds (**3**) are currently undergoing biological evaluation to assess their potential therapeutic applications, such as their use as pharmacological chaperones.[5]

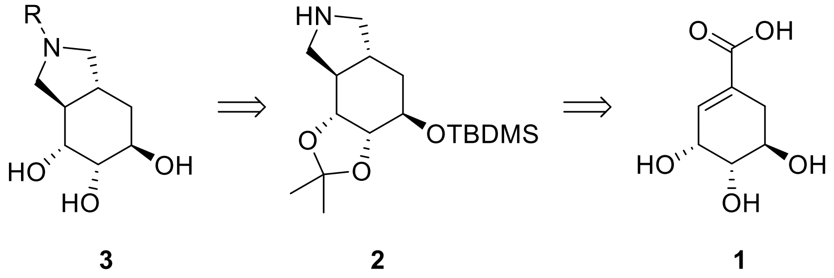

Figure 1. Retrosynthetic analysis for the synthesis of glycosidase mimetics (**3**)

References:
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Biomimetic Porphyrin-Based Molecular Cages: Conformational Control and Allosteric Behavior

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Keywords: *Porphyrin-cages, conformational control, supramolecular chemistry.*

Metalloporphyrins are a relevant molecular family involved in numerous crucial biological processes. In nature, these molecules are found in accessible catalytic sites and form well-defined environments. [1] Their diverse structural and functional features have inspired the development of artificial systems, such as molecular cages, in which porphyrins can be used to create confined pockets.[2] Such architectures can be obtained through supramolecular, covalent, or dynamic covalent strategies, and feature internal cavities capable of hosting guest molecules.

In the *Nanostructured Molecular Systems and Materials* research group, porphyrin cages are formed through the imine condensation of 4 units of tetra-aldehyde porphyrin and 2 units of di-amine linker, taking advantage of the reversibility of this linkage to access the thermodynamically product (**Fig. 1a**). According to the arrangement, imine bonds can adopt two main conformations: extended and compact. In examples previously studied, the extended conformation generally predominates, although in some cases the equilibrium has been shifted toward the compact conformation in response to different stimuli.[3]

In this work, we aim to obtain a metalloporphyrin-cage that preferentially adopts compact conformation stabilized by hydrogen bonds. To this end, we propose a porphyrin decorated with a hydroxyl group capable of forming an intramolecular hydrogen bond with the imine nitrogen (**Fig. 1b**) to study allosteric effects.

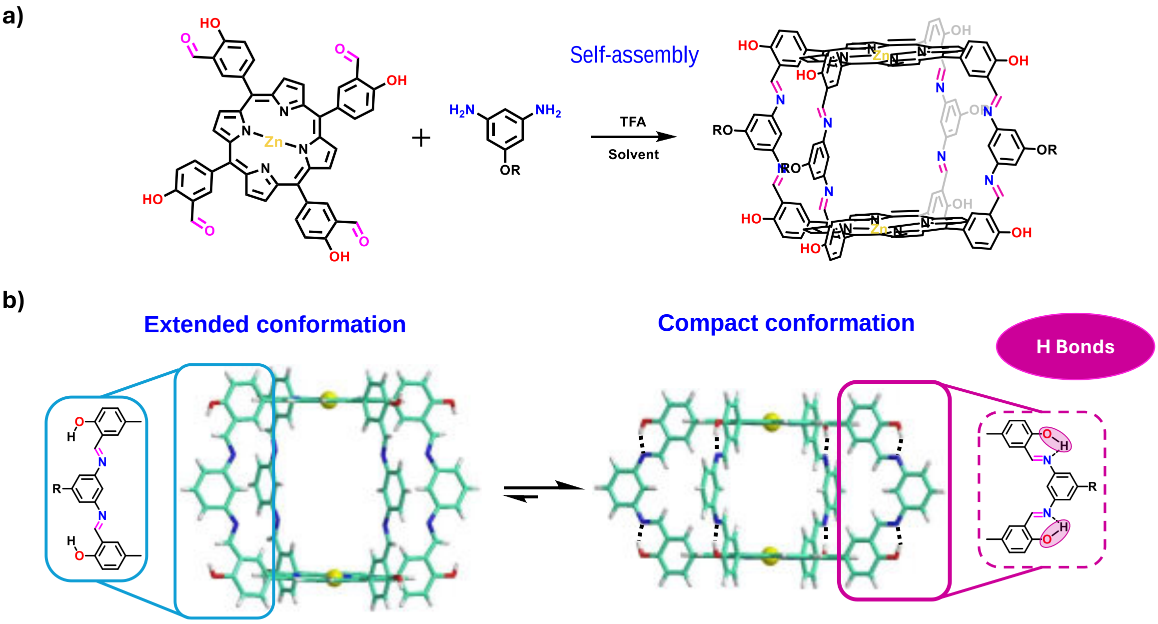

Figure 1. a) Synthesis of the metalloporphyrin-cage. **b)** Conformational equilibrium.

References:

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Fluorescent molecules for advanced biomedical applications

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***Keywords**:* *BODIPY,fluorescence, bioimaging.*

BODIPY dyes (boron-dipyrromethene derivatives) are a well-established class of highly fluorescent organic chromophores widely used in bioimaging. However, most reported BODIPY derivatives emit in the green-to-red region of the spectrum, while examples of blue-emitting analogues remain scarce. This limitation restricts their applicability in multicolor fluorescence microscopy, where efficient spectral separation and low background interference are essential.[1]

Herein, we present an exploratory study toward the development of a new family of blue-emitting BODIPY derivatives based on structural modification of the core. In particular, the introduction of sulfur atoms at the 1,7-positions leads to a novel class of 1,7-dithio-BODIPY systems (DTB). This core modification is expected to significantly alter the electronic properties of the chromophore, enabling access to the underexplored blue-edge emission region.

This work highlights the synthetic approach to these novel DTB scaffolds and their potential as fluorescent probes for advanced fluorescence microscopy applications, especially in multicolor imaging, where blue-emitting dyes are highly desirable.[2]

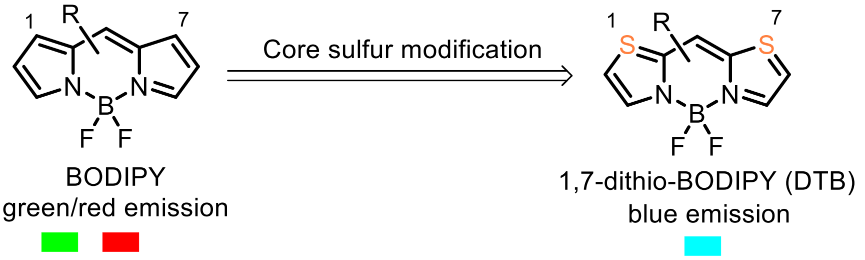
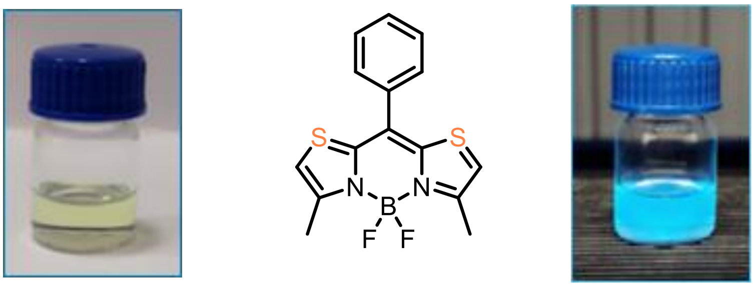


Figure 1. Structural modification of the BODIPY core toward blue-emitting DTB fluorophores



visible light

UV (366 nm)

Figure 2. Visible and UV-light emission of a DTB derivative

References:

[1] Kaur, P.; Singh, K. *J. Mater. Chem. C.* **2019**, *7*, 11361−11405.

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Bioorthogonal reactions for labeling supramolecular species via ruthenium-catalysed [2+2+2] cycloaddition reactions

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Keywords*: cyclopeptides, bioorthogonal chemistry, cycloadditions*

This work describes the solid-phase synthesis and characterization of cyclopeptides (CPs) designed to participate in ruthenium-catalysed cycloaddition reactions.[1],[2] A synthetic strategy was developed involving linear peptide synthesis, followed by cyclization and functionalization with a phenylacetylene group.[3] To optimize this process, different peptides with varying amino acid sequences were tested. The incorporation of hydrocarbon chains was also explored to promote peptide self-assembly and evaluate the cycloaddition reaction within assembled systems. [4]

Furthermore, the reaction is being studied in simpler systems, such as single amino acids, to better understand these processes.

The primary interest in these transformations stems from their mild reaction conditions—performed in water at room temperature—and the fluorescent properties of the resulting cycloadducts. These features, combined with the inherent versatility of cyclopeptide chemistry, open promising avenues for applications in bioorthogonal chemistry.

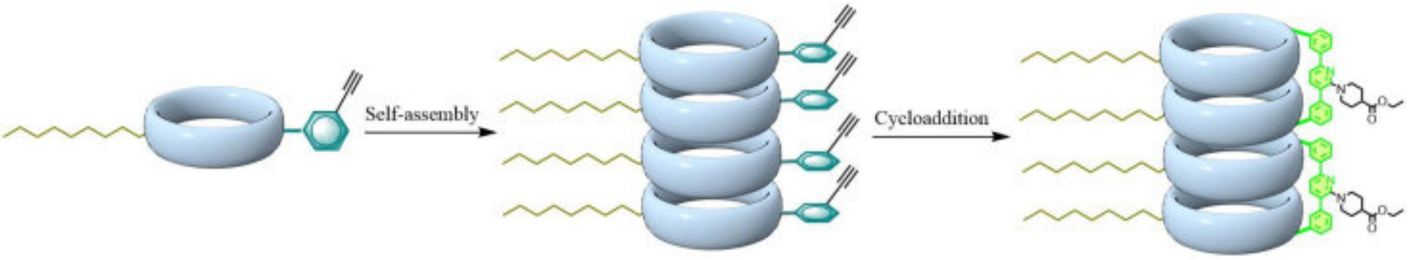

Figure 2. Schematic representation of the self-assembly of cyclopeptides, enabling their participation in [2+2+2] cycloaddition reactions.

References:

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Design and Synthesis of Photostabilizers for improving Membrane-Specific Fluorescent Probes.

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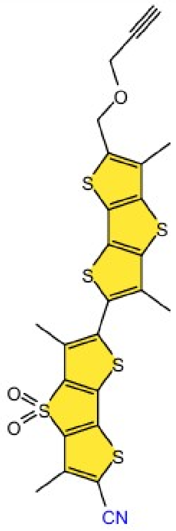
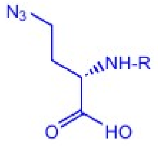
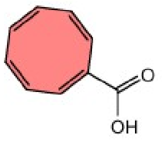
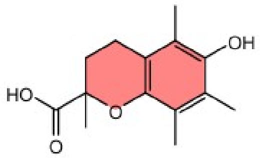
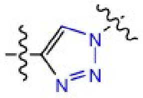
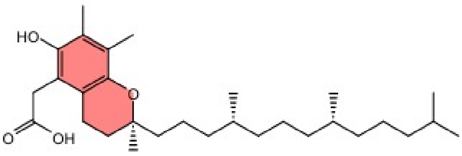
***Keywords**: Flippers, click chemistry, membrane tension.*

The use of fluorescent molecules for studying the properties of phospholipid membranes has demonstrated to be of great importance in cellular biology.[1] However, a significant limitation of these probes is the competition between fluorescence emission and the formation of reactive radicals. Over extended periods of irradiation, these the irradiation produces oxidative processes inducing cytotoxicity or fundamentally alter natural cellular behavior. In order to solve this issue, the idea of this investigation is to synthesize three well-known stabilizing ligands containing either Trolox (synthetic antioxidant), α-tocopherol (natural vitamin E) or cyclooctatetraene (COT) (a redox-active antiaromatic ring).[2] Those ligands will be anchored to a chromophore as a head group through the formation of a triazole ring (click chemistry).[3] Specifically, we plan to modify well-known chromophores used as mechanosensitive fluorescent probes that report membrane tension in living cells (Table 1). This strategy opens new avenues for correlating membrane tension with oxidative stress and redox state in real time within living cells.

Figure 1. Design of the three stabilizing ligands (COT, Trolox, and α-tocopherol) anchored to a common core.

Common core: Flipper-CN-Alkyne	**Head group:** Fmoc-Dab(N_3)-OH	**-R**
		**Probe 1:** Cyclooctatetraene-COOH 
	Linkage: Click (triazole)	**Probe 2:**Trolox 
		**Probe 3:** α-tocopherol-COOH 

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Anti-pollution molecular polymers

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***Keywords**: molecular polymers, π-π stacking, stereoisomers.*

The self-assembly of low-molecular-weight gelators (**LMWGs**) into 3D nanofibrillar networks represents a breakthrough in the design of *"smart"* materials for environmental remediation. Through non-covalent interactions, such as hydrogen bonding, π-π stacking, etc., these molecular polymers form gels capable of efficiently sequestering pollutants, including hydrocarbons, petroleum derivatives, and industrial dyes from water and soil. Despite their potential, practical implementation depends on overcoming some critical challenges, such as their adsorption capacity, selectivity, reversibility, biocompatibility and cost-efficiency.

This study explores how molecular design can address these barriers, providing a sustainable and high-performance alternative to traditional adsorbents in the global effort toward environmental restoration.

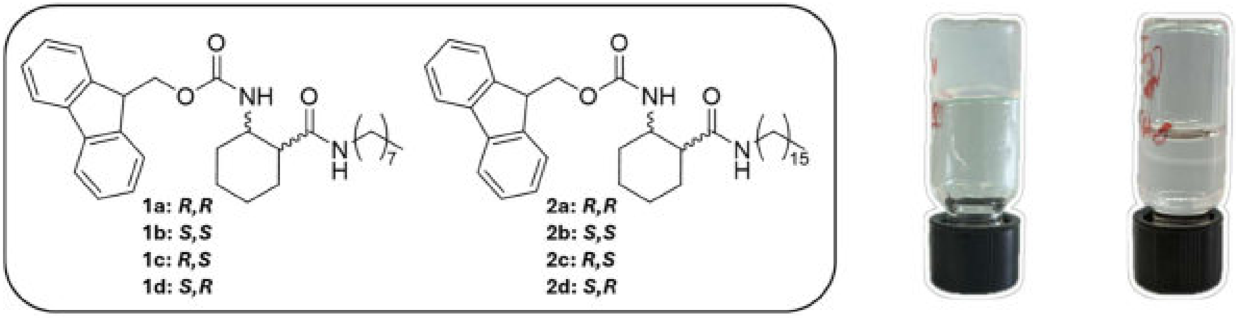

Figure 1: Representation of the different stereoisomers with an aliphatic chain of 8 and 16 carbon atoms (inside the box), and an example of a gelation test: below (left) and above (right) gelation limit.

This work focuses on the synthesis of a stereoisomeric family of alkylamide molecules (**1** and **2**) derived from 2-aminocyclohexanecarboxylic acids with the fluorenylmethoxycarbonyl (*Fmoc*) as protecting group to improved gelation promoted by π-π interactions.[1]

Furthermore, supramolecular studies on their structural organization in solution were carried out, along with the characterization of the resulting gels using a range of analytical techniques.[2]

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Synthesis of subporphyrazine-based fluorogenic probes for their activation under acidic pH

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Keywords: *subporphyrazines, pH, fluorogenic.*

Subporphyrazines (SubPzs) are contracted porphyrinoids composed of 3 pyrrole rings linked by aza bridges through their 2 and 5 positions. These compounds are 14 π-electron aromatic macrocycles with a conical shape and are only known as boron complexes due to their small central cavity.[1] Owing to the trigonal geometry of boron's orbitals, SubPzs contain an axial position on said central boron atom. Due to their unique structural features, SubPzs are highly versatile chromophores that give rise to highly tunable physical and chemical properties.[2,3] Thus, properties such as absorption, emission, and redox activity can be finely, or drastically adjusted, through peripheral functionalization of the macrocycle,[2,3,4] while axial functionalization can be used to introduce specific capabilities, such as hydrophilic, hydrophobic, amphiphilic, or targeted transport properties.[5] In this work, the synthesis and properties of SubPzs whose fluorescence can be switched on/off by the pH of the environment is described. To this end, the macrocycles are functionalized at their periphery with conjugated amine functions. Due to charge-transfer processes from the lone pair of the amine nitrogen atom to the macrocycle, the fluorescence properties of these compounds are quenched. However, protonation of the amine functionalities under acidic conditions is expected to suppress the charge-transfer ability of the nitrogen atoms, thereby activating the fluorescence of the SubPz. In order to enable the probe activation within cellular lysosomes, the basic amine functions are selected among aniline moieties with tabulated pK_a values ranging from 5.15 to 6.5. To enhance their biocompatibility, the SubPzs are also provided with a hydrophilic axial PEG ligand. The final goal is to evaluate the potential of these SubPzs as fluorogenic cellular markers and as optimized photosensitizers for PDT.

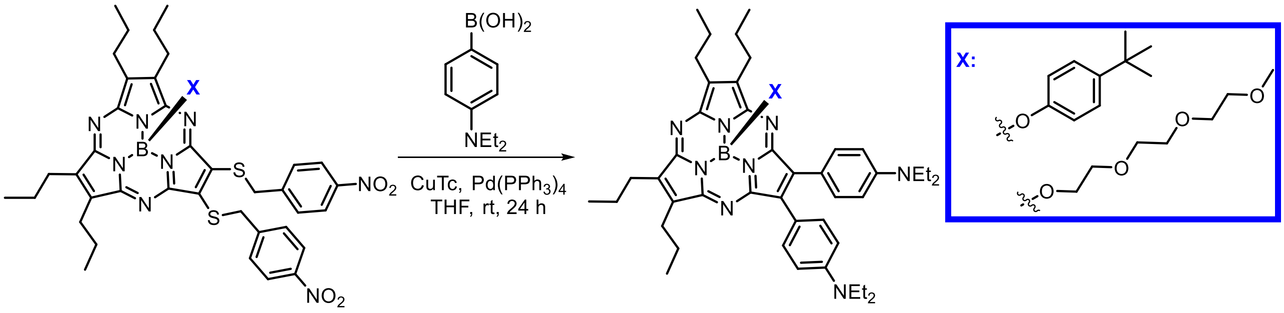

Figure 1. Synthetic procedure for the synthesis of the fluorogenic probes.

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Synthesis of molecular precursors for investigating selective unimolecular reactions

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Keywords: *On-surface science, acenes, AFM*

In recent years, the combination of organic chemistry and surface-science has enabled the visualization and manipulation of individual molecules with atomic precision, opening new opportunities in the fields of molecular electronics, nanotechnology, and artificial molecular machines. The development of suitable molecular precursors is essential for the development of this arising field of research. Recently, chlorinated acene derivatives such as **1** (Figure 1) have emerged as highly valuable precursors due to their ability to undergo selective voltage-induced transformations at the single molecule level.[1]

This project aims to expand the availability of molecular precursors derived from the tetrachloro-tetracene scaffold. With this aim, we prepared the brominated compound **3**. This compound provides direct access to tailored derivatives by using metal catalyzed cross coupling reactions. Concretely, the incorporation of ethynyl bridges enables the connection of two (**4**) or three tetrachloro-tetracene units while preserving a significant degree of electronic communication. The present work is developed as an international collaboration with the research group of Leo Gross (IBM Research Zürich), in the context of the ERC SyG MolDAM[2] (Diego Peña, Leo Gross, Jascha Repp. ID: 951519).

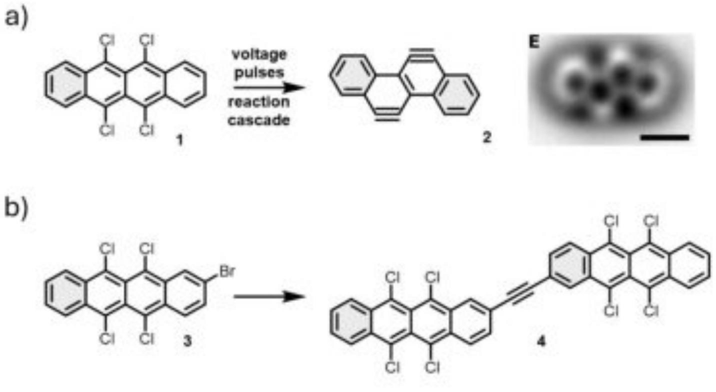

Figure 1. a) 5,6,11,12-tetrachlorotetracene (**1**) behaviour under voltage pulsage b) 2-bromo-5,6,11,12-tetrachlorotetracene (**3**) and derived dimeric structure (**4**).

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Chiral BODIPY G-Quadruplexes for Advanced Optoelectronics

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<u>Keywords</u>: *self-assembly, BODIPY, G-quadruplex.*

Molecular self-assembly enables the organization of molecules into well-defined structures through non-covalent interactions, such as hydrogen bonding, π-π stacking or electrostatic forces. Owing to their intrinsic reversibility and relative weakness compared to covalent bonds, these interactions permit the formation of dynamic supramolecular structures with adaptive functionalities. These features have paved the way for the development of supramolecular assemblies with applications in drug delivery, catalysis and electronics. In the latter field, π-conjugated systems are particularly attractive since their optoelectronic features can be significantly enhanced upon self-assembly compared to those exhibited by the discrete monomer unit.

The main aim of this project is the synthesis and characterization of discrete, chiral supramolecular assemblies with improved optoelectronic properties. Our strategy relies on the combination of guanosine (G) with the BODIPY dye.[1] Whereas the BODIPY scaffold showcase outstanding optoelectronic properties together with planarity, structural robustness and versatile functionalization sites, the G moiety provides the functional groups required to direct the selective and quantitative formation of well-defined supramolecular G-quadruplexes (G_4, G_8 or G_{12}) in the presence of alkali metal cations (Na^+ or K^+)[2]. Our approach is expected to afford dye-based G quadruplexes with enhanced chiroptical properties, including circularly polarized luminescence (CPL) and chiral induced spin selectivity (CISS) effect.

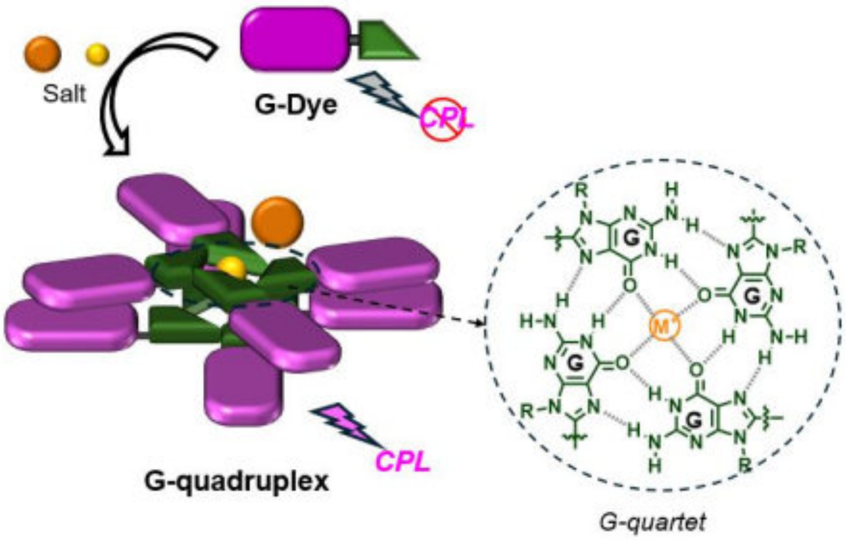

Figure 1. Schematic representation of G-quadruplex formation and subsequent CPL emission from the guanosine-BODIPY target molecule.

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Development and Optimization of the Schmidt Reaction on Flow Chemistry Platforms, Applied to the Preparation of Alkyl Lactams for Medicinal Chemistry

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***Keywords**: Schmidt, continuous flow, benzolactams.*

The Schmidt reaction provides atom-economical access to lactams from cyclic ketone precursors via acid-mediated transformation with hydrazoic acid and loss of N_2,[1] yet its application has been limited by the hazardous handling of HN_3 or alkyl azides.[2] To address this, we developed an optimized intermolecular Schmidt reaction of aryl-fused cyclic ketones using TMS-N_3 as a safe azide surrogate,[3] with explicit regioselectivity control at the key migration step (benzylic vs. homobenzylic). A multifactorial optimization approach, combining DoE and Bayesian optimization, was employed to rationally explore the reaction parameter space, identifying conditions that deliver 9:1 regioselectivity, 85% yield. These optimized conditions were subsequently translated to a continuous-flow platform, where precise independent control of temperature and residence time enabled consistent, scalable performance,[4] providing a robust and safe synthetic entry to benzolactam scaffolds of relevance to drug discovery programs.

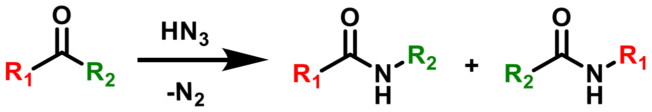

Figure 1. General representation of the Schmidt reaction between a ketone and hydrazoic acid.

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Pd-catalyzed regiodivergent access to benzocyclobutenes and indenes

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***Keywords**: regiodivergence, indenes, benzocyclobutenes.*

A fundamental goal in synthetic chemistry is the optimization of reaction conditions guided by the principles of green chemistry, such as atom economy, that is, maximizing the efficiency with which the reagents in a reaction are converted into products. In this context, regiodivergence is a powerful strategy, enabling a single substrate to yield different molecular entities through subtle variations in the reaction conditions. In metal- and organo-catalysis, regiodivergent transformations rely on the catalyst, ligand type/geometry, solvents and additives used to control the regioselectivity of each reaction. Representative examples of processes in which regiodivergence can be achieved include additions to unsaturated C-C bonds, (hetero)aromatic C-H activation reactions, cross-couplings and both intra- and intermolecular cyclizations.[1]

Typically, indenes have been synthesised via intramolecular Friedel-Crafts reactions or through Au, Rh and Pd catalysis,[2] whilst benzocyclobutenes (BCBs) have been accessed via [2+2] cycloadditions[3a] or carbene insertions.[3b] These structures, consisting of a benzene ring fused to a cyclopentene or cyclobutene ring respectively, are structurally simple, but fundamental, due to their widespread presence in natural[4a] and synthetic bioactive products[4b] and in materials science.[4c,d] In this work, based on our previous experience in the synthesis of *o*-allylbromobenzene derivatives and BCBs,[5] we present an unprecedented, regiodivergent, Pd-catalyzed process that allows the selective access to BCBs or indenes via modifications of the reaction conditions (Figure 1).

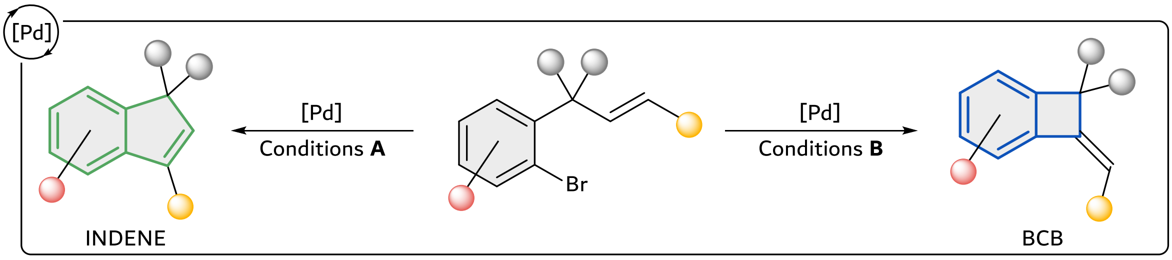

Figure 1. Regiodivergent synthesis of indenes and BCBs.

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Desing and Synthesis of hypoxia photoactivatable probes based on diazaxanthilidenes.

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***Keywords**: Diazaxanthilidenes, hypoxia, fluorescent sensors.*

Photoactivatable fluorescent probes are sensors that modify their emission upon light irradiation, typically classified as off/on systems (non-emissive to emissive) or photoconvertible on/on' systems (switching between two emissive states). These probes are highly valuable for biological studies, as they enable precise spatial and temporal control in fluorescence microscopy.[1] Recently, Chenoweth group described a new class of photoconvertible dyes based on a 1,1′-diazaxanthilidene (DXT) scaffold, undergoing a light-induced 6π electrocyclization/oxidation sequence that enables interconversion between two fluorescent states.[2]

In parallel, our group has initiated a collaboration with Chenoweth's group to develop novel photoactivatable systems derived from hypoxia-responsive probes. Hypoxia, a key feature of tumor progression, alters cellular redox balance, due to the lack of oxygen, and leads to overexpression of reductases such as azoreductases.[3] The detection of these enzymes by fluorescence bioimaging provides a non-invasive strategy for hypoxia sensing. In this context, our group previously developed hypoxia-activatable probes based on azo-BODIPY scaffolds.[4] Building on this work, we report the design and synthesis of two functionalized DXT derivatives that combine hypoxia-activated fluorescence with light-induced photoconversion, enabling dual-responsive probes for advanced bioimaging applications.

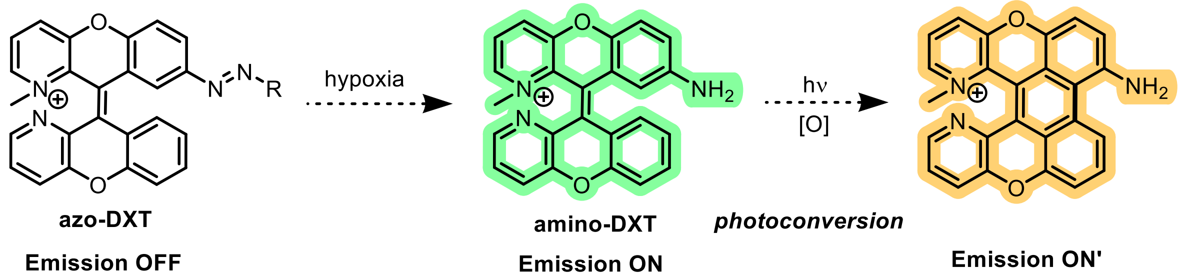

Figure 1. Off/On Hypoxia-activatable probe followed by on/on' photoconversion via a 6π electrocyclization/oxidation mechanism.

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Synthesis of Tetraphenylethene-Subporphyrazine (TPE-SubPz) conjugates for the visualization of SubPz columnar stacking.

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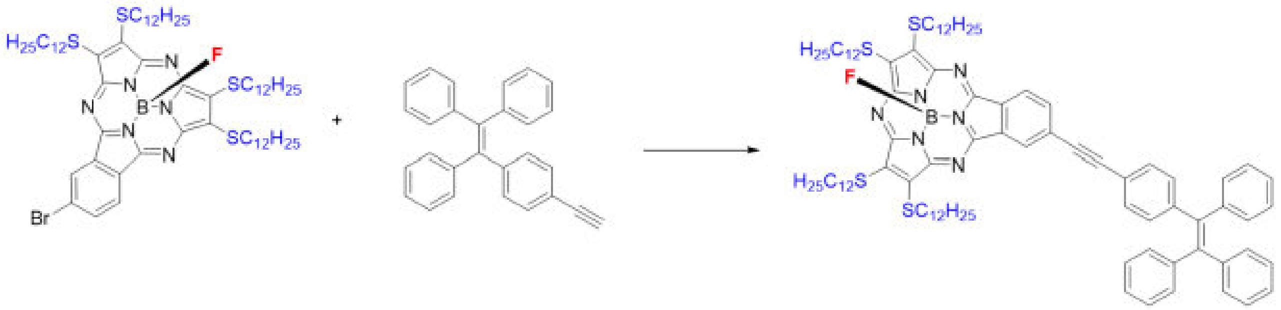
***Keywords**: subporphyrazines, tetraphenylethene, liquid crystals*

Subporphyrazines (SubPzs) are contracted porphyrinoids composed of three pyrrole units linked through aza bridges, featuring a 14 π-electron aromatic system and a characteristic non-planar, cone-shaped structure.[1,2] Owing to the presence of a central boron atom, SubPzs exhibit an axial position that, together with peripheral functionalization, enables fine tuning of their photophysical and redox properties. These features make them promising candidates for applications in photodynamic therapy (PDT), optical materials and photoresponsive systems.[2,3,4] Peripheral and axial functionalization with selected functions also enables their supramolecular organization into well-ordered structures, this constituting a useful tool to generate materials that provide enhanced properties related to their respective isolated molecules.[2,3] In this work, we are functionalizing a SubPz at one of the pyrrole units with the known tetraphenylethene AIEGEN moiety (TPE) (Scheme 1),[5] while the other two pyrroles bear long thioether chains, specifically selected to promote self-assembly of the SubPz macrocycle into columnar stacks with mesogenic behaviour.[1]

Scheme 1. Preparation of TPE-SubPz



The TPE-SubPz array is being constructed through Sonogashira coupling of ethynyl-TPE with an unsymmetric A_2B SubPz, bearing a bromine atom at the periphery. In the SubPz-TPE conjugate, molecular motions of the phenyl groups of TPE are expected to be effectively restricted upon SubPz columnar stacking, thereby activating the aggregation induced emission ability (AIE) properties of TPE.[5] As a result, we expect to monitor the SubPz self-assembly process by exploiting changes in the TPE fluorescence signal arising from its AIE properties.

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Enantio and Z-selective Cu-catalyzed allylic substitution of gem-diboryl alkenes

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***Keywords**: 1,1-diborylalkenes, copper, allylation*

1,1-Diborylalkenes are emerging as versatile bifunctional building blocks applied in the modular synthesis of complex molecules through boron-selective transformations. Chemoselective reactions on both geminal B-C(sp2)-B sites have attracted great research interest since they provide an efficient and flexible platform to construct molecular diversity.[1-5]

The presence of two geminal boryl moieties presents a significant challenge due to their closely similar reactivity. Consequently, achieving control over the E/Z selectivity constitutes a major obstacle in these transformations. Previous studies have reported only a limited number of methodologies for the selective synthesis of either the Z- or E-isomers, and to date, only a single example of a racemic Z-selective allylic substitution has been reported.[5]

We herein present the first methodology for the regio-, enantio and Z-selective allylic substitution of gem-diboryl alkenes. The method employs a chiral NHC-Cu complex as catalyst6 and affords synthetically versatile borylated 1,4-skipped dienes with good yields and excellent levels of selectivity

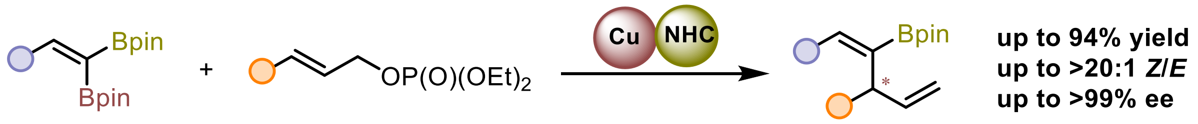

Figure 1. *Z*- and Enantioselective Cu-catalyzed allylic substitution of *gem*-diboryl alkenes

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Novel stapling methodologies to stabilize peptide extended conformation targeting MDM2-MDM4 interaction

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***Keywords**: Protein-protein interactions, Peptidomimetics, Stapling.*

The dysregulation of protein–protein interactions (PPIs) is implicated in numerous diseases, including cancer, making them therapeutic targets of considerable interest in biomedicine. However, the rational design of PPI modulators faces significant limitations as these interactions involve flat and extensive surfaces that hinder the development of effective small molecules. Peptides, by contrast, constitute a viable alternative, as they can span large interaction surfaces and adopt peptide secondary structure elements commonly involved in PPIs. Our interest is focused on the MDM2–MDM4 interaction, as it has been demonstrated that the C-terminal region of MDM4, which adopts an extended conformation, inhibits MDM2 and restores the pro-apoptotic function of p53 in certain tumor types, thus representing a relevant therapeutic target in cancer (Figure 1a).[1]

The objective of this work is to develop a stapling methodology to favor the extended conformation in peptides derived from the C-terminal region of MDM4. This strategy, based on the covalent linkage between side chains of a peptide to restrict its flexibility and promote a bioactive conformation, has been widely used to stabilize α-helices through crosslinks in *i* → *i*+4 or *i* → *i*+7 positions. Morerecently, this approach has been expanded to extended conformations through the *i* → *i*+2 pattern,in which the crosslinking between nearby residues imposes a more compact constrain that stabilizesspecific local geometries without inducing a helix.[2,3]

Starting from the native C-terminal sequence of MDM4, *i* → *i*+2 stapled peptides were designedby substituting two residues on the same face with amino acids bearing an alkyne group. Thepeptides were synthesized by automated solid-phase synthesis. For stapling, both oxidative couplingof the Glaser-type and two-component copper-catalyzed azide-alkyne cycloaddition (CuAAC) wereexplored, using a small library of diazide linkers (Figure 1b). The conformation of the resulting cyclicpeptides was analyzed by NMR and molecular modeling. In parallel, the optimal stapling positionand linker for binding with MDM2 were evaluated by molecular docking.

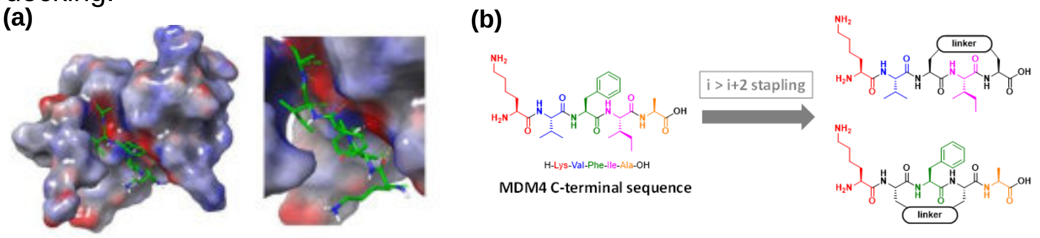

Figure 1. (a) Binding mode of C-terminal MDM4 peptide and MDM2 (adapted from PDB: 2VJF; (b) *i* > *i*+2 stapling as a novel strategy for the development of high-affinity peptides targeting MDM2.

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New molecules for Alzheimer's disease therapy

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***Keywords**: Alzheimer’s disease, Synthesis, Compound F*

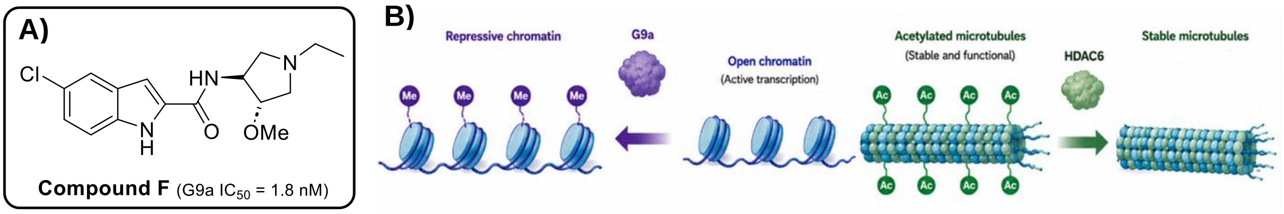
Alzheimer's disease (AD) is a neurodegenerative pathology that causes the deterioration of the central nervous system (CNS) due to the malfunctioning of some parts of the brain such as the hippocampus and the cortex, which leads to the loss of memory and the main cognitive functions.[1] The possible pathological causes of AD are based on the aggregation of some specific CNS proteins, such as β-amyloid peptide, or the hyperphosphorylation of tau protein, which cause the appearance of senile plaques and neurofibrillary tangles, respectively.[2] These extracellular deposits cause the progressive death of neurons and the loss of synaptic connections between them.[1]

AD is a multifactorial disease in which different biological targets are involved, that is why the identification and synthesis of multipotent molecules capable of acting on these biological targets simultaneously it is a strategy that is being widely studied.[2]

In this context, the histone lysine methyltransferase enzyme (G9a) establishes repressive chromatin states through the methylation of histone H3 at lysine 9 residues. (Figure 1B).[3] Dr. Griñán-Ferré's group has identified **compound F** as a potent inhibitor of G9a (Figure 1A),[4] showing promising results *in vivo* trials. This molecule not only crosses the blood-brain barrier but also prevents the methylation of histone H3 and reduces the concentration of β-amyloid plaques.[4]

On the other hand, histone deacetylases enzymes (HDACs), destabilize microtubule formation through deacetylation reactions of histone and non-histone substrates, affecting the DNA transcription and mitochondrial transport (Figure 1B).[3]

In this project we have designed a small molecule analogous to **compound F**, capable of simultaneously interact with different therapeutic targets involved in AD, such as G9a and HDAC. In this way, the isolation and characterization of the intermediates compounds is being carried out as well as the optimization of the protocols and strategies necessary for its obtainment.



Compound F (G9a IC_{50} = 1.8 nM)

Figure 1. A) Chemical structure of **compound F**. B) G9a methylation reaction on histone H3 at lysine 9 residues (left) and HDAC deacetylation reaction (right).

Finally, once this route is completed and the target molecule is synthesized, its pharmacological activity will be analyzed through *in vitro* and *in vivo* assays with the aim of identify a new molecule showing diverse and improved activity for the possible therapy of AD.

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Photocatalytic functionalization of propane under blue light

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***Keywords**: C–H bond functionalization, gaseous alkanes, photocatalysis*

Gaseous alkanes are one of the most abundant carbon-based feedstocks, with an annual production of 4 trillion m^3 per year (natural gas). However, due to their low reactivity, they remain highly underutilized. Currently, they are primarily used as fuel (for heating, propulsion or electricity generation) and in industrial processes such as steam cracking. These applications raise significant environmental concerns, as they are highly energy-intensive and lead to substantial greenhouse gas emissions. As a result, the development of novel protocols that allow the utilization of gaseous alkanes as alkylating agents is crucial.[1]

Oxime functional groups are found in many biologically active compounds and are excellent starting materials for a range of important transformations.[2] Nevertheless, the alkylation of oximes remains relatively unexplored. The few existing reports employ a C–H bond functionalization approach but tend to rely on the use of harsh UV-light irradiation and are limited to liquid alkanes and metal-based photocatalyst.[3] Alternative methodologies have been developed using different Hydrogen Atom Transfer (HAT) agents, such as pyridine *N*-oxides and DABCO derivatives.[4] Despite these advantages, the use of light gaseous alkanes, such as methane, ethane, propane, as alkylating reagents remains challenging.

In this regard, we hereby report a metal-free alkylation of oxime ethers using propane under visible-light (blue) irradiation (figure 1). This transformation provides the alkylated oximes in good yields with high regioselectivities. Notably, the reaction conditions favor the selective functionalization of the secondary C–H bond, despite its lower statistical abundance.

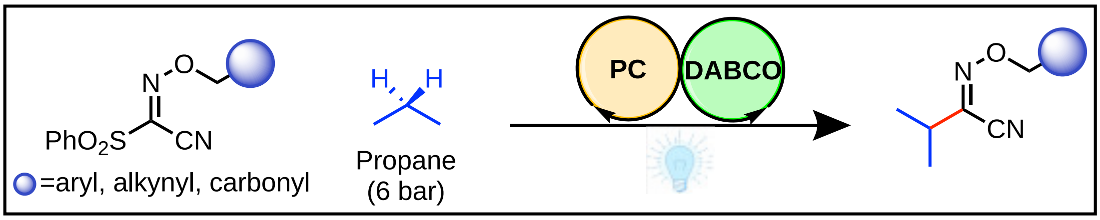

Figure 1. photocatalytic functionalization of propane under blue light.

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Multivalent Glycofullerene-Porphyrin Platforms for Targeted Photodynamic Cancer Therapy

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Keywords: *porphyrins, glycofullerenes, photodynamic therapy (PDT).*

Cancer is one of the leading causes of death worldwide, motivating the development of new therapeutic strategies within nanomedicine. In this context, porphyrins are promising biocompatible photosensitizers for non-invasive photodynamic therapy (PDT) due to their physicochemical properties. Furthermore, our group is pioneer in the development of carbon-based nanostructures based in glycosylated [60]fullerene, which have shown potential as antiviral agents due to their multivalent nature, enabling high-affinity interactions with cell membrane proteins.[1] In parallel, carbohydrate-functionalize [60]fullerene hexaadducts are also emerging as nanoplatforms for enhanced tumor targeting and cellular uptake by taking advantage of the overexpression of glucose transporters (GLUTs) on cancer cell membranes.[2]

Herein, we report the design and synthesis of a multivalent porphyrin platform functionalized with two glucose-bearing glycofullerenes for PDT applications. The porphyrinic core serves as the photosensitizing unit, while the carbohydrate moieties promote selective cancer cells targeting.

Ongoing work explores an asymmetric porphyrin bearing both a glycofullerene and a boron cluster for combined PDT and boron neutron capture therapy (BNCT), which could provide a synergistic multimodal therapeutic approach for improved cancer treatment.[3]

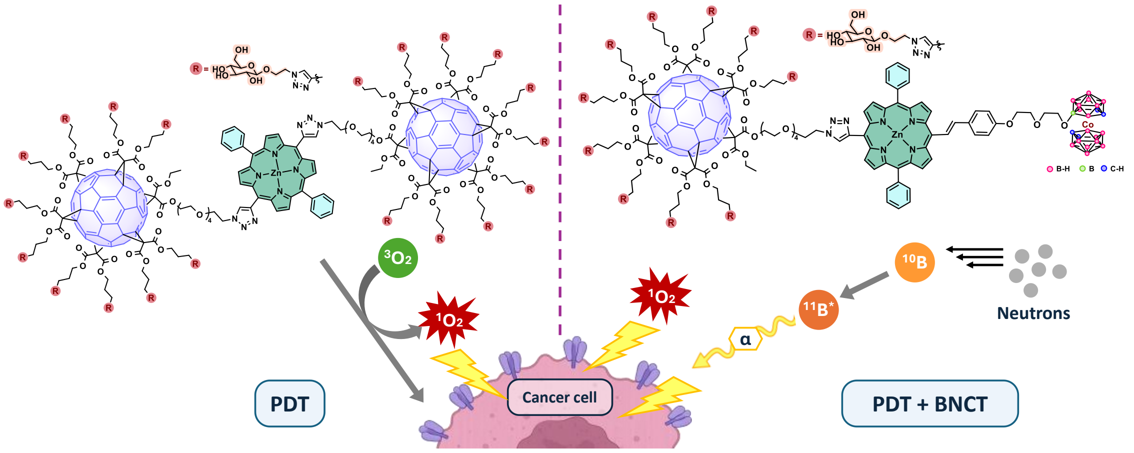

Figure 1. Multivalent porphyrin platforms functionalized with either two glycofullerenes (left) or combining glycofullerene with boron clusters (right), and their biological applications in cancer therapy.

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Superchaotropic Boron Clusters for Antibiotic Delivery Across Gram-Negative Bacterial Membranes

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Keywords: *Boron cluster, superchaotropicity, antibiotic resistance.*

Recently, superchaotropic boron clusters have emerged as one of the most promising transmembrane carriers, as an alternative to conventional amphiphilic delivery systems.[1] Their superchaotropic nature facilitates the translocation of diverse hydrophilic cargoes across lipid bilayers by promoting their desolvation. Unlike amphiphilic systems, these boron-based carriers can cross the lipid bilayers and release the molecules within the intracellular environment without compromising the structural integrity of the membrane and the cargo.[2]

Inspired by the behavior of boron clusters, this work explores whether superchaotropic carriers could extend the use of antibiotics that are only active against Gram-positive bacteria, enabling activity against Gram-negative pathogens with a double-membrane barrier. This could be an alternative strategy for the development of new antibiotic treatments due to the increasing bacterial resistance worldwide.[3]

This work presents the design and synthesis of a novel boron cluster platform based on the anionic dodecaborate cluster $[B_{12}H_{12}]^{2-}$ (Figure 1.A). To achieve this, we developed a strategy based on the orthogonal conjugation of the boron cluster with specific antibiotics such as Novobiocin (Figure 1.B) and Erythromycin (Figure 1.C) which are only active against Gram-positive bacteria. This process involves the chemical modification of the boron cluster and the selective functionalization of the antibiotics, yielding antibiotic–cluster conjugates for biological evaluation against Gram-negative infections.

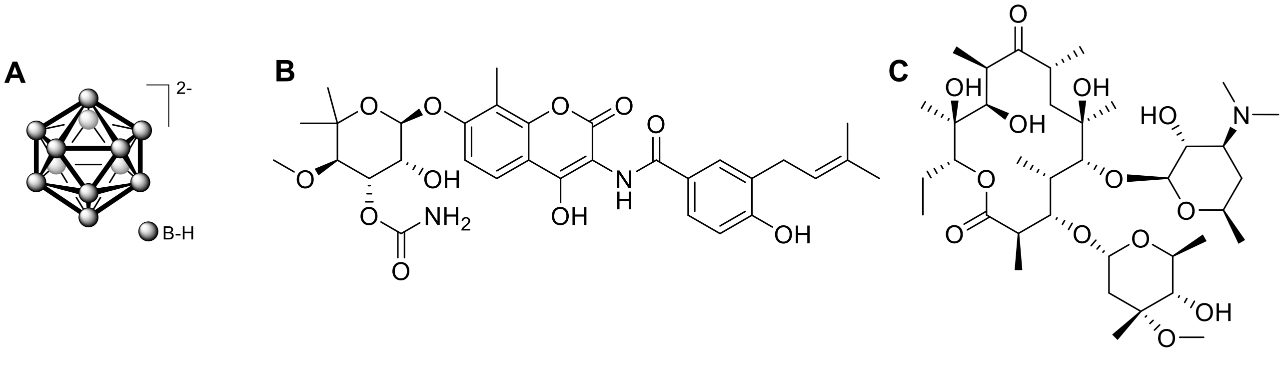

Figure 1. (A) Spatial structure of dodecaborate cluster $[B_{12}H_{12}]^{2-}$. (B) Chemical structure of the antibiotic agent Novobiocin. (C) Chemical structure of the antibiotic agent Erythromycin.

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Dominance of Atropisomerism over Point Chirality in the Self-Assembly of Arylene Diimides

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Keywords: *Point chirality; arylene diimides; self-assembly*

Chirality plays a fundamental role in molecular and supramolecular systems, affecting properties that range from catalysis to chiroptical response. Although point chirality has long been regarded as the primary determinant of supramolecular organization, growing evidence suggests that other forms of chirality-especially atropisomerism-may exert a dominant influence of self-assembly processes. These findings underscore the importance of disentangling the individual contributions of different chiral elements to enable the rational design of functional materials.[1,2] Herein, we report the synthesis of arylene diimides (**1**, Figure 1) decorated with peripheral chiral trialkoxybenzamide benzamide units.[3] The synthesis of these arylene diimides yields a mixture of two atropisomers (*M, M* and *P,P*) and a meso form (*M,P*) that can be separated by using chiral HPLC. Variable temperature ^{1}H NMR studies were initially performed as illustrated in Figure 1b. The amide functional group exhibited a downfield shift as the temperature increases, indicating the formation of pseudocycle through an intramolecular hydrogen bond. Futhermore, preliminary variable-concentration studies revealed the formation of a supramolecular polymer. The self-assembling and chiroptical features of these disatereomers will be presented to provide key insights into the hierarchical chiral organization of such chiral units.

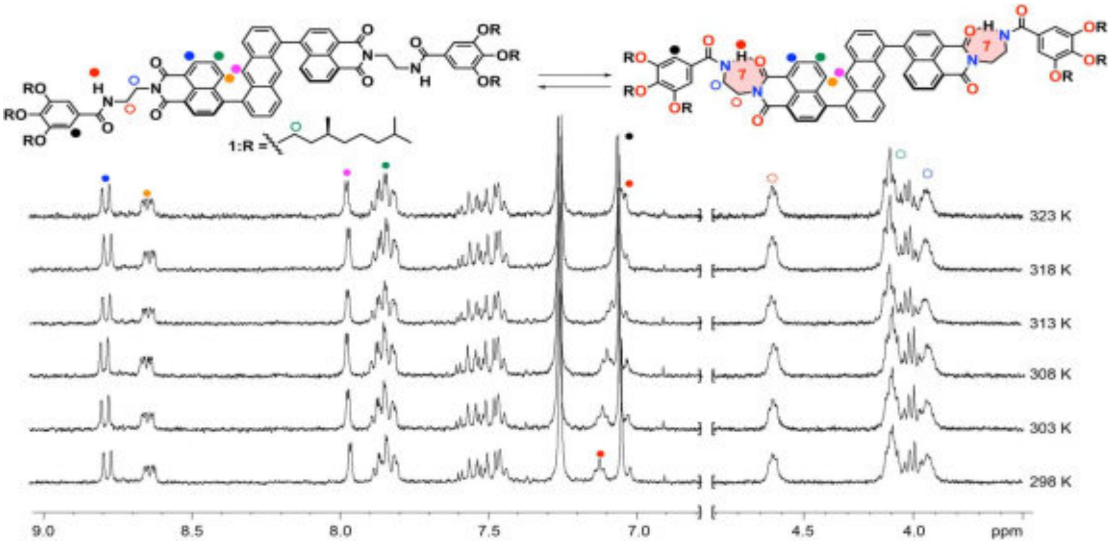

Figure 1. Chemical structure of arylene diimides **1** and partial VT ^{1}H NMR spectra of **1** showing the changes in the aromatic protons upon heating (1mM; $CDCl_3$; 700 MHz).

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Synthesis of multivalent carbon nanostructures–BODIPY glycoconjugates: a versatile platform for nanomedicine

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***Keywords**: carbon-nanomaterials, BODIPY, nanomedicine.*

The modification of the physicochemical properties of carbon-based nanostructures such as fullerenes and carbon nanoparticles through versatile functionalization strategies has significantly expanded their potential in nanomedicine. Carbon dots and fullerenes are zero-dimensional carbon nanomaterials, which have demonstrated excellent properties such as biocompatibility, high surface area and functional versatility.[1] Previous studies from our research group have shown that they can interact selectively with lectins highlighting their potential as antiviral materials.[2]

In recent years, there has been a growing interest in the development of methods to analyse the interactions between carbohydrates and their receptors. Among these strategies, the use of fluorescent biomarkers has been established as a useful tool for biosensing. In particular, BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene) derivatives have stood out due to their versatility and excellent optical properties.[3]

In this context, we aim to synthesize multivalent carbon nanostructures combined with BODIPYs and glucose, which represent an innovative strategy for the development of functional systems for nanobiotechnology. By combining the biocompatibility and abundant surface functional groups of carbon-based nanomaterials with the outstanding photophysical properties of BODIPYs, together with the cancer-cell selectivity and biocompatibility imparted by glucose units, a new family of materials is being developed for applications in diagnostics, targeted therapy and biosensing.

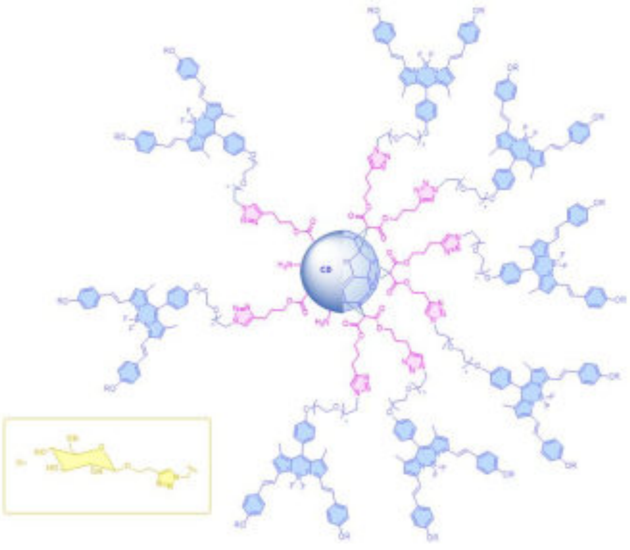

Figure 1. Carbon nanostructures–BODIPY glycoconjugates.

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o-Hydroxycarborane-Based Design of Vitamin D Receptor Agonists

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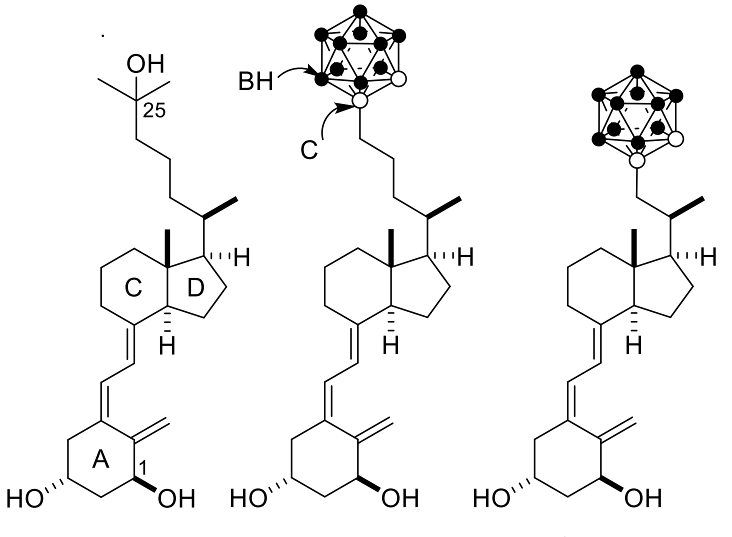
***Keywords**: 1,25 D3, carborane analogues, VDR*

Vitamin D_3, before eliciting its physiological functions, undergoes two hydroxylations, first in the liver and then in the kidney, to produce 1a,25-dihydroxyvitamin D_3 (1,25D_3, Fig. 1) which is the biologically active form of vitamin D_3. This secosteroidal hormone, through binding to the vitamin D receptor (VDR), regulates several physiological processes including calcium homeostasis, cell proliferation and differentiation, and immunomodulation.[1] Recent research has been devoted to the development of 1,25D_3 analogues with selective effects for medical use and some of them have already found clinical application.[2] We previously synthesized compound **2** (Figure 1) as the the first secosteroidal analogue of vitamin D_3, which contains an ortho-carborane unit at the side chain.[3] In comparison with the natural hormone 1,25D_3, the analogue **2**, which lacks the side-chain-C25-OH group, binds strongly to the VDR and induces similar biological activities though with reduced toxic calcemic effects. The carborane unit mimics the interaction of the side-chain-C25-OH of 1,25D_3 with the VDR and presents additional hydrophobic contacts between the boron atoms and important residues of the H12 helix. More recently we have discovered carborane analogue **3** as an antagonist of the VDR. It binds strongly to VDR preventing binding to 1,25D3. Therefore, compound **3** is of potential interest for treatment of hypercalcemic diseases such as Crohn's disease, sarcoidosis, and Paget's disease.



1 (1,25D_3) **2** **3**

Figure 1. Structures of the 1.25D3, *o*-Carborane analogue **2**, *o*-Carborane analogue **3**

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Synthesis of novel chiral gold (III) complexes via reaction with alkylidenecyclopropanes

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***Keywords**: Alkylidenecyclopropanes, C-H Activation, Au(III) carbophilic catalysts.*

Organometallic catalysis is a cornerstone of chemical synthesis, facilitating a wide array of transformations with excellent selectivity and efficiency. Historically, the most representative transition metals have been Pd, Ni, Rh, or Ru. In contrast, Au complexes were long ignored, partly because they were considered inert. This situation changed at the beginning of the century with the discovery that gold and platinum salts could act as carbophilic catalysts and activate π-bonds of unsaturated substrates. These metals offer ligand tunability, air and moisture tolerance and redox stability.[1]

Within this scenario, alkylidenecyclopropanes (ACPs), the combination of a highly strained cyclopropane ring and a C=C double bond, have emerged as compounds of great relevance in organic synthesis due to their easy access and high reactivity. That makes them especially likely to undergo transition metal-promoted transformations. In this context, while gold(I) complexes are generally limited to coordinating to pyridine-ACP ligands, gold(III) salts are capable of triggering ring-opening processes.[2] In particular, our group discovered that the activation of ACPs bearing an ortho-pyridine directing group with gold(III) salts delivers differe intriguing zwitterionic carboauracycles (Figure 1), featuring C(sp^2)-Au-C(sp^3) bonds.[3] These compounds have proven to be highly efficient catalysts for the functionalization of alkenes.

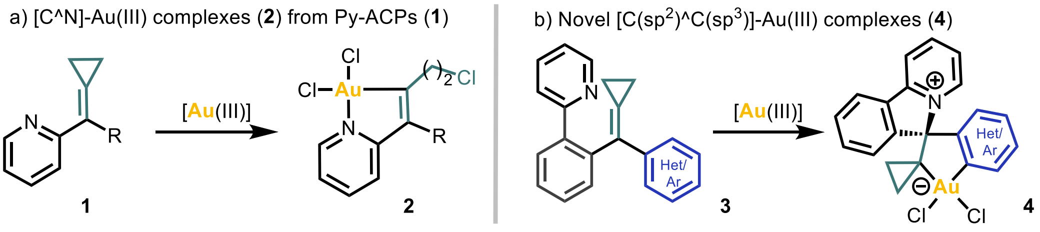

Figure 1. Synthesis of new gold complexes (III).[2,3]

In this context, the main goal of the project is expanding the development of chiral variants of these catalysts, introducing a chiral group at the ortho position of the pyridine moiety. In the current TFM work, several precursors were synthesized and their reactions with Au(III) salt, en route to the desired chiral carboauracycles have been performed.

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Design of Tumour Responsive Cleavable Linkers for Selective Drug Release

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***Keywords**: antibody-drug conjugates, self-immolative linker, Beckmann fragmentation.*

Antibody-drug conjugates (ADCs) are an advanced class of targeted cancer therapeutics that combine the tumour-targeting selectivity of monoclonal antibodies with the potency of highly cytotoxic payloads. Their efficacy critically depends on the chemical linker, which must ensure high circulatory stability while enabling efficient intracellular payload release upon internalization. This efficient intracellular relies on the incorporation of self-immolative spacers into the linkers, which undergo spontaneous and irreversible fragmentation upon activation by specific biological triggers.[1]

Current self-immolative systems are predominantly based on *p*-aminobenzyl carbamate scaffolds and related aromatic frameworks, which release the payload through 1,6-elimination cascades, as shown in Figure 1.[2] In this work, we explore the Beckmann fragmentation as a novel self-immolative trigger, building on previous work from our group on Grob fragmentation in 1,3-aminocyclohexanol systems.[3]

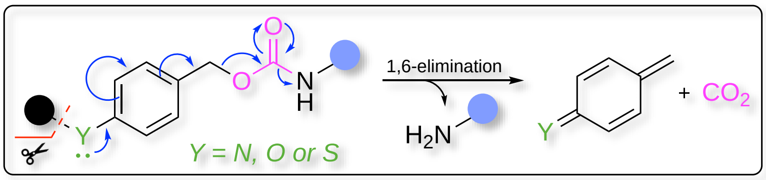

Figure 1. Self-immolative linkers based on electronic cascades.

In a similar manner, the Beckmann fragmentation can be triggered by the presence of the heteroatom bearing a free lone pair which promotes the anti-periplanar heterolytic C–C bond cleavage, generating a nitrile, an iminium ion and the free payload, as outlined in Figure 2.[4] Herein, we report the rational design and synthesis of novel Beckmann fragmentation-based spacers as modular building blocks for targeted delivery systems, thereby enabling new strategies for controlled payload release.

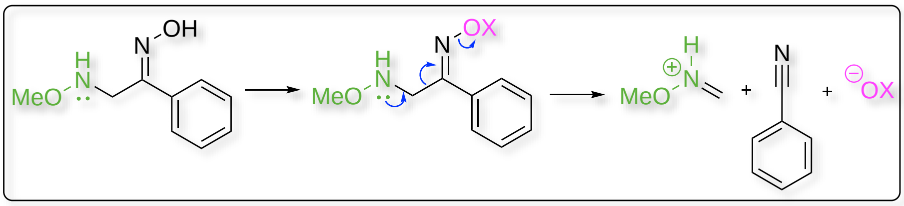

Figure 2. Beckmann fragmentation.

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Synthesis and evaluation of glutamate receptor antagonists to study the neurochemistry of the brain.

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***Keywords**: glutamate, GABA, receptors.*

Understanding how the human brain works remains a major scientific challenge, particularly in explaining how neuronal signaling gives rise to cognition and behavior. A key factor is the balance between excitatory and inhibitory activity,[1] primarily mediated by glutamate and γ-aminobutyric acid (GABA), the principal excitatory and inhibitory neurotransmitters, respectively. Studying the distribution of their receptors is essential for uncovering the neural basis of brain function, the mechanisms of neuronal signaling involved in sensory, cognitive, and behavioral processes, and the pathophysiology of numerous neurological and psychiatric disorders.[2]

Here we report the synthesis and evaluation of glutamate receptor antagonists as potential modulators of glutamatergic activity. We have synthesized 2,3-quinoxalinedione derivatives presenting bifunctional linkers for labelling with fluorophores and magnetic nanoparticles for imaging.

In parallel, we have attempted the heterologous expression in *Escherichia coli.* of a soluble glutamate receptor using the ligand-binding domain of the ionotropic kainate glutamate receptor GluR5, which plays a key role in regulating synaptic transmission. Finally, we are optimizing *in vitro* methods for validating the binding to glutamate receptors (Figure 1).

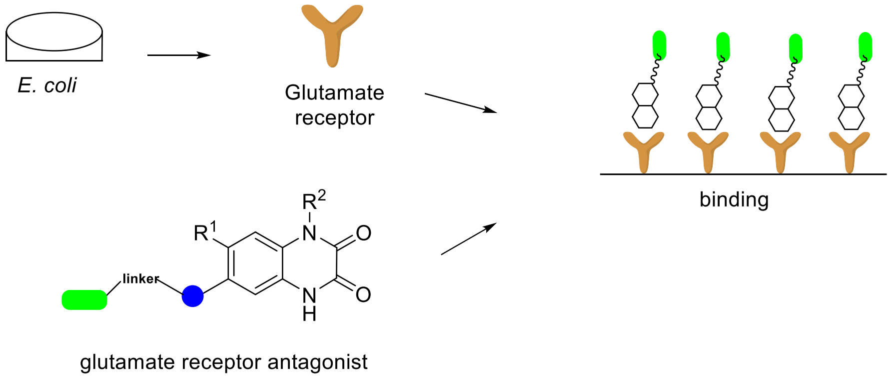

Figure 1. Scheme of the glutamate receptor antagonist structure and binding to the receptors.

All together, these efforts represent a step forward in our understanding of glutamatergic function in the human brain, as well as the development of novel pharmacological tools aimed at the treatment of glutamate-related brain disorders, as it plays an essential role in facilitating rapid neurotransmission and synaptic plasticity.

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Organic Reticular Chemistry: New Synthetic Routes for Functional Materials

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***Keywords**: covalent organic frameworks, post-synthetic modification, fluorophore.*

Covalent organic frameworks (COFs) are a type of crystalline porous materials formed by reticulating organic units into ordered two-dimensional (2D) or three-dimensional (3D) networks via covalent bonds. This enables the creation of permanent pores of a specific size and the integration of desired building units or active sites into the pores of these periodically ordered structures. Thus, COFs have great potential in photocatalysis, biomedicine, energy conversion, water purification or sensing due to their large surface area, high chemical stability and wide range of pore functionalization.[1]
This work focuses on the synthesis of a COF based on the monomers 1,3,5-tris(4-aminophenyl)-benzene, 2,5-dimethoxyterephthalaldehyde, and 2,5-bis(2-azidoethoxy) terephthalaldehyde.[2] This COF contains azide moieties within its pores, which will subsequently be used for post-synthetic modification via click chemistry with rhodamine B and fluorescein alkyne derivates. Moreover, the COF is obtained in the form of nanospheres, which facilitates its dispersion in organic solvents for subsequent deposition onto surfaces.[3] Thus, this work opens the way to new COF-based sensors harnessing the pH-dependent luminescence properties of the fluorophores.

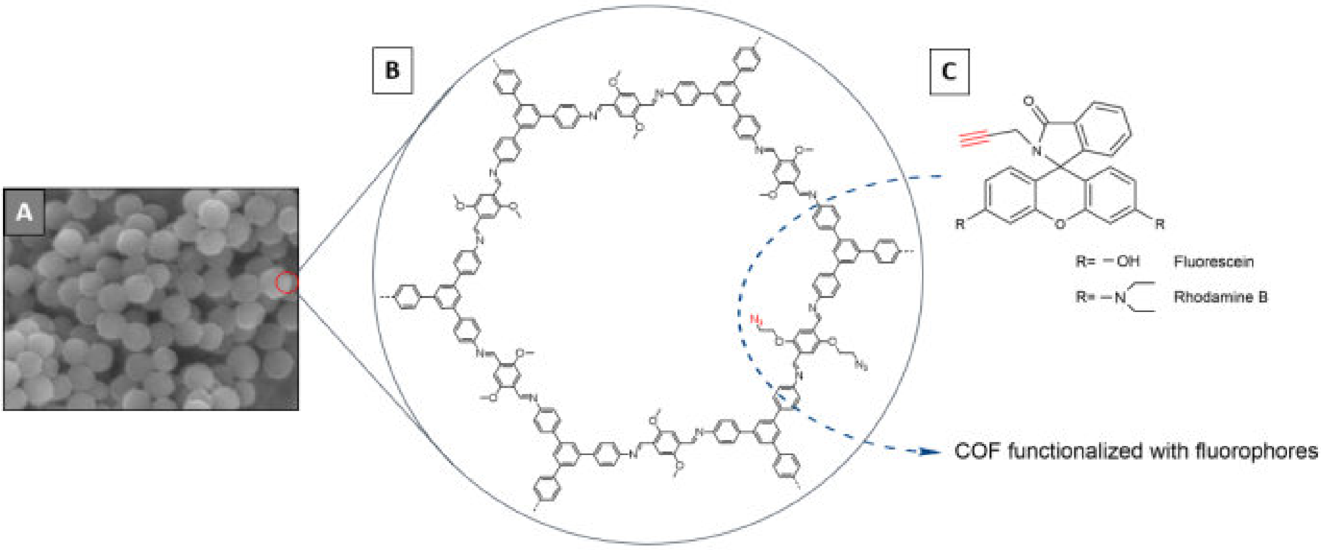

Figure 1. (A) SEM image of the COF nanospheres morphology, (B) chemical structure of the COF functionalized with azide moieties, (C) structure of the fluorophore alkyne derivates.

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Synthesis and resolution of [7]-helicene derivatives linked to chromophores

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Keywords: *chirality, helicenes, dyes.*

Helicenes are nonplanar molecules with a helical structure containing more than four ortho-fused aromatic rings.[1] Chromophores such as subphthalocyanines (SubPcs) and perylene monoimides (PMIs) are π-conjugated systems exhibiting notable optical and electronic properties, including strong light absorption and intense fluorescence emission. The combination of those chromophores with helicenes enables the integration of optoelectronic properties with chirality-induced features.[1,2] Previously SubPcs-[5]-helicenes prepared in our group did not show a fixed configuration and underwent racemization over time (Figure 1a). Therefore, the aim of this work consists on the preparation of new chiral chromophores linked to a [7]-helicene subunit to achieve a configurationally stable molecules with a stable helical chirality. The proposed synthetic strategy involves a Suzuki-type coupling between a boronic-SubPc or PMI derivatives and a Br-substituted [7]-helicene.[3]

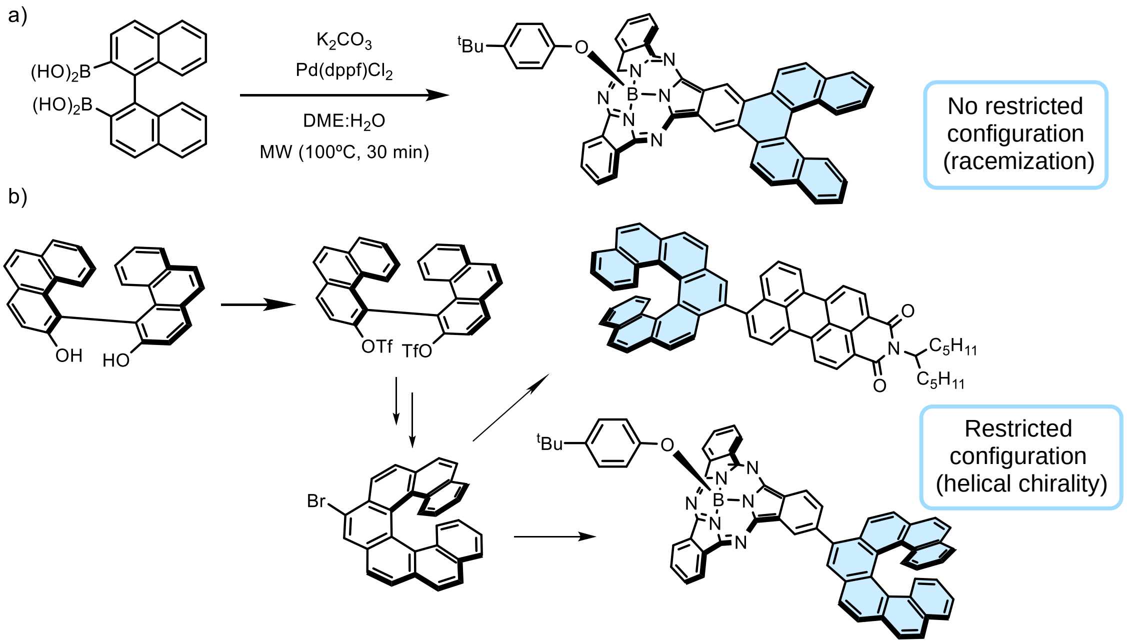

Figure 1. a) Subphtalocyanine fused [5]-helicene previously prepared in the group. b) Synthetic route of Subphtalocyanine and perylene monoimides linked to a [7]-helicene.

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Expanding the Scope of BODIPYs:
Approaching Water-Soluble CPL-active Small Organic Molecules

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***Keywords**: BODIPY, circularly polarized luminescence, water-soluble*

The development of small organic molecules that efficiently enable circularly polarized luminescence (CPL-SOMs) has gained significant interest in recent years.[1] This is due to the key advantages derived from their organic nature (e.g., synthetic versatility, photonic tunability, and access to flexible, lightweight materials) and small size (e.g., atom economy and membrane permeability), along with the unique properties of circularly polarized light, such as higher resolution and chiral character.[2] Such molecules are essential for the advancement of next-generation photonic organic materials and chiroptical technologies, ranging from high-performance CP-OLEDs to advanced bioprobes for emerging CPL bioimaging.[3,4] In this context, certain chiral BODIPYs (boron-dipyrromethenes) stand out due to their ready access in enantiopure form, fine tunability, and CPL efficiency.[5] Unfortunately, CPL-SOMs that work efficiently in water solutions have been scarcely reported,[6] despite the clear interest in advancing specific CPL-based applications, such as subcellular CPL imaging or sustainable CP-OLED illumination. In this communication, we report preliminary results on the development of water-soluble, CPL-active BODIPYs that combine synthetic accessibility, tunable emission spanning from blue to red, and high CPL brightness.

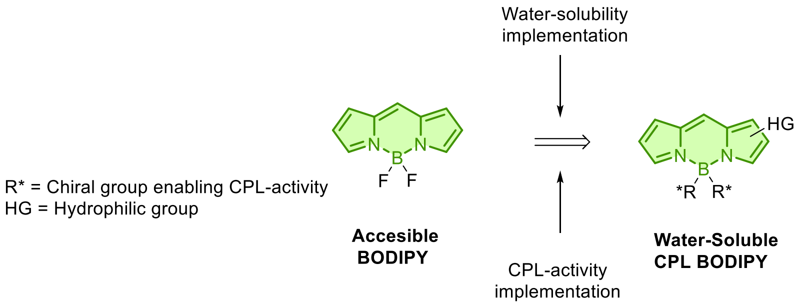

Figure 1. Structural modification of the BODIPY core for CPL induction and aqueous solubility

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Relevance of Thioester Chemistry for the Origin of Metabolism

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Keywords: *Prebiotic, thioester, acetyl-CoA.*

Prebiotic chemistry aims to understand how simple molecules could give rise to increasingly complex chemical systems under primitive Earth conditions. One of the central objectives of this field is to determine and explain how primitive networks could have emerged and functioned in the absence of enzymes. Some of the systems proposed as potential protometabolic candidates are the glyoxylate cycle and the tricarboxylic acid cycle [1], due to their ability to generate biomolecules of high biosynthetic value from simple molecules. In parallel, thioesters appear in this scenario as energy-rich molecules that could have played an important role in the emergence of these systems, acting as analogues of complex cofactors such as coenzyme A. Plausible prebiotic syntheses of these sulfur-based analogues have already been reported.[2, 3]

In this work, several thioesters were synthesized through organic methods in order to study their stability in aqueous media.[2] The kinetic study of the hydrolysis reactions of these thioesters helps us to understand their behaviour and why biology selected them as important and more complex substrates in different systems. Furthermore, we report a non-enzymatic reaction between glyoxylate and an acetyl-CoA derivative to reproduce one of the key steps of the glyoxylate cycle. An exhaustive screening was carried out to determine the optimal temperature and pH conditions, taking into account both conversion and the possible hydrolysis of the acetyl-CoA reactant. This discovery supports the theory that thioesters could have been key intermediates in the emergence of the first metabolic networks.

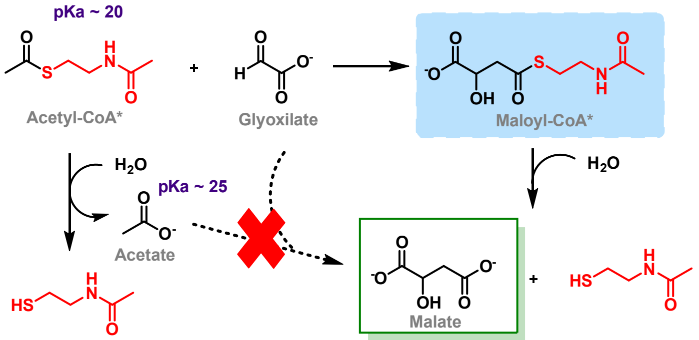

Figure 1. *Reaction between an acetyl-CoA analogue and glyoxylate to yield malate through a thioester intermediate.*

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Synthesis of Organic Compounds with Pharmacological Applications

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Keywords: *PET, BODIPY, aminophosphonation*

Molecular imaging plays a central role in medicinal chemistry for the study of disease-related processes at the molecular level. Among the available techniques, Positron Emission Tomography (PET) provides high sensitivity and quantitative whole-body imaging, while fluorescence imaging offers high spatial resolution and real-time detection at the cellular level.[1] The development of chemically distinct probes for each modality enables independent optimization toward specific biological targets and functions.

Our research group has identified oxindole-based structures as compounds with high selectivity and affinity for hyperphosphorylated tau, a key biomarker associated with neurodegenerative disorders, like Alzehimer or Parkinson.[2] This work focuses on the design and synthesis of an oxindole-based molecule that will be further functionalized with fluorine-18 to generate a PET radiotracer for the *in vivo* evaluation of tau pathology (**Figure 1a**).[3]

In parallel, we investigate the chemical modification of BODIPY derivatives through aminophosphonation reactions to modulate their photophysical properties.[4,5] Although BODIPY dyes are intrinsically characterized by high fluorescence quantum yields and photostability, the introduction of amino and phosphonate functionalities provides a strategy to fine-tune their electronic structure, potentially enhancing brightness, spectral behavior, and functional versatility (**Figure 1b**).

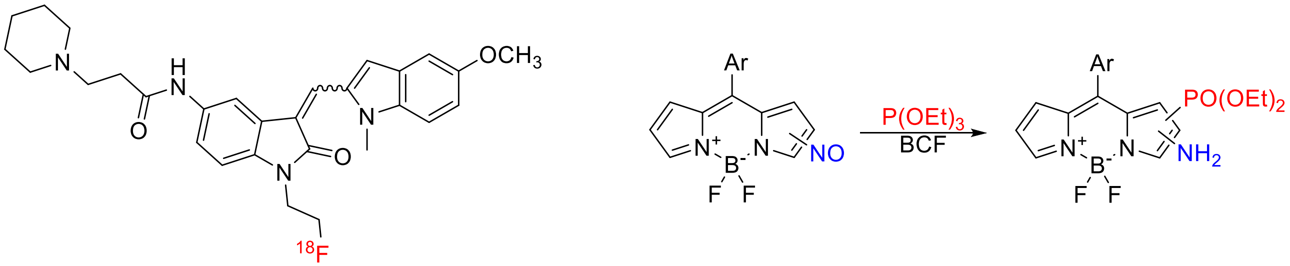

Figure 1a

Figure 1b

Figure 1. a) Synthesis of oxindole derivative for PET. **b)** Aminophoshonation of BODIPY derivatives.

References: (Arial 9, with 12 pts line spacing) **(Please do not insert references with the automatic tool nor in the footer)**

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Development of cannabidiol-based PROTACs

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***Keywords**: Cannabidiol (CBD), Molecular targets, Proteolysis targeting chimeras (PROTACs).*

Cannabidiol (CBD) is one of the most abundant phytocannabinoids found in the *Cannabis sativa* plant and it is known for exhibiting antitumor, anti-inflammatory, antioxidative and neuroprotective properties while being non-psychoactive.[1] Although some CBD-based drugs (Epidiolex®, Sativex®) have been currently approved for the treatment of certain neurological disorders, its molecular targets and specific mechanisms are yet to be fully elucidated.[1,2]

In this context, our research group has initiated a project focused on the identification of the molecular targets of CBD employing targeted protein degradation profiling, a method that combines the use of proteolysis targeting chimeras (PROTACs) with quantitative proteomics analysis.[3] A PROTAC is a heterobifunctional small molecule consisting of three elements: a ligand that binds to the protein of interest, a moiety responsible for the recruitment of an E3 ubiquitin ligase and a linker that connects these two moieties.[4] After administration, the PROTAC binds to its targets and marks them for degradation by the proteasome, thereby uncovering/revealing its specific target proteins by a decrease in their levels upon mass spectrometry processing.[2,3] To this aim, we have designed and synthesized a set of PROTACs based on the CBD scaffold (compounds **1-3**, Figure 1), by coupling different linkers through one of the hydroxy groups and incorporating pomalidomide as the ligand of E3 ligase. Subsequently, the cytotoxic capacity of these PROTACs has been tested to determine whether they retain the characteristic biological activity profile of CBD. Once verified that the structural modifications in the CBD core do not lead to a loss of activity, proteomic experiments will be conducted for target identification.

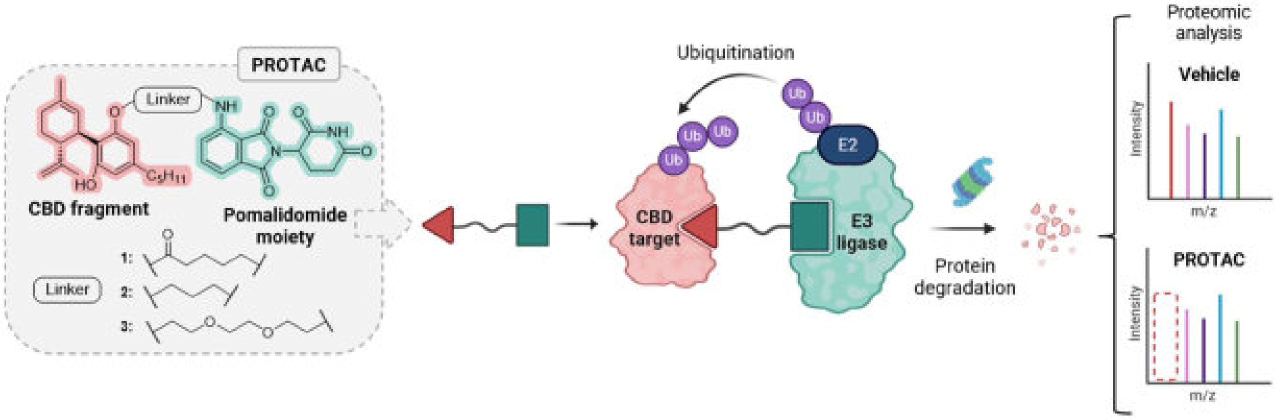

Figure 1. CBD-based PROTACs for target identification.

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Acyl azolium-promoted photochemical acylation of alkyl halides

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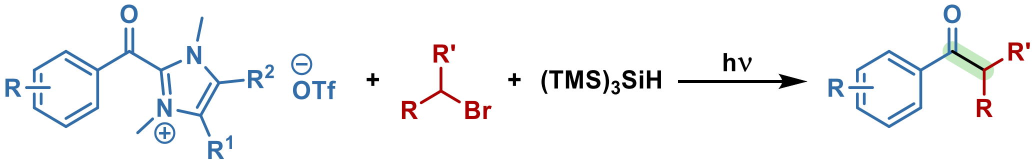
Keywords: *photochemistry, N-heterocyclic carbenes, radical C-C bond formation.*

Photochemistry has experienced a remarkable development over the past decades, and it has become one of the main tools to harness light as an energy source.[1] Carbonyl groups are among the most studied species, due to their immense potential for enabling photochemical transformations. One of the most significant reactivity modes of their biradical excited state is the Hydrogen Atom Transfer (HAT) process, either in its intra- or intermolecular version, to afford two different radicals, which can then couple with each other or lead to new reactions.[2] Acyl azolium intermediates exhibit an analogous photochemical reactivity to that of diaryl ketones, which are widely used in photochemistry. It is worth noting that reports of this reactivity are largely limited to UV light. Our group recently reported a study of the classical acyl azolium salts that enabled a deeper understanding of the photochemistry of these compounds.[3]

Taking advantage of this knowledge, in this work we present a new family of NHC-derived acyl azolium salts with photochemical activity at longer wavelengths. This work studies the photochemical acylation of alkyl halides mediated by acyl azolium salts through a HAT/XAT process in the presence of a silane (Scheme 1), offering a strategy for C-C bond formation with several advantages over conventional methods. For this purpose, multiple acyl azolium salts have been prepared, and the reaction with an alkyl bromide has been studied. Additionally, different alkyl halides have been explored, such as primary and secondary alkyl bromides, highlighting the reactivity of secondary alkyl bromides. Furthermore, a reaction mechanism is proposed based on the reactivity of the triplet excited state, which forms a biradical intermediate. This species initiates a Hydrogen Atom Transfer (HAT) with the silane, followed by a Halogen Atom Transfer (XAT) with the alkyl halide, which results in two radical species which can recombine to form a new C-C bond.



Scheme 1. Proposed photochemical acylation reaction.

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Synthesis of an orthogonal electron donor-acceptor spironanographene

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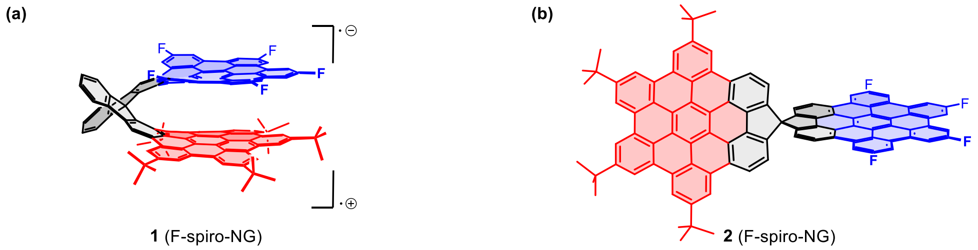
***Keywords**: molecular nanographenes, bottom-up synthesis, electron donor-acceptor systems.*

Graphene, the first two-dimensional atomic crystal isolated in 2004, attracted considerable scientific interest and increased attention toward carbon-based structures due to its exceptional properties. Among these, its high electronic mobility is particularly notable, making it a promising material for nanoelectronics applications.[1] However, although it is a zero band-gap semimetal, when its size is reduced to form graphene quantum dots or nanographenes, quantum confinement introduces a band-gap, making them suitable for use as field-effect transistors (FET).[2] In particular, molecular nanographenes obtained through bottom-up synthesis allow precise control over size and structure, providing monodisperse materials with tunable optoelectronic properties.[3]

Following this approach, our research group has recently developed the bottom-up synthesis of the bilayer F-spiro-NG (**1**, Figure 1a), composed of two substituted hexa-*peri*-hexabenzocoronene (HBC) units: one HBC unit endowed with *tert*-butyl substituents and the other substituted with fluorine atoms. This electron donor-acceptor bilayer nanographene showed an electron transfer process in the ground state that leads to the formation of an open-shell zwitterionic paramagnetic species.[4]

Herein, the synthesis of a new system, denoted as F-spiro-NG (**2**, Figure 1b), is proposed. This compound is a redesigned system based on **1**, in which the two HBC units are connected to the spirobifluorene core at different positions that leads to an orthogonal arrangement of the HBCs. This conformation prevents the formation of the bilayer by hindering the intramolecular *π-π* interactions. The ongoing synthetic work is based on three key steps, applied to both the donor and acceptor moieties: a regioselective Sonogashira coupling, a Diels-Alder [4+2] cycloaddition, and a Scholl reaction. This design will allow a direct comparison of the optoelectronic properties of **2** and **1**, as well as an analysis of how the absence of overlap affects charge transfer and carrier mobility. This approach is particularly relevant for gaining a better understanding of the role of interlayer coupling in electron donor-acceptor systems based on molecular nanographenes, which are of great interest for optimizing materials with potential applications in the semiconductor industry.



1 (F-spiro-NG)

2 (F-spiro-NG)

Figure 1. Structures of the electron donor-acceptor F-spiro-NGs: (a) bilayer system **1** with overlapping HBC units; (b) redesigned system **2** with orthogonal HBC units.

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Formic Acid Dehydrogenation catalyzed by Iridium-NHC Complexes

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***Keywords**: formic acid dehydrogenation, iridium complexes, catalysis.*

The safe transport of molecular hydrogen for its use as a sustainable alternative to fossil fuels remains a major challenge because of the risks involved in handling high-pressure gas. Liquid Hydrogen Carriers (LHCs) provide a stable and safer approach, with formic acid (FA) standing out as a promising candidate due to its high hydrogen capacity (4.4 wt%) and large-scale industrial production.[1] Consequently, the catalytic dehydrogenation of FA is under the scientific spotlight. Homogeneous catalysis using iridium-based complexes has been demonstrated to be among the most effective methodology for this transformation. However, the development of more robust systems remains essential to improve their performance.[2]

In this work, we report the synthesis and characterization of a series of [IrCp*(NHC-NH_2)Cl] complexes, where NHC-NH_2 is a functionalized N-heterocyclic carbene ligand. This design is supported by previous studies in which the presence of Cp* and NHC motifs in the catalyst improves the catalytic activity for the transformation of FA into H_2 (g).[3] Both optimization experiments and kinetic studies have been carried out to identify the ideal conditions for developing a highly efficient catalytic system for this process.

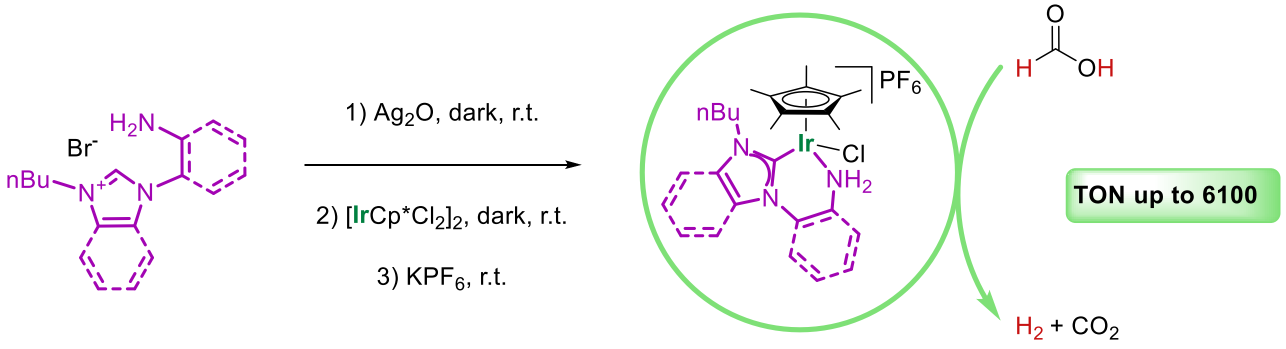

Figure 1. Catalytic dehydrogenation of formic acid with [IrCp*(NHC-NH_2)Cl] complexes.

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SYNTHESIS OF NOVEL CHIRAL BIANTHRACENE-BIS-PORPHYRIN CONJUGATES

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***Keywords**:* *bianthracene, chiral conjugates, porphyrin*

Chiral π-conjugated nanomaterials have recently attracted significant attention in several research fields due to their potential to exhibit chirality-dependent optical and electronic phenomena. Among them, porphyrins (PORs) stand out as versatile building blocks for the functionalization of chiral aromatic systems, such as nanographenes and polyaromatic hydrocarbons (PAHs), owing to their intense absorption, rich photophysical behaviour and remarkable stability. As a result, the obtained π-extended architectures display promising chirality-dependent photophysical and electronic properties.[1-3]

Herein, we report the synthesis of two new axially chiral bianthracene-bis-POR conjugates, in which a chiral bianthracene scaffold is covalently connected to two POR chromophores (**Figure 1**). The synthetic strategy is based on Suzuki-Miyaura couplings between 2,2’-dibromo-9,9’-bianthracene[4] and 5,15-functionalized metalloporphyrins,[2] obtained under classical Lindsey conditions.[5] The resulting racemic mixtures were fully characterized by mass spectrometry, NMR and UV-Vis spectroscopies. Each enantiomer was isolated by chiral HPLC, and their properties were studied in detail by CD spectroscopy.

Based on previous reports on related helicene-bis-PORs systems, these hybrids are expected to exhibit strong molecular circularly polarized luminescence (CPL), which is highly appealing for a wide variety of applications, including optoelectronics, spintronics, and biological imaging.[2] Beyond that, this study is anticipated to open new avenues for the rational design of bis-POR chiral platforms and enable the fine-tuning of their chiroptical properties.

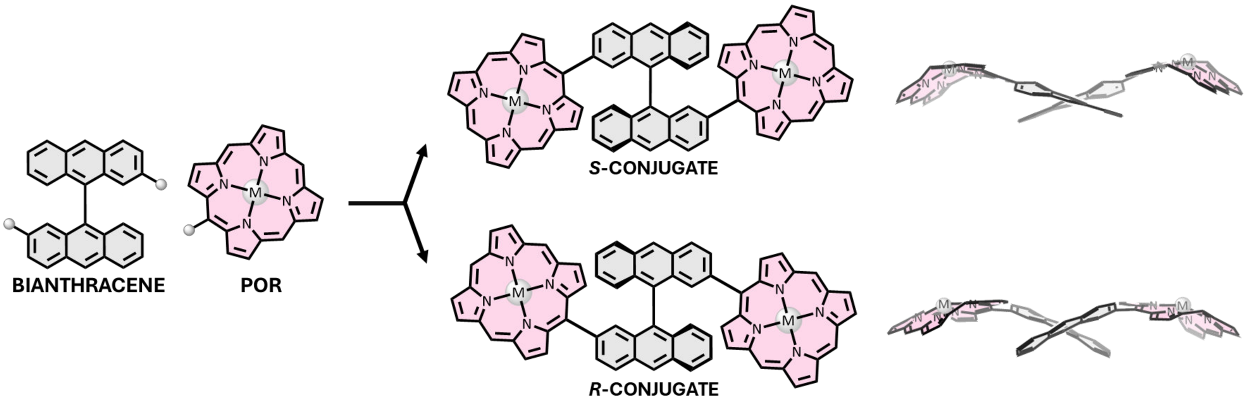

Figure 1. Synthetic route of the chiral bianthracene-bis-POR hybrids.

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Novel Precision Antibiotics Based on Shikimate Kinase Inhibition

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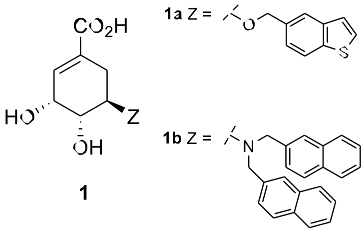
***Keywords**: precision antibiotics, bacterial resistance, shikimate kinase*

The efficacy of antibiotics in treating infectious diseases is being dangerously compromised by the abuse and misuse of broad-spectrum agents and the inherent evolutionary nature of bacteria, leading to the emergence of drug-resistant pathogens. The World Health Organization (WHO) estimates that, if the current trend persists, annual casualties caused by multidrug-resistant bacteria will surpass those from cancer by 2050, reaching around 10 million fatalities yearly.[1] The disappointing outcomes of the broad-spectrum approach, coupled with the remarkable success of precision medicine in oncology, have triggered a significant paradigm shift in antibiotic discovery toward a focus on narrow-spectrum agents. Precision antibiotics—characterized by well-defined functions and the targeting of novel therapeutic sites—are emerging as a strategic means to treat infections without disrupting the host microbiome or further driving the development of antimicrobial resistance. Our research group is addressing this challenge by developing inhibitors of the enzyme shikimate kinase (SK), an essential enzyme for relevant bacterial pathogens such as *Pseudomonas aeruginosa*, *Helicobacter pylori* or *Mycobacterium tuberculosis.*[2] This enzyme catalyzes the regiospecific phosphorylation of the C3-hydroxyl group of shikimic acid to afford shikimate-3-phosphate, using ATP as a phosphoryl donor. For inhibitor design, we implemented an innovative motion-based approach to target transient cavities that emerge during protein dynamics. These cryptic pockets are accessible in open or intermediate states but remain restricted or sequestered in the closed conformation.[3,4] As a result we identified compounds **1** that proved to be competitive reversible inhibitors in the nanomolar range. In this project, we address the synthesis of compounds **2** that incorporate a hydroxylamine moiety aimed at enhancing additional hydrogen-bonding interactions with the target. Furthermore, this modification is intended to minimize the protonation of the nitrogen atom within the active site—an environment highly enriched with positively charged residues. Several aromatic moieties, 2-naphthyl, benzo[*b*]thiophen-5-yl, and 5-indolyl, will be explored.



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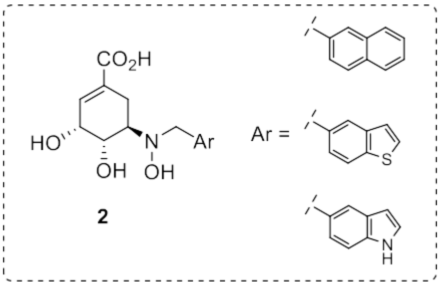

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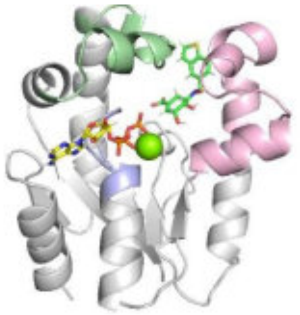

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