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Opening Lecture

Supramolecular Reactivity in the Non-Covalent Synthesis of Functional Systems and Materials

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The intriguing prospects of molecular electronics, nanotechnology, biomaterials, and the aim to close the gap between synthetic and biological molecular systems are important ingredients to study the cooperative action of molecules in the assembly towards functional supramolecular materials and systems. For chemists, the non-covalent synthesis of these supramolecular architectures is regarded as one of the most challenging objectives in science: How far can we push chemical assembly and can we get control over the reactivity, properties and functions of the responsive and adaptive architectures made? Moreover, the increasing number of different components in the assembly processes increases the complexity of the system, as many competing events occur, and pathway selection and controlled supramolecular reactivity are needed to arrive at the state required for the desired function.[1]

Mastering this complexity with a combination of experiments and simulations is a prerequisite to achieve the challenges set in creating functional materials and systems. In the lecture we illustrate our approach using supramolecular polymers as the main component in multicomponent assemblies. In all cases the control over the position of the molecules in time and space is required, where we are focusing on the emergence of homochirality. We will show the concept for their use as nanomaterials for electronics, novel nanomaterials for spin-controlled water-splitting and as active ingredients in biomedical applications, with supramolecular polymers as a key element.[2]

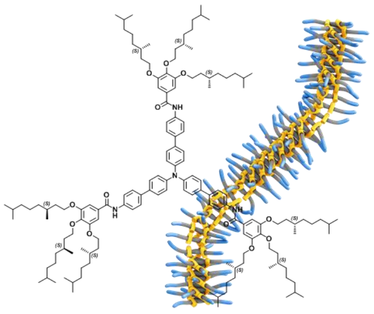

Figure. A chiral supramolecular polymer.

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Keynote Lectures

Electric Fields and the Metabolic Origin of Life

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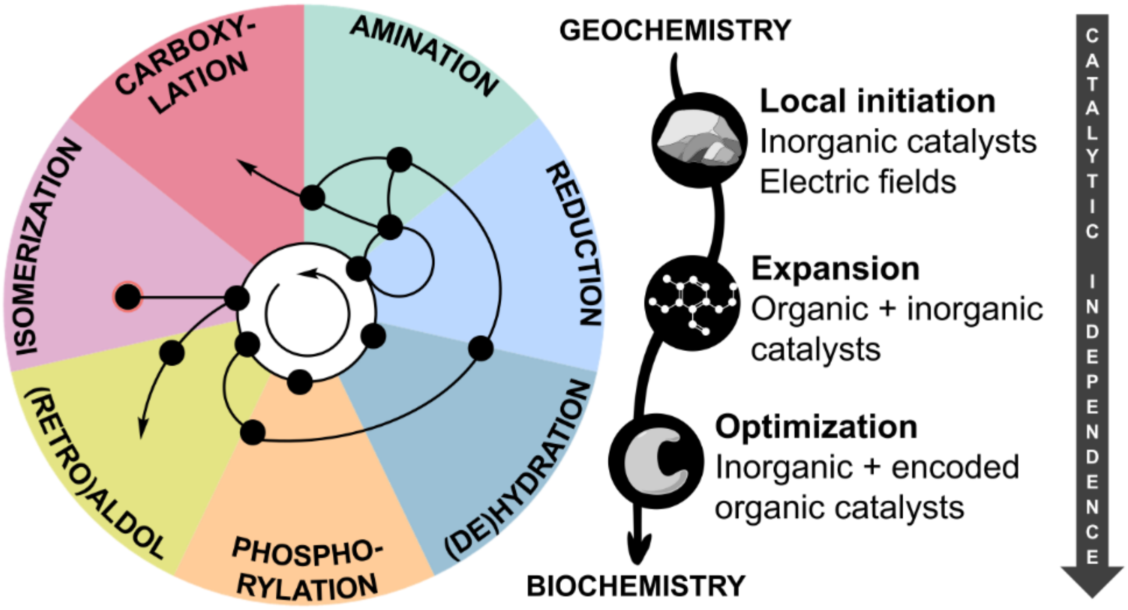
The Metabolism-First hypothesis for the origin of life posits that certain geochemical environments drove and facilitated dynamic organic reaction networks that were pruned and expanded through catalytic feedback effects. This process would lead to increasing catalytic autonomy of the reaction network from its original environment, ultimately resulting in the metabolic pathways found in chemoautotrophic organisms and a free-standing cell replete with catalysts for its own reactions.

But what lowered the kinetic barriers such that these reaction networks could have emerged in the first place? Metals and minerals were long proposed to have played this role, but extensive experimental work from my group and others has shown them to be promising yet insufficient. So what is missing?

Here I propose that strong electric fields, working together with metals, were life's first catalysts. Electric field catalysis is exceptionally general, maximizing the chance that complex reaction networks can emerge. An origin of metabolism under electric fields explains why enzymes operate predominantly by electrostatic effects, why phosphorylation is so central to metabolism despite being so challenging in water, and provides a fresh take on how proton gradients, catalysis, and phosphorylation became linked in membrane bioenergetics. Experiments and calculations supporting this hypothesis will be presented.



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KL2

Rethinking the Role of Quantum Mechanical Tunneling[1]

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Quantum mechanical tunneling (QMT) implies that a particle penetrates a potential energy barrier even though there is insufficient energy. In the last years has it become clear just how important QMT is for understanding chemical reactions. Here we emphasize the role that QMT plays in reactions of exemplary molecules. Once fully understood, the control[2] and application of tunneling in chemical synthesis, possibly stimulated through catalysts[3] or energy transfer, will open fascinating new ways of conducting chemical reactions. We expose QMT as the third reaction paradigm that can overwrite traditional kinetic control and govern reactivity, termed *tunneling control*.[1b, 2, 4] These findings are exemplified with the first full spectroscopic and theoretical characterization of the elusive hydroxycarbenes (R–C–OH)[5] that undergo facile [1,2]hydrogen QMT to the corresponding aldehydes under high barriers. We will demonstrate that this is a general phenomenon,[4a, 6] as exemplified by other OH-tunneling examples such as the rotational isomerization of a variety of carbocylic acids.[7] Such tunneling processes do not merely represent corrections to the reaction rate, they *are* the reaction rate, i.e., the completely *control* the reaction outome.[8] They can also override common notions such as the often invoked Curtin-Hammett principle.[9] We also demonstrate that *competitive carbon vs. nitrogen QMT* completely determines the outcome of some selected organic chemical reactions.[10] Finally, we will suggest that we need a fresh look at the role of the barrier width in chemical reactions by introducing the notion of "*intrinsic barrier width*" that has not been defined before.[11] This is also demonstrated with isotope-controlled selectivity (ICS).[8]

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Paradigm Shifts in Chemical Theory

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Despite decades of advancements in quantum chemistry, many foundational concepts in chemical theory still rely on empirical rules. While these rules help organize the vast experimental and computational data, they often lead to incorrect or conflicting predictions. Using quantitative molecular orbital (MO) theory and the Activation Strain Model (ASM) (1), I will challenge three key assumptions in chemical bonding and reactivity.

First, I will revisit the conventional view on why bond strength decreases as the electronegativity difference across the bond decreases, such as in the trend from C–F to C–I bonds (2). The traditional MO picture features the decreasing electronegativity difference as the physical principle behind this trend. I will show that this electronegativity model is fundamentally flawed in certain cases. Ironically, the textbook example often invoked to illustrate the electronegativity model (the carbon–halogen bond series) is such a case in point.

Second, I will examine the widely accepted belief that alkyl radicals ($R_mH_{3-m}C^{\bullet}$, m = 0-3) are stabilized with increasing substitution (methyl < primary < secondary < tertiary) and that this trend explains the corresponding decrease in C–H bond strength in the parent molecule $R_mH_{3-m}C$–H. Contrary to this, I will show that alkyl radicals are actually destabilized with increasing substitution, despite the observed bond strength trend (3).

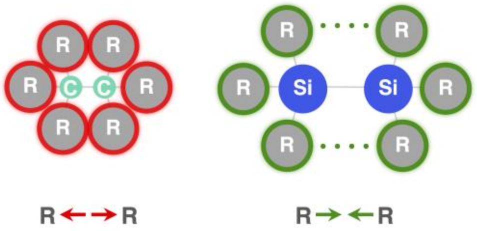

Figure 1. Tetrel–tetrel bonds and the effect of bulky substituents.

Finally, I will explore the intrinsic differences between C–C and Si–Si (and heavier tetrel–tetrel) single bonds, their relationship to atomic size, and why alkyl substitution weakens C–C but strengthens Si–Si bonds (see Figure 1). This trend extends to even heavier tetrel–tetrel bonds, revealing new insights into periodic trends in bonding (4).

These findings challenge long-standing chemical principles, offering a more accurate theoretical framework for understanding molecular interactions and reactions.

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Information processing in chemical reaction networks

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The flow of information is as crucial to life as the flow of energy. Living cells constantly probe their environment, and processing this information enables cells to adapt their behavior in response to changes in internal and external environmental conditions. Chemical reaction networks such as those found in metabolism and signalling pathways enable cells to sense physical properties of their environment, to search for food, or maintain homeostasis. Current approaches to molecular information processing and computation typically pursue digital computation paradigms and require extensive molecular-level engineering. Despite significant advances, these approaches have not reached the level of information processing capabilities seen in living systems.

In this talk, I will discuss our results on implementing concepts of reservoir computing in molecular systems. I will demonstrate how chemical/enzymatic reaction networks can perform multiple non-linear classification tasks in parallel, predict the dynamics of other complex systems, and can be used to time-series forecasting. This *in chemico* information processing paradigm provides proof-of-principle for the emergent computational capabilities of complex chemical reaction networks, paving the way for a new class of biomimetic information processing systems.

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Singlet Oxygen as a Tool for Biomolecular Ligations

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Within OBCR, we have developed a highly selective and efficient singlet oxygen mediated crosslink technology which is applicable to peptide-protein, peptide-nucleic acid and nucleic acid interstrand crosslink scenarios.[1] For this purpose, a furan ‘warhead’ is introduced into one of the biomolecular partners and subsequently activated by means of an oxidation trigger such as singlet oxygen which induces generation of a nucleophile-sensitive keto-enal moiety.[2] The overall procedure allows for spatiotemporal control of the crosslinking event. In the context of peptide ligand-receptor interactions, we have described, in live cells under normal growth conditions, spontaneous enzymatic activation and crosslinking of furan-modified peptide ligands to their membrane GPCR with zero toxicity, high efficiency and spatio-specificity.[3] Furan introduction into peptide and protein ligands and subsequent covalent modification of their natural targets was achieved after triggering photocatalytic singlet oxygen generation.[4] Furan-modified oligonucleotide probes were designed for efficient and selective crosslinking to natural nucleic acid targets,[5] including the elusive G-quadruplex and I-motif targets.[6] Singlet oxygen mediated furan oxidation was further applied to aptamer stapling.[7] Introduction of a slightly modified furan moiety into peptides and peptide nucleic acids (PNAs) allowed development of a triggerless proximity-induced click ligation with applications in nucleic acid biomarker detection and protein array design[8] as well as peptide cyclisation.[9] Furan[10] moieties were further converted, using singlet oxygen, into versatile building blocks for site-selective modification of proteins and synthesis of bioconjugates. The talk will highlight selected specific examples of these cross-linking and conjugation methodologies.

The work was supported by the FWO-Vlaanderen, the BOF-UGent, the IOF-UGent and the European Union’s Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 721613 (MMBio ITN), No 956070 (OligoMed ITN), No. 665501 (Pegasus^2 fellowship).

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Self-assembled molecular cages for transition metal catalysis and applications in living cells

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The interface between supramolecular chemistry and transition metal catalysis has received surprisingly little attention in contrast to the individual disciplines. It provides, however, novel and elegant strategies that lead to new tools for the search of effective catalysts, and as such this has been an important research theme in our laboratories.[1] In this context we have intensively explored the use of well-defined nanospheres[2,3] that form by self-assembly in transition metal catalysis. These nanospheres create catalysts (and substrates) at high local concentration, just like in enzymes, higher reaction rates are observed for several reactions that operate via binuclear mechanism. Also, they provide new tools to control catalytic events in complex media, showing substrate selective catalysis, effector controlled catalysis and catalysis with feed back loops. More recently we have translated the chemistry from the typical organic solvents to aqueous media and biorelevant conditions. This allows to use these nanostructures for new functions as gene delivery and nonnatural catalytic conversions in living cells.[4] In this lecture I will outline the various strategies in catalysis and discuss the application for gene delivery, with a focus on the general concepts and most recent results.

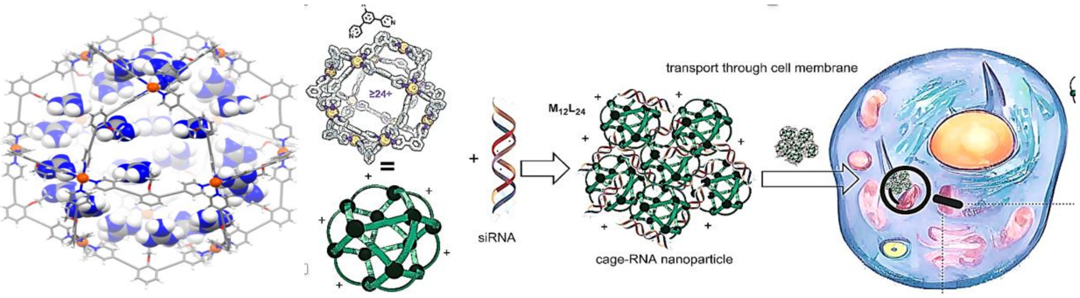

Figure 1. *An example of a M12L24 nanosphere as scaffold to bind catalysts (left) and functionalized nanospheres for gene delivery (right).*

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Hybrid Organic-Inorganic Interfaces for Supramolecular Photosynthesis: The Quantasome Vision

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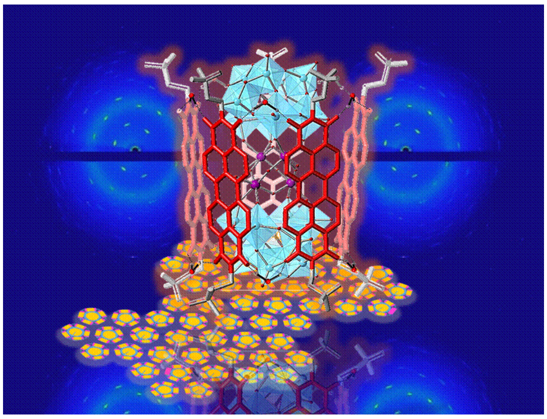
Photosystem II (PSII) organization in natural thylakoids sets key guidelines to rethink the molecular design of innovative artificial photo-electrolysers. Building on the early "quantasome" hypothesis (Science 1964, 144, 1009-1011), PSII mimicry can be pared down to essentials by shaping a photocatalytic ensemble (from the Greek term "soma"= body) where light-quanta trigger a water oxidation.[1-4] We have recently reported on PSII-inspired nanodimensional quantasomes (QS) that readily self-assemble into hierarchical photosynthetic nano-stacks, made of bis-cationic perylenebisimides as chromophores and deca-anionic tetraruthenate polyoxometalates (Ru_4POM) as water oxidation catalysts.[2-4] A combined supramolecular and click-chemistry strategy allows to interlock the multi-lamellar architecture emerging from the perylene aromatic stacking in water, while installing tetraethylene glycol (TEG) cross-linkers thus enhancing water harvesting and transport in proximity of the oxygen evolving center. The resulting nanostacks evolve oxygen using low energy green photons ($\lambda >$ 450 nm, FEO2 > 95 %).[4-5] Action spectra, mass-activity, light-management, photoelectrochemical impedance spectroscopy (PEIS) together with Raman mapping of hydration shells, point to a key role of the supramolecular nano-arrays, where the interplay of hydrophilic, hydrophobic domains is reminiscent of PSII-rich natural thylakoids.[1-5]



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Invited Lectures

Programmable release in compartmentalized enzyme systems: insights from kinetic modelling

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Compartmentalized enzymes have been widely studied as models of cell-like behaviour and the encapsulation of urease in self-organised structures such as liposomes and double emulsions provides the prototypical example [1]. The urease reaction produces ammonia in the presence of urea with an increase in pH that in turn influences the transport rates of species across the membrane barrier. Herein, we use kinetic simulations and experiments to investigate the role of the interface in the control of pH in the compartmentalized urease reaction. We show how the timing of pH changes in double emulsions is likely governed by formation of micelles in the oil layer [2], whereas electrical gradients across phospholipid bilayers play an important part in liposome pH [3]. We explore how these factors might be exploited for programmable release of an internal cargo in, for example, sensing and pharmaceutical applications.

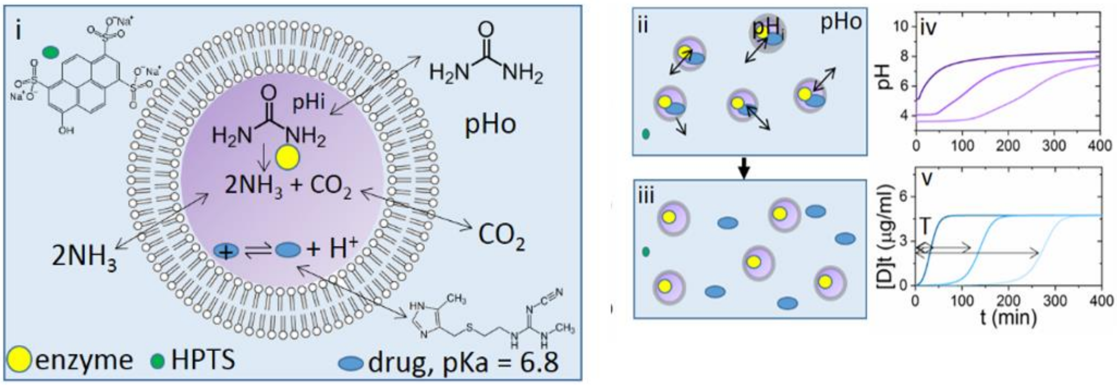

Figure 1. Programming pH changes and drug release in urease-encapsulated liposomes or emulsions

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What can we learn from and do to kinetic-thermodynamic responsiveness?

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We present a conceptual framework for rethinking reactivity, from absolute values to system-level responsiveness. Between competing pathways at the transition state (TS), an under-explored aspect is that each pathway has a distinct kinetic-thermodynamic responsiveness: how much can a given change in reaction free energy impact reaction rate constants. Adjusting the thermodynamic driving force can alter the differences in energy discrimination at the TS between competing paths, thereby increasing and even switching selectivity. The difference in this sensitivity between competing pathways is crucial in determining how responsive the selectivity is to thermodynamic changes. We showcase our early examples where this responsiveness is treated as a tunable variable, and how it can be utilized as a design principle in reactions. We aim to provide a causal complementary to **system-specific** and **data-driven approaches**, telling us not just *what happens*, but *how sensitively* a system responds, whether reactivity is **incidental or systematic**. This opens up a new design logic: we can begin targeting tunability, not just outcomes.

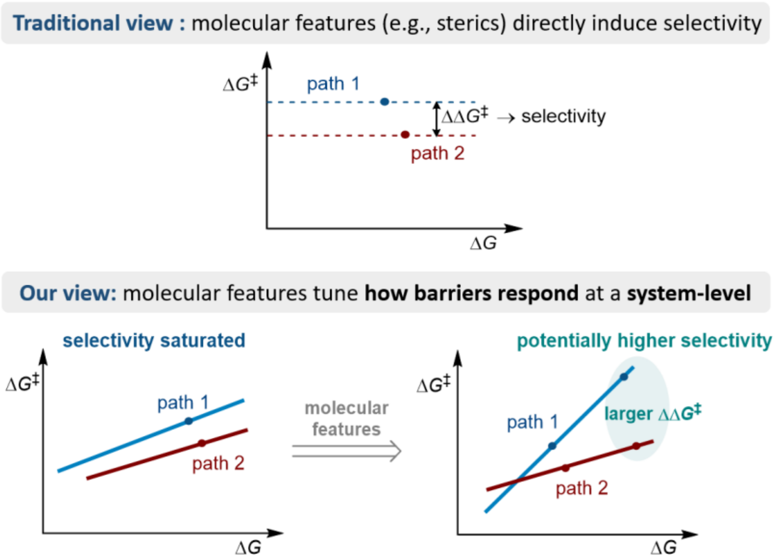

Figure 1. **Traditional view:** Molecular features (e.g., sterics) directly bias the outcome by lowering one transition state barrier more than another. **Our view:** Molecular features modulate how barriers respond to thermodynamic driving force, tuning selectivity at a system level.

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Breaking Covalent Bonds with Mechanical Force

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Chemical reactions require energy to start. Typically, this is provided through heat (thermal), photons (photochemistry), or electron/holes (electrochemistry). The use of mechanical energy to drive chemical reactions, while uncommon nowadays, is at the very beginning of chemistry, when materials were ground together to produce a different product. Different from the other energy sources, mechanical energy is directional, and can lead the same reactants into different products according to the relation between the force vector and the chemical bonds in the molecules. In macromolecules, in which segmental translation and truncation does not allow for full dispersion of mechanical stress, interesting non-classical reactions become dominant, such as homo- and heterolytic bond scissions. In this talk, I will discuss this bond-scission mechanochemistry using some recent examples from our group - looking how stereochemistry[1] and electronic effects from heteroatoms[2] affect (mechano)chemical reactivity.

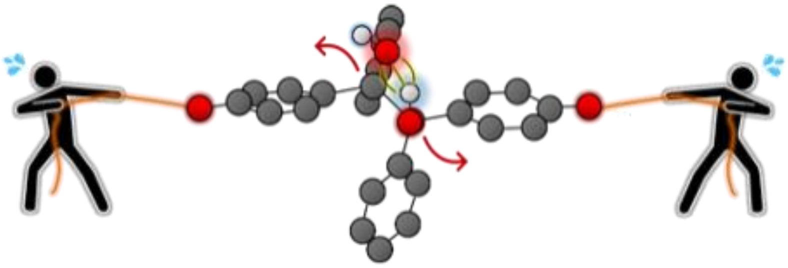

Figure 1. H-bond affecting mechanochemical torsion and C-C bond scission.

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Double 2D- and 3D-aromaticity in triplet tropylium trication, oxidized closo icosahedral dodecaiodo-dodecaborate cluster, and periodo-polycyclic aromatic hydrocarbons

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The most widely known example of a species with double 2D-aromaticity is the hexaiodobenzene dication, $[C_6I_6]^{2+}$.[1] This species shows π-aromaticity in the benzene ring and σ-aromaticity in the outer ring formed by the iodine substituents. To our knowledge, no species with double 3D-aromaticity nor double Hückel-Baird 2D-aromaticity have been reported to date. Inspired by the hexaiodobenzene dication example, in this work, we explore the potential for double aromaticity in three different type of compounds: periodo-polycyclic aromatic hydrocarbons,[2] double 2D-aromaticity in tropylium (tri)cation and anion derivatives,[3] and double 3D-aromaticity in $[B_{12}I_{12}]^{0/2+}$.[4] Our results based on electronic, magnetic, and energetic indicators of aromaticity show the presence of double aromaticity in several periodo-polycyclic aromatic hydrocarbons, in triplet $C_7Br_7^{+3}$ with an internal Hückel aromatic tropylium ring and an external incipient Baird aromatic Br_7 ring, but not in $[B_{12}I_{12}]^{0/2+}$.

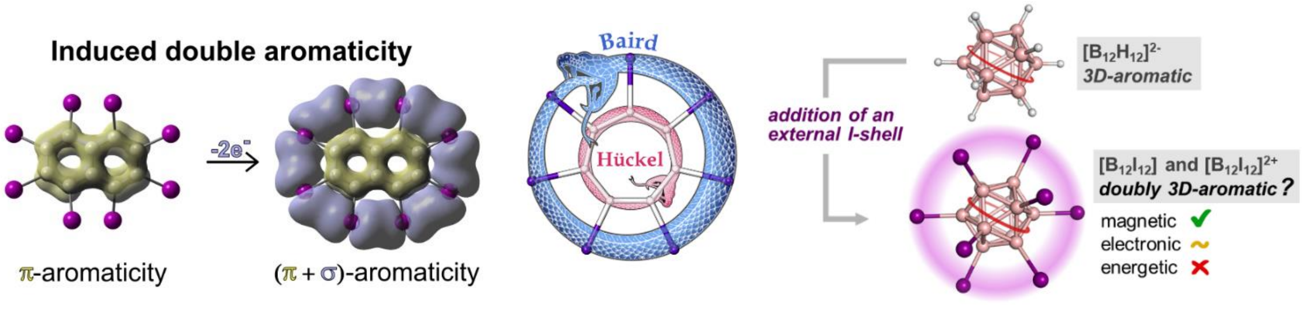

Figure 1. Some of the species described in this lecture

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Old Ideas, New Tricks: Additivity in Polycyclic Aromatic Systems

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Delocalization is one of the foundational principles of modern chemical theory. From resonance structures to band theory, it provides the framework for how we understand conjugated systems. Yet delocalization also carries an implicit assumption: that a molecule's electronic behavior is an emergent, holistic property—not reducible to the sum of its parts.

And yet… what if it is?

In this talk, I explore the surprising success of additivity in predicting magnetic properties of conjugated molecules. Through a series of studies on NICS-XY-Scans,[1,2] bond currents, and current densities,[3] we show that even large polycyclic systems can be modeled accurately using only a small set of mono-, bi-, and tricyclic subunits. This is not merely a computational convenience—it is also a window into the behavior of polycyclic aromatic systems.

Strikingly, this pattern of locality also emerges from an entirely different direction: deep learning. Using graph neural networks trained only on small molecules, we achieve accurate predictions of magnetic behavior in systems many times larger.[4] That these models succeed reinforces a central point: delocalization, at least in its magnetic manifestation, behaves as though it is fundamentally local.

This rethinking opens new avenues for how we understand, predict, and ultimately design π-conjugated systems—not by ignoring delocalization, but by redefining its scope.

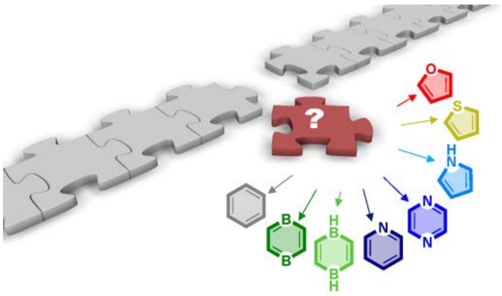

Figure 1. Breaking polycyclic aromatic systems into smaller components.

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IL6

Electron-Deficient Aromatics
Multiredox Systems, Near-Infrared Dyes, & Brønsted Acids

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Systematic tuning of electronic energy gaps in organic molecules can be achieved by homologation (oligomerization) of linear π-conjugated motifs, by ring expansion of π-conjugated macrocycles, or by extension of fused ring systems in two dimensions. A complementary approach relies on combining donor and acceptor (D–A) moieties, with diverse recent applications in small-molecule and polymer chemistry. The D–A paradigm is particularly suitable for the development of tunable building blocks, which can be constructed by judicious merging of existing electron-deficient and electron-rich motifs. A simple and potentially productive design of such a hybrid structure is achieved by combining naphthalenemonoimide (NMI, red) and pyrrole (blue), as shown below.[1] We will discuss the application of these and similar pyrroles as building blocks for the synthesis of diverse polycyclic aromatics, including macrocycles,[1,2] heteroatom-doped nanocarbons,[3,4] and small-molecule dyes.[5] These systems reveal rich redox chemistry, spanning multiple oxidation levels, tunable optical signatures extending into the near infrared, an ability to form complex supramolecular assemblies, and surprising acid–base properties. We will also discuss our efforts to extend the concept of NMI fusion to non-pyrrolic heterocycles and carbocycles.[6,7]

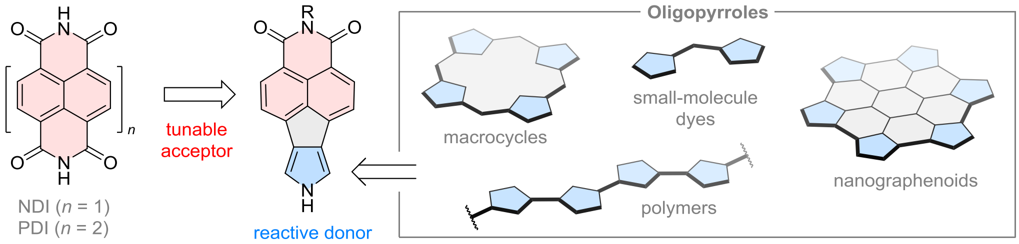

Figure 1. NMI-fused oligopyrroles.

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Enabling endergonic processes through catalysis

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Energy conversion is a pillar of our society, which is heavily based on chemical-to-thermal energy conversion, with massive efforts dedicated to light-to-electrical energy conversion using solar panels. Biology is different: it is grounded into chemical-to-chemical energy conversion, thanks to catalytic processes. A significant biological parallel is the synthesis of adenosine triphosphate in our body, which occurs under energetically unfavored conditions, thanks to the energy provided by a proton gradient.

In this talk, I will present how my group is enabling chemical-to-chemical energy conversion in fully artificial systems, thanks to catalytic processes involving small molecules.

Our latest experimental efforts will serve as a basis to discuss how energy can be exploited to drive chemical reactions,[1] adaptation phenomena,[2] and active transport,[3] revealing common underlying principles.[4],[5],[6] A unique feature shared by these catalytic systems is that the focus is not on the product obtained (e.g., transformation achieved, yield, e.e.); instead, the focus is on how the catalyst itself is modified during the catalytic cycle. I hope that this uncommon perspective will stimulate practicioners working in catalysis to consider systems they are working on under a different light.

These studies tackle the general problem of realizing endergonic reactions ($\Delta G > 0$).[5] Mastering these reactions has far-reaching implications in energy harvesting, transduction, and exploitation, in both biological and technological settings.

Figure 1. Cartoon representation of an endergonic process leading to the self-assembly of a thermodynamically unstable species.

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IL8

Mechanistically Guided Strategies for the Design and Synthesis of Organophosphorus Compounds

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In recent years, the field of visible light-mediated organic transformations has undergone a significant revival, profoundly influencing the methodologies for synthesizing organic molecules.[1] This lecture will explore the crucial role of physical organic chemistry in both understanding and innovating photoinduced chemical reactions.

The first part of the talk will focus on the formation of carbon-carbon and carbon-heteroatom bonds facilitated by visible light, while the second part will examine how well-designed phosphorus molecules can activate inert chemical bonds when exposed to light.[2]

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Reactivity Scales as Tools for Analyzing Polar Organic Reactions: Dos and Don'ts

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Predicting the reactivities of organic compounds or the rates of organic reactions has remained a challenge though it has been in the center of physical-organic chemistry since its beginnings [1]. For simple electrophile-nucleophiles reactions, in which only one new σ-bond is formed in the rate-determining step, Equation (1) was proposed, which makes it possible to describe the reactivity of electrophiles and those of nucleophiles in a certain solvent by only three parameters: the solvent-independent electrophilicity E and the solvent-dependent nucleophilicity parameters N (and s_N) [2, 3]. These reactivity descriptors can be used to construct comprehensive reactivity scales.

Recent examples for the further expansion of the reactivity scales by integrating new classes of electrophiles and nucleophiles will be highlighted (Figure 1a) [4-6]. This presentation will also shed light on how true or pretended limitations of Equation (1) can be used to analyze the mechanisms of [4+2] cycloadditions (Figure 1b) [7].

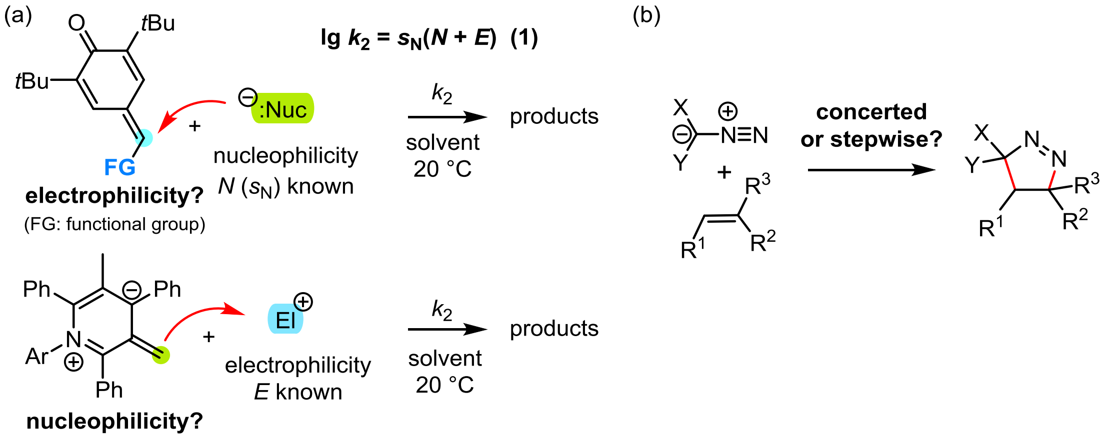

Figure 1. (a) Recently integrated classes of nucleophiles and electrophiles in Mayr's reactivity scales. (b) Cycloadditions are a challenge for the application of Equation (1).

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New Trends in Enantioselective Cu-Catalyzed Sequential Transformations

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Enantioselective Cu-catalyzed sequential transformations typically involve the initial nucleometallation of an olefinic substrate to form an organocopper catalytic intermediate that can be trapped by a suitable electrophile.[1] These emerged as a powerful strategy in modern organic synthesis, integrating multiple bond-forming events into a single operational step, thus streamlining synthetic routes and enabling the efficient construction of complex chiral molecules from simple precursors. However, the range of substrates and electrophiles suitable for these transformations is generally limited to a few classical C(sp^2)-electrophiles, which limits the scope of attainable products.

In this lecture, recent contributions from our group will be presented that show how, by designing new substrates, this chemistry can be expanded to include new reactivity or previously inaccessible products. A new synthetic strategy named asymmetric olefinative conjugate addition (AOCA)[2,3] developed in our lab will be presented, as well as new approaches towards chiral cyclopropanes[4] and cyclopentadienes that rely on CuH-catalysis.[5] Key mechanistic aspects of each of these transformations will be discussed.

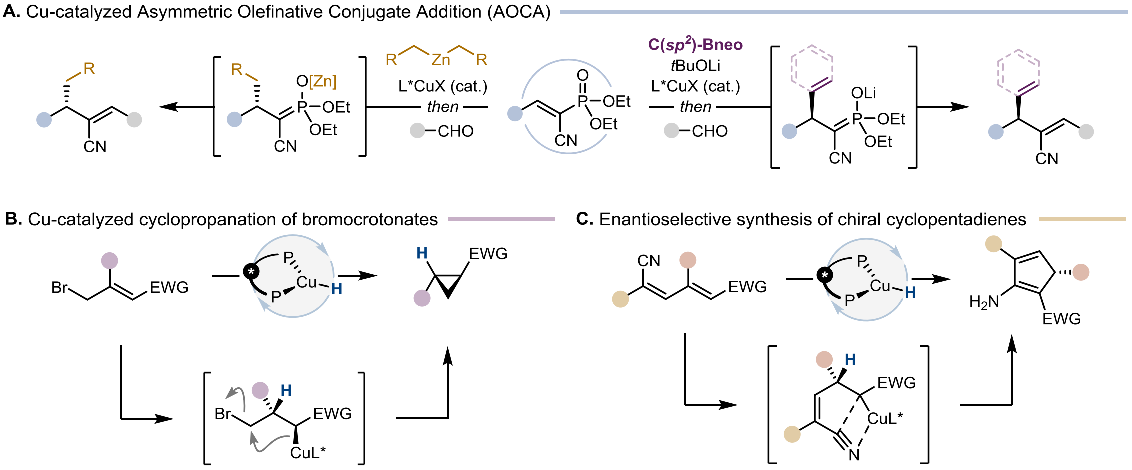

Figure 1. Cu-catalyzed sequential transformations developed in our group.

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Surface-Mounted Molecular Devices

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Molecular devices anchored on surfaces offer a versatile platform for developing responsive materials that can be controlled by external stimuli. These systems are of growing interest due to their ability to modulate interfacial properties, enable light-controlled processes, and contribute to areas such as molecular electronics. At their core, such architectures rely on two key components: a stimuli-responsive unit that performs the desired function, and a molecular scaffold that ensures effective surface integration and optimal performance. The platform element is critical - it must provide robust surface attachment, maintain adequate separation between individual molecules, suppress electronic interactions with conductive substrates to preserve excited-state lifetimes, and arrange functional units in a predictable and spatially defined orientation above the surface.[1]

In this talk, three fundamentally different strategies for creating photoresponsive molecular layers on surfaces will be discussed: Langmuir–Blodgett films,[2] self-assembled monolayers, and incorporation of molecular guests within surface-accessible pores of nanocrystalline hosts.[3,4] These approaches differ in terms of molecular packing, structural precision, and functional stability, and their suitability for specific applications will be discussed.

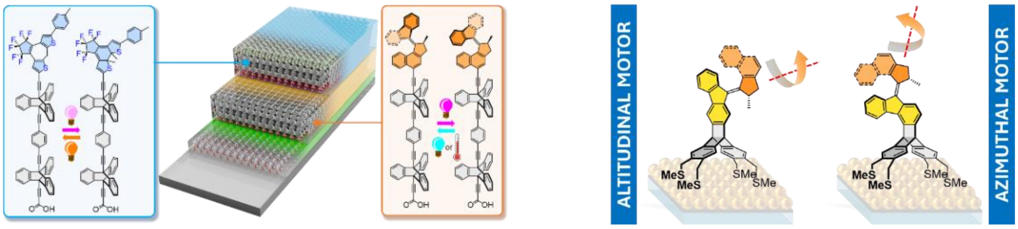

Figure 1. Photoswitchable Langmuir-Blodgett films (left) and self-assembled arrays of tetrapodal light-driven molecular motors (right).

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Light-driven reactions assisted by organic molecules or materials

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Sunlight is one of the most abundant and clean energy sources available on Earth. Thus, exploiting the energy of light to trigger chemical reactions has been the subject of extensive research for many decades. Light-induced chemical transformations involve the synchronization of several steps starting with light absorption by a molecular chromophore or semiconductor. It is then necessary that this absorbed energy is transferred to the reaction substrate or to the catalyst responsible for the chemical transformation, either by electron transfer or direct energy transfer phenomena. In this talk, the use of organic chromophores or materials as photocatalysts for organic transformations or solar fuel production will be discussed. In addition, the description of new electron donor-acceptor (EDA) complexes that open new chemical space in organic chemistry will be presented. Emphasis will be given to the mechanistic pathways leading to the transformations proposed on basis of electrochemical analysis, steady state or time resolved spectroscopic techniques and the detection or trapping of reaction intermediates.

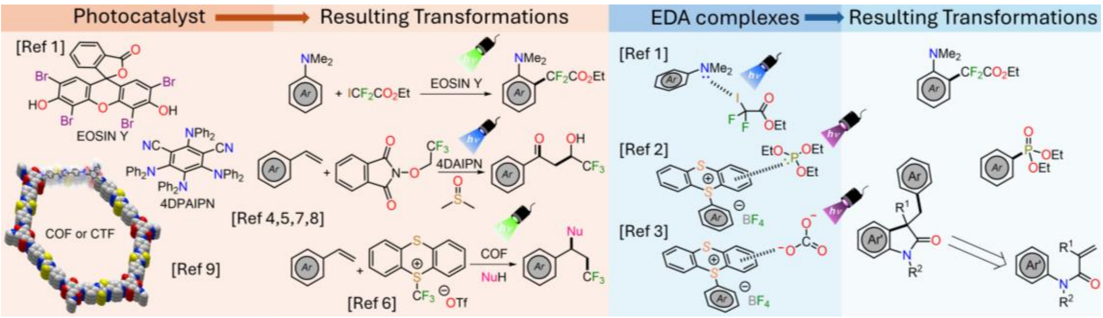

Figure 1. Representative photocatalysts, EDA complexes and resulting transformations. CTF: Covalent Triazine Framework. COF: Covalent Organic Framework.

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Helical Frameworks as Catalytic Platforms: Controlling Reactivity Through Molecular Geometry

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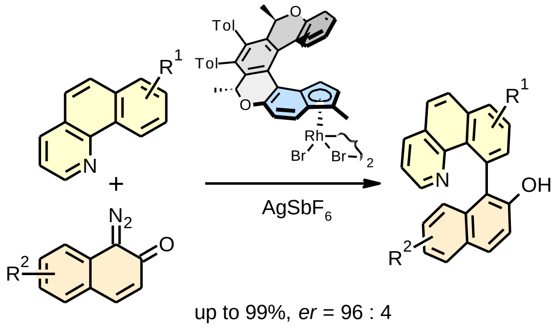
Despite remarkable recent progress in the synthesis of nonplanar chiral aromatics, particularly helicenes, their application in asymmetric catalysis remains rather underexplored.[1] Inherently chiral helicenes with their rigid, π-conjugated helical architecture, and distinctive electronic features, represent promising scaffolds for enantioselective catalysis. Their chirality, encoded in the molecular framework rather than arising from stereogenic centers, offers a uniquely well-defined chiral environment that can effectively steer asymmetric induction at the molecular level. When incorporated into transition metal complexes, helicenes have the potential to serve as versatile platforms for the development of highly selective catalytic systems.

In this lecture, I will examine how helically chiral ligands modulate catalytic outcomes, focusing on recent advances in rhodium- and iridium-catalyzed transformations[2] where the interplay between structure and reactivity is key to achieving high enantioselectivity (Scheme 1).



Scheme 1

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Chemoselective C(sp^3)–H bond oxygenations guided by solvent induced polarity enhancement

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Oxygenated groups are common functionalities in natural products and bioactive molecules and accordingly, reactions that introduce oxygen atoms into hydrocarbon frameworks represent important synthetic transformations. Among the available reagents, metal-oxo species[1] and dioxiranes[2] have found extensive application in view of their ability to efficiently promote C(sp^3)–H bond hydroxylations and C=C bond epoxidations under mild conditions. Within these transformations, the possibility to achieve highly chemoselective hydroxylations in C(sp^3)–H rich molecules and chemoselective C(sp^3)–H bond hydroxylation of substrates bearing C=C bonds remain standing issues, with the latter transformation that is recognized as a major challenge in the field.[3]

Herein we address these problems, leveraging on polarity enhancement effects induced by solvent hydrogen bonding to electron withdrawing functional groups. The interaction of fluorinated alcohol solvents with these groups determines a strong electronic deactivation toward oxygenation by electrophilic Mn-oxo species and dioxiranes of proximal over remote C(sp^3)–H bonds and of electron poor C=C over remote tertiary, secondary and primary C(sp^3)–H bonds, enabling highly selective hydroxylation at remote sites, thus providing a powerful methodology to govern the intramolecular chemoselectivity of these processes.

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Oral Communications

Tracking Propagating Perturbations in Chemical Reactions

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Periodic perturbations propagate through chemical reactions. For instance, modulations of reactant concentration result in distinct phase delays and amplitude dampening in the concentration profile of downstream species, which are governed by the reaction topology and kinetics of the individual steps (**Figure 1A**).[1] Tracking the propagation of such perturbations presents a powerful approach for probing reaction connectivity and rates of individual reaction steps. Here, we harness Electrospray ionization-mass spectrometry (ESI-MS) to monitor the propagation of periodic perturbations in chemical reactions under continuous flow conditions.

As a first example, we investigate the organocatalytic addition of cyclopentadiene to α,β-unsaturated aldehydes (**Figure 1B**).[2] Upon perturbation of input concentrations, ion intensities of key species detected by ESI-MS oscillate with characteristic time delays, providing quantitative insights into the kinetics of individual reaction steps, as demonstrated by substituent effects.[3]

We then extended the approach to a chemical reaction network promoted by ferrous iron, that converts pyruvate and glyoxylate into intermediates of the biological Krebs cycle.[4] The network is composed of 23 compounds formed by aldol condensations, oxidation/reduction and hydration/dehydration reactions. Perturbating the input concentration of either pyruvate or glyoxylate yields propagation patterns, suggesting that both reactants are characterized by different entry points in the network. Overall, this work describes a novel approach for online reaction monitoring and highlights ESI-MS as an exceptionally informative analytical tool.

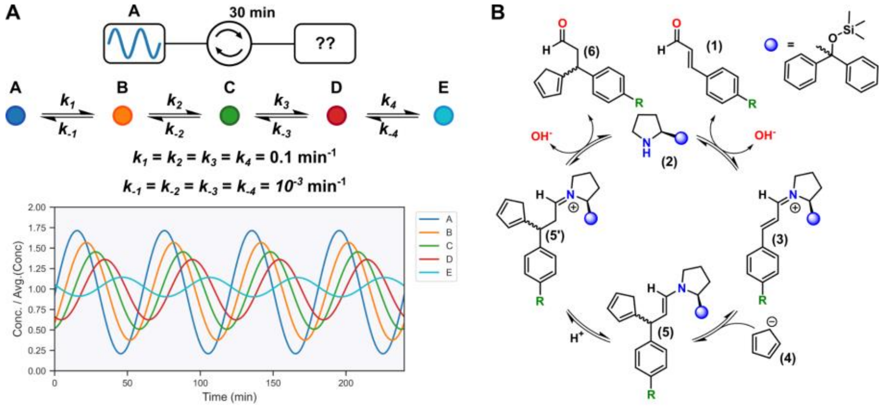

Figure 1. Numerical simulation of a model reaction in conditions of a continuous stirred-tank reactor. **B.** Proposed reaction mechanism for the addition of cyclopentadiene to α,β-unsaturated aldehydes.[2]

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Structure-Reactivity Relationships in the Dihydroazaborinine Molecular Solar Thermal System

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Molecular solar thermal energy storage (MOST) systems offer an approach to harnessing solar energy by converting, storing, and releasing it within chemical bonds.[1] 1,2-Dihydro-1,2-azaborinines (dihydroazaborinines) show promising properties for utilization as MOST system.[2-5] In the search of optimization of the properties of dihydroazaborinines for MOST application, report on the impact of substituents on i) the photochemistry of dihydroazaborinines and ii) the thermal stability of their Dewar (2-aza-3-bora-bicyclo[2.2.0]hexene) photoisomers using experimental physical-organic techniques. We also report the synthesis of derivatives with high energy densities approaching 1 MJ/kg.[6]

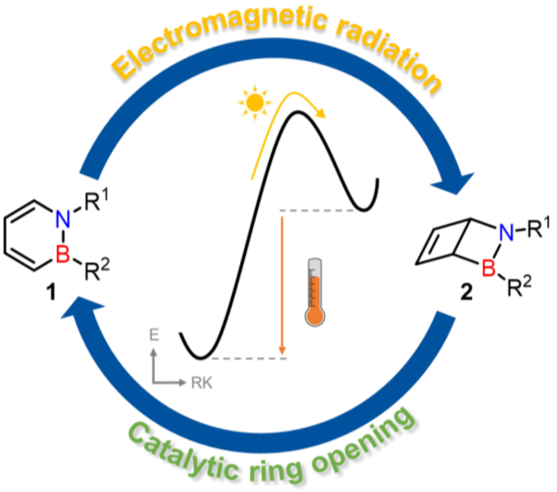

Figure 1. Principle of dihydroazaborinine based molecular solar thermal system.

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Electron Chemistry

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It's about using an electron flow as the sole reagent of a C-C bond formation, with the substrate being a binding empty molecular orbital such as the LUMO of a host assembly. In fact, this LUMO results here from the sigma-type overlap of $2p_z$ atomic orbitals associated with vicinal electrophilic centers C(γ) of pyridiniums in close van der Waals contact ($d(C\gamma\text{-}C\gamma) < 3.40$ Å; Figure). Upon two-electron acceptance, the LUMO transforms into an emerging elongated carbon-carbon covalent bond (HOMO), which is an integral new part of the thus reduced host assembly. We have therefore called this host a "structronic"[1,2] entity, based on a neologism derived from "structure" and "electronics", and the electrochemically formed bond is regarded as a "two-electron reservoir", insofar as reoxidation of the loaded assembly leads to specific cleavage of this reservoir bond (localized electro-chemistry). Because this relatively localized LUMO, which is to be filled with electrons, strides over the redox-innocent scaffold that positions the pyridiniums to enable their through-space interaction (see Figure), it is referred to as a supra-molecular orbital (supra-MO), regardless of whether the scaffold is rigid,[1] semi-rigid,[3] or even saturated and flexible.[4] It is worth emphasizing that the underlying electrochemical mechanism is fundamentally unrelated to a process resembling intramolecular sigma-dimerization of geminate pyridinyl radical species. The structronic paradigm is characterized by (i) a two-way inversion of standard potentials, yielding one-step two-electron processes, and (ii) the emergence of electrochemical hysteresis associated with the reductive formation (charging) and oxidative cleavage (discharging) of the C–C reservoir bond.[1,2]

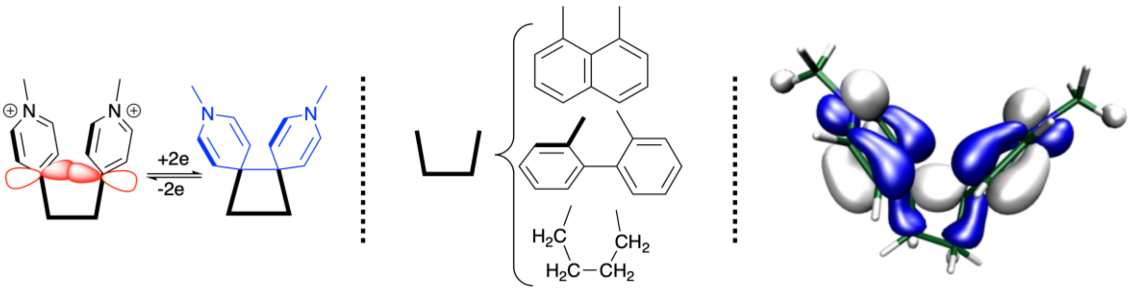

Figure. Working principle of the structronic paradigm implemented for energy storage.

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Counterintuitive Steric Activation in the Electrocyclization of Highly Substituted π-Cations

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Increasing steric bulk is typically considered an impediment to bond formation due to increased steric hinderance. In a counterintuitive discovery, we have identified that the electrocyclization of π-cations, such as in the Nazarov reaction (Figure 1),[1] are actually activated through the incorporation of additional substituents, including at the end-carbons that are involved in σ-bond formation. This has enabled the rapid assembly of multiple all-carbon quaternary stereogenic-centres with exquisite stereochemical control: diastereospecifity and enantioselectivity. These findings have been rationalized using experimental and theoretical methods and arise from steric activation of the π-cation, where increasing substitution disfavors planar (stablized) conformers of this cation and promote its cyclization.

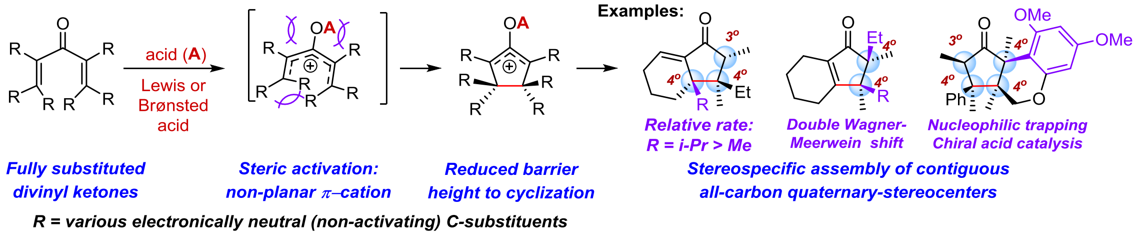

Figure 1: Steric Activation of the Nazarov Cyclization

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Organic reaction mechanisms and fractals

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The analogy between the theory of fractals, the basic principles of the linear correlations in the mechanistic organic chemistry such as linear free energy relationship (LEFR), Gunwald-Winstein correlations, and the laws of the general acid catalysis are discussed.
Fractal growth is characterized with the parameter called fractal dimension (D) defined by the relation

$$Y = X^D$$

whose logarithmic form is $\log Y = D \log X$

The real meaning of the notion of fractals is analyzed by investigating the analogy of this equation with the equations used for the determination of the organic reaction mechanisms in solutions, for instance, the analogy with the Hammett correlation

$$\log(k/k_0) = \rho \log(K/K_0)$$

Here, the parameter ρ is the measure of the sensitivity of the reaction on the structure of the reactant, and it is the characteristics of a particular reaction mechanism. From the analogy between ρ and D, the parameter ρ can be regarded as a sort of fractal dimension.
I argue that, as the reaction mechanistic linear correlations are valid only within the relatively narrow temperature range (as well as within the specific reaction conditions such as solvent, structure of the reactant, etc.), the same ought to be also with the fractal growth in general. In such a way, the mechanistic chemistry could motivate the redefinition of fractals theory on the way that fractals does not exist as structures in the nature but, rather, that fractals (with fractal dimension) describe the mechanism of the appearance of self-similarity, but only within the narrow range of space.

Screening and activation of a full hidden intermediate on the PES of E1cB/E2 borderline eliminations and of the Schmittel cyclization of enyne–allenes

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Full hidden intermediates have been elusive to locate on a given potential energy surface (PES) (see Figure 1); mainly, we focused on the E1cB/E2 borderline eliminations and the Schmittel cyclization of enyne–allenes as case studies. The electronic structure of these hidden species remains entirely uncoupled from the reaction coordinate. Therefore, we propagate forward and backward quasiclassical trajectories initialized in the transition state ensemble of the rate-determining step. Our screening strategy considers that a few so-called 'hot' trajectories will eventually reach the full hidden intermediate [3], higher in energy over the minimum energy path (MEP) connecting the reactant and product. Once this has been spotted, we rationalize how we can stabilize the full hidden intermediate to be coupled to the reaction coordinate. Naturally, replacing a substituent in the reactant should change the landscape of the PES, although it is possible that PES's evolution could be studied systematically. With this in mind, we get the necessary insights from a diabatic model of intermediate stabilization (DMIS) complemented with valence bond state correlation diagrams (VBSCD) [2,3]. That was the case for the mechanism of Schmittel cyclization of enyne–allenes, on which a biradical intermediate was featured as a full hidden. Through its stabilization, the partially hidden intermediate in formation transits from the biradical to a zwitterionic structure [3]. To enrich the discussion, the reactive normal modes of this reaction [4] will also be considered.

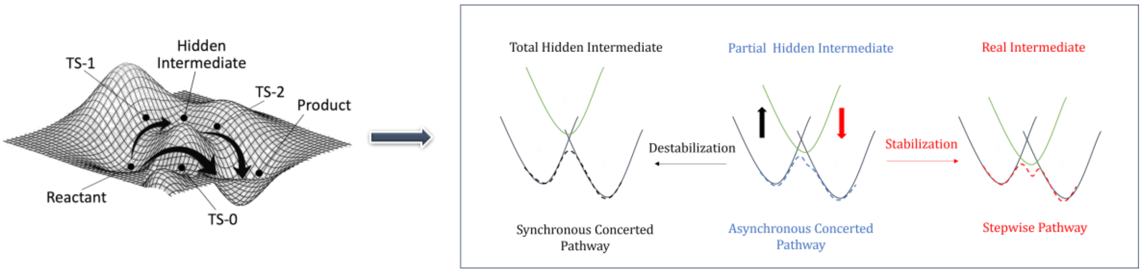

Figure 1. Schematic representation of the activation of a full hidden intermediate on the PES

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The quantum chemical nature of hydrogen bonds demystifies misconceptions

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In this work, we present a quantum chemical description of hydrogen bonding and clarify misconceptions arising from its classical mechanical interpretation. Hydrogen bonding is a crucial chemical interaction across many areas of chemistry, including reactivity and catalysis,[1] and fundamental physicochemical properties such as boiling points.[2] Classically, hydrogen bonding is described as a strong Coulombic interaction between a protonic hydrogen-bond donor, Y–H$^{\delta+}$, and a negatively charged region on the hydrogen-bond acceptor. According to the classical understanding, as recognized by IUPAC,[3] hydrogen bonds cannot form with hydridic Y–H$^{\delta-}$ donors.

Recently, the intermolecular interaction in Me$_3$Si–H$^{\delta-}$•••ICN has been incorrectly claimed to be a hydridic hydrogen-bonded system. This apparent breach of the classical rules led to a proposal to revise the IUPAC definition, extending the scope of hydrogen bonding beyond protonic Y–H$^{\delta+}$ donors to include hydridic Y–H$^{\delta-}$ donors.[4] However, the quantum mechanical interpretation of hydrogen bonds, based on Kohn–Sham molecular orbital (KS-MO) theory, challenges this proposal.

Herein, we demonstrate that interactions involving protonic and hydridic hydrogens are fundamentally distinct.[5] In fact, these represent two different bonding mechanisms, characterized by charge transfer in opposite directions. Contrary to typical hydrogen bonds, Y–H$^{\delta-}$ fragments act as acceptors in other well-established Lewis acid-base interactions, such as halogen, chalcogen, and pnictogen bonds. Quantum mechanics shows that hydridic hydrogen bonds cannot exist because of the Pauli exclusion principle. An increased overlap between same-spin occupied orbitals not only weakens hydrogen bonds but completely prevents their formation in the case of hydridic Y–H$^{\delta-}$ fragments.[5]

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Why do some heteroaromatics have n,π* states as their first excited states, while others have π,π* states as these?

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Heteroaromatic molecules are found in areas ranging from biochemistry to photovoltaics.[1] Hitherto there is no rationale as to which heteroaromatic compounds have π,π* states as their lowest excited state and which ones have n,π* states as these. We explore to what extent (anti)aromatic character is a decisive factor, yet, Baird's 4*n* rule on excited state aromaticity is applicable only to the lowest π,π* states.[2] Thus, a different rationale needs to be developed for the n,π* states, and we start at Mandado's 2*n*+1 rule for aromaticity of separate spins.[3,4] Heteroaromatics with (4*n*+2)π-electrons in S_0 and in-plane lone-pairs (n_σ, herein n), will in their n,π* states have 2*n*+2 π_α-electrons and 2*n*+1 π_β-electrons (or *vice versa*), and becomes π_α-antiaromatic and π_β-aromatic. However, the antiaromatic π_α- and aromatic π_β-components may not cancel, leading to residual aromatic or antiaromatic character (Figure 1A). We explore vertically excited triplet n,π* states (^{3}n,π*), which are most readily analyzed, but also singlet n,π* states (^{1}n,π*), and first explain which compounds have n,π* states with aromatic residuals as their lowest excited states. We can conclude that six factors impact on the order between the n,π* and π,π* states (Figure 1B): (*i*) the electronegativity of the heteroatom(s), (*ii*) the valence angle at the heteroatom impacting the lone-pair orbital energy, (*iii*) the number of π-orbitals and π-electrons, (*iv*) the degree of (anti)aromatic character of the n,π* state, (*v*) the electronegativity of atoms adjacent to the heteroatom, and (*vi*) the spatial extent of the n orbital affecting the intra-orbital electron repulsion.[5]

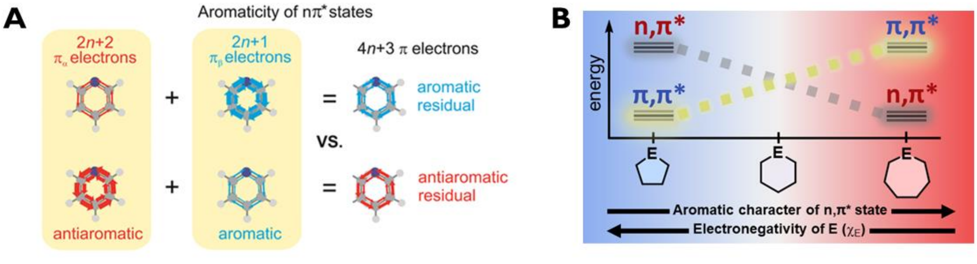

Figure 1. (A) Illustration of why n,π* states have aromatic or antiaromatic residuals. (B) Illustration of factors that influence on the energy order between the lowest n,π* and π,π* states of heteroaromatics.

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Synthesis of azulene-embedded PAHs via Scholl oxidation

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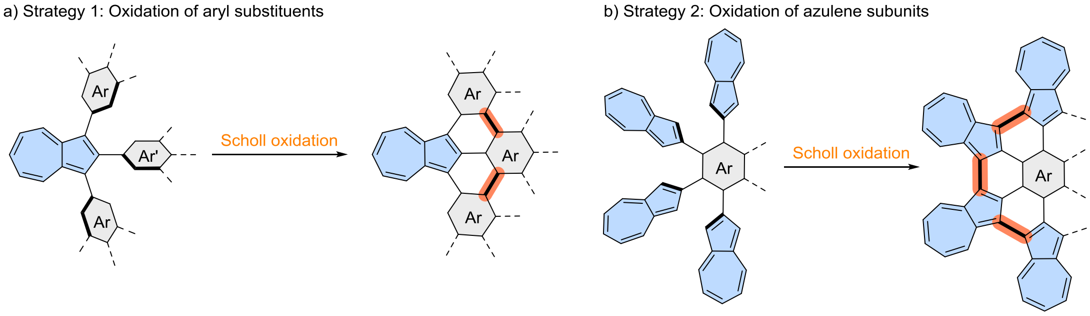
Recently, there has been growing interest in non-alternant polycyclic aromatic hydrocarbons (PAHs) for applications in organic materials.[1] Among these, azulene-containing π-scaffolds are particularly significant.[2, 3] PAHs incorporating an azulene moiety exhibit unique properties, such as biradical character[4] and near-infrared (NIR) absorption.[5] However, general synthetic methodologies for constructing such molecules remain limited, highlighting the need for further development.

Here we present a systematic study of two synthetic strategies involving Scholl-type oxidation. The two main approaches are: **(1)** the oxidation of benzenoid aromatic substituents surrounding the azulene core (Scheme 1a)[6] and **(2)** the oxidation of the reactive 1- and 3-positions of azulene subunits (Scheme 1b).[7, 8] By fine-tuning reaction conditions and substitution patterns, both strategies successfully yielded the unprecedented large nanographenes containing up to six azulene subunits. However, unexpected side products, including 1,2-phenyl shifts and dimerization, were also isolated. The target PAHs exhibit highly promising properties for organic materials, including red-shifted optical absorption extending beyond 1300 nm, a small electrochemical gap, and good solubility.


a) Strategy 1: Oxidation of aryl substituents

b) Strategy 2: Oxidation of azulene subunits

Scheme 1. Synthetic strategies for azulene-embedded PAHs via Scholl oxidation.

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On-Surface and Matrix-Isolation Strategies for Accessing Elusive Phosphorus–Nitrogen Species

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The isolation and characterization of exotic main group species continue to deepen our understanding of chemical bonding, with broad implications ranging from materials science to astrochemistry. In this talk, we present the formation of an elusive *o*-benzoquinone–PN complex, generated by UV irradiation (λ = 254 nm) of (o-phenyldioxyl)phosphinoazide. Upon subsequent irradiation with light at λ = 523 nm, the complex recombines to form (o-phenyldioxyl)-λ^5-phosphinonitrile,demonstrating, for the first time, the reactivity of PN with an organic molecule (Figure 1A).[1] We also report the on-surface synthesis of cyclotriphosphazene (P_3N_3), an inorganic aromatic analogue of benzene, via voltage pulse-induced dechlorination of $P_3N_3Cl_6$ on a Cu(111) surface at 5.2 K. Real-space imaging confirms its planar D_{3h}-symmetric structure, which is further corroborated by matrix isolation spectroscopy following photolytic conversion of a hexaazide precursor (P_3N_{21}) (Figure 1B).[2] Additionaly, we showcase the synthesis of hitherto unpreported neutral hexanitrogen (N_6), a long-sought allotrope of nitrogen, achieved via room temperature gas-phase halogenation of silver azide and subsequent cryogenic isolation. Spectroscopic analyses and high-level computations confirm its identity and reveal its surprising kinetic stability, even at the temperature of liquid nitrogen (Figure 1C).[3]

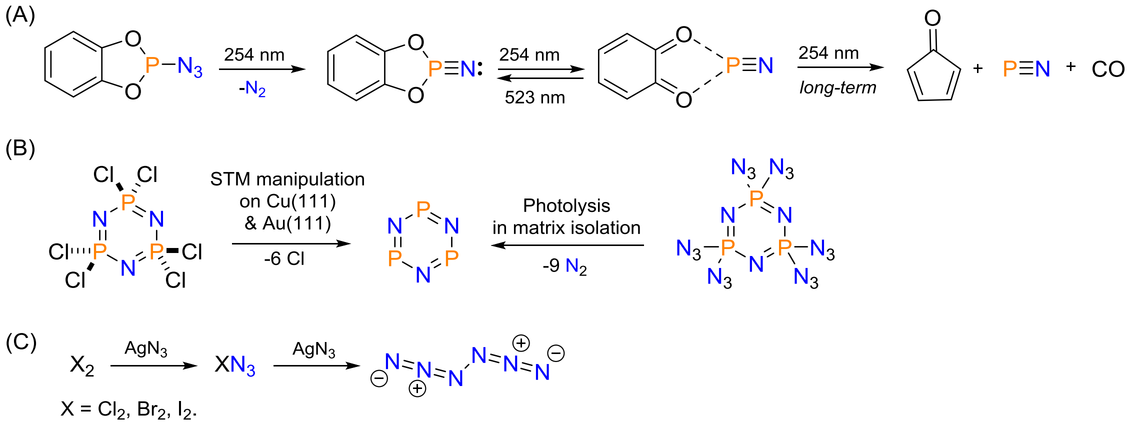

Figure 1. Reaction sequences employed in the studies.

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Dissolved or assembled reactants? The case of the Formose reaction

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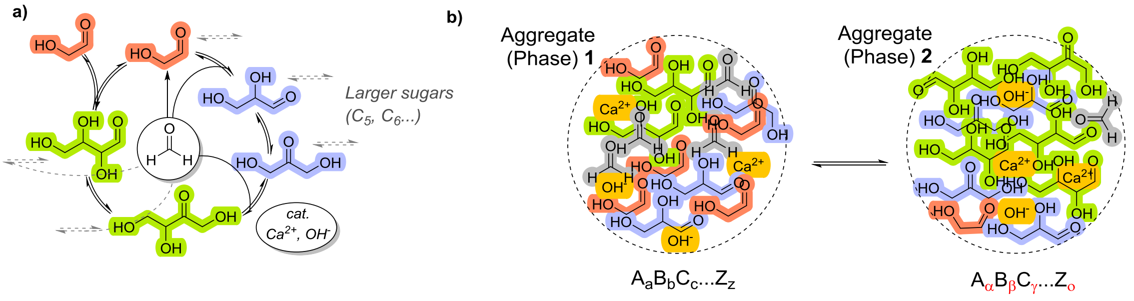
By default, chemicals in reaction mixtures are supposed to be in solution-phase when there is no evident sign of phase separation, such as a hazy or milky appearance resulting from solid particles or liquid droplets. Though, this can be deceiving: small molecules can aggregate to assemblies large enough to behave like a separate phase, but still small enough not to cause any visible turbidity.[1] This can have a profound impact on chemical reaction networks, as these are then governed by phase equilibria instead of molecular equilibria.

Under this perspective we are currently revisiting the Formose reaction, a reaction network that forms a combinatorial explosion of sugars from formaldehyde, catalysed by Ca^{2+} and basic pH (cf. Figure 1a). It is discussed in the context of the origin of life, namely in the prebiotic formation of sugars and nucleic acids.[2] Despite being discovered over 150 years ago,[3] the reaction network as a whole is still not understood.[4] Recent results from Dynamic Light Scattering (DLS), Nanoparticle Tracking Analysis (NTA) and other analytical techniques suggest that the sugars are in aggregated form instead of solution-phase, which might be a key factor that has been overlooked so far.



Molecular equilibria... *... or phase equilibria?*

Figure 1. a) Autocatalytic Breslow cycle, which is at the heart of the Formose reaction. The depicted sugars can add to further formaldehyde, C_2 or higher sugars to make larger sugars (C_5, C_6..., grey dashed arrows); b) illustration of Formose constituents assembled into large aggregates. Here, equilibria are not between individual molecules but between phases, i. e. ensembles of aggregates of same composition and fix constituent ratio.

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OC12

Autonomous mobile robots for exploratory synthetic chemistry

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Autonomous laboratories can accelerate discoveries in chemical synthesis, but this requires automated measurements coupled with reliable decision-making. Most autonomous laboratories involve bespoke automated equipment and reaction outcomes are often assessed using a single, hard-wired characterization technique. Any decision-making algorithms must then operate using this narrow range of characterization data. By contrast, manual experiments tend to draw on a wider range of instruments to characterize reaction products, and decisions are rarely taken based on one measurement alone. Here we show that a synthesis laboratory can be integrated into an autonomous laboratory by using mobile robots that operate equipment and make decisions in a human-like way.

Our modular workflow (Figure 1) combines mobile robots, an automated synthesis platform, a liquid chromatography–mass spectrometer and a benchtop nuclear magnetic resonance spectrometer. This allows robots to share existing laboratory equipment with human researchers without monopolizing it or requiring extensive redesign. A heuristic decision-maker processes the orthogonal measurement data, selecting successful reactions to take forward and automatically checking the reproducibility of any screening hits. We exemplify this approach in the three areas of structural diversification chemistry, supramolecular host–guest chemistry and photochemical synthesis. This strategy is particularly suited to exploratory chemistry that can yield multiple potential products, as for supramolecular assemblies, where we also extend the method to an autonomous function assay by evaluating host–guest binding properties.[1]

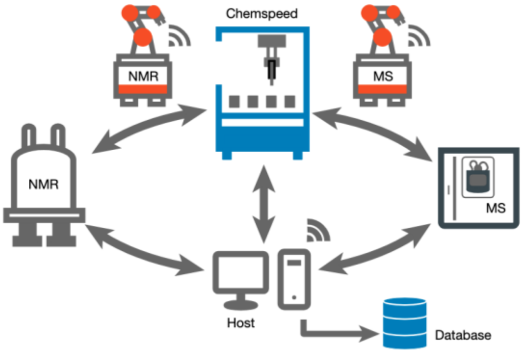

Figure 1. Workflow for autonomous synthesis using mobile robots, synthesizer, MS, and NMR analysis.

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OC13

Kinetics-guided aqueous synthesis of phosphoramidates and thiophosphoramidates from P(V) dichloridates

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The preparation of phosphate-containing and phosphate-mimicking molecules underpins areas of enzyme, nucleoside, inositol and bioconjugate chemistry. Most of these phosphate systems find their applications in aqueous media, and thus their preparation in aqueous media is a logical approach. We will describe a combination of experimental and theoretical studies that deliver understanding on how phosphodichloridate and thiophosphodichloridate ions function as electrophiles towards amines in water to deliver (thio)phosphoramidates, which are phosphate mimics. Direct access to phosphoramidates from P(V) chlorides offers a general approach to P(V)–N systems that avoids the use of condensing agents.

Phosphodichloridate ($PO_2Cl_2^-$) and thiophosphodichloridate ($PSOCl_2^-$) ions react selectively with amines in aqueous media to produce phosphoramidate ($R'RNPO_3^{2-}$) and thiophosphoramidate ($R'RNPSO_2^{2-}$) ions. Aminolyses of $PO_2Cl_2^-$ and $PSOCl_2^-$ with anilines, primary alkyl amines, secondary alkyl amines and hypernucleophilic amines revealed Brønsted relationships between rate coefficients for aminolysis k_N and amine pK_{aH}. Rate constants were used to predict the outcomes of aminolysis experiments in aqueous media and our predictions matched experimental outcomes. Exploitation of Hammett and Bronsted LFER analyses alongside DFT calculations allows us to present strong evidence for an associative $S_N2(P)$ mechanism.

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Bis(Phosphazenyl Phosphines) as Potential Metal-Free Catalysts for CO_2 Reduction

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CO_2 emissions have been steadily increasing each year, exacerbating the global warming crisis. However, over the past decade, research has shown that CO_2 can serve as a promising carbon source for synthesizing various important chemicals, including formic acid, methanol, urea, and others. Among these, the hydrogenation of CO_2 to formic acid is of particular interest, as industrial production currently relies on use of methyl formate and formamide [1]. However, CO_2 hydrogenation is challenging because it usually requires the simultaneous activation of both H_2 and CO_2, and both molecules exhibit high stability. For example, cleavage of the C=O bond in CO_2 requires 192 kcal mol^{-1} whereas breaking the H-H bond requires 104 kcal mol^{-1}. To address these challenges, numerous noble metal-based catalysts, have been employed in CO_2 hydrogenation reactions. Despite their efficacy, the high cost of these noble metals presents a major limitation for their widespread use as catalysts. Recently, inspired by natural photosynthesis, where CO_2 reduction is achieved using NADPH cofactors, biomimetic metal-free hydride donors have been explored as catalysts for the selective reduction of CO_2 to formate [2]. A critical consideration here is that hydride donors for CO_2 reduction should possess higher hydride donor strength than formate anion. The hydride donor strength is commonly expressed via thermodynamic hydricity ($\Delta G H^-$), defined as the standard Gibbs energy required for hydride ion release: $R\text{-}H \rightarrow R^+ + H^-$. Herein we will present the unexpected ability of protonated electron-rich phosphazenyl phosphines [3] to act as highly effective hydride donors, offering a potentially novel pathway for CO_2 reduction. Moreover, we explore the feasibility of closing the catalytic cycle of CO_2 reduction through the heterolytic cleavage of a dihydrogen (H_2) molecule within a frustrated Lewis pair framework. This process aims to generate formic acid while simultaneously regenerating the phosphine catalyst.

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Heterogeneous photocatalysis in continuous flow systems

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An innovative deep-coating technique was developed to produce coated glass pipes for flow photocatalysis. The system was tested for antibiotic residues transformation, enabling its application in a custom-designed continuous flow reactor powered by a sustainable light source, such as sunlight. Coating was tested with inorganic semiconductors and also with semiconductor polymers. Batch experiments were conducted for comparison, with the catalyst in powdered form under both ultraviolet (UV) and visible (Vis) light irradiation, achieving up to complete (100%) transformation under UV and up to 55% transformation under Vis light. The experimental data were well described by the Langmuir-Hinshelwood (L-H) kinetic model. This system achieved over 60% transformation under sunlight irradiation. LC/MS analysis of the transformation by-products revealed different pathways, that will be discussed.

A multi-site adsorption model allowed to explain the observation of biphasic kinetic traces in these kind of systems.

Cysteine Thioaldehydes – Generation and Reactivity

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Cysteine thioaldehydes are proposed as fleeting intermediates in a small number of important biological pathways, including the activation of sulfatases and the biosynthesis of penicillin, coenzyme A and a few families of ribosomally synthesised and post-translationally modified peptides (RiPPs).[1-5] However, the highly reactive nature of the carbon–sulfur double bond makes the study of thioaldehydes challenging.[6] We have studied the reactivity of cysteine thioaldehydes in biological media by generating them through Norrish Type II photolysis of the corresponding phenacylsulfide derivatives.[7,8] Depending on the conditions (pH, buffer) and peptide sequence, cysteine thioaldehydes can be transformed along different pathways to give a complex distribution of products, including enethiols, isothiazolones, 1,2,4-trithiolanes, formylglycine, thiazoles and oxazoles (Figure 1). These studies have revealed important insights into some of the biological pathways mentioned above, especially the activation of sulfatases, which involve the aerobic or anaerobic transformation of a cysteine residue into a formylglycine residue via a thioaldehyde.

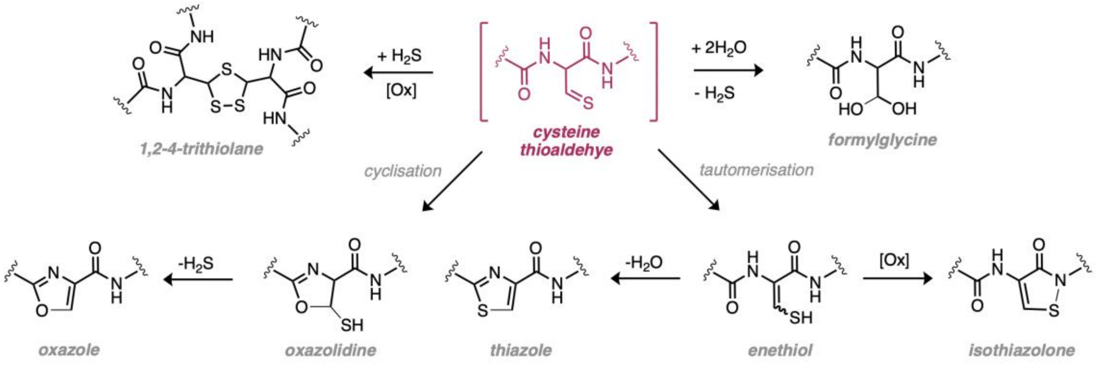

Figure 1. Products derived from cysteine thiolaldehydes in aqueous media

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Anionic calixarenes oppose α-synuclein oligomers and their toxicity effects in a Parkinson's disease model

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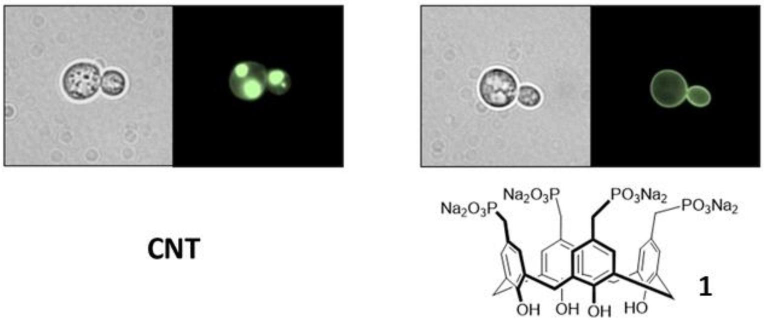
Parkinson's disease (PD) is the most common neurological disorder together with Alzheimer, with a growing trend and a heavy impact on persons and public health systems, in particular in developed countries with elderly populations. A PD hallmark is the accumulation of intracellular inclusions (Lewy bodies) containing misfolded α-synuclein (AS) aggregated in toxic oligomeric forms.[1] AS is a small protein abundant in the brain, primarily found in nerve terminals, involved in regulating the vesicle trafficking network. Exploiting a host-guest approach and starting from the well-known ability of some negatively-charged calix[4]arenes to complex lysine side chain,[2] we prepared different anionic calix[4]arenes as potential ligands of AS. AS, jn fact, is characterized at the N-terminal domain by the presence of the repeating partially conserved motif KTKEGV playing a role in the pathological aggregation. The calixarene derivatives were tested in engineered *Saccharomices cerevisiae* cells, used as consolidated model of human PD. We observed that some of the calix[4]arenes, mainly **1**, indeed counteract AS-induced toxicity, through the reduction of oligomer formation, restoring different metabolic pathways impaired by AS oligomers and hindering other damaging events such as oxidative stress. NMR studies confirmed the ability of the macrocyles to interact with the AS N-terminal domain and, in particular, with Lys residues.



CNT

1

Figure 1. α-Synuclein oligomers in intracellular foci observed in untreated yeast cells (CNT; left), are absent in cells treated with anionic calixarene **1** (right).

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Artificial Supramolecular Signal Transduction Systems

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Many of the unique properties and functions of complex biological systems arise from the compartmentalisation afforded by lipid bilayer membranes. These membranes form an important barrier between the cell's internal fluid and the external medium. However, extracellular molecules, such as hormones, nutrients and pathogens, can change the intracellular chemistry by signalling across the cell membrane via membrane-spanning proteins.

Inspired by this, we have long been interested in creating entirely synthetic systems that functionally mimic this process by coupling an external molecular recognition event with an internal catalytic process [1]. As well as the fundamental challenge of creating life-like artificial cells, this approach has the potential to interface with biological systems in sensing applications, to supplement natural systems with artificial components that can recover lost function and to create responsive systems that can deliver material to specific sites and act as controllable microreactors [2]. Our most recent approach to transmembrane signaling has involved controlling the location of a transducer within a membrane to modulate its catalytic activity [3]. However, a weakness in the current systems is that they suffer from low catalytic activity, so the nature of the substrates, the capacity for turnover and the difference between the on and off states are all limited, reducing their potential. In this contribution, we report a much more efficient catalytic transducer, and show how it can be controlled by a new signaling analyte. We also broaden the overall configuration of the system to provide new opportunities in the types of constructs that can be formed, for example facilitating intervesicular communication for.

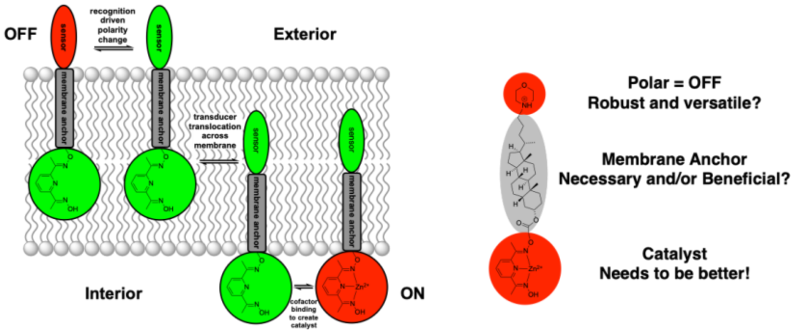

Figure 1. Schematic of artificial transduction system and the questions addressed in this contribution.

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Toward bimetallic nanowires: Insights from the co-impregnation of block copolymer films

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Bimetals and alloys often display synergistic effects that give rise to non-linear properties at specific composition ranges. Confining these materials in nanowires is particularly beneficial for applications in catalysis, magnetism, and sensing owing to the high surface area and nanoscale confinement effects.

To date, ordered arrays of *mono*-metallic nanowires have been obtained by employing block copolymer films as sacrificial templates. In this approach, periodic arrays of nanoscale domains formed by phase separation are selectively impregnated by metal precursors. Subsequent plasma treatment eliminates the polymer film, and the metal precursors are reduced *in situ* into metallic nanostructures in the process.[1,2] Selective co-impregnation with two metal precursors in solution seems like the next logical step toward obtaining *bimetallic* nanowires.[3] However, the need to tune their composition to a desired range poses a challenge, because the resulting metal composition seldom matches the ratio of metal precursors in the impregnating solution.

In the presentation, I will describe the intricate competitive-cooperative mechanisms of impregnation that were unraveled by a deep exploration into the nature of interaction between pairs of three metal precursors (Pd, Pt, and Co) and the functional groups in the block copolymer domains. The different behaviors were successfully modelled using a single equation, which provides intuitive physical insights into the interplay between the metal precursors as they compete over binding sites.[4]

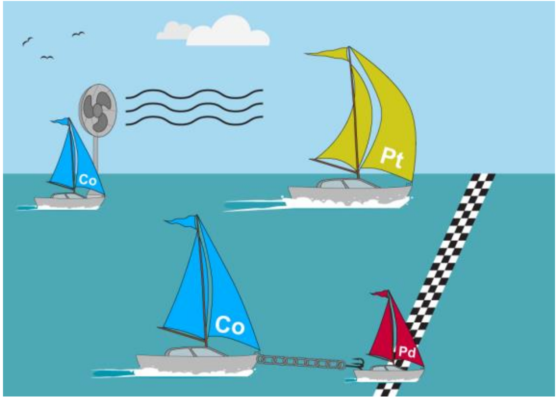

Figure 1. Illustration of the competitive-cooperative co-impregnation mechanism

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Predicting Reactivity and Catalysis in Water Based on High-Throughput Kinetic Experimentation

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Understanding the molecular origins of chemical reactivity and catalysis in water remains a fundamental challenge with far-reaching implications across the chemical sciences — from deciphering complex reaction networks in systems chemistry, rationalizing enzymatic catalysis, to advancing green chemistry. Yet the vast combinatorial space of substrates, catalysts, and reaction conditions in aqueous environments[1] currently precludes the reliable quantitative prediction of reaction rates. In this work,[2] we present the development and implementation of a high-throughput experimental pipeline designed to measure reference-quality rate constants in water (Figure 1). Focusing on acid/base catalysis, we have compiled an extensive dataset comprising several thousand experimentally determined rate constants across a diverse range of conditions and molecular structures. Through a combination of classical free-energy relationship analyses and modern machine-learning regression techniques, we have constructed predictive models that not only quantitatively deconvolute competing catalytic mechanisms but also establish a robust framework for predicting rate constants across substrates and environmental parameters. These models advance our mechanistic understanding of chemical reactivity in aqueous media and represent a step toward general, quantitative prediction of chemical kinetics in water.

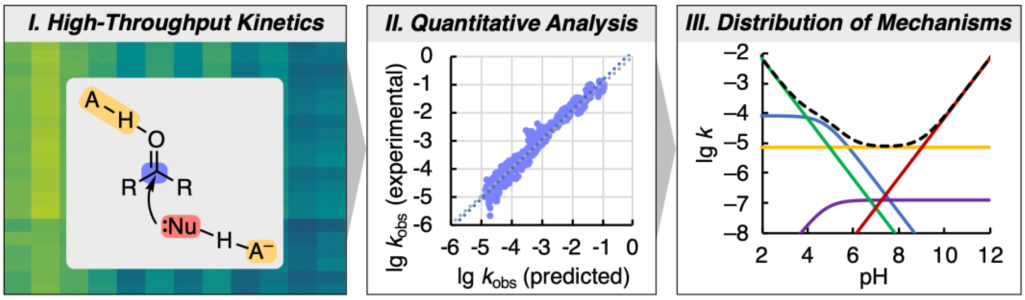

Figure 1. (I) High-throughput kinetics enable exploring the kinetic space of nucleophilic addition reactions in water. (II/III) Models built on the basis of the kinetic data allow for both quantitative predictions of rate constants and for the deconvolution of the competing mechanisms of catalysis.

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Quantifying solvent effects in mixtures containing ionic liquids

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Ionic liquids have long been suggested as alternatives for organic solvents in preparative chemistry.[1] However, changes in reaction outcome relative to molecular solvents[2] have limited their application. Our group has focused on understanding these ionic liquid solvent effects, with interactions in solution being able to explain how such effects vary with the amount and nature of the ionic liquid.[3]

Lacking at this stage is the ability to quantitatively predict these solvent effects - we can identify the optimum proportion of the best ionic liquid(s) to affect reaction outcome; whether this results in a change in (say) rate constant of two-, ten- or one hundred-fold remains elusive. This presentation will introduce a range of questionably successful solvent parameters, introduce the possibility for machine learning approaches,[4] identify that structural features might correlate to reactivity[5] but show that, ultimately, resorting to formal physical organic reactivity parameters[6] does the trick (Figure 1a).[7] In doing so, correlations between features in solution and these parameters (Figure 1b) may explain the fundamental changes observed.[8]

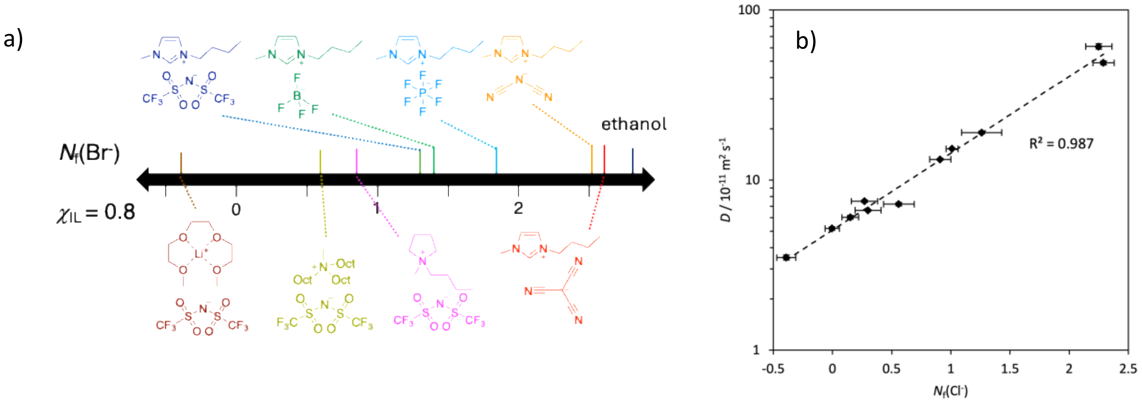

Figure 1. (a) The nucleofugality of bromide in ethanol and each of a series of ionic liquids (χ_{IL} = 0.8). (b) Linear correlation of D_{cation}, normalised for cationic charge, with $N_f(Cl^-)$ for a series of mixtures of ethanol and ionic liquids.

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OC22

Hydrogen Transfer Mechanisms in the Anthraquinone Process

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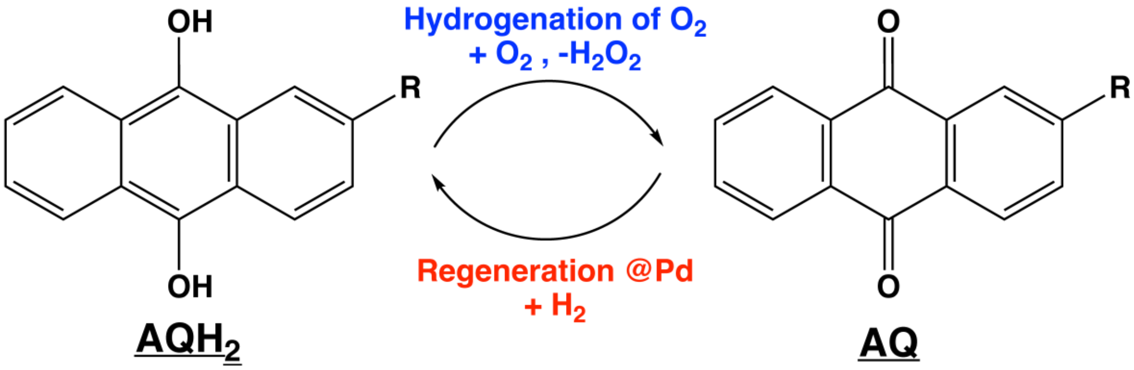
The anthraquinone (AQ) process (Riedel–Pfleiderer process) is the key industrial method for production of hydrogen peroxide. Within this process anthrahydroquinone (AQH_2) is oxidized to hydroxyanthraquinone (AQH_2) whereupon O_2 is reduced to H_2O_2 (Scheme 1). Despite its large-scale implementation, the mechanistic details of the reduction of O_2 still remain unclear. Traditionally, it was described to proceed through an endoperoxide intermediate in a spin-forbidden reaction. However, a more recent computational study suggested subsequent hydrogen atom transfers to O_2 via an anthrasemiquinone ($AQH^\bullet$) radical to be more likely, including an intermediate cross-over from the triplet to the singlet potential surface preceding the second H transfer. Here, we have reacted substituted anthrahydroquinones with O_2 in controlled gas phase experiments within the collision cell of a modified mass spectrometer. The experimental findings, supplied with our own quantum chemical computations, provides support to the stepwise mechanism.



Scheme 1. In this study R = $-CH_2NMe_3^+$, CO_2^- and SO_3^-. Only the forward reaction was studied.

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The Dynamic Chemistry of the $\equiv\mathrm{B}^{-}\text{—}{}^{+}\mathrm{N}\equiv$ Bond

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Dynamic combinatorial chemistry (DCC) is a prominent field due to its relevance to several areas where fast bond breaking and formation are central such as supramolecular chemistry, catalysis, dissipative systems, and systems chemistry.[1] Both covalent and supramolecular bonds have been exploited for the construction of dynamic libraries (DLs) which are sets of compounds that interconvert under equilibrium conditions. Typically, covalent bonds form and break more slowly than supramolecular bonds in the absence of a catalyst.

Although not traditionally categorized within DCC, the reversible bonding of boron and nitrogen compounds has been exploited to synthesize (supra)molecular architectures such as molecular cages,[2] rotaxanes,[3] supramolecular adducts,[4] and polymeric materials.[5] In this work, we investigate the properties of the dative $\equiv\mathrm{B}^{-}\text{—}{}^{+}\mathrm{N}\equiv$ bond in the adducts between phenylboronic acid catechol ester and several *N*-heteroaromatic amines (see Figure 1). Such compounds interconvert rapidly even in the absence of a catalyst. Then, we build DLs of increasing complexity involving multiple amines (both *N*-heteroaromatic and aliphatic) and phenylboronic acid catechol ester. Finally, we transiently alter the population of such DLs employing tribromoacetic acid as a stimulus.

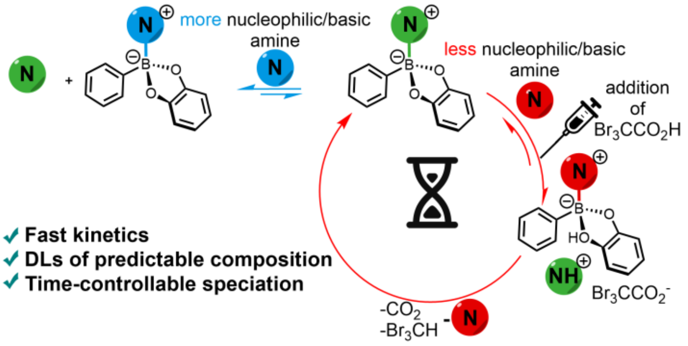

Figure 1. Schematic representation of a DL based on the dynamic B-N bond and transient alteration of its population by means of tribromoacetic acid.

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Light-Controlled Magnetic Levitation

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Light-driven, remote-controlled movement has been achieved with microscopic and nanoscale objects, typically below 100 micrometers in size, with optical tweezers. Larger objects need extremely high laser power leading to overheating and damage. Expanding the size range of objects that can be moved contactlessly would open up new applications across multiple fields, such as biomedicine, materials science, robotics, precise placement in microelectronics or assembly of optoelectronic components.

Larger objects (up to the size of a frog) can be lifted using diamagnetic levitation. However, they cannot be precisely positioned by remote control. We now achieved light-controlled magnetic levitation by the design and synthesis of photoswitches that change their magnetic susceptibility upon irradiation reversibly with blue-violet and green light. We achieved the levitation and light-driven position control of particles with a diameter of 1 mm.

Tautomerism and Conformational Effects in Protonated and Copper(I)-Coordinated Bis(oxazoline) Ligands: Insights from Spectroscopy and DFT

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Tautomerization and conformational flexibility play a central role in shaping the structure and reactivity of bis(oxazoline) (BOX) ligands, both in their free protonated forms and when coordinated to metals. We present a combined spectroscopic and computational study of (S,S-Ph-BOX)H$^+$, its dimethylated analogue (S,S-Ph-diMeBOX)H$^+$, and their corresponding copper(I) complexes. IRMPD spectroscopy and ion mobility measurements, supported by DFT calculations, reveal tautomerism in the protonated (S,S-Ph-BOX)H$^+$ and a broader conformational ensemble in the sterically constrained diMeBOX derivative.[1] For copper(I)-BOX complexes, large variations in calculated ligand dissociation energies (BDEs) are traced to the choice of conformer and tautomer. Comparison with experimental IRMPD spectra confirms that only the correct tautomeric form yields reliable agreement with measured BDEs. These findings underscore the importance of tautomer control for accurate structure-energy relationships in BOX-based catalytic systems.

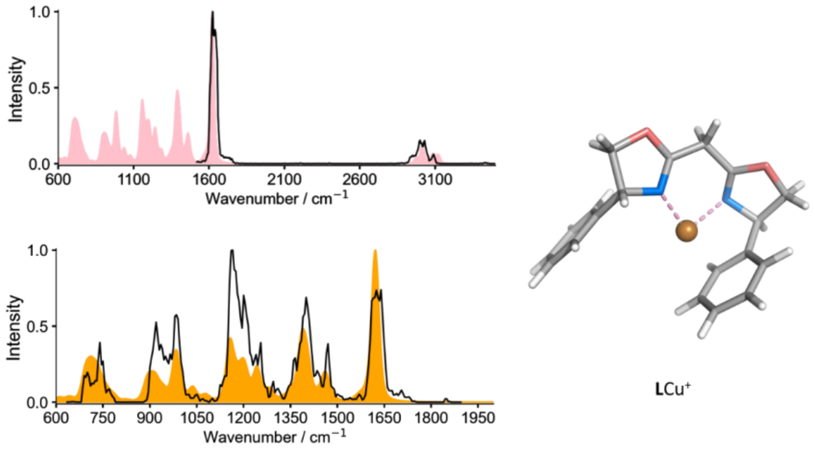

Figure 1. IRMPD spectra (black lines) together with the DFT-predicted (BP86/def2-TZVP) IR spectra for the most stable isomer of the BOXCu$^+$ in the region 600 to 3500 cm^{-1} (top) and 600 to 2000 cm^{-1} (bottom).

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Crystallizing the Transient: Phthalaldehyde-Based Species as a Gateway to Functional Hybrid Materials

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Phthalaldehyde is a highly reactive dialdehyde known for forming dynamic mixtures with nucleophiles, making isolation of well-defined crystalline products challenging.[1] In this work, we investigate its reactions with selected nucleophiles—Tris, 2-picolylamine, and 2-hydrazinopyridine—in the presence of transition metal ions (Cu, Co, Zn, Mn, V, La) under aerobic and anaerobic conditions. By leveraging hydrogen-bonding design and symmetry principles, we succeeded in isolating and structurally characterizing a variety of transient species, including a tetranuclear oxovanadium cluster with near-infrared absorption of light,[2] porous coordination networks incorporating 1-iminoisoindoline units,[3] and novel dicopper(I)-bishydrazone-based halometallate[4] and nitrate salts.[5] These materials not only provide insight into the coordination chemistry of unstable intermediates but also exhibit functional properties. In particular, the nitrate-stabilized bishydrazone complexes enabled the preparation of graphite-based hybrid materials with enhanced surface area and chemiresistive response on gold interdigitated electrodes. Our findings demonstrate how careful control of reaction conditions and molecular interactions can steer complex systems toward isolable, functional products, with implications for materials chemistry and sensor design.

Acknowledgements: The research leading to these results was supported by the Johannes Amos Comenius Programme, European Structural and Investment Funds, project 'CHEMFELLS VII‘ (No. CZ.02.01.01/00/22_010/0008809).

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Quantitative detection of free radical intermediates in organic reactions

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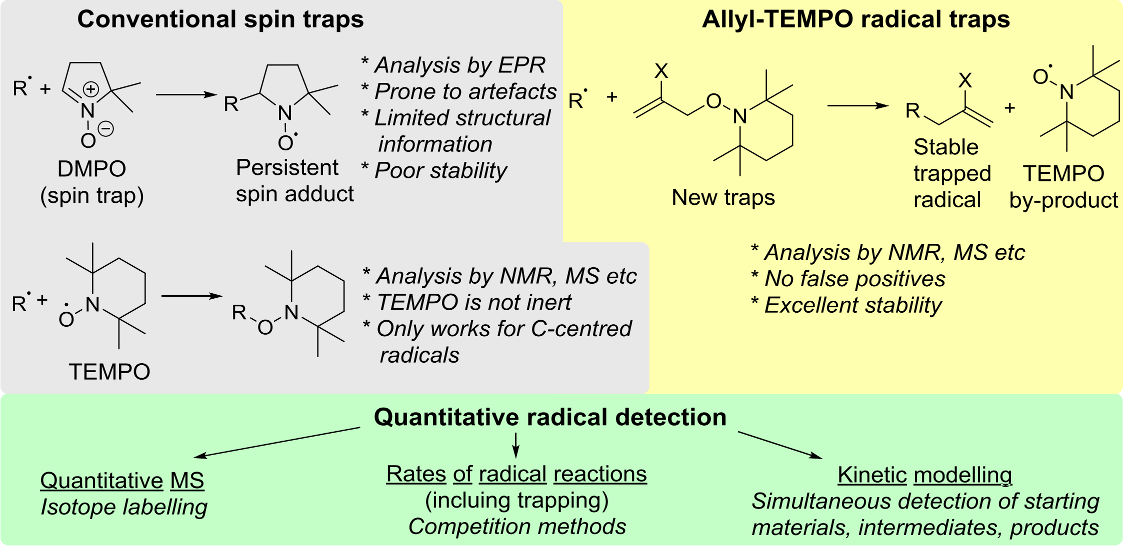
Detection of short-lived free radical intermediates is a challenging task mostly due to their low steady-state concentration in reaction mixtures. Therefore, these intermediates are often trapped using nitrone- or nitroso-derived spin traps (e.g., DMPO) or stable free radicals such as TEMPO (recombination traps).[1] While very powerful, these methods suffer from many drawbacks including limited structural information, artefact formation etc. We have recently developed a new type of allyl-TEMPO radical traps which can be used in combination with conventional analytical techniques such as NMR or MS; this new method resolves many of the disadvantages of the conventional radical trapping.[2]

Here, we will demonstrate how the allyl-TEMPO traps have helped to improve our mechanistic understanding of selected free radical reactions.[3] A particular challenge is quantitative radical detection. This not only requires the quantification of trapped radicals (which is a challenge for MS!) but also the knowledge of the rate constants of radical formation and the rate constants of their further competitive reactions (including trapping).



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Understanding selectivities in radical reaction: the case of Truce-Smiles rearrangement

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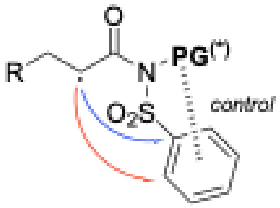
The Truce-Smiles rearrangement (TSR) in its radical version is a transformation involving the migration of an aromatic ring to a previously created radical carbon, through a photocatalytic [1] or an electrochemical [2] process in the last developed versions. An aryl group can therefore be regioselectively installed at a position that would be difficult to achieve under more classical approaches and more recent approaches also allow to design compounds in a diastereoselective manner.[1,3]
One of the main problems of the radical Truce-Smiles rearrangement is the competition between the 5-*exo* and the 6-*endo* cyclisation which can occur during the rate determining step (Scheme 1). We will show that this can be controlled by establishing specific non-covalent interactions with protective groups.
We will subsequently show that these protective groups, needed for the acrylamide moiety involved in the TSR, have a profound impact on the mechanism by locking some specific conformations, which allows subsequently to understand the physico-chemical parameters controlling the reaction.
Finally, it will be demonstrated how the same non-covalent interactions allow to develop a stereoselective version of the TSR in its radical version, through the unlocking of unstable, but thus more reactive, conformations.



Scheme 1.5-*exo* *vs*. 6-*endo* in radical TSR

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Poster Presentations

P1

Multifunctional calixarene platforms for the selective delivery of nucleic acids

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Calixarenes have been extensively used as scaffolds for the design of preorganized molecular receptors for ions and small molecules until, in the latest 20 years, they became attractive as building blocks for the preparation of ligands able to interact with macromolecules of biological interest, also showing surprising and peculiar properties that strongly depend on their size, structure and conformation.[1] Amphiphilic cone calixarenes (e.g. **1-3**)[1,2] bearing basic amino acids or guanidinium ions at the upper rim have been shown to bind nucleic acids of different type (DNA, RNA, PNA)[3-5] and to efficiently transfect cells.[6] The knowledge acquired so far sheds a bright light on the future applications of calixarenes in bionanotechnology and nanomedicine.

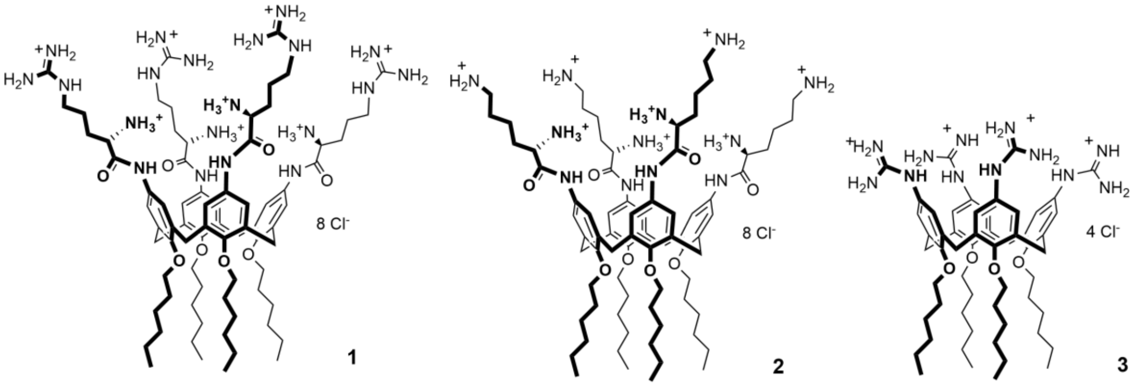

Figure. Selected calixarene-based delivery systems for natural/artificial nucleic acids.

Acknowledgements: This work was funded under the National Recovery and Resilience Plan (NRRP), M4 C2 Investment 1.1— Project "National Center for Gene Therapy and Drugs based on RNA Technology", code MUR CN00000041 – CUP [E63C22000940007], Call for Tender D.D. No. 3138 of the 2021.12.16 modified with D.D. No. 3175 of the 2021.12.18 by Italian Ministry of University and Research, PNRR–M4C2–BAC - CUP D53C23003990007 – funded by the European Union–NextGenerationEU, CASN_A_23_PNRR_BAC-MUNUS_01 – "Multifunctional synthetic platforms for the precision delivery of Nucleic AcidS –MUNUS".

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Molecular engineering of kinetically stable quaternary ammonium salts for renewable energy applications

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Quaternary ammonium groups (QA) are a necessary element in renewable energy devices (fuel cells, flow batteries).[1] They are embedded in anion-exchange membranes (AEMs), which are the separator materials in these devices, responsible for selective transport of anionic charge carriers, while blocking gases, electrons, and cations.[2] The major drawback in AEMs' is their chemical stability, particularly in high-power operating conditions (high pH, low hydration, elevated temperatures) leading to undesired chemical reactions between hydroxide anions and the QA groups, limiting the lifetime of the device.[3,4]

In this research, we combine *in silico* modeling and experimental results to conceive general design rules for kinetically stable QA functional groups. We investigate different degradation pathways (i.e., substitution, elimination, or electron transfer) while varying electronic and steric parameters of multiple families of QA (Figure 1). This, to identify their weak spots, and connect simple structural parameters such as bond lengths, partial charges, and free volume around possible reaction centers to kinetic stability towards the nucleophilic hydroxide.[5]

To support our computational predictions, we synthesize the most promising QA and test their stability experimentally, adding to our already large experimental database used to create the predictions. Our combined approach will allow us to gain better understanding of the structure-property relationships in bottom-up QA design as well as to address the technological challenge of achieving real long-life operations.

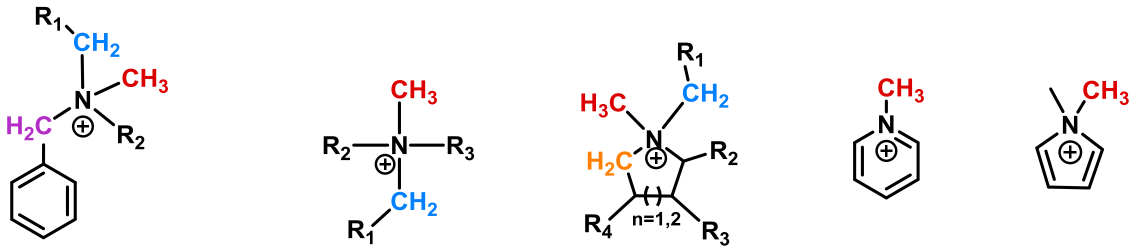

Figure 1: Families of molecules studied in our research.

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Tunable Preparation of α-Aminoacyl Fluorides and α-Fluoroamides via Base-Induced Cascade Multiple-Cleavage Processes from Bromodifluorohydrin Reagents and Amines

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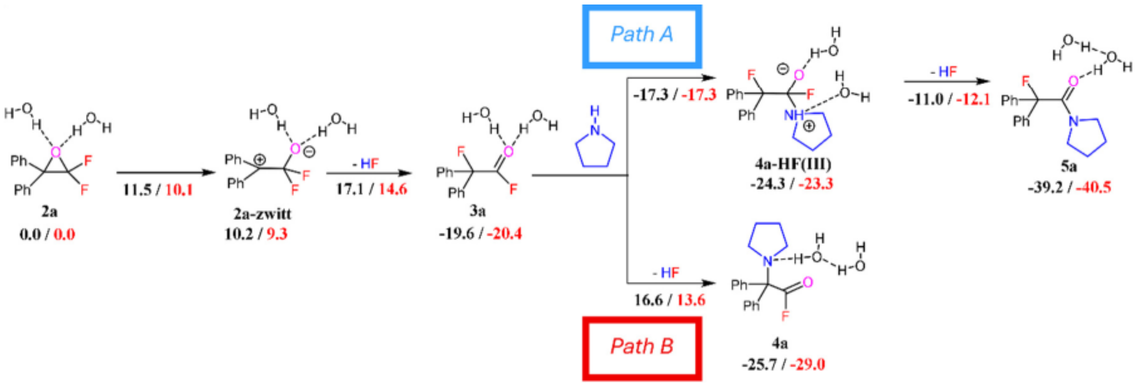
The demand for organofluorine and halodifluoromethyl compounds in organic synthesis is increasing.[1] Recent advances have made these compounds versatile building blocks,[2] with various cleavage modes.[3] A novel strategy for the synthesis of α-fluoroamides and α-aminoacyl fluorides using 2-bromo-2,2-difluoroalcohols and amines is proposed. This research explores experimentally and computationally a base-induced cascade multiple-cleavage process, forming these fluorinated compounds under mild conditions.

The computational part of this study investigates the reaction mechanism and role of hypothetical gem-difluoroepoxide. DFT and DLPNO-CCSD (T) single-point calculations were used to map the energy profiles. The reaction is studied in acetonitrile and acetonitrile-water mixture. Epoxide **2a** (Scheme 1), which is formed from an alkoxide intermediate, shows zwitterionic character (**2a-zwitt**) due to water molecule stabilization. Calculations reveals that the presence of water made α-fluoroamide **5a** formation more favorable and lowers the activation energy barriers compared to pure acetonitrile reactions, influenced by the **2a** amphionic nature.



Scheme 1. Reaction in acetonitrile and water. Free energies in kcal mol^{-1} at 293 K at the M06-2X/def2-TZVP (black) and DLPNO-CCSD(T)/def2-TZVP//M06-2X/def2-TZVP (red) levels of calculation.

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Synthesis and characterization of fluorescent cholesterol derivatives for production of Nano-Ghosts

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Access to novel labeled lipids has become increasingly straightforward over the past decades, owing to their broad application in imaging and drug-delivery technologies. In particular, the development of fluorescent cholesterol analogues that retain the physicochemical and biological properties of native cholesterol is experiencing growing interest, given cholesterol's pivotal role in regulating membrane packing, protein dynamics, permeability, and intracellular trafficking. Notably, such fluorescent derivatives are especially valuable for investigating the in vitro behavior of nano-ghost systems, as they allow for real-time visualization of membrane movement, fusion, and localization via optical microscopy. Nano-ghosts represent an emerging class of nanocarriers composed of empty cellular membranes, specifically engineered for targeted therapeutic delivery. Their biomimetic architecture confers immune-evasive properties and intrinsic targeting capabilities, thereby minimizing systemic toxicity and enhancing therapeutic efficacy. These features position nano-ghosts as highly promising tools in oncology, regenerative medicine, and immunotherapy [1-3].

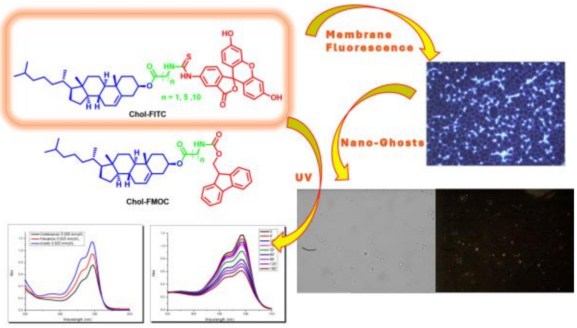

Figure 1. Labeled cholesterol structures and study.

In this study, three distinct aminated linkers of varying lengths were synthesized on the cholesterol backbone and subsequently conjugated to fluorescent labels (FITC and Fmoc-OSu) with the aim of evaluating the influence of both linker length and fluorophore nature on the physicochemical properties of the labeled cholesterol derivatives. The fluorescein-labeled compounds (Chol-FITC) were successfully employed in the preparation of nano-ghosts, whose membranes could be visualized by optical microscopy.

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Investigation into the *N*-dealkylation of protected chelating agents

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To match the specific coordination properties of a certain metal ion, it is often necessary to decrease the substitution degree on the nitrogen atoms of well-known poly(aminocarboxylate) ligands used as chelators for the preparation of diagnostic or therapeutic probes. In order to achieve this goal, two main synthetic approaches are adopted: (1) using a reduced amount of alkylating agent (e.g., tert-butyl bromoacetate) or (2) selectively protecting one of the N-positions, then alkylating the remaining ones, and finally deprotecting. Unfortunately, both strategies usually lead to unsatisfactory yields, either due to the formation of multiple partially alkylated products (in the first case), or because of the additional synthetic steps required (in the second case). In this work, we investigated the applicability of the iron-Polonovski *N*-dealkylation reaction to obtain a library of useful ligands starting from the *tert*-butyl-protected derivatives of chelators widely used in biomedical fields such as CDTA, EDTA, NOTA, AAZTA and PCTA (Figure 1). This method involves the use of an oxidant to form an N-oxide of the aminocarboxylate compound, and then the use of an iron(II) salt to promote the release of the oxygen atom as a water molecule, followed by the formation of an iminium species that is finally hydrolyzed to the desired secondary amine with the release of an aldehyde.[1],[2] Surprisingly, we found that a stoichiometric excess of oxidizing agent was sufficient to start the N-dealkylation process without the use of the iron(II) catalyst, and proposed an alternative mechanism to explain such behavior. In addition, we evaluated the role of substrate rigidity in promoting selective mono-N-dealkylation.[3]

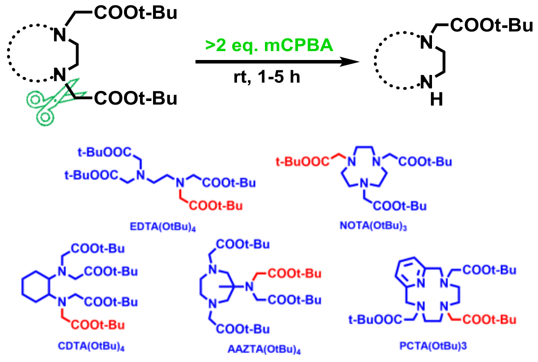

Figure 1. General representation of the investigated N-dealkylation and structures of the well-known chelators used as substrates (in protected form)

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Functionalized azulenes – from synthesis to applications as molecular colorimetric probes

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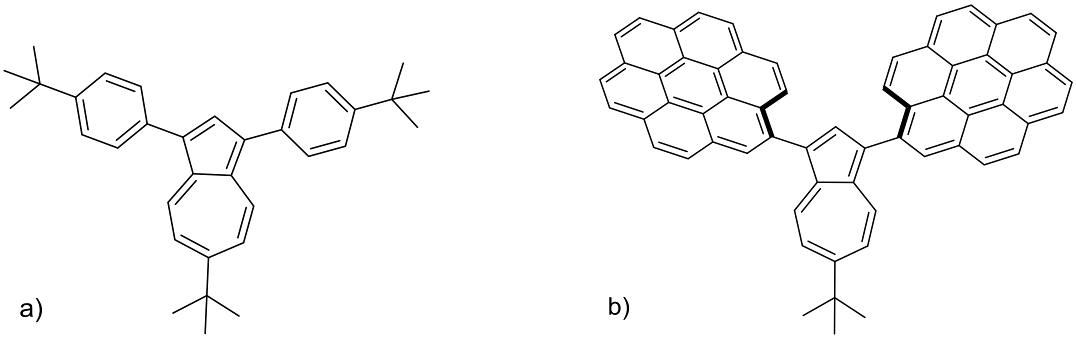
Azulenes, as non-benzenoid aromatic compounds, have attracted interest in organic synthesis. Their derivatives can be used for various purposes, including as components in cosmetics, dyes, or functional materials such as chemical sensors or molecular probes for environmental pH[1]. Thanks to reactions such as *ortho*-metalation or Suzuki–Miyaura coupling, azulenes can be transformed into highly interesting compounds with a wide range of applications.

Borylation, when combined with cross-coupling strategies, enables the efficient introduction of diverse substituents onto the azulenic core. By fine-tuning the conditions of the borylation reaction, the substitution pattern on the molecule can be precisely controlled. Subsequent application of the Suzuki–Miyaura coupling further expands the synthetic versatility, offering access to a wide array of structurally varied azulenic derivatives[2].

The aim of this research was the synthesis of azulenic derivatives that could serve as molecular probes for environmental pH. The first step involved the synthesis of 6-(*tert*-butyl)azulene and the optimization of the borylation conditions. The resulting compound served as a precursor for further transformations. As a result of borylation followed by Suzuki–Miyaura cross-coupling, two compounds were successfully obtained. Their potential application as molecular pH probes was subsequently evaluated.



Scheme 1. Synthesized compounds: a) 6-(tert-butyl)-1,3-bis(4-(tert-butyl)phenyl)azulene, b) 1,1'-(6-(tert-butyl)azulene-1,3-diyl)dicoronene.

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Environmentally relevant hydrolysis of anticancer drugs explored by DFT calculations

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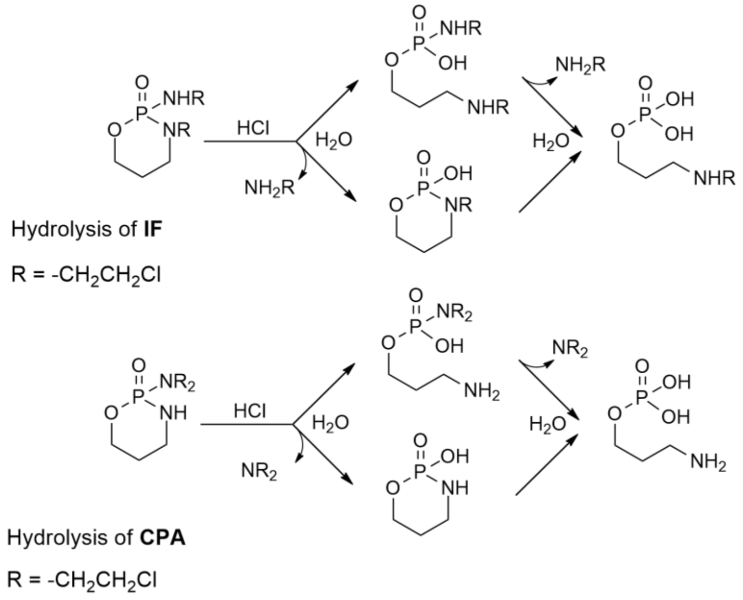
Anticancer drugs cyclophosphamide (**CPA**) and ifosfamide (**IFO**) undergo hydrolysis when dissolved in a neutral or acidic aqueous solution. After both phosphorous-nitrogen bonds are cleaved, the stable acyclic products are obtained. There are two possible reaction pathways, depending on whether the first step is the opening of the ring or the cleaving of the 2-chloroethylamine group [1,2].

We performed DFT calculations to assess the reaction pathways of **CPA** and **IFO** hydrolysis. Global minima found by conformation analysis, as well as transition states were optimized and their energies in aqueous environment compared in order to produce the potential energy surface of the reaction. We determined that both **IFO** and **CPA** hydrolysis proceed by first opening the ring, followed by cleaving of the 2-chloroethylamine group in the intermediate product.

In order to explain this ordering, multiple derivatives of different ring sizes and side chains were drawn and evaluated to assess the impact of the ring size and side chain effects.



Scheme 1. Possible hydrolysis pathways of CPA and IFO

Acknowledgements. This work has been supported by Croatian Science Foundation (projects IP-2022-10-2634 (“Pharma-Eco”) and DOK-NPOO-2023-10-7238).

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Development of a new tool for the theoretical study of isomerization mechanisms for MOST materials

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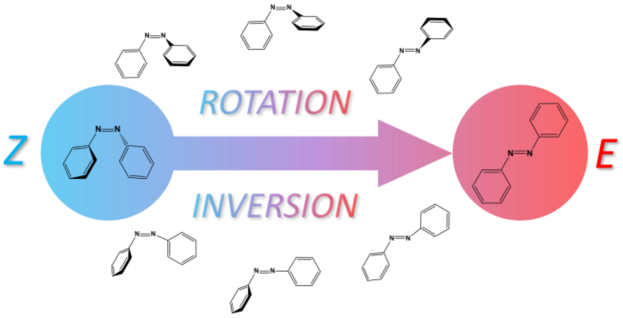
Among the renewable energies, a new technology emerged during the last decade: MOlecular Solar Thermal (MOST) technology. Starting from a thermodynamically stable isomer, it can undergo photoisomerization to form a metastable isomer. The energy is then stored in chemical bonds. This metastable form subsequently reverts to the stable isomer through a spontaneous thermal-back isomerization process and releases energy as heat; this energy can be used in practical applications in household. One promising candidate for this kind of technology is the azobenzene. This molecule can photoisomerize from the trans (E) isomer to the cis (Z) isomer and then it can reconvert back to the trans form. Previous studies [1] have identified two potential mechanisms for the thermal-back isomerization of azobenzene: the inversion and the rotation pathways. Early computational investigations, primarily based on Density Functional Theory (DFT), suggested that the inversion mechanism represents the minimum-energy pathway for the transition from the cis to the trans form. However, DFT-based predictions exhibit certain limitations, such as a significant overestimation of the activation entropy. This led to recent research [2-4] to rethink the rotation mechanism; during this pathway, the azo double bond is broken and consequently a triplet state is involved during the reaction. These investigations successfully reproduced the experimental thermodynamic parameters, including entropy and enthalpy, associated with the thermal-back isomerization of azobenzene. The scope of this study is double: reproduce these results with a computationally cheaper alternative method which is the Spin-Flip Time-Dependent DFT (SF-TDDFT), and finally estimate the rate of the back isomerization process via the semi-classical Marcus and Marcus-Levich-Jortner (MLJ) formalism, which is suitable for calculating rate of reaction involving an intersystem crossing.



Scheme 1. Schematic representation of the two mechanisms involved in the back-isomerization of azobenzene from cis (Z) isomer to trans (E) isomer.

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Transient Changes in Conductivity of a Water Solution by Means of an Activated Carboxylic Acid

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Dissipative chemical systems, in which chemical or photophysical stimuli are consumed to maintain a nonequilibrium (and hopefully functional) state, are currently the object of intense investigation due to the prospect of achieving time-programmable chemical transformations.

In this context, activated carboxylic acids (ACAs) have been extensively used as chemical stimuli to drive a vast number of different acid-base-responsive dissipative systems.[1]

Nowadays, an interesting area of research is represented by the development of ACA-powered systems in which the expressed phenomenon is not, per se, acid-base in nature. We recently showed that ACAs can be used to control non-pH-responsive devices via signal transduction, by coupling a pH-dependent galvanic concentration cell with a comparator circuit to enable the time-programmability of electric devices in a "fire-and-forget" fashion.[2]

Here, we investigated the possibility of using nitroacetic acid to control, over time, the electrical conductivity of an aqueous solution. In this case, the addition of the ACA directly affects the conductivity of the solution, removing the need for a signal transductor.

The aqueous solution must be initially characterized by a very low ion content, thus a low electrical conductivity. The addition of nitroacetic acid produces an immediate and remarkable increase in conductivity, which persists until the acid is entirely consumed by the system. Varying the experimental conditions in which the measurements are performed allowed us to control the time required for the system to return to the low conductivity state, and to tune the maximum conductivity value reached by the system.

We then interfaced this newly designed dissipative system with simple electric circuits, where it behaved as a chemically driven variable resistor.

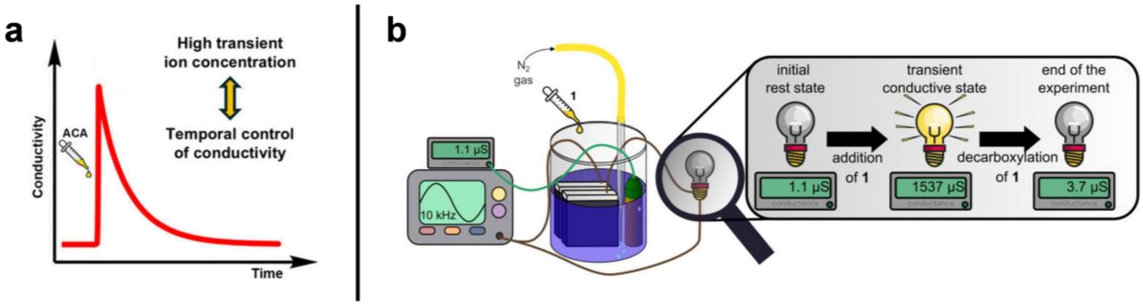

Figure 1. a) Typical conductivity profile of the aqueous solution after the addition of nitroacetic acid. b) Pictorial representation of the circuit involving the system as a variable resistor.

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Synthesis of Cu-complexes for water oxidation sol-gel materials

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The production of benign fuels from clean and renewable sources of energy is a stimulating goal.[1] In this context, the scientific community draws inspiration from nature to design artificial photosynthetic systems.[2] Artificial photosynthesis aims to achieve the light-induced water splitting ($2H_2O \rightarrow O_2 + 2H_2$), that consists in the hydrogen evolution reaction, HER ($4H^+ + 4e^- \rightarrow 2H_2$), for which protons and electrons are supplied by the water oxidation reaction, WOR ($2H_2O \rightarrow O_2 + 4H^+ + 4e^-$). Since WOR is thermodynamically and kinetically demanding, it requires efficient water oxidation catalysts (WOCs) to overcome its activation barrier.[3] The best WOCs reported today are made of Ru and Ir. However, it is highly desirable to use more Earth-abundant transition metals.[4]

In this project, we design an anodic catalytic layer to be incorporated in a water splitting electrochemical cell based on a hybrid thin film of SiO_2 containing WOC units based on first-row transition metal catalysts. This approach aims to achieve protection against degradation and the attachment of an active WOC capable of sustain operational current at low overpotentials. We present the synthesis of three macrocyclic ligand precursors and their derivative Cu complexes, based on a Cu macrocyclic unit (Cu-MAC, Figure 1) known to be an efficient WOC at different values of pH.[5] These WOC units will be incorporated into stabilizing SiO_2 matrixes to later be incorporated in a water splitting (photo)electrochemical cell as an anode.

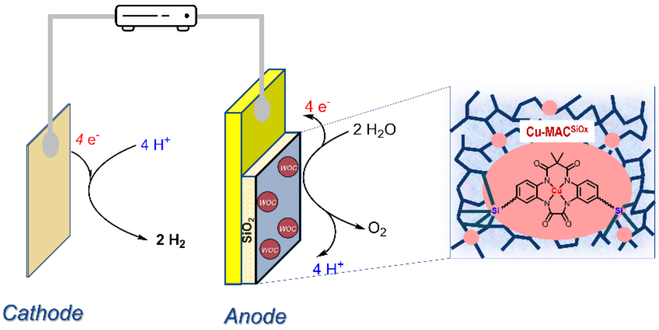

Figure 1. Schematic water splitting electrochemical cell based on an anodic Cu-MAC^{SiOx} catalytic layer.

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Chemical Ratchets and Nonequilibrium Reaction Cycles

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In recent years, conceptual advances arising from the field of molecular machines have led to a proliferation of counter-intuitive chemical systems:[1] (supra-) molecules that display unidirectional bond rotation,[2] chiral molecules that deracemize,[3] diffusion of particles *against* a concentration gradient,[4] and reactions that appear to disequilibrate.[5] These examples are functioning as Maxwell's Demons,[1] and just as with this famous *Gedankenexperiment*, for understanding the origin of these effects, the devil is in the detail. They use kinetic selectivity within a nonequilibrium reaction cycle to ensure that dissipation of one energy gradient (converting a fuel reagent to a waste product) proceeds most quickly while driving another process away from equilibrium.[1] This is known as a ratchet mechanism, as the forwards pathway occurs more readily than the corresponding backwards pathway.[1] While designing systems that function in this way remains non-trivial, ratchet mechanisms have now been demonstrated for single molecules, in supramolecular chemistry and self-assembly, in DNA nanotechnology and even across mesoscopic scales.[1] The availability of the new settings for chemical ratchets leaves the way open to exploit the counterintuitive functions that chemical ratchets enable under nonequilibrium conditions.

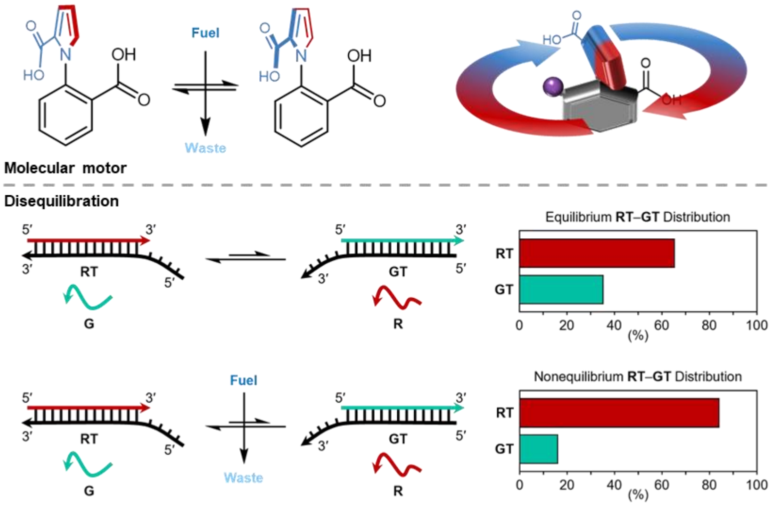

Figure 1. Ratchet mechanisms use diverse chemical structures to perform nonequilibrium tasks such as a molecular motor performing unidirectional rotation or biasing a DNA duplex distribution.

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(Bey)on(d)-water catalysis: an investigation into the impact of salts in on-water catalysis and on-polyol catalysis

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The use of on-water catalysis has become an area of increasing interest in green chemistry due to the potential to both replace volatile organic solvents and to enhance desirable organic reactivity.[1] The mechanism of this type of catalysis is usually attributed to enhanced hydrogen bonding effects[2] or enhanced acidity due to adsorption of hydroxide[3] at the water-organic interface caused by the disruption of the hydrogen bonding network at the interface and the resultant poorly solvated hydrogen atoms facing the organic phase.[4]

The addition of salts to water is also known to significantly affect the hydrogen bonding networks present in water.[5] This effect is most explored in the context of protein solubility as the Hoffmeister series which orders cations and anions from kosmotropic to chaotropic depending on their ability to salt-out or salt-in proteins from water.[6] The microscopic origin of the change in protein solubility is the stabilisation (for kosmotropic ions) or destabilisation (for chaotropic ions) of water-water interactions in bulk solution.[7] It has also been observed that the order of ions in the Hoffmeister series remains constant across many different trends in their physicochemical properties when dissolved in water, and in organic solvents. [8, 9]

Polyols also exhibit complex hydrogen bonding networks[10] and have sufficient organophobicity to form an interface with many organic molecules. This interface has occasionally been observed to improve desirable organic reactivity and has been compared to on-water catalysis in that context.[11] The impact of salt solutions in on-water catalysis has also only been observed sporadically and has not been investigated systematically.[12, 13] This presentation outlines our preliminary investigations into the relative effects of on-polyol and on-water catalysis as well as the role of dissolved salts on this activity.

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Vinylogous electrochemical carboxylation of dienones

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Electrochemical carboxylation is an emerging strategy for valorizing carbon dioxide (CO_2) into valuable single carbon atom building blocks.[1] This class of transformations typically involves the reaction between an electrochemically generated carbanion and CO_2, leading to the for the formation of a new C-C bond.[2] In this work, we report the first example of δ-selective electrochemical carboxylation of dienones (**1**), affording 6-oxo-carboxylic acid derivatives (**2**) in yields up to 56%.[3] The protocol was extended to poly-conjugated carbonyl derivatives ($\alpha,\beta,\gamma,\delta$-unsaturated esters, thioesters, and amides), highlighting that a vinylogous electrochemical activation generally occurs for this class of extended conjugated systems.

Mechanistic investigations conducted on the model compound **1a** – using cyclic voltammetry and DFT calculations – reveal that under electrochemical reduction conditions, nucleophilic species ($\mathbf{1a}^{\bullet-}$ and $\mathbf{1a}^{2-}$) are generated, which can react with CO_2. However, only the electro-generated double-reduced forms are the productive intermediates. These undergo regioselective CO_2 addition on the δ-carbon atom (vinylogous position). The crucial role of CO_2 in directing this transformation was also studied.

Given the broad industrial utility of carboxylic acids, this protocol enables the synthesis of novel 6-oxo-carboxylic acid scaffolds, with potential application as core structures for new biologically active compounds.

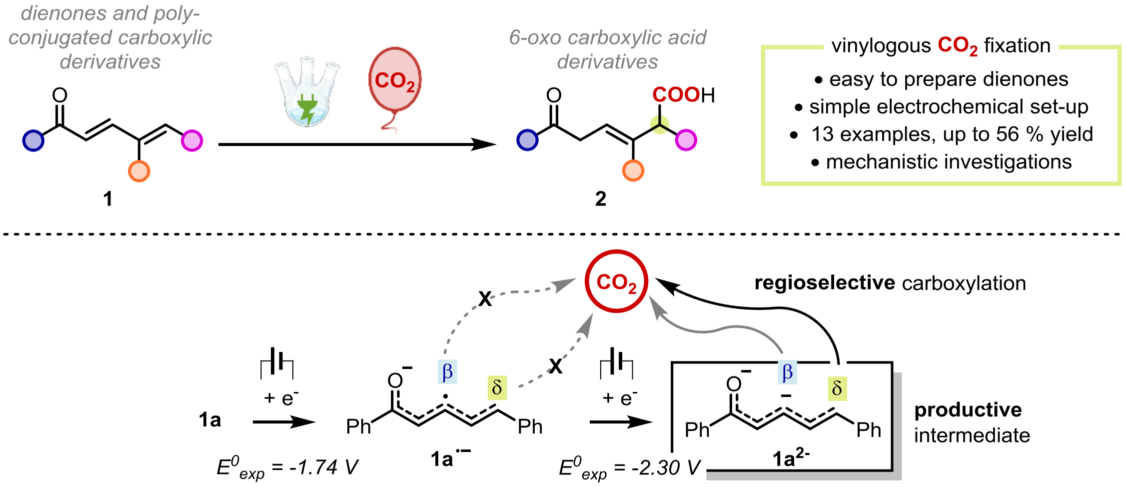

Figure 1. General representation of the transformation and carboxylation pathways for **1a**. Potentials are referred to Fc^+/Fc couple.

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Towards the first enantioselective total synthesis of quartromicins; an approach to the enantioselective synthesis of spirotetronate fragment precursor

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Quartromicins **1**, a subgroup of six natural products, contain four spirotetronate moieties embedded in a large macrocycle. The first members were partially characterized in 1991, and their related aglycon was identified a year later.[1,2] Isolated from a strain of *Amycolatopsis orientalis*, quartromicins showed potent antiviral activities against various pathogens.[2] One unique feature of quartromicins is the presence of two-fold, both *endo* and *exo* spirotetronates, each one bearing two contiguous quaternary stereocenters. The 12 stereocenters, 8 quaternary carbons, and high proportion of unsaturation make this 32-membered macrocycle very challenging. Until now, there have been no reports of its total synthesis, although some groups have developed approaches for its fragments.[3,4] Spirotetronates are very interesting moieties, both chemically and biologically.[5] With our well-planned retrosynthesis, we perceive that the identical spirotetronates placed diagonally opposite to each other are the desired synthons, and these in turn can be synthesized by cycloaddition. We envisaged that an enantioselective Lewis acid-catalyzed Diels-Alder reaction for the synthesis of cycloadduct **1a** would be an excellent route, which can be transformed into spirotetronates. Here, we will discuss the results of our enantioselective synthesis of the fragments and the challenges encountered in achieving them.

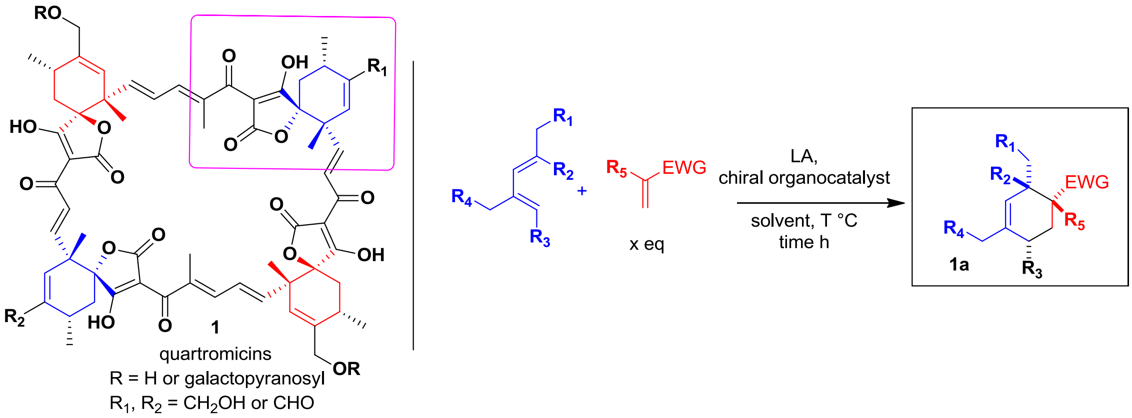

Figure. Structure of quartromicins **1** and the synthesis of the fragment **1a**.

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Interfacial and aqueous-phase oxidation of salicylic acid: from spontaneous ·OH generation to HOONO and UV-driven photolysis

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Organic aerosols are abundant in the atmosphere and significantly influence climate, air quality, and human health. These particles engage in heterogeneous and multiphase reactions with oxidants such as hydroxyl (·OH), nitrate (NO_3), and ozone (O_3). Although ·OH formation is typically linked to photochemical processes, recent studies report its spontaneous generation at the air/water interface of aqueous droplets, even without light or added precursors [1]. This has been attributed to strong interfacial electric fields or differences in ion solvation, which promote charge separation and redox reactions that yield ·OH and solvated electrons [2].

In this study, we explored the oxidative degradation of salicylic acid (SA), a model aromatic acid [3], under three conditions: (1) Spontaneous oxidation at the air–water interface in humidified air, without light or oxidants, using laboratory-generated SA-containing droplets analyzed by LC-HRMS [1]; (2) Aqueous-phase reactions with peroxynitrous acid (HOONO), monitored by stopped-flow spectrophotometry to assess kinetics and products [4]; and (3) Photolytic degradation via H_2O_2/UV and NO_3^-/UV advanced oxidation processes, to evaluate efficiency and transformation pathways.

Results show that SA undergoes notable transformation through all pathways. Interfacial oxidation produces unique products not observed in bulk or photolytic systems, underscoring the atmospheric relevance of this mechanism. HOONO and UV systems induce selective aromatic oxidation and hydroxylation. Overall, the findings highlight the importance of both interfacial and aqueous-phase oxidation in shaping the atmospheric fate of organic compounds.

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Graphene derivatives as fillers for nanocomposite hole transporting layers in perovskite solar cells

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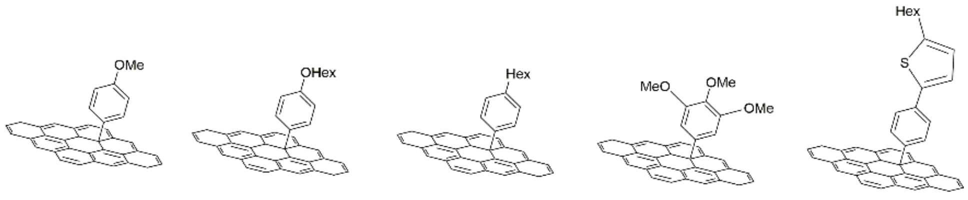
Perovskite Solar Cells (PSCs) are a type of photovoltaic device which stand out for of their high power-conversion efficiencies and broad absorption spectrum. However, this technology lacks long-term stability due to degradation of the perovskite layer when it is exposed to environmental factors.[1]

In this work, we make use of the electrical properties of graphene materials, by exploring the potential of a composite hole transporting layer (HTL) with reduced graphene oxide (rGO) and poly(3-hexylthiophene) (P3HT), combination that has been already shown to improve the stability of the cells.[2,3]

To address the tendency of graphene derivatives to aggregate, we covalently functionalized different types of graphene-based materials with various functional groups, to improve their dispersibility in the P3HT matrix. The derivatives were synthesized through diazotization chemistry and characterized through Raman, TGA and dispersibility measurements.



D_1 rGO-PhOMe

D_2 rGO-PhOHex

D_3 rGO-PhHex

D_4 rGO-Ph(OMe)3

D_5 rGO-PhThHex

Figure 1: f-rGO derivatives

The blends of functionalized graphene derivatives and P3HT were obtained through a sedimentation-based separation and were characterized by dispersibility measurements, UV-Vis, SEM and TEM, showing that, among all, functionalized rGO (f-rGO) derivatives (Figure 1) were more homogeneously dispersed in the polymeric matrix. Further studies will highlight the stability advantages of depositing f-rGO/P3HT composite material as HTL in PSCs.

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Substituent effect on the carbon–carbon bond strength

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The carbon–carbon bond is the universal connector in organic molecules. Understanding its nature and strength is therefore essential for rationalizing and tuning the properties of numerous compounds and the chemical transformations they undergo. The single $R_3C–CR_3$ bond is remarkably strong and stable compared to other homodiatomic analogs.[1] However, its strength can be significantly reduced upon alkyl substitution, for example, as hydrogens are replaced by methyl groups. Alkyl substituents introduce steric repulsion that weakens the $R_3C–CR_3$ bond, and the magnitude of this effect depends both on the number and on the size of the substituents. Extending this analysis to a broader range of substituents, from electron-withdrawing to electron-donating groups, reveals a related but distinct weakening mechanism known as the lone-pair shielding effect.[2] In these so-called lone-pair-shielded radicals (Figure 1), the substituent contains a high-energy lone-pair-type orbital that interacts with the carbon radical center, effectively shielding it and opposing electron-pair bond formation. Interestingly, this C–C bond weakening occurs contrary to the commonly accepted rationale that such substituents stabilize the resulting $CR_3^{\bullet}$ radical.[3]

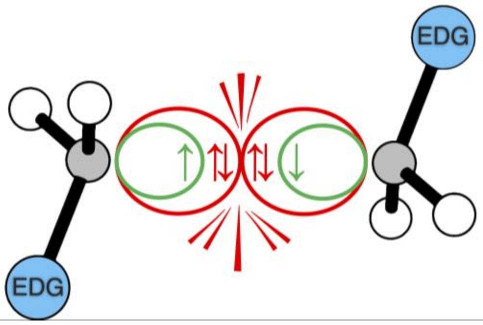

Figure 1. Schematic representation of lone-pair shielded radicals and how they induce a C–C bond weakening.

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Chiral Perylenebisimide-Ru_4POM Assemblies: Probing Interactions in Modular Photoactive Systems for Water Oxidation

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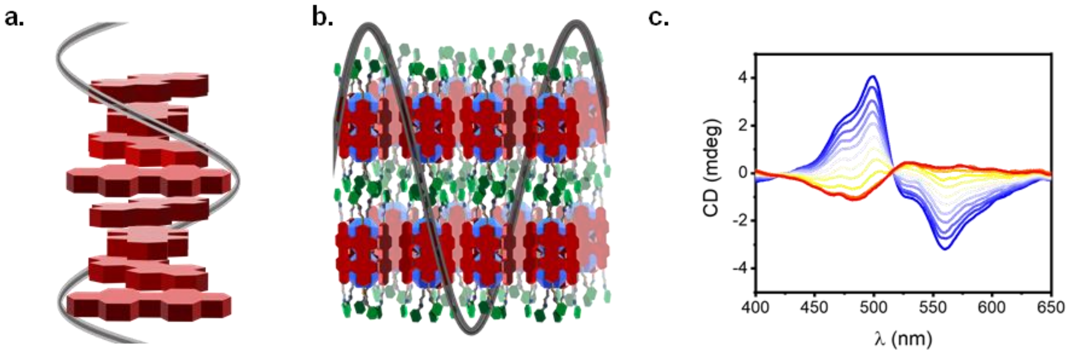
Understanding the molecular interactions between photoactive dyes, catalytic centers and substrate is critical for optimizing artificial photosynthetic systems.[1] Here, we investigate the supramolecular binding between chiral perylenebisimide (PBI) derivatives and a ruthenium-based polyoxometalate (Ru_4POM) catalyst within modular assemblies for light-driven water oxidation. Our system builds upon the quantasome (QS) platform,[2,3] which integrates PBI dyes, serving as light-harvesting antennas, with transition metal polyoxometalates as oxidation catalysts. By introducing chiral carbohydrate moieties onto the PBI framework via click chemistry, we enhance both water dispersibility and optical activity, enabling more detailed investigation of PBI-Ru_4POM interactions. Binding affinities and structural organization were characterized using UV-Vis spectroscopy, circular dichroism (CD), fluorescence quenching, and isothermal titration calorimetry (ITC). These studies reveal the role of electrostatic and π–π interactions in complex formation, as well as the influence of chirality on aggregate morphology and performance in water oxidation. Our findings provide molecular-level insight into dye-catalyst organization, offering design principles for tuning charge transfer and catalytic efficiency in supramolecular photocatalytic QS assemblies.



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New Insights into Proton Sponges: The Case of Phosphazenyl Phosphines

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We investigated the basicity of a series of proton sponges derived from phosphazenyl phosphines in both the gas phase and acetonitrile solution. By incorporating aromatic and aliphatic scaffolds with varied spacing between phosphazenyl phosphine units, we were able to modulate their superbasic properties. The strongest system identified reaches a pK_a of 42.0 in acetonitrile and gas-phase proton affinity (PA) of 307.0 kcal mol^{-1}, values close to but not exceeding those of benchmark phosphazenyl phosphines[1]. Analysis of bis- versus mono-substituted derivatives showed that the proton-chelating effect (ΔPA) is moderate in these systems and cannot be explained solely by electron-pair repulsion or hydrogen bonding. Instead, mesomeric, inductive, and dispersion contributions play an essential role. Topological (AIM) analysis revealed weak P^+–H···P and P^+–H···N interactions, in contrast to the strong N^+–H···N bonds of classical nitrogen-based proton sponges, which accounts for the reduced chelating effect. Unlike previously known phosphazenyl phosphines, these proton sponges can accommodate a second proton while retaining superbasic character (pK_{a2} = 26.2–36.6), highlighting their distinctive bifunctional nature.

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Molecular Engineering of Covalent Organic Frameworks for Hydrogen Evolution

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Due to the current worldwide situation, the use of green fuels is on the rise, and it is common knowledge that one of the most promising renewable energy sources is green hydrogen. In this context, generation of hydrogen through water splitting under visible-light irradiation has been widely studied topic since the 1970s.[1],[2] Photochemical water splitting is a complex process in which different components are required to fulfill the overall reaction, each of them having a key role including (i) harvesting the light, (ii) separation of charges, (iii) breaking and (iv) formation of chemical bonds.

Organic semiconductors have recently emerged as promising materials to be used in photocatalysis. Prominent examples are 2D-covalent organic frameworks (COFs), which are reticular materials with high crystallinity and porosity.[3] They have been applied in photocatalysis processes including visible light-induced hydrogen evolution reactions (HER) with great success.[4][5] One of the advantages of COF materials is their versatility to control their chemical and electronic structure, allowing to rationally design better photocatalytic materials by enhancing solar light harvesting, charge separation, interaction with co-catalysts or dispersibility in water.[6]

In this work we have prepared a family of 2D-COF materials decorated with different moieties in the organic skeleton and tested for light-induced HER in combination with well-defined co-catalytic centers and suitable electron donors.

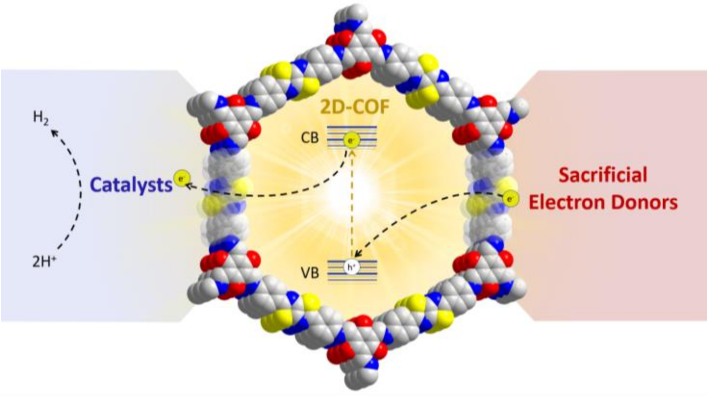

Figure 1. Components of the photocatalytic system tested in this work for HER reactions.

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Lights, Camera, Disproportionation: Imine Synthesis from Hofmann-Löffler-Freytag Intermediates

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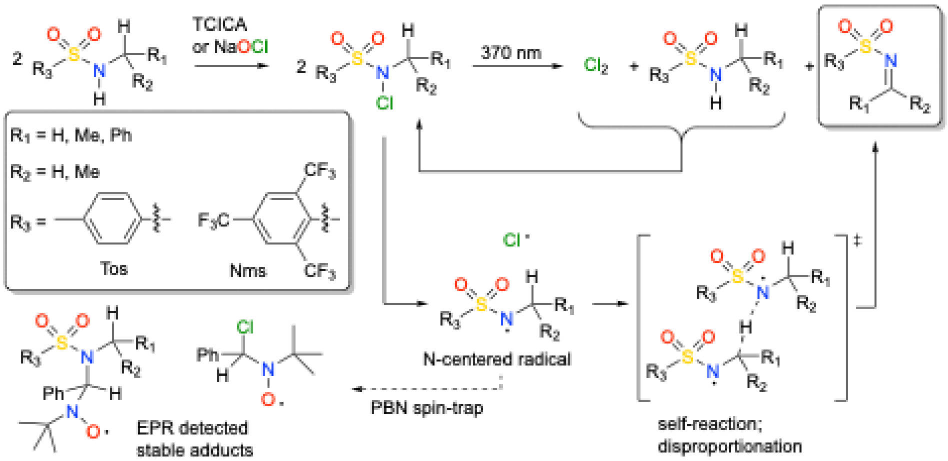
The Hofmann–Löffler–Freytag (HLF) reaction is a fundamental, metal-free approach for site-selective C–H functionalization, pivotal in synthesizing heterocycles such as pyrrolidines and piperidines. While recent efforts by researchers have advanced its synthetic utility, less attention was provided towards byproducts and limitations of the HLF reaction.[1] Using *N*-halogenated tosylamide species, under irradiation by UV light, pyrrolidine and piperidine structures are predominately formed, which is a useful technique in late-stage functionalization in drug discovery. Detailed mechanism of the observed regioselectivity (more pyrrolidine than piperidine) has been recently described, as well as imine as a byproduct.[2]

Using combined advanced experimental techniques—spin-trapping EPR spectroscopy and NMR spectroscopy with irradiation inside the cavity, alongside computational DFT modeling we managed to fully characterize the reaction mechanism, potential side-reactions, and byproducts of the HLF reaction, and used this knowledge to propose facile imine synthesis from *N*-chlorinated tosylamides.[3]



Scheme 1. Utilization of the HLF side-reaction in the synthesis of imines via *N*-centered radicals

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Towards ionoids: Synthesis of tetracationic macrocycles and study of their self-assembly process with dianionic salts.

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In the pursuit of novel polymers formed through non-covalent molecular interactions, a new class of colloidal ionic clusters, termed ionoids, was discovered in 2012.[1] These spherical, self-assembling aggregates exhibit hydrodynamic radii of 6–8 nm and are notable for their exceptional stability in solution. They spontaneously form after ten days of incubation at room temperature in a specific solvent mixture (DMSO:glycerol:water at a 50:43:7 v/v/v ratio), resulting from the association between multicationic molecular boxes—such as the “Texas-sized molecular box”—and dianionic salts, including dipotassium methanedisulfonate (MDS) and Fremy’s salt.[2] The assembly mechanism is driven by synergistic factors, such as preferential solvation, medium viscosity, van der Waals interactions, and long-range correlated electrostatic forces.[3]

This work focuses on the synthesis of new cationic building blocks for ionoid formation. Ten tetracationic macrocycles, including the “Texas-sized molecular box”, were synthesized via high-dilution macrocyclization strategies using two common heterocyclic heads and five distinct linkers. All intermediates and final macrocycles were characterized by mass spectrometry and one- and two-dimensional nuclear magnetic resonance (NMR) spectroscopy.

To investigate early stages of ionoid formation, electron paramagnetic resonance (EPR) spectroscopy was employed using Fremy’s salt as spin probe. Additionally, dynamic light scattering (DLS) was used to study ionic aggregates formed from the interaction of MDS with two selected macrocycles. Ongoing efforts are directed towards the development of new linkers, heterocyclic heads, macrocycles, and ionoid structures.

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Molecule to Functional Supramolecular Materials for Energy Harvesting Applications

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The growing demand for wearable and flexible electronics has led to the development of soft electronics. Supramolecular approach offers immense potential in this field and its applications have largely been confined to solution-phase systems, where favorable solute–solvent interactions promote self-assembly by overcoming entropic penalties. However, translating these ordered solution structures into functional bulk materials remains a significant challenge due to the loss of such directional interactions in the bulk state. This work aims to address the challenges associated with anchoring functional units to supramolecular scaffolds without compromising their self assembled structure and translating solution structures into bulk materials. Several supramolecular scaffolds based on benzene 1,3,5-tricarboxamide (BTA) cores with naphthalene diimides (NDI) at the periphery were synthesized to exploit synergistic interactions between H-bonding and charge-transfer (C-T) complexation. Among different hydrocarbon spacer lengths, the six-carbon spacer was found optimal for achieving self-assembled hierarchical structures. The introduction of C-T complexation to the BTA-C_6-NDI_3 scaffold with electron-rich guest molecules (pyrene) at the periphery led to the formation of an organogel and the solution structure effectively translated into the bulk state while preserving ordered morphology. The resulting bulk material exhibits ferroelectric switching behavior, along with notable piezoelectric and pyroelectric responses at room temperature (T_c ~ 47 °C) as demonstrated in figure A.[1] Next, organic multiferroic material was addressed using a similar supramolecular strategy by introducing another functional element (TEMPO radical) into the polar BTA scaffold. The resulting scaffold [BTA-(NDI-TEMPO)$_3$] behaves as organic multiferroic material at room temperature. The device fabricated from the C-T mediated scaffold displayed a remarkable magnetoelectric coefficient (α = 220 mV/Oe-cm) in the bulk state and acts as potential material for magnetic and pyroelectric energy harvesting at room temperature.[2] This approach presented the utility of supramolecular design in bridging the gap between molecular-level assembly and practical application for soft materials.

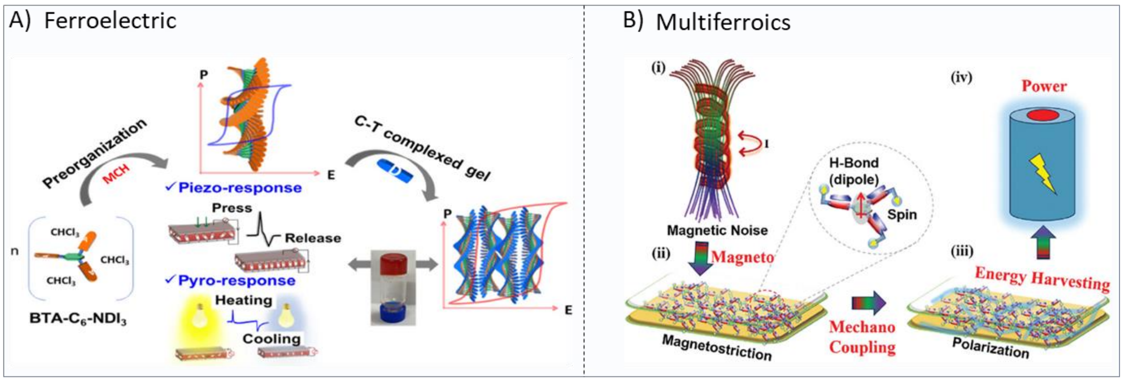

Figure 2. Schematic representation of supramolecular functional materials (A) BTA based organogel for FE switching. (B) Magnetic field induced voltage generation due to magnetoelectric coupling.

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The physical organic chemist’s toolbox for designing singlet fission chromophores

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Singlet fission (SF), a photophysical process where the energy of an incident photon is divided across multiple excitons, promises a substantial increase in efficiency of photovoltaic devices.[1] As such, the search is on for organic molecules that undergo singlet fission efficiently and are stable to UV radiation. Our research leverages aromaticity concepts to understand known SF chromophores such as DKPP[2] and DPND[3] and to identify new compounds with SF potential, then exploits organic reactivity to assemble and functionalise these structures.

Here, we explore the spectroscopic properties of ‘isopyrocoll’, an underexplored π-system that was discovered in 1968.[4] Using microwave-assisted thionation followed by silver(I)-mediated malononitrile condensation, the excited-state photophysics of this molecule as measured by ultrafast transient absorption spectroscopy can be radically altered. We also describe synthetic progress towards a modular, adaptively aromatic π-system with predicted SF capability.

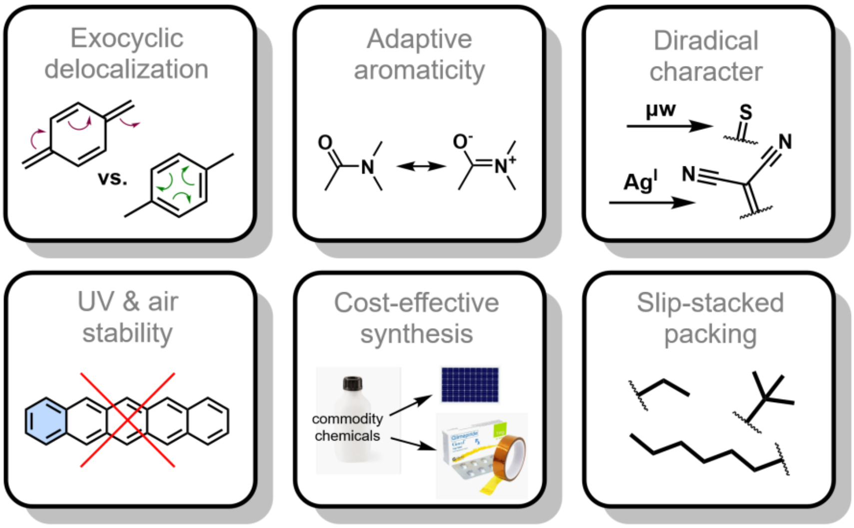

Figure 1. The physical organic chemist’s toolbox for designing singlet fission chromophores.

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Combinatorial Probabilities in the C–N Bond Metathesis of Tertiary Amines

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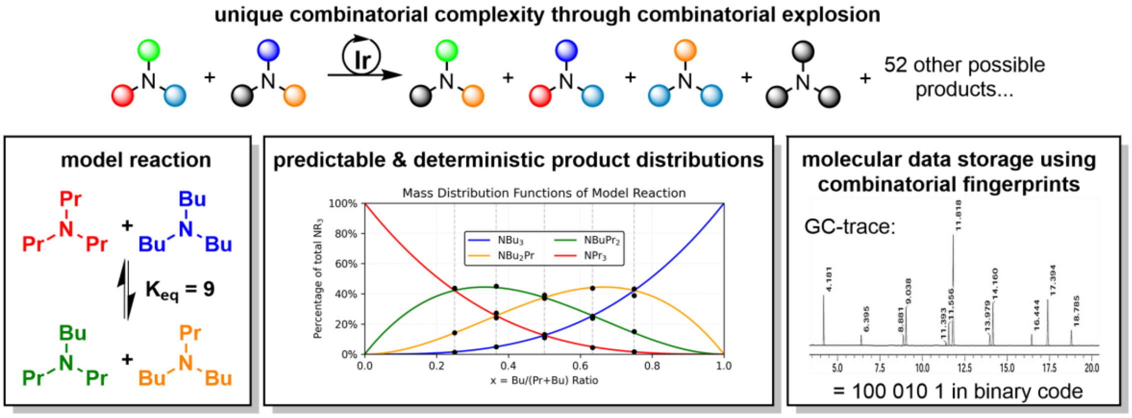
Tertiary amines are an important motif in many bioactive molecules.[1] Herein we report an iridium-based system that allows for the homodesmotic C–N bond metathesis in tertiary alkyl amines. In the absence of any substrate feature controlled selectivity, this reaction is poised to result in complicated product mixtures due to a combinatorial explosion.[2] We demonstrate how the combinatorial space of the metathesis process can be tailored for targeted synthesis and other applications accordingly.[3]

For simple model systems, the resulting product distributions can be readily predicted by combinatorial probabilities. This results in a deterministic reaction outcome following a multinomial distribution, where the mixing entropy in the system is maximized. Finally, we demonstrate how combinatorial fingerprints of metathesis product mixtures obtained from gas-chromatography can be used for the encoding of information.



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The Global Kinetic-Thermodynamic Relationship Derived from First Principles: The Origin of Responses in Chemical Reactivity

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The effect of reaction energy on reaction rates has always been a central question in physical organic chemistry. Its analysis prompted the development of many models to explore how the thermodynamics may affect the kinetics. The existing models, however, are inherently limited in their applicability, often valid only in small spans of reaction energy, being constructed on practical yet oversimplified assumptions, or requiring highly reaction-specific corrections.[1] In addition, deviations from linear trends are frequent and rarely addressed.[2]

We have derived a non-linear equation that links the activation energies and reaction energies in a generalisable manner, with only a minimal assumption about the local preservation of the Hammond postulate. Thus, this constitutes the first fully deductive approach in modelling the kinetic-thermodynamic relationship. Mathematical evaluation shows that the Leffler equation constitutes a local approximation to our function, which also shows behaves similarly to the Marcus equation given an idealised, perfectly symmetric, thermoneutral reaction. The non-linear equation explains the global response of the barrier through three thermodynamic-independent parameters: E_{min}, E_{eq} and θ.

We demonstrate the validity of this model in several sets of reactions with DFT calculations, where values for these parameters can be obtained. Unlike models stemming from empirical data fitting, by construction, our equation inherently ensures generality across different reaction classes allowing comparisons among completely different families of reactions without requiring system-related correction factors. The universality of this relationship suggests broader implications for reactivity theory beyond the studied reactions, and opens new orthogonal ways of evaluating design of reaction methodologies systematically.

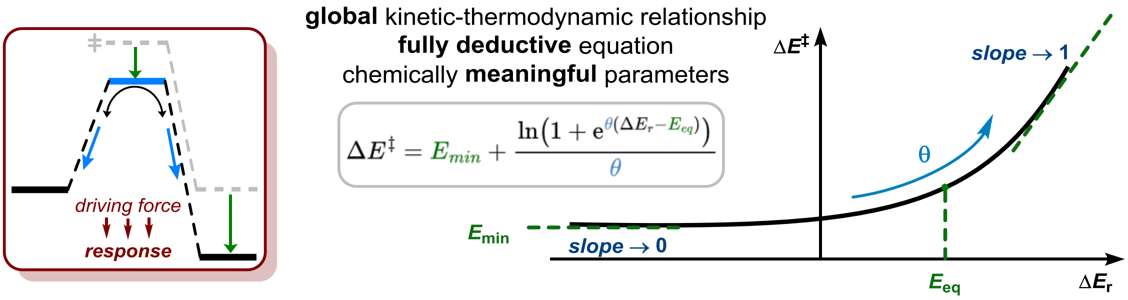

Figure 1. Derived non-linear equation for the kinetic-thermodynamic relationship of chemical reactions.

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Engineering of Light-Harvesting Systems (LHSs) based on O-doped nanoribbons in Liquid Crystals

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This study focuses on the engineering of light-harvesting systems (LHSs) using oxygen-doped nanoribbons based on the peri-xanthenoxanthene (PXX) scaffold as chromophores in a liquid crystalline medium (4-cyano-4'-pentylbiphenyl). Photophysical investigations at room temperature revealed a systematic bathochromic shift in the UV–vis absorption and emission spectra upon the introduction of fused phenyl ketone groups and π-extension. These modifications led to molecules with strong spectral overlap, ideal for Förster Resonance Energy Transfer (FRET). Two two-step LHSs, denoted as **$8^{1000}/1^{500}/6^{250}$@5CB** and **$8^{1000}/1^{500}/4^{250}$@5CB**, were constructed in the nematic liquid crystalline phase. Differential scanning calorimetry (DSC), polarize optical microscopy (POM), and small-angle X-ray scattering (SAXS) confirmed the formation of the liquid crystalline phase of the LHSs at room temperature. The FRET efficiencies for the first step were 0.91 and 0.81, and for the second step 0.76 and 0.73, for **$8^{1000}/1^{500}/6^{250}$@5CB** and **$8^{1000}/1^{500}/4^{250}$@5CB**, respectively.

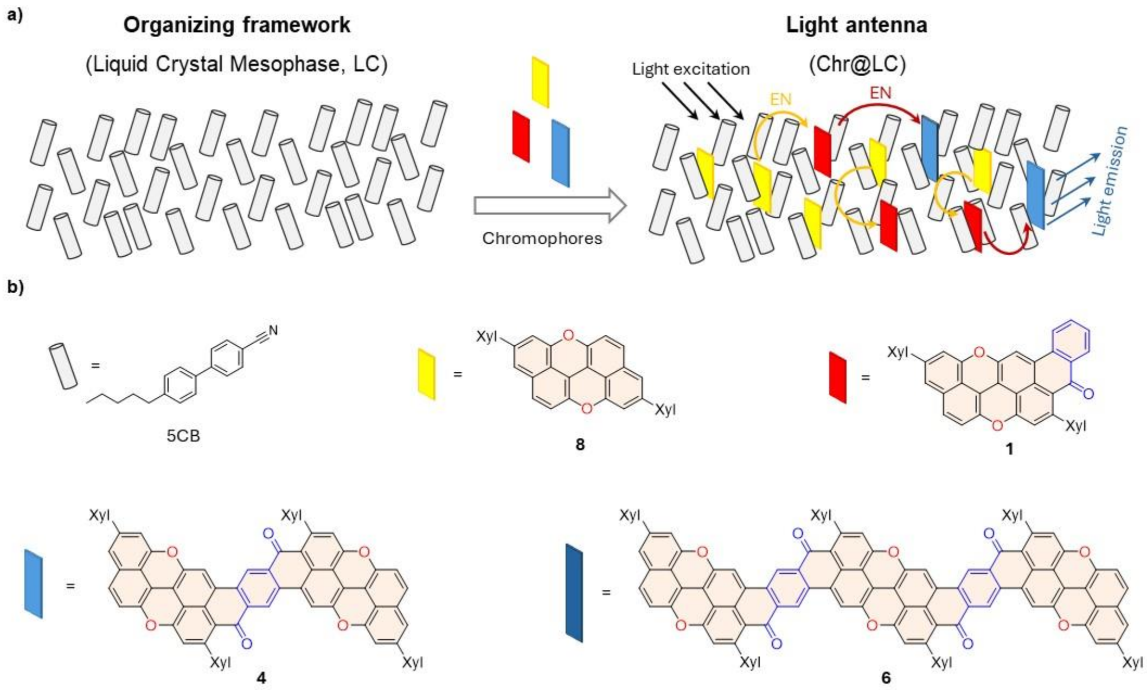

Figure 1. Light-harvesting system based on PXX scaffold as chromophores in a liquid crystalline medium.

On the mechanism of photodriven hydrogenations of N_2 and other substrates by Hantzsch ester: Buffer is key to reactive H-atom donors

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The Hantzsch ester (HEH_2) ha been widely used as a photoreductant for activated substrates, but its application in photodriven transfer hydrogenation has remained limited. Recently the pairing of HEH_2 with a collidine/collidinium triflate buffer [(ColH)OTf/Col] enabling photochemical reduction of N_2 to NH_3 using a molybdenum catalyst has been demonstrated—an unprecedented reaction under such mild conditions[1]. This result points to a strong driving force for proton-coupled electron transfer (PCET) generated upon HEH_2 photoexcitation in the presence of the Col-buffer. Here, we investigate how this buffer combination unlocks HEH_2 reactivity. Wavelength-dependent studies confirm HEH_2 excitation governs reactivity, and the HEH_2/Col-buffer combination proves uniquely effective. Spectroscopic data suggest static quenching of HEH_2 via electron transfer to $[ColH]^+$ within a hydrogen-bonded complex, generating $ColH^•$ and $[HEH_2]^{•+}$(Figure 1), followed by rapid deprotonation of $[HEH_2]^{•+}$ by Col yielding $HEH^•$—a potent H-atom donor. Interestingly, transient absorption and EPR experiments support this mechanistic pathway. The applicability of this system is demonstrated by efficient photoreduction of a library of C=O and N=O π-bonds, with marked increases in rate, yield, and reactivity profile upon Col-buffer addition. $ColH^•$ is proposed as a powerful PCET donor (BDFE_N–H ≈ 28 kcal/mol), expanding the use of HEH_2 in photoredox chemistry.

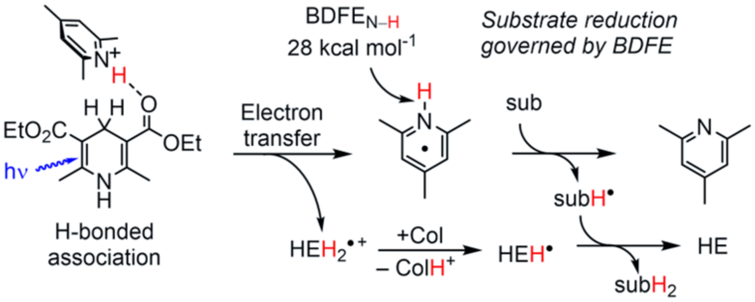

Figure 1: The mechanism proposed for the photoreduction by HEH_2 and Col-buffer.

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Solvation and Photochemistry of 1,4-Naphthoquinone: A Computational Study

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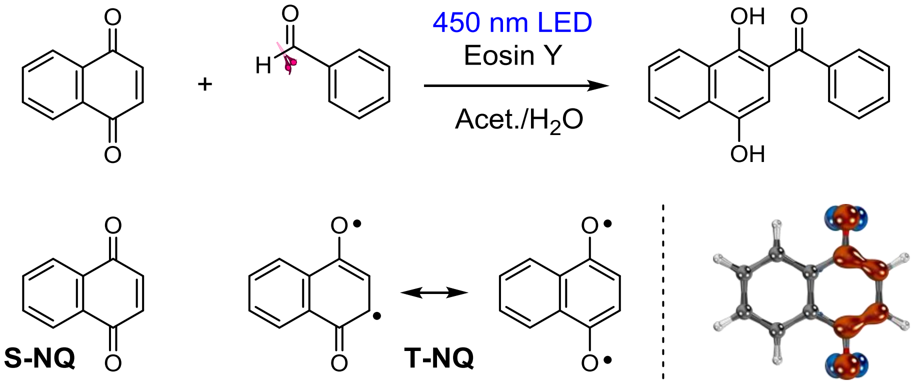
Solvation is a complex phenomenon involving electrostatic and van der Waals forces as well as chemically more specific effects such as hydrogen bonding. Herein, we investigate the impact of both micro- and macrosolvation on the photochemical acylation of 1,4-naphthoquinone (**NQ**) using a combination of quantum chemical methods and complementary solvation models.[1] The reaction proceeds via triplet–triplet energy transfer from the visible-light photocatalyst Eosin Y to singlet **NQ**, populating its triplet state **T-NQ**.[2] This is followed by H-abstraction from formaldehyde and subsequent radical recombination.

T-NQ exhibits a rich electronic structure with several low-energy nπ* and ππ* excited states, revealed under both C_2v and Cs symmetry using DFT and multiconfigurational methods. The singlet–triplet energy gap of **NQ**, along with the acylation reaction free energies, shows a clear dependence on solvent polarity. Hydrogen-bonded 1:1 and 1:2 **NQ**···H_2O complexes are analyzed on both the singlet and triplet potential energy surfaces in the gas phase and by means of bulk water solvation models. Additionally, TD-DFT calculations reveal pronounced solvatochromic effects for Eosin Y due to a solvent-induced shift in the tautomeric equilibrium between its spirocyclic lactone (closed) and carboxylic acid (open) forms.[3] Overall, water plays a key role rather than a bystander in facilitating the visible-light-driven photoacylation of quinone **NQ**, of significant synthetic interest for the pharmaceutical industry.



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Hybrid Nanoparticles as Drug Delivery Vectors

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In recent times a new class of therapeutics has attracted considerable attention: the small interfering RNAs that are able to target genes that are causally involved in the pathological process. However, these RNAs present some features that make them difficult to use in clinical practice, as the poor biodistribution and the ability to trigger the immune system. To overcome these issues several nano-delivery systems have been proposed and used over the years, the most successful ones being solid lipid nanoparticles (SLNs). The goal of our research group is to develop nanoparticles for nucleic acid delivery featuring biodegradability, resistance to water, structural stability, the ability to avoid the immune system and triggered nucleic acid release at the site of action. To this goal, we developed a delivery vehicle based on a poly(lipoic acid) matrix stabilized by a PEG-ended surfactant[1]. These nanoparticles, while featuring the targeted characteristics, with the added bonus of passive targeting of cardiac tissues[2], demonstrated only moderate RNA encapsulation efficiency. In this communication, we report on our studies on a second generation of poly(lipoic acid) with high RNA encapsulation efficiency. These new nanoparticles take inspiration from SLNs in terms of constituents, while maintaining a polymeric core based on lipoic acid derivatives (figure 1).

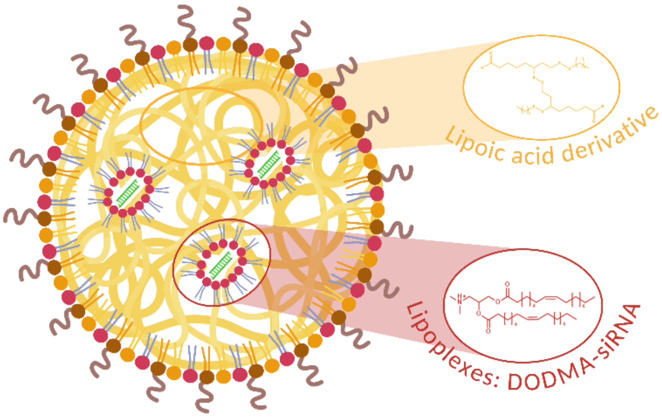

Figure 1. Schematic representation of hybrid nanoparticles encapsulating siRNA.

Results obtained show how the chemical features of the nanoparticles components influence both encapsulation efficiency and glutathione-triggered degradation. The flexibility of the synthetic protocols allows the encapsulation of both small siRNAs and large mRNA.

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Going Explicit: How Surrounding Species Inclusion Enhances DFT Mechanistic Studies

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In the computational treatment of chemical reactions, it is common to simplify the system in order to reduce the complexity of the calculation. In particular, in simulations of reactions in solution, only the reactants are often considered, neglecting the surroundings. However, the omission of species not directly involved in the reaction, such as solvent molecules, can compromise the correct description of the reaction mechanism. This theoretical study highlights how, in some cases, micro-solvation of the system or reproduce a more complex system,[1] is fundamental to accurately reproduce experimental data. By means of DFT calculations with an explicit description of those molecules that participate indirectly, we demonstrate how the consideration of microsolvation provides a more realistic model of the system, allowing experimental results to be explained and offering a deeper understanding of the reaction mechanism.

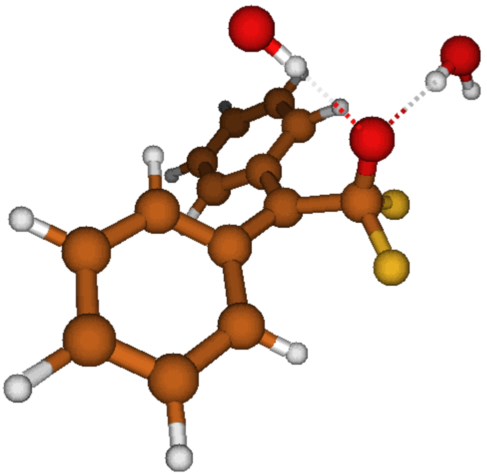

Figure 1. **Zwitterionic species observable only upon micro-solvation in the calculation.**

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Molecular thermometers to study photothermal catalysis at the nanoscale.

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Among several light-driven process, the photothermal effect have attracted a renewed interest over the last years. A relevant emergent application is photothermal catalysis (PTC), where selected nanoabsorbers (nPTAs) under low intensity irradiation are exploited for the green synthesis of useful products, as fuels.[1] Inorganic systems like plasmonic nanoparticles (mostly gold) are particularly effective as nano-photothermal agents (nPTAs). The localized heating effect provided by nPTAs allows to supply energy in a well-controlled spatio-temporal way, allowing to create an energy-rich nano-environment in their close proximity. With respect to conventional chemistry processes based on the unspecific heating of the whole reaction environment, photothermal catalysis is thought to proceed mainly by generation and injection hot electrons or by localized heating, but the relative importance of these processes are still unclear.[2]

Measuring the temperature in close proximity to the surface of photothermal nanoabsorbers is fundamental to dissect the contributions to catalysis. Our hypothesis is that this problem can be addressed by the use of thermolabile species as temperature-time indicators. In this work, we developed time-temperature indicators based on thermolabile linkers. These probes undergo irreversible cleavage/dissociation when heated, providing a tool to measure the heating efficiency and profiles with high spatial resolution. Additionally, at difference from standard temperature chemosensors, where only the molecules present in the heated volume produce a signal, thermolabile indicators, undergoing an irreversible transformation when being in the heated area, provide a mechanism for signal amplification.

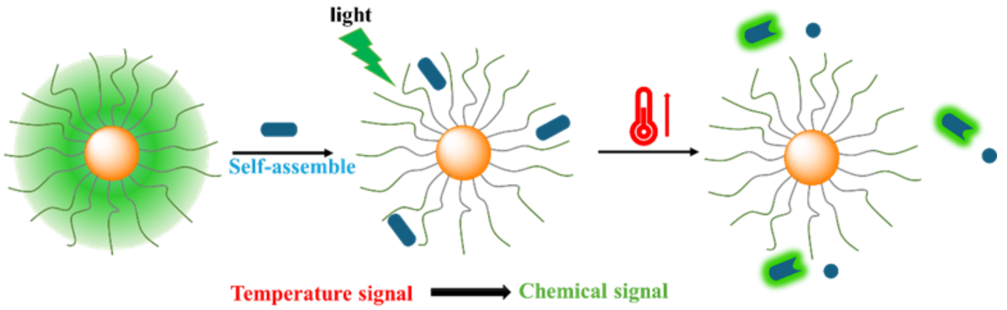

Figure 1. The structure of molecular thermometers connected to gold nanoparticles and irreversible cleavage after heating.

Acknowledgements

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Synthesis of Chiral BTBT Derivatives for the Study of the CISS Effect

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Interest in the field of organic electronics has been growing for more than four decades, leading to the design and synthesis of a wide variety of organic semiconductors – of which, thienoacenes are currently one of best performing materials for charge transport.[1][2][3] One class of thienoacenes, derivatives of [1]benzothieno[3,2-b][1]benzothiophene (BTBT), have been shown to exhibit charge carrier mobilities on the order of 10 cm2 V−1 s−1.[4][5] These high charge carrier mobilities have been shown to be a result of their favourable frontier orbitals and propensity to form herringbone style packing in the solid state.[6][7][8]
The introduction of chiral moieties to organic semiconductors can allow for the organic molecules to act as spin filters and the exploitation of this effect, known as the chiral-induced spin selectivity (CISS) effect, offers potential opportunities for the development of magnet-free spintronic applications.[9][10]
We, hereby, present the design, synthesis, and characterization of chiral BTBT derivatives. The BTBT are linked to the chiral molecule through different functional groups. With the view to determine their suitability for spintronic applications.

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Design of Ferrocene–Peptide Conjugates as Potential Anticancer Agents

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Cancer remains one of the most significant health challenges in modern society. Existing therapeutic strategies often suffer from limited selectivity and numerous side effects. In this study, we aim to design, synthesize, and evaluate peptide–ferrocene conjugates as potential anticancer agents. The peptide component is intended to selectively target integrins, proteins that play a crucial role in cancer initiation and progression, while the ferrocene moiety is expected to exert cytotoxic effects through the generation of reactive oxygen species (ROS) [1].

Inspired by previous studies [2,3], we designed and synthesized conjugates composed of three key components: (i) a ferrocene moiety serving as an electroactive unit; (ii) an aromatic linker to modulate the oxidation potential of ferrocene to physiological conditions; and (iii) a short peptide sequence, including the well-known RGD motif, capable of interacting with overexpressed receptors on cancer cells.

The synthesized compounds were subjected to conformational analysis in solution using ^{1}H NMR, IR, and circular dichroism (CD) spectroscopy, as well as detailed electrochemical characterization via cyclic voltammetry. In addition, we assessed their resistance to proteolytic degradation both by individual enzymes and in human serum. As expected, the ferrocene moiety provided protective effects for the peptide segment, with significant amounts of the conjugates remaining intact after 24 hours. Notably, the best stability was observed in constructs featuring the shortest linker, likely due to the closer proximity of the ferrocene unit to the peptide.

The evaluation of the potential anticancer activity of these compounds is currently ongoing on different cancer cell lines.

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Transient Induction of Chirality by an Activated Carboxylic Acid

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A dissipative system is maintained in a non-equilibrium state by the consumption of a chemical stimulus, e.g. an ACA[1] such as **1** (see Figure 1, left). We reported that using enantiomerically pure **1**, a transient and temporally programmed transfer of chirality from the ACA stimulus to the metal complex **2** can be achieved. In the presence of DIPEA as a base, the conjugate base of **1** occupies a coordination site of **2**, as expected[2], inducing helicity, enantiomeric excess and therefore Circular Dichroism (CD) signal (see Figure 1, right). Then, the carboxylate loses CO_2 and is reprotonated, generating a racemic and CD-silent waste and restoring the initial equilibrium (see Figure 1, left). In addition, the complex **2** with and without the carboxylate ligand was characterized with NMR techniques. The system dissipative cycle was also meticulously studied with NMR over time using enantiopure and racemic **1**. In the former case, the symmetry breaking is recognizable and the half-life of the species was estimated. In the latter, a ligand exchange process simplifies the spectra. Remarkably, it is possible to control the duration of the chirality transfer modulating the excess **1** added and perform subsequent cycles without loss of efficiency.

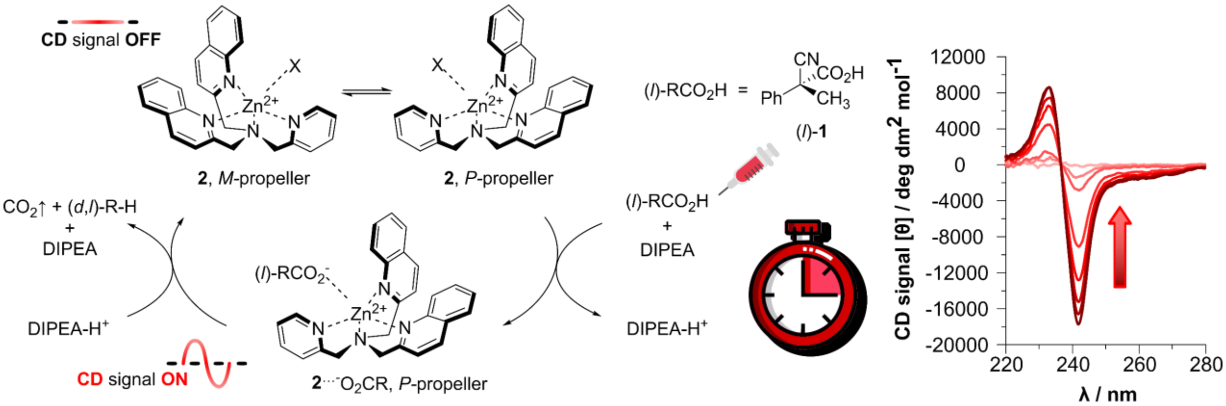

Figure 1. Left) Reaction cycle described above Right) Time evolution of CD spectra after addition of 1.

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Artificial Water Channels Enhance Solar Water Oxidation

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In natural Photosystem II (PSII), structured water channels ensure directional delivery of water and protons to the oxygen-evolving complex, thus enhancing catalytic performance. Inspired by this architecture, we report the synthetic design of artificial water channels in supramolecular quantasomes (QS), assembled from cationic perylenebisimides (PBI^{2+}) and anionic Ru_4POM catalysts. Polyethylene glycol (PEG) linkers of variable length (QS_{PEG}-n, n = 2–140) are covalently introduced to cross-link the QS framework, enabling internal hydration domains that mimic PSII-like water channeling.

Small-angle X-ray scattering (SAXS) and low-field NMR reveal dual hydration dynamics—confined water within the QS interior and mobile water at the surface. Among the series, QS_{PEG}-6 exhibits the optimal balance of porosity and 2D paracrystalline order, resulting in a significant enhancement of photocatalytic oxygen evolution and excellent faradaic efficiency under simulated solar irradiation. In contrast, longer PEG chains destabilize the lamellar structure, reducing catalytic performance and highlighting the structural limits of hydration tuning.

These findings establish a new design strategy for integrating hydration control into artificial photosystems. By modulating supramolecular porosity via PEG-mediated cross-linking, we provide a platform for scalable, robust solar water oxidation catalysis.

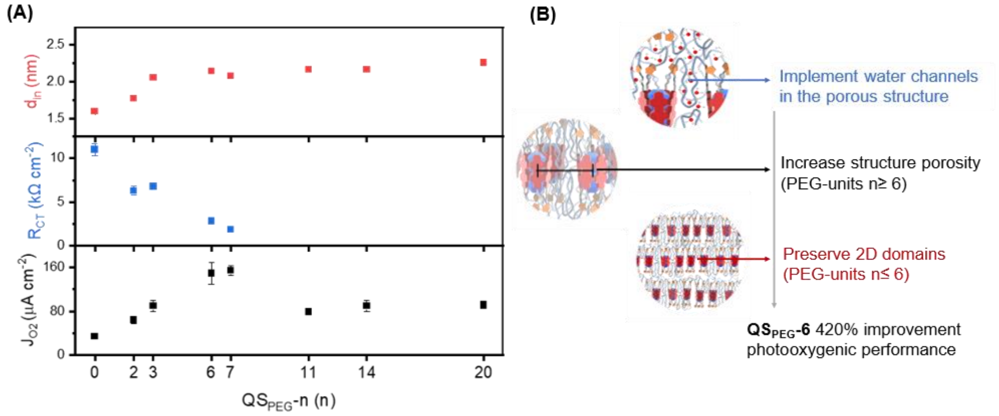

Figure. A) Correlation between the intralamellar distance d_{in}, the structure morphology (from SAXS fitting results) (red), the R_{CT} (blue), and oxygenic photocurrent densities of IO-ITO|**QS_{PEG}-n** (n=0, 2, 3, 6, 7, 11, 14, 20) (black), and the length of the PEG linkers in the **QS_{PEG}-n** structure. **B)** Model of **QS_{PEG}-n** key structural properties to enhance photooxygenic activity.

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Oxidation of Carbonyl Compounds Formed in Biomass Burning Initiated by HOONO

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Biomass burning produces nearly 90% of global primary organic aerosols and emits large quantities of organic pollutants, such as carbonyl compounds.[1] Once in the atmosphere, carbonyl compounds react with various oxidants in both aqueous and gas phases. These oxidants include hydroxyl radicals (OH), peroxynitrite (HOONO), chlorine atoms (Cl) or ozone (O_3). Particularly, HOONO is present in sea water [2], and it is responsible for 1/3 of the oxidation processes by nitrogen compounds in cloud droplets.[3] On the other hand, peroxynitrite is produced in particulate matter from photoisomerization of nitrate [4] or by decomposition of nitrogenous organic compounds. The oxidation products may produce harmful secondary pollutants, in the atmosphere, provoking respiratory infections, even lung cancer.[5] Moreover, HOONO chemistry in cloud microdroplets and its environmental implications are not fully understood.

In the aqueous phase, the oxidation kinetics and mechanisms of the reactions of carbonyl compounds initiated by HOONO were studied under controlled laboratory conditions (pH, ionic strength and temperature) using a stopped-flow spectrophotometric technique.[6] This work enhances the understanding of the environmental chemistry of carbonyl compounds in the aqueous phase.

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Towards A Solar Fuel Device: Light-Driven Water Oxidation Catalyzed by a Supramolecular Assembly

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Pushing the boundaries of solar fuel research, wireless artificial photosynthetic systems are being designed to mimic Nature's way. These devices envision a machinery that harnesses sunlight to transform readily available resources like water and carbon dioxide into valuable products like H_2, carbon derivatives, and O_2. Such bio-inspired molecule-based systems require four key elements: a photosensitizer, a catalyst, an electron shuttle, and a vesicle acting as a nano-reactor. PLANKT-ON project (EIC Pathfinder Open 2022) inserts in this scenario, proposing polyoxometalate membranized vesicles as micro-compartmentalized protocells for artificial photosynthesis.[1] Photocatalytic active units named artificial quantasomes (QS) are encapsulated in the vesicle, emulating the Photosystem II (PSII). The supramolecular structure of QS self-assembles spontaneously in water, due to the complementary electrostatic interactions between bis-cationic perylene bisimide derivatives, acting as light-harvesting antennae, and a deca-anionic polyoxometalate ruthenium-based water-splitting catalyst.[2,3] This work presents our research on designing and characterizing these building blocks to achieve light-induced water oxidation within a confined environment.

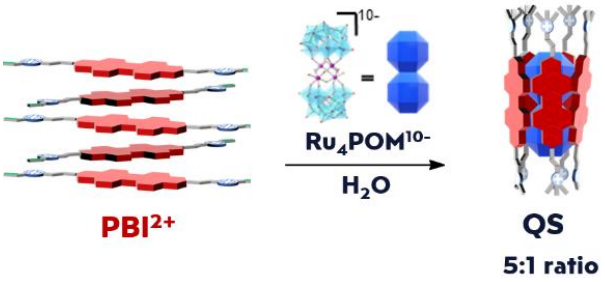

Figure 1. Self-assembly of Artificial Quantasome unit.

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On Deep Eutectic Solvent Catalysis

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Hydrogen bonds are critical to the success of many organic processes.[1] As a result, hydrogen bond catalysis has become an area of intense interest.[2] In the toolbox of modern organic synthesis, poly- and perfluorinated reagents such as 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) and trifluoracetic acid (TFA) are some of the most heavily used hydrogen bond donating catalysts.[3,4] These highly fluorinated catalysts are both toxic and persistent environmental pollutants. Another well-known hydrogen bond catalyst is water. The interface between water and an immiscible non-polar phase is known to exhibit a unique hydrogen bonding environment,[5] which has been exploited by Sharpless[6] and others[7] to catalyse a wide range of processes in what has been dubbed 'on-water catalysis'.

Deep Eutectic Solvents (DESs) are a class of 'green solvent' containing a mixture of hydrogen bond acceptor and hydrogen bond donor.[8] This combination results in mixtures containing highly associated hydrogen bonding networks.[8] Our group has recently demonstrated that some DESs exhibit hydrogen bond donating abilities comparable to or exceeding that of HFIP as well as having exceptional organophobicity.[9]As a result these DESs are exceptionally good at affording biphasic mixtures with organic reagents and solvents. This presentation will outline work undertaken to investigate the ability of these DES-oil interfaces to effectively facilitate hydrogen bond catalysis.

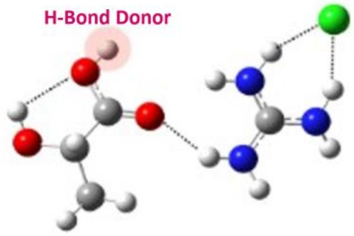

Figure 1: Representation of the strongest hydrogen bond in the associated DES.

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Quantum-chemical calculations as a powerful tool for predicting the course of a chemical reaction

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Computational methods play a key role in modern chemistry [1], as they allow a deeper insight into the nature of the chemical process and the explanation of the experimental data obtained [2]. Thanks to the rapid development of information technologies in the last decades, they have become an equal and necessary collaborator of experimental research. In this study, the thermal transformations of various thienyl and phenyl derivatives of o-divinylbenzene in an acidic media were investigated using an integrated experimental-theoretical approach [3]. Several derivatives led to cyclization products when heated under acidic conditions, while some proved to be non-reactive. The reactivity or non-reactivity of the investigated compounds was found to be closely related to the position of the preferred proton entry site in the investigated compounds, which was demonstrated by DFT calculations. If the preferred position of proton entry into the molecule coincides with the protonation position required for cyclization, the reaction proceeds, otherwise the derivatives are not reactive. By blocking a preferred proton position with a suitable substituent in the non-reactive precursors, proton formation at the undesired site can be prevented and proton entry can be redirected to the site where the reaction can proceed.

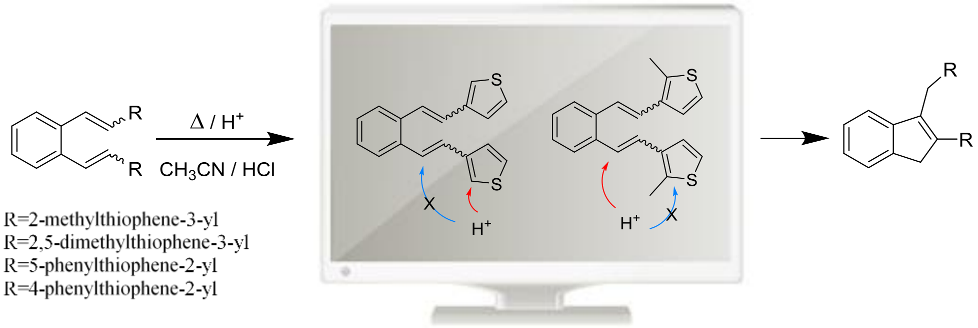

Figure 1. Thermal transformations of *o*-divinylbenzene derivatives.

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Exploring the Impact of Topological Variations on the Stability of the Ground Singlet and Lowest-Lying Triplet States of Catacondensed Hexabenzenoids

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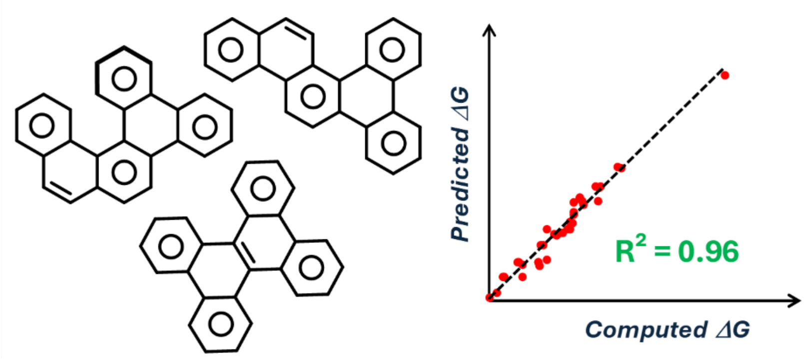
Polybenzenoid hydrocarbons (PBHs) are very popular in material science[1], organic electronics and spintronics[2] due to aromaticity and unique electronic properties. The impact of topological variations on the relative stability of PAH isomers in different electronic states is poorly understood, with limited insights into how Clar π-sextets[3] and topological features[4] like bay, cove, fjord, and K-regions influence stability in their ground singlet (S_0) and lowest-lying triplet (T_1) states. In this work, we perform density functional theory calculations of the S_0 and T_1 states of the 37 catacondensed hexabenzenoids. We use a multivariate linear regression model with relative energy as the dependent variable and a series of topological parameters as the independent variables to quantify the effect of topology in the relative stability of the catacondensed hexabenzenoids. Our analysis shows that, in S_0, stability is enhanced by an increase in the number of Clar π-sextets and K-regions and decreased by the presence of coves and fjords. In T_1, the main stabilizing factors are the number of Clar π-sextets and the number of rings involved in the antiaromatic region, whereas topological regions like K-edges, bays, coves, or fjords are destabilizing.



The influence of topological features on the stability of 37 catacondensed hexabenzenoids in their S_0 and T_1 states using a multivariate regression model.

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Photogeneration of azomethine ylides : toward the dearomatization of electron-poor arenes via (3+2) cycloaddition

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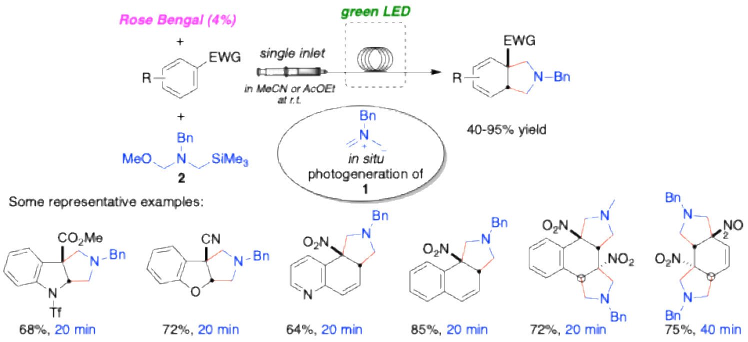
In the search for novel molecules with tridimensional structures, dearomative processes have become a hot topic due to the large number of starting materials available. Among them, electron-poor arenes are of interest since they are easily accessed through electrophilic aromatic substitution, and the presence of an electron-withdrawing group (such as a nitro or cyano group) can serve for post-functionalization. The non-stabilized ylide **1** is an attractive electron-rich dipole allowing construction of the popular pyrrolidino fragment. Due to its ability to self-condense, **1** must be generated *in situ* in the presence of the dipolarophile. For this, a common source of **1** is the hemiaminal ether **2**, which decomposes, at room temperature, into the target ylide through acid catalysis, usually.[1]

We report herein that Rose Bengal can be used as photocatalyst for the friendly generation of **1** at room temperature under flow conditions. In these conditions, it allows the dearomatization of structurally diverse electron-poor arenes, including the challenging benzenic derivatives, by (3+2) cycloaddition within less than 1 h (Scheme 1).[2]



Scheme 1: Flow (3+2) Dearomative cycloaddition under photocatalyzed conditions

The (3+2) cycloaddition takes place between various electron-depleted aromatics and the non-stabilized ylide **1**, photogenerated from **2** through a radical cationic intermediate. Computational studies suggest a stepwise mechanism involving azomethine ylide **1** as reactive species toward the arene. With the Rose Bengal as photocatalyst, a broad range of substrates from hetarenes (indole, benzofurane, quinoline, pyridine) to naphthalene and benzene were efficiently transformed into valuable 3D structures. This photocatalysed (3+2) cycloaddition under green light irradiation can also advantageously be performed in the friendly ethyl acetate as solvent.

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London dispersion between confined alkyl groups

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Despite its image as a weak interaction, London dispersion (LD) can be decisive in the structure and reactivity of organic molecules.[1] To date, efforts to experimentally quantify the strength of dispersion interactions have proven challenging, partly due to competition with surrounding solvent.

Here, we show that self-assembled coordination cages featuring endohedral alkyl groups serve as a versatile platform for the study of London dispersion, both in the gas phase and in solution. Specifically, by systematically varying the alkyl groups constricted to the interior of these cages – formed by subcomponent self-assembly[2] of tritopic pyridyl-imine ligands around metal cations such as Zn^{2+} – we can observe dramatic changes to their stability. Moreover, LD can govern the stereochemical preferences of these dynamic systems, as well as the self-sorting of systems containing two or more alkyl groups.

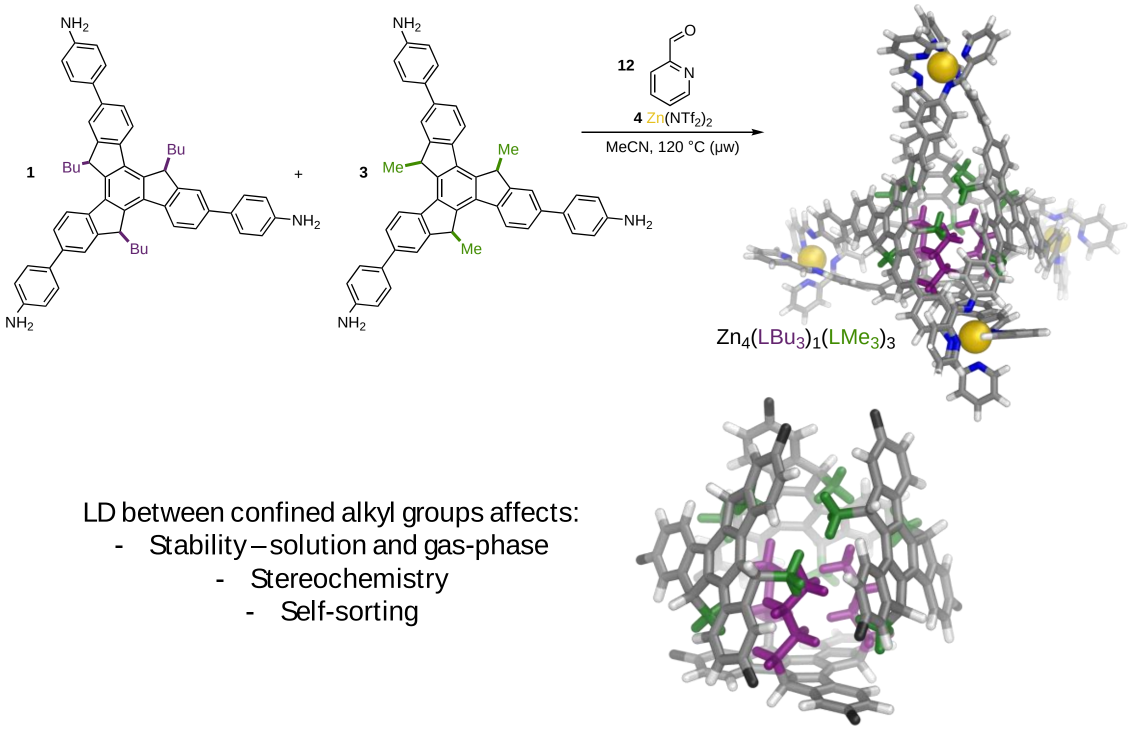

Figure 1. Self-assembly of a heteroleptic Zn_4L_4 cage encapsulating closely interacting alkyl groups.

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π - Complexes of Benzoannulated TBD with Arenes – Theoretical Prediction of Basicity and UV-Vis Spectra

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Guanidine moiety is well known anion recognition site in a vast number of artificial anion receptors. [1] Due to its Y-shaped structure, it possesses high intrinsic and solution basicity [2] which ensures its protonation over a wide range of pH. It can form strong multiple hydrogen bonds which makes it a suitable active subunit not only in anion sensors, but in organocatalysis [3] and the bridging component in the photoactive D-A systems as well. [4,5]

In this work, we will focus on the dibenzo derivative of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) and its complexation with a series of arenes (benzene to pentacene) as a simple model for developing multicomponent molecular systems consisting of a guanidine binding site and nanotubes or graphene fragments as electron accepting groups.

Structures of guanidines, their protonated forms and π-stacked complexes with arenes, basicity and pK_a values, as well as complexation energies, were calculated using DFT M062X/6-311G(d,p) model in acetonitrile (solvent effects by SMD model of solvation). The basic photochemical properties of selected complexes (excitation energies, oscillator strengths and absorption spectra) were simulated from data obtained by employing the TD-PBE0/aug-cc-pVTZ//M062X/6-311G(d,p) approach.

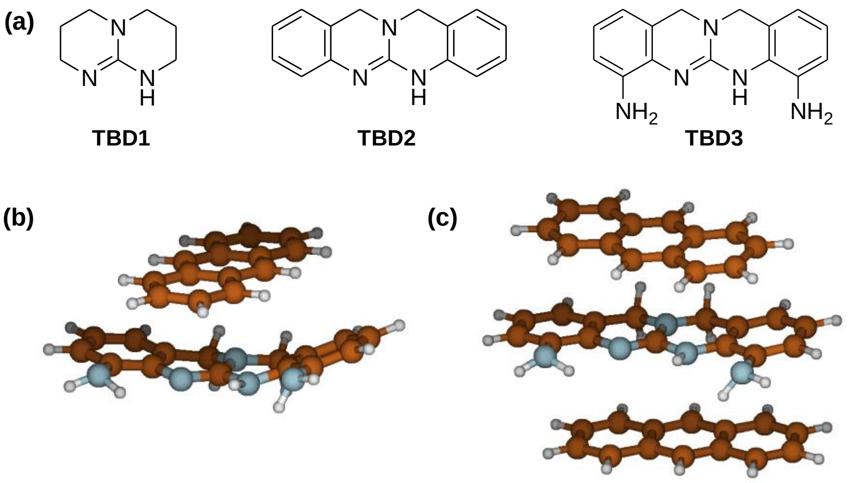

Figure 1. (a) Structures of (a) investigated guanidines; (b) **TBD3** complex with anthracene and (c) sandwich **TBD3** complex with two molecules of anthracene

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Selenium nanoparticles as drug delivery system for levodopa in the treatment Parkinson's disease

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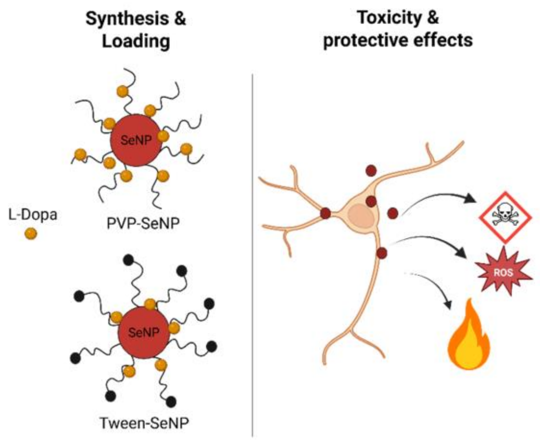
Parkinson's disease (PD), neurodegenerative disease that affects thinking, skilled movements, feelings, cognition and memory, is characterized by the degeneration of dopaminergic neurons which causes massive depletion of dopamine. Main therapeutic strategy for PD is to increase level of dopamine by administration of its precursor levodopa (LD). However, levodopa treatment is responsible for different side effects in PD patients, many of them being caused by increased oxidative stress.

We aimed to design safer and more efficient LD nanoformulation by employing selenium nanoparticles (SeNPs) with two different stabilization agents: Tween 20 and poly(vinylpyrrolidone). Using *in vitro* model of dopaminergic neurons, safety and biocompatibility of Tween-SeNP and PVP-SeNP were evaluated as LD nanodelivery systems. Obtained results showed that both nanoformulations were non-toxic to dopaminergic neurons under *in vitro* settings. Moreover, PVP-SeNP exhibited protective action against levodopa-induced oxidative stress and cellular damages. Efficiency of such nanodelivery system was tested using hemiparkinsonian rat model, generated by injection of 6-hydroxydopamine into the right hemisphere of the rat brain according to the stereotaxic atlas. Rats were treated orally with LD alone or LD-dopped SeNPs 28 days after stereotaxic surgery. Behavioral assays including Accelerating Rotarod Test, Gait Analysis Test and Neurological Severity Score were performed to evaluate the changes in motor activity before and after the treatments. Obtained results showed great improvement in locomotor behavior of male rats after the treatment with LD-dopped SeNPs (+CD) compared to the efficacy of LD(+CD).



Scheme. SeNP as drug delivery systems for neurodegenerative disease.

Acknowledgements: This study was financially supported by the "Research Cooperability" Program of the Croatian Science Foundation funded by the European Union from the European Social Fund under the Operational Programme Efficient Human Resources 2014 – 2020 (grant HRZZ-PZS-2019-02-4323), Horizon 2020 project PHOENIX (Grant Agreement no. 953110), the European Regional Development Fund project KK.01.1.1.02.0007 "Research and Education Centre of Environmental Health and Radiation Protection – Reconstruction and Expansion of the Institute for Medical Research and Occupational Health" and the European Union – Next Generation EU (Program Contract of 8 December 2023, Class: 643-02/23-01/00016, Reg. no. 533-03-23-0006).

Encoding free-form locomotion in photo-responsive soft microrobots

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Living systems express propulsion at the microscale mostly due to non-reciprocal motions. At low Reynolds number (drag-dominated regime), motility is achieved only when displaying non-reciprocal shape transformations.[1] Likewise, terrestrial propulsion escapes friction forces by exploiting non-reciprocal movements, resulting in directional motility.[2] While non-reciprocal motions are well established in microorganisms, artificial micro walkers or swimmers are currently facing multiple challenges to achieve such deformations and, therefore, motility. Soft architectures based on liquid crystal elastomers (LCEs) not only present structural integrity but they can also be polymerized with well-defined molecular alignments to encode macroscopic motions in a non-reciprocal fashion, as observed in biological systems.[3] The latter is a crucial feature as it allows for inter-media life-like locomotion at the microscale in synthetic matter, encompassing both aquatic and terrestrial environments. By using photo-responsive mesogens in bioinspired, single-material LCE microstructures, we investigate the emergence of multimodal locomotion in synthetic matter and in different media, towards the creation of soft robotics and intelligent materials that perform amphibious-like motions under dissipative conditions.

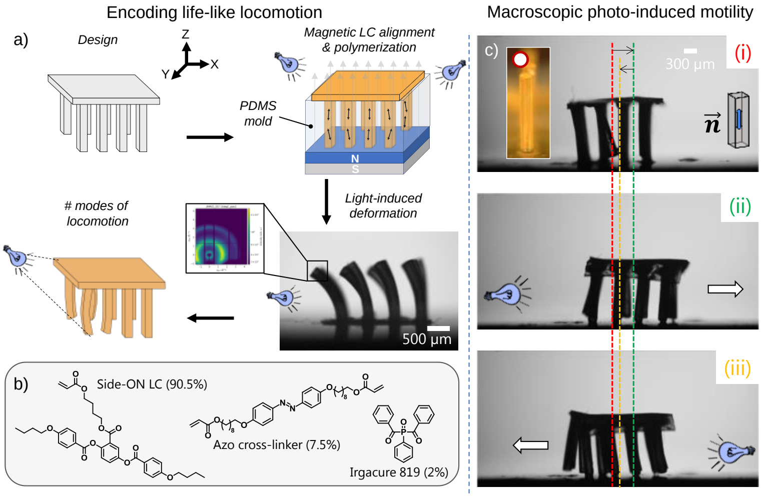

Figure 1. a) Design and fabrication of photo-responsive LCE structure, characterized by WAXS (inset). b) Chemical moieties used, comprising Side-ON mesogen and azobenzene photo-switch. c) Directional locomotion of the free-standing microstructure upon varying the direction of incoming UV light.

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2-Nitreno-9-fluorenylidene – A Quintet Ground State Carbenonitrene

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Due to their promise in developing organic magnetic materials and their utility in quantum information science, organic high-spin molecules derived from polycarbenes and polynitrenes have attracted considerable interest.[1,2] Prerequisites for these applications are a robust spin ground state, high yields of the high-spin species, and a rigid backbone facilitating the ferromagnetic interaction of spin centers.

This presentation will focus on the investigation of 2-nitreno-9-fluorenylidene (**1**). In this molecule a carbene and a nitrene center are linked ferromagnetically via the rigid fluorene scaffold, resulting in a high-spin quintet ground state. The synthesis of **1** was achieved by photolysis of its precursor, 2-azido-9-diazofluorene (**2**), in an argon matrix at 3 K. Its high-spin ground state was verified by analysis of IR, UV-vis and EPR spectra in combination with DFT calculations.

The photochemical pathway from **2** to **1** was investigated by matrix isolation spectroscopy at cryogenic temperatures and by ultrafast time-resolved spectroscopy in solution at room temperature. Our investigations revealed that the carbenonitrene is generated via a stepwise cleavage of the azide and diazo group. The photolysis of **2** closely resembles a combination of the photochemical pathways observed for the reference systems 2-azidofluorene, a nitrene precursor, and 9-diazofluorene, a carbene precursor. However, the photochemistry of **2** is cleaner than that of the reference compounds, and no side reactions, such as cyclization to a benzazirine or ketenimine,[3] were observed.

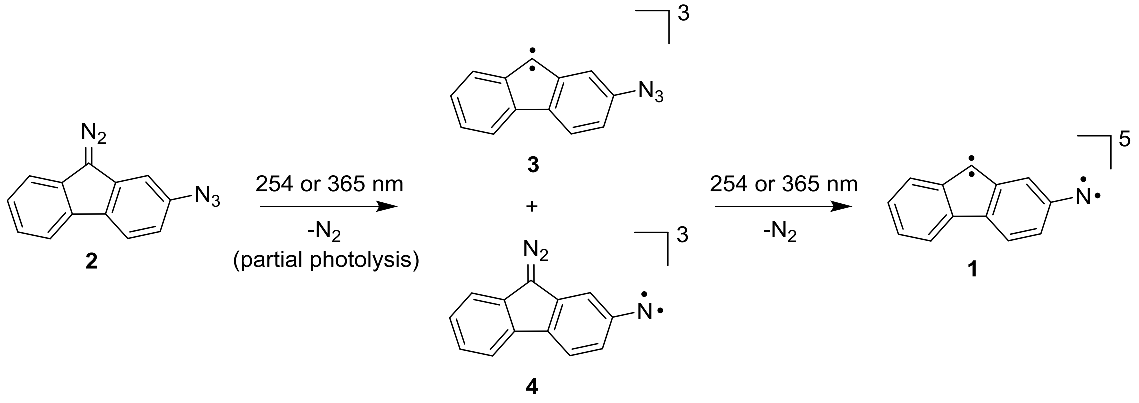

Figure 1. Generation of quintet 2-nitreno-9-fluorenylidene (**1**) from its precursor **2** by photolysis, eliminating two nitrogen molecules forming the triplet carbene and nitrene intermediates **3** and **4**.

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Computational Study of the Through-Resonance Effect in Phenylaminomethyl Cations

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Substituent effects on the stabilities of cations of benzene derivatives are well described by the Yukawa-Tsuno equation (1):

$$-\Delta E_X = \rho(\sigma^0 + r^+\Delta\bar{\sigma}_R^+) \tag{1}$$

The normal substituent constant (σ^0) measures the fundamental electron-donating or -withdrawing capability of all ring substituents. The resonance substituent constant ($\Delta\bar{\sigma}_R^+ \equiv \sigma^+ - \sigma^0$) measures the capability of the through-resonance for *para* -R groups. The σ^+ and σ^0 were determined on the stabilities of α,α-dimethylbenzyl cations (**1**) and **1(ϕ=90˚)** where the vacant p-orbital in **1** was fixed orthogonally to the benzene π-electron system, respectively. The resultant r^+ value reveals the degree of the through-resonance effect in a given system.

We have reported a negligible r^+ value of -0.04 for N-phenylguanidinium ions.[1] On the other hand, substituent effect analyse of a series of R-(phenylamino)methyl cations gave a wide range of r^+ values, although relevant canonical structures cannot be drawn.[2] In this study, we extended the study to R,R-(phenylamino)methyl cations to discuss the inducement mechanism of the through-resonance effects in detail. Relative gas-phase stabilities of ring-substituted cations **2**–**7** were computationally determined using isodesmic reactions (B3LYP/6-311+G(2d,p)). Their substituent effects were analyzed by Eq. 1.

Obtained r^+ value (Scheme 1) increase with increasing electron-withdrawing ability of the substituents (R) connected to the cationic center. A variety of the through-resonance effects were observed in these cations. NBO analyses suggested that the π–π^* and π–σ^* orbital interactions between benzene π-electron systems and side chains determine the degree of the through-resonanc effects.

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Computational Study of the Saturation Effect in Benzylic Cations

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Substituent effects on the stabilities of cations of benzene derivatives are well described by the Yukawa-Tsuno Eq (1)[1]:

$$-\Delta E_X = \rho(\sigma^0 + r^+\Delta\bar{\sigma}_R^+) \tag{1}$$

The normal substituent constant (σ^0) measures the fundamental electron-donating or -withdrawing capability of all ring substituents. The resonance substituent constant ($\Delta\bar{\sigma}_R^+ \equiv \sigma^+ - \sigma^0$) measures the capability of the through-resonance for *para* -R groups. The resultant r^+ value reveals the degree of the through-resonance effect in a given system. Eq. (1) has been successfully applied to various reaction rates and gas-phase stabilities to give insights on reaction mechanism and cation structure, and was computationally reproduced to reveal theoretical background.[2]

On the other hand, we have developed a linear free energy relationship (LFER) for anions. It has become apparent that anions are stabilized by not only the fundamental and through-resonance effects but also the saturation effect, and their substituent effects are described by three-term extended Yukawa-Tsuno Eq. (2):[3]

$$-\Delta E_X = \rho(\sigma^0 + r^-\Delta\bar{\sigma}_R^- + s\Delta\bar{\sigma}_S) \tag{2}$$

The saturation substituent constant ($\Delta\bar{\sigma}_S \equiv \sigma^- - \sigma^0$) at the third term in Eq. (2) measures the capability of the saturation for EDGs. The resultant *s* value reveals the degree of the saturation effect.

This situation raises a question: Why substituent effects of cations can be analyzed by two-term Eq. (1)? To make clear if cations can be stabilized by the saturation effect caused by EWGs, substituent effects on the gas-phase stabilities for various benzylic cations were computationally determined using isodesmic reaction (3). Increased number of ring substituents (X) were used compared to former studies for the detailed study.

(3)

Obtained substituent effects were compared with one another to discuss the presence of the saturation effect induced by EWGs to stabilize the cation that demands the third term to Eq. (1).

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Dynamic Covalent Bonds for Optical Data Storage: Harnessing $^1O_2$ -Self-sensitization and Photoperoxidation for Information Encoding

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As digital information multiplies at an unprecedented rate, the challenge of developing advanced storage technologies has intensified, driven by the need for systems that can handle vast amounts of data while remaining efficient, scalable, and durable. Herein, anthracene-based chromophores are employed to develop a photowritable fluorescent system that enables information encoding by exploiting the reversible stimuli-induced covalent bond formation and breaking of a corresponding endoperoxide (EPO) species. Specifically, O-doped anthracenyl derivatives capable of efficient $^1O_2$ -self-sensitization and reversible EPO formation via [4 + 2] cycloaddition is investigated. Integration of these derivatives into polymeric matrices allows the production of photowritable films without affecting the molecule's capability to generate $^1O_2$ and form an EPO[1]. A series of anthracene-based chromophores is prepared, to showcase the influence of electron density and twisting of the anthracene backbone on the rate constant of the EPO formation and the release of $^1O_2$ and – depending on these rate constants – suggest the eventual function of the individual chromophores in optical data storage systems.

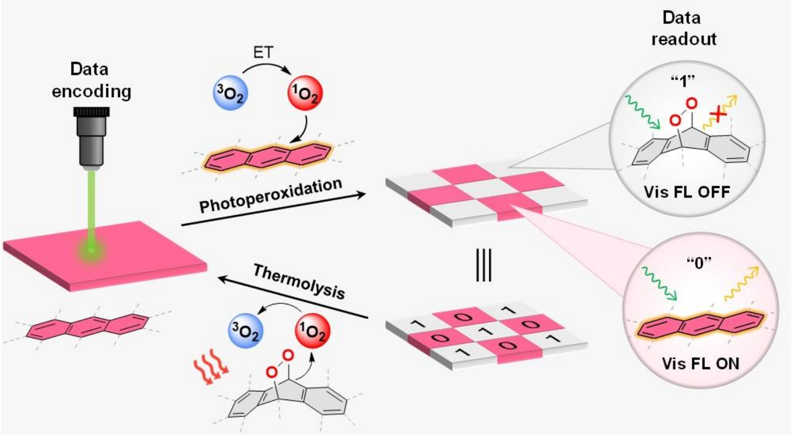

Figure 1. The concept of photowritable fluorescent polymeric thin films.

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Quinazolinones as prospective phytoeffectors

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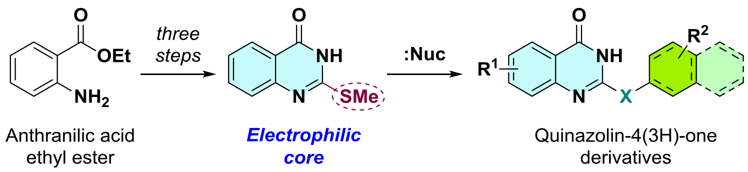
Upon drought stress, plants reduce their transpiration by closing their stomata. Besides hindering their further growth, this innate response provokes the so-called oxidative stress, characterized by larger amounts of reactive oxygen species (ROS). ROS damages all classes of biomolecules including DNA which could lead to mutations and disrupt plant reproduction. One of the several plant defense mechanisms to repair ROS-damaged DNA relies on Poly-(ADP-Ribose) polymerases (PARP) enzymes. This mechanism, though efficient, consumes a lot of energy, hindering other physiological processes like growth. In this chapter we report on the *in-silico* study, synthesis, *in vitro*, and *in vivo* biological evaluation of a library of potential PARP inhibitors derived from anthranilic acid 118 as a continuation of previous research within our group. The AtPARP1 enzyme was used as a model receptor for the theoretical and inhibition assays, while *Lemna minor* plants were used to evaluate the capacity of the synthetic molecules to induce drought stress tolerance. The synthesis route comprised a three-step derivatization of 118 to obtain the intermediate 120, which was then reacted with a set of different nucleophiles comprising anilines, thiophenols and benzylamine derivatives. A modified route was designed to obtain a phenol derivative through a one-step Oxone®-mediated oxidation/substitution reaction. Another modified route was employed for the preparation of alkynylated derivatives by means of the Sonogashira cross coupling reaction. While no significant results were found during the *in vitro* screening, four 2-quinazolin-4(3H)-one derivatives showed herbicidal activity, and other four increased plant growth in the *in vivo* bioassays.



- Wessjohann's group (previous work):

X = NH **R^1**: 4-, 5-NO_2 or -NH_2
R^2: EWG, EDG

- Wessjohann's group, **this work:**

X = O, S, NH, $NHCH_2$ **R^1**: 4-I, 4-(TMS)ethynyl
R^2: EWG, EDG

Multivalent interactions between functionalized gold nanoparticles and DNA

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Sensing of ultralow analyte concentrations is of crucial importance for many applications such as in detection of biomarkers for faster disease diagnosis. DNA sensing and the ability to detect single nucleotide polymorphism is emerging as an essential element of molecular diagnosis and in forensics science.[1] Gold nanoparticles (AuNP) have become key components of diagnostic assays thanks to their attractive properties, such as their ease of preparation, the organized structure of the nanoparticle surface monolayer, and the intrinsic optoelectronic properties of the gold core. Taking advantage of these favorable properties, AuNPs were employed in diagnostic assays for nucleotides, peptides, enzymes and small biomolecules.[2-4]
Here we present an in depth study of a novel multivalent system capable of ultrasensitive detection of specific molecular targets in the form of nucleic acid strands. Three different nanoparticles with different terminal groups (TACN·Zn^{2+}, TACN, NMe_3^+) were employed and their interactions with DNA strands of different length and hybridization level were studied.
The results obtained through this research will be used to develop a responsive system towards DNA-RNA hybrid double strands exploiting the well known catalysis of RNA hydrolysis by TACN·Zn^{2+} complexes. [5]

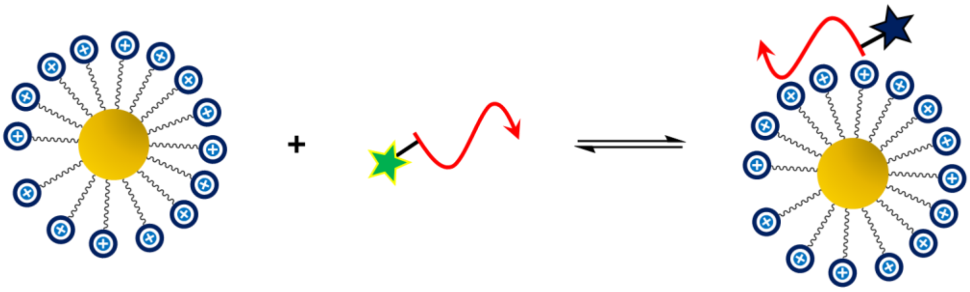

Figure 1. Schematic representation of the interaction between the AuNP and a single strand DNA, functionalized with a fluorophore. Once the DNA strand is bound to the nanoparticle, its fluorescence emission is quenched.

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A Scalable Automated Reaction Pathway Finder using the NEB Method

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Locating the reaction pathway, or minimum energy path, on the potential energy surface is a high-dimensional problem, for which multiple methods have been developed. One popular method is the Nudged Elastic Band (NEB) approach, which approximates the reaction path as a series of images leading from the reactant to the product structure. These images are optimised while also considering the tangent direction of the reaction path, as well as an artificial spring force that connects them. The efficiency and accuracy of this optimisation process depend on various parameters and definitions. After analysing the influence of the chosen starting path, the tangent definition, and the chosen step predictor, it became possible to significantly reduce the number of iterations required by the NEB to produce a reaction pathway. Furthermore, alternative reaction paths identified using different methods offer valuable insights into the NEB process and the quality of the optimised reaction pathway.

Towards systematic initiations of minimum energy path calculations

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The exploration of reaction pathways lies at the heart of understanding chemical processes, with applications ranging from catalysis to drug design. A reaction path in its fundamental form describes the rearrangement of atoms between reactant and product state along a connected set of structures, providing insight into the kinetics of the reaction. With the advancement of computational hardware and quantum chemical methods in the recent years, computational and data-driven reaction network discovery has become accessible, revolutionizing the way chemical space is explored, thus accelerating the development of novel molecules and materials [1,2,3]. However, at the heart of this endeavor still lies the efficient generation of minimum energy paths (MEP), which are often needed *a priori* as feedstock for data driven methods. It has been shown that the MEP generated by common use gradient-based methods such as the Nudge Elastic Band (NEB)[4] or string[5] method heavily rely on the initial path and the coordinate space chosen[6].

In this regard we present a systematic and broad comparison of representations used in MEP generators, as well as a curated dataset of benchmark reactions for reaction-exploration algorithms. Our dataset shows wide chemical diversity, containing molecules with up to 21 heavy (non-hydrogen) atoms from the reaction space spanned by C, H, O, N, S, P, B, F, Cl and Br. By including larger and chemically more diverse molecules than previously established datasets [7,8] we provide an opportunity to test the robustness and predictive capabilities of established methodologies.

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Catalytic polymerization of 1-bromo-2-phenylacetylene derivatives by using palladium complexes as catalysts

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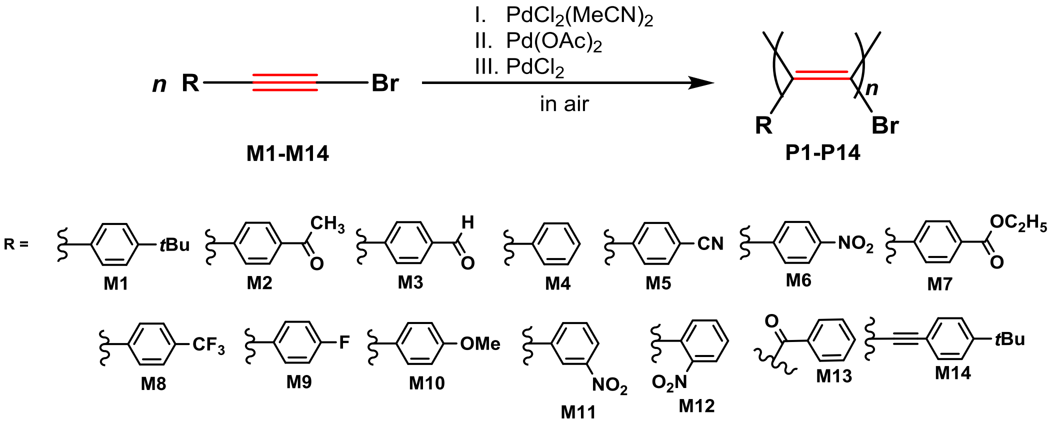
Haloalkynes have been of great interest to the scientific community for years. These compounds are interesting due to their biological activity and the enormous application potential associated with nonlinear optical properties and electrical conductivity [1]. In recent years, there has been a increased interest in disubstituted acetylene polymers due to their high gas permeability, unique elastomeric behavior in various conjugated fluorescent polymers, and improved thermal stability compared to their monosubstituted counterparts [2]. The use of transition metal catalysts has contributed to gaining insight into the polymerization reaction mechanism as well as to the development of controlled polymerization systems [3]. In 2014, the polymerization of 1-chloro-2-(4-*tert*-butyl)phenylacetylene using palladium complexes was studied [4]. In 2018, the polymerization of 1-chloro-2-phenylacetylene derivatives was carried out using Brookhart-type catalysts [2]. Catalytic polymerization reactions using palladium salts for 1-chloro-2-phenylacetylene derivatives are known in the literature.

During the research, using derivatives of 1-bromo-2-phenylacetylene in a catalytic polymerization reaction using palladium salts as catalysts, a series of polymers were obtained (Figure 1). The reaction conditions for the catalytic polymerization of 1-bromo-2-(4-*tert*-butyl)phenylacetylene were optimized. It was checked how time, temperature, type of solvent, type of catalyst and its amount affect the polymerization reaction. GPC analysis of the DCM-soluble parts revealed that the M_w and PDI were 29 965 and 1.19 for P1 after 72 hours.



Scheme 1. Catalytic polymerization reaction of 1-bromo-2-phenylacetylene derivatives.

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Active materials based on dynamic self-assembly processes

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The transition from inactive to active matter is one of the defining moments in the emergence of life. The transition to active matter requires self-organized non-equilibrium structures able to extract energy from the environment to carry out work. The transient fluorescence signal generation in response to ATP concentration has been reported exploiting the supramolecular interactions between positively charged gold nanoparticles (Au-NPs) and negatively charged coumarine.[1] In the meantime, ATP is a key component of a tumour microenvironment, with low concentrations in healthy cells, but elevated levels up to hundreds in extracellular tumour tissues. This makes it a good candidate for cancer detection. Inspired by this system reported, we want to create a new model of mixed monolayer Au-NPs covalently decorated with two different thiols: an ATP receptor and a reporter thiol. In a 3D matrix, this approach prevents coumarin from diffusing away, thus allowing this system to detect an analyte with spatial resolution. Hence, the reporter thiol will be equipped with a hydrophilic poly(ethylene glycol) (PEG) grafted with a negatively charged fluorescence probe that can be reversibly released in the presence of a specific stimulus.[2] And we also investigated how to optimize the surface architecture.

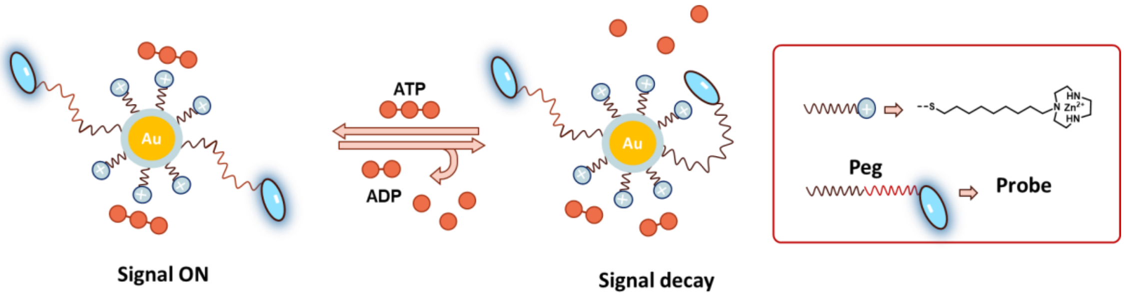

Figure. The system can be reversible activated, and the presence of apyrase degrades ATP to cause signal decay

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Solvent Effects on the Reactivity of a Solvatochromic Phenolate Betaine

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The kinetics of methylation of solvatochromic 4-(2,4,6-triphenylpyridinio)phenolate **1**[1] was followed in six solvents and four binary mixtures with variable compositions, in search of solvent effects that govern the reactivity of the betaine phenolate.

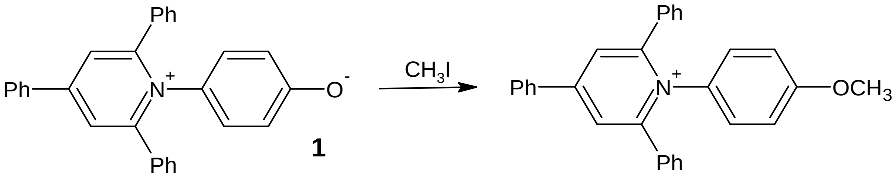


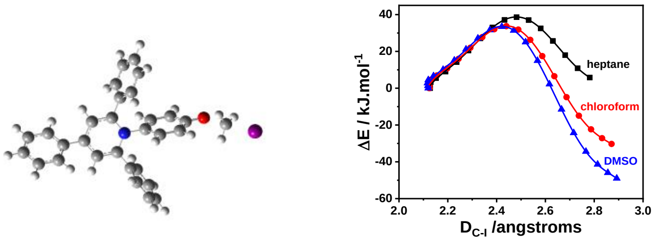
Figure 1. Reaction of betaine phenolate **1** with methyl iodide at 25°C

In small (C_1-C_4) acidic alcohols the process, besides being too slow, competed with the reaction of CH_3I with the nucleophilic solvent, preventing the determination of trustworthy rate constants. Thus, the choice of solvents was restricted to media with negligible acidities ($CHCl_3$, CH_2Cl_2, $(CH3)_2CO$, CH_3CN, DMSO and 2-octanol).

The dependence of the second-order-rate constants on solvent effects was expressed as a multiparametric equation of the medium *SP* (polarizability) and *SdP* (dipolarity) parameters.[2]

$$\text{Log } k_2 = -9.92 + 6.01\,SP + 4.66\,SdP \qquad (N = 6 \quad r^2 = 0.962)$$

Calculations with a polarizable continuum model at a semi-empirical PM3 level confirmed the above dependence. IRC plots of reaction energies *vs* C-I bond breakage showed that increasing the solvent dipolarity/polarizability had the effect of reducing transition energies, with more endergonic processes and earlier transition states.



(a) (b)

Figure 2. a) Transition state for the methylation of **1;** b) theoretical plots of reaction energies *vs.* CH_3-I bond breakage in solvents of increasing polarizability/dipolarity (heptane < chloroform < DMSO)

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Studying self-assembly of peptides through nucleobase recognition: how to build a biomolecular wire

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The creation of long biomolecular wires able to perform tasks such as electron transfer needs perfect control of the self-assembly process, via directional and reversible secondary interactions.[1] Elucidation of the rules mediating the macroscopic organization and leading to functional properties would offer a fascinating prospect for technology and open up the way towards many new applications.[2] In this work, peptide-nucleobase monomers have been used to realize different structures on gold surfaces. Three building blocks have been designed to be non-covalently linked to a gold electrode and self-assemble in an ordered manner (Figure 1).[3]

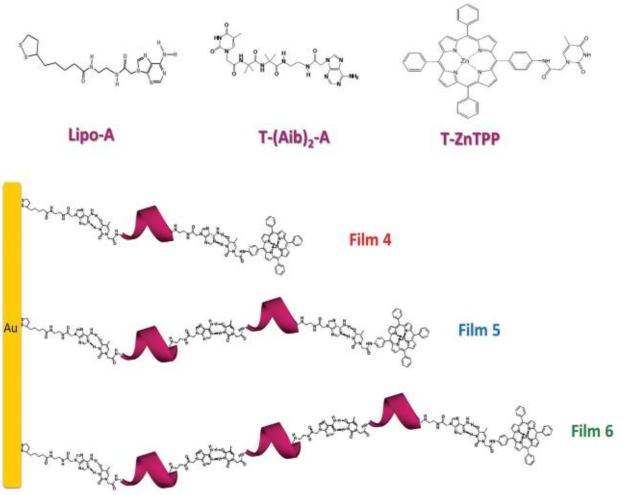

Figure 1. Chemical structures of the building blocks and biomolecular wires.

Consecutive deposition of the three complementary building blocks via thymine-adenine hydrogen bonds afforded three films, composed of one, two, and three helical peptide layers, respectively, with the ZnTPP dye as the external layer. Spectro-electrochemical and spectroscopic characterizations revealed that all films are able to generate current under illumination, with photoresponse and stability depending on the number of peptide layers.

In this presentation, we will show how the efficiency of the photoconversion process is controlled by both the molecular organization of the porphyrin dyes on the film and the length of the biomolecular peptide bridge between the porphyrin and the gold surface.

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Novel hybrid inorganic–organic building blocks based on polyhedral oligomeric silsesquioxane for poly(1-haloacetylene)s: thermal, solid-state polymerization.

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Previous studies on 1-haloacetylene polymerization have focused on catalytic reactions, with examples involving molybdenum-based catalysts for 1-bromoacetylene [1] and tantalum, molybdenum [2], or palladium-based catalysts for 1-chloroacetylene [3]. Brookhart-type catalysts also showed activity for 1-chloroacetylene polymerization [4]. However, thermal polymerization in the solid state remains largely unexplored, and no examples of such processes for 1-haloacetylenes have been reported in the literature.

Polyhedral oligomeric silsesquioxanes (POSS) are hybrid materials with a silicon-oxygen core $(RSiO_{1.5})$⍰ (R = H, alkane, alkene, or aryl; n = 6, 8, 10, or 12) and organic side groups R [5].

In this work, we synthesized poly(1-haloacetylenes) from POSS-based blocks functionalized with 1-haloacetylene groups, featuring eight symmetrically arranged haloalkyne groups around a cubic core. These systems underwent a novel thermal solid-state polymerization. For the first time, we report catalyst-free polymerization of 1-chloro-, 1-bromo-, and 1-iodoacetylenes, producing thermally stable polymers. The direct band gaps for **polyPOSS-C_2Cl**, **polyPOSS-C_2Br**, and **polyPOSS-C_2I** were 2.79, 2.74, and 2.38 eV, with indirect band gaps of 2.19, 1.57, and 1.47 eV, respectively. Thermal stability reached 267 °C for **polyPOSS-C_2Cl**, 287 °C for **polyPOSS-C_2Br**, and 309 °C for **polyPOSS-C_2I**.

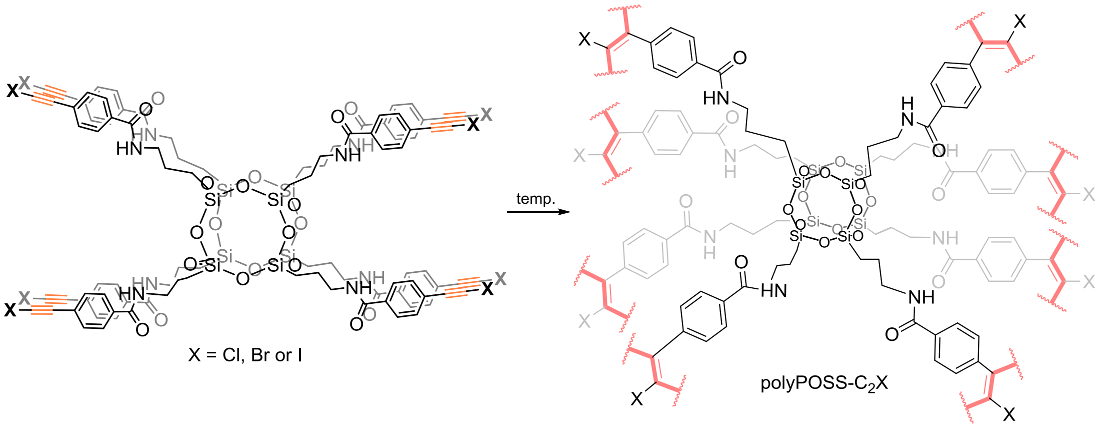

Figure 1. Synthetic route for the preparation of disubstituted polyacetylenes from 1-haloalkyne-substituted POSS derivatives (X = Cl, Br or I).

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Organic Pigments: new Super-Reductants for electro-photochemical synthesis

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A super-reductant is a highly reactive species that can facilitate chemical reactions that would not normally occur under normal reducing conditions. Such species are typically generated via photoexcitation of an electrochemically reduced state of a photocatalyst (PC), thereby accessing excited-state reduction potentials that are significantly more negative than those attainable through ground-state redox processes (Figure1). This approach has been recently employed with dicyanoanthracene[2] and dicyanobenzene derivatives (4-DPAIPN)[1] for reductive activation of aryl halides or aryl ammonium salts (Figure1). In this study, we aim to employ the use of organic pigments as an innovative class of super-reductants in electro-photochemical synthesis. These pigments such as quinacridone and indigo are insoluble compounds, but can be functionalized at N-H sites to yield soluble derivatives. These functionalized derivatives exhibit multiple reversible reduction waves while retaining significant absorption within the visible light spectrum. The derivatives are subsequently tested under electro-photochemical conditions to evaluate their capacity as super-reductants in benchmark organic reductions.

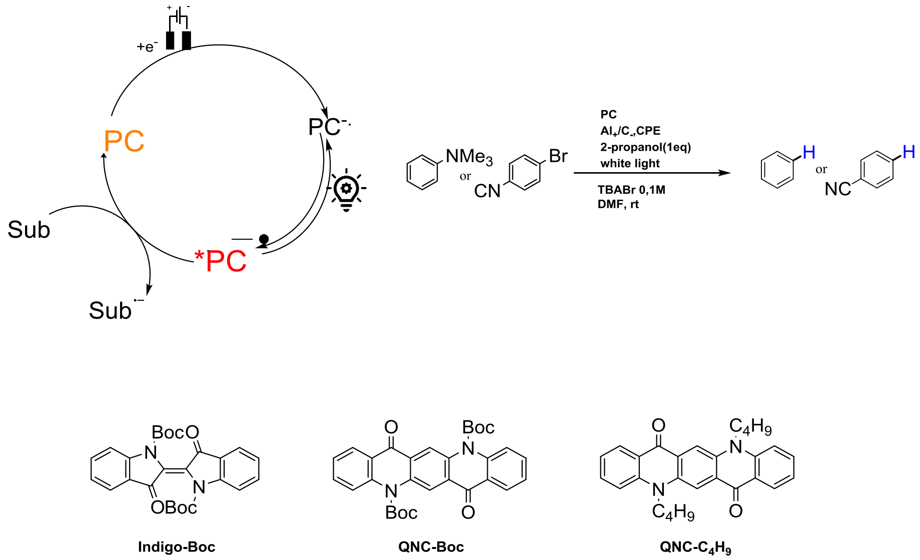

Figure 1(a). A photo-electrochemical cycle of a PC; (b) Example of benchmark reaction; (c)The structures of Indigo-Boc, QNC-Boc and QNC-C_4H_9

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Ionic Liquids as Stable Carbene Precursors for Organocatalysis and Biomass Applications.

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Carbenes possess incomplete electron octets and coordinative unsaturation, making them inherently unstable compounds. This stability can be improved for many N-heterocyclic carbenes (NHCs), with electronic and steric stabilisation enabling their use as relatively stable and effective organocatalysts.[1] Activation conditions for NHCs vary, but may involve strong base addition, photoactivation, or the use of transition metals.[2]

Ionic liquids (ILs) are compounds composed solely of ions with melting points below 100 °C.[3] ILs exhibit unusual ion-pairing effects, enabling NHC formation using a relatively weak base as an anion, reducing the need for highly corrosive or hazardous materials. These IL species form in situ carbenes without the need for additional activation conditions, making them ideal as both reaction media and catalytic species, representing an attractive alternative route to traditional carbene catalysis.[4]

The primary aim of this research is to understand the extent to which the concentration of in-situ carbenes can be tuned by appropriate selection of IL anion or cation and the ability of these IL-based carbenes to facilitate carbene-catalysed reactions. This presentation will outline our investigation into the relationship between ion structure and carbene reactivity using the model reaction illustrated in Figure 1. The use of selected IL-based carbenes for reactions of relevance to biomass valorisation will also be presented.

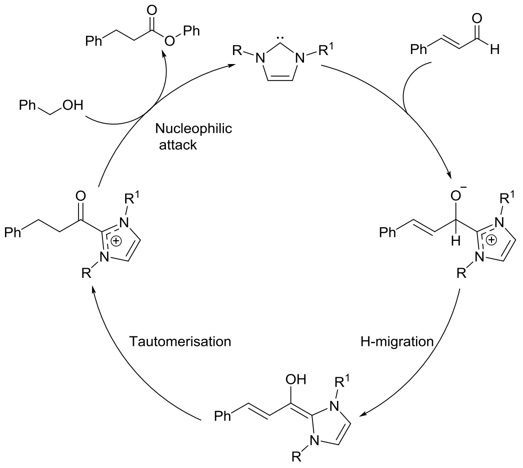

Figure 1. Catalytic cycle for the NHC-catalysed Umpolung addition of cinnamaldehyde with benzyl alcohol.

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Amphiphilic BODIPY-Based Fluorophores: Synthesis, Photophysical Characterization and Bio-Relevant Aggregation Studies

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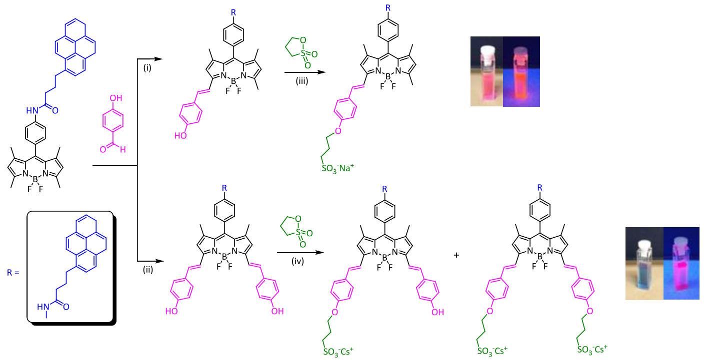
Fluorescent nanostructures are becoming key components of next-generation smart materials, particularly in the fields of bioimaging, biosensing, and biomimetic systems [1]. In this study, we present the rational design and synthesis of three novel amphiphilic BODIPY-based fluorophores. These molecules are functionalized with a pyrene moiety and bearing either mono- or bis-sulfonic acid groups on styryl arms. They combine water solubility, membrane permeability, and strong π–π stacking capabilities, enabling their self-assembly into nanostructures in aqueous media. Synthetic strategies include selective Knoevenagel-type condensation reactions, which afford mono- or distyryl derivatives by modulating solvent polarity and aldehyde stoichiometry, thus toluene favoring mono-substitution and acetonitrile enabling efficient bis-substitution. Subsequent sulfonation with 1,3-propane sultone under optimized basic conditions yields the target amphiphilic sulfonates in good to excellent yields (Scheme 1). The successful derivatization has been demonstrated by spectroscopic characterization, which has revealed solvent and conjugation- dependent optical properties. Cellular uptake studies and preliminary self-assembly assessments highlight their potential for bioimaging applications. Beyond their biological relevance, the presence of pyrene units suggests opportunities for integration with graphenic materials, expanding their application to hybrid optoelectronic systems [2]. Overall, this work emphasizes the structural versatility and functional tunability of BODIPY scaffolds for the development of next-generation fluorescent probes.



Scheme 1. (i) Piperidine, AcOH, Toluene$_{dry}$, Dean-Stark, 24 h, Ar; (ii) Piperidine, TsOH, ACN$_{dry}$, Dean-Stark, 24 h, Ar; (iii) NaH, THF$_{dry}$, reflux, 6 h, Ar; (iv) Cs_2CO_3, Acetone$_{dry}$, reflux, 48 h, Ar.

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Design and Synthesis of HSP90 Small Molecules for Senescence Therapy

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Cellular senescence is a stable and terminal state of growth arrest in which cells are unable to proliferate, despite optimal growth conditions and mitogenic stimuli. Cellular senescence contributing to age-related pathologies, highlighting a therapeutic potential and a critical priority in this topic.[1] Heat Shock Protein 90 (HSP90) inhibitors have shown potential as senolytic agent but with several issue in formulations, toxicity and cost.[2] To overcome these limitations, by a virtual screening approach, compound **1**, structurally related to the xanthine family, was emerged as a promising pharmacologically active compound with a powerful nM IC_{50}.[3] This project seeks to improve compound **1** activity and to obtain a better pharmacologically active compound as HSP90 inhibitors so, guided by computational predictions, a library of compound **1** derivatives was designed and synthesized. Herein, is reported the development of an optimized synthetic route for compound **1** and its derivatives, emphasizing efficiency, scalability, and reliablity. This approach not only facilitates an access to compound **1** but also serves as a versatile foundation for systematic derivative synthesis.

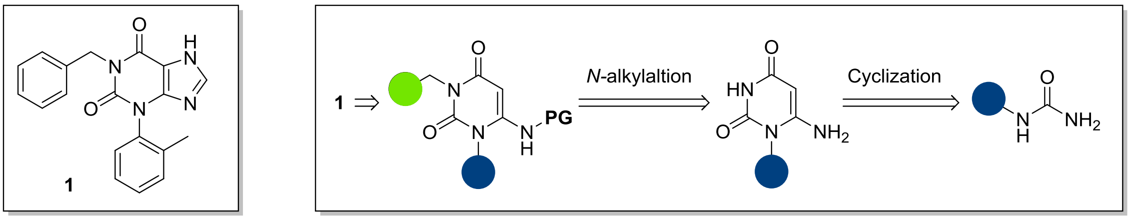

Figure 1. Structure of compound **1** and retrosynthetic analysis.

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Development and Characterization of Cu(I)-Lipoic Acid Nanoparticles in the Framework of Novel Strategies for Anticancer Therapy

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The use of metal complexes in the context of anticancer therapy has a long history, dating back to the U.S. FDA approval of cisplatin in 1978 for treating genitourinary tumors.[1] Since then, an extensive number of complexes has been synthesized, investigated and studied to discern the therapeutic properties offered by this wide class of compounds.

The exploration of different metals has provided several insights into their different mechanisms of action and collateral effect profiles with respect to platinum-based drugs, characterized by significant side effects and resistance issues.[2] In particular, complexes of endogenous metals, such as copper, have been emerging as a promising and effective alternative to traditional metal-based anticancer therapies due to their prominent antitumor activity, encouraging safety profile and desirable capability of overcoming resistance phenomena to platinum-based drugs.[3]

Nevertheless, even though these compounds possess a huge therapeutic potential, poor pharmacokinetic properties frequently emerge as a pivotal issue that impedes the progression of investigation throughout clinical trials.

In order to improve the pharmacokinetic features of these molecules and, consequently, improve the therapeutic index of the candidate drug, a recently developed lipoic acid-based nanocarrier was exploited. Poly(lipoic acid) nanoparticles possess a variety of interesting properties in the context of anticancer drug delivery: they are inherently biocompatible and biodegradable, present high stability in biological media and absence of *in vitro* and *in vivo* toxicity; furthermore, lipoic acid itself has been investigated as for its possible contribution to anticancer therapy.[4]

In this work, two different strategies for conjugating the antitumor therapeutic efficacy of copper(I) complexes with the promising pharmacokinetic-enhancing potential of poly(lipoic acid) nanoparticles are presented, discussed and compared in the ambit of the development of novel and innovative nanoplatforms for anticancer therapy.

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Dual Emission of Discotic Columnar Liquid Crystals

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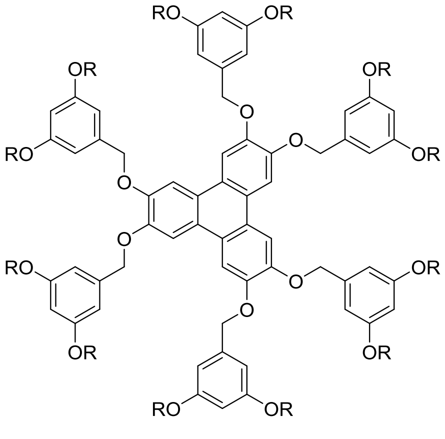
Discotic columnar liquid crystals (LC) represent a class of LC with potential applications in optoelectronics, such as OLEDs or photovoltaic devices.[1] We synthesized a novel class of columnar LC at room temperature confirmed by Differential Scanning Calorimetry (DSC) and Polarized Optical Microscopy (POM). The compounds are based on a triphenylene core functionalized with benzyl moieties, which present alkyl chains as solubilizing groups. The LCs were achieved through a convergent synthesis, resulting in symmetrical molecules via multistep modification of the residues and coupling with a hexahydroxy triphenylene core via Williamson ether synthesis. The introduction of the benzyl spacer between the triphenylene core and the solubilizing chains access the liquid crystal phase at room temperature. Therefore, we studied how different length hydrocarbon chains (C6, C8, C10) in the solubilizing groups affect the possibility of achieving the different phases, both in the mesophase and solution aggregation. We observed the presence of two possible columnar phases, one with the triphenylene core in a staggered and one with an eclipsed fashion. The different columnar phases display different spectroscopical properties, achieving different fluorescence states due to the supramolecular assembly. Lastly, we investigated how the different chain length impacts the spectroscopic properties at different temperatures.



R= C_6H_{13}, C_8H_{17}, $C_{10}H_{21}$

Figure 1. Liquid crystals.

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Synthesis and Reactivity of Fluorinated Terphenyl Nitrenes beyond Cryogenic Conditions

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Nitrenes are reactive intermediates with a robust triplet ground state and, owing to their electron deficiency, are fleeting species with a short lifetime at room temperature. Due to their magnetic properties, potential applications lie in the field of novel materials and organic magnets. The aim of this work is to investigate triplet nitrenes that are kinetically stabilized by steric hindrance and to suppress intramolecular ring insertion by blocking the adjacent positions with fluorinated phenyl substituents.[1,2]

The parent *meta*-terphenyl azide as well as its fluorinated derivative **1** were synthesized and deposited in inert gas matrices at 3 K. Upon UV irradiation, the triplet nitrene **2** is generated and characterized by IR, UV-vis and EPR spectroscopy. Secondary photochemistry of nitrene **2** with 365 nm leads to a so far unidentified photoproduct assumed to be the corresponding azirine **3**. Furthermore, the reactivity towards molecular oxygen was analyzed. **2** was stable in oxygen-doped xenon as well as pure oxygen matrices up to the degradation of the matrix. Analogous experiments in KBr matrices were conducted and the thermal decay of the nitrene was monitored from 12 K to room temperature. Nitrene **2** was found to persist in KBr matrices up to 80 K. At higher temperatures, a complex product mixture is obtained, containing amines and carbazoles. Overall, triplet nitrene **2** is stable against reactions with oxygen at low temperatures and KBr matrices provide a convenient method to immobilize and extend the lifetime of sterically-hindered aryl nitrenes beyond cryogenic conditions.

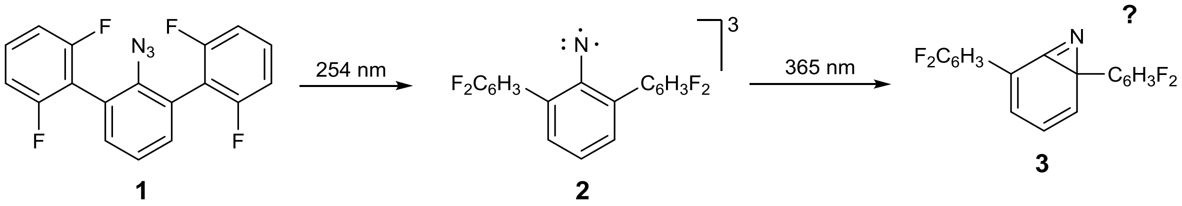

Figure 1. Photochemical synthesis and rearrangement of fluorinated terphenyl nitrene.

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The search for prebiotically relevant C_3H_5NO isomers: spectroscopic characterization and photochemistry of a heterocyclic azide

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The chemical origin of life remains one of the most profound mysteries in science. In terrestrial prebiotic chemistry, the Strecker synthesis[1] is considered to play an important role for the amino acid formation, involving the reaction of an aldehyde with ammonia and hydrogen cyanide – molecules that have been detected in the interstellar medium (ISM). In recent years, the detection of molecules in the ISM has focused heavily on cyano-containing species. However, the discovery of compounds such as formaldimine ($H_2C{=}NH$),[2] ethanimine ($CH_3HC{=}NH$),[3] and cyanoformaldimine ($NCHC{=}NH$)[4] has drawn considerable attention to imines – a key intermediate in the Strecker synthesis – and highlights their potential relevance in both astrochemistry and prebiotic chemistry. Despite their importance, spectroscopic data on simple imines remain sparse due to their instability, emphasizing the need for laboratory-based reference studies. Recently, our group successfully characterized simple imines, such as 2-iminoacetaldehyde[5] and glycine imine[6], by photochemical decomposition of the respective azide precursors using the matrix isolation technique. Building on this approach, this work describes the IR and UV-vis spectroscopic characterization and photochemistry of imines with the formula C_3H_5NO, generated from an *O*-heterocyclic azide precursor. To date, molecules with this chemical composition have not been detected in the ISM. Characterizing these imines and understanding their photochemistry could provide valuable insights into their abiotic synthesis and the complex chemical processes occurring in space.

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Dearomative Diels-Alder Cycloadditions between Nitroarenes and Silyloxydienes: a Rational Design of the Reactivity

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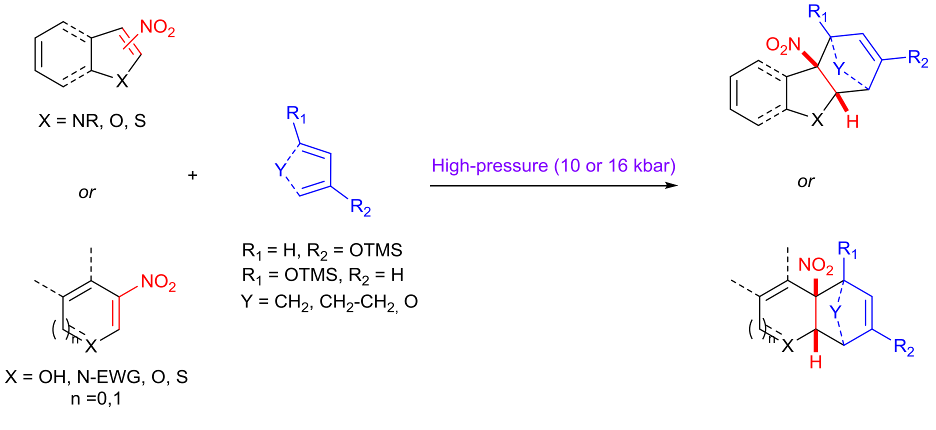
Dearomative [4+2] cycloadditions have the potential to convert planar structures into three-dimensional complex polycyclic molecules. In this context, we recently reported formal Diels-Alder cycloadditions of electron-deficient arenes with Danishefsky's diene and 2-(trimethylsiloxy)-1,3-cyclohexadiene. Depending on the aromatic dienophile/silyloxy diene couple, high-pressure activation was required, or not.[1]

These stepwise cycloadditions can be considered as a reaction between a nucleophilic diene and an electrophilic arene. We are currently calibrating the electrophilicity E of electron-deficient arenes and the nucleophile-specific reactivity descriptors N and s_N of silyloxydienes using the Mayr-Patz equation,[2] $\log k(20°C) = s_N(N + E)$. These results have allowed us to launch a scale of reactivity of different arenes and silyloxydienes.

Based on this work, we have performed the formal [4+2] cycloadditions of different nitro-substituted electron-deficient arenes with less reactive siloxy-dienes, under different operating conditions, depending on the electrophilicity of the aromatic and the nucleophilicity of the diene (Scheme 1). The reaction can provide intricate complex polycyclic structures that can be associated with active and/or natural compounds. Results regarding these reactions, their selectivities and mechanisms will be presented and analyzed in the context of the diene/dienophile couple involved in the reactions.



Scheme 1. Diels-Alder cycloadditions of electron deficient arenes with less reactive siloxy dienes.

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Synthesis and investigations of monoketone-bridged acene precursors towards analysis of higher acenes

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Acenes are polycyclic aromatic hydrocarbons (PAHs) consisting of linearly fused benzene units. In comparison to their topological isomeric PAHs, acenes show the smallest HOMO-LUMO gap leading to an enhanced diradical character and charge transport in the solid state.[1,2]

Pushing the limits in synthesis of longer, unsubstituted acenes and their optical characterization gives further insight into their intriguing electronic structure.[3] Since acenes become less soluble and more sensitive towards oxidation or dimerization with increasing length, synthesis and characterization of acenes requires special techniques like on-surface methods or matrix isolation.[4-6] In synthesizing suitable precursor molecules it is established to insert removable α-diketone or monoketone bridges as stabilizing units.[7,2]

We report the synthesis of long monoketone-bridged acene precursors utilizing a Diels-Alder sequence.[8] The parent acene is then generated via thermal or photochemical CO-extrusion. This allows the solid state and spectroscopic analysis of acenes of unprecedented lengths and paves the way for a better understanding of these systems.

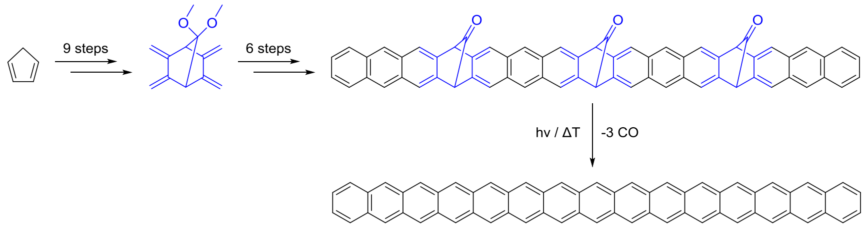

Figure 1. Synthesis of a monoketone bridged pentadecacene precursor.

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A Nonenzymatic Analog of Pyridoxal Biosynthesis

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To understand and recreate the origin of life, our lab is searching for conditions under which geochemistry might organize itself into dynamic reaction networks that pre-patterned metabolism and its bioenergetics.[1] In order for the network to change over time, an important feature would be its ability to produce small molecules that could catalyse existing reactions within the network or turn on new ones, allowing the network to be expanded and pruned in the absence of genetic control. We have recently shown that several coenzymes, including pyridoxal-5-phosphate (PLP), are able to promote their associated reactions in the core of metabolism nonenzymatically.[2] However, it is yet to be demonstrated whether the biosynthetic pathways leading to the formation of these coenzymes can occur nonenzymatically. Here, we show a nonenzymatic analog of PLP biosynthesis. Dihydroxyacetone phosphate (DHAP), ribose and ammonia react in water to give PLP, supporting the feasibility of catalytic feedback effects within protometabolic networks.

The observation that ribose leads to PLP, whereas the biological substrate ribose-5-phosphate does not, provides insight into the environment needed to establish protometabolic networks that pre-pattern biological metabolism.

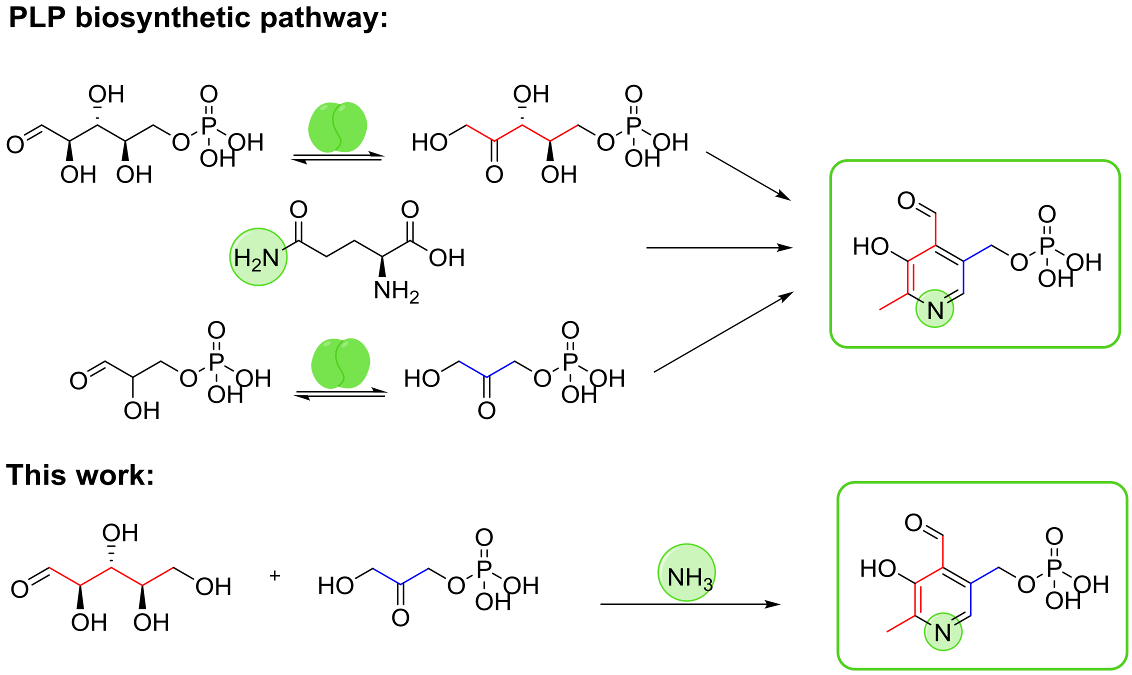

Figure 1. Biosynthetic pathway and possible nonenzymatic route for PLP synthesis.

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Twisting Curvature of Current Density Susceptibility for Aromaticity Characterization in Benzenoids

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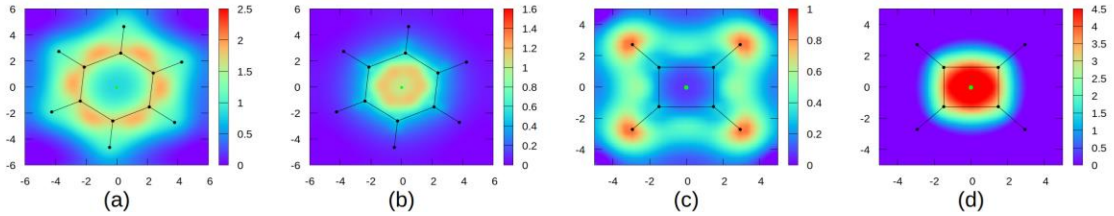
Twisting curvature is measure of how a surface bends in two directions. We present profiles of twisting curvature of magnetically induced current density susceptibility (MICDS)[1] ($\partial^2\mathbf{J}/\partial x\partial y$ in (nA/T)/Å^2) to identify diatropic and paratropic dominant regions of benzenoids. These can be calculated by integrating strength of current density on all possible planes through a vortex—the point about which current circulates—dissecting molecular plane. This method provides clear visualization of local aromaticity, but sensitive to vortex position. Benzene with vortex at the ring center (Fig. 1a-b) reveals a paratropic interior and diatropic exterior, with overall diatropic dominance confirming aromaticity. In cyclobutadiene (Fig. 1c-d), the interior paratropic current exceeds the exterior diatropic contribution, consistent with antiaromaticity. For fused ring systems (FRS) like azulene, when the vortex is centered on the 5-MR, the diatropic current is stronger outside the 5-MR than the 7-MR, suggesting greater aromaticity in the 5-MR. Shifting the vortex to the 7-MR reveals a stronger paratropic response within it, supporting its reduced aromatic character. We extended this methodology to various FRS, including **naphthalene, indene, fluorene, coronene, and anthracene**. In all cases, the analysis provided a consistent and nuanced description of **local aromaticity**, depending on the relative positioning of vortices across different rings. These findings demonstrate that **twisting curvature analysis of MICDS** offers a powerful and flexible tool for characterizing local aromatic and antiaromatic regions in both simple and complex π-conjugated systems. Also, this complements to traditional approaches to describe aromaticity like NICS and bond current analysis.[2]



(a) (b) (c) (d)

Figure 1: The twisting curvature of MICDS profiles for (a) diatropic, (b) paratropic contributions in benzene and (c) diatropic, (d) paratropic contributions in cyclobutadiene.

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Bond Delocalization Function: Decoding Resonance and Electron Delocalization in π-Conjugated Systems

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We introduce the Bond Delocalization Function (BDF), a new approach for analyzing the π-electron structure of molecules. Unlike traditional models that superimpose atomic orbitals to form bonds, BDF is built on the fundamental superposition principle applied at the level of bond orbitals (BO). Within the Electron Density of Delocalized Bonds (EDDB) formalism [1], BDF allows simultaneous visualization of both the electrons localized in π-bonds (exhibiting *olefinic* character) and the electrons delocalized across the π-conjugated systems (displaying *aromatic* character). By decoding the complex wavefunction interference patterns into intuitive, colorful maps, BDF provides a direct and accessible visualization of π-resonance without the necessity of identifying all possible resonance forms. We demonstrate the interpretative and predictive power of this method through applications to several poly- and macrocyclic systems [2].

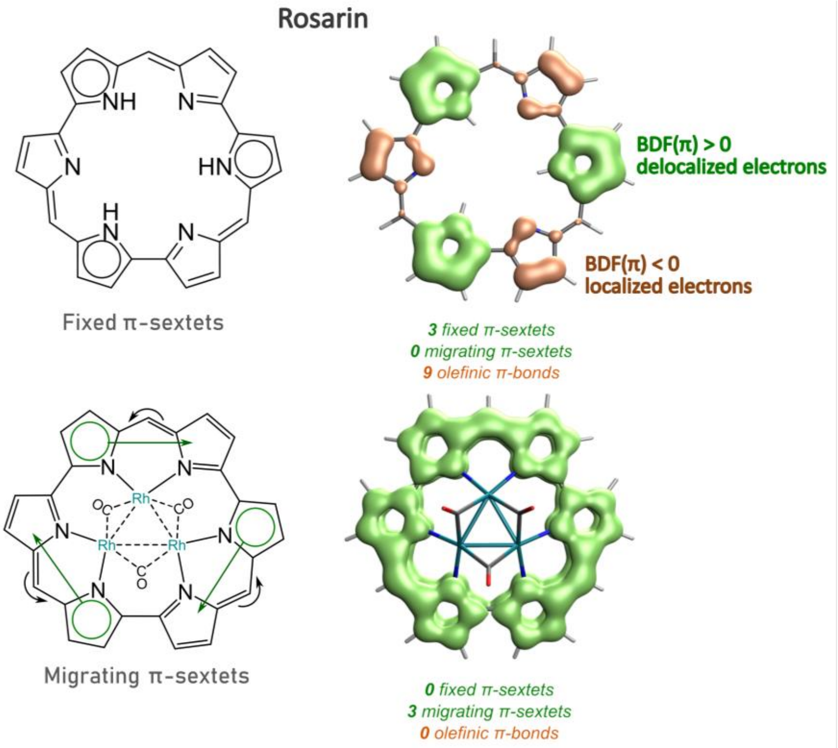

Figure 1. The Clar's structure of Rosarin and its rhodium complex, revealed by the BDF(*r*) function.

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Organic Reactivities in BioRenewable Solvents: A Sustainable and Safer Alternative to Conventional Organic Solvents

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Conventional organic solvents, typically derived from fossil fuel feedstocks, are extensively used in organic synthesis but pose environmental and health hazards due to their volatility, toxicity, and non-renewable nature. Biorenewable solvents (BRS), such as Cyrene™, represent a greener alternative, offering reduced environmental impact, improved safety, and enhanced biodegradability.[1] In this study, we examine the nucleophilicity of various nucleophiles, specifically phosphines and enamines in Cyrene (Fig. 1) and compare their reactivities to those observed in other solvents.

To quantify nucleophilicity, second-order rate constants were measured via time-resolved UV-Vis spectroscopy and correlated with electrophilicity data using the *Mayr-Patz equation (1)*:

$$\lg k_2\ (20\ °\mathrm{C}) = s_\mathrm{N}(N+E) \qquad (1)$$

where N and s_N are nucleophile-specific parameters and E is the electrophile parameter.

The nucleophilicity (N) parameters of phosphines and enamines were consistently lower in Cyrene™ than in dichloromethane (DCM),[2] as determined using the Mayr-Patz equation (1), indicating reduced reactivity in the biorenewable solvent. This decrease is likely due to Cyrene's higher dielectric constant, dipolarity, and hydrogen-bond accepting ability,[3] which can stabilize transition states and interact with nucleophilic lone pairs. These results highlight the importance of solvent effects on reactivity and the need to determine nucleophilicity parameters directly in green solvents.

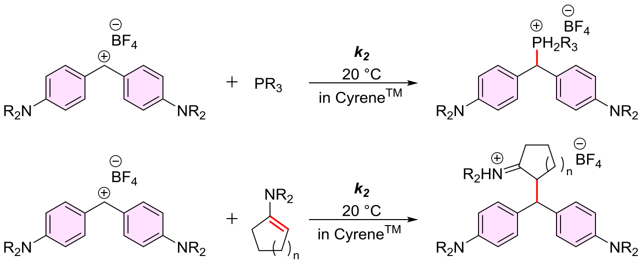

Figure 1. Nucleophilic reactivities of phosphines and enamines with benzhydrylium cations in Cyrene™.

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Eco-Friendly Synthesis of Ag and Au Nanoparticles Using Lactic Acid from Fermentation Waste and Cyclodextrins as Colloidal Stabilizers.

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Nanoparticles of metals (MNPs) such as gold (AuNPs), silver (AgNPs), platinum (PtNPs) and palladium (PdNPs), among the most prominent, are gaining significant attention due to their exceptional catalytic properties that enhance their effectiveness in various chemical reactions.[1]

A key aspect in the synthesis of MNPs is the development of sustainable and innovative reducing agents. In that sense, we focus on the valorization of industrial waste, particularly fermentation byproducts rich in lactic acid, as an eco-friendly alternative for nanoparticle synthesis.

For the other hand, a significant challenge in the practical application of nanoparticles is their stability in aqueous environments, which can limit their effectiveness, particularly in catalysis. Cyclodextrins (CDs), which are cyclic oligosaccharides composed of glucose units, have emerged as promising stabilizers for metal nanoparticles. Research has shown that cyclodextrins (CDs) not only stabilize nanoparticles but also serve as reducing agents, thereby improving the synthesis process.[2]

In this study, we demonstrate a novel, environmentally friendly approach to synthesizing gold (AuNPs) and silver (AgNPs) nanoparticles using industrial lactic acid as a reducing agent and amphiphilic β-cyclodextrins modified with dodecenyl succinic anhydride (β-CDMod) as stabilizing ligands. The synthesized nanoparticles, AuNPs@CDModDS1, AuNPs@CDModDS5, and AgNPs@CDModDS5, exhibit stable surface plasmon resonance band characteristics, and remain colloidally stable in water for up to three weeks.

The MNPs were spherical with varying sizes: AuNPs@CDModDS1 (6.7 ± 0.1 nm), AuNPs@CDModDS5 (17 ± 12 nm), and AgNPs@CDModDS5 (9 ± 6 nm). The nanoparticles demonstrated remarkable catalytic efficiency in the reduction of 4-nitrophenol, with AgNPs@CDModDS5 showing the highest catalytic activity ($\kappa = 27\ \mathrm{L{\cdot}s^{-1}{\cdot}m^{-2}}$). The pH-sensitive β-CDModDS5 ligand enhanced nanoparticle stability, facilitated substrate anchoring, and stabilized reaction intermediates, presenting a versatile and sustainable approach to nanoparticle synthesis.

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Mechanistic Switchover in Fe-catalyzed Amination controlled by Hydroxylamine-Derived reactants: from free radical to metal-based reactivity

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The relevance of amine functions in biologically active compounds calls for the design of amination reactions with improved efficiency, selectivity, and sustainability. Fe-mediated amination with hydroxylamine-derived reactants has gained significant attention in recent years [1], as it relies on iron salts or complexes that are non-toxic, cheap, and abundant and bench-stable reactants. Moreover, this reaction enables NH_2 insertion in a single step, making this chemistry remarkably attractive. Over the years, different types of hydroxylammonium-derived reactants have been designed, all including electron-withdrawing O-substituents.

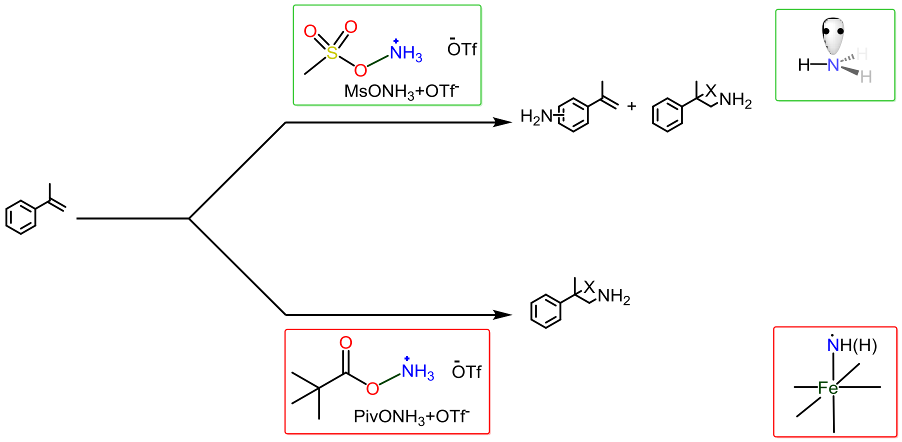

Figure 1: Radical vs metal-based pathways in Fe-catalyzed amination with $MsONH_3^+$ and $PivONH_3^+$

In this context, we investigate how two prototypical reagents, O-sulfonyl hydroxylammonium ($MsONH_3^+$) and O-pivaloyl hydroxylammonium ($PivONH_3^+$), affect the amination mechanism of arenes and olefins. Both hydroxylammonium salts react well with olefins, giving doubly amino-functionalized products [2], whereas only $MsONH_3^+$ reacts efficiently with isolated arenes. We associated this change in reactivity to a mechanism variation and a consequent change in the structure of the aminating agent. Tailored mechanistic experiments confirmed that the radical cation $NH_3^{+\cdot}$ is the aminating species formed with $MsONH_3^+$, leading to a free radical process where the metal acts as an initiator. On the other hand, $PivONH_3^+$ shows a different behavior, forming an iron-nitrenoid intermediate as the reactive species [3].

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C_2NH Isomers: Key Intermediates in Prebiological Chemistry Relevant to Both Endogenic and Exogenic Abiogenesis?

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Understanding the origins of life will probably first require understanding abiotic formation of nitrogenated compounds. The atmosphere of Saturn's moon Titan is a useful analogue for early Earth's atmosphere, and nitrogen incorporation is thought to initiate in the upper atmosphere of Titan by photolysis of molecular nitrogen. Photochemical models of Titan's atmosphere and crossed molecular beam experiments have identified reactive molecules that are created when post-photolysis atomic nitrogen collides with organic compounds.[1-3] These reactive molecules (e.g., cyanocarbene HCCN). are thought to be key intermediates in abiotic nitrogen incorporation, but these molecules are so extremely reactive that experimental observations of their reactivity are quite limited.[1,3-5]

Our study uses matrix isolation infrared (IR) spectroscopy at low temperatures (10–30 K) to observe what products form when cyanocarbene reacts with molecules known to be in Titan's atmosphere (e.g., water, hydrogen cyanide, formaldehyde, ect.).[2] We generate HCCN by photolysis of diazoacetonitrile frozen and diluted in argon ice.[5] Doping the ice with molecules of interest followed by heat cycling (annealing) of the inert frozen matrix, selectively induces bimolecular reactions through controlled diffusion. These experimental results together with quantum chemical computations provide foundational insights into photochemical models of abiotic nitrogen incorporation, a process potentially vital to abiogenesis on early Earth.

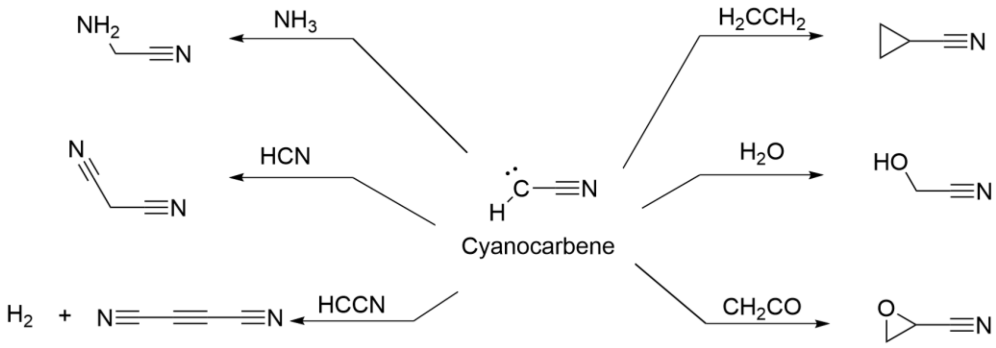

Figure 1. Proposed reactions of cyanocarbene with molecules of interest to Titan's atmosphere. Reaction with HCN as calculated by Vieira *et al.*[6], water as calculated by Guerrero-Méndez *et al.*[7], HCCN as calculated by Yung[3], and formaldehyde as calculated by Behnke *et al.*[8].

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Facile Synthesis and Application of Biodegradable Poly(γ-butyrolactone) and Copolymers via base assisted Ring-Opening Polymerization

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Poly(γ-butyrolactone) (pGBL) and its copolymers are emerging as promising sustainable alternatives to conventional plastics, owing to their full biodegradability, potential bio-based origin, and thermal recyclability.[1-2] However, conventional synthetic approaches often require elaborate catalysts, extremely low temperatures, or dilute reaction conditions, limiting industrial scalability. In this study, we report a simplified, cost effective and scalable anionic ring-opening polymerization (ROP) strategy using potassium tert-butoxide and mono- or polyfunctional alcohols as initiators in green solvents such as 2-methyltetrahydrofuran (2-MeTHF). This method enables efficient polymerization at higher temperatures (−10 to −20 °C), achieving high yields (up to 94%) and moderate to high molecular weights (Mn ≈ 9,000–15,000 g/mol) with tunable end-group functionalities. Importantly, copolymerization of γ-butyrolactone with other lactones (e.g., δ-valerolactone, ε-caprolactone) yields bifunctional and even liquid copolyesterols suitable for polyol applications such as polyurethane foams. The resulting materials exhibit thermal re-monomerization behavior, with pGBL depolymerizing to monomer at ~300 °C, enabling closed-loop material lifecycles. Differential scanning calorimetry (DSC) and GPC analysis confirm the formation of well-defined linear and cyclic polymer topologies with pseudo-eutectic behavior observed in copolymers.This accessible and solvent-flexible methodology, compatible with large-scale synthesis, paves the way for sustainable applications of pGBL as thermoplastics, coatings, inks, medical materials, or polyol precursors in circular materials design.[3]

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Diametrically Different Enantioselective Enzyme Catalysis in Disparate Biocondensates

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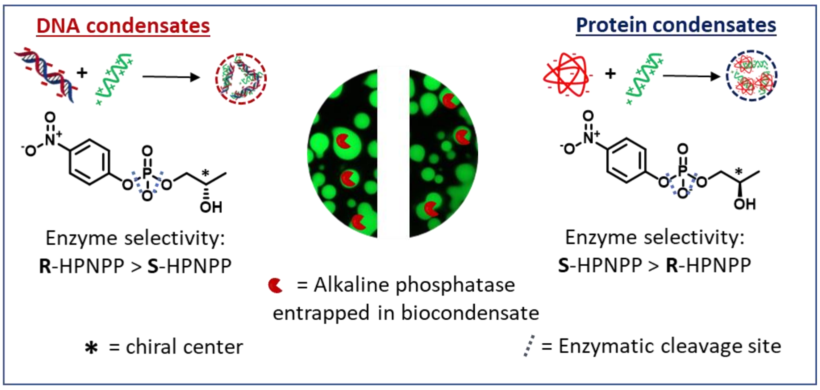
The discovery of membrane-less biocondensates resulted in a paradigm change in our understanding of how biological systems function. Condensates can selectively partition molecules based on their physicochemical properties. Enzymes and substrates with certain affinities for the condensate phase may be preferentially concentrated within the condensates, while others remain in the surrounding solution. This selective partitioning can alter the effective concentration of substrates seen by the enzyme, potentially affecting its selectivity for specific substrates. Enantioselective catalysis is a crucial field in modern chemistry and is especially significant in the field of medicine. The different enantiomers or diastereomers of a molecule may have distinct biological activity. It is well recognized that biomolecules, including proteins, RNA, enzymes, and DNA, exhibit remarkable selectivity when carrying out their respective tasks within our bodies. Due to their potential for high efficiency, selectivity and specificity, high yield, and biodegradability in a range of applications, biocatalysts are currently receiving a lot of interest. Here, we describe the enatioselective phosphodiesterase activity of the enzyme alkaline phosphatase (ALP) in protein (bovine serum albumin (BSA)) and DNA-based biocondensates utilizing both the R- and S-form of the RNA-model substrate, 2-hydroxypropyl p-nitrophenyl phosphate (HPNPP). The enantiomeric ratio (E) $[\{(k_{cat}/K_M)_S-(k_{cat}/K_M)_R\} / \{(k_{cat}/K_M)_S + (k_{cat}/K_M)_R\} \times 100]$ value of approximately 33% indicates that the ALP enzyme's natural preference is for S-HPNPP in aqueous buffer. However, when ALP is encapsulated in BSA condensate, the preference over S-HPNPP drops to about 7-25%. It's interesting to note that in DNA-based complex coacervate stabilized with chiral macroion, L- or D- Polylysine, a complete reversal of the E-value (-20 to -45%) was noted because in this case, ALP reacts faster with R-HPNPP. Finally, we show that the conformational dynamics of the enzyme within the coacervate environment are linked to the catalytic activity and reversal of enzyme enantioselectivity in the condensed phase. We did discover that the enantiopreference to the enzyme alkaline phosphatase (ALP) depending on the components of the biocondensate.



Scheme: Schematic representation of Alkaline Phosphatase (ALP)-encapsulated BSA- or DNA-based condensates, showing different selectivity towards hydrolysis of R- or S-HPNPP.

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High-Throughput Kinetics of the Reactions of Urea with Aldehydes Allow Predicting Rates and Mechanisms of Catalysis in Water

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Most organic reactions happen between electrophiles and nucleophiles. In aqueous environments, electrophiles containing the carbonyl moiety play a central role, e.g., in biochemistry, green chemistry, and the reactions considered relevant to the origin of life. However, predicting the rate of nucleophilic additions to carbonyl groups and the specific underlying mechanism, especially in water, remains largely impossible, as catalysis by acid and base can dramatically change how these reactions proceed.[1] As a result, reaction discovery and optimization in water involve extensive trial-and-error experimentation instead of rational predictions. We herein report using automated liquid handling robots for high-throughput reaction screening to create a comprehensive dataset of experimental rate constants for the reaction of urea as a test nucleophile toward a library of aldehydes, considering a broad array of reaction parameters (Figure 1). Having established a systematic dataset allows us to test for both classical physical organic techniques to derive correlations and the benchmarking of machine learning regression algorithms. This work establishes a foundation for general predictions of reactivity in aqueous environments, providing new insights into the reaction mechanisms crucial for our understanding of fundamental organic chemistry.

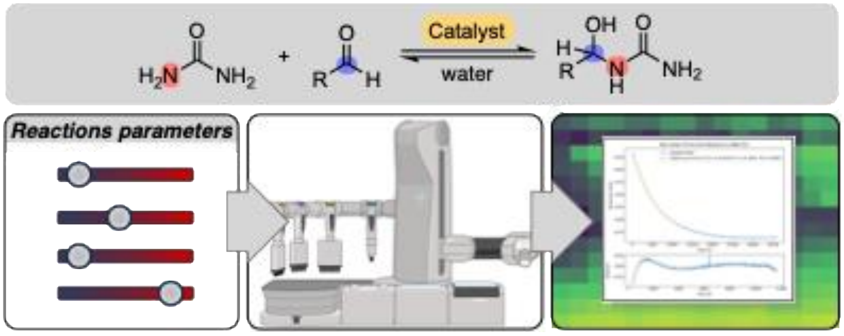

Figure 1. Workflow for kinetic high-throughput screening of carbonyl addition reactions.

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Chemical models for allosteric disulfide and amyloid assembly

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Cyclic peptides represent a significant category of molecules with a wide array of applications, including therapeutic agents, materials, and ionophores. The combination of peptides with non-peptidic components results in hybrid cyclopeptides that exhibit enhanced properties and greater resistance to proteolytic degradation. This work introduces a collection of isomeric disulfide-based hybrid cyclic peptides featuring various ring sizes. The water-soluble pseudopeptidic macrocycles exhibit a strong inherent propensity for self-assembly. Microscopic investigations showed a fibrillar morphology resembling amyloid, along with autofluorescence. The crystal structure of the 23-membered macrocycle revealed various noncovalent interactions. We outline that the macrocyclic framework serves as an excellent platform for generating diverse classes of disulfide conformations. Further, the single crystal X-ray structure of the macrocycle revealed a unique allosteric disulfide topology.

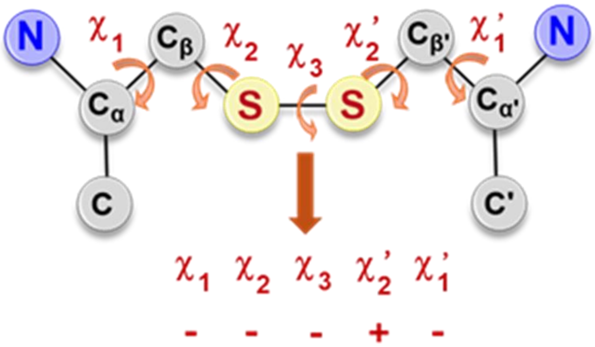

Figure1. General depiction of the various dihedral angles of the disulfide bond which define all 20 possible conformations.

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Organic Semiconductors Frameworks for Artificial Photosynthesis

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Nature uses extended hierarchical architectures of antennas and catalytic centres to drive photosynthetic reactions.[1] Organic semiconductors (OSC) offer a unique platform to design artificial photoactive frameworks with defined molecular synthons and donor-acceptor interfaces, allowing for a deep understanding of the critical interplay between the structural and opto-electronic properties of the building blocks, charge localization, and framework morphology.[2] Herein, we present a family of imine-linked OSC frameworks (**PBI-1-COFs**) built from a bay-substituted PBI chromophore (**PBI-1**), designed to introduce within the architecture a high concentration of N-rich donor sites and a core twisted moiety. A modular platform of aryldiamine linkers (Ph, *b*Ph, *t*Ph) directs the framework topology, yielding an isoreticular series with optical bandgaps of ~ 1.9 eV and light absorption extending to 700 nm. Notably, the framework with the shortest linker **PBI-1-COF-Ph** evolves into onion-like π-stacked nanodomains and monodisperse spherical microparticles (D = 700 ± 100 nm) composed of staggered nanosheets, suggesting a morphological progression from curved nanodomains to fully folded spheroidal structures. The longer *b*Ph and *t*Ph analogues display mixed spherical and rod-like architectures, indicating an intricate structure-morphology relationship governed by linker length and **PBI-1** core distortion. On 3D-tungsten oxide nanosheets (WO_3 3D-NS),[3] the in-situ growth of **PBI-1-COFs** affords robust OSC@WO_3 photoanodes with high photocurrent densities (up to 590 ± 50 μA cm^{-2}) and minimal recombination under visible-light irradiation in presence of hydroquinone photo-redox shunts. This work sets a blueprint for the rational design of twisted chromophore-based OSC frameworks where molecular curvature, interfacial functionality, and supramolecular order collectively modulate light harvesting and photoelectrocatalytic performance.

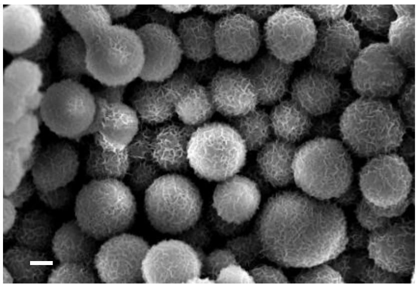

Figure 1. SEM image of **PBI-1-COF-Ph** microparticles. Scale bar is 400 nm.

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Electron-Poor Acridiniums as Versatile Electrophilic Catalysts

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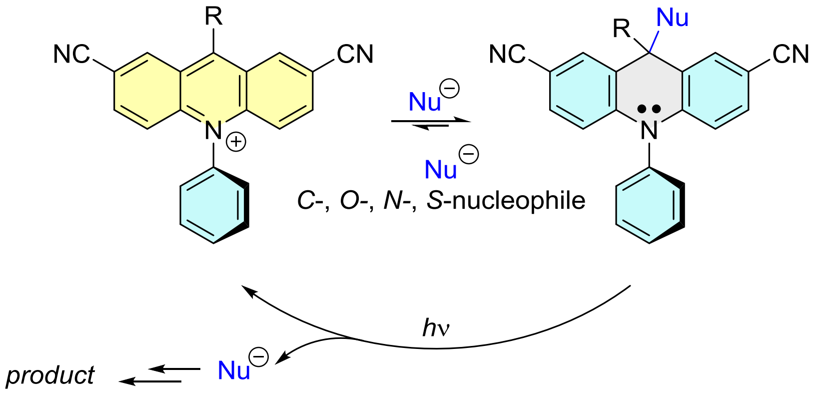
Acridiniums are exceptionally versatile, highly oxidizing photocatalysts, whose cationic nature stabilizes the acridinyl radical generated via photoinduced electron transfer from a suitable donor substrate.[1] Structural modifications of the acridinium scaffold have historically focused on mitigating unwanted side reactions, such as *N*-dealkylation, attack of radicals and nucleophiles at position 9 (Scheme 1).[2] Here, we introduce a complementary strategy: the design of electrophilic acridiniums through the incorporation of electron-withdrawing nitrile substituents into the acridinium core.[3] These electrophilic acridiniums exhibit remarkable catalytic versatility, enabling the reversible addition of diverse *C*-, *O*-, *N*-, and *S*-nucleophiles at the 9-position with subsequent nucleophile release upon irradiation.

Leveraging these unique properties, we advance electron-poor acridiniums as photo/organocatalysts for the activation of alcohols, arenes, thiols, and amines. In this work, we show that acridinia, commonly used in photoredox catalysis as oxidants, are flexible and multimodal catalysts for the activation of inert chemical substrates.



Scheme 1. Catalytic activity of electron-poor acridiniums.

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Synthesis and characterization of novel viologens

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ECVs (π-extended conjugated viologens) based material have recently attracted attention for their potential applications in materials and supramolecular chemistry.[1]
Building on the expertise acquired in a recent project focused on the synthesis of novel ECVs to for incorporation into in the crystalline structure of hybrid perovskites,[2] our group decided to synthesize new ECVs and pyridinium salts derivatives. The aim was to investigate their non-covalent interactions with different anionic systems for the development of stimuli-responsive materials.[3]
Following the challenging synthesis of our three targets, we established an interdisciplinary collaboration to optimize the non-covalent interaction in aqueous solution of our most characterized ECV with hydrophilic silver nanoparticles coated with an anionic functionalization agent AgNPs-3MPS reaching the loading percentage of viologen on the surface of AgNPs-3MPS of **80 ± 12 %** determined via UV-Vis spectroscopy. The loaded nanoparticles were analyzed and, notably, the comparative FTIR analysis of AgNPs-3MPS sample before and after the showed spectral shifts consistent with a non-covalent interaction between the two systems supported by analogous evidence in literature.[4]
This project will be a starting point for different subsequent research directions with the long-term goal of developing novel chemosensors and electrochromic devices.

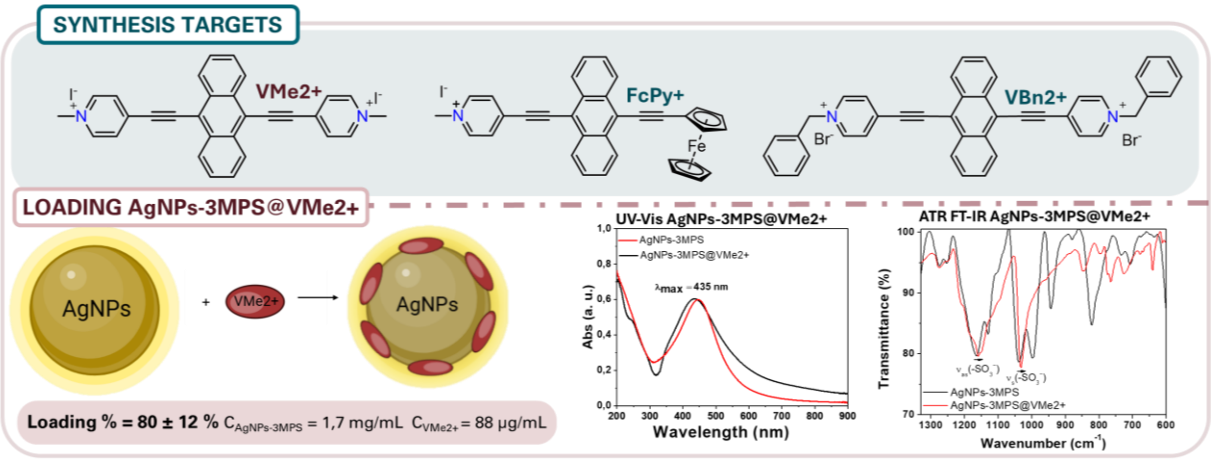

Figure 1. Graphical abstract of the project

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The effect of light on the *N*-chlorination of anticancer drugs

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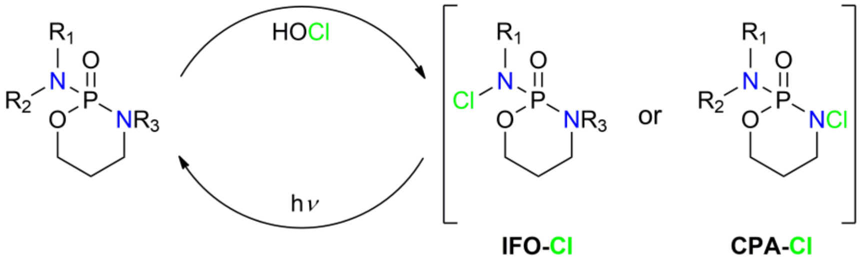
The two anticancer drugs cyclophosphamide (**CPA**) and ifosfamide (**IFO**) undergo *N*-chlorination in the reaction with hypochlorous acid in water (Figure). The reaction was followed by ^{1}H and ^{31}P NMR spectroscopy. In case of **IFO** the exocyclic nitrogen was chlorinated and the ^{31}P signal was shielded by *ca*. 4 ppm, whereas the chlorination of endocyclic nitrogen in **CPA** resulted in its downfield shift. As expected, the trophosphamide analogue (**TPA**) does not react with chlorinating agent. The chlorinated products **IFO-Cl** and **CPA-Cl** are stable in dark, but decompose back to the parent structures when exposed to the light. To investigate the effect of light, the mixture (**CPA/IFO** and HOCl) was irradiated during the reaction. Optical fiber, coupled to different light sources, was inserted into the coaxial NMR tube setup, allowing *in situ* NMR monitoring of the chlorination under UV or simulated sunlight. A slight inhibition of the reaction was observed, mostly due to photo-induced cleavage of the N-Cl bond in the corresponding products. Assessment of the environmental relevance of these findings is currently in progress.



IFO $R_1 = R_3 = CH_2CH_2Cl$, $R_2 = H$
CPA $R_1 = R_2 = CH_2CH_2Cl$, $R_3 = H$
TPA $R_1 = R_2 = R_3 = CH_2CH_2Cl$

Figure. *N*-Chlorination of antineoplastic agents and photo-induced decomposition of the products.

References

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On-Chip Dissipative Self-assembly for Neuromorphic Information Processing

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Dissipative self-assembly involves the emergence of supramolecular structures that reside in low-entropy states by dissipating energy to the environment, thereby increasing its entropy.[1] Actin polymerization is one such example of dissipative self-assembly. Actin remodeling in neurons involves morphological changes in dendritic spines (structural plasticity) that further influences synaptic plasticity (short-term plasticity and long-term potentiation).[2] We describe a neuromorphic electrochemical device capable of emulating structural and synaptic plasticity in a synchronized manner. We achieved this by employing organic monolayer-protected gold nanoparticles that form emergent semiconducting dissipative structures in response to low operating voltages. Supramolecular self-assembly of semiconducting dissipative material between synaptic electrodes reminisces the actin remodeling of neurons. The device is capable of demonstrating hallmarks of habituation, including frequency sensitivity and intensity sensitivity. Systematic investigations revealed the memory effects and nonlinearity in the system. Additionally, the system was also capable of temporal information processing. We elaborate on the mechanism of memory formation in comparison with an appropriate control system that does not undergo self-assembly.

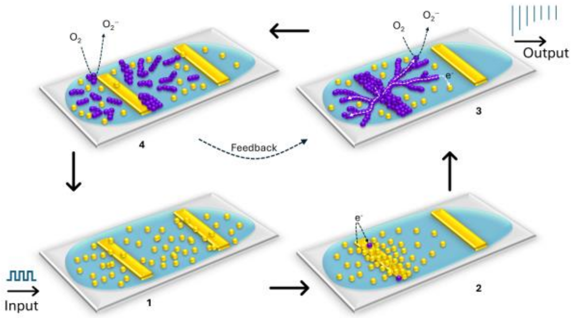

Figure1. On-chip dissipative self-assembly.

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Generation and UV-photolysis of *N*-methyleneformamide

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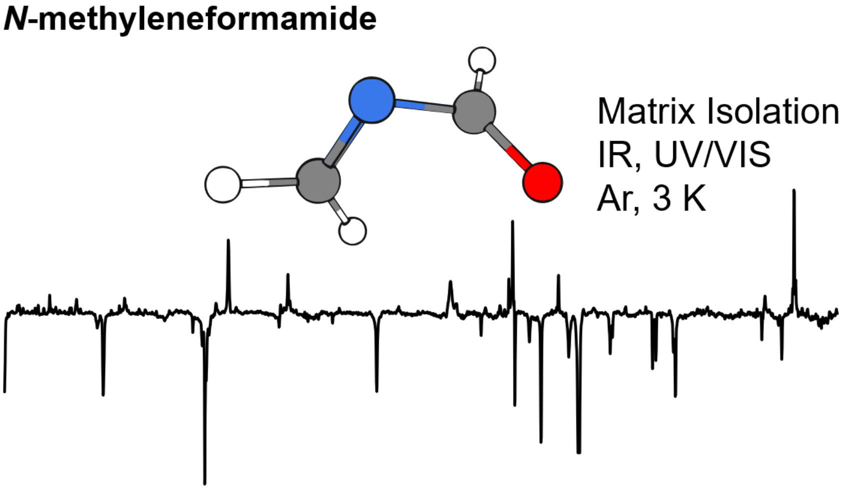
Simple imines have been detected in space and are considered as building blocks to larger heteroaromatic, cyclic and biological relevant compounds. Herein we revisited the formation of the simplest acylimine, namely *N*-methyleneformamide, by high-vacuum flash pyrolysis (HVFP) as well as its spectroscopic characterization by cryogenic matrix isolation infrared (IR) and UV/Vis spectroscopy.[1]

N-methyleneformamide prefers a gauche over a *s*-trans conformation in contrast to parent 1,3-butadiene. In UV-photolysis experiments we identified formaldehyde:HCN and formaldimine:CO complexes as the major decomposition products. As further photolysis products we observed the HCN:CO and HNC:CO complexes. All experimental findings are supported by deuterium labeling experiments and high-level ab initio coupled cluster calculations. *N*-methyleneformamide should be considered as a candidate for an interstellar search. The sequence R2C=N–RC=O also occurs in cytosine making the title compound highly relevant for prebiotic chemistry and the search for the molecular origins of life.



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Bioresponsive Chemiluminescence via Logic Gate Design: Towards Selective Intracellular Photodynamic Applications

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Conventional photodynamic therapy (PDT) suffers from limited selectivity and off-target effects due to its reliance on external light. To overcome this, we developed a bioresponsive chemiluminescent agent, Diox@Ru, whose activation is controlled by a Boolean AND-gate logic.[1] This system combines a dioxetane-based chemiluminescent scaffold with a ruthenium-based photosensitizer via stimuli-responsive linkers. Diox@Ru is activated only upon simultaneous encounter of two tumor-specific intracellular stimuli: mildly alkaline pH and elevated ROS levels. It remains inert under physiological conditions and in the acidic extracellular tumor microenvironment. Upon intracellular co-activation, it autonomously produces light, which triggers localized singlet oxygen generation without external irradiation. In both 2D and 3D tumor models, Diox@Ru induced potent and selective cytotoxicity. This logic-gated platform enables precise spatiotemporal control of PDT, minimizing off-target effects and offering a targeted strategy for intracellular cancer therapy.

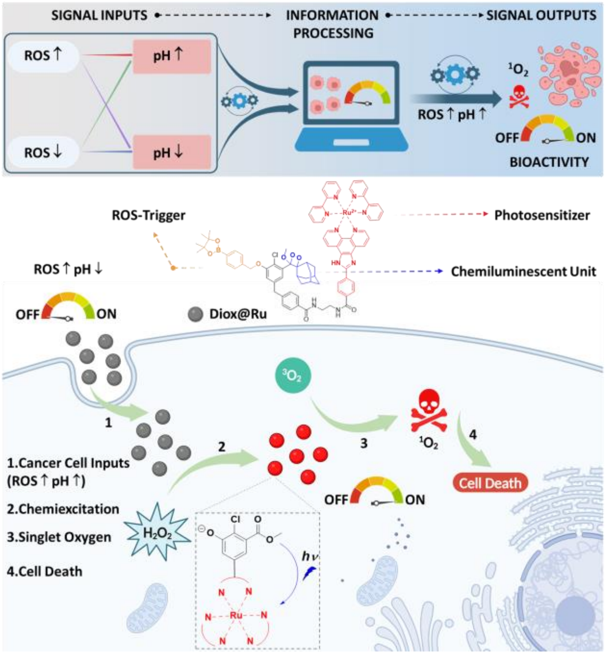

Figure 1. Design of the self-activating "AND" gated chemiluminescent photosensitizer for controlled chemiluminescent photodynamic applications in glycolytic tumor cells.

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The Electrophilicities of Dialkyl Acetylenedicarboxylates

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Dialkyl acetylenedicarboxylates (DAAD) represent versatile building blocks in multiple fields of organic synthesis. The electron-deficient triple bonds of DAAD are frequently used in cycloadditions, Michael additions, and multicomponent reactions.[1]

Our work characterizes the electrophilicities of DAAD at their triple bonds by studying the kinetics of DAAD reactions with carbanions (Fig. 1a). The carbanions, which were chosen as reference nucleophiles, have reported nucleophilicities *N* (and s_N), which made it possible to use the Mayr-Patz equation (1) to determine the electrophilicity *E* of DAAD.[2,3] Thus, the quantification of the DAAD electrophilicity facilitates the comparison of their reactivity with >350 structurally diverse electrophiles in Mayr reactivity scales (Fig. 1b).[3,4]

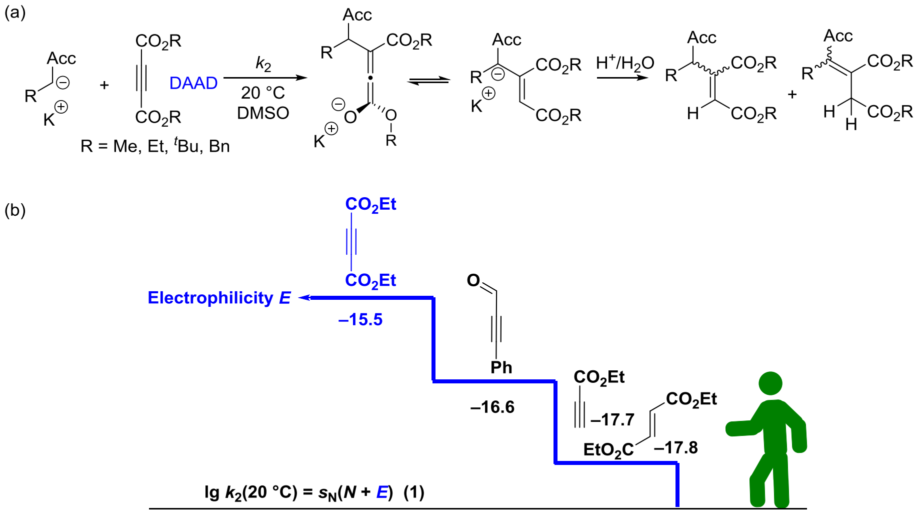

Figure 1. (a) Nucleophilic attack of carbanions at the electron-deficient π-system of DAAD. (b) Electrophilicity ranking according to the Mayr *E* scale.

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Novel Thiourea and Guanidine Functionalized Diaminoterephthalate Fluorophores

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Diaminoterephthalates are typical representatives of the single benzene-based fluorophores, and they became important building blocks for devising new organic optoelectronic materials [1,2]. The typical fluorescence band of the simple N-alkylated 2,5-diaminoterephthalates (DATA, Fig. 1) falls above 500 nm, with the observed Stokes shift larger than 100 nm [1]. This was attributed to the specific arrangement of the electron-donating and the electron-accepting groups, leading to the S_1 with highly pronounced charge-transfer character [3]. Besides that, geometry changes triggered by the antiaromaticity in the S_1(FC) region were also recognized as the mechanism that strongly contributes to the large Stokes shift [3,4]

Herein we presenting novel thioureas and guanidines as the potential anion–sensing subunits constructed upon the DATA backbone and its diamide (**DATAm**, Fig. 1) analogue. Their basic photochemical properties (absorption and emission maxima) were investigated computationally by employing PBE0/6-31G(d)//M06-2X/6-31G(d) approach [5]. Selected structures were also prepared and their response toward selected anions were investigated by UV/Vis and fluorescence spectroscopy.

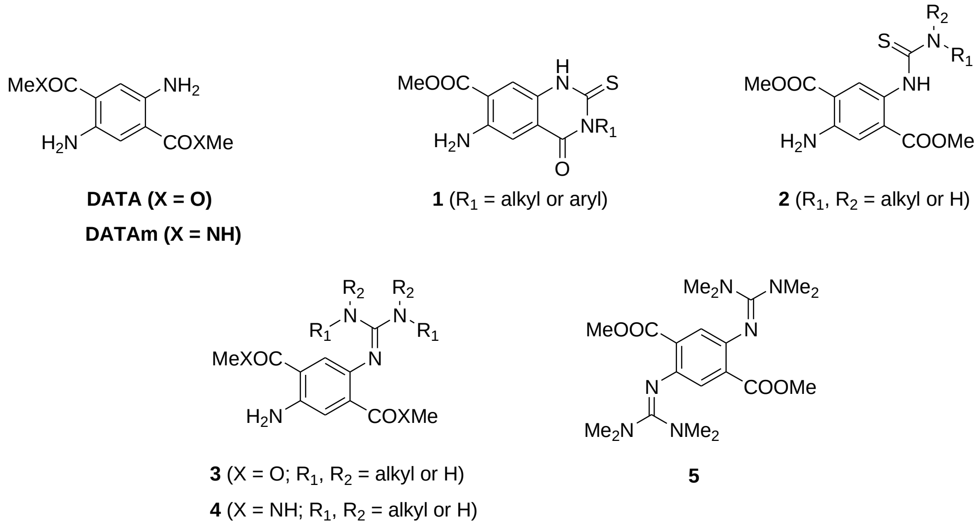

Figure 1. Schematic structures of the investigated groups of compounds

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Development of a Synergistic Hybrid Catalytic System Based on Gold-doped MOF/COF Composites for Enhanced Photocatalysis

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To develop photocatalysts with continuous electron extraction and rapid proton transfer could kinetically accelerate the photocatalysis.[1] Herein, we have prepared a heterogeneous COF@Au@UiO-66-NH_2 nanostructures consisting in Au nanoparticles supported on a metal organic framework,(MOF) followed by a topologically guided synthesis of highly crystalline triazine covalent organic frameworks (COFs) on the surface. The intercalated Au nanoparticles with the localized surface plasmon resonance (LSPR) effect[2] act as generators of hot electrons and also transfer channels for the photo-generated electrons from the COF shell to the UiO-66-NH_2 core. It is showed that the introduction of appropriate Au and COF could not only broaden the visible-light absorption band but also promote the separation of photoinduced charge carriers and enhance the photocatalytic performance. The catalytic system photocatalytically converted benzyl alcohol and oxygen into benzaldehyde and H_2O_2 at room temperature in an oxygen atmosphere under visible-light.[3]

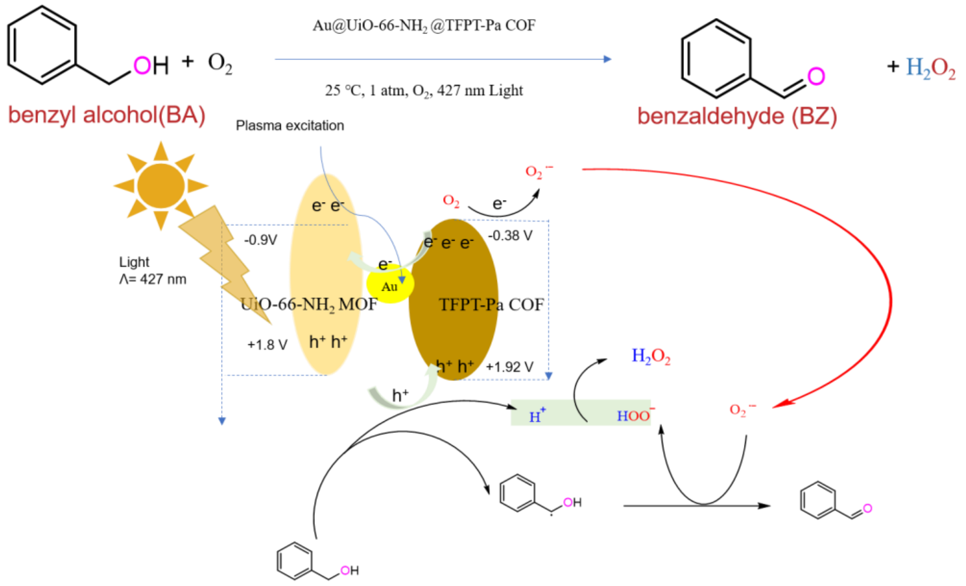

Figure 1: Hypothesis Scheme of photocatalysis reaction of benzyl alcohol and Oxygen.

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