Book of Abstracts

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Dear participants, guests and colleagues!

It is our great pleasure to welcome you to **Balticum Organicum Syntheticum 2026** in Tallinn, Estonia. BOS 2026 brings together an outstanding international community of scientists, including established leaders, emerging researchers, and students. The scientific programme combines plenary and invited lectures of academic and industrial speakers, contributed presentations, and poster sessions designed to encourage discussion, stimulate new ideas, and strengthen connections across disciplines and sectors. The conference has always valued the balance between fundamental research and practical application, and we are pleased to continue this tradition in Tallinn.

We are particularly delighted to host this BOS in Estonia's capital city. Tallinn, with its unique blend of historical heritage, vibrant scientific community, and forward-looking innovation ecosystem, provides an ideal setting for scientific exchange and international collaboration.

We would like to express our sincere gratitude to all authors, speakers, participants and sponsors whose efforts have made BOS 2026 possible. Most importantly, we thank all contributors to this Book of Abstracts for sharing their latest research and helping to create a stimulating and inspiring scientific programme.

Welcome to Tallinn!

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Programme

Sunday, June 28

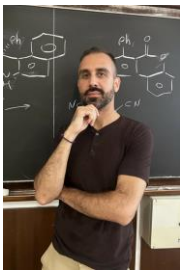
13:00	Registration desk opens	
13:00-15:30	Walking Tour in Old Town	
15:00-15:45	Coffee break	
15:45-16:00	BOS committee welcome	
16:00-17:00		Junichiro Yamaguchi Professor Waseda University **Exploring Ring Transformation: Opening, Formation, and Swapping of Cyclic Structures** Abstract here
17:00-18:00		Oliver Kappe Professor The University of Graz **Going With the Flow – the Use of Continuous Processing in Organic Synthesis** Abstract here
18:00-20:00	Welcome reception	

Monday, June 29

8:00	Registration desk opens	
9:30-10:00	Conference opening	
10:00-11:00		Martin Burke Professor University of Illinois **Blocc Chemistry: Imagine a World Where Anyone Can Make Molecules** Abstract here
11:00-12:00		Christophe Allais Research Fellow Pfizer Inc. **Process Enablement of Next Generation COVID-19 Inhibitor Ibuzatrelvir and Overview of Pfizer Sustainability Strategy** Abstract here

12:00-12:30	Group photo
12:30-14:00	Lunch break/ Presentation: SOURCES (13:30-14:00)
14:00-15:00	 Gints Smits Professor National Institute of Research and Innovation **From Esters to Aldehydes and Beyond: Triarylborane-Catalyzed Hydrosilylation** Abstract here
15:00-16:00	 Christina White Professor University of Illinois **Site-Selective C—H Oxidation** Abstract here
16:00-16:30	Flash poster presentations (5x5 min) 1. Bui, L.; RWTH Aachen University; **Asymmetric Hydrogenation of 3H-Azepines via Catalytic Kinetic Resolution: Access to Anti-disubstituted Azepanes**; P012 2. Das, A.; Latvian Institute of Organic Synthesis; **Iodine(III) Reagent Enable Catalyst- and Light-Free Fluoromethyl Radical Cascade Reaction**; P017 3. Dey, P.; Czech Academy of Sciences; **Enabling Diversity-Oriented Synthesis of Drug-Like Atropisomers**; P020 4. Domack, J.; University of Münster; **Divergent Housane Synthesis via Intramolecular [2 + 2] Cycloaddition of 1,4-Dienes**; P021 5. Indu, S.; Johannes Kepler University; **Enantioselective α-Amination of Carbonyl Compounds Using Ammonia**; P032
16:30-18:30	Poster session I (odd numbers)/Coffee – List of Abstracts
19:00-21:00	Walking Tour in Old Town

Tuesday, June 30

8:00	Registration desk opens	
8:45-9:00	Welcome and BOS updates	
9:00-10:00		Maud Reiter Vice President dsm-firmenich **From Pine to Perfume: Sustainability-Driven Perfumery Ingredient** Abstract here
10:00-11:00		Luca Dell'Amico Professor University of Padova **Synthesis and Functionalization of Small Rings via Photochemical Methods** Abstract here
11:00-11:30	Coffee break / Presentation: WAB-Group (11:00-11:30)	
11:30-12:30		Gabriel Schäfer Project Manager Dottikon Exclusive Synthesis AG **Oldie but Goldie: the Use of HOSA in Accessing Classical Functional Groups on Scale in an Innovative Way** Abstract here
12:30-13:30		Artiom Cernijenko Senior Principal Scientist Novartis BioMedical Research **Discovery of WIZ and NEK7 Molecular Glue Degraders** Abstract here
13:30-15:00	Lunch break / Presentation: CAS (14:30-15:00)	
15:00-16:00		Franziska Schoenebeck Professor RWTH Aachen University **Creating Tools for Synthesis From Mechanistic Foundations** Abstract here

16:00-16:30	Flash poster presentations (5x5 min) 1. Krech, A.; Tallinn University of Technology; **Electrochemical Enantioselective Azidation of α-Branched Aldehydes Through Iodine-Mediated Electrocatalysis**; P046 2. Orbach, N.; Israel Institute of Technology; **Stereocontrolled Synthesis of Polysubstituted Housanes via *gem*-Bismetalated Cyclopropanes**; P076 3. Smyrnov, V.; University of Chicago; **Single-Step Conversion of Furans to Pyridines**; P108 4. Tual, L.; University of Strasbourg; **Rh(II)-Catalyzed Diazo Decomposition for the Synthesis of Thiolanes and Thiazepines: Towards Application in Continuous Flow Chemistry**; P118 5. Žurauskas, J.; Vilnius University; **From Bench Neglect to Bench-Stable C1 Reagent**; P138
16:30-18:30	Poster session II (even numbers)/ Coffee – List of Abstracts
20:00-22:30	Conference dinner (only with pre-booked entrance cards)

Wednesday, July 1

8:00	Registration desk opens
8:45-9:00	Welcome and BOS updates
9:00-10:00	 Cristina Nevado Professor University of Zurich **"Capturing" the Golden Snitch: Reactive Gold(III) Species as Mechanistic Tools for Reaction Design** Abstract here
10:00-11:00	 Maksim Ošeka Professor Tallinn University of Technology **Merging Electrosynthesis With Asymmetric Organocatalysis** Abstract here
11:00-11:30	Coffee break/ Presentation: TFTAK (11:00-11:30)

11:30-12:30		Carsten Bolm Professor RWTH Aachen University **Mechanochemistry: The Use of Mills in Organic Synthesis** Abstract here
12:30-13:30	Lunch break/ Presentation: Kerox (13:00-13:30)	
13:30-14:30		Benjamin Martin Network Leader Novartis Pharma AG **Sustainable Pharmaceutical Process R&D Enabled by Flow Chemistry** Abstract here
14:30-15:30		Richmond Sarpong Professor University of California, Berkeley **Break-it-to-Make-it Strategies for Chemical Synthesis Inspired by Complex Natural Products** Abstract here
15:30-16:00	Conference closing and prizes	

EXPLORING RING TRANSFORMATION: OPENING, FORMATION, AND SWAPPING OF CYCLIC STRUCTURES

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Cyclic structures—ranging from all-carbon rings such as benzene to nitrogen- and oxygencontaining heterocycles—are ubiquitous in organic molecules and play decisive roles in determining their physical, chemical, and biological properties. Their importance continues to drive the development of new strategies for cyclic framework manipulation.

This talk highlights three transformations that dramatically remodel cyclic skeletons. A ring-opening strategy for cyclic amines is achieved under blue-light irradiation in the presence of a Lewis acid and a photoredox catalyst, enabling selective C–C bond cleavage via carbon radical intermediates under mild conditions. A complementary ring-formation approach relies on the in situ generation of highly reactive ortho-quinodimethane intermediates through a simple multicomponent process, providing an efficient and modular route to polycyclic structures. Finally, a heteroaromatic swapping reaction is described, in which aromatic ketones are converted into heteroaromatic frameworks through a Claisen/retro-Claisen pathway, offering a practical method for selective aromatic editing.

GOING WITH THE FLOW – THE USE OF CONTINUOUS PROCESSING IN ORGANIC SYNTHESIS

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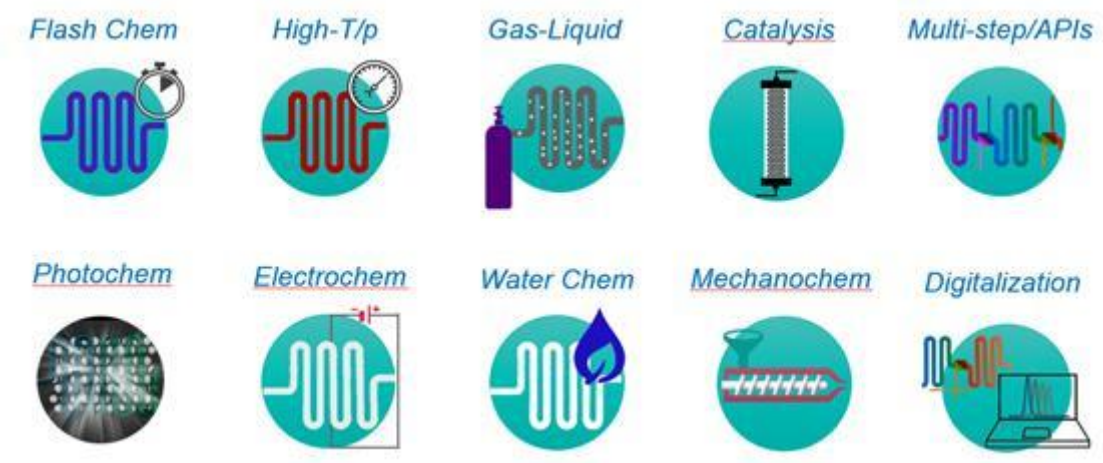
Continuous flow processes form the basis of the petrochemical and bulk chemicals industry where strong competition, stringent environmental and safety regulations, and low profit margins drive the need for highly performing, cost effective, safe and atom efficient chemical operations. In contrast to the commodity chemical industry, the fine chemical industry primarily relies on its existing infrastructure of multipurpose batch or semi-batch reactors. Fine chemicals, such as drug substances and active pharmaceutical ingredients (APIs), are generally considerably more complex than commodity chemicals and usually require numerous, widely diverse reaction steps for their synthesis. Flow technology has considerable advantages in mass- and heat transfer, safety and ease of scale-up, when compared to traditional batch reactions. Furthermore, hazardous chemistries such as highly exothermic reactions, or those involving unstable or toxic intermediates can be operated safely in flow, whereby this technology acts as a powerful route-enabler. In this lecture, contributions from our research group in the field of continuous flow processing in the areas shown will be highlighted.[1]



1. Gutmann, B.; Cantillo, D.; Kappe, C. O. *Angew. Chem. Int. Ed*. **2015**, 54, 6688-6729.

BLOCC CHEMISTRY: IMAGINE A WORLD WHERE ANYONE CAN MAKE MOLECULES

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Molecules built primarily from carbon–carbon bonds, or "small molecules," underpin countless aspects of modern life, yet their immense functional potential remains largely untapped. Innovation in this space is constrained by the fact that only a small number of specialists can synthesize such molecules—fewer than can fit in one building worldwide. The difficulty lies in forming carbon–carbon bonds repeatedly and reliably, particularly on automated platforms.

Blocc chemistry offers a transformative solution by enabling iterative carbon–carbon bond formation through the use of MIDA and TIDA ligands, which reversibly attenuate boronic acid reactivity. This discovery allows small molecule synthesis to be performed in a way that is compatible with robots, AI, and non-specialists. A further breakthrough—that MIDA/TIDA boronates display binary elution behavior on silica—established a universal, automation-friendly purification strategy.

Now adopted globally, blocc chemistry has enabled over 1,000 publications and 300 patents spanning natural products, pharmaceuticals, agrochemicals, and materials. In the Burke lab, it has yielded molecular prosthetics for cystic fibrosis and other diseases, and renal-sparing antifungal agents now in clinical trials. Integration with AI and automated functional testing is advancing closed-loop discovery, while the Molecule Maker Lab is translating this approach into a democratized platform for molecular innovation.

PROCESS ENABLEMENT OF NEXT GENERATION COVID-19 INHIBITOR IBUZATRELVIR AND OVERVIEW OF PFIZER SUSTAINABILITY STRATEGY

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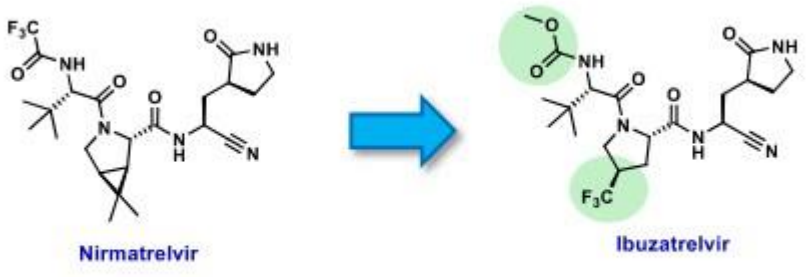
Shortly after the COVID-19 pandemic was declared in March 2020 by the WHO, Pfizer initiated a multi-front approach to combat the virus, which included a vaccine but also recognized very early the need for an orally dosed treatment able to help infected patients. This initiative resulted in the discovery of nirmatrelvir, active ingredient of PAXLOVID®, which was then developed at unprecedented speed.

In parallel to this massive effort, Pfizer continued to seek additional options for patients, and ultimately discovered ibuzatrelvir, an orally bioavailable, next-generation clinical candidate developed for the treatment of COVID-19 infections. Advantages of this asset will be discussed, along with its accelerated timeline and synthetic challenges such as the chiral CF_3-proline throughout development of a commercial route.

Emphasis on the sustainability aspects of the latest route will also be highlighted as well as an overview of Pfizer Drug Substance strategy in this space as we commit to Net Zero engagements.



FROM ESTERS TO ALDEHYDES AND BEYOND: TRIARYLBORANE-CATALYZED HYDROSILYLATION

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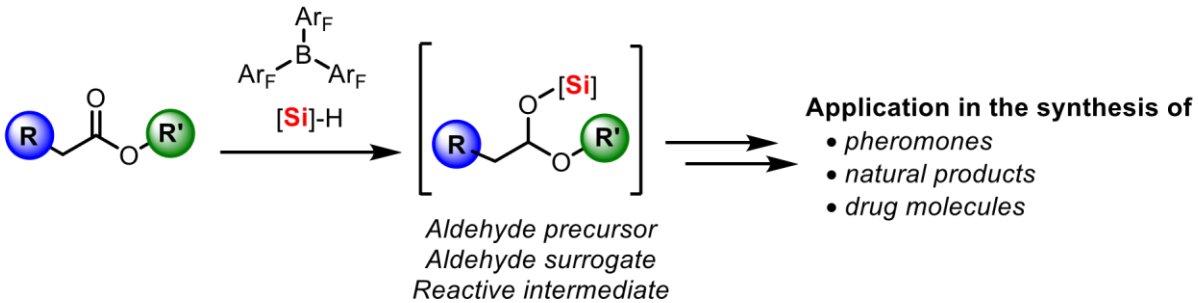
Ester-to-aldehyde reduction remains a persistent challenge in organic synthesis. Although aluminum hydride reagents can effect this transformation, their limited chemoselectivity and poor functional-group tolerance restrict broader application. Catalytic hydrosilylation has recently emerged as an alternative strategy, proceeding via silylacetal intermediates.

This presentation describes our recent advances in triarylborane-catalyzed ester hydrosilylation. Systematic structure–reactivity studies have enabled the extension of this methodology to a diverse set of polyfunctional ester substrates. Beyond serving as intermediates en route to aldehydes, the resulting silyl acetals are shown to function as synthetically useful aldehyde surrogates in downstream transformations.

Mechanistic studies, supported by DFT calculations, reveal unconventional catalytic pathways underlying this process. Notably, subtle modifications to the ester substrate, catalyst structure, or silane reagent can induce pronounced changes in reaction outcome, leading to divergent product formation.



SITE-SELECTIVE C—H OXIDATION

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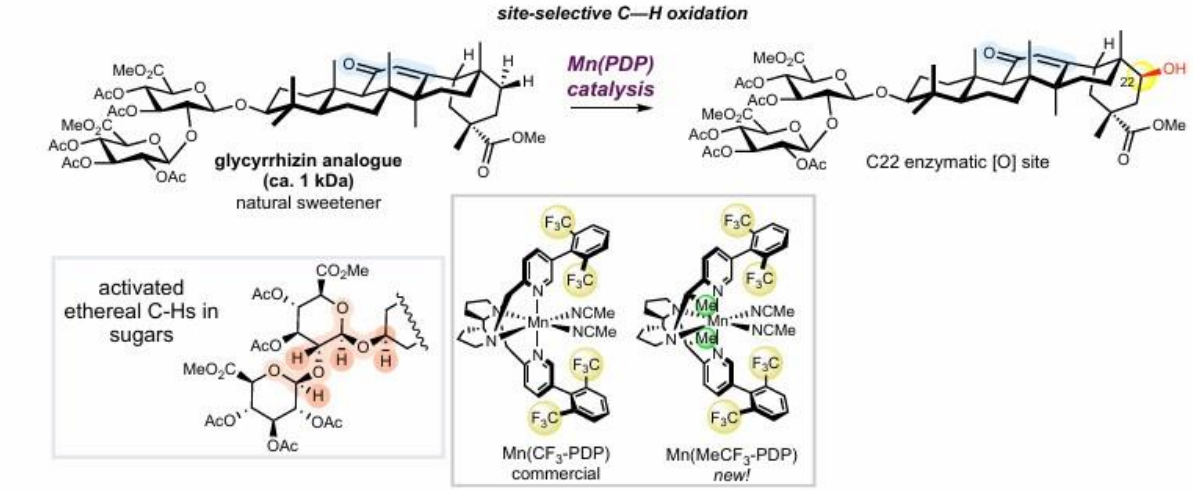

FROM PINE TO PERFUME: SUSTAINABILITY-DRIVEN PERFUMERY INGREDIENT INNOVATION

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The present presentation follows the sustainability-driven journey of perfumery ingredient discovery and development starting from pine-tree derived feedstock. Impact on people and planet will be evaluated using a holistic sustainability metrics tool EcoING Compass®[1] and quantitative full life cycle assessment (LCA).

1. Reiter et al., Curr. Opinion in Green and Sustainable Chemistry, 2022, 33, 100583 & to dsm-firmenich: WO2023152091

SYNTHESIS AND FUNCTIONALIZATION OF SMALL RINGS VIA PHOTOCHEMICAL METHODS

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In this presentation I will discuss recent reports from my group on the photochemical construction and functionalisation of oxetanes[1], azetidines[2] and cyclobutanes[3]. These studies show how visible light can drive the selective formation of strained small-ring systems and enable their controlled transformation into complex molecular architectures. I will focus on the underlying reaction mechanisms and on the nature of the key radical intermediates that define reactivity and selectivity.

I will then show how the design and development of new organic photocatalysts can unlock reaction pathways that were previously inaccessible.

By combining mechanistic understanding with catalysts development, we have opened new opportunities for molecular synthesis and gained access to structural motifs that were beyond reach using conventional methods[4].

Looking ahead, we aim to further expand the scope of light-driven chemistry by exploring new photocatalyst families and reactivity modes that can transform the way we build and modify small, strained molecules[5].

1. Mateos, J., Rigodanza, F., Costa, P., Natali, M., Vega-Peñaloza, A., Fresch, E., Collini, E., Bonchio, M., Sartorel, A., Dell'Amico, L. *Nat. Synth.* **2022***, 2*, 26–36.
2. Rodríguez, R. I., Corti, V., Rizzo, L., Visentini, S., Bortolus, M., Amati, A. Natali, M., Pelosi, G., Costa, P., and Dell'Amico, L. *Nat. Catal.* **2024***, 7*, 1223–1231.
3. Corti, V. Simionato, G. Rizzo, L. Serapian, S. A. Pelosi, G. Natali, M. Dell'Amico, L. *Nat. Chem.* **2025**.
4. Franceschi, P., Cuadros, S., Goti, G., Dell'Amico, L. *Angew. Chem. Int. Ed.* **2023**, *62*, e202217210.
5. Rosso, C., Barison, G., Droghetti, F., Michelazzo, N., Sartorel, A., Pelosi, G., Bortolus, G., Costa, P., Natali, M., Dell'Amico L. *ChemRxiv* **2024**

OLDIE BUT GOLDIE: THE USE OF HOSA IN ACCESSING CLASSICAL FUNCTIONAL GROUPS ON SCALE IN AN INNOVATIVE WAY

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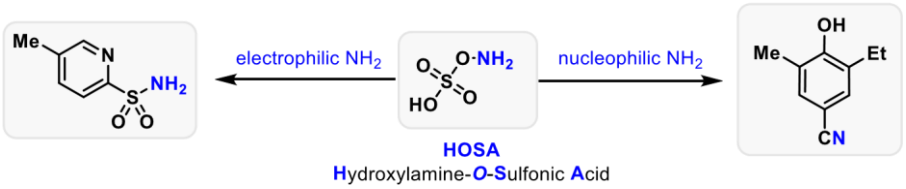
Hydroxylamine-*O*-sulfonic acid, or short HOSA, is an easily handled, stable solid, which is produced on ton-scale by reaction of hydroxylamine with oleum/sulfuric acid or chlorosulfonic acid/sulfuric acid. Despite being a bulk chemical, HOSA has not been extensively used in the manufacturing of pharmaceuticals, which is surprising given the great versatility of this reagent to act as an electrophilic or nucleophilic source of nitrogen.



We have disclosed two new manufacturing routes, for which HOSA was used on scale and took advantage of its modular reactivity. In the first example, a novel route to 5-methyl2-pyridinesulfonamide was developed. The new route relied on the selective oxidization of the thiophenol starting material to the sulfinate salt, followed by amination of the nucleophilic sulfinate sulfur-atom with HOSA acting as an electrophilic amine source. This oxidation/electrophilic amination sequence worked well as a "one-pot" procedure by simply adding HOSA to the reaction mixture after completed oxidation of the thiophenol. The new process was performed on 22 kg scale, delivering the desired product in 69% overall yield and excellent purity.[1]

In the second example, a new manufacturing route for 3-ethyl-4-hydroxy-5methylbenzonitrile was urgently needed. Therefore, a conceptually novel route to the nitrile with HOSA, this time reacting as a nucleophilic amine source, was developed. The idea was to convert the corresponding aldehyde into the HOSA-derived oxime, followed by elimination of sulfuric acid to form nitrile. This reaction sequence worked well on scale and provided the product in 89% yield and high purity.[2]

1. Schäfer, G.; Fleischer, T.; Kastner, M.; Karge, R.; Huang, Q.; Libang Wu, B.; Tang, J.; Aiglstorfer, I. *Org. Process Res. Dev.* **2023**, *27*, 1377-1383.
2. Schäfer, G.; Fleischer, T. *Helv. Chim. Acta* **2023**, *e202300167*.

DISCOVERY OF WIZ AND NEK7 MOLECULAR GLUE DEGRADERS

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Targeted protein degradation has emerged as a promising therapeutic strategy, enabling the removal of disease-driving proteins rather than simply inhibiting their function. Among these approaches, molecular glues represent a unique class of small molecules that induce proximity between an E3 ubiquitin ligase and a target protein, leading to selective ubiquitination and proteasomal degradation. This seminar will explore the design and application of cereblon-based molecular glue degraders, focusing on two interesting targets: WIZ, implicated in fetal hemoglobin induction for the treatment of sickle cell disease, and NEK7, a regulator of NLRP3 inflammasome activation in inflammatory disorders.

CREATING TOOLS FOR SYNTHESIS FROM MECHANISTIC FOUNDATIONS

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This presentation will give an overview of our group's recent research activities at the interface of synthetic organic, mechanistic chemistry and homogeneous catalysis. The emphasis will be on novel strategies that were recently identified in our laboratory to simplify and accelerate the synthesis of structurally diverse molecules. These include, for example, the (i) use of organogermanes as orthogonal coupling partners in Csp2 and Csp3 space, (ii) metalloradical-catalyzed stereomutations, (iii) late-stage alkylations & (iv) routes to synthesize previously inaccessible fluorinated motifs. The development, scope and mechanistic underpinnings (based on experimental & computational/data science studies) of these novel processes will be discussed.

"CAPTURING" THE GOLDEN SNITCH: REACTIVE GOLD(III) SPECIES AS MECHANISTIC TOOLS FOR REACTION DESIGN

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Identifying the structure and electronic nature of key reactive intermediates in catalysis is essential for the development of new synthetic methods. Despite their widespread application in catalysis, material science and biomedical research, the development of gold(III) complexes remains limited by challenges associated with their synthesis. The use of bidentate and tridentate ligands is crucial to prevent the facile reduction to gold(I) or decomposition to elemental gold(0). However, most of the existing protocols to attain both, mono and bis-cycloaurated complexes, rely on harsh conditions and/or require the use of stoichiometric additives or toxic reagents (e.g. Ag or Hg). Here, we will present our contributions in this area which underscore the critical role of gold(III)-stabilized frameworks in unlocking new reactivity paradigms.

MERGING ELECTROSYNTHESIS WITH ASYMMETRIC ORGANOCATALYSIS

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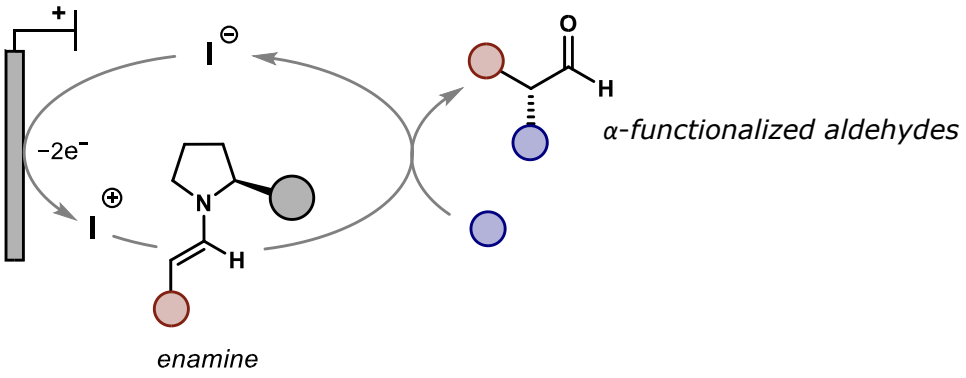
Asymmetric catalysis plays an important role in modern organic chemistry providing methods for the synthesis of biologically active compounds and pharmaceuticals. Merging well-developed aminocatalysis with electrochemistry opens new horizons for asymmetric transformation beyond classical thermochemical activation. This approach is sustainable, since it employs harmless organocatalysts to induce chirality and electrons as traceless and green reagents avoiding the utilization of hazardous stoichiometric oxidants. We have developed iodine-mediated asymmetric functionalization of carbonyl compounds. The transformation is driven by the mild and controlled electrochemical generation of electrophilic iodine species in catalytic amounts, which allows to protect the organocatalyst from decomposition.



MECHANOCHEMISTRY: THE USE OF MILLS IN ORGANIC SYNTHESIS

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IUPAC defines a "mechano-chemical reaction" as a "chemical reaction that is induced by the direct absorption of mechanical energy".[1] Such activation mode can be useful and beneficial in both synthesis and catalysis.[2] Mills play a central role in such processes. Selected recent examples from our group will be covered in the presentation.[3] In addition, it is demonstrated how the vessel geometry (Figure 1) affects the milling efficiency.[4]

Figure 1: Vessels with different geometries used in a mixer mill

1. IUPAC. *Compendium of Chemical Terminology*, 2nd ed. (the "Gold Book"), Blackwell Scientific Publications, Oxford, 1997 and cited in *PAC* **2004**, *76*, 889.
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SUSTAINABLE PHARMACEUTICAL PROCESS R&D ENABLED BY FLOW CHEMISTRY

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Continuous Manufacturing is the result of industrializing flow chemistry, and the focus of this presentation will be the application to synthesizing medicines.[1] The fundamental principles of how continuous processes can impact a chemical reaction are outlined, and the connection to green chemistry is given.

The key learnings from three case-studies in the areas of hydrosilylative reduction and organometallic chemistries will be highlighted,[2-3] taking the listener from the lab discoveries to the final processes and equipment rigs used for manufacturing on kilogram scale. Decision making as to when to use flow equipment, and when to use batch, as well as strengths and weaknesses of the new processes will be shared.

The aim is to showcase continuous manufacturing as a mature enabling technology which has green credentials, and can be relied upon to support the synthesis of complex pharmaceutical building blocks.

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BREAK-IT-TO-MAKE-IT STRATEGIES FOR CHEMICAL SYNTHESIS INSPIRED BY COMPLEX NATURAL PRODUCTS

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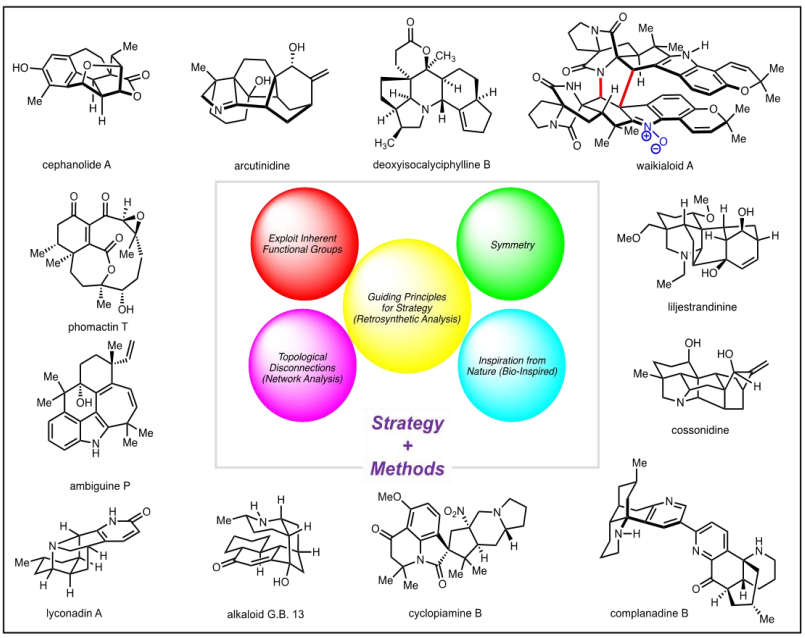
Natural products continue to inspire and serve as a basis of new medicines. They also provide intricate problems that expose limitations in the strategies and methods employed in chemical synthesis. Several strategies and methods that have been developed in our laboratory and applied to the syntheses of architecturally complex natural products will be discussed. In particular, new ways to employ the cleavage of core bonds such as C–C and C–N bonds (i.e., break-it-to-make-it strategies) to achieve skeletal editing will be presented.



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HYDROQUINONE/QUINONE CYCLE FOR REDUCTIVE PHOTOCATALYTIC TRANSFORMATIONS

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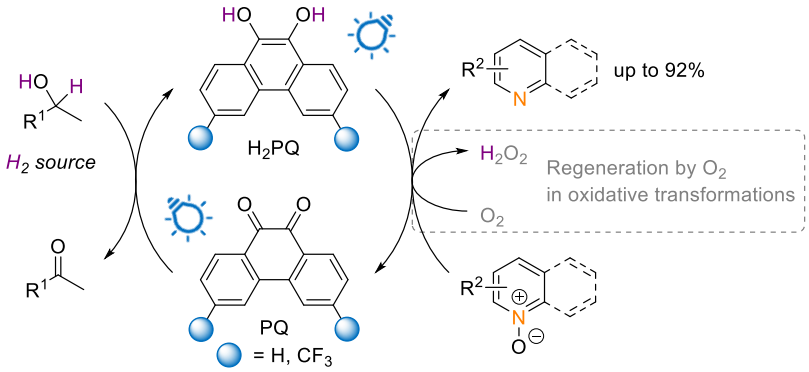

Over the past decade, the shift from metal-based to organic photocatalysts has motivated the exploration of quinones as photoredox catalysts. Seminal work by Fukuzumi and co-workers showed that phenanthrenequinone (PQ) can act as a photoactivated oxidant in alcohol oxidations.[1a] Building on this concept, we have enhanced the redox properties of PQ through strategic incorporation of CF_3 substituents.[1b]

As oxidative transformations require terminal oxidants to regenerate PQs, we questioned whether this cycle could be repurposed for reductive organic transformations. To test this concept, we investigated the photocatalytic deoxygenation of N-heterocyclic *N*-oxides. Traditionally, this transformation has been conducted using phosphines or boranes, or metal-mediated methods,[2] and more recently applying photoredox systems such as Hantzsch ester, acridinium salt/isopropanol, or thioxanthone/TfOH.[3]

We have developed an efficient photocatalytic deoxygenation of pyridine and quinoline *N*-oxides using isopropanol as a simple hydrogen source.[4] Experimental and computational studies suggest that *in situ* generated phenanthrenehydroquinones (H_2PQs) act as photoactived reductants enabling the transformation.

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ONE-POT SYNTHESIS OF NOVEL FLUORESCENT DIPYRAZOLOPYRIDINES

Zagorskytė, I.[a]; Razmienė, B.[a]; Ambrazaitytė, E.[a]; Račkauskienė, G.[a]; Belyakov, S.[b]; Holzer, W.[c]; Šačkus, A.[a], and Arbačiauskienė, E.[a]

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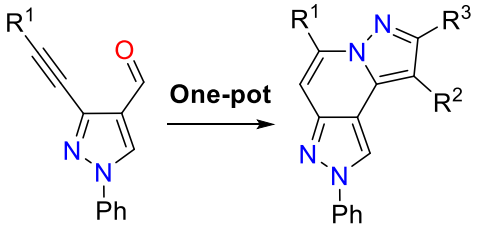
One-pot reactions represent a sustainable approach to synthesis, in which at least two reaction steps are carried out in the same reaction vessel without separating intermediate compounds. By eliminating the workup of a multi-stage procedure, this strategy promotes faster, more efficient, and more straightforward organic synthesis[1,2].

In this work, the effective synthesis and derivatization of 2*H*-dipyrazolo[1,5-*a*:4',3'-*c*]pyridines are described. 3-Alkynylpyrazole-4-carbaldehydes, *p*-toluenesulfonyl hydrazide, and an acidic α-hydrogen atom-containing aldehyde, ketone, or nitrile were reacted in a silver (I) catalysed one-pot reaction to afford 2*H*-dipyrazolo[1,5-a:4',3'-*c*]pyridine compounds with substituents at 2-, 5-, 8-, and 9-positions. The photophysical properties of the obtained compounds were investigated using spectroscopic techniques, including UV-vis and fluorescence spectroscopy[3].



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ALKENE AMIDATION BY ORGANOPHOTOCATALYTIC N–H-ACTIVATION

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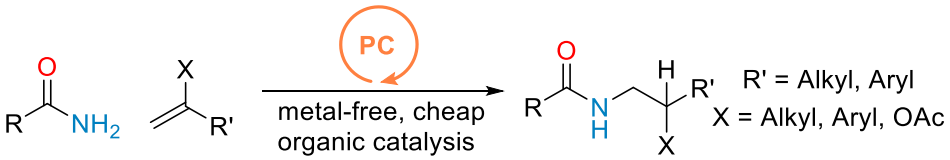
Photocatalysis has seen a resurgence in the last decade due to its ability to effect novel organic reactivity. A major advantage of photocatalytic transformations lies in homolytic X–H bond activation, bypassing the need for the preparation of highly reactive species *ex situ*. While selectivity in traditional hydrogen-atom-transfer processes is usually governed by X–H bond dissociation energy, proton-coupled electron transfer (PCET) can allow for a cooperative activation selective towards those hydrogen atoms involved in hydrogen bonding.[1]

Knowles *et al.* have previously demonstrated selective activation of amide N–H-bonds in intramolecular cyclisation by the resulting N-centered radical. Most interestingly, a singular example of intermolecular hydroamidation reactivity was disclosed.[2] Intrigued by this reactivity, we decided to explore this intermolecular addition. Among other results, we were able to replace the expensive, tailor-made, highly-fluorinated Iridium catalyst previously reported with an easily-preparable organic photocatalyst while shortening reaction times. An expansion of the utilizable alkenes for the reaction also allowed for the construction of protected 1,2-aminoalcohols from protected enols and phenethylamine derivates from styrenes by an inexpensive, scalable method. Intermediate trapping by HRESI-MS and photophysical kinetic experiments show the reaction to run via photodependent generation of N-centered radical species in the presence of a reversible trap likely acting as a radical reservoir.



steric hindrance tolerated up to X = R' = tBu

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VISIBLE-LIGHT-MEDIATED THREE-COMPONENT REACTION OF α,β-UNSATURATED ESTERS, STYRENES AND CARBOXYLATES

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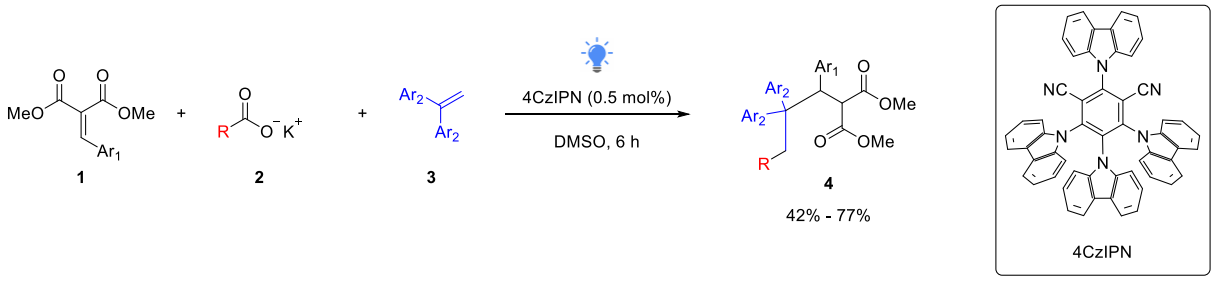
Photocatalytic multi-component reactions (MCRs) have emerged as a powerful tool for the rapid assembly of complex molecular scaffolds with high atom economy.[1] Merging the decarboxylative oxidation of abundant carboxylic acids with a radical-to-anionic crossover relay offers a sustainable, metal-free alternative to traditional cross-coupling methods.[2]

Herein, we report a highly efficient, visible-light-mediated three-component reaction that combines radical and anionic pathways within a single catalytic cycle. Utilising a robust organic photoredox catalyst based on the isophthalonitrile core (4CzIPN),[3] we successfully coupled diverse aliphatic carboxylates (**2**) with 1,1-diphenylethylene derivatives (**3**) and dimethyl benzylidenemalonate acceptors (**1**). The protocol operates through a sequence of single-electron transfer (SET) steps, effectively transforming transient radical intermediates into nucleophilic carbanions for subsequent C–C bond formation. This transition from radical to anionic reactivity enables precise assembly of polyfunctionalized products (**4**) with high regioselectivity under mild, metal-free conditions. We have successfully applied this strategy to a wide range of substrates, including diverse aliphatic carboxylates and Michael acceptors bearing both electron-donating and electron-withdrawing groups, achieving yields up to 77%.



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VISIBLE-LIGHT-INITIATED DECARBOXYLATIVE RADICAL ADDITION TO ELECTRONICALLY MISMATCHED ALKENES AND ALKYNES

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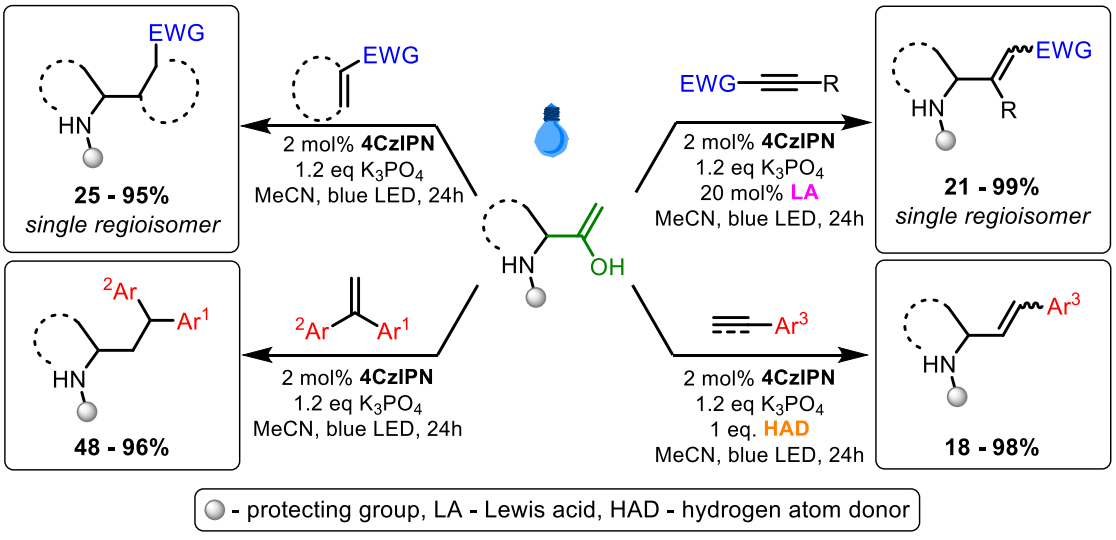
Amino acids are versatile building blocks in natural product and drug synthesis. Radical decarboxylation is particularly attractive for forming carbon-carbon bonds from amino acids, especially when initiated by visible light. Yoshimi showed that UV irradiation of an external photocatalyst initiates a photoredox process that couples carboxylic acids with electron-deficient alkenes.[1] MacMillan adapted this protocol to visible-light conditions in 2014.[2] Since then, this methodology has emerged as a powerful tool in organic synthesis with broad utility. However, the nucleophilic nature of the radical restricts its use primarily to electron-deficient acceptors.[3]

We aimed to develop an efficient strategy for activating both electron-deficient and electron-rich alkenes and alkynes. Our methodology reliably engages common Michael acceptors as well as styrene derivatives.[4] Introducing a hydrogen-atom donor to the discovered protocol substantially broadens the scope to include electron-rich alkenes and alkynes. Moreover, in the presence of a Lewis acid, internal alkynes afford the corresponding products in high yields and with good diastereoselectivity.



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SINGLET–TRIPLET GAP: POTENTIALLY USEFUL PARAMETER FOR PREDICTING CATALYTIC ACTIVITY OF CARBENE AND CARBENOID-BASED COMPLEXES

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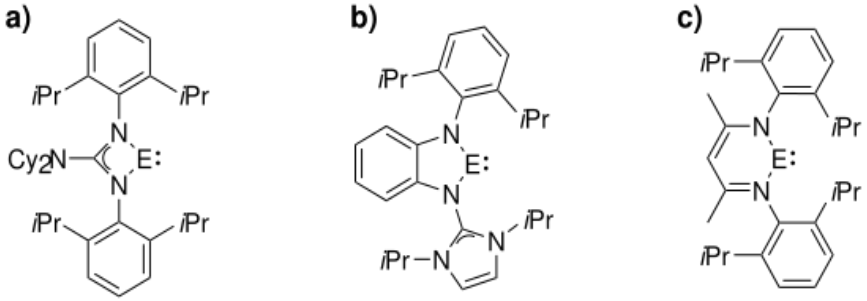
In the design of new catalysts one can take various multiple approaches. One of relatively recent ones is the search for easy-to-calculate structural or electronic parameters of known substances which correlate to their reactivity. Such parameters can later be used for the computational exploration of new structures with desirable properties[1], with possible use of machine learning[2].

As a part of our studies on cyclic triel carbenoids as potential ligands for olefin metathesis catalysts we screened multiple parameters to correlate them to our results on the predicted activity of Tl(AmIm)-based ruthenium complexes in olefin metathesis as well as towards the paths of their undesirable decomposition. The comparison of carbenoids with known structures of NHCs and CAACs showed that the best parameter for this purpose is singlet–triplet gap, which clearly separates NHCs and CAACs while placing triel carbenoids between them. Importantly, as S–T gap requires calculations on bare ligands and not whole complexes, it is cost efficient and, thus, allows for very fast screening of multiple structures.



Three important families of cyclic triel carbenoids: a) E(Giso), b) E(AmIm), c) E(NacNac).

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SULFONDIIMIDOYL-CONTAINING HYPERVALENT IODINE(III) COMPOUNDS: SYNTHESIS AND REACTIVITY

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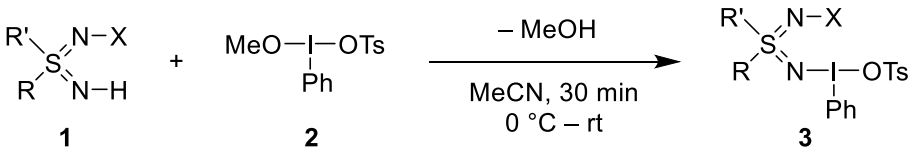
The interest in sulfur-containing scaffolds has grown steadily in the recent years. Prominent representatives of this group are sulfoximines or sulfonamides, which are used in many areas, such as medicinal chemistry and crop protection. However, very little is known about their aza-analogues, the sulfondiimines **1**.

Here, we present a new substance class: *N*-sulfondiimidoyl hypervalent iodine (III) compounds **3**. They can be obtained in excellent yields (81–99%) by reaction of sulfondiimine **1** with methoxy(tosyloxy)iodobenzene (MTIB, **2**). After 3–30 min, only simple filtration of the reaction mixture is necessary to obtain pure products. Many *S*-substituted sulfondiimines are tolerated and can be converted into the new substance class **3** with *S*,*S*-aryl, *S*,*S*-alkyl and *S*-alkyl, *S*-aryl backbones. They are stable for several months under argon at low temperatures (–20 °C). At room temperature, they can be handled for a short time without any signs of decomposition.

To investigate the reactivity profile and general behavior of *N*-sulfondiimidoyl hypervalent iodine (III) compounds **3**, they were tested in several different organic transformations.[1]



1 **2** **3**

X = Ph, Ns; R, R' = alkyl and/or aryl

81–99% yield

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MODULATION OF ANTIOXIDANT AND SOLUBILITY PROPERTIES OF MELDRUM'S ACID DERIVATIVES

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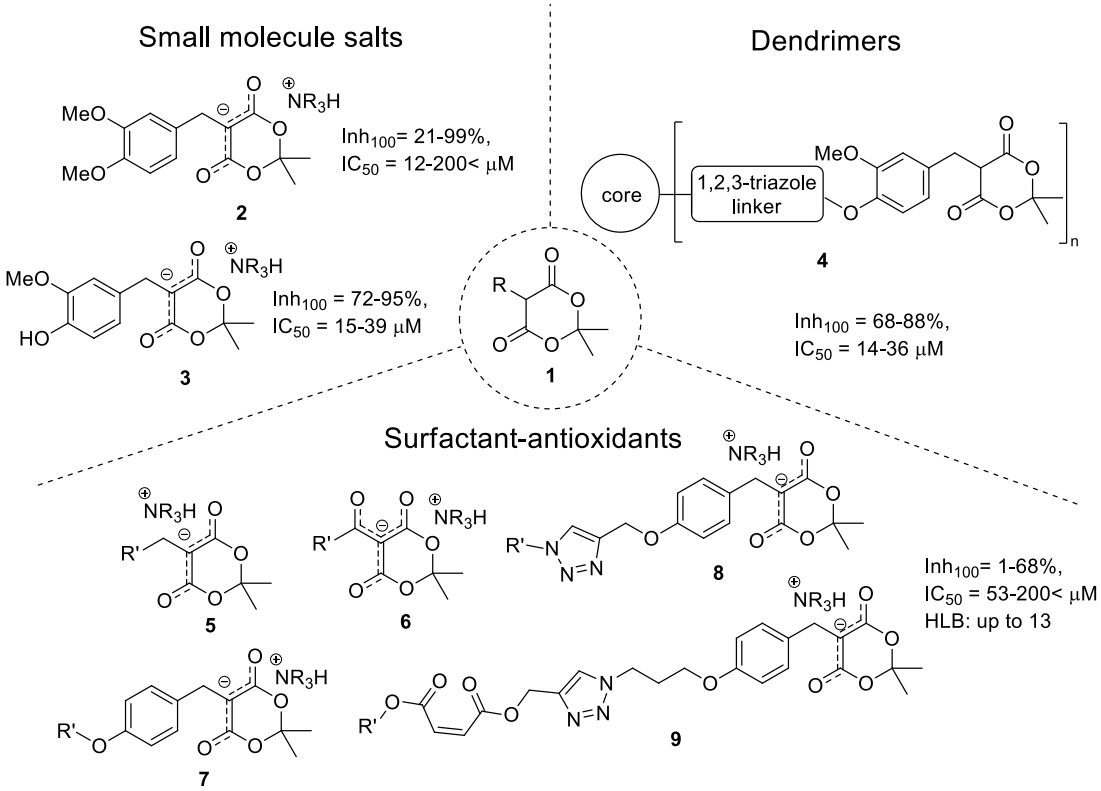
Meldrum's acid derivatives **1** are potent radical scavengers[1] belonging to the 1,3-dicarbonyl type antioxidant class.[2] To further enhance the antioxidant activity of arylmethyl Meldrum's acids we have employed 2 strategies: formation of small molecule ammonium salts **2**,**3** and dendrimeric structures **4**. Additionally, salts of various lipophilic Meldrum's acid derivatives **5**-**9** were investigated as potential dual-purpose molecules: surfactant-antioxidants.



Acknowledgements: This work was supported by the EU RRF (5.2.1.1.i.0/2/24/I/CFLA/003, grant ID 1028), ERDF (1.1.1.8/1/24/I/007, grant ID 8131), and Latvian Council of Science (lzp-2025/1-0442).

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SYNTHESIS OF 2′-AZIDO-2′-DEOXYRIBOFURANOSYL PURINES

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2′-Azido-substituted analogues of ribonucleosides are valuable compounds for oligonucleotide functionalization. The 2′-azido moiety is biocompatible and can be further selectively modified via Click chemistry[1]. Azide−alkyne cycloaddition is the leading technology to effectively conjugate selected molecules to the oligonucleotides, and its implementation has enabled researchers to generate a wide variety of tools for application in molecular biology[2].

A synthetic methodology for the preparation of 2′-azido-2′-deoxyribofuranosyl purines from readily accessible uridine has been developed. The synthetic route proceeds in only three steps and relies on a direct transglycosylation strategy, providing facile access to the target nucleoside analogues. It also expands beyond typical nucleosides by enabling the introduction of readily functionalised bases.

Acknowledgements

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SYNTHETIC APPROACH TOWARD APTAMER-DRUG CONJUGATE FORMATION FOR BIOLOGICAL VALIDATION

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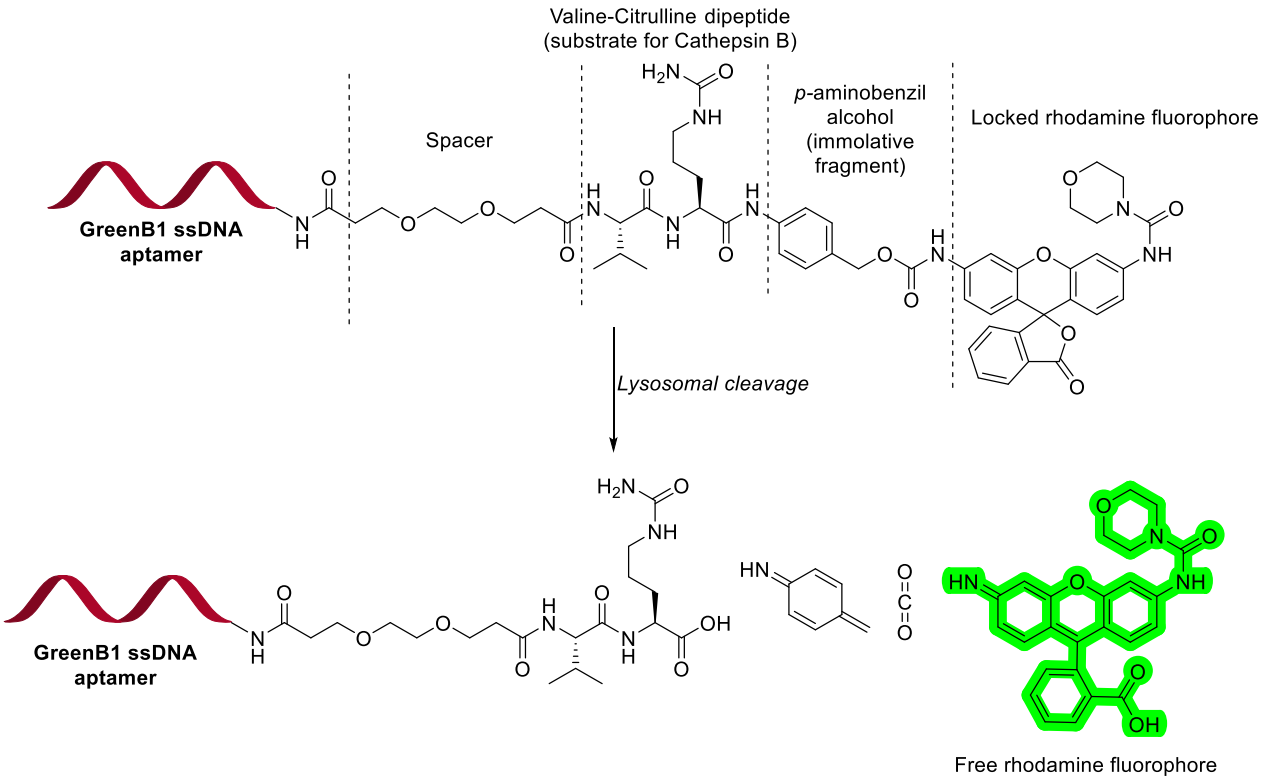
This work is concerned with the synthesis of an aptamer-drug conjugate for use in targeted therapy. For our purposes, we have elected to utilize the previously studied β1-integrin targeting GreenB1 aptamer.[1] Herein we report the synthesis of a Cathepsin-B responsive ssDNA aptamer-fluorophore[2] conjugate, which will allow us to validate the mechanism of targeted cell internalization and subsequent lysosomal payload release.



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FORMATION OF KERATIN FILM IN RAW WOOL

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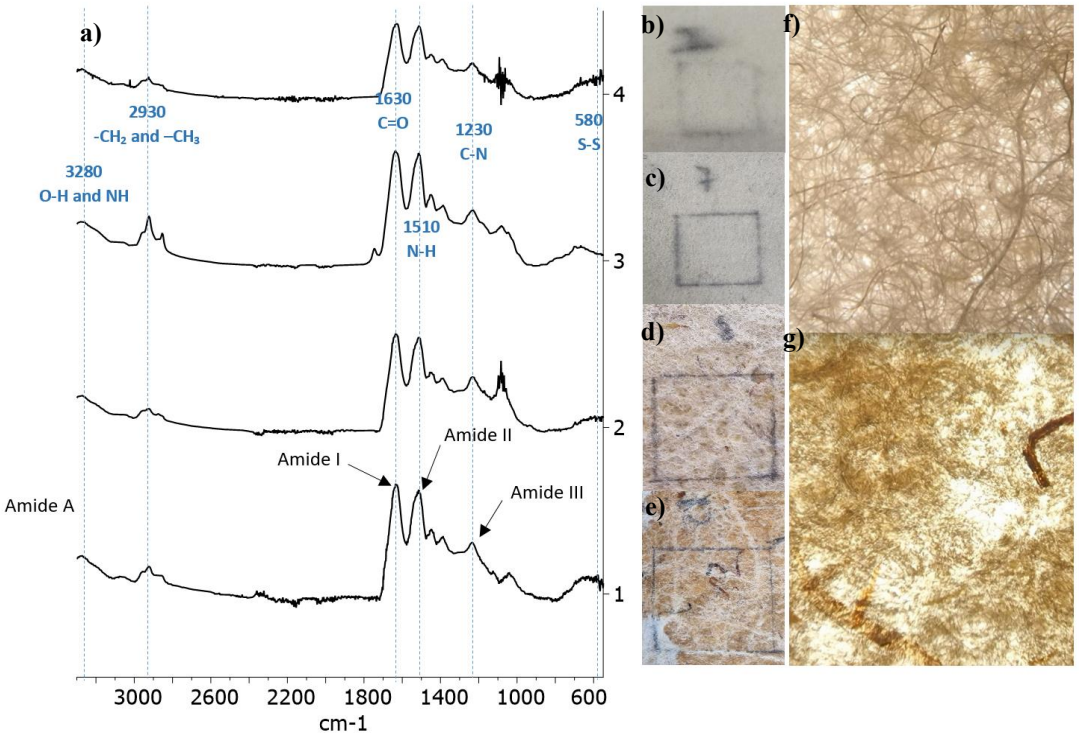
Wool fibers contain approximately 95% keratin, one of the most abundant structural proteins; however, a significant portion of wool waste remains underutilized.[1] Wool consists largely of keratin, a cysteine-rich protein whose disulfide bonds provide structural stability while enabling chemical and physical modification.[2] In this study, ATR-FTIR spectroscopy combined with machine learning was used to investigate chemical changes in wool after mechanochemical treatment. A Random Forest model achieved high accuracy (0.97), identifying key spectral regions related to amide and disulfide groups. Hot pressed wet sheep wool samples showed increased oxidation and disulfide bond cleavage, indicating keratin structural rearrangement associated with film formation.



a) ATR-IR spectra of representative wool sheet samples: b) M1 (raw wool sheet), c) M2 (hot-pressed wool sheet), and d)-e) M3–M4 (hot-pressed wet wool sheets). Stereo microscopy images of M1 and M4, respectively. (f, g), 10x magnification.

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ASYMMETRIC HYDROGENATION OF 3H-AZEPINES VIA CATALYTIC KINETIC RESOLUTION: ACCESS TO ANTI-DISUBSTITUTED AZEPANES

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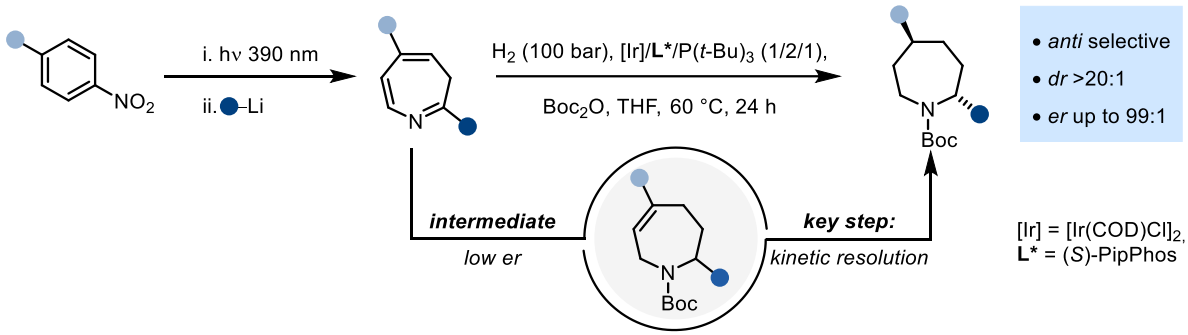
Azepane is one of the most important *N*-heterocyclic systems used in drug discovery, being present in natural products and bioactive molecules.[1] Yet compared to other saturated *N*-heterocycles, the preparation of azepanes usually requires tedious multistep synthesis, with enantioselective approaches being limited to monosubstituted substrates.[2] When escaping flatland is at the forefront of drug discovery strategy, developing methods to access architecturally complex molecules and different isomers of one core is paramount.

In this work, we report the diastero- and enantioselective synthesis of *anti*-disubstituted azepanes via Ir-catalyzed hydrogenation of the azepine precursors.[3] A mixed-ligand approach leads to the selective formation of the *anti*-stereoisomer by kinetic resolution. Several di-aryl, alkyl and heteroaryl substituted azepanes were synthesized with a high diastereoselectivity (dr >20:1) and enantioselectivity (up to 98:2 er). Mechanistic experiments showed the reaction proceeds first *via* the formation of a partially reduced intermediate with a low enantiomeric ratio. The last hydrogenation step is controlled by kinetic resolution and leads exclusively to the enantiopure *anti*-isomer.



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SYNTHESIS OF PURINE-INDOLE CONJUGATES IN TWO STEPS FROM TRIAZOLYLPURINES

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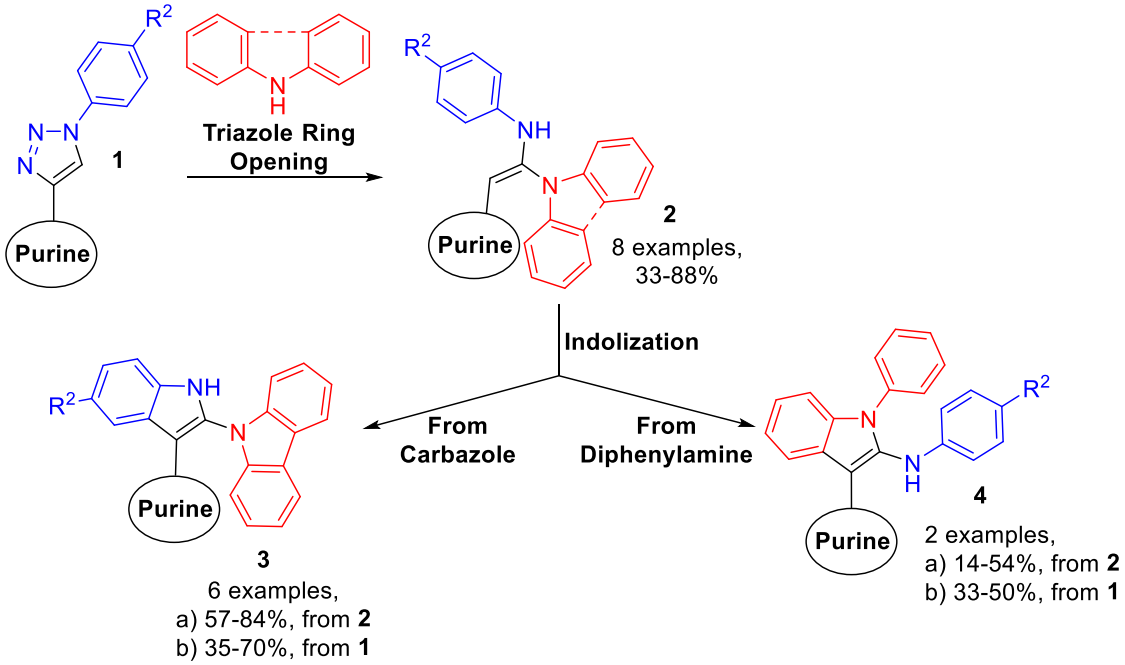
A metal-free synthetic approach towards purine-indole conjugates from triazolylpurines was developed by our group in 2025.[1] Synthesis started with the triazole ring opening reaction of triazolylpurines **1** with aromatic *N*-nucleophiles, which led to the formation of *N*-aryl ethene-1,1-diamines **2**. Afterwards, compounds **2** underwent cyclization reaction in the presence of iodine with the formation of indole ring containing products. Depending on the applied *N*-nucleophile, the last step provided selectively 1*H*-indoles **3** or 1-aryl-1*H*-indoles **4**. Reactions were done in step-by-step or one-pot reaction approaches. This method allowed the synthesis of indole derivatives with *N*-heteroatom-containing substituents at the indole *C*2 position.



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A RAPID ONE-POT STRATEGY TO FUNCTIONALIZED THIETANES AND THEIR OXIDIZED DERIVATIVES FROM OXETANES

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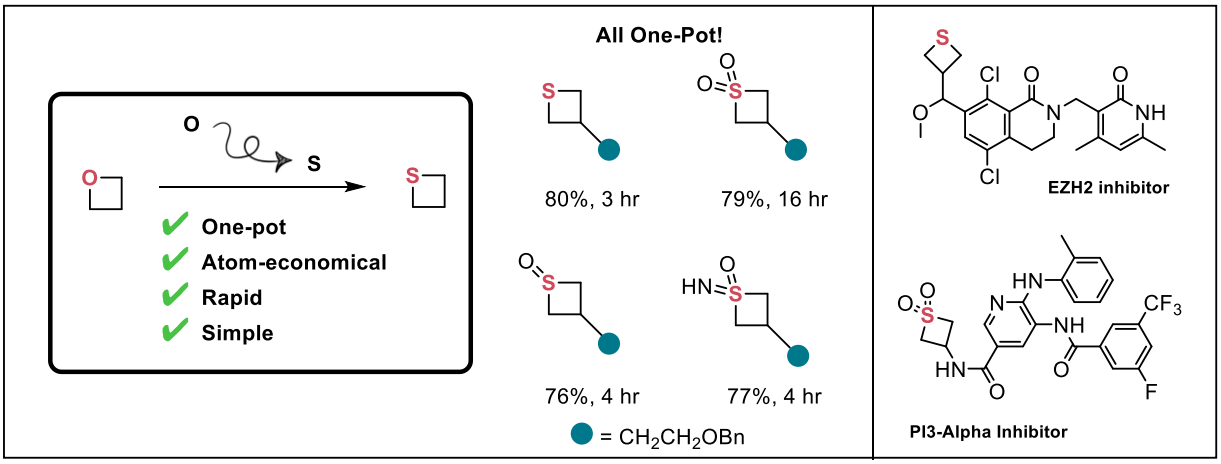
Four-membered heterocycles are valuable motifs in medicinal chemistry and synthetic methodology.[1] While oxetanes have emerged as versatile and readily accessible building blocks, their sulfur analogues, thietanes, remain comparatively underexplored due in part to the limited availability of efficient synthetic methods. Among the different approaches reported to access thietanes, strategies involving formal O-to-S atom exchange using oxetanes as substrates are particularly attractive, especially in the context of medicinal chemistry. However, these methods typically rely on multistep sequences, often involve relatively unstable dibrominated intermediates, and are limited in scope or require specialized photochemical protocols, thereby reducing their practicality. Herein, we report a streamlined one-pot strategy for the direct conversion of oxetanes into thietanes, thietane monoxides, thietane dioxides, and thietane sulfoximines. This operationally simple transformation enables rapid and relatively atom-economical access to functionalized thietanes and their derivatives from readily available oxetane precursors while avoiding the isolation of reactive intermediates. This approach offers a practical route to thietane scaffolds and may facilitate their broader exploration in synthetic and medicinal chemistry.



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A CRYSTALLINE PHOTOCAGE WITH ADIABATIC QUANTUM CHAIN FOR EFFICIENT TWO-PHOTON UNCAGING AND IMAGING

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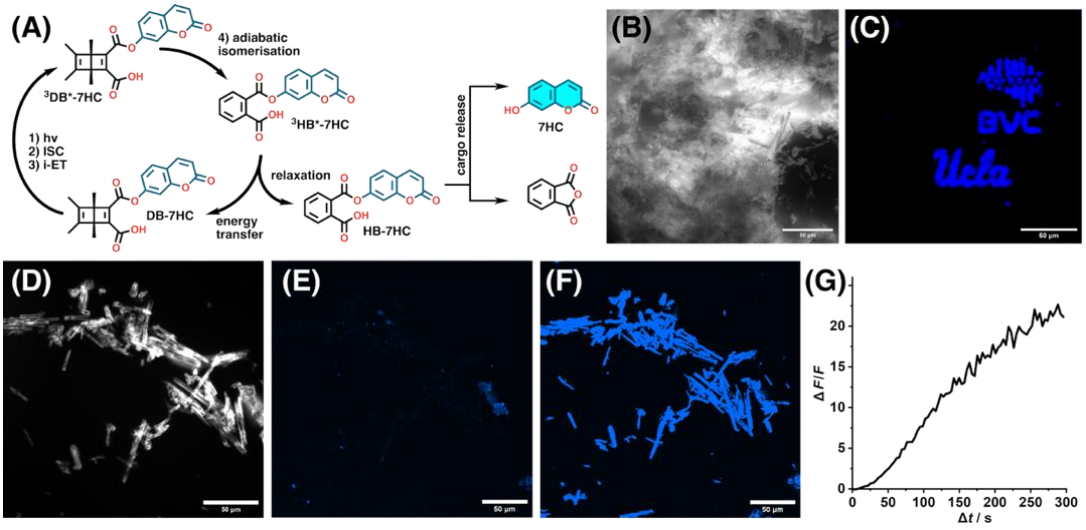
Two-photon (2P) excitation is the simultaneous absorption of two low-energy photons happening in exceptionally high photon flux, obtained by focused laser light. 2P microscopy is a useful imaging method employing this phenomenon to enable 3D imaging. Photocaging is a process, where a bioactive cargo is masked by a photolabile protecting group (photocage) to be released by targeted illumination. This is attractive in 2P imaging, where the release (uncaging) can be precisely controlled by manipulating the focal point of the laser. However, 2P excitation is a sporadic event, limiting the efficiency. Herein we present a chemical amplification platform using a crystalline system of dewar-benzene-7-hydroxycoumarine ester, in which an adiabatic quantum chain reaction proceeds, generating hundreds of uncaged cargo per absorbed photons. During adiabatic excited-state reactions the photoproducts can transfer their excitation energy to the neighbouring molecule and start a new uncaging cycle. A quantum yield of Φ=400 has been measured, orders of magnitude higher than the theoretically achievable Φ=1.0 in solution and the 2P uncaging has been carried out successfully at 690-770 nm wavelength range. The power- and wavelength dependence of the uncaging has been quantified and photopatterning experiments showcasing complex structures, such as the logos of our institutes have been carried out using directed two-photon irradiation. [1]



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ELECTROCHEMICAL SYNTHESIS OF SPIRO-HEMIAMINAL ETHERS FROM FURFURAL DERIVATIVES

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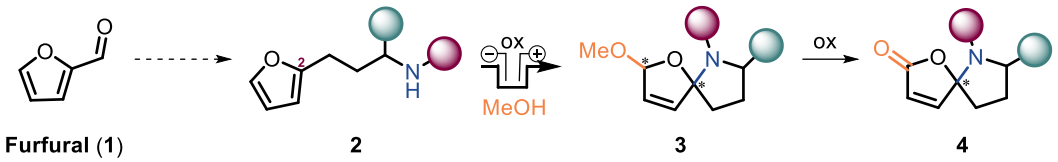
Furfural (**1**), a furan derivative, is one of the products obtained in large quantities during biomass processing.[1] As part of the effort in our group to transform furfural derived substrates into value-added building blocks employing electrosynthesis, we have developed new method for obtaining [4.4]-spirocyclic hemiaminal ether scaffolds **3** from furan derivatives **2**.



The [4.4]-spirocyclic scaffolds **3** were assembled through electrochemically induced *C-N* bond formation between amide and furan ring in substrates **2**. Lactones **4** could be obtained by further oxidative transformation of the methoxy group into a carbonyl group. The method provides a simple way to construct the [4.4]-spirocyclic hemiaminal ether motif observed in several biologically active natural products.

Acknowledgements: This work has been funded by Recovery and Resilience Facility (RRF) (5.2.1.1.i.) grant Nr. 34/OSI/DG (2025) and project TRANSPHARM (European Union Horizon Europe research and innovation program grant No. 101057816).

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IODINE(III) REAGENT ENABLE CATALYST- AND LIGHT-FREE FLUOROMETHYL RADICAL CASCADE REACTION

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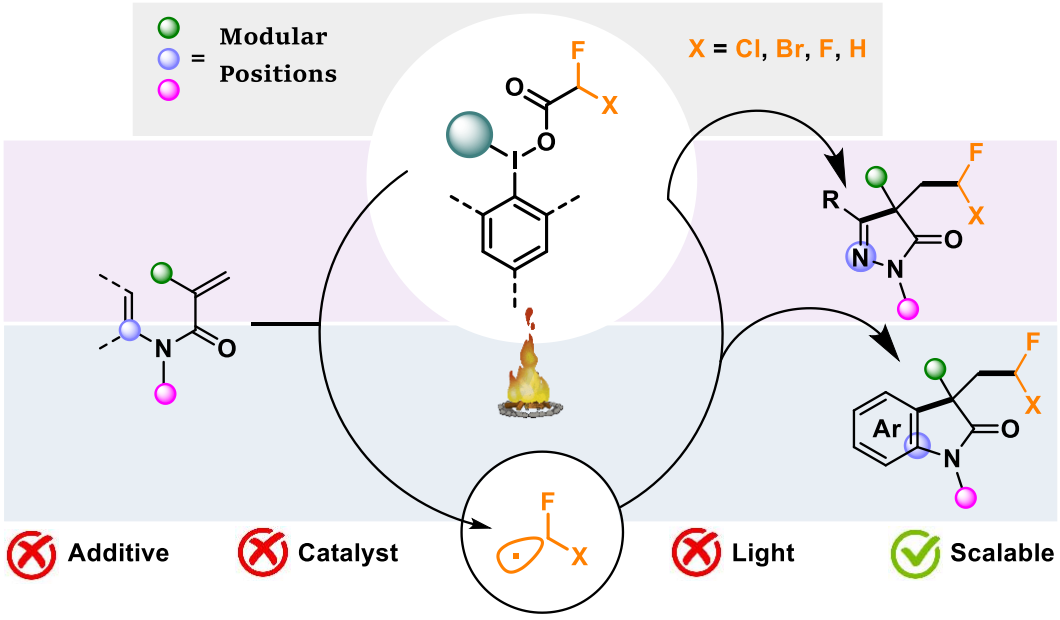
While conventional radical fluoroalkylation typically necessitates exogenous catalysts or photoactivation to surmount significant kinetic barriers, here we report a versatile cascade cyclization of alkenes enabled by newly developed iodine(III) reagents as autonomous radical triggers. This protocol operates under remarkably mild, catalyst- and light-free conditions, requiring no chemical additives. The innate reactivity of the iodine(III) species facilitates the direct generation of diverse fluoromethyl radicals (-CHFX where X = Cl, Br, F, H), providing expedient access to functionalized pyrazolones, oxindoles, and related heterocycles. By obviating the requirement for external activation, this strategy establishes a robust and sustainable paradigm for the precise installation of fluorinated motifs into complex molecular frameworks.



Acknowledgement
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CONTROLLED MONO-, DI-, AND TETRA-BORYLATION OF DABNA-TYPE MR-TADF SCAFFOLDS

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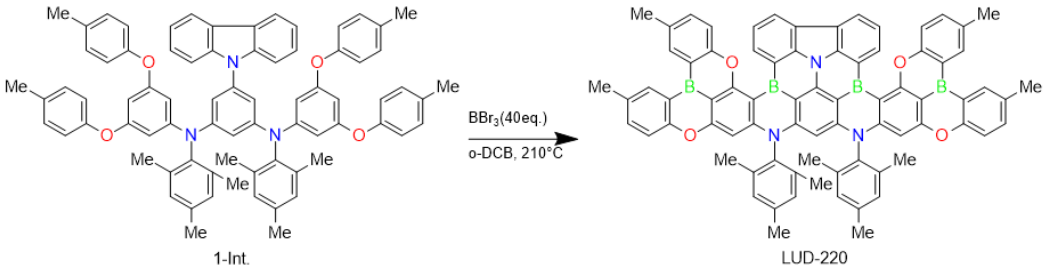
B/N-doped multiple-resonance thermally activated delayed fluorescence (MR-TADF) emitters are attractive OLED materials because they combine narrowband emission with efficient exciton harvesting[1,2]. However, their broader development remains limited by demanding, substrate-specific syntheses. Here, we examine BBr_3-mediated one-shot electrophilic borylation as a concise route to multi-boron MR frameworks and evaluate how precursor architecture controls the number of C–H borylation events.

Under optimized BBr_3/o-DCB conditions, a few extended DABNA-type precursors underwent fourfold borylation (see below), whereas related carbazole/dibenzofuran-containing substrates afforded diborylated products. More sterically or electronically constrained analogues gave only monoborylated compounds, defining clear structural limits for productive multiple borylation. During attempted synthesis of F-DABNA, the same conditions promoted fluorine-to-bromine substitution, giving Br-DABNA as the major product and revealing a useful late-stage halogen-exchange/diversification pathway for DABNA-type frameworks.



The resulting emitters were characterized by steady-state and time-resolved PL, with emission centered at 444 nm, narrow emission bands with FWHM of 19 nm, and PL quantum yields of 36%. These results establish BBr_3-mediated one-shot borylation as a practical entry to structurally diverse MR-TADF scaffolds and clarify the substrate features required for mono-, di-, and tetra-borylation.

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SYNTHESIS OF BENZOXAZINONE DERIVATIVES BY SIMULTANEOUS ACTIVATION OF CO AND CO_2

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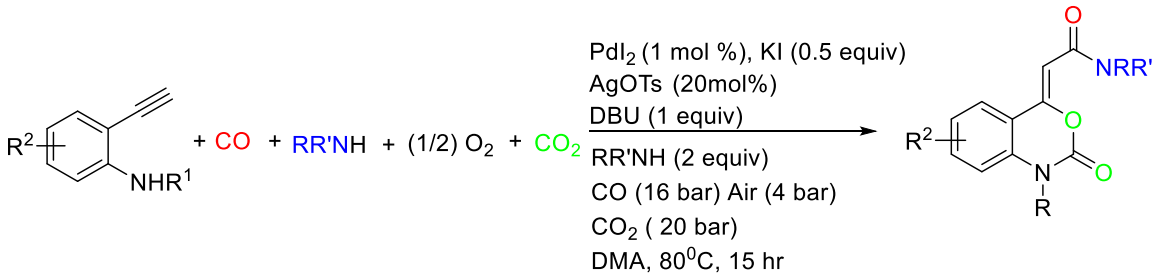
The activation of CO and CO_2 as a C-1 source in organic synthesis is an important area of research. The activation of carbon oxides leads to the synthesis of heterocycles having significant importance for the development of mankind.[1,2] Among heterocyclic derivatives, 1,4-diihydro-2*H*-benzo[*d*][1,3]oxazin-2-ones are of significant importance due to their biological properties.[3] Here, we have successfully performed the synthesis of benzoxazinone derivatives by simultaneous incorporation of CO and CO_2 onto 2-ethynylanilines.[4] The synthetic process consists of PdI_2-catalyzed oxidative monoaminocarbonylation of the triple bond of 2-ethylnylanilines followed by DBU/Ag^+–promoted CO_2 insertion with 6-*exo*-*dig* cyclization. Reactions were carried out by using PdI_2 (1 mol%) and KI (0.5 equiv) in DMA as solvent at 80^0C under 20 bar of a 4:1 mixture CO–air and 20 bar of CO_2 in presence of a secondary amine (2 equiv), DBU (1 equiv) and AgOTs (20 mol%). Products were obtained from differently substituted 2-ethynylanilines and various secondary amines in moderate to high yield (50-95%). The compounds obtained were characterized by various spectroscopy techniques (^{1}H NMR, ^{13}C NMR, HRMS, IR, and XRD for representative examples).



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ENABLING DIVERSITY-ORIENTED SYNTHESIS OF DRUG-LIKE ATROPISOMERS

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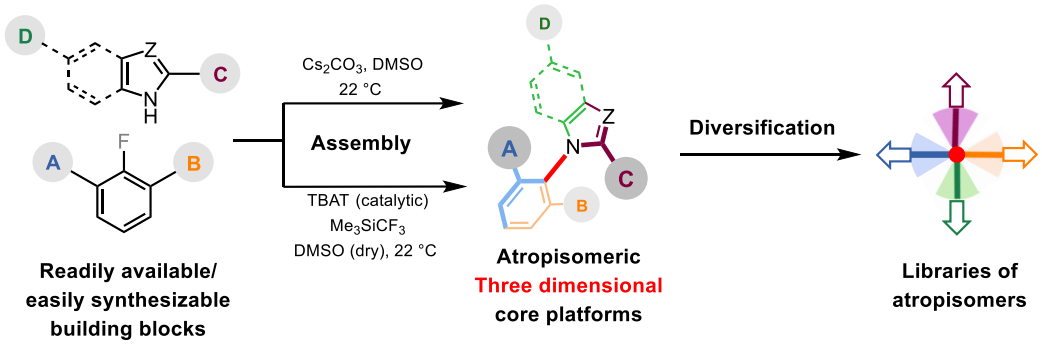
Atropisomers are chiral conformational isomers originating from restricted rotation around a sterically hindered single bond.[1] These compounds possess unique three-dimensional shape and are intrinsically sterically hindered, a feature which renders their synthesis more challenging than for analogous non-atropisomeric compounds. Atropisomerism is becoming increasingly more attractive in medicinal chemistry, as a way to tune pharmacological properties.[2] The Paioti research group has been interested in developing ways to synthesize rapidly a broad range of drug-like atropisomers by diversity-oriented synthesis approaches. In our first foray, we have shown that nucleophilic aromatic substitution (S_NAr) reaction enables synthesis of highly modifiable and difficult-to-access heterobiaryl C-N atropisomers.[3] We identified that fluoroarenes react with a large assortment of N-H heterocycles promoted by Cs_2CO_3 in DMSO, or catalytically, based on a



fluoride-catalyzed reaction promoted by Me_3SiCF_3. Reactions are fast, usually complete in seconds to hours, and enabled synthesis of a large, diverse and diversifiable library of >250 atropisomeric compounds which will be tested in medicinal chemistry screenings.

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DIVERGENT HOUSANE SYNTHESIS VIA INTRAMOLECULAR [2 + 2] CYCLOADDITION OF 1,4-DIENES

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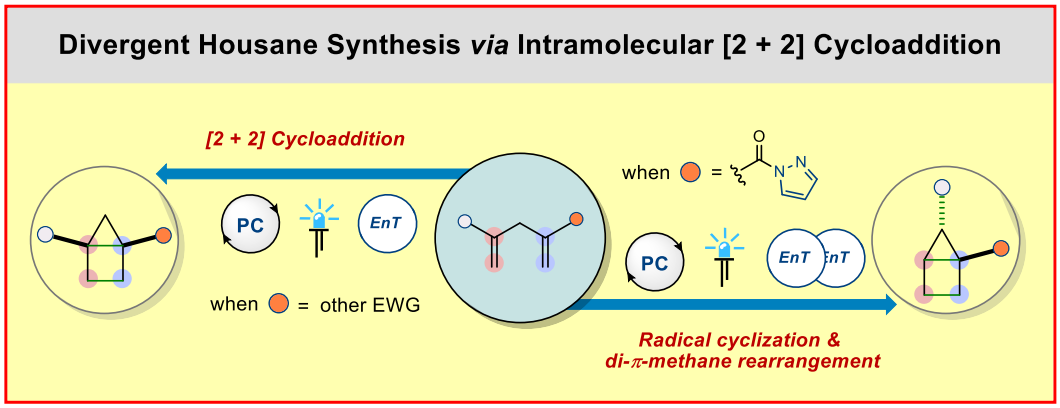
Highly strained ring systems serve as privileged building blocks for the synthesis of sp^3-rich, three-dimensional scaffolds, which are increasingly recognized as beneficial motifs due to their improved lipophilicity and metabolic stability.[1,2] One of these promising precursor platforms is the bicyclo[2.1.0]pentane framework, better known as "housanes", which has been challenging to access synthetically for the need to build up a high degree of ring strain. Here, we disclose a novel, divergent strategy to access a broad family of housanes through an intramolecular energy-transfer-mediated [2 + 2] cycloaddition of 1,4-dienes. The employed method favors strain build-up over the competing di-π-methane rearrangement, thereby expanding the toolkit for efficient exploration of housane chemical space. Substituent engineering enables switching between single and double energy-transfer pathways to deliver 1,3- and 1,2-disubstituted housanes with excellent stereocontrol and broad functional group tolerance. Mechanistic studies and density functional theory calculations support an energy-transfer pathway and rationalize the observed selectivity.



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SYNTHESIS OF PYRIDINIUM LUMINOPHORES FOR DEVELOPMENT OF BIOGENIC AMINE SENSORS

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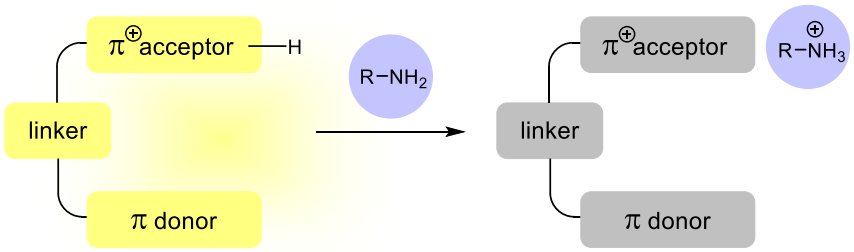
In recent years solid state organic luminophores have garnered attention for their potential uses in light-emitting diodes because of their low cost of production. One of the breakthroughs in solid-state organic luminophores was the discovery made by K. Leduskrasts in 2019[1] where solid-state luminescence was achieved by utilizing $\pi^+ - \pi$ interactions in a pyridinium – carbazole system. Further research by K. Leduskrasts and his team led them to discover the structure of derivatives achieving quantum yields up to 85 %.[2]

In collaboration with the Institute of Atomic Physics and Spectroscopy, we've found that such type of luminophore can change it's optical properties when exposed to ammonia and acetic acid vapors, which suggests their potential use as a solid-state gas sensor.[3] Further modifying the structure of pyridinium based luminophores led us to a structure that is capable of detecting ammonia in concentrations as low as 20 ppm.



Luminescent *Loss of luminescence*

Acknowledgements

The research is financed by the "Biomedical and Photonics Research Platform for the Development of Innovative Products" – "BioPhoT" – implemented within the framework of the long-term national research program "Innovation Fund – Long-Term Research Program", financed by the Ministry of Economics (No IVPP-EM-Innovation-2024/1-0002), grant no. OSI_PIP_BioPhoT-2025/1-0013 "Optical Sensor Solution for the Smart Packaging of Fresh Seafood – FRESHWAVE".

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SYNTHESIS OF POLYMER-SUPPORTED LEWIS BASE CATALYSTS FOR DYNAMIC KINETIC RESOLUTION IN CONTINUOUS FLOW

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Dynamic kinetic resolution (DKR) of secondary alcohols is a powerful synthetic method for the transformation of racemic starting materials into optically pure products.[1] It relies on two parallel processes – kinetic resolution (KR) and simultaneous racemization of the unreacted enantiomer (Fig. 1).

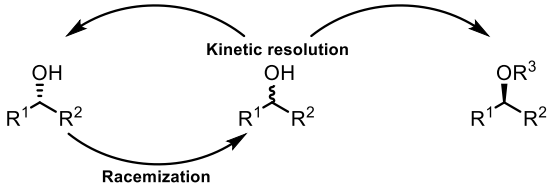

Fig. 1. DKR of secondary alcohols.

A vast majority of the DKR protocols described in the literature use enzymes to carry out the KR. This is because transition metal racemization catalysts can form complexes with various organocatalysts, therefore stopping both catalytic cycles. This can be circumvented by attaching both catalysts to an insoluble matrix, therefore isolating the catalysts and preventing the unwanted complexation. Furthermore, this would enable the use of these catalysts in packed-bed reactors under flow chemistry conditions.[2] In this work, chiral acylation catalysts were immobilized onto *Merrifield* resin. The obtained catalysts were tested in the KR of 1-phenylethanol (Fig. 2).

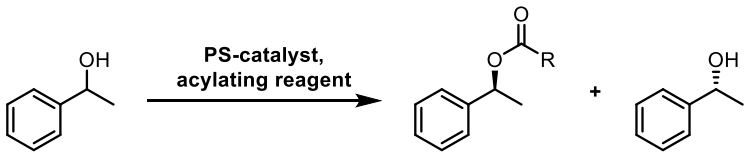

Fig. 2. KR of 1-phenylethanol using polymer supported organocatalysts.

Acknowledgements. The research is financed by the Recovery and Resilience Facility project "Internal and External Consolidation of the University of Latvia" (No.5.2.1.1.i.0/2/24/I/CFLA/007) grant no. ESS2025/492d27 "Dynamic kinetic resolution of secondary alcohols and hemiaminals under flow chemistry conditions".

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CATALYTIC DESYMMETRIZATION OF [2,2]PARACYCLOPHANES

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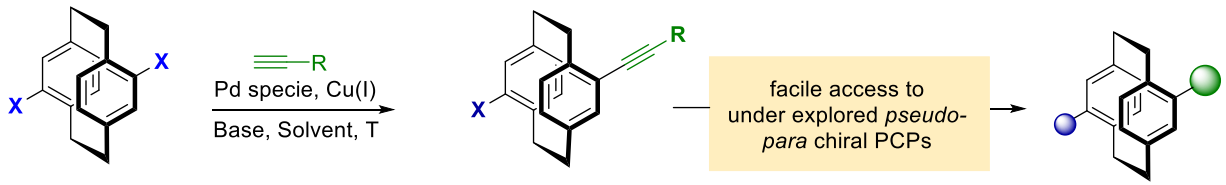
During the last few years, intensive research is being carried out on chiral backbones based on rigid and stable [2.2]cyclophanes (PCPs), as they are becoming attractive chiral ligands in asymmetric catalysis and other fields.[1a] From a synthetic point of view, selective functionalization at specific positions of the PCP backbone has encountered acceptable success,[1b] but stereoselectivity is a crucial pitfall, as enantiopure PCPs are still obtained by methodologies based on chromatographic resolutions.[2] We will present our preliminary results applying the state of the art in asymmetric alkynylations to pursue desymmetrization of pseudopara[2.2]paracyclophanes.[3]



Acknowledgements: We thank the Basque Government (EJ, grant IT1741-22) and Agencia Estatal de Investigación (grant PID2023-147050NB-I00//MICIU AEI/10.13039/501100011033) for financial support. D. A. acknowledges EJ for fellowship.

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CHEMICAL TRANSFORMATIONS OF SUGAR DERIVATIVES IN LIQUID SO_2

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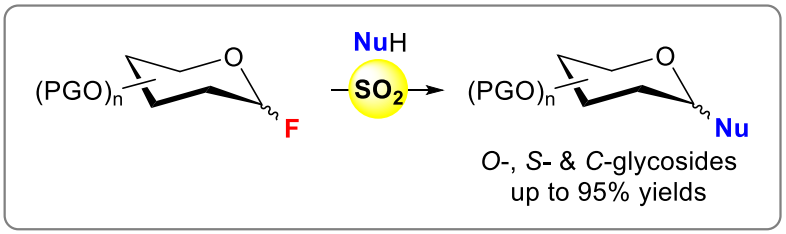
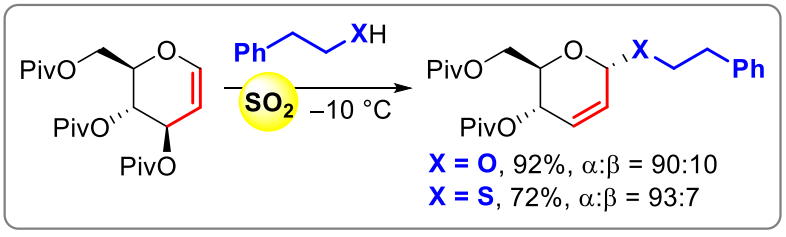
Liquid SO_2 is one of the few polar aprotic solvents that possess Lewis acidic properties. Thus, it can be applied as an alternative for conventional solvents for traditionally Lewis acid promoted and/or carbenium ion mediated chemical transformations.

Herein we present chemical transformations of sugar derivatives that can be facilitated by liquid SO_2 as a reaction medium in the absence of any external additive. Firstly, glycosylation reaction between differentially protected glycosyl fluorides as glycosyl donors and various nucleophiles have been developed.[1] Similarly, glycosylation between 2-deoxyglycosyl fluoride and alcohol has been observed in high yield and stereoselectivity. Secondly, reactivity of glycals containing different protecting groups has been studied towards Ferrier rearrangement with variable results.

Glycosylation



Ferrier rearrangement



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POLY(ITACONIC ACID) BASED HYDROGELS LINKED BY DYNAMIC COVALENT AND SUPRAMOLECULAR CROSS-LINKS

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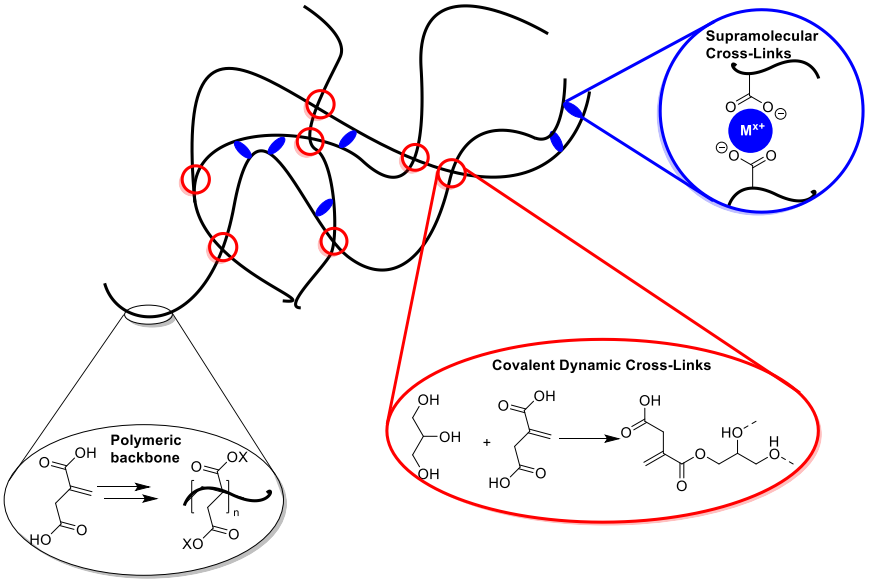
Finding alternatives for fossil-fuel derived materials is an important challenge in the task for more sustainability. However, the advantages of lower costs, easier modification and processibility, in comparison to most sustainable alternatives, results in e.g. acrylates being so widely used.

In here, we show the synthesis and optimisation of a fully bio-sourceable poly(itaconic acid) based hydrogel for a multitude of different applications. We show a significant increase of properties through a synergy of dynamic covalent (ester) and supramolecular (metal-ligand coordination) cross-links. While the polymeric backbone of the hydrogel is poly(itaconic acid), we first optimised the polymerisation process of itaconic acid by changing the degree of deprotonation. Furthermore, we developed a fully bio-sourceable method for a glycerine based cross-linker, that outperformed commercial fossil-fuel derived ones. Additionally, we investigated further doping of the material by introducing different types of metal-ion addition, which allowed us to significantly vary the materials properties. Solely by changing from no supramolecular cross-linkage to stronger coordination by exchanging sodium ions with calcium ions we changed the material from a soft, superabsorber to a strong material.



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SUSTAINABILITY-GUIDED DESIGN OF A MULTICATALYTIC SYSTEM FOR THE AEROBIC SYNTHESIS OF BENZIMIDAZOLES

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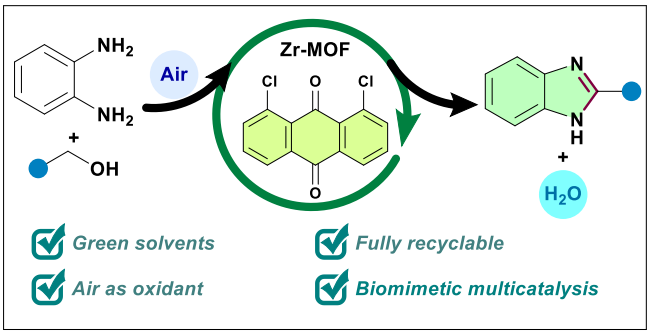
Benzimidazoles are important heterocycles in pharmaceuticals and fine chemicals;[1] yet numerous syntheses depend on mostly harsh reagents, stoichiometric oxidants, transition metals including toxic or noble metals, and/or non-benign solvents. On the other hand, our group has recently developed a tuneable MOF/co-catalyst based multicatalytic system to promote diverse aerobic oxidation reactions simply by altering the co-catalysts.[2] This past study opened the door for us to further proceed with a new multi-catalytic tool to oxidize commercially available alcohols which can be utilized as intermediates to synthesize some crucial heterocycles like benzimidazoles. Herein, we have reported a sustainability-guided design of a fully recyclable Zr-MOF-808/1,8-dichloroanthraquinone (1,8-DCA) to resolve recurring sustainability drawbacks in the synthesis of benzimidazoles, resulting in the development of a one-pot aerobic oxidative coupling of primary alcohols with 1,2-phenylenediamines to access 2-substituted benzimidazoles in good yields and functional group tolerance, using atmospheric air as the terminal oxidant. Using a green solvent like anisole for the reaction, developing a new water-based synthesis of the MOF rather using conventional DMF, enabling open air system instead of using pure oxygen, not only recycling the solid catalysts but also recovering and reusing the co-catalysts for further cycles were the primary attributes we have effectively emphasised in this work concerning sustainability.



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COPPER-CATALYZED ASYMMETRIC DEAROMATIVE CYCLIZATION TO ACCESS HEXAHYDROPYRROLIZINOINDOLONES

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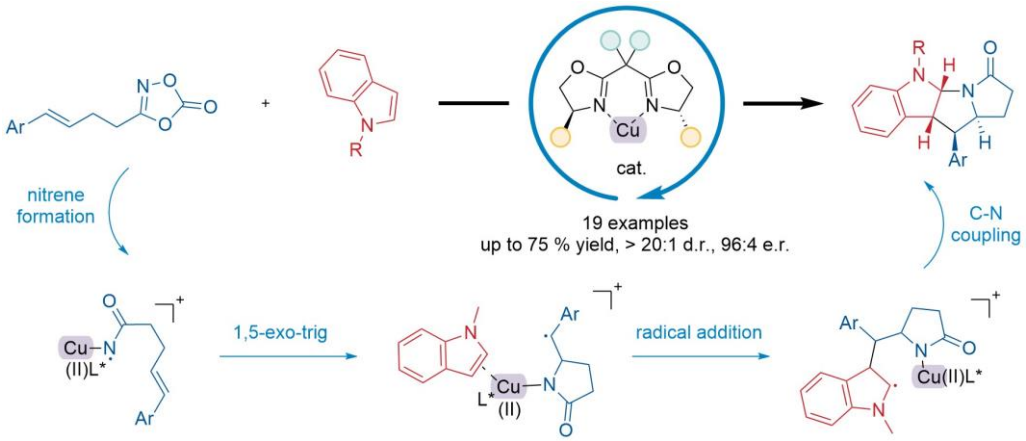
The catalytic asymmetric dearomatization (CADA) of indoles is a powerful strategy to access chiral polycyclic indolines, yet intermolecular cascade processes with precise regio- and enantiocontrol remain challenging.[1] Herein, we report a copper-catalyzed intermolecular asymmetric dearomative cyclization of indoles initiated by nitrene transfer, enabling efficient construction of pyrroloindoline scaffolds—key motifs in bioactive alkaloids[2]. Using a chiral copper catalyst and nitrene precursors, this method delivers complex polycycles bearing vicinal quaternary/tertiary stereocenters in up to 75% yield and 96:4 e.r. Mechanistic studies support a cascade pathway involving a high-valent copper-nitrenoid species, stereoselective radical addition at indole C3, and cyclization.

This work not only demonstrates a broad substrate scope and high functional group tolerance but also provides fundamental insights into transition-metal-catalyzed nitrene transfer dearomatization. These findings offer a robust synthetic tool for the late-stage functionalization of heterocycles and the total synthesis of complex indole-based natural products.



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ORGANOCATALYTIC DESYMMETRIZATION AS AN ACCESS TO ORTHOGONALLY PROTECTED *MYO*-INOSITOLS

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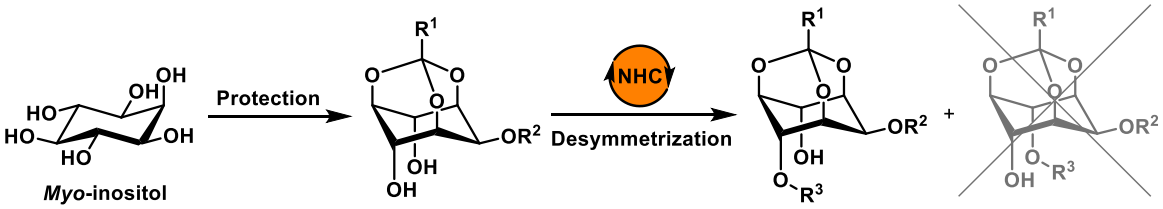
Myo-inositol and its derivatives possess important yet not deeply explored biological activities in living cells. Among both eukaryotic and prokaryotic organisms, inositol derivatives have multiple roles, e.g. during cell signalling or membrane transfer.[1] It is not surprising that there is a high demand for the synthesis of specific enantioenriched inositols. Some approaches have already been developed, such as desymmetric phosphorylation by Scott J. Miller *et al.*.[2]

In this project,[3] we present *N*-heterocyclic carbene (NHC) catalyzed approach to enantioenriched *myo*-inositol derivatives based on the desymmetrization process. After reaching the optimal reaction conditions, we analyse the feasibility of the methodology by reacting with different reaction partners or using various protecting groups on inositol. Subsequently, we report the synthetic utility of the products by their application in selected post-transformations. All of the results will be thoroughly discussed.



Acknowledgements: This work was supported by the Czech Science Foundation (24-12575S).

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SYNTHESIS OF FUCOSYLATED HUMAN MILK OLIGOSACCHARIDE ANALOGUES

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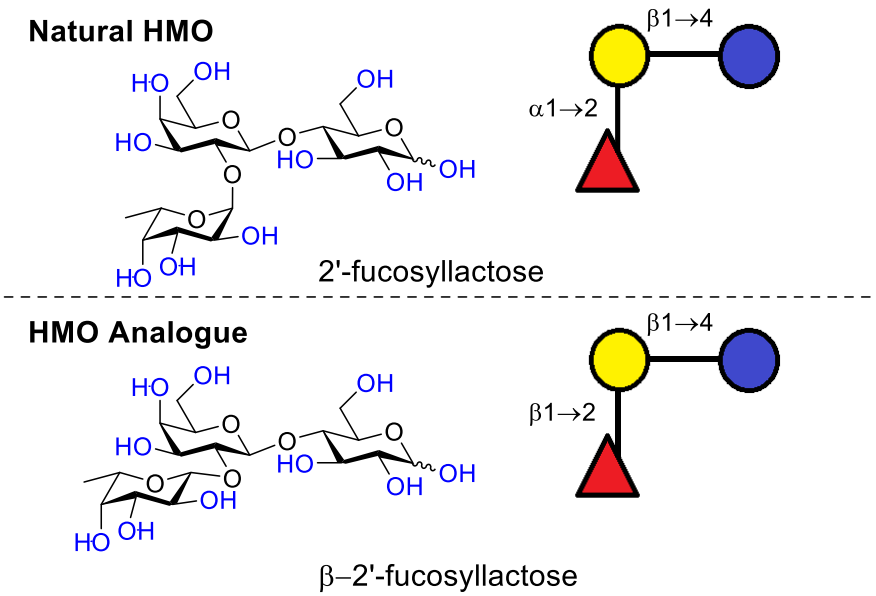
Human milk oligosaccharides (HMOs) mainly function as prebiotics. Additionally, HMOs help to regulate the T-cell production, act as decoys and antiadhesive antimicrobials to pathogens, alleviate allergy symptoms and even help to develop the brain.[1] HMO structures start from relatively simple linear trisaccharides and end up as branched oligosaccharides 30 monosaccharide units in size. The most common HMOs are fucosylated HMOs, in which in nature fucose is connected with α-glycosidic bonds to other saccharides.[2] While α-glycosidic bond is the thermodynamic one, it is harder to synthesize.[3] As such, we have synthesised HMO analogues using a simpler route, where fucose is connected to lactose with a β-glycosidic bond. These analogues have been tested on different bacteria for prebiotic activity.



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ACCESSING MEDIUM-SIZED BRIDGED HETEROCYCLES VIA ENT-CATALYZED INTERMOLECULAR DEAROMATIVE (5+4) CYCLOADDITION OF FURANS AND OXAZOLES

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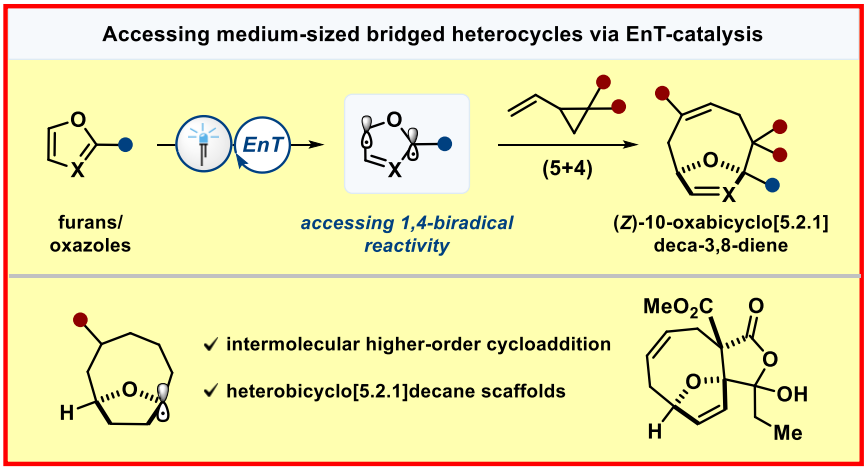
Medium-sized bridged heterocycles constitute highly valuable structural motifs frequently encountered in bioactive natural products and medicinal chemistry. Nevertheless, their broader exploration remains limited because concise and modular synthetic approaches are scarce, owing to unfavorable enthalpic and entropic factors associated with their synthesis. To address this issue, energy-transfer-mediated dearomatization of monocyclic heteroarenes, in combination with suitably designed biradical acceptors may offer new opportunities for higher-order intermolecular cycloaddition reactions.

In this work, we report an energy transfer (EnT)-catalyzed intermolecular (5+4) dearomative cycloaddition of furans and oxazoles with vinyl cyclopropanes, affording direct access to (*Z*)-10-oxabicyclo[5.2.1]deca-3,8-diene scaffolds in a single step. This reactivity, inaccessible under thermal conditions, proceeds through a distinct diene-type 1,4-biradical intermediate generated *via* visible light triplet sensitization. The resulting partially unsaturated cycloadducts provide versatile handles for downstream functionalization, enabling modular access to heterobicyclo[5.2.1]alkane motifs and highlighting their potential as versatile building blocks in synthetic chemistry.



ENANTIOSELECTIVE α-AMINATION OF CARBONYL COMPOUNDS USING AMMONIA

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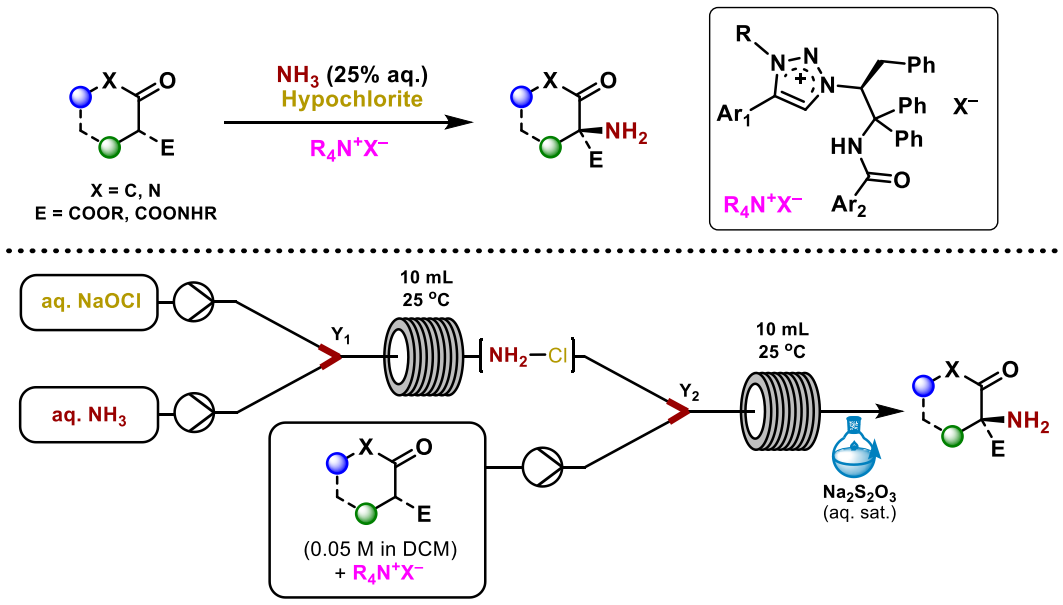
A direct and operationally simple α-amination protocol on carbonyl compounds has been reported. Ammonia solution in presence of hypochlorites provides the necessary oxidative conditions which can affect this versatile transformation using ammonium ion based phase transfer catalysis.[1] Most importantly, an enantioselective protocol has been established using triazolium salts as chiral phase transfer catalysts to achieve the desired α-amination with good enantioselectivity on β-ketoesters and oxindoles.



For further applications of the method, we designed a continuous flow setup where the reactive intermediate (NH_2Cl) is generated prior to reacting with the enolate. With this setup, the competing α-chlorination pathway can be completely avoided and reaction times can be reduced to five minutes with up to 99% NMR yield.

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SYNTHESIS OF NOVEL CHIRAL PYRROLIDINE-BASED BIHETEROCYCLIC AMINO ACID ESTERS

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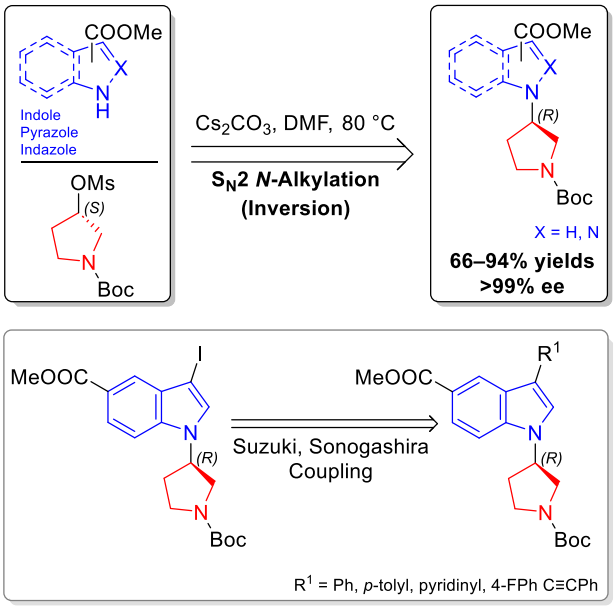
Biheterocycles are important scaffolds in medicinal chemistry owing to their structural diversity and biological relevance[1]. Herein, we report the stereoselective synthesis of new chiral indole-, pyrazole- and indazole–pyrrolidine hybrids as heterocyclic *N*-Boc-amino acid esters. The method involves nucleophilic substitution of heterocyclic carboxylates with enantiomerically pure *N*-Boc-3-methanesulfonyloxypyrrolidines, affording the desired products in good to excellent yields with inversion of configuration. Additional diversification was achieved through Suzuki–Miyaura and Sonogashira cross-coupling reactions, enabling aryl, heteroaryl, and alkynyl substitution. Structural and stereochemical assignments were confirmed by chiral HPLC, X-ray crystallography, and advanced NMR analysis.



1 Singh, A. K.; Kumar, A.; Singh, H.; Sonawane, P.; Paliwal, H.; Thareja, S.; Pathak, P.; Grishina, M.; Jaremko, M.; Emwas, A.-H.; Yadav, J. P.; Verma, A.; Khalilullah, H.; Kumar, P. *Pharmaceuticals* **2022**, *15*, 1071.

SYNTHESIS OF 7-SUBSTITUTED AMINOQUINAZOLINES AND THEIR PLASMEPSIN X INHIBITORY POTENCY

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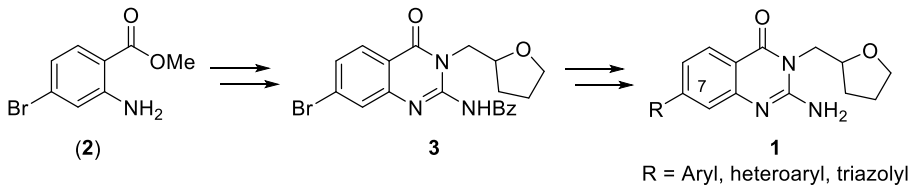
Malaria is a parasitic infection caused by *Plasmodium spp.* WHO report estimated ~282 million malaria cases with over 600 000 deaths in 2024.[1] Emerging drug resistance stipulates need for development of novel antimalarials acting on yet unexploited drug targets. One of such targets are malaria aspartic proteases (AP). *Plasmodium spp.* expresses 10 AP called plasmepsins (plm). Some of plms, like plm X, play an intricate role in parasite's survival.[2] Based on our previous research[3] we report synthesis of 7-substituted aminoquinazolines **1** and their plm X inhibitory potency. The synthesis begins with commercially available 4-bromoanthralic acid methyl ester (**2**) which is transformed into core quinazolinone **3**. Phenyl or pyridyl fragments were introduced by using Suzuki or Stille coupling while triazole ring was introduced by using Sonogoshira and CuAAC reactions.



Enzymatic assay against plm X showed IC_{50} values of several aminoquinazolines **1** at submicromolar range, rendering these compounds as promising hits for further optimization studies.

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THE ESSENCE OF *CINCHONA* CATALYST

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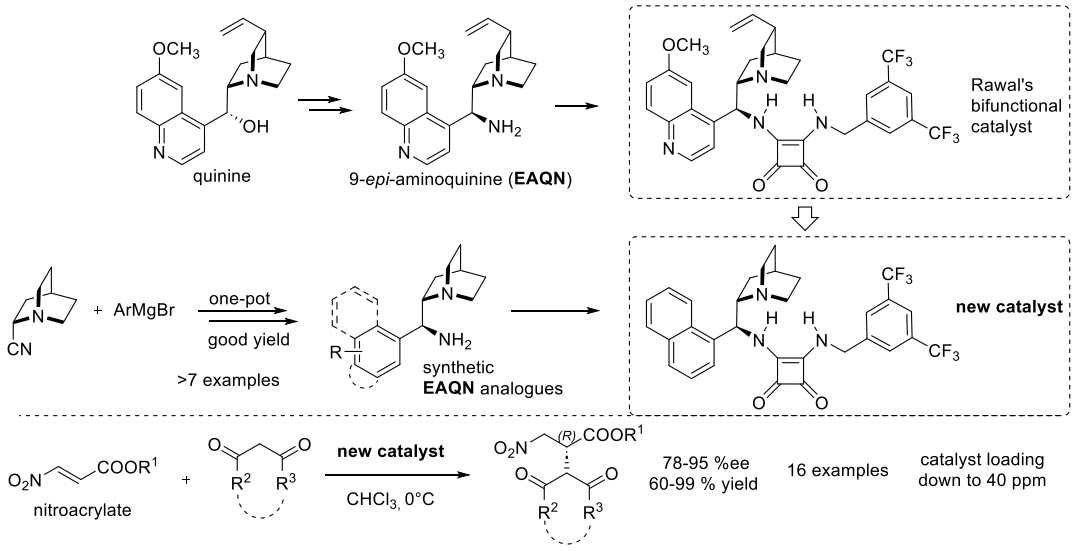
A limited set of chiral, mostly natural scaffolds forms the backbone of contemporary organocatalysis. These include *Cinchona* alkaloids, modified by replacing the hydroxyl group with amine and further converted to a hydrogen-bond donor moiety, as in Rawal's squaramide. The multitude of functional groups, including a hydrogen bond donor, quinoline ring, tertiary amine, and pendant alkene may interplay in the catalytic reactions, but some of the roles are obscured while others act as mere spectators.



With this in mind we decided to remove most of the redundant complexity of the alkaloid, and streamline the synthesis of new fully synthetic *Cinchona*-inspired catalysts. Indeed, Grignard addition of arylmagnesium halides to an *α*-cyano-heterocyclic base followed by *in situ* reduction of intermediate imine formed an array of compounds resembling 9-*epi*-aminoquinine. These analogues, lacking the vinyl group and featuring simplified aromatic cores, were converted into bifunctional squaramides. In model addition reactions, these catalysts performed comparably to their natural counterparts. Furthermore, we applied them to the previously unexplored enantioselective addition of dicarbonyl nucleophiles to alkyl 2-nitroacrylates. The catalysts demonstrated superior activity, providing up to 99% yield and 95% ee. Notably, the system remained active at loadings as low as 40 ppm, maintaining modest yields and reasonable enantiocontrol.

VISIBLE-LIGHT SURFACE PATTERNING USING A MEROCYANINE PHOTOACID

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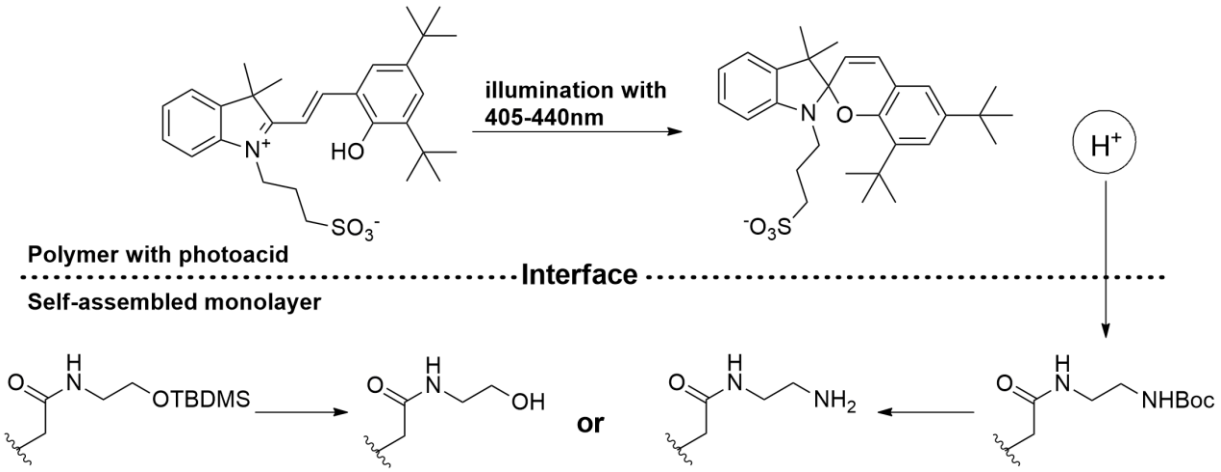
Surface patterning is central to modern materials science because it allows the creation of spatially resolved chemical, physical, or topographical domains, which are required for sensors, (bio)interfaces, microfluidics, and information-storage devices. Our previous work demonstrated that photoinduced local acidification within a merocyanine-photoacid-loaded PDMS stamp allows maskless, reversible, and microscale chemical patterning under visible light.[1] Herein, we present a FlexDym polymer stamp enriched with a photoacid for the generation of terminal –OH and –NH_2 groups on self-assembled monolayers. Furthermore, we produced patterns of various sizes using different illumination devices, thereby expanding the toolbox of soft-lithographic methods.



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NONLINEAR OPTICAL ACTIVITY OF THROUGH SPACE CHARGE TRANSFER ORGANIC SALTS

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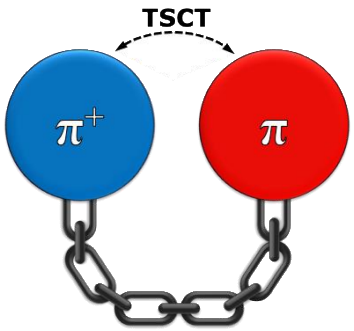
In nonlinear optics (NLO), intense light fields produce unusual material responses including frequency conversion and intensity-dependent refractive indices, that are used in telecommunications, imaging, data processing, and laser technologies.[1] NLO responses are classified by order (e.g., second, third, fifth), reflecting the degree of a material's NLO susceptibility. While organic materials with strong second- and third-order responses have been extensively studied, the fifth-order NLO behaviour of small organic molecules remains virtually unexplored.

Herein, we demonstrate that organic NLO material design featuring a heteroaromatic π^+- system placed in close spatial proximity to an electron-donating π system achieves efficient intramolecular through space charge transfer (TSCT), together with a strong NLO response. Compounds with a general structure **1** exhibited a pronounced negative fifth order NLO response without measurable third-order contribution as measured using the Z-scan method in solution. These findings highlight π^+-system containing TSCT architecture as a powerful design motif for engineering tailored, high-order optical nonlinearities in small-molecule systems and open new avenues for organic material development in advanced photonic devices.



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Acknowledgements
This work was funded by RRF grant No.30/OSI/PG (RRF project No.5.2.1.1.i.0/2/24/I/ CFLA/001) and Latvian Quantum Technologies Initiative under European Union Recovery and Resilience Facility no. 2.3.1.1.i.0/1/22/I/CFLA/001.

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STEREOSPECIFIC SUFEX REACTIVITY OF HIGHLY ENANTIOENRICHED SULFONDIIMIDOYL FLUORIDES

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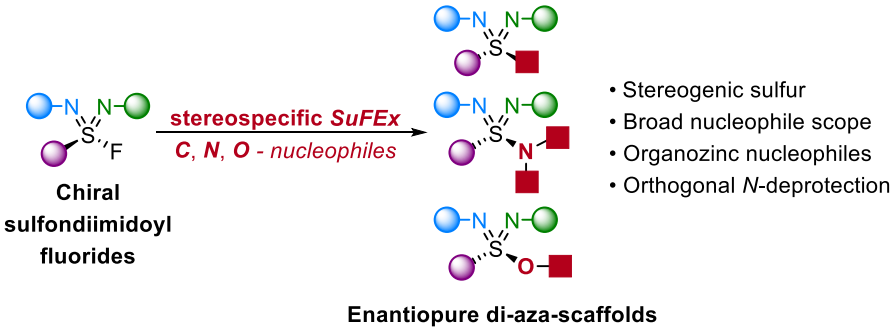
Sulfondiimidoyl fluorides are established SuFEx platforms, yet their potential in asymmetric synthesis remains largely unexplored. Herein we report stereospecific SuFEx transformations of highly enantioenriched sulfondiimidoyl fluorides to access sulfone diimines, sulfondiimidamides and sulfondiimidates with complete chirality transfer. For sulfone diimine formation, heteroleptic triorganozincates serve as mild and chemoselective carbon nucleophiles, enabling exclusive stereospecific allyl and benzyl transfer with broad functional group tolerance. The accomplished orthogonal deprotection of sulfondiimidoyl scaffolds demonstrates their additional synthetic flexibility. Collectively, this work establishes sulfondiimidoyl fluorides as robust chiral SuFEx building blocks for asymmetric synthesis.



Acknowledgements: This work was financially supported by RRF grant No. 02/OSI/ZG (RRF project No. 5.2.1.1.i.0/2/24/I/CFLA/001).

MECHANOCHEMICAL REDUCTIVE CLEAVAGE OF PHENOL ETHERS

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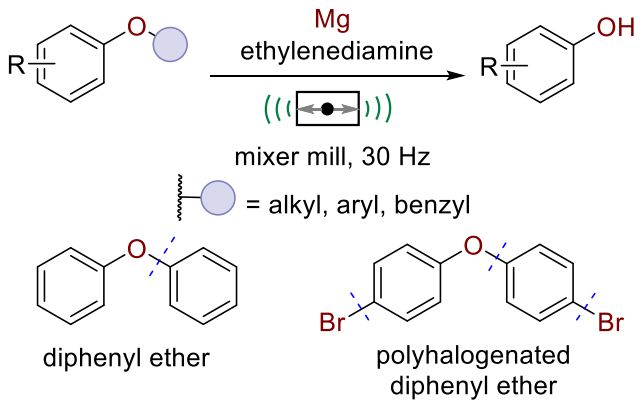
Phenolic moieties are common in a wide range of organic compounds, including natural products, pharmaceuticals, dyes, and agrochemicals. Their frequent presence requires chemists to develop reliable methods for preparation and cleavage of phenol ether, including selective protection and deprotection of phenolic hydroxyls during multi-step synthesis. However, carbon-oxygen bond in phenyl ethers is strong (dissociation energy: 200–347 kJ·mol^{-1}) and its cleavage typically requires harsh conditions and prolonged reaction times. For example, the reductive cleavage is typically performed by using alkali metals in liquid ammonia or amine solvents.[1] Mechanochemistry provides an attractive alternative, accelerating reaction rates and enabling efficient product formation under mild, solvent-free conditions.

Built on our prior work,[2] we report a mechanochemical method for the reductive cleavage of aryl ethers using magnesium metal and ethylenediamine under ball-milling conditions. This method enables efficient and quantitative cleavage of diverse aryl alkyl ethers, including the highly resilient diphenyl ethers. The reaction is solvent-free, operates at room temperature, and offers a practical approach for the degradation of polyhalogenated pollutants. The results of mechanistic studies will also be presented.



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2. Nallaparaju, V.J.; Satsi, R.; Merzhyievskyi, D.; Jarg, T.; Aav, R.; Kananovich, D.G. *Angew Chem Int Ed*. **2024**, *63(20)*, e202319449.

MECHANOCHEMICAL GENERATION AND SYNTHETIC APPLICATIONS OF SOLID ALKALI METAL AMIDE BASES

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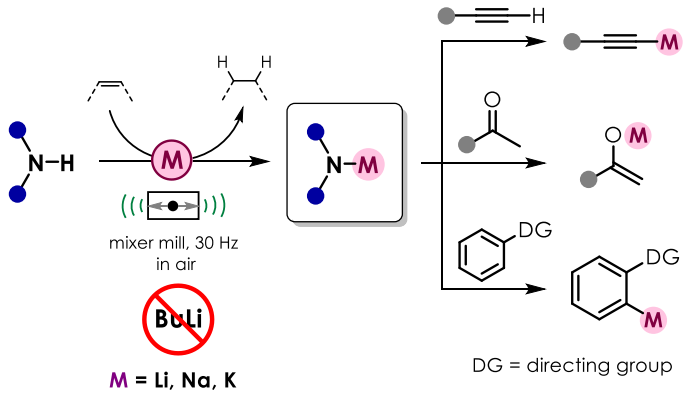
Herein, we present the mechanochemical generation of solid alkali metal amide bases, including their diisopropylamide and tetramethylpiperidide derivatives, directly from the respective alkali metals, olefins as sacrificial oxidants, and the corresponding amines using a mixer mill. This Birch-type reductive transformation avoids the use of BuLi, which is required for their preparation in solution.[1] The reaction proceeds efficiently without any solvents, although the presence of THF or hexane as liquid-assisted grinding agents accelerates the process. The reactions were performed at ambient temperature and can tolerate air. The solid-state generated amide bases were successfully applied to a range of transformations, including the enolization of ketones, the conversion of terminal alkynes into acetylides, and the directed ortho-metalation of aromatic substrates. We also present mechanistic studies performed using *in situ* PXRD and Raman monitoring to elucidate the role of mechanical force in initiating and sustaining this solid-state transformation.



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AGING EFFECTS IN MECHANOCHEMICAL AMIDE COUPLING MEDIATED BY CARBODIIMIDE AND URONIUM-TYPE COUPLING REAGENTS

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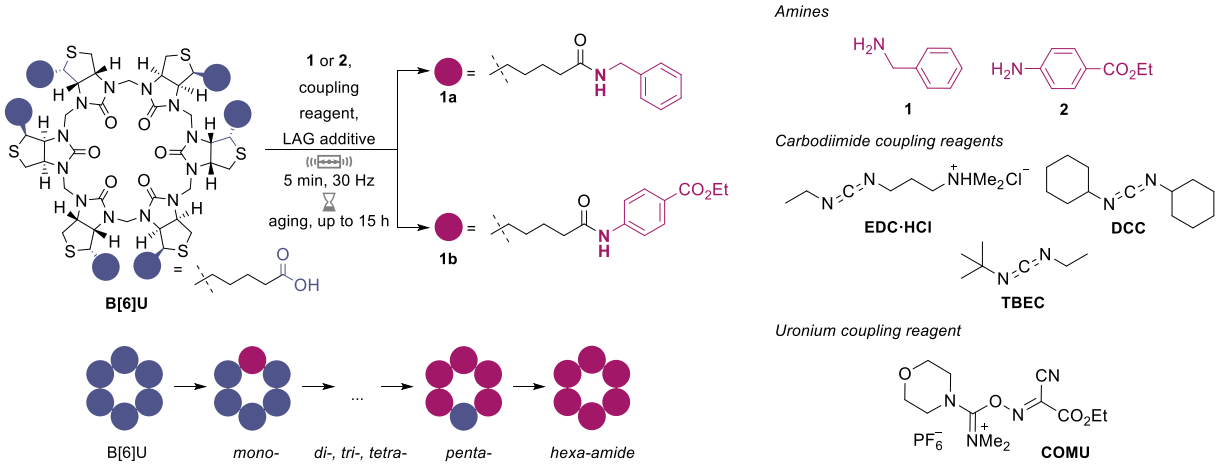
Amide coupling is one of the most widely adopted organic transformations in mechanochemistry, as it produces valuable amides and peptides without the use of hazardous solvents while leading to low *E*-factor values.[1] Aging is a methodology in mechanochemistry that involves a short initial mechanical activation followed by diffusion-controlled reaction under static conditions.[2] Here, we demonstrate that mechanochemical amide coupling reactions can be performed under aging conditions. In this context, biotin[6]uril, a macrocyclic hexacarboxylic acid, serves as a sensitive model that requires six consecutive couplings to yield the hexa-amide product. For carbodiimides (EDC, DCC, TBEC) the reaction proceeds under aging conditions after a short period of ball milling (2–5 min), with no significant dependence on continued ball impacts. The reaction rate at aging is accelerated by mild heating and polar LAG solvents, indicating the importance of a liquid phase to facilitate aging-driven reactivity. Consistent with the findings, amide couplings with COMU showed reagent-dependent behaviour, occurring under continuous ball impacts for solid inorganic base (K_2HPO_4) while switching to aging regime with liquid organic base (DIPEA).



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DIPHENYLAMINE-PYRROLIDIN-2-ONE-HYDRAZONE DERIVATIVES: SYNTHESIS AND QUANTUM CHEMISTRY EVALUATION

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Lithuania
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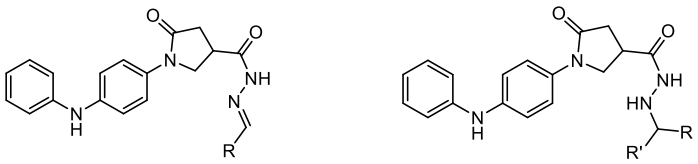
Pyrrolidin-2-one and hydrazone scaffolds are important pharmacophores in drug design due to their versatile biological activities and tunable structural features. Pyrrolidine moiety provides benefits in drug design because of the ring's unconstrained conformation, which may be locked and tuned with the suitable substituents. Biological activity of hydrazone derivatives is associated with the presence of the active azomethine pharmacophore.

A series of target hydrazones were synthesized from 5-oxo-1-(4-(phenylamino)phenyl)pyrrolidine-3-carbohydrazide and various aldehydes bearing aromatic and heterocyclic moieties and acetophenones.



Their probable activity was evaluated by quantum chemistry simulations Optimization of ground state molecular structure for several conformers was carried out by means of *Gaussian16* software using density functional CAM-B3LYP method and 6-31G(d,p) basis set supplemented with polarization functions (d,p). Solvation effects (water surrounding) were estimated using PCM method. Electronic excitations were simulated using semiempirical TD method (for singlets). For population of excited lowest electronic state using transition S0→S1, in all cases dominant and most significant electron jump is not of homo→lumo type, but homo-1→lumo or homo→lumo+1.

The quantum chemistry simulations identified hydrazone derivative bearing thiophene moiety as the most reactive one showing that its high reactivity is associated with the movement of the five-membered heterocyclic fragment relative to the core and following reorientation of charge-donor-charge acceptor fragments.

ENERGY-TRANSFER-MEDIATED MODULAR ALKENE (HETERO-)ARYL-AMINATION

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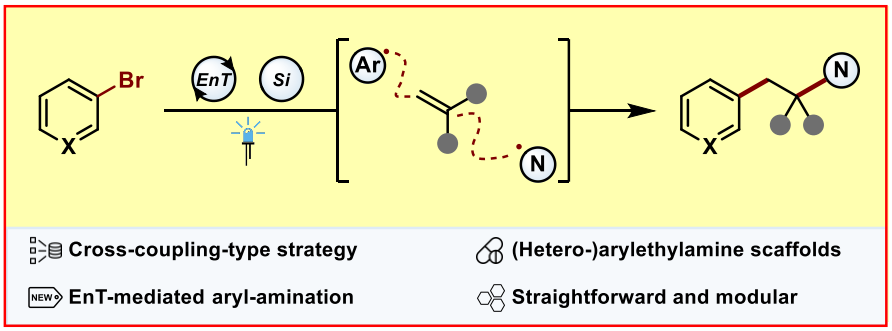
The phenethylamine scaffold serves as the structural backbone for a wide range of biologically active compounds and drugs, including neurotransmitters such as dopamine.[1] Owing to the central role of this manifold in medicinal chemistry, bioisosteric benzene-to-heteroaromatic ring replacement is an evident scaffold-hopping strategy during lead optimization.[2] As synthetic chemistry remains a key driver in drug discovery, enabling rapid access to these frameworks from readily available feedstocks through straightforward and step-economic strategies is of paramount interest.[3] We herein present an innovative solution by solving the long-standing problem of a cross-coupling-type approach for energy-transfer-mediated aryl-aminative difunctionalizations of alkenes. An unprecedented class of aminative-coupling-reagents was developed, activating feedstock (hetero-)aryl bromides in situ to generate highly reactive aryl-radicals, which add to common alkenes. Selective amination is achieved by the so-called persistent radical effect (PRE). In this straightforward modularity-driven approach, a wide range of (hetero-)aryl bromides as well as alkenes could be employed, yielding an array of drug-like (hetero-)arylethylamines.



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DEVELOPMENT OF REVERSIBLE COVALENT INHIBITORS FOR PLASMODIUM SERINE PROTEASE SUB1

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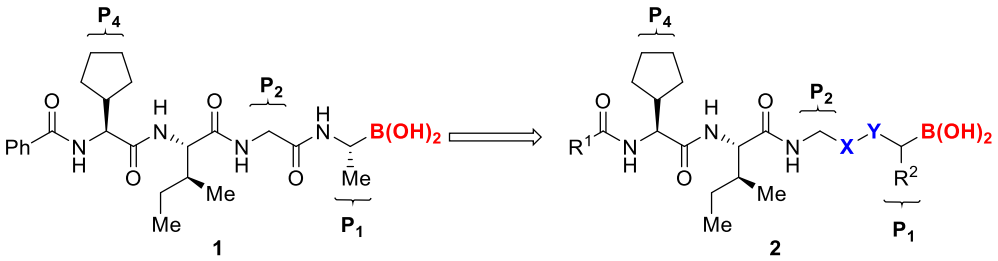
Malaria – a disease transmitted by mosquitoes and caused by the *Plasmodium* parasite – is responsible for over 600 000 deaths annually[1]. Due to the increasing drug resistance to known anti-malarials, drugs acting by novel parasite growth inhibition mechanisms are urgently needed. In the blood stage of the disease, merozoites infect and replicate within healthy blood cells. The escape of parasites from blood cells is facilitated by a subtilisin-like serine protease SUB1 which makes it as an attractive target for novel anti-malarials.

In our previous work we reported that peptidic boronic acid **1**[2] acts as an inhibitor of SUB1 by forming a covalent reversible bond with serine in the catalytic site of the enzyme. In search for more drug-like scaffolds we developed P_1 – P_2 depeptidized analogues **2** of peptidic boronic acid **1**. In this work, we report synthesis and SUB1 inhibitory potency of depeptidized analogues **2**.



Acknowledgements: This project is funded by student grant from National Institute of Research and Innovation (Latvian Institute of Organic Synthesis) (IG-2026-06).

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EXPLORING THE REACTIVITY OF TRIS(PENTAFLUOROPHENYL)BORANE TOWARDS ADDITIVES IN CATALYTIC REACTIONS

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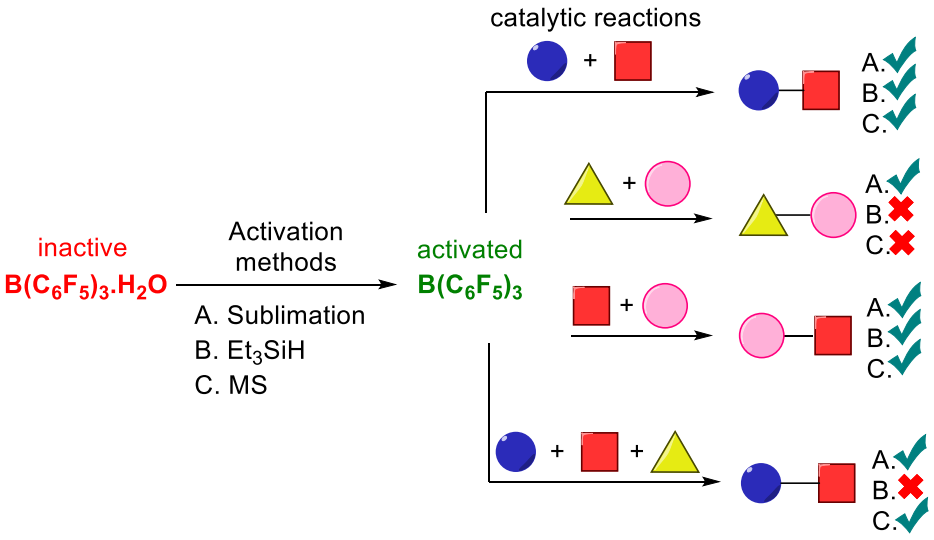
Borane catalysis, involving boron-based frustrated Lewis pairs (FLPs) has recently gained attention for hydride abstraction from amines, generating reactive iminium hydroborate salts that can participate in a variety of stoichiometric and catalytic reactions.[1] Tris(pentafluorophenyl)borane (BCF) is widely used due to its unique reactivity and stability.[2] However, its moisture sensitivity leads to the formation of a water adduct, reducing its Lewis acidity and catalytic efficiency and often requiring inert handling conditions or activation additives. To address this limitation, we investigated molecular sieves (MS) as a simple and practical method for BCF activation. The MS-BCF system demonstrated effective reactivity across various catalytic reactions and provides a useful alternative to conventional additives that may cause undesired side reactions.



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ELECTROCHEMICAL ENANTIOSELECTIVE AZIDATION OF α-BRANCHED ALDEHYDES THROUGH IODINE-MEDIATED ELECTROCATALYSIS

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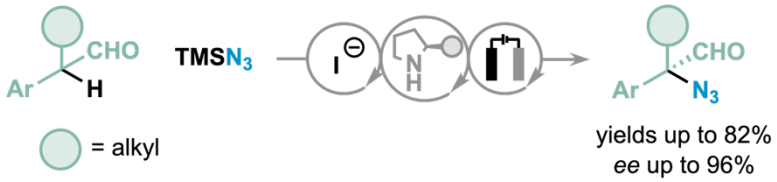
Construction of quaternary stereocenters remains a longstanding challenge in organic chemistry.[1] Although asymmetric organocatalysis, which employs small organic molecules for enantioinduction, has undergone rapid development over the past two decades, its integration with electrochemical methods offers new opportunities to access unique reactivities and overcome limitations of conventional synthetic approaches.[2]

Herein, we report the enantioselective synthesis of α-azido quaternary aldehydes from readily available aldehydes through a dual catalytic strategy combining asymmetric enamine catalysis and iodine-mediated electrocatalysis. The method affords the desired products in good yields and excellent enantioselectivities. In addition, comprehensive mechanistic investigations and computational studies were conducted to elucidate the reaction pathway. Notably, straightforward derivatization of the obtained products provides efficient access to valuable chiral quaternary amino acid derivatives.[3]



❍ *dual catalytic strategy* ❍ *mild and robust electrochemical conditions*
❍ *computational studies* ❍ *access to chiral quaternary amino acids*

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SYNTHESIS OF FUSED HETEROCYCLES BY A NOVEL CASCADE 1,2-SILYL SHIFT – FRIEDEL-CRAFTS CYCLIZATION

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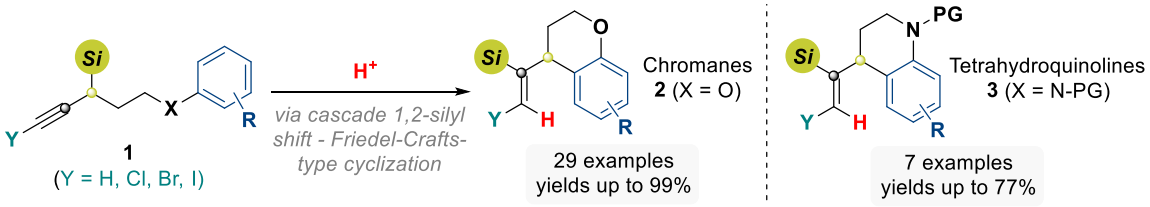
Chromanes **2** and tetrahydroquinolines (THQs) **3** are widespread motifs in antioxidants[1-2] and alkaloids that exhibit high pathogen toxicity and anticancer potential.[3-5] For the synthesis of their 4-vinyl group-containing analogs, we propose harnessing the intrinsic 1,3-dipole character of propargyl silanes.[6-7] The latter is enabled by the possibility of a 1,2-silyl shift once the propargylic system is activated by an electrophile. This leads to the formation of reactive allyl cation intermediates or their equivalents. The intramolecularly offered aryl moiety, acting as a π-nucleophile, triggers an intramolecular Friedel–Crafts reaction, affording chromanes **2** or THQs **3**. Terminally halogenated propargyl silanes **1** (Y = Cl, Br, I) afford products **2**-**3** with a geometrically controlled (*Z*)-2-halo-1-(trialkylsilyl)vinyl moiety.[8]



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C-H AMINATION OF LUPANE TYPE TRITERPENOIDS

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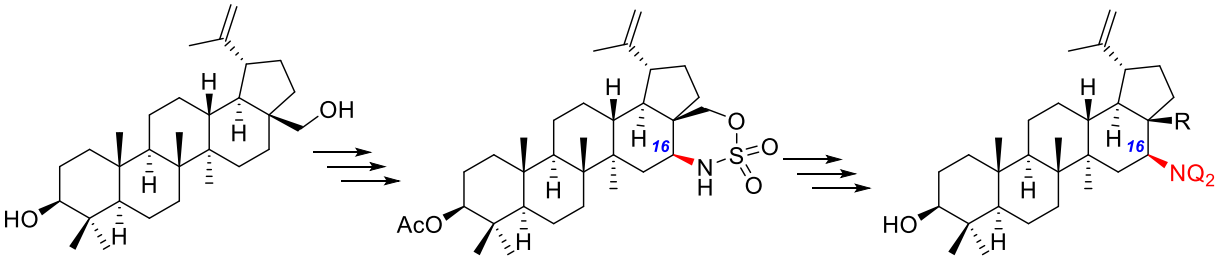
Betulin is pentacyclic triterpenoid natural product that is obtained as secondary metabolite in more than 200 different types of plants. Betulin and its derivatives exhibit several important pharmacological properties such as antitumor, anti-inflammatory, antiparasitic, and anti-viral activities.[1] However, deeper studies showed that medicinal application of the majority of betulin derived molecules have been hindered by their poor water solubility. A possible option to overcome the low bioacessability of lipophilic triterpene core is introduction of polar functional groups. The aim of this work is to obtain novel amino group bearing betulin derivatives by site-selective C-H amination at C(16) of betulin core.[2]



R = CH_2OH, COH, COOH, CH_2N_3, CH_2OSO_3Na, $CH_2OSO_2NH_2$
NQ_2 = NH_2, NHBoc, NHCBz, NHAc, N_3

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CONTACT-ELECTRO-CATALYTICALLY DRIVEN ADVANCED OXIDATION OF BENZOIC ACID DERIVATIVES

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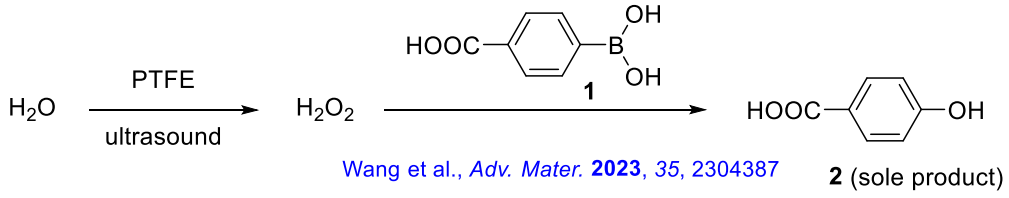
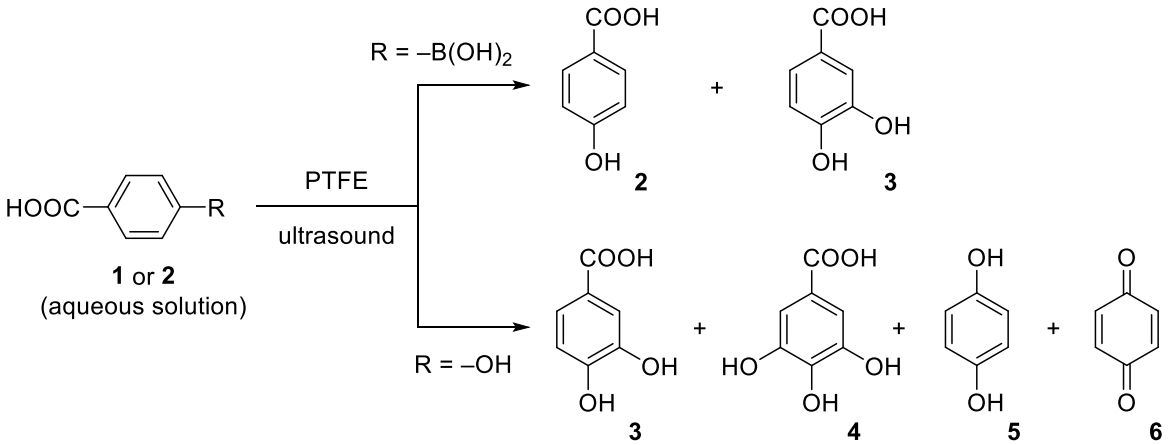
Benzoic acid derivatives, including 4-boronobenzoic acid **1** and 4-hydroxybenzoic acid **2,** are important synthetic precursors used in academic and pharmaceutical research. The oxidation of aryl boronic acids to phenols is an important organic transformation that requires peroxide addition. Recently, Wang group reported the *in-situ* production of H_2O_2 in an aqueous medium at ambient temperature and pressure *via* ultrasonically driven contact electrocatalysis (CEC), which transforms aryl boronic acid **1** into phenol **2**.[1]

Here, we report that the CEC of an aqueous solution of aryl boronic acid **1** itself leads to initially unexpected dihydroxylation product **3** in addition to the desired phenol **2**. We also demonstrate the further oxidation of hydroxybenzoic acid **2** under CEC conditions, which very likely proceeds through HO• generation and gives a variety of products **3**–**6**.





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MECHANOCHEMICAL DERIVATIZATION OF KUKERSITE KEROGEN

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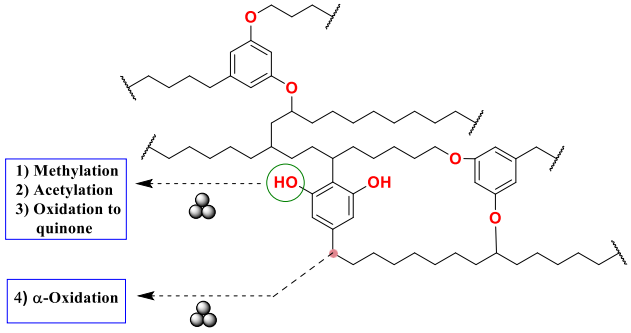
Kerogen, a solid organic component comprising 10–60 wt% of oil shale, represents one of the most abundant yet underutilized fossil organic matter resources on Earth.[1] Structurally, kerogen is a natural polymer enriched in resorcinol-type aromatic units cross-linked by aliphatic side chains. Chemical derivatization and valorization of kerogen to obtain low-molecular-weight phenolic compounds is highly appealing due to the value and versatility of these products but remains challenging because it requires mild oxidative cleavage of carbon–carbon bonds within the kerogen backbone. Previously developed oxidation methods demand harsh conditions, which typically oxidize the sensitive phenolic motifs to CO_2 and H_2O, yielding aliphatic dicarboxylic acids only.[2]



As a prerequisite for developing milder oxidative strategies for kerogen conversion, we developed derivatization protocols that enable protection of phenolic hydroxyl groups. Because kerogen is an insoluble cross-linked polymer and is poorly compatible with conventional solution-phase chemistry, mechanochemical derivatization offers a practical alternative. Here, we report the mechanochemical methylation and acetylation of kerogen under mild, ambient-temperature conditions, in contrast to previously reported high-temperature method.[3] Preliminary results on the mechanochemical oxidation of kerogen model compounds will also be presented.

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WATER SOLUBLE TRIAZOLYLPURINE DERIVATIVES AS CORROSION INHIBITORS IN ACIDIC MEDIA

Kumpiņš, V.; Sebris, A.; Burcevs, A.; Ušacka, U.; Iesalnieks, M.; Drunka, R.; Valkovskis, K.; Novosjolova, I.; and Turks, M.

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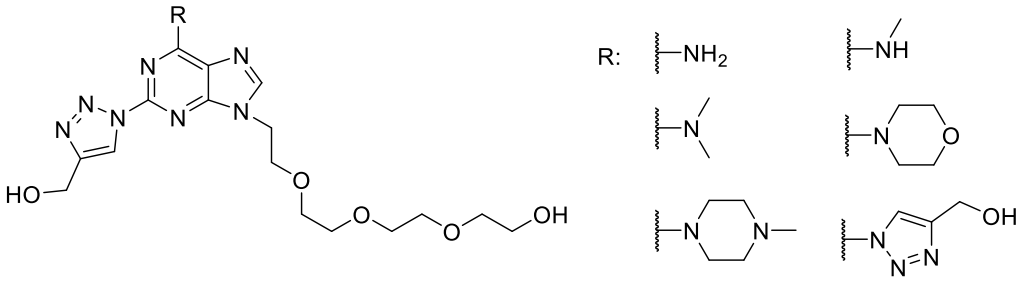
Corrosion is a chemical process, which leads to deterioration of materials and is caused by the surrounding environment. Corrosion inhibitors form a thin protective layer on the metal surface through adsorption or by interacting with metal atoms on the surface. Most efficient inhibitors possess Lewis basic groups, which contain heteroatoms (N, O, P, S) or π-electron systems.[1]

Herein we propose substituted triazolylpurines as corrosion inhibitors, as they possess multiple nitrogen atoms and an extended π-electron system. Derivatives with different substituents at purine C(6) position were prepared to determine the effect of hydrogen bond donors as well as electron donors and acceptors. Inhibition efficiency of target compounds were tested on mild steel in aqueous 1 M HCl using gravimetric and electrochemical methods. 2,6-Bistriazolylpurine showed the highest inhibition efficiency, reaching up to 97% at 10^{-3} M concentration. Synthetic pathway towards the products and determination of their anticorrosion activity will be discussed in detail.[2]



Acknowledgements: This work was supported by the grant No. RTU-ZG-2024/1-0025 as part of project No. 5.2.1.1.i.0/2/24/I/CFLA/003.

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ADVANCING ELECTROCHEMICAL SOMO-ORGANOCATALYSIS TOWARD NEW TRANSFORMATIONS

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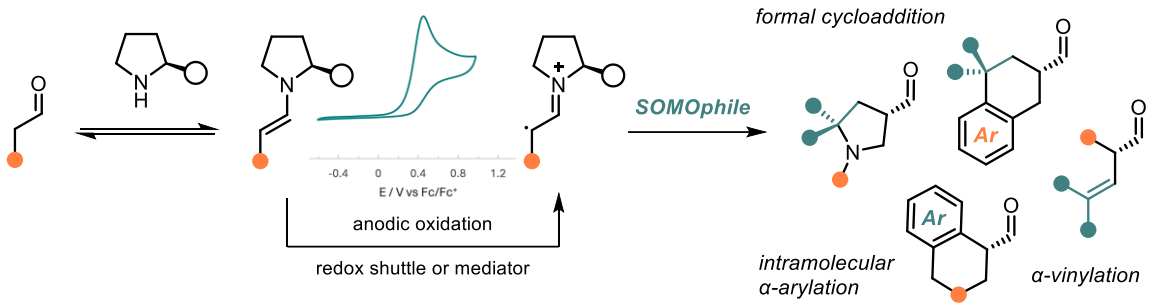
Organic electrochemistry has emerged as an attractive tool for performing umpolung transformations. In this context, it has recently been shown to efficiently promote asymmetric SOMO-organocatalytic reactions, in which nucleophilic enamine intermediates are transformed into electrophilic species through single-electron oxidation at the anode and subsequently react with SOMOphiles to furnish α-functionalized aldehydes in an enantioselective manner. Electrochemical conditions allow these transformations to be performed at ambient temperature without special precautions, whereas analogous reactions employing stoichiometric oxidants, such as ceric ammonium nitrate (CAN), typically require low temperatures, an inert atmosphere, and prolonged reaction times.[1] Importantly, recent studies have shown that the use of a redox shuttle under electrochemical conditions helps prevent the degradation of the chiral aminocatalyst, a major challenge in oxidative organocatalysis.[2] Building on these advantages, we report an extension of this methodology toward new asymmetric transformations.



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SYNTHESIS OF CLOVANE-RELATED SESQUITERPENOIDS: RUMPHELLCLOVANES A–D

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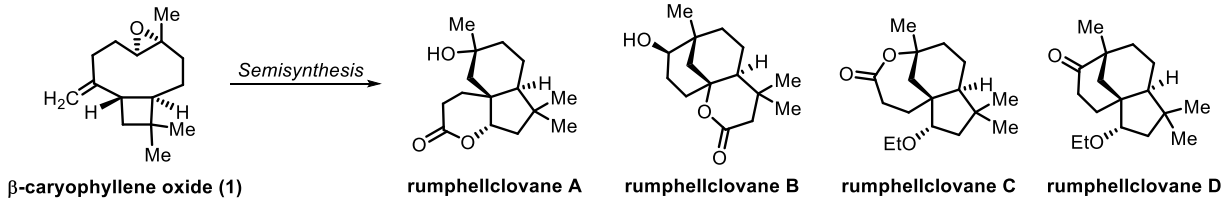
Rumphellclovanes A–D are clovane-type sesquiterpenoids isolated from gorgonian coral *Rumphella antipathies*, it is also known that some of these derivatives exhibit modest anti-inflammatory activity.[1–3]

In this work, we present the semisynthetic approach toward rumphellclovanes A–D (**2**–**5**) starting from readily available β-caryophyllene oxide (**1**). Starting material **1** provided the necessary carbon skeleton that could be rearranged to these naturally occurring lactones and ketone via a short synthetic route, enabling the preparation of rumphellclovanes A–D in substantial amounts.



Acknowledgements: This project is funded by Latvian Council of Science 1.1.1.9. activity "Post-doctoral research" (grant agreement no. 1.1.1.9/LZP/1/24/038).

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HYDROGEN BOND-DRIVEN CO-CRYSTALLIZATION OF NITROGEN-RICH ENERGETIC NUCLEOBASE ANALOGUES: UNEXPECTED TETRAMERIC ASSEMBLY

Līpiņš, D. D.;[a] Kons, A.;[b] Bērziņš, A.;[b] Tchoń, D. M.;[c] Saršūns, K.;[b] Mishnev, A.;[d] Klapötke, T. M.;[e] Turks, M.;[a] and Novosjolova, I.[a]

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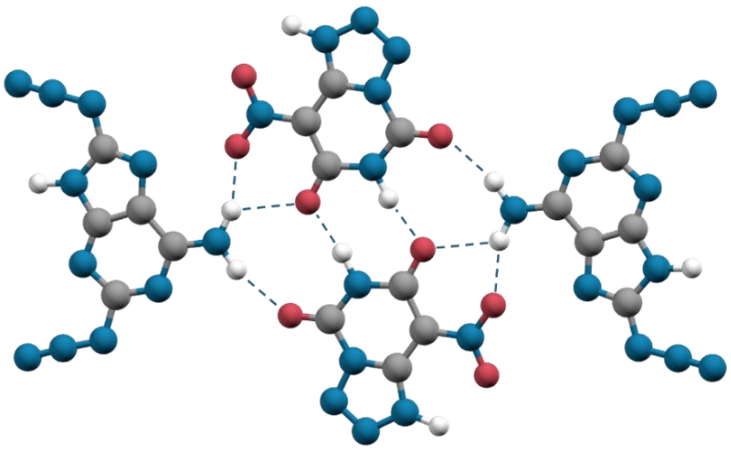
The field of energetic materials has a constant demand for more energetic but, at the same time, safer materials. One novel approach to accessing these polar opposite properties is co-crystallization, as a means of stabilizing the crystal lattice while simultaneously obtaining higher energy density.[1]

Natural nucleobases are well-established hydrogen bond donors and acceptors with planar geometry and high nitrogen content, making them attractive structural motifs for the design of highly stabilized energetic materials. However, the introduction of energetic functional groups into the nucleobase framework and their effect on co-crystallization behaviour remains largely unexplored.

Herein, we report the co-crystal of 2,8-diazidoadenine and 5-nitrotetrazolouracil, which exhibits a non-canonical planar hydrogen-bonded tetramer. The effect of co-crystallization on the stability and detonation parameters of the material is explored.



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FROM ESTERS TO SILYL ENOL ETHERS: MECHANISTIC INSIGHTS AND SCOPE OF TRIARYLBORANE-CATALYZED ESTER HYDROSILYLATION

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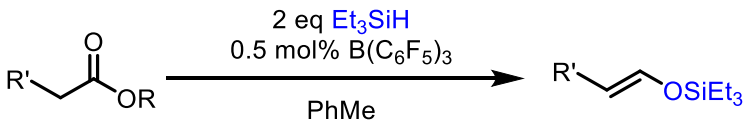
Triarylborane-catalyzed ester hydrosilylation is a powerful transformation but it is often limited by overreduction. Meanwhile, the direct one-step synthesis of valuable silyl enol ethers from esters remains underdeveloped. In this work, we investigate the mechanism of tris(pentafluorophenyl)borane-catalyzed ester hydrosilylation using NMR-based kinetic studies, with a focus on understanding the origin of reactivity pathways. Our studies reveal the formation of both silyl ethers and previously unreported silyl enol ethers as key products arising from competing reaction pathways.

Our mechanistic investigation reveals key factors controlling selectivity in triarylborane catalysis and the pathways leading to overreduction. Building on these findings, we develop a straightforward and general method for the direct synthesis of silyl enol ethers from esters. The transformation proceeds with good yields and broad functional group tolerance, offering a practical route to valuable synthetic intermediates.



Acknowledgements

This research is partially funded by the Latvian Council of Science, project "Application of catalytic hydrosilylation in the valorization of renewables," project No. lzp-2023/1-0413 and Recovery and No.1.1.1.8/1/24/I/007 «RTU doctoral grants for supporting research excellence in smart specialization areas»

EFFICIENT ACCESS TO PLANAR-CHIRAL [2.2]PARACYCLOPHANES VIA ENZYMATIC DESYMMETRIZATION

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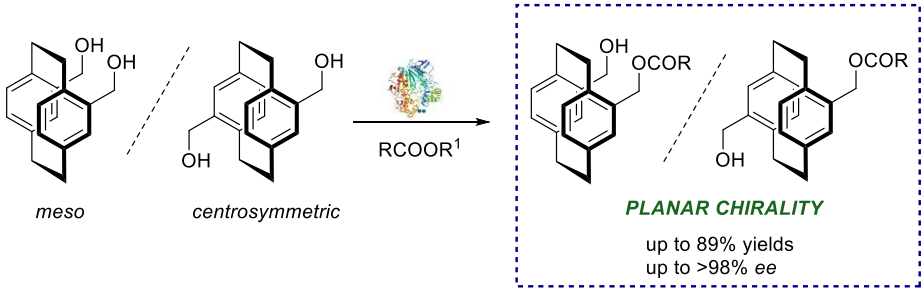
Recently, considerable research efforts have been devoted to chiral backbones based on rigid and conformationally stable [2.2]paracyclophanes (PCPs), as they have emerged as highly promising chiral ligands for asymmetric catalysis and related fields.[1] The unique physical and chemical properties of PCPs further expand their utility as π-stacked conjugated polymers, hole-transport materials, … among others. From a synthetic point of view, substantial progress has been made in the selective functionalization of defined positions on the PCP scaffold. Nevertheless, achieving stereoselective control remains a major challenge, since access to enantiopure PCPs still largely relies on chromatographic resolution techniques.[2] To address this limitation, we have focused on catalytic carbon–heteroatom bond-forming strategies that enable the efficient differentiation of enantiotopic groups in *meso* and centrosymmetric disubstituted PCPs. Herein, we report a biocatalytic transesterification protocol that exploits the high activity and broad substrate tolerance of lipases. This method offers a rapid and versatile route to two important PCP building blocks obtained in good yields and with excellent enantioselectivities, and suitable for a broad range of downstream applications.[3]



Acknowledgements: We thank the Basque Government (EJ, grant IT1741-22) and Agencia Estatal de Investigación (grant PID2023-147050NB-I00//MICIU AEI/10.13039/501100011033) for financial support. D. A. acknowledges EJ for fellowship.

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DIRECTING GROUP *VS* PCT: WHAT REALLY CONTROLS SITE SELECTIVITY OF Pd-CATALYZED C(sp^3)–H FUNCTIONALIZATION IN PENTACYCLIC TRITERPENOIDS?

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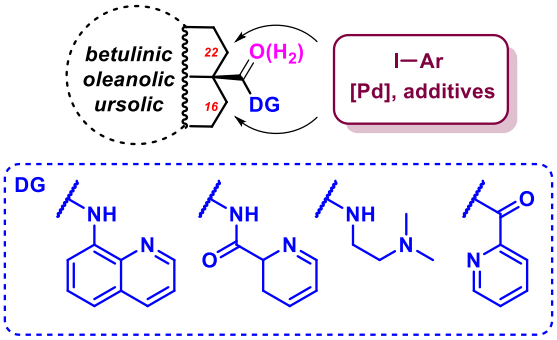
Pentacyclic triterpenoids (PCTs) are numerous and structurally diverse natural products that are widely distributed in plants and possess a wide range of biological functions. Existing work on PCTs derivatization has focused on versatile modification of functionalities at C(3)/C(28) positions leaving widely available C(sp^3)-H largely underexplored.



Here, we present a method for the functionalization of dormant C(22) and C(16) positions using Pd-catalyzed C(sp^3)–H activation reactions and evaluate the influence of different directing groups on C(sp^3)–H activation efficiency and positional selectivity.[1] For this purpose, we designed a series of betulin-, oleanane- and ursane-based model substrates bearing varied bidentate-directing groups that differ in coordination mode, bite angle, rigidity and electronic properties. Our study investigates whether site selectivity in Pd-catalyzed C(sp^3)–H functionalization of PCT is predominantly governed by attached directing group or by the intrinsic sterics of the PCT scaffold. Our work clarifies the extent to which directing-group design can be used as a reliable tool to steer Pd-catalyzed C(sp^3)–H functionalization of complex triterpenoids and outlines guiding principles for future late-stage diversification strategies in this scaffold class.

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CONTROLLING ISOMERISM IN NONPLANAR PORPHYRINS

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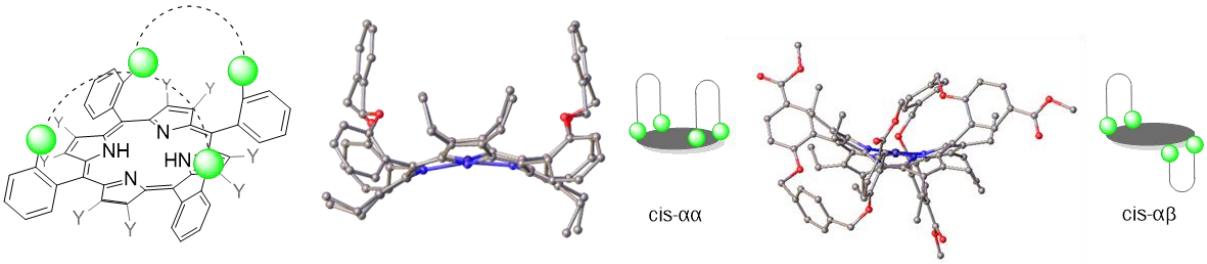
The ability to control the shape of a porphyrin macrocycle and its surrounding environments is highly coveted. Strapped porphyrins offer dual control over both the peripheral porphyrin environment and degree of macrocycle deformation by decorating the porphyrin with covalent linkers connecting either meso-meso or β-β positions.[1,2] The tunability of the three-dimensional shape of this scaffold has led to their heavy utilisation as biomimetic models for the active sites of metalloproteins.[3] Since the inception of strapped porphyrins, there has been expansive work into understanding their properties and devising of their efficient synthesis. However, despite the plethora of methods that exist today, strapped porphyrins remain challenging molecules to synthesise, with their preparation requiring long multi-step syntheses or shorter synthesis hampered by low yields. Given the emerging utility of nonplanar porphyrins as organocatalysts and enzyme mimics, we sought to exploit the flexibility of the nonplanar macrocycle for the efficient one step synthesis of a new class of strapped "subnecto" porphyrins. This method enables facile access to a diverse porphyrin tool kit for the selective design of functional three-dimensional architectures.



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AMINO-*N*-HETEROCYCLES: *N*-ACYLATION AND BIOLOGICAL ACTIVITY

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Preliminary antibacterial screening against the *E. coli DH5α* cell line was performed on a series of randomly chosen compounds. Highly promising activity was observed for two 2-(3-chlorophenyl)-*N*-(pyridinyl)acetamides. Based on these findings, it was decided to expand the compounds library and evaluate the antibacterial potential of related 2-(chlorophenyl)-*N*-(heteroaryl)acetamides.

The target molecules were prepared *via* amide coupling. Selection of proper reaction conditions was conducted using 4-aminoisoquinoline a model for *N*-acylation reaction with 3-chlorophenylacetic acid applying various activating agents. The most effective conditions were applied to the syntheses of remaining target compounds.

To reliably prove the structure of the obtained compounds, spectral analysis IR and NMR along with mass spectrometric analysis (MS) methods were used. All compounds prepared for biological studies were purified to at least 97% purity (LC-MS).

ELECTROOXIDATIVE IODINATION OF CARBONYL COMPOUNDS: A MILD, SIMPLE, AND SCALABLE ACCESS TO α-IODOCARBONYLS

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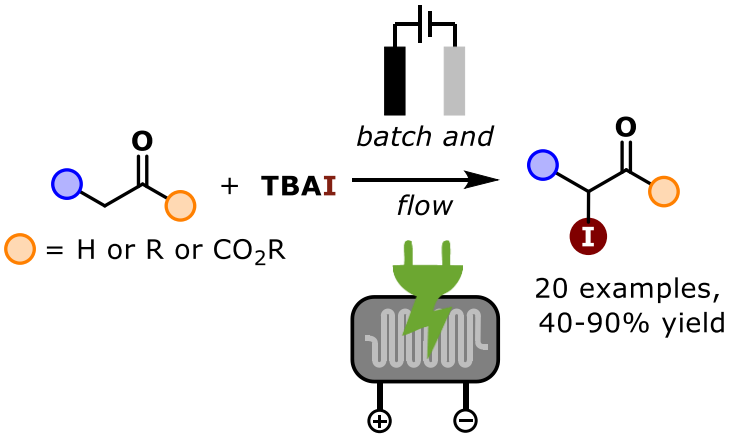
α-Iodinated carbonyl compounds represent an important class of molecules owing to their broad synthetic versatility. The coexistence of an iodine atom and a carbonyl group generates multiple reactive centers, allowing these compounds to participate in a wide range of chemical transformations. Conventionally, these compounds are synthesized by direct iodination of the carbonyl compounds with iodinating reagents. Although numerous methods have been reported, these transformations often require stoichiometric oxidants, acidic conditions, or catalysts. As a result, many existing protocols have poor compatibility with oxidation-sensitive substrates like aldehydes and are limited to ketones.[1]

Herein, we report a general method for α-iodination of carbonyl compounds through electrochemical generation of reactive electrophilic iodine species under mild reaction conditions. This work comprises quaternary ammonium salt as a stable and inexpensive iodine source. By employing electric current as a controllable and traceless alternative oxidant, our work eliminates the use of wasteful oxidants and hazardous reaction conditions. Thus, it demonstrates excellent tolerance towards oxidation-sensitive substrates featuring aldehydes and heterocycles. Additionally, the reaction can be scaled up upon the introduction of a continuous flow setup.



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CLICK-CHEMISTRY FUNCTIONALITIES IN ADOMET ANALOGUES BASED NUCLEIC ACID TAGGING

Malikėnas, M.;[1] Masiulis, D.;[1] Petraitytė, G.;[1] Masiulionytė, B.;[2] Vilkaitis, G.[2] and Masevičius, V.[1]

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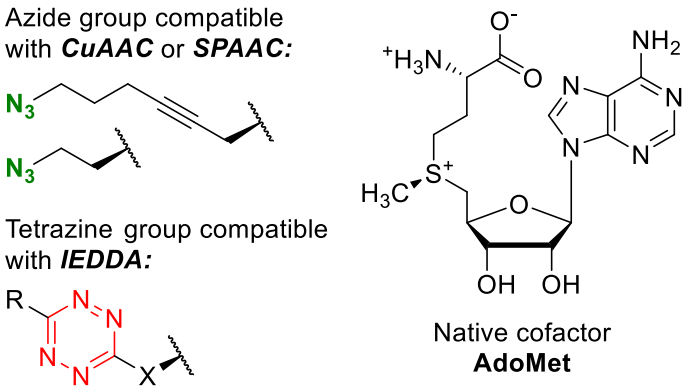
S-adenosyl-L-methionine (AdoMet) is a methyl donor in various methylation reactions catalysed by methyltransferases. *In vivo* targets of this essential reaction include biopolymers and small molecules, making it a cornerstone of epigenetics, epitranscriptomics, and metabolic regulation. To apply this reaction in various nucleic acid tagging techniques, a transferable reporter group or biorthogonal functional group is introduced in place of the native methyl group. Among the transferable biorthogonal functional moieties, the azido group and its counterpart, the terminal alkyne, are among the most frequently used, although slow reaction rates and the toxicity of copper (I) salts to cells hinder the usability of this reaction. Other click-chemistry biorthogonal pairs are also used as moieties in AdoMet analogues (primary amino – NHS-esters; thiols – maleimide). Herein, we present a new AdoMet tool—IEDDA click-chemistry—which is at least several orders of magnitude faster, more sensitive, and potentially useful to single-cell applications.



OVERCOMING MAJOR CHALLENGES IN THE SYNTHESIS OF NEW TRIPEPTIDES

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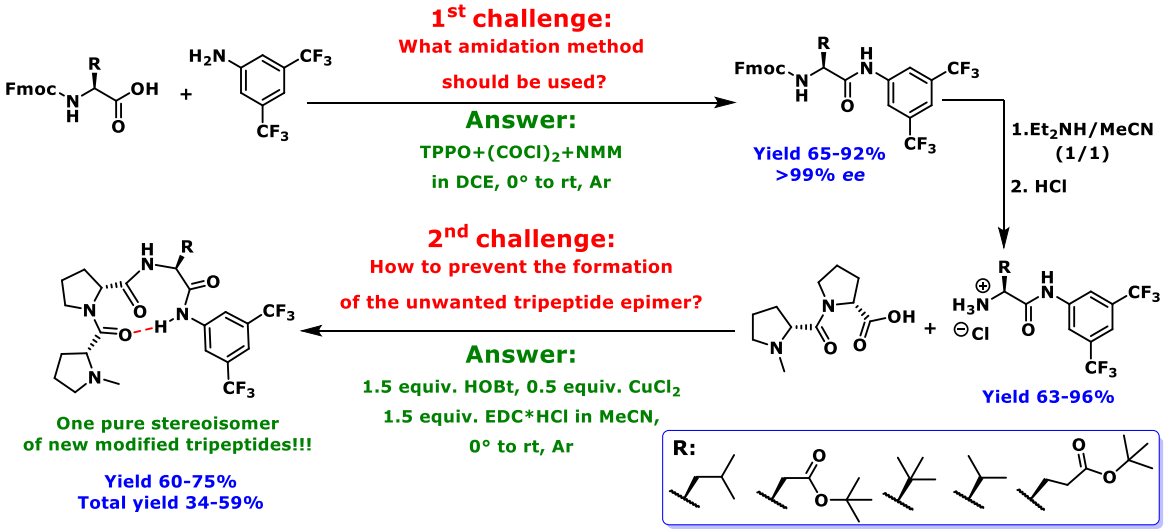
In asymmetric organocatalysis, oligopeptides have been widely investigated for C–C bond formation through enamine activation of the nucleophile and hydrogen-bond coordination of the electrophile. In contrast, examples in which peptides activate and coordinate the nucleophile via a tertiary amine acting as a Brønsted or Lewis base remain scarce. Consequently, the potential of such oligopeptides in enantioselective catalysis remains largely unexplored.

We investigated the synthesis of tripeptides containing *N*-methyl-diproline and amino acid amide moieties and tackled two major challenges. The first involved the amidation of Fmoc-protected amino acids with a poorly nucleophilic aniline to obtain the corresponding amides in high yields and enantiomeric purities. Screening of various coupling reagents revealed that the combination of triphenylphosphine oxide (TPPO), oxalyl chloride ($(COCl)_2$), and *N*-methylmorpholine (NMM) provided the desired products in good yields (65–92%) and excellent enantiomeric excess (ee > 99%). Secondly, epimerization at the second proline chiral center was observed during the coupling of *N*-methyl-diproline with the amino acid amide hydrochloride. This issue was successfully addressed by employing appropriate amounts of hydroxybenzotriazole (HOBt), $CuCl_2$, and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl). NMR analysis confirmed that epimerization was completely suppressed. The last step yielded 60-75% of the tripeptides, where total yield of the tripeptides ranged from 34-59%.



INTRINSIC VERSUS IMPURITY EFFECTS IN PURELY ORGANIC ROOM-TEMPERATURE PHOSPHORESCENCE

Mazarevics, A.[a,b]; Leduskrasts, K.[a]; Krukle-Berzina, K.[a]; and Suna, E.[a,b]

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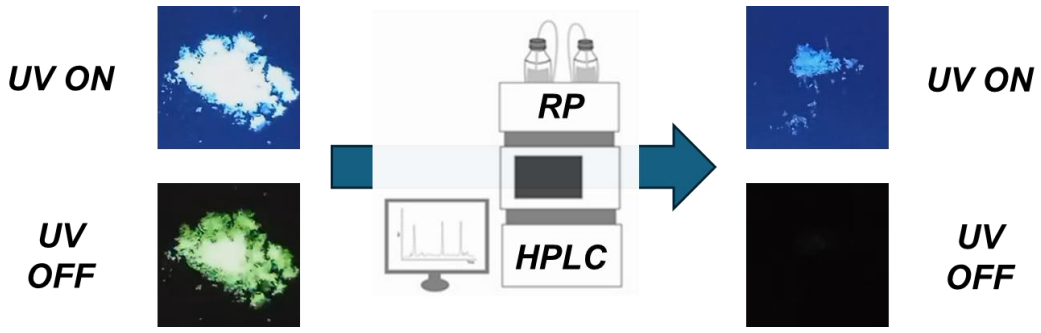
Purely organic phosphorescent materials (phosphors) have been utilized in lighting, bioimaging, and sensing to replace their toxic and high-cost inorganic and organometallic counterparts.[1] Purely organic phosphors are obtained by incorporating (**a**) aromatic heterocycles, (**b**) carbonyl groups, and (**c**) halogen atoms into their molecular structure. The **a**–**c** structural elements induce various second-order effects in the crystal lattices of organic phosphors, which are generally considered to be responsible for the observed room temperature phosphorescence (RTP).[2] However, recent studies have demonstrated that RTP disappears in the absence of impurities for various organic phosphor classes, including carbazoles, boronic esters, aryl boranes, benzoic acids, triphenylamines, pyrazines, and phenothiazines. Nevertheless, the observed RTP from the vast majority of organic phosphors is still ascribed to structural elements **a**–**c** and their second-order effects.

Herein, we systematically investigate a structurally diverse set of literature reported phosphors, which incorporate structural elements **a**–**c**, and demonstrate that trace-level impurities, which can be removed through reversed phase HPLC, appear to be responsible for the observed millisecond-scale RTP. These results provide compelling evidence that impurities are responsible for the observed ultra-long RTP in all crystalline organics.



Acknowledgements:

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SYNTHESIS AND MODIFICATION OF 1-PHENYL-1*H*-PYRAZOLE-4-CARBIMIDOYL CHLORIDE

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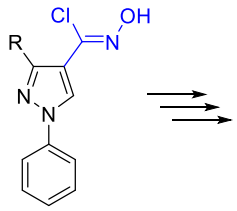
The pyrazole derivatives are important in organic synthesis due to their wide range of applications across various fields, including agriculture and insecticide/herbicide development[1]. Pyrazole-based compounds also have medicinal properties such as analgesic, anticancer, antipyretic, etc[2]. Isoxazole and pyrimidinamine derivatives are known to exhibit biological activity. However, very few studies on fused systems of these scaffolds have been reported in the literature. Despite that, available evidence suggests that pyrimidinamines combined with different five-membered rings exhibit antitumor activity[3,4].



Based on scientific findings about the importance of pyrazole and the fact that isoxazole-pyrimidinamines are poorly studied, it was decided to synthesize isoxazole[5,4-*d*]pyrimidin-4-amine derivatives. We performed the well-known synthesis of pyrazole carbaldehyde[5], and from the resulting compound, 1-phenyl-1*H*-pyrazle-4-carbimidoyl chloride was obtained in two steps. After formation of the isoxazole ring and, in several stages, the pyrimidine ring, the final products were obtained.

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CONFORMATIONAL ANALYSIS OF TRANSITION STATES MAY REVEAL SOME ALTERNATIVE REACTION PATHS

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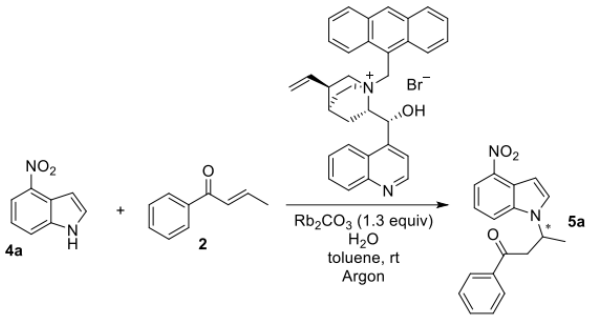
The reaction of 4-nitroindole and trans-crotonophenone[1] was studied by quantum chemical density functional method using M06-2X DFT functional with def2-SVP basis set. A reaction coordinates scan for the formation of the C-N bond was performed and the corresponding transition states (TS) for the ***S***- and ***R***-enantiomers were found. Conformational analysis was performed for both transition states (***S*** and ***R***). It was found that several TS conformations have close energy values, thus opening up some alternative (parallel) reaction channels. These channels may increase the overall reaction rate. In contrast to our previous studies[2], where the rate-determining reaction step was related to torsional degrees of freedom, this reaction appears to proceed in a more conventional manner, i.e. the rate-determining step is related to the reaction coordinate associated with the covalent (C-N) bond.



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RESEARCH ON CYCLIZATION PATHWAYS OF 1-ALKYNYL-2-THIOBENZIMIDAZOLES UNDER VARIOUS REACTION CONDITIONS

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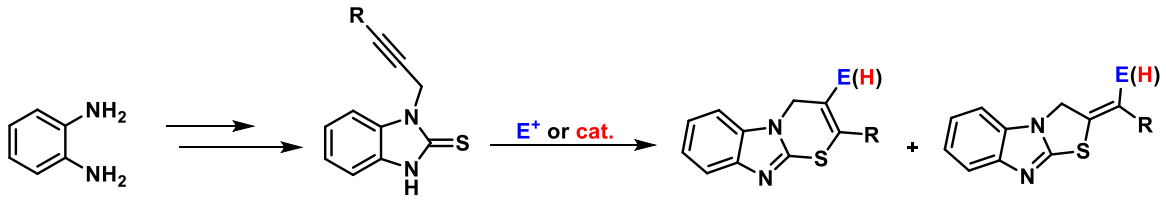
Intramolecular alkyne cyclization provides a versatile approach to structurally defined heterocycles. These transformations can be driven by nucleophiles, electrophiles, coinage-metal catalysts, or bases, and typically proceed through competing 5-*exo*-dig and 6-*endo*-dig pathways. Regioselectivity is highly sensitive to reaction conditions and substituent electronic properties. Although cyclizations involving O-, N-, and C-centered nucleophiles are well-established, sulfur-mediated variants remain comparatively underdeveloped, despite their utility in the synthesis of biologically active heterocyclic motifs.

Building on the limited development of sulfur-mediated cyclizations, this work examines the intramolecular cyclization of 1-alkynyl-2-thiobenzimidazoles as a strategy for the synthesis of novel benzimidazo[2,1-*b*][1,3]thiazine frameworks. The model substrate was derived from *o*-phenylenediamine via *N*-propargylation with (3-bromoprop-1-yn-1-yl)benzene, followed by condensation with thiocarbonyldiimidazole. A screen of coinage-metal catalysts and halogen electrophiles identified optimal reaction conditions for the highest selectivity toward the six-membered ring product. The effect of substituent electronics on regioselectivity was further examined by introducing both electron-donating and electron-withdrawing groups.



SQUARAMIDE BASED ORGANOCATALYSTS IN GLYCOSYLATION REACTIONS

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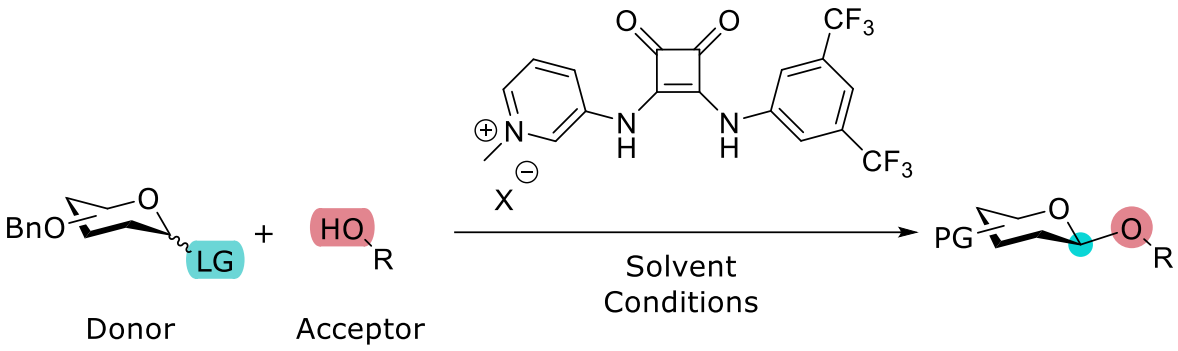
Squaramide organocatalysts have emerged as powerful hydrogen-bonding catalysts in a wide range of organic transformations, yet their application in glycosylation chemistry remains largely unexplored. In this work, novel squaramide catalysts bearing a 3,5-bis(trifluoromethyl)phenyl moiety on one side and a pyridine unit on the other were investigated for glycosylation reactions. Subsequent quaternisation of the pyridine scaffold and variation of the corresponding counteranions enabled systematic evaluation of catalyst structure and counterion effects on glycosidic bond formation under mild conditions. These findings demonstrate the potential of tailored squaramide-based systems as new organocatalytic tools for selective glycosylation chemistry.



WET AIR OXIDATION OF WOOD TREATMENT WASTEWATER: A POTENTIAL ROUTE TO BIO-BASED ACETIC ACID FOR DE-ICERS FROM OIL SHALE ASH

Muldma, K.; Närep, A.; Mets, B.; Umerenkova, V; Lopp, M; and Kaldas, K.
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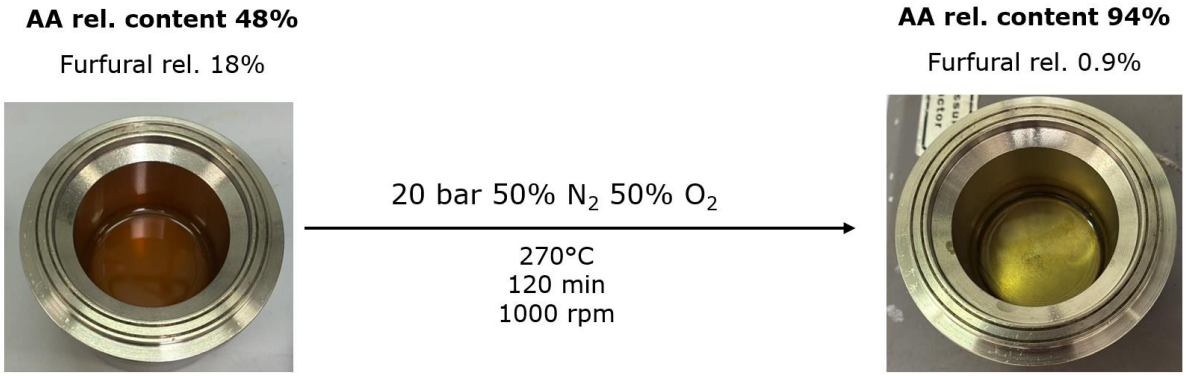
Acetic acid is an important platform chemical used in the food, pharmaceutical, and chemical industries. Global demand reached 17 million tons in 2022 and is expected to increase by 25% by 2030. However, around 90% of acetic acid is still produced from fossil resources. This work explores wood thermal treatment wastewater as a renewable source of acetic acid, enabling the valorisation of both wood-derived waste streams and Estonia's oil shale ash to produce biodegradable de-icing agents.

Initial WAO (wet air oxidation) experiments were conducted under conditions similar to those reported for bio-based acetic acid production from high-furfural wastewaters (270 °C, 20 bar synthetic air, 180 min)[1]. Under these conditions, only a slight increase (3%) in acetic acid concentration was observed, while its relative concentration based on GC–MS analysis increased from 48% to 88%. WAO represents a promising method for wood thermal treatment wastewater valorisation into bio-based acetic acid but further optimisation is needed.



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ONE-POT NUCLEOPHILIC ORGANOCATALYTIC ENANTIOSELECTIVE [8+2]-CYCLOADDITIONS OF PHOTOGENERATED KETENES

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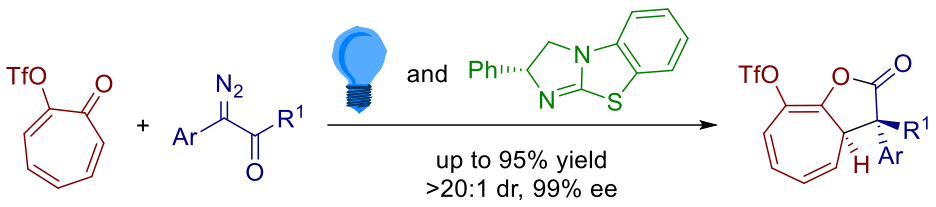
Cyclic structures are prevalent in numerous natural products and can be efficiently synthesised via well-developed cycloaddition reactions of alkenes. However, the use of longer polyenes in higher-order cycloadditions (HOCs) remains challenging due to issues of regio-, stereo-, and periselectivity. Recent advances in asymmetric organocatalysis have significantly improved the feasibility of such transformations.[1] Herein we demonstrate the use of diazoketones as precursors for photochemically generated ketenes in asymmetric organocatalytic HOCs for the synthesis of 7,5-fused heterocyclic compounds. This structural motif is found in several members of the sesquiterpene lactone class of natural products. We report the synthesis of unique representatives of this scaffold incorporating an all-carbon quaternary stereocenter and demonstrate the potential for further diversification of the scaffold.[2]



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SELECTIVE FUNCTIONALIZATION OF 1,8-NAPHTHALIMIDES WITH WEAK NUCLEOPHILES UNDER MILD METAL-FREE CONDITIONS

Mutovska, M.[1]; Zagranyarski, Y.[1]; Konstantinov, K.[1,2]; Zagranyarska, I.[3]; Sánchez, D.[4]; Allain, M.[4]; David, A.[4]; Angelova, S.[5]; Stoyanov, S.[1]; and Cabanetos, C.[4]

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Functionalized 1,8-naphthalimide derivatives are an important class of π-conjugated compounds with applications in fluorescence sensing, organic electronics, and bioactive systems. However, their selective modification with weak nucleophiles remains challenging due to low reactivity and competing side reactions.

Herein, we report an efficient and transition-metal-free strategy for the controlled functionalization of the 1,8-naphthalimide core under mild conditions. Careful optimization of the base and reaction temperature enabled the synthesis of diverse difluoro-, dialkoxy-, and mixed alkoxy-substituted derivatives in excellent yields (80–97%) and short reaction times (up to 30 min).

Mechanistic studies indicate a Halex-type pathway involving peri-difluoro intermediates followed by nucleophilic aromatic substitution with weak nucleophiles such as alcohols. The methodology is scalable to gram quantities and allows precise control over the substitution pattern.

The obtained compounds exhibit characteristic photophysical properties of naphthalimide systems, including near-UV absorption and strong blue–cyan emission, with optical behaviour strongly influenced by the substitution pattern.

Overall, this work provides a practical and versatile route to functional 1,8-naphthalimide derivatives, expanding their potential applications in sensing, photonic materials, and biomedicine.

Acknowledgements: Authors are grateful to the Bulgarian National Science Fund project NSF KP 06-H79/8

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FUNCTIONALIZED 2-(TRIFLUOROMETHYL)BUTA-1,3-DIENES DERIVED FROM HFO GAS

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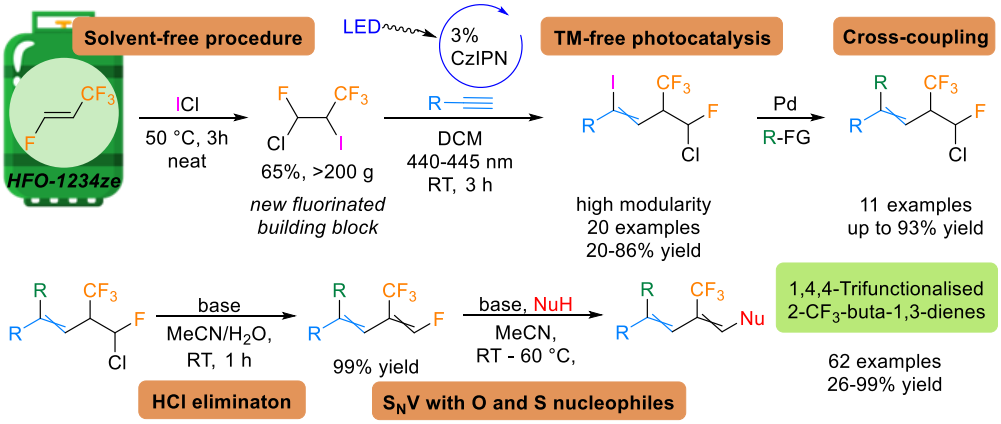
In 2025, out of 29 small molecule drugs approved by FDA, 14 were fluorinated compounds. As various fields continue to benefit from fluorinated compounds and demand increases, questions regarding the environmental impact and sustainability of fluorine have also arisen. Hydrofluoroolefins (HFOs) represents suitable alternative fluorine sources. They have low ecological footprint as they are the result of a lengthy and closely monitored research process as refrigerant gases,[1] but their exploration for organic synthesis remains limited.[2] In recent years, our research group has aimed to expand the synthetic application of HFOs.[3] In our latest work, we used HFO-1234ze, an HFO that has been used rarely in synthetic applications to date. First, we performed an ICl addition on the molecule, then optimized a photoaddition step that allows it to react with various acetylenes. Thanks to the iodine present, we were able to selectively perform cross-coupling reactions on the resulting photoadduct. We then noticed that butadienes could be easily formed from the photoadducts by HCl elimination. This added another point of modularity to the molecules, as the electron-deficient vinyl fluoride allowed us to perform nucleophilic vinylic substitution reactions on the butadiene. As a result of our work, we achieved a novel incorporation of the trifluoromethyl group into a highly modular synthetic building block from a sustainable fluorine source.



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SYNTHESIS OF ADENOSINE 5'-CARBOXAMIDE CONTAINING METTL1 INHIBITORS

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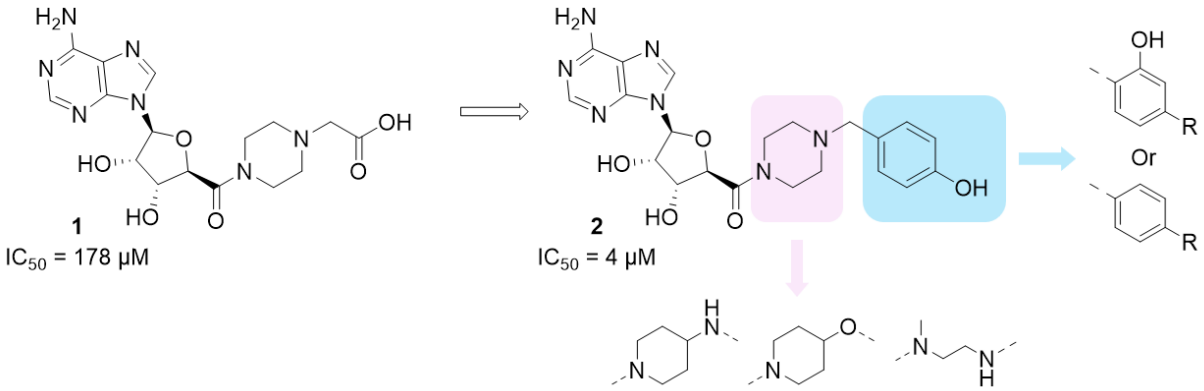
Methyltransferase-like protein 1 (METTL1) is an important protein in the human organism, responsible for catalysing RNA *N*7-guanosine methylation involved in multiple cellular processes. However, dysregulation of this modification pathway has also been associated with cancer progression. Studies have shown that reduction of METTL1 expression in cancer cells induces apoptotic features, highlighting METTL1 as an attractive therapeutic target.

In this work, we report a novel class of METTL1 inhibitors exhibiting low micromolar activity. These compounds are based on the adenosine 5'-carboxamide **1** scaffold reported by Nai et al. 2024[1]. Several analogues were synthesized by varying substituents on the aromatic ring and introducing modifications within the piperazine scaffold. Compound **2** was obtained with a 44-fold increase in activity in respect to the previous compound **1**.



Acknowledgements

This work was financially supported by Latvian Institute of Organic Synthesis student grant Nr. IG-2026-17 and Latvian Recovery and Resilience grant No.29/OSI/PG (No.5.2.1.1.i.0/2/24/I/CFLA/001).

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ETHERIFICATION OF CELLULOSE USING MECHANOCHEMISTRY AND AGING

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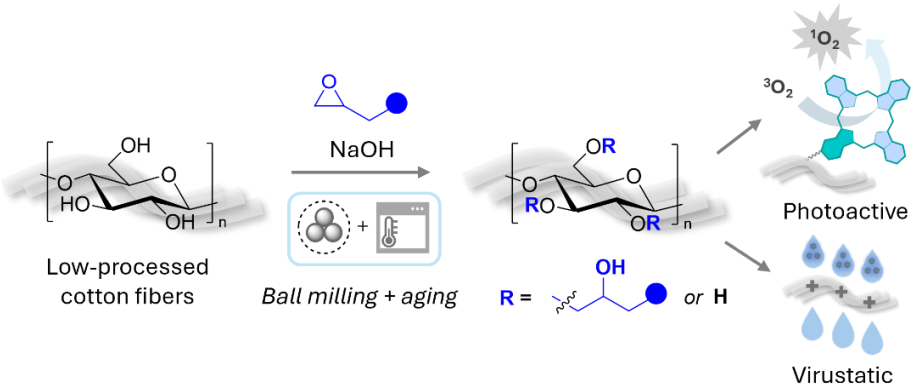
Cellulose is a valuable natural resource for the development of innovative biomaterials with diverse applications, driving the growing demand for advancing sustainable and efficient methods for its modification.[1] Solid-state approaches, such as mechanochemistry[2] and accelerated aging, enable direct functionalization of inherently insoluble cellulose without dissolution, offering efficient, fast and lower waste reactions.[3,4] Here, we present our recent work on developing virustatic[4] and photoactive cellulose-based materials via solid-state etherification reaction.



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MECHANOCHEMICAL SYNTHESIS OF MONO- AND DI-STYRYL BODIPY DYES AND THEIR SENSING APPLICATIONS

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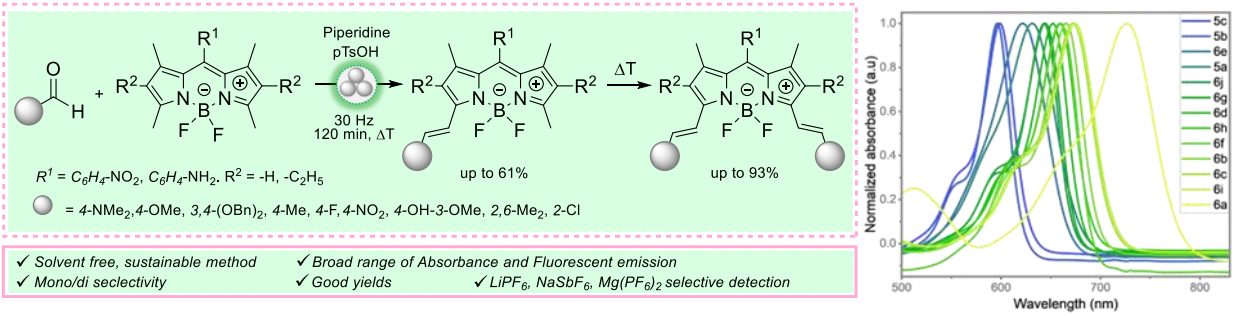
Styryl-BODIPY dyes are widely used as red and near-infrared fluorophores, but their synthesis by Knoevenagel condensation is typically limited by poor mono/di selectivity and requires reflux in toxic, high-boiling solvents.[1,2] In this study we report a mechanochemical synthesis in which the post-milling aging temperature serves as a selectivity switch, affording either mono- or di-styryl products at will. The synthetic method gives access to a wide variety of substituted benzaldehydes on two BODIPY scaffolds in good yields, with tunable absorption and emission of dyes across 550-750 nm. As an application, a dimethylamino-styryl derivative was conjugated to a mono-biotinylated hemicucurbit[8]uril macrocycle via amide coupling, giving a fluorescent probe for the selective detection of lithium, sodium, and magnesium electrolyte salts with big anions.



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BIO-INSPIRED NITROGEN-RICH ENERGETIC MATERIALS: SYNTHESIS AND CHARACTERIZATION OF AZIDO AND NITRO MODIFIED NUCLEOBASES

Līpiņš, D. D.;[a] Briedis, U. O.;[a] Valkovskis, K.;[a] Mishnev, A.;[b] Reinhardt, E.;[c] Klapötke, T. M.;[c] Turks, M.;[a] and Novosjolova, I.[a]

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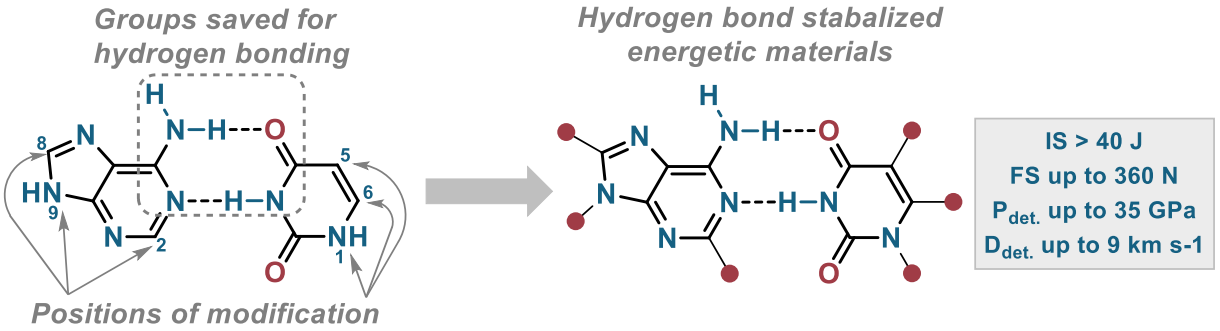
Improving both the energetic performance and safety of primary explosives simultaneously remains one of the central challenges in the field of energetic materials. The incorporation of hydrogen bond donors and acceptors into energetic frameworks has proven to be an effective molecular-level strategy for simultaneously improving crystal packing and reducing sensitivity to mechanical stimuli.[1]

The planar geometry, high nitrogen content, and well-defined hydrogen bonding patterns of natural nucleobases make them promising building blocks for the design of highly stabilized energetic materials. Nevertheless, these heterocycles have scarcely been explored in this context.

Herein, we report the synthesis and energetic properties of purine and uracil energetic materials. Their detonation velocity ($D_{det.}$) and detonation pressure ($P_{det.}$) reach values of up to 9 km s^{-1} and 35 GPa, respectively, while still having low impact sensitivity (IS) and friction sensitivity (FS) of over 40 J and up to 360 N.



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STEREOCONTROLLED SYNTHESIS OF POLYSUBSTITUTED HOUSANES VIA *GEM*-BISMETALATED CYCLOPROPANES

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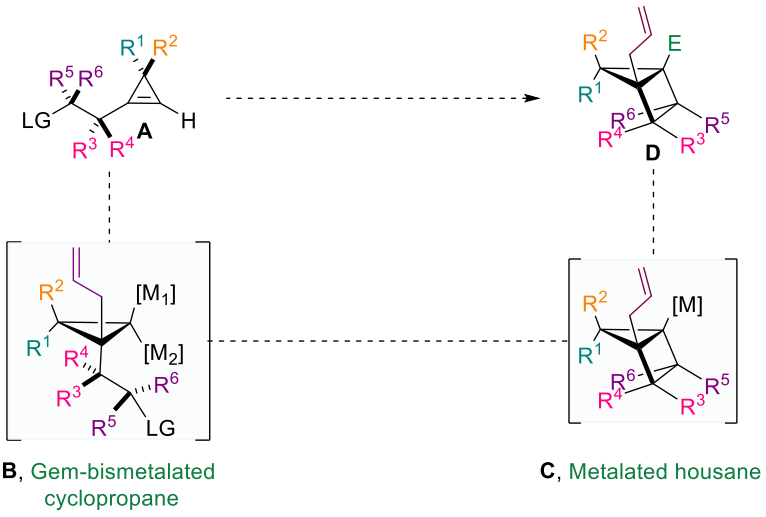
Bicyclo[2.1.0]pentanes, also known as housanes, have attracted increasing attention in recent years because of their potential role as bioisosteres and their strain-release chemistry.[1] Despite this interest, the synthesis of polysubstituted, stereodefined housanes remains a significant challenge. To address this problem, we envisioned the use of bismetalated cyclopropyl intermediates.[2] Our strategy begins with cyclopropene **A**, which contains an alkyl iodide side chain. Deprotonation of **A** generates a cyclopropenyl lithium intermediate. In the presence of allylmagnesium bromide and zinc bromide, a diastereoselective allylzincation reaction occurs, forming the bismetalated cyclopropyl species **B**.[3] Intramolecular cyclization then generates the metalated housane **C**. Subsequent electrophile trapping and cross-coupling reactions enable diversification of the resulting housanes **D**. This process provides a one-pot, diastereoselective synthesis of housanes from cyclopropenes.



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DESIGN AND SYNTHESIS OF HIGHLY POTENT AND SELECTIVE GRK2 INHIBITORS FOR POTENTIATING ANALGESIA

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This research is a synthetic medicinal chemistry project focused on pain. G-protein coupled receptor kinases (GRKs) are implicated in conditions ranging from heart failure to μ-opioid receptor (MOR) desensitization (Fig. 1), which the latter potentially causing the tachyphylaxis of opioid analgesics. Chronic opioid administration, such as morphine, leads to tolerance, with GRK2 identified as a key contributor through its role in MOR internalization. In our published study (Janet Lowe *et al.*), we investigated GRK involvement in acute agonist-induced MOR desensitization using Takeda compound 101, a membrane-permeable, potent, and selective GRK2 inhibitor (Fig. 2A).

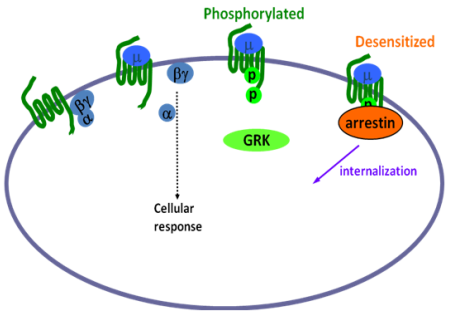

Figure 1. μ-Opioid receptor desensitization mechanism involving agonist-induced receptor and G-protein activation, GRK-mediated receptor phosphorylation, arrestin binding, arrestin-dependent signalling, and receptor internalization, recycling, and downregulation.

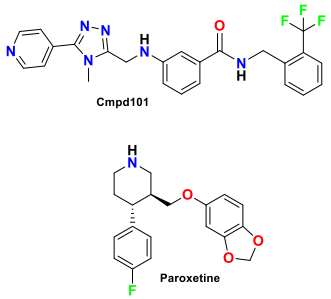

Figure 2. A) Structure of Cmpd101; an optimised 9-step synthesis developed by M. Ostovar. B) Structure of paroxetine, primarily known as a selective serotonin reuptake inhibitor, which also acts as a direct and selective GRK2 inhibitor.

To date, numerous GRK2 inhibitors have been reported; however, most lack either high potency or exclusive selectivity for GRK2 over other kinases, highlighting the need for a novel scaffold combining both properties. In this research, Takeda 101 and paroxetine analogues, two promising scaffolds for GRK2 inhibition, were used as the basis for high-throughput screening and in silico design to identify new lead-like scaffolds. Five scaffolds were identified and synthesised alongside Takeda- and paroxetine-based analogues to enable structure–activity relationship (SAR) studies. Selected compounds underwent biological evaluation. This poster presents the identification, synthesis, and biological profiling of these scaffolds and analogues, providing a foundation for future rational design of GRK2 inhibitors with enhanced potency, selectivity, and improved drug-like properties.

DEVELOPMENT OF *S*-ADENOSYL-L-METHIONINE ANALOGUES RESISTANT TO CLASSICAL DEGRADATION PATHWAYS

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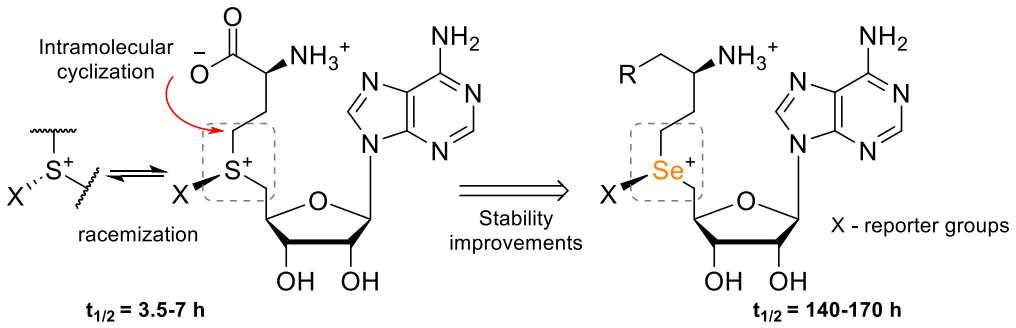
S-adenosyl-L-methionine (AdoMet or SAM) serves as a methyl group donor in the methylation of biopolymers and small molecules, a crucial reaction catalyzed by methyltransferases. To expand the utility of this cofactor, various AdoMet analogues with transferable functional or reporter groups have been developed. However, these AdoMet analogues demonstrate low chemical stability, limiting their application in certain biomolecule labelling experiments. Herein, we present the synthesis protocols for biologically active AdoMet analogues that are resistant to intramolecular cyclization and exhibit a reduced rate of racemization. To accomplish this, non-proteinogenic amino acids have been effectively employed as building blocks for AdoMet analogues.



EXPLORING S(IV)/S(VI) CHEMICAL SPACE THROUGH A UNIFIED ISOTHIAZOLIDINE STRATEGY

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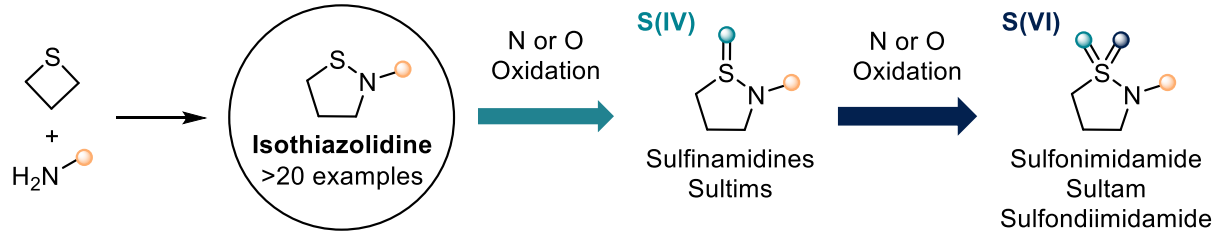
Sulfur-containing heterocycles, particularly S(VI) derivatives, have emerged as valuable motifs in medicinal chemistry and agrochemical discovery. [1] The growing interest in these frameworks arises from their potential as bioisosteres of lactams, additional vectors for functionalization, and the possibility of central chirality. While cyclic sulfonamides have historically dominated the medicinal chemistry landscape, the interest has recently expanded to sulfonimidamides and sulfondiimine. Yet, access to such heterocycles remains limited, thereby restricting medicinal and agrochemical efforts to the most common sulfonamide building blocks. In this context, we considered that isothiazolidines could offer an underexplored yet versatile platform for accessing diverse sulfur oxidation states from a common intermediate. However, limited attention has been brought to this structural motif mainly due to lengthy and low-yielding syntheses as well as narrow substrate scope. We report the results of our investigations in this area which have led to the development of a telescoped synthetic route that allows the initial formation of isothiazolidines from thietanes. Subsequent one-pot controlled oxidation to diverse sulfur oxidation states enabled rapid exploration of S(IV) and S(VI) chemical spaces from a common scaffold. The method exhibits broad substrate scope, tolerating substitution at all positions of the thietane ring as well as a wide variety of functional groups.



Simple reagents · One-Pot · No over oxidation · Modular synthesis · Rapid · Efficient

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ELECTROPHILE-PROMOTED CYCLIZATION OF 2-ALKENYLTHIOIMIDAZOLES FOR THE SYNTHESIS OF IMIDAZO[2,1-*b*][1,3]THIAZINE DERIVATIVES

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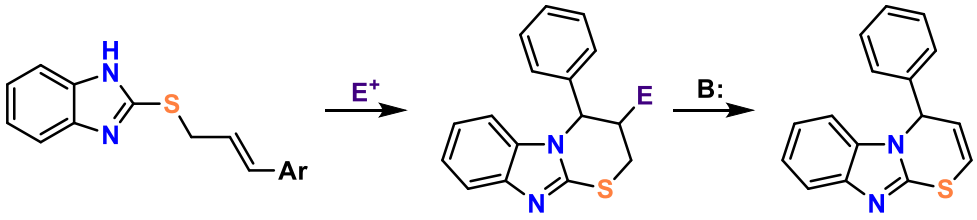
Imidazo[2,1-*b*][1,3]thiazine derivatives are of interest in medicinal chemistry due to their biological activities. In this work, the cyclization of 2-alkenylthioimidazoles, promoted by an electrophile, was applied to the synthesis of imidazo[2,1-*b*][1,3]thiazine frameworks. Using 2-cinnamylthiobenzimidazole as a model substrate, reaction conditions were optimized by varying the electrophilic source, solvent, and temperature. The cyclization products were subsequently further treated with base-promoted elimination to obtain compounds with the desired heterocyclic structures. The developed methodology provides a simple approach for obtaining imidazo[2,1-*b*][1,3]thiazine derivatives for further chemical and biological studies.



THE STEREOSELECTIVE PRENYLATION OF ARYL- AND HETEROARYL HALIDES: γ-SELECTIVE COUPLING AS A GENERAL TOOL FOR ASYMMETRIC Csp^2-Csp^3 CROSS-COUPLING

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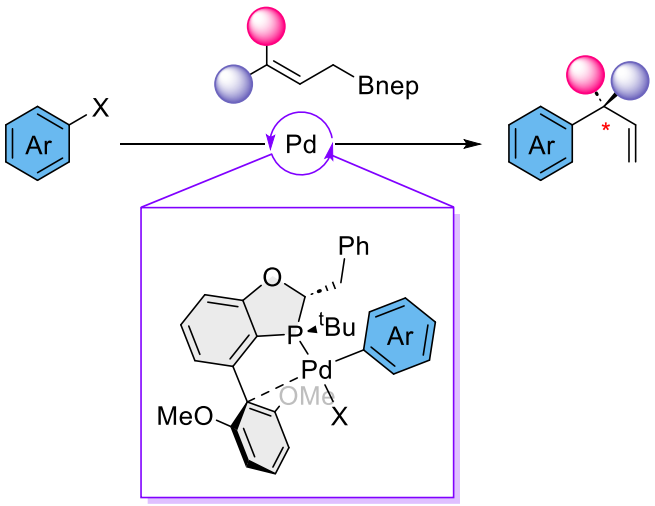
The asymmetric construction of all carbon quaternary stereogenic centers on heteroarenes is a long-standing challenge for synthetic chemists, due to the significant steric congestion around the central carbon atom. In our work, we describe a catalytic solution that promotes the stereoselective γ-selective Suzuki-Miyaura cross-coupling of aryl halides and allyl boronic acid esters and forms all carbon quaternary stereogenic centers in one step. The γ-selective coupling approach overcomes the need for a preformed stereogenic center, gives selective access to both stereoisomers and starts with readily available starting materials.[1]



- Regio- and stereoselective sp^2-sp^3 coupling
- excellent regioselectivity up to 99:1 (γ:α)
- enantioselectivity up to er 96:4

1. C. Pawlowsky, T. Leipertz, B. Henßen, M. Haase, J. Pietruszka, *J. Org. Chem.* **2026**, *91*, 6929-6937.

DIVIRGENT SYNTHETIC APPROACH TO HSP90 INHIBITORS INCORPORATING RESORCINOL AND THIADIAZOLE SCAFFOLDS

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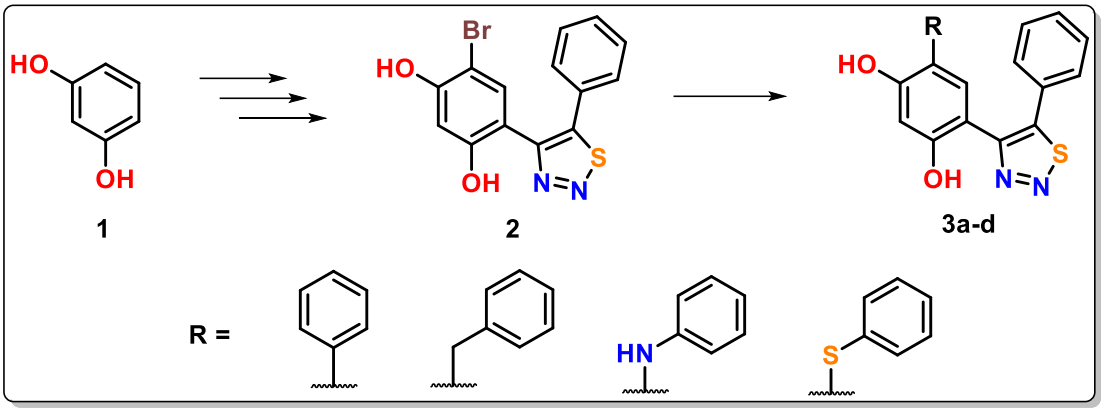
Hsp90 (heat shock protein 90) is a highly conserved molecular chaperone of approximately 90 kDa, found ubiquitously across eukaryotes and in numerous bacterial species. Its overexpression in cancer cells renders Hsp90 a compelling yet demanding target for anticancer drug development.[1] Despite the considerable number of compounds investigated to date, the C-4 position of the resorcinol ring remains relatively unexplored.[2]



This work aimed to prepare a series of Hsp90 inhibitors bearing hydrophobic substituents at the 4th position of the resorcinol moiety. Employing palladium-catalyzed cross-coupling strategies, four distinct compound classes (**3a–d**) were accessed via Buchwald–Hartwig amination and Suzuki coupling conditions. The presentation will discuss the divergent synthetic route, the challenges encountered, and the outcomes obtained.

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ELECTROOXIDATIVE SELENYLATION OF CARBONYL COMPOUNDS

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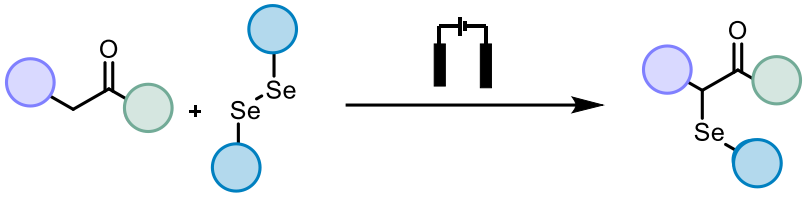
The incorporation of selenium-containing functional groups into organic molecules has attracted growing interest in recent years and have found broad applicability of organoselenium compounds in synthetic chemistry.[1] Beyond their utility as versatile synthetic building blocks, selenium derivatives have also found promising applications in materials science[2] and medicinal chemistry.[3]

In this work, we report a direct electrochemical anodic selenylation of carbonyl compounds, enabling the selective synthesis of α-selenocarbonyl derivatives under mild reaction conditions. The methodology employs commercially available and bench-stable diselenides $(RSe)_2$ as selenium sources, providing an atom-economical approach to C-Se bond formation. In contrast to conventional protocols that rely on prefunctionalized selenium reagents such as phthalimide selenides or the use of stoichiometric external oxidants to activate diselenides, our strategy uses electricity as a clean, controllable, and traceless oxidant. This electrochemical protocol offers a straightforward and sustainable alternative for the preparation of valuable organoselenium compounds.



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PHOTOINDUCIBLE DECARBOXYLATION IN REACTIONS WITH ALKYNES: REGIOSELECTIVE ADDITION OF ALKYL RADICALS TO THE TRIPLE BOND

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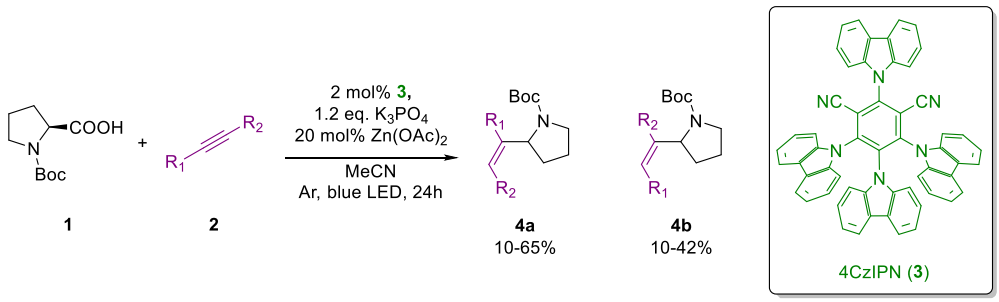
Visible-light photocatalysis should be considered as catalysis based on chemical processes initiated by the absorption of electromagnetic radiation from the visible range (380-750 nm). This technique has received growing interest due to its considerably milder and more economical reaction conditions when compared to thermal methods.[1] Recently, this approach has gained immense popularity, leading to significant progress in the area.[2] Numerous transformations initiated by visible light have been reported, including the decarboxylation of carboxylic acids, which generates free radicals that can react with alkynes, enabling the formation of C–C bonds.[3,4,5]

In this research, we examined the application of light-initiated radical decarboxylation of proline in reactions with unsaturated compounds while utilising external photocatalysts (**3**). The reaction conditions were optimised by examining the effect of various factors (solvent, photocatalyst, base) on the desired product (**4**) yield and the isomers **4a/4b** ratio. Preliminary findings suggest that the presence of a Lewis acid (LA) may play a role in favouring the formation of a single isomer of the product. Consequently, we also analysed the impact of various additives and LA, including metal salts (i.e. zinc, copper, scandium, ytterbium). The optimised conditions were subsequently employed to promote the addition of the resulting alkyl radical from **1** to a range of substrates bearing triple carbon-carbon bonds.



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SYNTHESIS OF AMARYLLIDACEAE ALKALOID ANALOGUES VIA TANDEM ALKYNE CARBOPALLADATION/ SUZUKI CROSS-COUPLING REACTION

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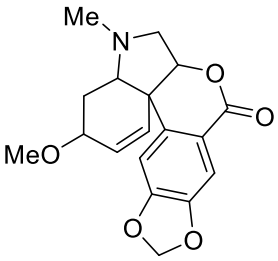
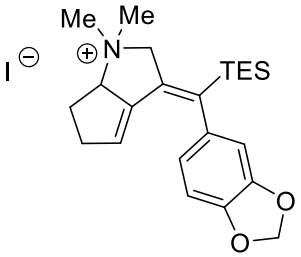
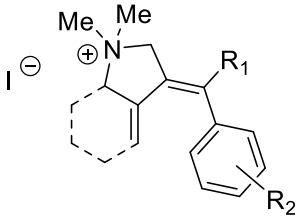
Alkaloids isolated from the Amaryllidaceae plant family have been extensively studied for their biological properties.[1] In prior studies of our group, several synthesised alkaloid analogues were found active against cholinesterases,[2] and the derivatives containing quaternary ammonium centre were also screened for their affinity towards muscarinic receptors. Biological evaluation revealed that two analogues displayed mild affinity for muscarinic receptors.



Macronine
(Amaryllidaceae alkaloid)



Previous work[2]



This work

Guided by these findings, we synthesised new series of compounds, diversified through tandem alkyne carbopalladation/ Suzuki cross-coupling reaction with a variety of boronic acids. In the subsequent series, structural modifications were introduced in other parts of the molecule. The resulting compounds were tested for their binding affinity to muscarinic receptors. The bioactivity results provided insights into structure-activity relationships, offering opportunities to further modify the compounds for improved properties. The selected compounds were also screened for cytotoxic activity showing some promising results.

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SYNTHESIS OF STRUCTURALLY SIMPLIFIED DIAZONAMIDE A ANALOGS

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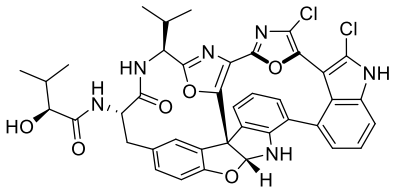
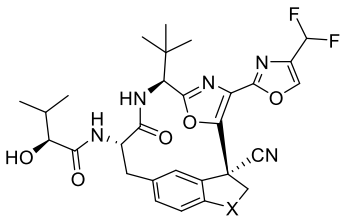
Diazonamide A (**1**) is a structurally unique naturally occurring compound that exhibits high antiproliferative activity against several malignant tumor cell lines.[1] Due to its high biological activity and complex structure, many research groups have focused on studies of diazonamide A, resulting in the development of several structurally simplified analogs.[2,3,4] Our group has also developed a series of analogs by replacing the tetracyclic hemiaminal with an indane moiety. The lead compound of the series, **2**, demonstrates high antiproliferative activity against several malignant tumor cell lines, high metabolic stability, and effective inhibition of tubulin polymerization. However, **2** lacks aqueous solubility which renders it from entering preclinical studies.[3]

We designed a series of compounds, **3a–f**, by replacing the indane moiety in **2** with the more polar benzofuran, benzothiophene, and indoline moieties. This resulted in a 10-fold improvement in solubility, while maintaining high antiproliferative activity and strong inhibition of tubulin polymerization.



Diazonamide A (1)



2 (X = CH_2)
3a-f (X = O, S, SO_2, NR)

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METAL-FREE PHOTOREDOX MANIFOLD FOR DEHYDROGENATIVE C-N COUPLING UTILIZING PROTONS AS OXIDANTS

Radzevičius, N.[1]; Žurauskas, J.[1]; Vaickūnas, P.[1]; Snarskis, G.[2]; Chatinovska, B.[1]; Kreiza, G.[3]; Raišys, S.[3]; Šimėnas, M.[3]; Kalendra, V.[3]; Zakarauskas, K.[4]; Kazlauskas, K.[3]; and Orentas, E.[1]

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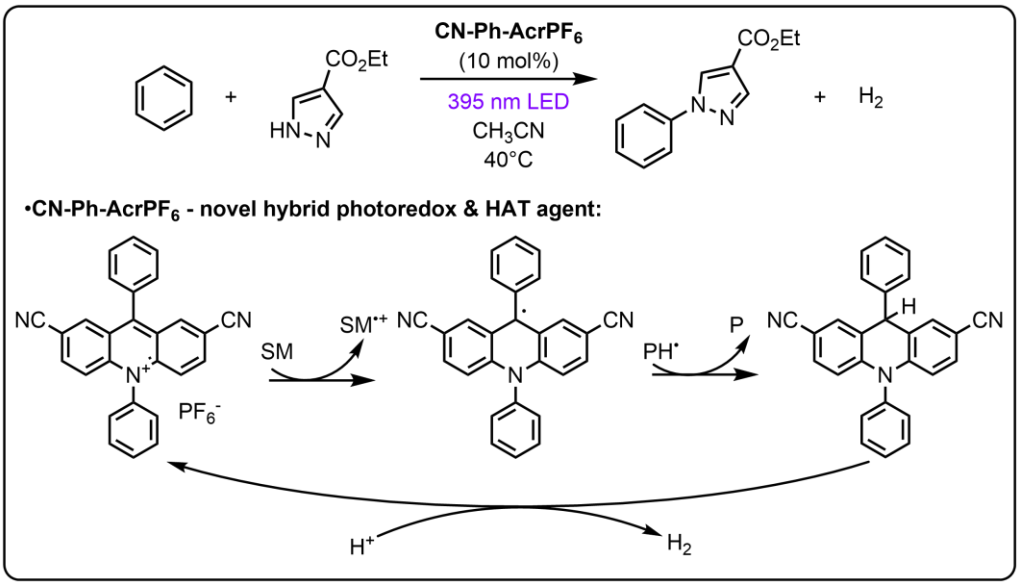
C-H functionalization in the absence of directing motifs represents a powerful strategy for simplifying otherwise long and resource-intensive synthesis routes. While visible light photoredox catalysis has emerged as a cost-effective and environmentally benign approach to C-H functionalization, existing methods utilizing acridinium photocatalysts have consistently required an external oxidant to mediate hydrogen-atom-transfer (HAT). Alternatively, avoiding these external oxidants previously necessitated the use of toxic and costly transition metal-based hydrogen-evolving catalysts. This research introduces a conceptually new, metal-free photocatalytic process for arene C-H functionalization that employs a structurally modified acridinium-type catalyst. Throughout the catalytic cycle, the modified catalyst functions sequentially as an oxidizing agent, a HAT agent, and a proton-reducing agent. This concept has been applied to a C-N coupling between arenes and pyrazoles.



CARBANION-INITIATED DIAGONAL GROB FRAGMENTATION IN SUBSTITUTED CYCLOBUTANES

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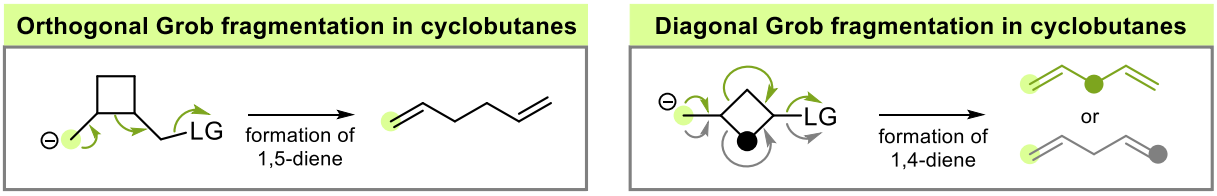
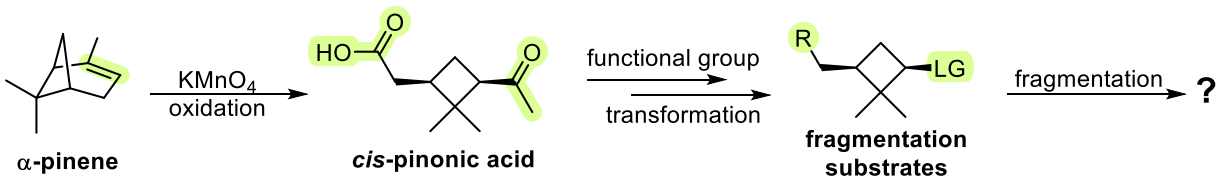
Cyclobutane ring opening is a valuable organic chemistry tool[1] applied in total synthesis and pharmacy. Grob fragmentation is one of the cyclobutane ring opening strategies which usually occurs orthogonally[2] rather than diagonally[3] due to the preferred orbital overlap. Only a few examples of diagonal fragmentation exist, whereas carbanion-initiated diagonal fragmentation is unknown; the regioselectivity and stereoselectivity also remain unclear for non-fused cyclobutanes.



Herein we report a new synthetic approach towards substrates that are potentially suitable for diagonal Grob fragmentation initiated by the carbanion. As a result, it was demonstrated that carbanion-initiated fragmentation in cyclobutanes is possible and proceeds with high regio- and stereoselectivity, but is substrate-dependent.



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EXPANDING AMINE REACTIVITY: LEWIS ACID-ENABLED REMOTE C–H FUNCTIONALIZATION OF AMINES

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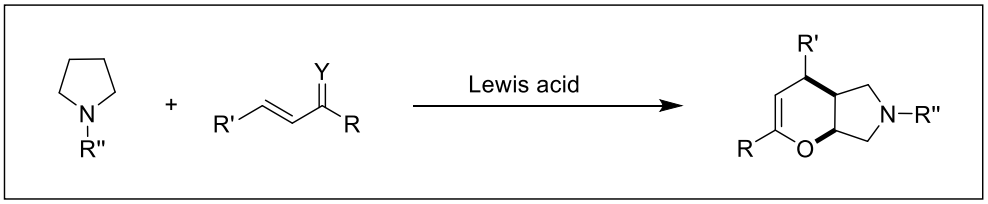
Catalytic C–H activation of amines has emerged as a powerful strategy for the construction of structurally diverse nitrogen-containing molecules. While significant advances have been achieved in the α-functionalization of amines through transition-metal catalysis and Lewis acid-mediated processes[1,2] , although only a limited number of studies have addressed remote C–H activation in tertiary amines.[3] Herein, we report an unprecedented Lewis acid-mediated transformation that enables the sequential and selective activation of multiple C–H bonds in tertiary amines under mild reaction conditions. This unique reactivity reveals a distinct mode of amine activation that diverges from conventional α-functionalization pathways, providing efficient access to structurally diverse nitrogen-containing molecular frameworks. These results expand the scope of Lewis acid-mediated amine activation, offering new mechanistic insights and highlighting its potential for the development of remote C–H functionalization strategies in tertiary amines.



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STEREOCHEMICAL STUDY OF STRAINED, FUSED RING SYSTEMS

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Chirality is a fundamental concept that plays a significant role in science. It is also of tremendous importance to the chemical, pharmaceutical and agricultural industries. Conformational chirality is a specific type of chirality that occurs when a molecule lacks a permanent chiral centre yet still adopts a particular three-dimensional shape which cannot be superimposed on its mirror image. Examples include sterically congested biaryls, helicenes and certain cyclohexane derivatives. Nevertheless, for a molecule to be useful or observable as a chiral entity, there must be a sufficiently high energy barrier to rotation to prevent it from shifting back and forth instantly at room temperature. Thus, the strategic use of steric congestion to lower or block this rotation is important element in this area. As a result, steric factors can force molecules into rare, asymmetric landscapes, opening up new possibilities in chiral catalyst design. Along these lines, this study investigates the unique conformational behaviour of a 4a, 8a-substituted cis-decalin scaffold bearing vicinal methyl esters.

While the straightforward synthesis (**Figure 1A**) and DFT calculations would suggest a highly symmetrical ground state - characterized by both carbonyl groups oriented toward the ring system, our experimental data reveal a more complex conformational reality. X-ray crystallographic analysis (**Figure 1B**) reveals a striking symmetry-breaking event: the molecule adopts a "locked" rotameric state where one carbonyl is oriented toward the bridgehead while the other faces the cyclohexane rings. This rare form of conformational superchirality suggests that transannular strain and subtle non-covalent interactions can override predicted symmetries. Furthermore, crystallographic analysis reveals an emergent form of conformational homochirality, wherein the molecule selectively populates only two of the four theoretically possible conformers.

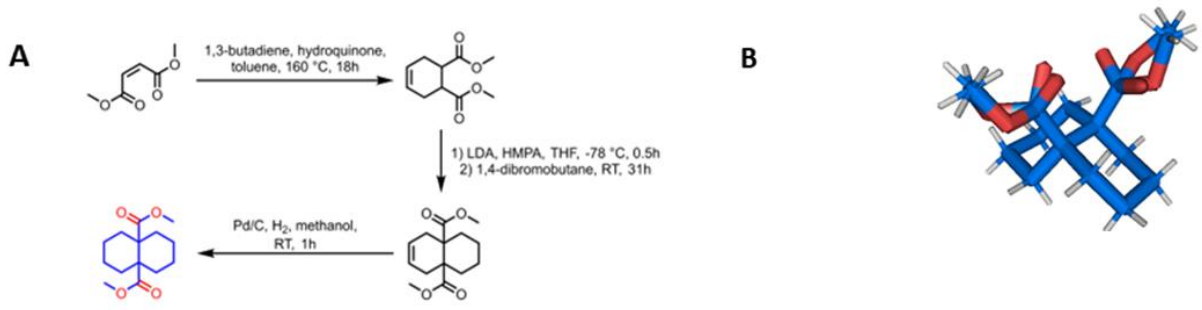

Figure 1: Synthesis of target molecule (A) X-ray crystallography structure (B)

PCT AND IMATINIB FORMULATIONS FOR SYNERGISTIC IMPROVEMENT OF BIOLOGICAL ACTIVITY

Lugiņina, J.;[1] Rjabovs, V.;[1] Kroškins, V.;[1] Turks, M.;[1] Ieviņa, L.;[2] Dubņika, A.;[2] and Juhņeviča, I.[3]

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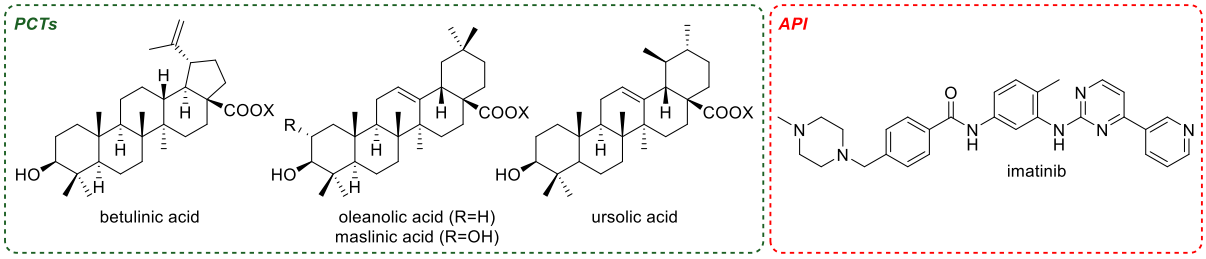
Pentacyclic triterpenoids (PCTs) possess various biological activities[1] that, in some cases, rival those of commercial APIs. A limited number of studies indicate that there's a potential of an improved synergistic effects of PCT and API combinations. Here, we report on evaluation of biological activity of binary salts of PCT-derived natural carboxylic acids (betulinic, maslinic, oleanoic, and ursolic acids) and chemically modified phosphonic acids[2] with imatinib. We have tested these combinations for potential treatment of human osteosarcoma (MG63) and observed synergistic improvement compared to pure imatinib treatment.[3]



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FROM BENCH TO PLANT: LARGE-SCALE AMIDATION USING CONTINUOUS FLOW MECHANOCHEMISTRY FOR GREEN CHEMISTRY MANUFACTURING

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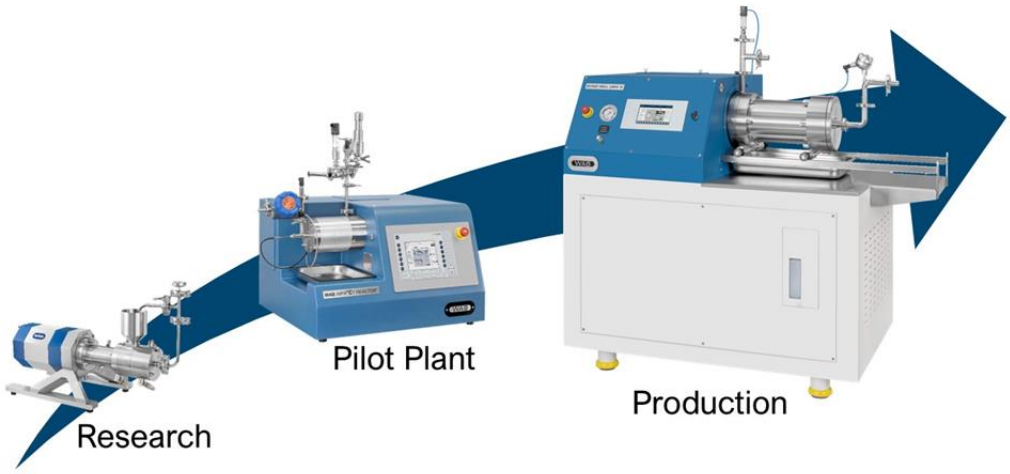
Mechanochemistry, powered by mechanical energy rather than heat or solvents, is emerging as a key enabler of sustainable chemical manufacturing by reducing waste, lowering energy consumption, and eliminating hazardous solvents. To accelerate industrial-scale adoption, WAB-GROUP®'s developed an advanced technologies and integrated into large-scale continuous mechanochemical processes, The WAB IMPA°CT REACTOR®, a unique system combining continuous flow chemistry with bead milling.



There are broad applicability of mechanochemistry through representative transformations—including Diels–Alder reactions, Wittig reactions, amidations,[1,2] esterifications, material synthesis, and the formation of MOFs—underscoring its value as a scalable, cost-effective, and environmentally responsible approach for industrial manufacturing.[1]

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2. Otvos S., Kappe, O.*, Chimica Oggi*, **2026**, 44, 2, March / April

ENHANCING THE KEROX PROCESS: FROM KEROGEN METHYLATION TO ESTERIFICATION IN FLOW

Rõuk, K.;[1] Staškevitš, K.R.;[1] Kimm, M.;[1] Heinmaa, I.;[2] Pehk, T.;[2] Silm, E.;[1] Lopp, M.;[1] and Kaldas, K.[1]

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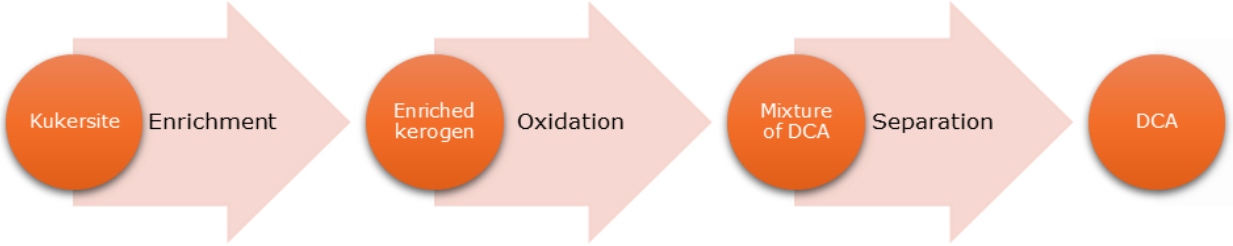
Kukersite, a type of oil shale found in northern Estonia that contains 30-50% of organic material called kerogen, has served as the country's primary energy source for many decades. However, its conventional use in combustion and oil production no longer meets environmental standards, prompting the development of new technologies that utilize kukersite as a source of organic matter and chemicals. One such technology, developed at the Industrial Chemistry Laboratory in cooperation with KEROGEN OÜ, is the KEROX process, which enables the direct conversion of kukersite—without intermediate steps such as oil or energy production—into valuable aliphatic dicarboxylic acids or DCAs. However, some steps in the process could be further improved through continued research and development. For example, the oxidation step, which generates aliphatic DCAs, could also yield aromatic acids if the resorcinol moieties present in kerogen were protected. This complex mixture of dicarboxylic acids would then undergo esterification to enable separation by distillation. However, this step remains challenging and requires further optimization.



Herein, we report the successful methylation of kukersite kerogen as a way to protect the resorcinol moieties during oxidation. Furthermore, we report our preliminary studies on the esterification of complex mixtures of aliphatic dicarboxylic acids under flow conditions.

BRIDGING DISCOVERY AND PRACTICALITY: VISIBLE-LIGHT AZA PATERNÒ–BÜCHI ACCESS TO BICYCLIC FUSED AZETIDINES

Shpotya, I. S.;[a,b] Parikh, S. G.;[c] Sham, V. A.;[a,d] Volochnyuk, D. M.;[a,b,d,e] Schindler, C. S.;[c,f,g] and Ryabukhin, S. V.[a,b,e]

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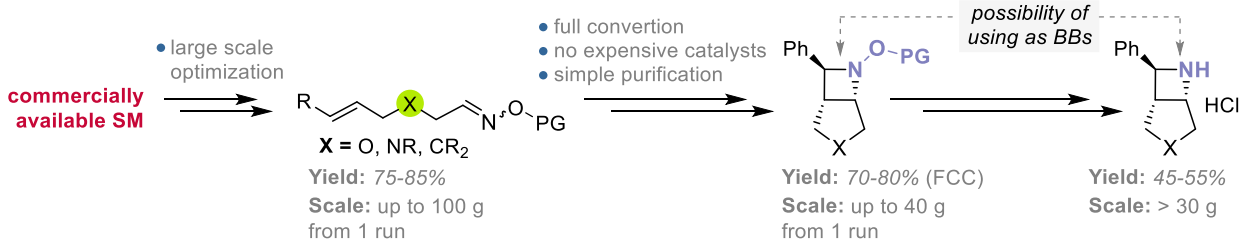
Although the azetidine core is becoming increasingly popular in medicinal chemistry, its commercial availability and diversity remain limited, particularly for bicyclic fused structures. This limitation drives the creation of new synthetic methods, often utilizing novel disconnection strategies. Visible-light-based procedures stand out from other approaches due to their cost-efficiency, environmental friendliness, lower resource requirements, and easier operation. Nevertheless, the pharmaceutical industry is still reluctant to implement these strategies because of scale-up and optimization difficulties, including poor yields, challenging separation and purification processes, restricted diversity, and/or scarce availability of starting materials in the market. These obstacles frequently render the "rocket" innovations impractical or difficult to apply in large-scale production of useful synthetic building blocks. In this study, we show how working directly between industry and method developers can address this critical limitation. Through partnership with Professor Corinna Schindler's research group, building upon their groundbreaking work published in Nature Communications, we present a comprehensive expansion of a reliable method for synthesizing various bicyclic fused azetidines. The compounds are produced at scales ranging from tens to hundreds of grams with commercially viable yields at a cost-efficient rate. We also demonstrate the potential use of these compounds as building blocks in medicinal chemistry applications.



COREY–CHAYKOVSKY RING EXPANSION OF THIIRANES AS A PRACTICAL ENTRY TO 2-SUBSTITUTED THIETANES

Babchenko, I. E.;[a,b] Obushak, M. D.;[b] Granat, D. S.;[a,c] Lomaka, M. A.;[a,c] Leha, D. O.;[c,d] Volochnyuk, D. M.;[a,c,e] and Ryabukhin, S. V.[a,c,e]

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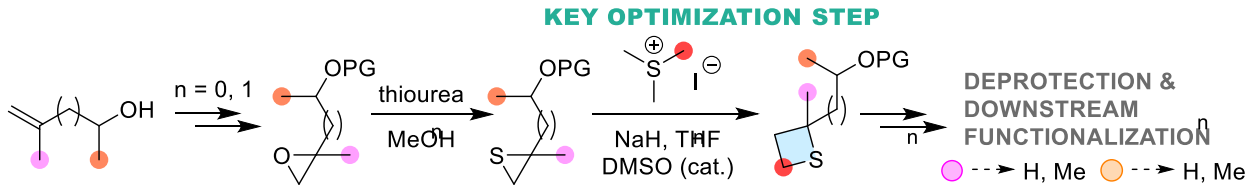
Thietanes are valuable four-membered sulfur heterocycles with potential applications in medicinal chemistry and as intermediates for the synthesis of more complex sulfur-containing molecules. However, their broader use remains limited by the lack of general and scalable approaches to functionalized derivatives. Among the available strategies, ring expansion of three-membered sulfur heterocycles offers an attractive yet underexplored entry to substituted thietane scaffolds.

In this work, we developed a concise route to 2-substituted thietanes based on Corey–Chaykovsky-mediated ring expansion of thiiranes. The thiirane precursors were prepared from readily available allylic or homoallylic alcohol derivatives *via* epoxidation and subsequent thiourea-mediated thionation. The key ring-expansion step was optimized with particular focus on the protecting group of the hydroxyl functionality, which was found to be essential for efficient and reproducible formation of the thietane ring. The developed protocol provides scalable access to hydroxyl-functionalized 2-substituted thietanes and can be applied to enantiomerically enriched substrates, enabling the synthesis of chiral thietane building blocks. The obtained products can be further oxidized to the corresponding sulfones, thereby expanding the structural and physicochemical diversity of the resulting scaffolds. Thus, the proposed thiirane-to-thietane ring-expansion strategy offers a practical platform for accessing underexplored sp^3-rich sulfur-containing building blocks relevant to medicinal chemistry. Among other things, this report will discuss the substrate scope, scalability options, and the peculiarities of the synthetic sequence leading to thietane products.



SCALABLE THIA-PRINS CHEMISTRY FOR THE CONSTRUCTION OF sp^3-RICH SULFUR-CONTAINING SCAFFOLDS

Lomaka, M. A.;[b,c] Babchenko, I. Y.;[c] Granat, D. S.;[b,c] Leha, D. O.;[a,b] Volochnyuk, D. M.;[a,b,c,d] and Ryabukhin, S. V.[a,b,c]

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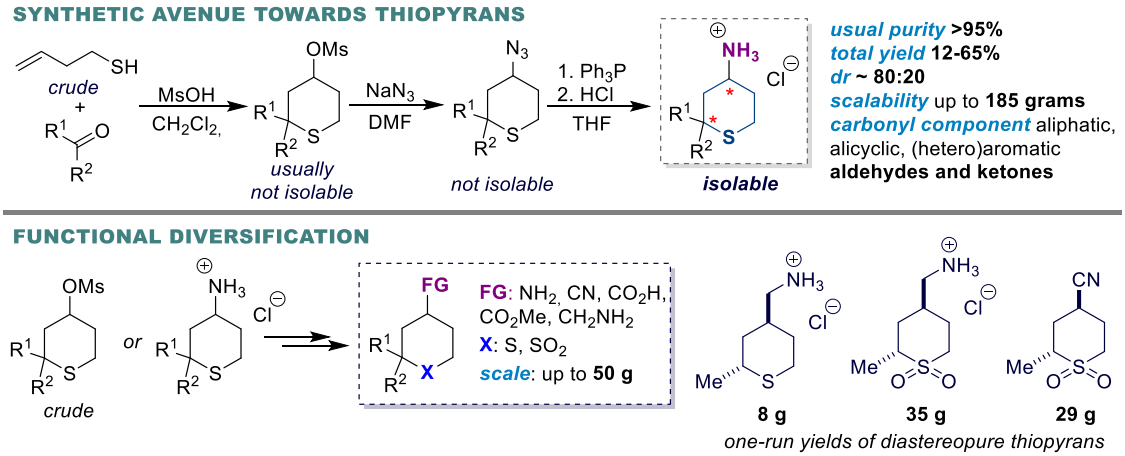
Saturated sulfur-containing heterocycles represent attractive structural motifs for medicinal chemistry, offering opportunities to modulate lipophilicity, polarity, molecular shape, and conformational behavior. However, tetrahydrothiopyran scaffolds remain considerably less explored than their oxygen- and nitrogen-containing analogs, largely due to the limited availability of practical, scalable synthetic methods.

Herein, we present a scalable thia-Prins-based platform for the preparation of functionalized tetrahydrothiopyran building blocks. The approach relies on the acid-promoted cyclization of homoallyl thiol with diverse carbonyl compounds, followed by *in situ* functional-group manipulation to give isolable water-soluble aminium salts. This feature proved crucial for practical purification, enabling efficient separation of target thiopyran derivatives from complex reaction mixtures without chromatographic purification. The developed protocol was demonstrated on a multigram scale, yielding 4-amino-substituted tetrahydrothiopyrans with good diastereoselectivity. The synthetic utility of the obtained intermediates was further expanded through C4 diversification. Crude mesylate and azide intermediates, as well as isolated aminium salts, were employed for the preparation of thiopyran derivatives bearing nitrile, carboxylic acid, aminomethyl, sulfone, and triazole-linked fragments. In addition, oxidation of the sulfur atom enabled access to the corresponding S,S-dioxides, further increasing the diversity and medicinal-chemistry relevance of the resulting scaffolds.



DESIGN, SYNTHESIS, AND BIOPHYSICAL EVALUATION OF NOVEL TPP RIBOSWITCH LIGANDS BASED ON FRAGMENT OPTIMIZATION

Ryczkowska, M.[1]; Brokāne-Ķikure, K.[1]; Todoran, O.[2]; Panchal, V.[2]; Silva, C. F.M.[3]; Haug, B. E.[3]; Brenk, R.[2]; and Šmits, G.[1]

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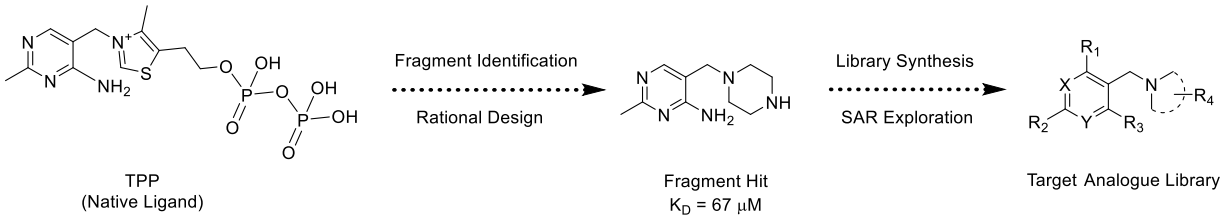
The fast rise of multidrug-resistant bacteria creates an urgent need for new antibiotics with novel modes of action. Bacterial riboswitches, especially the thiamine pyrophosphate (TPP) riboswitch, are very promising molecular targets. These non-coding RNA elements regulate essential metabolic pathways in bacteria and are not present in humans. Therefore, blocking their function is a good strategy to develop new antimicrobial drugs.[1,2] In this work, we present a structure-based design and synthesis of new ligands for the TPP riboswitch. Our project starts from a previously found fragment hit, which shows a binding affinity with a dissociation constant (K_D) of 67 μM. To systematically study the structure-activity relationships (SAR) and improve the interactions in the binding pocket, we designed a library of structural analogues. Their binding profiles are being evaluated using surface plasmon resonance (SPR) and isothermal titration calorimetry (ITC). The preliminary SAR trends provide important information about the structural requirements for riboswitch inhibition and help to develop high-affinity antibacterial agents.



Acknowledgements

This research is co-funded by the European Union (European Regional Development Fund), No.1.1.1.9/LZP/1/24/010 "Novel TPP riboswitch ligands as potential antibiotics"

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BRINGING PTERINS TO THE FLAVIN ERA: BENZOPTERINS AS PROMISING PHOTOCATALYSTS AND FLUORESCENT MARKERS

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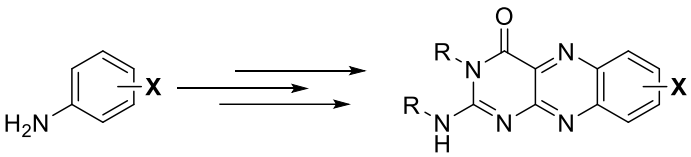
Nature gave pterins a minor role in biological systems. Its reduced solubility and lack of stability during redox processes made them unappealing compared to its flavin counterpart, which is found in the well-known FAD(H_2) cofactor.[1] As a result, pterins have been relegated to coordinating cofactors or pigmentation in animals.[2,3]

However, these limitations did not stop them to be reactive compounds with an interesting photochemistry. On the former, it has been associated with the degradation of tyrosine by phenol coupling or photooxidation of tryptophan on the skin.[4] On the later, the close proximity between low-laying singlet states ($S_{n\pi^*}$ and $S_{\pi\pi^*}$) gives an outstanding playground to tune its properties.[5]



- ***6-steps synthesis, up to 15% overall yield***
- ***Only 3 purifications required***
- ***LQY from 4,5%-60%***

X= H, OMe, COMe, NEt_2, F, Cl...

Aided with predictions from TD(A)DFT calculations, substituted *N*-alkylated benzopterins were synthesized to improve its singlet or triplet formation. The photophysical, redox and catalytic properties are measured to confirm the desired effect. We develop a versatile molecular photosystem for both biological and synthetic applications.

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MECHANOCHEMICAL SYNTHESIS AND STRUCTURE OF POSITIONAL ISOMERS OF NEW CHIRAL HEMICUCURBITURILS

Satsi, R.; Viderman, A.; Prigorchenko, E.; Merzhyievskyi, D.; Lootus, K.-M.; Jarg, T.; Reitalu, R.; Öeren, M.; and Aav, R.

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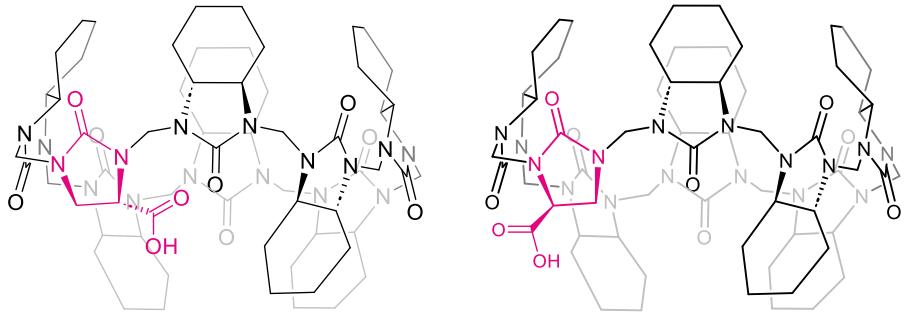
Chiral hemicucurbiturils are promising receptor molecules that have been used for sensing and separation, and their synthesis can be done mechanochemically.[1-4] In this work, a new chiral cyclohexanohemicucurbituril incorporating a carboxylic acid bearing ethyleneurea monomer was synthesized. Milling and subsequent aging were applied to facilitate the acid-catalyzed polycondensation and template-driven macrocyclization. Design of experiments approach was used for optimization of the reaction conditions and identification of key parameters influencing macrocycle formation. Product was synthesized in 35% HPLC yield. The reaction was found to produce two positional isomers of the macrocycle with distinct conformational dynamics. Computational chemistry enabled the identification of which structure corresponds to the more dynamic and which to the less dynamic isomer.



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ACYCLIC DIARYL λ³-BROMANES: SYNTHESIS AND USE IN CYCLOADDITION REACTIONS VIA ARYNE GENERATION

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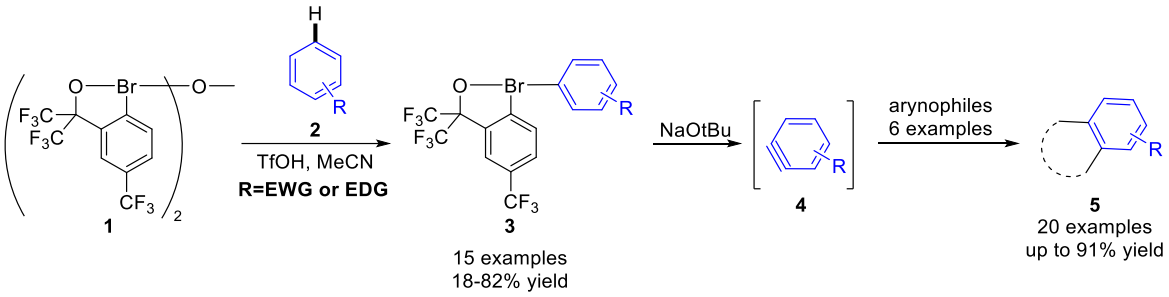
The chemistry of hypervalent bromine(III) compounds is rapidly advancing. Cyclic biaryl λ³-bromanes exhibit unique reactivity – they can generate arynes under rather mild conditions.[1] By contrast, acyclic diaryl λ³-bromanes, which could offer conversion of a single aryl group into an aryne, remain underexplored, and all reported methods for their preparation from non-prefunctionalized arenes rely on the use of highly toxic BrF_3.[2]

Herein, we report the use of a stable, electrochemically generated Br(III) compound **1** in the synthesis of the acyclic diarylbromanes **3** via Friedel-Crafts reaction with arenes **2**, containing different electron-donating or electron-withdrawing groups.[3] Diarylbromanes **3** are used in cycloaddition reactions with various arynophiles through aryne generation in the presence of a strong base.



Acknowledgements: This research is funded by the Latvian Institute of Organic Synthesis internal student grants IG-2025-07, IG-2026-09.

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PROPARGYL SILANE ARYLATION-1,2-SILYL SHIFT-HETERO-CYCLIZATION CASCADE REACTION

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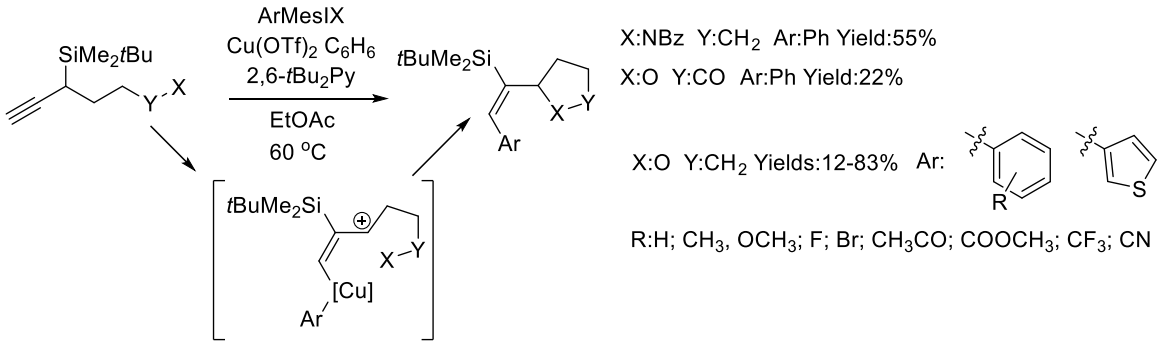
Previously we published synthetic methodology for propargyl silane 1,3-difunctionalization using 1,2-silyl shift.[1] Our current work involves copper catalyzed arylation of propargyl silanes with diaryliodanes, followed by a 1,2-silyl shift. This creates an electrophilic carbon center that can react with an internal nucleophile, leading to a formation of a heterocycle. Diaryliodanes with electron donating and electron withdrawing aromatic groups and some heteroaromatic groups, as depicted below, can be used to form a substituted tetrahydrofurans. Pyrrolidine and furan-2-one cycles may also be formed, albeit with lower yields and narrow diaryliodane scope.[2]



Acknowledgements: The Latvian Council of Science Grant LZP-2023/1-0576 is kindly acknowledged for financial support.

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PROGRESS IN TOTAL SYNTHESIS OF NOSTOLACTONE 4

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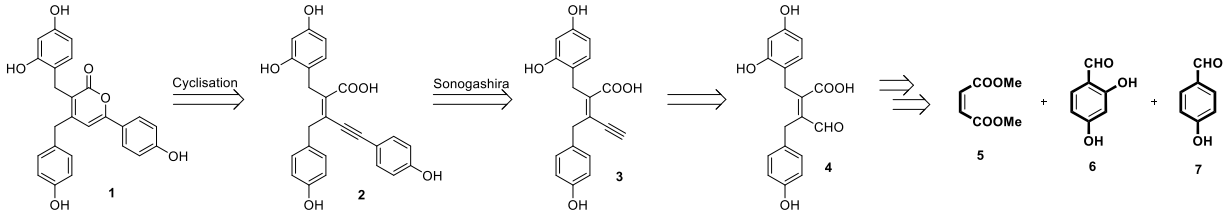
Nostolactone 4 (**1**) is a polyphenolic compound isolated from the cyanobacterial strain *Nostoc sp.* possessing biological activity against some Gram-positive bacteria.[1] Its skeleton is composed of 2,3,5-trisubstituted δ-lactone ring and it has not been synthesized yet. The aim of this work is to develop the total synthesis of nostolactone 4, to optimize the reaction steps, to prepare a library of its analogues and then to test their biological activities.

One of the possible ways studied (Scheme 1) is based on the generating alkynyl from aldehyde **4** using different reaction conditions (Corey–Fuchs, Bestmann–Ohira, Seyferth–Gilbert). Derivatization of the terminal triple bond of **3** via Sonogashira coupling would furnish the opened analogue **2**, whose cyclization in acidic conditions would give us the desired compound nostolactone 4 (**1**). Herein, we present the initial attempts towards the acid 4 as well as other synthetic approaches.

Scheme 1. – Retrosynthetic approach to synthesis of nostolactone 4



Acknowledgements: This work was supported by Charles University (SVV 260661, GAUK 149124)

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SYNTHESIS OF *N*-HETEROCYCLIC BODIPY DYES FOR APPLICATIONS IN ANTIMICROBIAL PHOTODYNAMIC THERAPY

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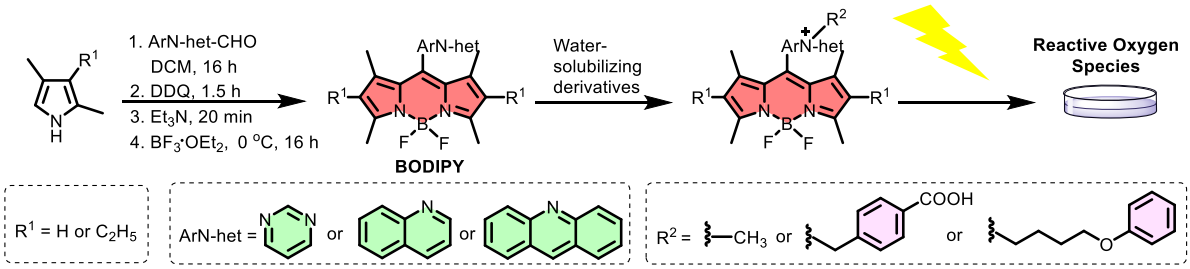
BODIPY (4,4-difluoro-4-bora-3*a*,4*a*-diaza-*s*-indacene) dyes are fluorophores recognized for their high fluorescence quantum yields, strong chemical stability and adjustable absorption/emission profiles. Derivatization of the BODIPY core is known to augment the biochemical and photophysical properties of these dyes, resulting in their biomedical application as probes, for fluorescence imaging and photosensitizers (PSs) in photodynamic therapy (PDT).[1,2]Although BODIPYs have been widely investigated as PDT agents for cancer treatment, their use in antimicrobial PDT (aPDT) against prokaryotes has potential for further exploration with the rise in microbial resistance to conventional antibiotics. Previous studies on meso-pyridinium BODIPYs gave promising results in photodynamic applications against prokaryotes, highlighting their potential in aPDT.[3] This work presents the synthesis and functionalization of a small library of cationic meso-*N*-heterocyclic BODIPY derivatives capable of being investigated in a biological medium. Finally, the suitability of these scaffolds was examined for deep tissue treatments.



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STIMULI-RESPONSIVE H-BONDED SUPRAMOLECULAR SYSTEMS

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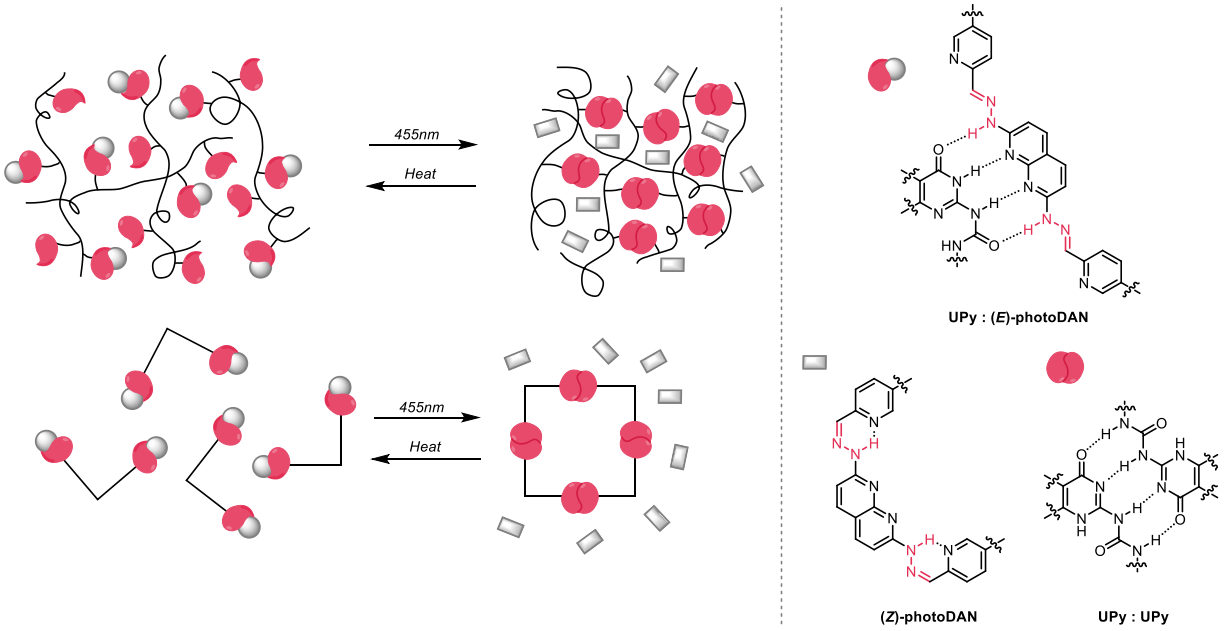
Stimuli-responsive supramolecular systems have emerged as promising materials for adaptive and reconfigurable systems due to their dynamic and reversible non-covalent interactions. However, designing smart hydrogen-bonded materials that exhibit controlled and predictable switching behavior under external stimuli remains challenging.

In our report, we design and investigate H-bonded supramolecular systems constructed from ureidopyrimidinone (UPy) and 1,8-naphthyridine-2,7-diamine (DAN) motifs incorporated with stimuli-responsive hydrazone functional groups. These systems dynamically reorganize their structures in response to external stimuli, undergoing E→Z isomerization upon light exposure and reverting to the E isomer upon heating. NMR, UV–VIS spectroscopy, and viscosity measurements were employed to establish structure–property relationships and confirm quasi reversible switching behavior.

The rational design principles presented in this research provide a framework for engineering next-generation adaptive materials, such as smart coatings, self-healing materials or drug delivery systems, with programmable and reversible functionalities.



NOVEL PYRIDINE-1,2,4-TRIAZOLE-3-THIONE DERIVATIVES AS PROMISING ANTIMICROBIAL AGENTS

Šermukšnytė, A.; Stasevych, M.; Komarovska-Porokhnyavets, O.; Zvarych, V.; Kantminienė, K.; and Tumosienė, I.

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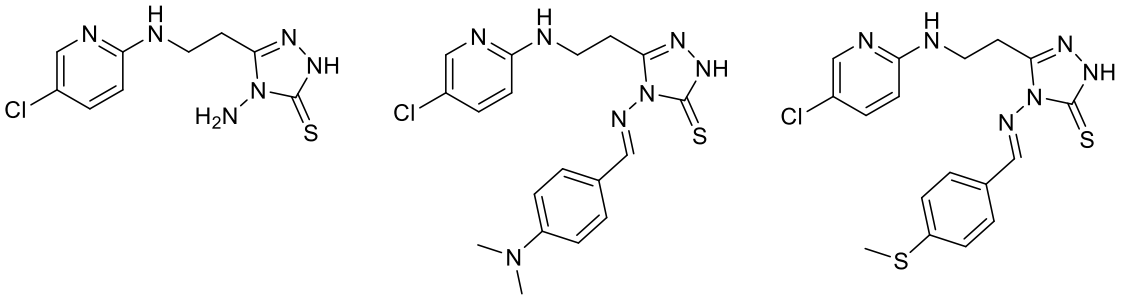
1,2,4-Triazole derivatives are widely explored in medicinal chemistry because of their unique pharmacophoric properties. As both pyridine and 1,2,4-triazole exhibit notable bioactivity, their combination may enhance anticancer and antimicrobial properties.

In this work, a series of novel pyridine-1,2,4-triazole-3-thione derivatives bearing hydrazone moieties was synthesized and evaluated for their antimicrobial potential. The synthetic route involved the preparation of *β*-alanine intermediates by reacting 2-aminopyridine and 2-amino-5-chloropyridine with acrylic acid under reflux conditions. Subsequent cyclization with thioacetohydrazide yielded the corresponding 4-amino-1,2,4-triazole-3-thione derivatives. Their subsequent condensation with various aldehydes afforded the target compounds in moderate to good yields. The structures of all synthesized compounds were confirmed by ^{1}H and ^{13}C NMR spectroscopy as well as mass spectrometry.

Among the tested compounds, 5-chloropyridine-based 4-amino-1,2,4-triazole-3-thione and its hydrazone derivatives bearing 4-dimethylaminobenzylidene and 4-methylthiobenzylidene substituents exhibited the highest antimicrobial activity. These compounds showed strong antibacterial effects against *M. luteum* and antifungal activity against *C. tenuis*. Overall, several of the synthesized pyridine-1,2,4-triazole-3-thione derivatives demonstrated promising antimicrobial activity and may act as lead compounds for further development.



ORGANOCATALYTIC ACTIVATION OF HYDROGEN PEROXIDE BY PYRIDYL-3-BORONIC ACIDS FOR SUSTAINABLE OXIDATION

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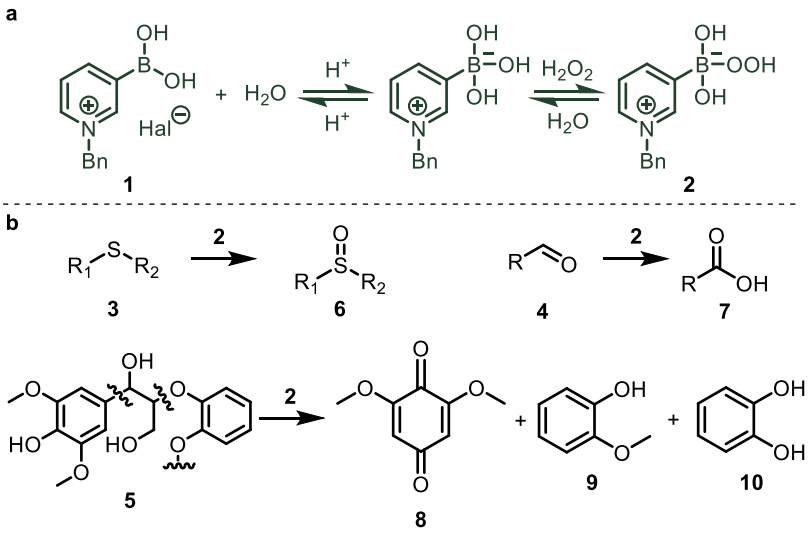
Hydrogen peroxide is regarded as an attractive and environmentally benign oxidant owing to its low cost, high active oxygen content, and the formation of water as byproduct. Nevertheless, the efficient oxidation of most functional groups typically requires catalytic activation of H_2O_2 to achieve sufficient reactivity and selectivity.[1] The demand for sustainable oxidation processes for the synthesis of active pharmaceutical ingredients (APIs), their intermediates,[2] and for biomass valorization, particularly lignin conversion,[3] continues to grow steadily.

In this work, hydrogen peroxide was activated by 1-benzyl-3-boronopyridinium bromide **1** to generate peroxoboronic acid **2** *in situ*. The resulting oxidation system was evaluated using sulfides **3**, aldehydes **4**, and the lignin β-O-4 model compound **5** as substrates. Consequently, the corresponding sulfoxides **6**, carboxylic acids **7**, and β-O-4 bond cleavage products (2,6-dimethoxy-p-benzoquinone **8**, 2-methoxyphenol **9**, and benzene-1,2-diol **10**) were obtained.



Acknowledgements: This work was supported by the Estonian Research Council via project TEM-TA49.

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DESYMMETRIZATION OF *PSEUDO-PARA* DIFORMYL-[2.2]PARACYCLOPHANE VIA BRØNSTED ACID–CATALYZED REDUCTIVE AMINATION

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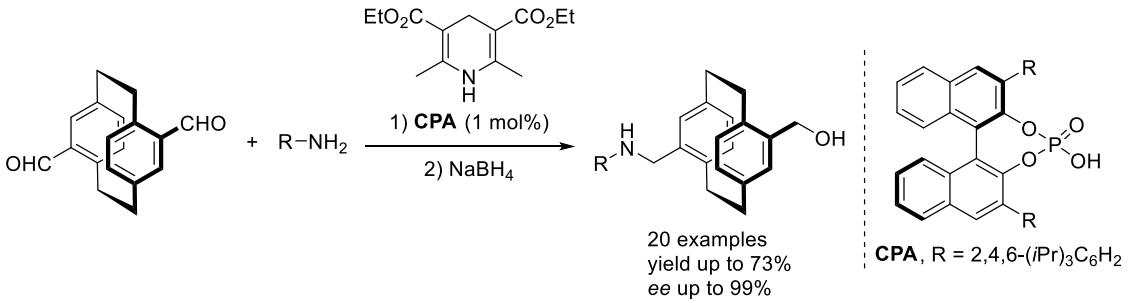
Accessing planar-chiral molecules remains a major challenge in asymmetric synthesis. Enantiopure [2,2]paracyclophane derivatives have attracted increasing attention over the past decade for their significant applications in asymmetric synthesis and in diverse areas of materials science. As a result, developing efficient asymmetric synthetic methods for these compounds is of great importance and remains a focal point in the field.

Building on our earlier contributions to this field[1], we report a highly stereoselective organocatalytic desymmetrization of prochiral *pseudo-para* diformyl-[2.2]paracyclophanes via chiral phosphoric acid-catalyzed reductive amination.[2] Using a BINOL-derived Brønsted acid catalyst and a Hantzsch ester as the hydride source, the method delivers planar chiral paracyclophane derivatives in good yields (up to 73%) and excellent enantioselectivities (up to 99% *ee*) under mild conditions, with catalyst loadings as low as 1 mol%. The reaction exhibits a broad amine scope and enables efficient access to versatile enantioenriched paracyclophane building blocks. Mechanistic studies indicate that stereocontrol arises from enantioselective desymmetrization. Subsequent product derivatizations further demonstrate the synthetic utility of the planar-chiral scaffolds obtained.



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SINGLE-STEP CONVERSION OF FURANS TO PYRIDINES

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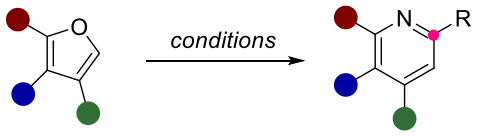

Skeletal editing, recently popularized by Levin, Sarpong, and others, represents a highly promising approach for the core diversification of molecular scaffolds, often possible in the late stage of the synthetic sequence.[1] Even though this concept has already received a lot of attention from the synthetic and medicinal chemistry community, the current portfolio of available methods for skeletal editing remains quite limited, and further developments in this area are needed. In particular, novel methods to access pyridines from other heterocycles are desirable, as pyridine represents the second most popular core in FDA-approved drugs.[2] Furans constitute the perfect starting point for such skeletal modifications, as they are widely available from bio-based sources, but less common in bioactive compounds.

We developed a method for conversion of furans to pyridines with insertion of C2-substituent. After thorough optimization, optimal conditions for such transformation were established. The reaction possesses wide scope in terms of accessible substitution patterns, identity of the substituents on the inserted carbon atom, and functional group tolerance. The efficiency of the reaction was further demonstrated by late-stage transformation of furan-containing natural products to their pyridine analogues. Based on our mechanistic scenario, we also developed conversion of industrially relevant furfural derivatives to pyridines, as well as pyridylation of carbon nucleophiles.

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FLUOROIODOCARBENE ADDITION TO BICYCLOBUTANES: A RADICAL HANDLE FOR QUATERNARY FLUORINATED BICYCLO[1.1.1]PENTANES

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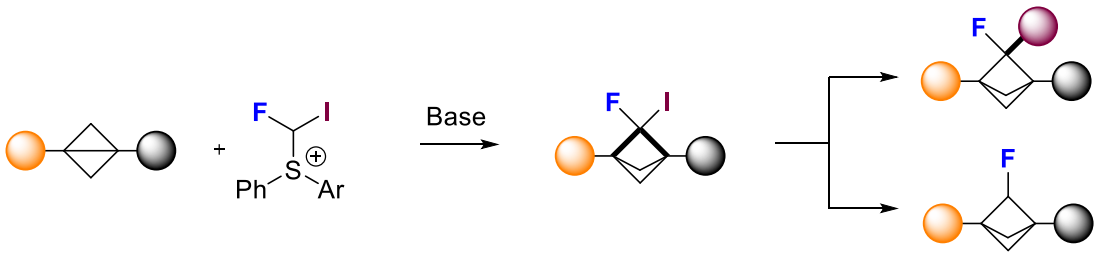
Fluorinated bicyclo[1.1.1]pentanes (BCPs) represent attractive motifs in medicinal chemistry, combining the pharmacological benefits of fluorine incorporation with the utility of BCPs as saturated, three-dimensional bioisosteres of benzene.[1] Although fluorinated BCPs have attracted increasing interest in drug discovery, bridge-monofluorinated derivatives remain scarce[2, 3], and quaternary fluorinated analogues are still unknown. These unexplored architectures could provide valuable opportunities to modulate molecular properties and expand chemical space.

Herein, we report the synthesis of bridge-fluorinated BCPs through fluoroiodocarbene addition to bicyclobutanes from a sulfonium salt[4] under mild conditions, enabling access to 2-fluoro-2-iodobicyclo[1.1.1]pentanes. The resulting C-I bond serves as a versatile synthetic handle for functionalization, in particular for C-C bond formation with activated alkenes as well as dehalogenation under photochemical conditions.

This strategy provides access to bridge-fluorinated and previously unknown quaternary fluorinated BCPs, expanding the chemical space of fluorinated saturated bioisosteres for medicinal chemistry.



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SYNTHESIS OF AN OXYGENATED METHANOINDENE CAGE TOWARD LIBIGUIN A

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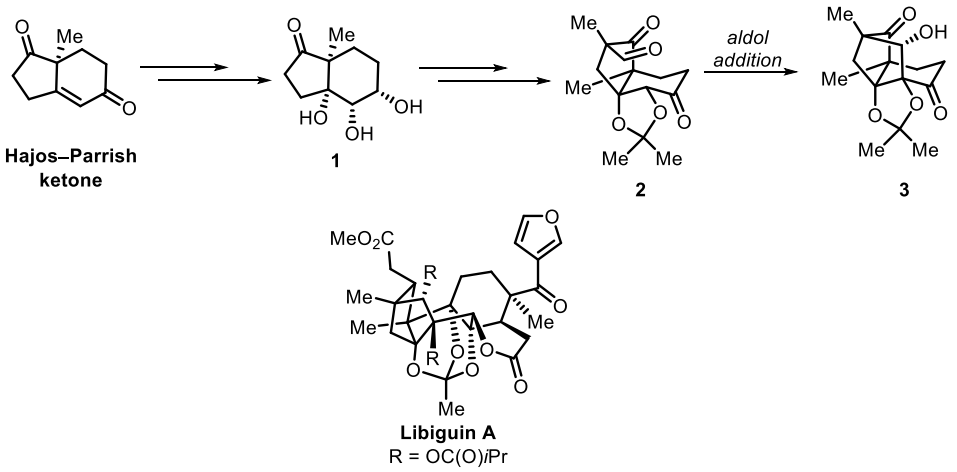
Phragmalin-type natural products are characterized by an octahydro-1*H*-2,4-methanoindene core within their carbon skeleton. Among them, Libiguin A has attracted significant attention because of its potential as a treatment for erectile dysfunction.[1] As part of our ongoing efforts toward the total synthesis of Libiguin A and its analogues, we previously constructed the methanoindene cage through an intramolecular aldol addition.[2] Herein, we describe the incorporation of oxygenated bridgehead positions into this scaffold via the transformation of the Hajos–Parrish ketone to triol precursor **1**, enabling the synthesis of the oxygen-rich methanoindene cage **3**, an advanced intermediate that more closely reflects the highly oxygenated framework of Libiguin A.



Acknowledgements: This project is funded by Latvian Council of Science 1.1.1.9. activity "Post-doctoral research" (grant agreement no. 1.1.1.9/LZP/1/24/032).

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DECONJUGATIVE CARBON INSERTION INTO ACYCLIC π-SYSTEMS

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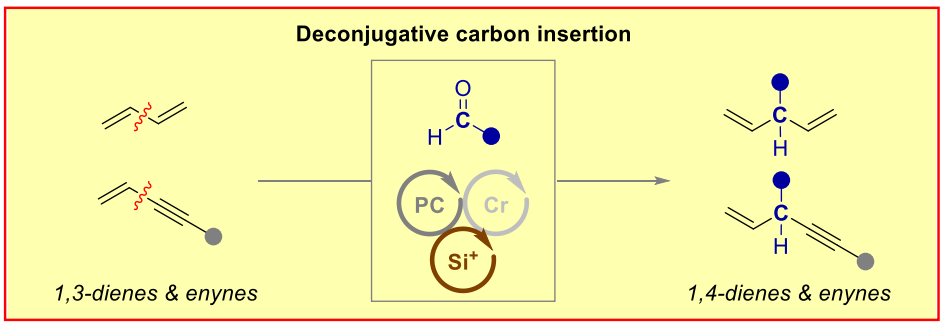
Contrary to their conjugated 1,3-counterparts, 1,4-dienes are significantly underrepresented building blocks despite their considerable synthetic potential.[1] A major challenge in their synthesis and handling can be attributed to the pronounced tendency to isomerize to the thermodynamically favored conjugated 1,3-dienes, which contributes to their scarcity and high cost. Accordingly, previously reported methodologies typically rely on specifically designed substrate cores and exhibit limited tolerance towards substitution patterns.[2,3]

To address this limitation, this work presents a deconjugative carbon insertion strategy that enables the direct conversion of simple acyclic 1,3-dienes and enynes into valuable 1,4-dienes and enynes. The transformation uses readily available aldehydes as single-carbon source and proceeds *via* a photocatalytically initiated Nozaki–Hiyama–Kishi reaction, furnishing stable homoallylic alcohol intermediates. In a subsequent step, activation with trimethylsilyl triflate induces a 1,2-alkenyl or alkynyl migration, followed by elimination to deliver the deconjugated products with high efficiency.

Importantly, the stable intermediates can be readily functionalized at the terminal alkene prior to migration, enabling streamlined access to unsymmetrical 1,4-dienes with excellent chemo-, regio-, and *E/Z*-selectivity. Diverse derivatization efforts and an extensive scope demonstrate the potential of the product motif as a platform for rapid access to complex and bioactive molecules.



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NAPHTHALIMIDE DERIVATIVES WITH EXTENDED HETEROCYCLIC SYSTEMS—SYNTHESIS, SPECTRAL AND SENSING PROPERTIES

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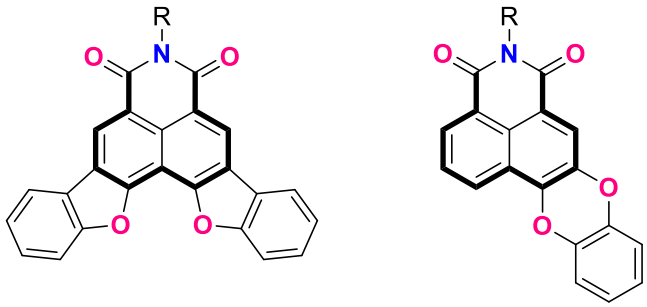
Benzofuran- and benzodioxin-annulated naphthalimides bearing either a dimethylaminoethyl receptor or a non-donating alkyl substituent at the imide nitrogen were synthesized using tailored synthetic strategies. Their photophysical properties were investigated by absorption and fluorescence spectroscopy, while sensing performance was evaluated by fluorescence titrations. Quantum chemistry calculations were employed to rationalize experimental observations. The study demonstrates that heterocyclic annulation critically governs the electronic structure and sensing performance of naphthalimide fluorophores, providing guidelines for the rational design of PET-based optical sensors.[1]



Acknowledgments: This research was funded by the Bulgarian National Science Fund, grant number KP-06-H61/1.

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CONTINUOUS-FLOW ELECTROCHEMICAL FERRIER REARRANGEMENT OF GLYCALS

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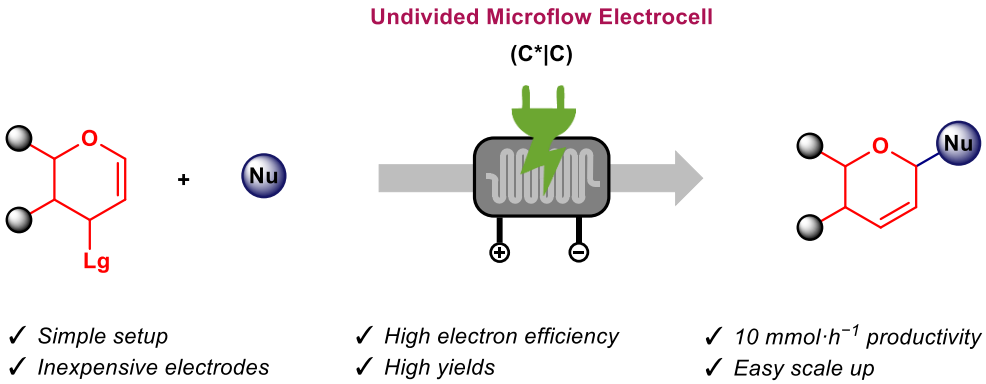
The integration of electrochemistry with flow chemistry offers an efficient and sustainable platform for organic synthesis. The favourable reactor characteristics improve mass transfer and reaction efficiency while reducing supporting electrolyte requirements.[1]

In this work[2], we report a flow-enabled electrochemical variant of the Ferrier rearrangement, a transformation that typically relies on strong acids or stoichiometric oxidants to convert glycals into unsaturated glycosyl derivatives. This work demonstrates broad substrate compatibility, allowing various glycals and nucleophiles to furnish 2,3-unsaturated glycosyl derivatives efficiently. Notably, the reaction performs reliably at faster flow rates, making it readily scalable for continuous synthesis. This approach outperforms the earlier batch version and represents a significant advancement in the application of flow electrochemistry for the carbohydrate synthesis.[3]



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4-METHYLENE-γ-SULTINE SYNTHESIS THROUGH PALLADIUM-CATALYZED [3+2] CYCLOADDITION OF METHYLENECYCLOPROPANES WITH SULFUR DIOXIDE

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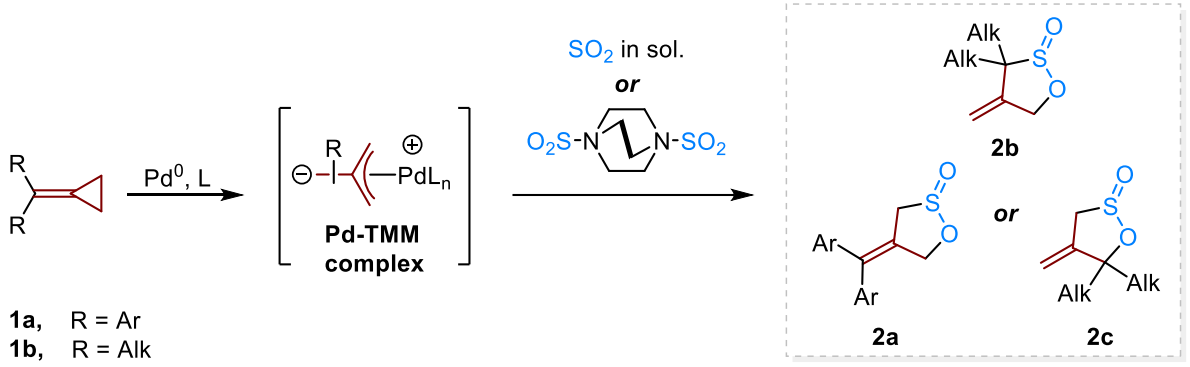
γ-Sultines are a class of compounds with various applications, mainly stemming from the chirality of the sulfur atom and their utility as synthetic intermediates.[1-3] Their synthesis via formal cycloaddition of trimethylenemethane (TMM) with sulfur dioxide is not reported in the literature.

Our group developed a novel method for 4-methylene-γ-sultine synthesis, which employs methylenecyclopropanes **1** as a TMM source, which through palladium catalysis reacts with sulfur dioxide to form sultines **2**. Interestingly, substrate-dependent sultine isomerism was observed. For diaryl-MCPs **1a**, only one isomer **2a** was isolated. However, for dialkyl-MCPs **1b** or aryl-/alkyl- substrates, it was dependent on substituents, SO_2 source, and reaction time. Sultine isomers **2b** and **2c** dominate for dialkyl-MCPs. Obtained sultines **2a-c** are versatile synthetic intermediates that undergo various further synthetic transformations that will be discussed in detail.



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SCALABLE MECHANOCHEMICAL SYNTHESIS OF BIOTIN[6]URIL AND SELECTIVE LANTHANIDE RECOGNITION BY ITS DERIVATIVES

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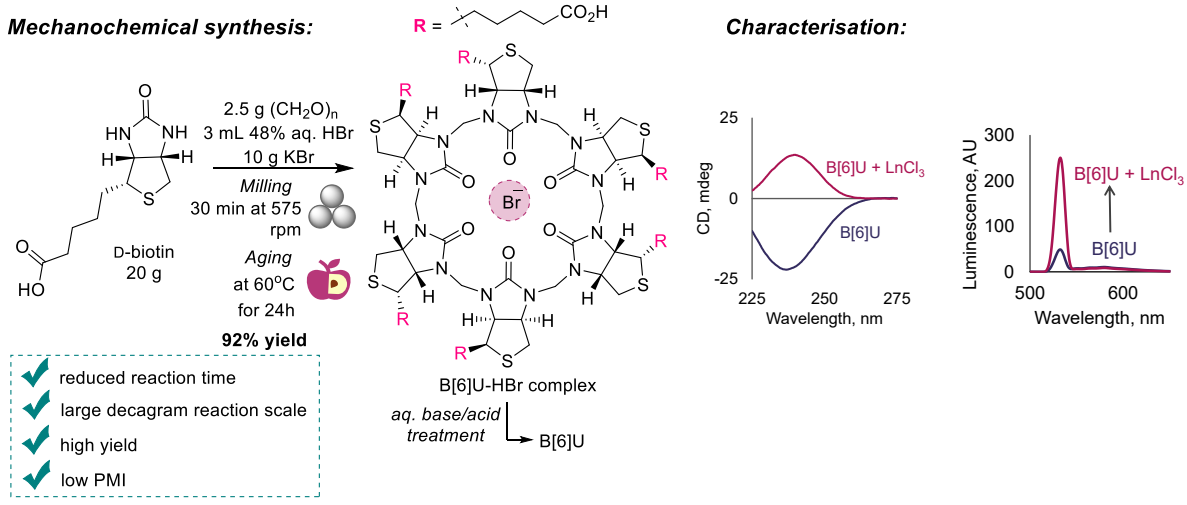
Biotin[6]uril (B[6]U) is a chiral, water-soluble cavitand with anion binding properties. The presence of six carboxylic groups allows for versatile functionalization, supporting the development of B[6]U derivatives with diverse structural and electronic characteristics.[1,2] Previously B[6]U has been synthesized via the solution-based approach in moderate yields.[3] We present a solvent-free mechanochemical route using shaker and planetary ball mills, enabling efficient scale-up to decagram quantities.[4] Optimization of templating additives, aging time and milling parameters led to an 82-fold scale-up, yielding ca 20 g B[6]U (92% isolated yield, 91% purity). Compared to solution-based synthesis, this approach provides higher yields, shorter reaction times, enhanced scalability, and very low process mass intensity. Since B[6]U is easily available in large quantities, we explored the impact of its substituents – featuring ester and amide functionalities – on lanthanide binding selectivity. Host-guest interactions were screened in solution via circular dichroism and luminescence spectroscopy, providing insights into binding affinities and structural preferences. Our findings offer new perspectives for selective binding, sensing and separation strategies.



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ANION EFFECTS IN THIOUREA-CATALYZED GLYCOSYLATION: A COMBINED EXPERIMENTAL AND COMPUTATIONAL STUDY

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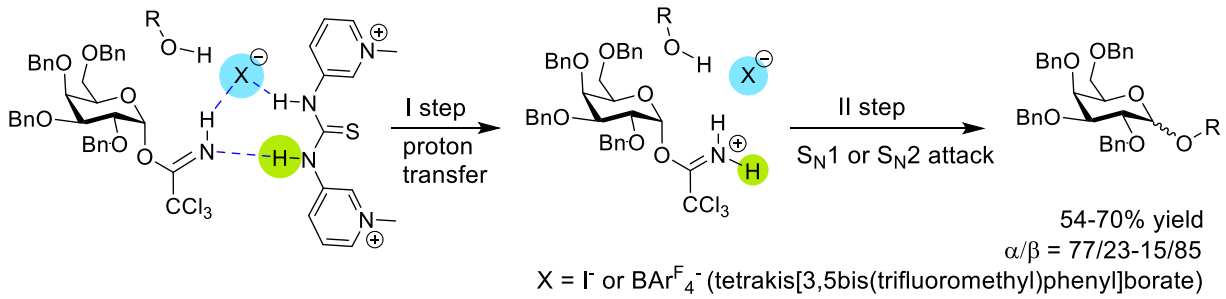
Within carbohydrate chemistry, glycosylation is a field of considerable contemporary importance. Thiourea-based catalysts, known for their efficient hydrogen-bond donor ability, have been widely used in asymmetric organocatalysis[1] and, more recently, also in stereoselective oligosaccharide synthesis.[2] Incorporation of positively charged moieties, such as quaternized pyridyl groups, into the thiourea framework is expected to further enhance both hydrogen-bonding and catalytic activity. Catalysts of this type have shown promising activity in glycosylation reactions involving glycosyl picolinates.[3]



Based on our previous study,[4] which demonstrated the critical role of the counteranion in the reaction mechanism, we investigated the influence of different anions on glycosylation catalysed by quaternized pyridyl-substituted thioureas. The corresponding neutral thiourea analogue was also investigated for comparison. Combined experimental and computational study revealed that the anion strongly influences reaction selectivity and that the cationic thiourea acts primarily as a Brønsted acid catalyst rather than a conventional H-bond donor catalyst.

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DESIGN AND SYNTHESIS OF Π-CONJUGATED INDOLOCARBAZOLE DERIVATIVES AS FUNCTIONAL ORGANIC MATERIALS

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Indolocarbazole-based π-conjugated systems have attracted increasing attention due to their unique electronic properties and potential applications in organic electronics and photonic materials. In this study, we report the design, synthesis, and characterization of novel indolocarbazole derivatives as functional organic materials with tunable photophysical properties.

A series of indolocarbazole-based compounds were synthesized using efficient synthetic approaches, including transition metal-catalysed cross-coupling reactions. Structural modifications were introduced through the incorporation of electron-donating and electron-withdrawing substituents, enabling precise control over the electronic structure and extension of π-conjugation.

The photophysical properties of the synthesized compounds were systematically investigated, revealing strong absorption in the UV–visible region and tunable emission behaviour. Particular attention was given to the role of molecular design in promoting intersystem crossing and the formation of triplet excited states, which are crucial for applications involving phosphorescence and thermally activated delayed fluorescence (TADF).

The results demonstrate that indolocarbazole-based systems represent a promising platform for the development of advanced metal-free organic materials. Their tunable electronic and photophysical properties make them attractive candidates for applications in organic light-emitting diodes (OLEDs), sensing, and optoelectronic devices.

Acknowledgements: Authors are grateful to the Bulgarian National Science Fund project NSF KP 06-H99/2

Rh(II)-CATALYZED DIAZO DECOMPOSITION FOR THE SYNTHESIS OF THIOLANES AND THIAZEPINES: TOWARDS APPLICATION IN CONTINUOUS FLOW CHEMISTRY

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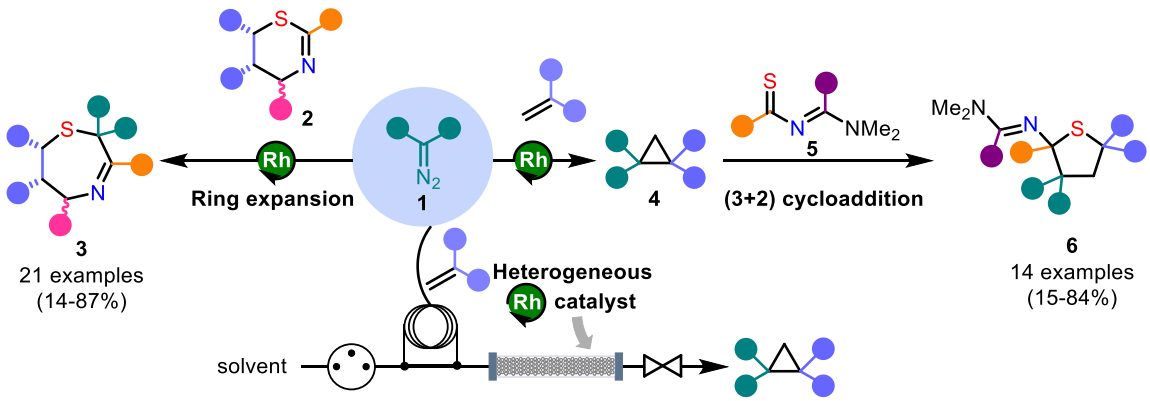
S- and (*N,S*)-containing heterocycles have emerged as privileged scaffolds in bioactive molecules.[1] The continuous demand from the pharmaceutical industry for molecular diversity and structural originality highlights the need for rapid and efficient synthetic methodologies.

Herein, we report the development of two methods for the synthesis of *S*- and (*N*,*S*)-heterocycles, both mediated by *in-situ*-generated metallocarbenes from the rhodium(II)-catalyzed decomposition of diazo compounds **1**. First, we describe a ring expansion of 1,3-dihydrothiazines **2** which react with a metallocarbene to afford 1,4-thiazepines **3**.[2] Second, we present a (3+2)-cycloaddition to access polysubstituted thiolanes **6** featuring an amidine moiety. This approach involves the reaction of donor-acceptor cyclopropanes **4**, prepared via cyclopropanation of alkenes with diazo compounds, with (*N*,*S*)-heterodienes **5**.[3]

To overcome the challenges associated with the high cost of homogeneous rhodium catalysts and the safe management of N_2 release, we are developing a continuous-flow protocol using a heterogeneous rhodium catalyst cartridge. This approach aims to enhance scalability, safety, and cost-efficiency in the decomposition of diazo compounds for synthetic applications.



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NOVEL 4-PHENYL-1,2,4-TRIAZOLE-3-YL THIOACETAMIDE DERIVATIVES BEARING PYRIDINE MOIETY: SYNTHESIS AND EVALUATION OF ANTIMICROBIAL ACTIVITY

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One of major global health issues of the 21st century is antimicrobial resistance (AMR), which poses a growing and serious threat to public health, medical treatment, and economic systems worldwide. AMR makes effective treatment with available antibiotics more difficult, leading to longer hospital stays, higher medical expenses, and increased mortality. As conventional antibiotics lose their effectiveness, the pursuit of innovative treatment approaches and the discovery of new antimicrobial compounds has become essential. Pyridine derivatives exhibit strong antimicrobial properties against a wide range of bacterial and fungal pathogens, often disrupting cell wall synthesis, protein function, or nucleic acid metabolism[1]. The 1,2,4-triazole framework serves as a key pharmacophore, exhibiting strong interactions with biological receptors due to its dipolar nature, hydrogen bonding capabilities, structural rigidity, and enhanced solubility[2].

A series of thioacetamide derivatives, incorporating pyridine and 1,2,4-triazole pharmacophores, were synthesised from 5-(((substituted pyridin-2-yl)amino)methyl)-4-phenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thiones by *S*-alkylation with various bromoacetamides bearing substituted benzene and pyridine moieties. The antibacterial and antifungal properties of the target compounds were evaluated against selected bacterial and fungal strains via serial dilution method. The compound bearing two pyridine moieties in its structure has been shown to possess higher antifungal activity against *C. tenuis* than antifungal drug nystatin and the same level antibacterial activity against *M. luteum* as antibacterial drug vancomycin.

Acknowledgement: the research received funding from the Research Council of Lithuania (LMTLT), agreement No S-MIP-25-22.

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1,2,3-FUNCTIONALIZATION OF PROPARGYL SILANE SYSTEMS BY A CASCADE ELECTROPHILE ACTIVATION – 1,2-SILYL SHIFT – NUCLEOPHILE TRAPPING

Turks, M.; Kroņkalne, R.; Ubaidullajevs, A.; Gercāns, K.; Lācis, R.; Turka, S.; Beļaunieks, R.; Rogaļevs, R.; Sebris, A.; and Puriņš, M.

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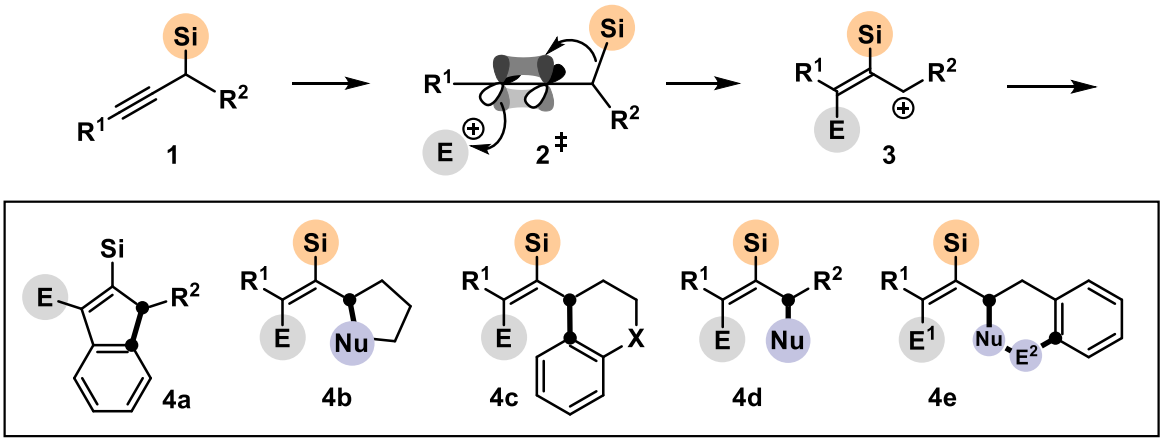
Propargyl silanes can act as precursors of 1,3-dipols, if their electrophilic activation is followed by 1,2-silyl shift.[1] Herein, we report propargyl silane **1** activation by electrophiles (H^+, X^+, RSe^+, R-Cu^{III}) that results in allyl cation **3** formation. The latter is trapped with various *N*-, *O*-, *S*-, *C*-nucleophiles in either intramolecular or intermolecular fassion.[2] This provides highly 1,2,3-functionalized systems **4a-e** with possibilities for further derivatization. Preliminary investigations indicate that the enantioselective transformations are also feasible in the presence of chiral Brønsted acids.



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ELECTROPHILE-INDUCED GERMANIUM MIGRATIONS IN PROPARGYL GERMANES

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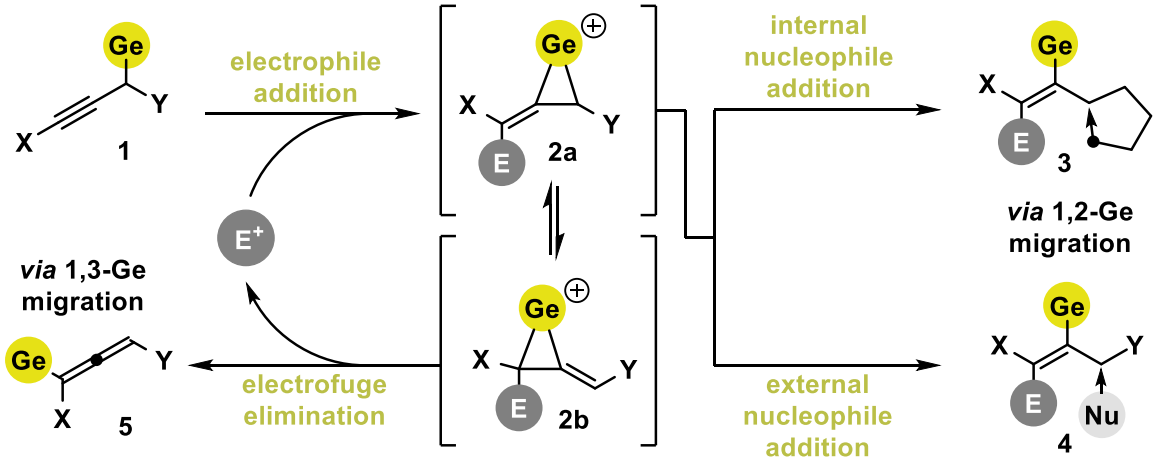
Many reports highlight organogermanium(IV) compounds for their anomalous resistance towards nucleophilic attack including fluoride, while electrophilic activation converts them into highly reactive and labile functionalities.[1] This feature can be successfully applied in various reactions that follow cationic pathway. Herein we report novel electrophile-induced germanium rearrangements in propargyl germanes **1** utilizing carbocation β-stabilization effect by group 14 elements.[2] Using our previously developed 1,2-silyl shift methodology,[3] we observed that cationic germiranium intermediate **2a** can be effectively trapped by intrenal or external nucleophile to afford substituted vinyl germane products **3** or **4**, instead of protodemetalation. Alternatively, in the absence of nucleophiles, allenyl germanes **5** are preferentially obtained.



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TOTAL SYNTHESIS OF EMETINE AND IT'S STUCTURAL ANALOGUES VIA IRELAND-CLAISEN REARRANGEMENT APPROACH

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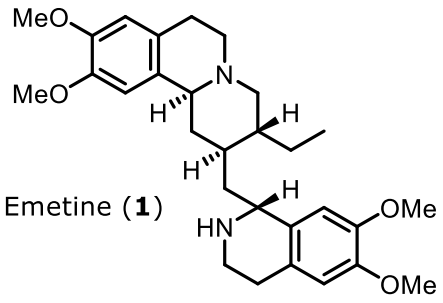
Alkaloid emetine (**1**) is a natural product found in *Carapichea ipecacuanha* and is one of the active compounds in syrup of ipecac. While emetine was used in the first half of the 20th century as an anti-protozoal and vomiting-inducing drug (emetic), it was eventually withdrawn from the market due to its cardiotoxicity. However, recent studies have shown that emetine exhibits anti-viral activity against a vast array of viruses such as SARS-CoV-2, MERS-CoV, influenza A, Zika, and Ebola. [1,2]

Although total synthesis of emetine is already known[3], here we present progress towards a novel, much shorter total synthesis of emetine based on Ireland-Claisen rearrangement. This newfound route would give us straightforward access to structural analogues of emetine, which are available in limited scope, enabling the exploration of structure-activity relationships.



Emetine (**1**)

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WOOD WASTEWATER PURIFICATION WITH ACTIVATED CHARCOAL AND PURITY ANALYSIS VIA GC-MS AND CAPILLARY ELECTROPHORESIS WITH DIRECT UV DETECTION

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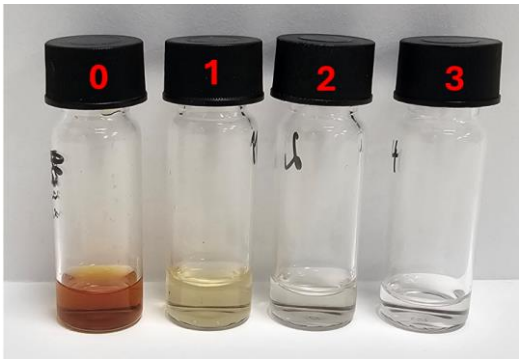
Acetic acid is an organic acid widely utilized across food, chemical, pharmaceutical, textile, packaging and other industries. Due to high global demand, recovering and valorizing it from industrial waste streams presents an economically attractive alternative. Various methods exist for recovering acetic acid, including liquid-liquid extraction, reactive extraction, membrane extraction, and reactive distillation. However, to implement methods like reactive extraction, it is best to use activated carbon to clear the sample of any interfering compounds.

The objective of the present study is to optimize the parameters of activated carbon filtration: carbon type, carbon amount, sonication time, filtration amount. Filtration efficiency was evaluated using Gas Chromatography-Mass Spectrometry (GC-MS) and capillary electrophoresis-UV. The primary target for filtration was furfural. The concentration of acetic acid was monitored using both analytical techniques to ensure if there were any losses. Preliminary results indicate that while activated carbon filtration is highly effective, the process requires further optimization. Visually, the treatment successfully transforms dark brown wastewater into a clear effluent. To minimize product loss and maximize efficiency, future work will focus on utilizing activated carbons specifically tailored for wood wastewater treatment.



Filtration stages. 0 – original sample. 1 – after 1 filtration. 2 – after 2nd filtration. 3 – after 3rd filtration.

γ-C_6N_{16}: A METAL-FREE PRIMARY EXPLOSIVE

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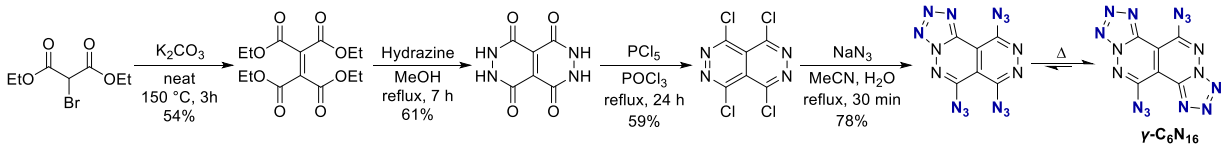
Legacy primary explosives – lead azide and lead styphnate, have been extensively used in primers and detonators since their discovery in the 1920s and are still in use due to their chemical and thermal stability, reliable performance and low cost of production. As a result, police and civilian shooting ranges and training grounds (environment in general) are continuously contaminated with lead. Lead pollution and toxicity along with non-ideal physical properties of lead explosives have emerged growing interest for safer alternatives. Prevention of lead toxicity risk requires development of next-generation environmentally and human safe (emphasis on *heavy metal free*) primary explosives.

We report a nitrogen-rich metal-free primary explosive, 4,10-diazidotetrazolo[1,5-*d*]tetrazolo[1′,5′:1,6]pyridazino[4,5-*d*]pyridazine (***γ*-C_6N_{16}**), designed through strategic exploitation of nitrogen isomerism from *α*-C_6N_{16} isomer previously designed in our group.[1] The compound is readily accessible from simple precursors and features a planar, highly nitrogen-rich framework. The ***γ*-C_6N_{16}** exhibits high density (1.79 g/cm^3), excellent thermal stability (T_{onset} = 201 °C), and high heat of formation (5631 kJ/kg). Calculated detonation parameters are D = 8001 m/s and P = 24.2 GPa. Successful initiation of PETN standard detonator demonstrates its practical application as a metal-free primary explosive. In addition, ***γ*-C_6N_{16}** has good UV light stability, near zero aqueous solubility, hygroscopicity, and significantly lower aquatic toxicity compared to lead-based systems. These properties combined position ***γ*-C_6N_{16}** as a promising candidate for next-generation environmentally benign primary explosive.



Acknowledgments. This research is funded by 1.1.1.9 Research application No 1.1.1.9/LZP/1/24/060 of the Activity "Post-doctoral Research" "Nitrogen-Rich Annulated Diazines as Novel Energetic Materials".

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SCALABLE ACCESS TO 3-SUBSTITUTED AND 3,3-DISUBSTITUTED THIETANES IN THREE SULFUR OXIDATION STATES FOR MEDICINAL CHEMISTRY

Vashchenko, B. V.; Doroshenko, I. O.; Stepaniuk, O. O.; Gavrylenko, O. V.; Ogurok, V. M.; Tarasiuk, T. M.; Volosiuk, V. V.; and Grygorenko, O. O.

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A robust and scalable synthetic platform providing broad access to thietane-based building blocks across three sulfur oxidation states is disclosed. Starting from readily available thietan-3-one and epithiochlorohydrin, a diverse set of 3-substituted and 3,3-disubstituted thietanes was prepared. Systematic pK_a and Log*D* measurements, benchmarked against oxetane, azetidine, and cyclobutane analogs, revealed clear structure–property trends: S(II) thietanes remain close to cyclobutane in lipophilicity, while S(IV) and S(VI) counterparts surpass even oxetane in polarity. The utility of the platform was illustrated by the synthesis of analogs of sulfacetamide, highlighting thietane as a versatile "three-in-one" fragment for tuning ionization and lipophilicity in sp^3-rich drug design.

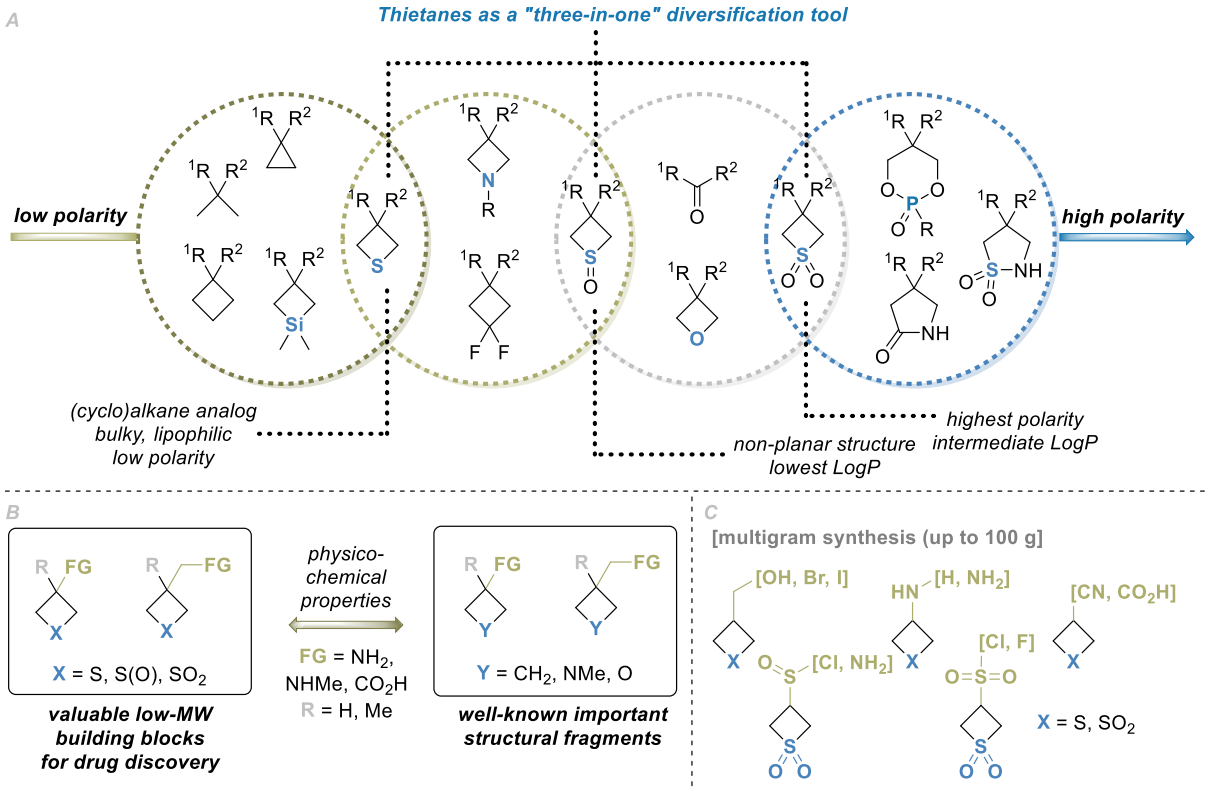

Figure 1. Thietanes as a "three-in-one" diversification tool. *A)* Polarity range of S(II), S(IV), and S(VI) thietanes *vs* common four-membered rings and isosteric fragments. *B)* Concept of this work. *C)* Representative building blocks accessible by multigram synthesis.

SYNTHESIS OF BICYCLIC AMINO ACID DERIVATIVES VIA X-H INTRAMOLECULAR INSERTION OF DIAZOCOMPOUNDS

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Diazocompounds are widely used in organic synthesis, particularly in X-H insertion reactions, which allow for the "alkylation" of heteroatoms (*N*, *O*, *S*) or activated Carbon. Due to its higher reactivity compared to conventional alkylation, the intramolecular variant of this reaction allows for the formation of strained rings, including bicyclic ones.

In this study, derivatives of 2-azabicyclo[3.1.1]heptane and 2-azabicyclo[3.2.1]octane, functionalized at the 3- and 4-positions, were synthesized using the X-H insertion method. The starting compounds are available amino acids, and the key intermediate is the bicyclic ketoester, which is functionalized by decarboxylation or by reductive removal of the ketone group (Figure 1, A). The most relevant compounds obtained are the corresponding bicyclic α- and β-amino acids (and their variously protected derivatives) (Figure 1, B); additionally, as part of the study of the reactivity of bicyclic ketones, diamines, aminoalcohols, and difluoroamines were obtained (Figure 1, C).

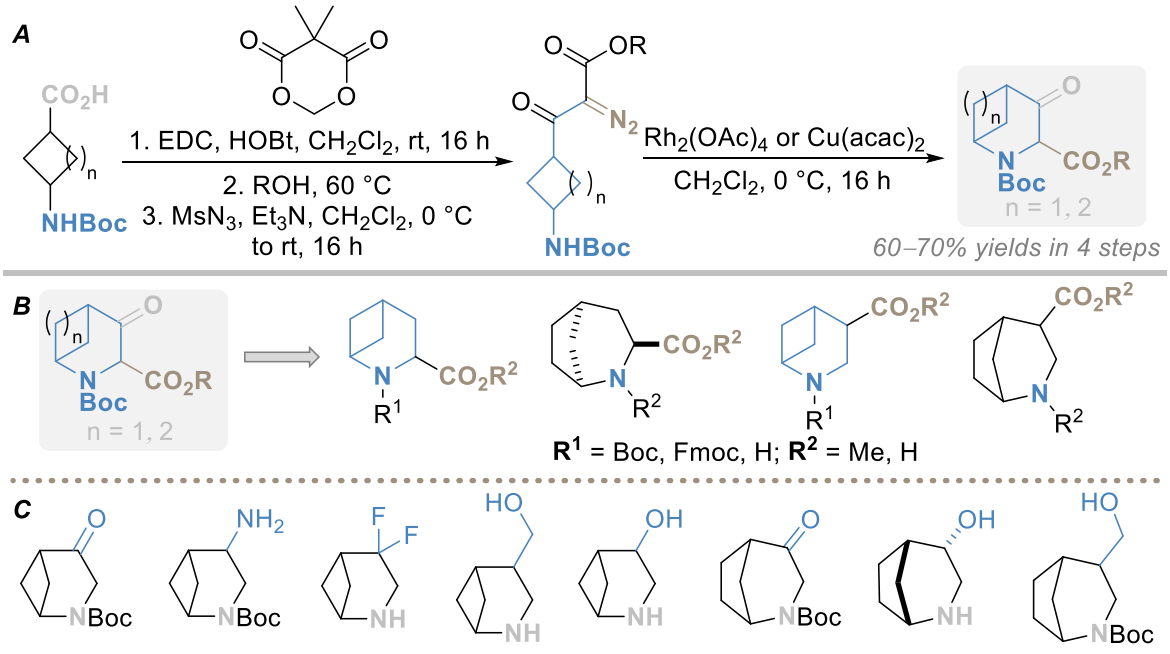

Figure 1. (A) Synthesis of bicyclic ketoesters; (B) Synthesis of amino acid derivatives; (C) Additional compounds obtained

INTRODUCTION OF THE CF_2Cl-FRAGMENT INTO ELECTRON-RICH HETEROCYCLES

Savchenko, V. S.;[a,b] Ryabukhin, S. V.;[a,b,c,d] and Volochnyuk, D. M.[a,b,c,d]

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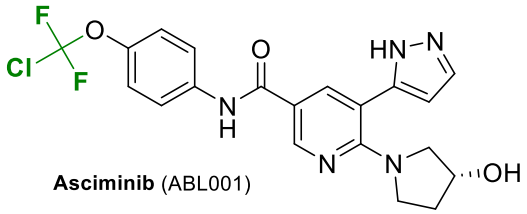
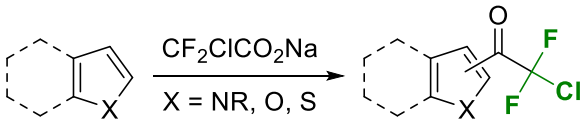
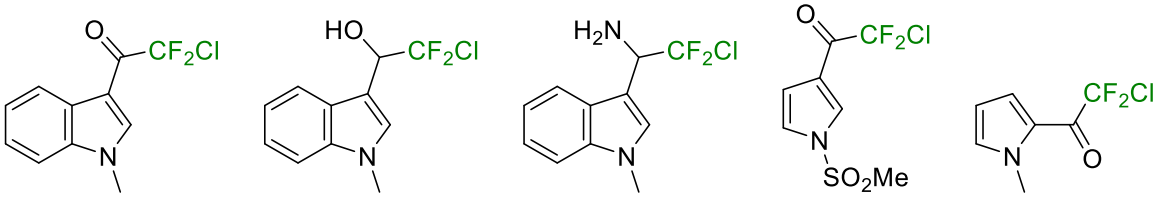
The popularity of the CF_2Cl-fragment in medicinal chemistry programs increased after Asciminib (ABL001) was proposed as a novel drug. However, this group remains rare due to the limited number of preparative procedures available for its introduction and functionalization of related molecules. In our report, we present a robust and effective methodology for the implementation of this group into heterocycles using a widely available and inexpensive reagent, CF_2ClCO_2Na. The further derivatizations and functionalizations of the molecules obtained will also be demonstrated. The scope and limitations, as well as the problems and advantages of the proposed procedures, will be discussed. All the procedures developed are working in 10-100 gram scales with a good perspective for further scale-up.



Asciminib (ABL001)





SCALABLE MULTI-KILOGRAM SYNTHESIS OF CYCLOPROPANOL: STABILITY PROFILING AND REPRODUCIBLE PROTOCOLS FOR MEDICINAL CHEMISTRY APPLICATIONS

Kibalnyi, M.;[a,b] Dmitriv, Yu.;[a] Pashenko, O. Ye.;[a,b,c,d] Ryabukhin, S. V.;[a,b,c,d] and Volochnyuk, D. M.[a,b,c,d]

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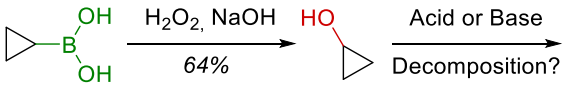
Cyclopropanol has become an important strained-ring building block in medicinal chemistry, with growing interest driven by its use as a radical precursor, homoenolate equivalent, and strain-release partner in C–C bond-forming reactions. However, cyclopropanol is still a difficult synthetic intermediate to access and use on scale. Its tendency to undergo ring opening under acidic or basic conditions has long limited both its preparative production and its practical use in downstream chemistry.

Here, we report a robust, optimized protocol for the multi-kilogram synthesis of cyclopropanol by oxidation of cyclopropylboronic acid. The process was successfully carried out on a preparative scale using a standard industrial reactor setup. It gives reproducible isolated yields and is suitable for routine production, addressing a key supply limitation for this valuable building block. To define practical handling conditions, we performed a systematic stability study using real-time NMR monitoring under acidic, strong basic, and weak basic conditions in different solvent systems. The results showed that decomposition strongly depends on both pH and solvent. Fast degradation was observed under strongly basic aqueous conditions, while acidic media led to moderate instability. In contrast, protic organic solvents and weak organic bases provided much better stability, with no significant decomposition detected over an extended time. These stability data were then used to develop a set of reliable and medicinal-chemistry-relevant protocols for cyclopropanol functionalization, including acylation, sulfonylation, alkylation, and arylation.



System	*k*		Result
CF_3CO_2D	0.0181	38.2 m	mod. dec.
KOH/DMSO-d_6/D_2O	0.0591	11.7 m	fast dec.
KOH/CD_3OD	0.0020	346.5 m	stable
DBU(DIPEA)/DMF	n. d.	>3 d	no dec.

AZETIDINE-CONTAINING DIAZASPIROALKANES: PRACTICAL SYNTHESIS OF ORTHOGONALLY PROTECTED sp³-RICH DIAMINE BUILDING BLOCKS

Virstiuk, I. Yu.;[c,d] Levchenko, K. V.;[c,d] Pokhodylo, N. T.;[d] Leha, D. O.;[a,b] Ryabukhin, S. V.;[a,b,c,e] and Volochnyuk, D. M.[a,b,c,e]

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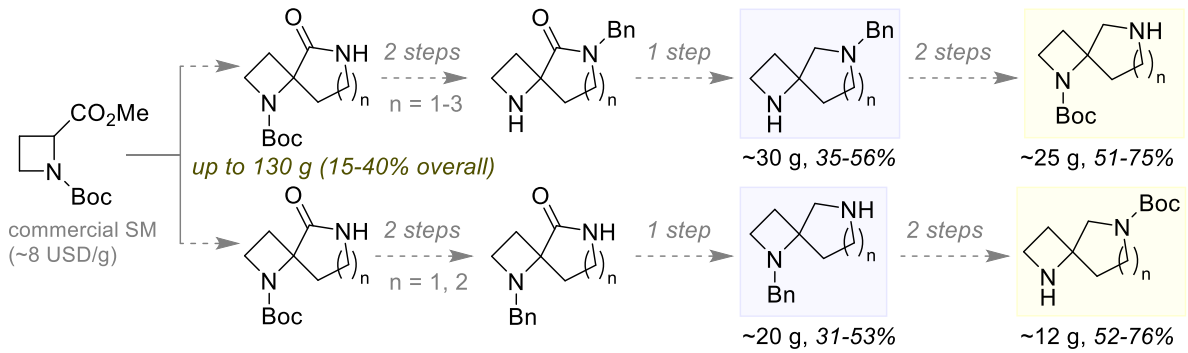
Saturated nitrogen heterocycles such as piperazine, piperidine, and morpholine are widely used in medicinal chemistry, but their extensive application increasingly motivates the search for structurally novel, three-dimensional replacements. Spirocyclic azetidines and diazaspiroalkanes offer attractive opportunities for scaffold hopping because they combine conformational rigidity, high sp^3 character, and defined spatial orientation of nitrogen atoms. However, azetidine-containing diazaspirocycles remain underrepresented due to the limited availability of practical, scalable synthetic methods.

In this work, we developed a concise route to diazaspiroalkanes in which an azetidine ring is spiro-fused with aza-heterocyclic fragments of different ring sizes. The approach starts from readily available *N*-Boc-protected azetidine-2-carboxylate derivatives and terminal bromo-nitriles. A sequence involving α-alkylation, nitrile reduction, intramolecular lactamization, and lactam reduction provides access to the target diazaspiroalkane cores on a multigram scale. For larger ring systems, additional activation of the amino group was required to enable efficient ring closure. A key feature of the developed methodology is the possibility to obtain orthogonally protected derivatives containing two independently addressable endocyclic nitrogen atoms. This enables controlled, sequential functionalization and makes the synthesized scaffolds valuable building blocks for medicinal chemistry library design. The resulting azetidine-based diazaspiroalkanes represent conformationally restricted, sp^3-rich analogs of piperazine-type motifs with defined geometry and broad potential for further application in drug discovery.



PENTAFLUOROSULFANYLATION OF UNACTIVATED ALKENES AND STYRENES FROM SF_6 VIA NET-REDUCTIVE PHOTOREDOX CATALYSIS

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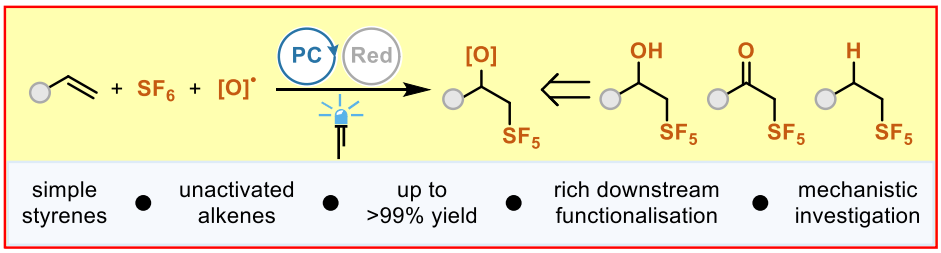
While fluorinated molecules play a crucial role in life sciences,[1] most of the common functional groups belong to the class of per- and polyfluorinated alkyl substances (PFAS) that cause environmental problems and their use could be restricted in the near future. The SF_5-group has gained increasing interest recently, as it also exhibits the appealing properties of fluorinated functional groups but is a non-PFAS motif as demonstrated by environmental studies.[2] However, the broad application of the SF_5-group is strongly hampered by its synthetic accessibility, usually involving the highly toxic gas SF_5Cl. Ideally SF_6 – a cheap, non-toxic greenhouse gas – could be used as a SF_5-source for organic synthesis. A study by Rombach and Wagenknecht demonstrated such a transformation using photoredox catalysis.[3] However, all currently known methods to functionalize alkenes from SF_6 are highly limited to biased, electron-rich substrates restricting the broad application of SF_6 as a SF_5Cl alternative.

We have developed a net-reductive photoredox-catalyzed pentafluorosulfanylation leveraging TEMPO as a highly efficient radical trap and as a handle for further postfunctionalization to enable the pentafluorosulfanylation of styrenes and unactivated alkenes from SF_6.



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ANOMERIC AMIDES AS VERSATILE REAGENTS FOR THE BUILDUP OF COMPLEXITY AT NITROGEN

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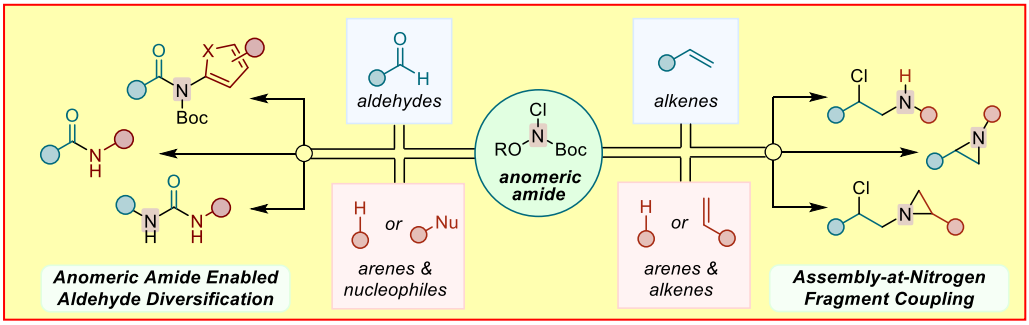
The rapid generation of molecular complexity from simple precursors is a key objective in synthetic organic chemistry.[1] This project develops a unified strategy for amine synthesis and diversification based on "assembly-at-nitrogen" logic, using anomeric amides as versatile linchpin reagents.

In the first study, an anomeric amide-enabled aminative fragment coupling allows regioselective alkene–arene and alkene–alkene C–N bond formation via a one-pot cascade involving chloroamination, N-deprotection, and formal nitrene transfer.[2] This operationally simple, catalyst-free process provides efficient access to complex amine architectures.

In the second study, a complementary divergent aldehyde functionalization platform converts a single precursor into diverse products, including ureas, carbamates, thioesters, amines, and amides.[3] Key *N*-Boc hydroxamate intermediates enable orthogonal activation pathways, such as LOSSEN-type rearrangements and single-electron transfer.

Together, these studies establish anomeric amides as powerful reagents for both convergent and divergent synthesis, enabling efficient exploration of chemical space from simple starting materials.



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PHOTOINDUCED DERACEMIZATION ENABLED BY HYDROGEN ATOM RELAY VIA NON-COVALENT CATALYST ASSEMBLY

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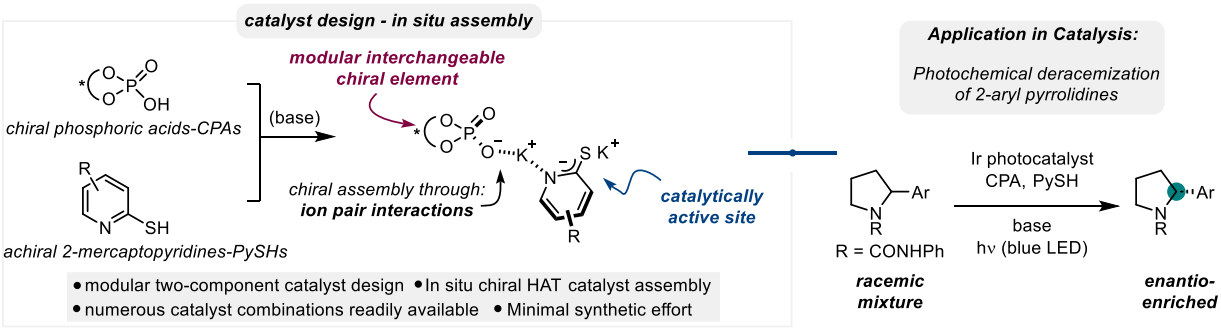
Visible light-driven deracemization through hydrogen atom transfer (HAT) provides a powerful editing strategy for converting racemic substrates into single enantiomers under mild, non-equilibrium conditions. Despite its potential, achieving stereocontrol in HAT processes remains a fundamental challenge in radical chemistry because open-shell intermediates are highly reactive and difficult to regulate within a chiral environment. Conventional approaches therefore rely on structurally elaborate chiral HAT catalysts whose preparation often requires multistep synthesis and extensive optimization.

We disclose a conceptually distinct strategy in which chiral HAT catalysts are generated in situ through non-covalent self-assembly between privileged chiral phosphoric acids and commercially available 2-mercaptopyridines. In this system, the phosphoric acid serves as a modular and interchangeable chiral source that renders the achiral thiol effectively chiral, thereby enabling access to a previously unexplored combinatorial space of chiral HAT catalysts. This platform enabled the photochemical deracemization of 2-aryl pyrrolidines, a prevalent scaffold in active pharmaceutical ingredients. Mechanistic studies reveal that Optical enrichment occurs via enantioselective hydrogen atom relay in which the chiral HAT assembly mediates both hydrogen atom abstraction and hydrogen atom delivery within a confined chiral environment. In this way, a simple self-assembled catalyst system achieves the function of a tailored chiral hydrogen atom transfer catalyst without requiring its pre-synthesis. More broadly, these findings establish non-covalent catalyst assembly as a general design principle for controlling hydrogen atom transfer in asymmetric photochemical transformations.



HETEROCYCLE-FUSED 1,8-NAPHTHALIMIDES WITH PROMISING ANTITUMOR ACTIVITY

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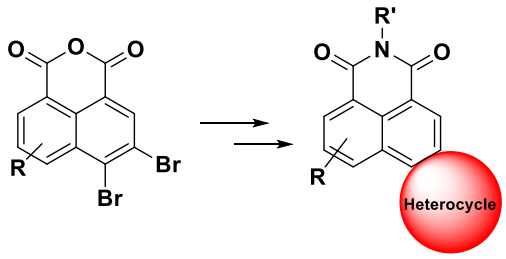
Recent anticancer research has focused on small molecules that interact with DNA. Among these, 1,8-naphthalimides and their derivatives have demonstrated significant anticancer activity against various human and murine cells. Studies show that their efficacy is greatly affected by the fusion of aromatic or heteroaromatic rings and by modifications to the position and size of their side chains.

In our laboratory, we have developed an excellent building block for the synthesis of heterocyclic extended 1,8-naphthalimides. The target structures are highly suitable as DNA intercalators.



Acknowledgements: Authors are grateful to the Bulgarian National Science Fund project NSF KP 06 N61/1

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SKELETAL EDITING OF CYCLIC AMINES THROUGH NITROGEN ATOM INSERTION

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Skeletal editing offers a direct way to reshape nitrogen-containing molecules beyond the limits of traditional substitution chemistry by modifying the molecular framework itself.[1-3] Nitrogen atom insertion enables controlled ring expansion of saturated amines in a single step, providing an efficient route to molecular diversification. Cyclic amines, particularly pyrrolidines, are attractive targets because of their widespread presence in pharmaceuticals and bioactive compounds.[1-3] Here, we describe a nitrogen-atom insertion strategy that converts cyclic amines into higher-order nitrogen heterocycles through deliberate skeletal reorganization. The transformation proceeds under mild conditions, tolerates a broad range of functional groups, and allows access to structurally distinct aza-heterocycles that are difficult to obtain by conventional methods. Overall, this work highlights skeletal editing via nitrogen insertion as a practical and versatile approach for advancing synthetic and medicinal chemistry.

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ALKENYL FLUOROSULFATES AS VERSATILE PARTNERS IN PALLADIUM-CATALYZED CROSS-COUPLING REACTIONS

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Alkenyl fluorosulfates were evaluated as substrates for palladium-catalyzed cross-coupling reactions and compared with the more commonly used triflates and halides.[1] Firstly, practical multigram synthetic procedures based on the reaction of carbonyl compounds with SO_2F_2 were developed for the preparation of the target fluorosulfates. Then, their reactivity in Suzuki, Sonogashira, Heck, Stille, Buchwald-Hartwig, and Miyaura borylation reactions was investigated under standard conditions, and the principal limitations of these transformations were established. In most cases, alkenyl fluorosulfates demonstrated reactivity comparable to or exceeding that of the corresponding alkenyl triflates.

1. Hnativ, V.; Aleksandrenko, S.; Zhersh, S.; Grygorenko, O. O. *Chem. Eur. J.* **2026**, *in press*.

STABILITY STUDY OF AROMATIC HETEROCYCLIC SULFONYL HALIDES

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Heteroaromatic sulfonyl halides are valuable building blocks, although their applicability is often limited by insufficient stability. In the presented study,[1] decomposition was evaluated for more than 200 heteroaromatic sulfonyl chlorides, most of which were prepared for the first time, enabling the formulation of practical guidelines for choosing between sulfonyl chlorides and fluorides. The main degradation pathways include SO_2 extrusion, hydrolysis, and competing transformations at other functional groups. SO_2 extrusion is characteristic of 2- and 4-substituted six-membered heterocycles, whereas hydrolysis predominates for more stable systems, including pyridine-3-sulfonyl chlorides and many five-membered heterocycles. Overall, pyridine-3- and most five-membered heteroaromatic sulfonyl chlorides are sufficiently stable for routine use, while for pyridine-2- or -4- and diazine-derived analogues, the corresponding fluorides are better alternative.

1. Shevchuk, O. I.; Vashchenko, B. V.; Doroshenko, I. O.; Stepannikova, K. O.; Hys, V. Yu.; Karpenko, O. V.; Kozachenko, O. P.; Cherepakha, A. Yu.; Kozytskyi, A.; Tolmachova, K. A.; Zhersh, S.; Tolmachov, A. O.; Grygorenko, O. O. *Chem. Eur. J.* **2026**, *32*, e70739.

ENANTIOSELECTIVE DEAROMATIZATION OF INDOLES VIA AN ALLYL-CATION-TYPE [3+2] CYCLOADDITION

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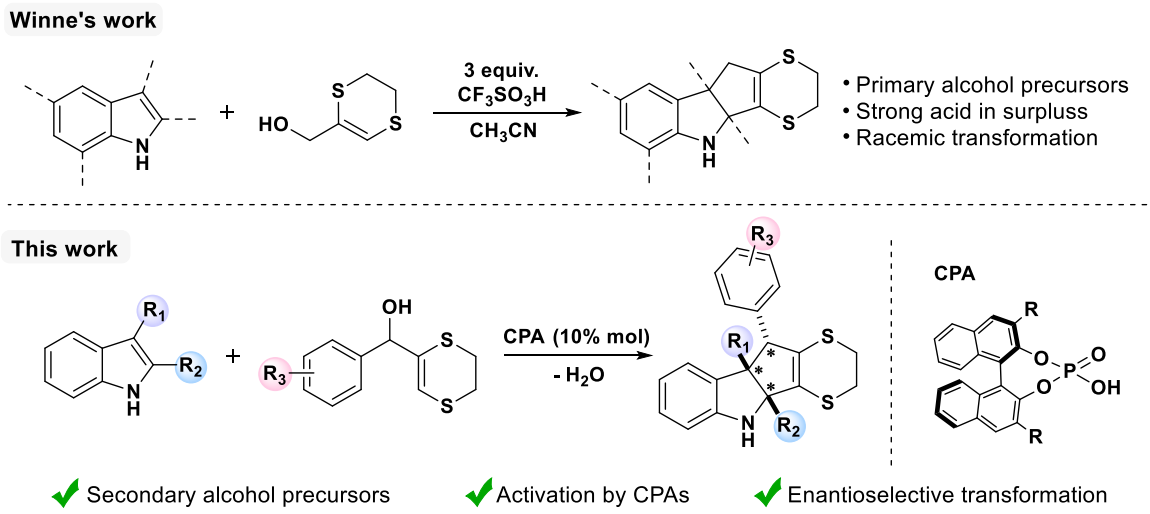
Polycylces derived from indoles can be efficiently assembled via catalytic asymmetric dearomatization reactions (CADA) that simultaneously form multiple stereocenters, providing rapid access to natural products, their enantiomers, and diverse analogs. By bypassing the chiral pool, product stereochemistry is fully dictated by the chiral catalyst, making CADA a versatile tool for natural-product synthesis and drug discovery. Herein, we report a stereoselective dearomatization of indoles via a formal [3+2] cycloaddition using a dithiane-derived alcohol as a dithioallyl-cation precursor, affording tetrahydrocyclopentaindole polycycles with three contiguous stereogenic centers, including one quaternary center. Building on Winne's work,[1,2] secondary alcohol precursors are activated by chiral phosphoric acids (CPAs) to enable an enantioselective variant of this transformation, overcoming limitations of racemic approaches that require strong acids.



Acknowledgments

This work was supported by the Croatian Science Foundation (IP-2022-10-5184).

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FROM BENCH NEGLECT TO BENCH-STABLE C1 REAGENT

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Direct C1 functionalization of unactivated arene C–H bonds remains a fundamental challenge, as existing methods — electrophilic hydroxymethylation, halomethylation, and Minisci-type approaches — are restricted in scope and deliver static functional groups rather than diversifiable synthetic handles. We disclose a photoredox platform using methylenedipyridinium salt (DiPyM) — an air-stable, multigram-accessible reagent prepared in one step from dihalomethane and pyridine. Under blue LED irradiation (455 nm, Ir or fully organic dye) DiPyM undergoes single-electron reduction to release the electrophilic radical, which adds to arene C–H bonds. Downstream rearomatization closes the redox-neutral cycle; the liberated pyridine elegantly serves as a base for deprotonation.

The benzylpyridinium products serve as pseudo-benzylic halides for downstream elaboration: nucleophilic substitution delivers amines, sulfones, sulfides, and alcohols; Pd-catalysed Suzuki–Miyaura, Hiyama, and Sonogashira couplings give diarylmethanes and propargylbenzenes; reductive cleavage under Pd/H_2 delivers the formally methylated arene (“magic methyl”). The protocol tolerates halogens, esters, amides, and phenols, and has been demonstrated in late-stage functionalization of ibuprofen, naproxen, paracetamol, guaifenesin, and silodosin, sildenafil core, CBN, CBL, chlorotadalafil, estrone and other pharmaceutical structures.

ORTHO SUBSTITUTED AND META SUBSTITUTED TRIFLUORO BENZENESULFONAMIDES FOR SELECTIVE CAIX INHIBITION

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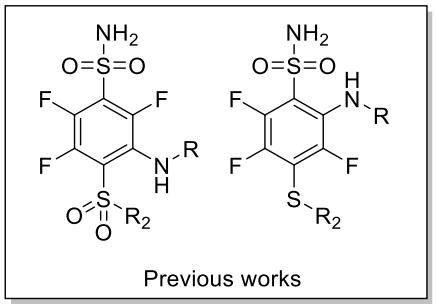
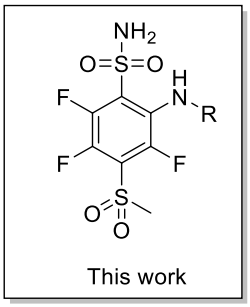
Carbonic anhydrase IX (CAIX) is significantly overexpressed in hypoxic tumors, making it a promising therapeutic target and biomarker. While sulfonamide derivatives are potent inhibitors of the carbonic anhydrase family, their current lack of selectivity poses a major challenge. To address this, we have developed a series of fluorinated benzenesulfonamide inhibitors.

Previous scaffold modifications, including *meta*-para and *ortho*-para substitutions, achieved high potency but failed to deliver optimal selectivity for CAIX. Furthermore, lead compounds were binding to multiple isoforms (e.g., XII, XIII, XIV) or faced solubility limitations for *in vivo* application. To overcome these selectivity and pharmacokinetic hurdles, we designed and synthesized novel fluorinated benzenesulfonamides. Specifically, we focused on *ortho*-substituted analogues containing an aliphatic fragment with an incorporated methylsulfone group at the *para*-position. We also synthesized *meta*-substituted analogues to systematically compare how the position of substituents influences binding affinity and selectivity toward the CAIX isoform.





DUAL-INTERACTION CARBONIC ANHYDRASE IX INHIBITORS BEARING HYDROPHOBIC AND HYDROPHILIC MOIETIES

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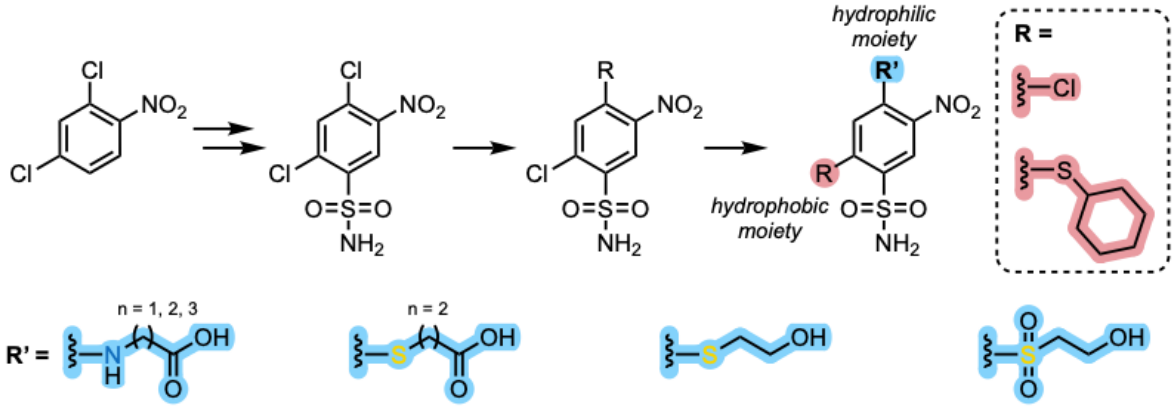
Carbonic anhydrase IX (CA IX) is a well-established target for cancer therapy, particularly in hypoxic tumors. Because of highly conserved active site of different CA isoforms, development of isoforms specific inhibitors continuous to be a notorious task. In this work, we explore the strategy of incorporating both hydrophobic and hydrophilic moieties on the same nitrobenzenesulfonamide scaffold to simultaneously engage the hydrophobic pocket and the hydrophilic half of the active site. This dual-interaction approach is intended to enhance selectivity toward CA IX over other isoforms.



Acknowledgments

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ORTHO- AND META-SUBSTITUTED BENZENESULFAMATES AS INHIBITORS OF CARBONIC ANHYDRASE

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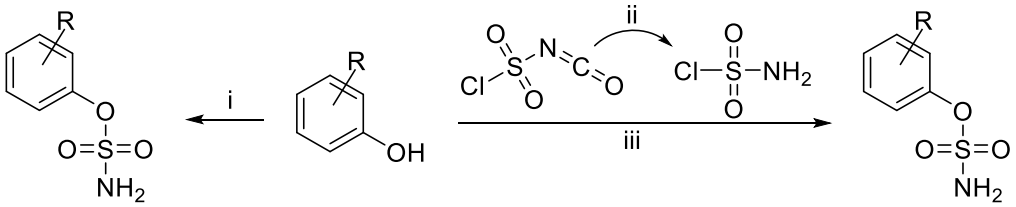
Carbonic anhydrases (CAs) are involved in physiological and pathological processes such as respiration, pH regulation, and tumor progression. Most clinically used inhibitors are sulfonamides, which efficiently coordinate the catalytic Zn^{2+} ion but often lack isoform selectivity, resulting in side effects. To overcome this limitation, alternative zinc-binding groups (ZBGs), including sulfamates, hydroxamates, phenols, and coumarins, have been explored. Among these, sulfamates represent a particularly promising scaffold.

We have designed and synthesized a series of novel aryl sulfamates as CA inhibitors. Binding affinities were measured by FTSA, and representative complexes were solved crystallographically to establish structure–activity relationships that can guide the design of isoform-selective CA inhibitors. Variations of substituents on the benzenesulfamate ring led to compounds **11a** and **16**, which exhibited high observed binding affinity to CAIX; the K_d was 0.52 nM and 0.40 nM respectively.



SYNTHETIC ACCESS TO FLUOROHALOMETHYL ESTERS

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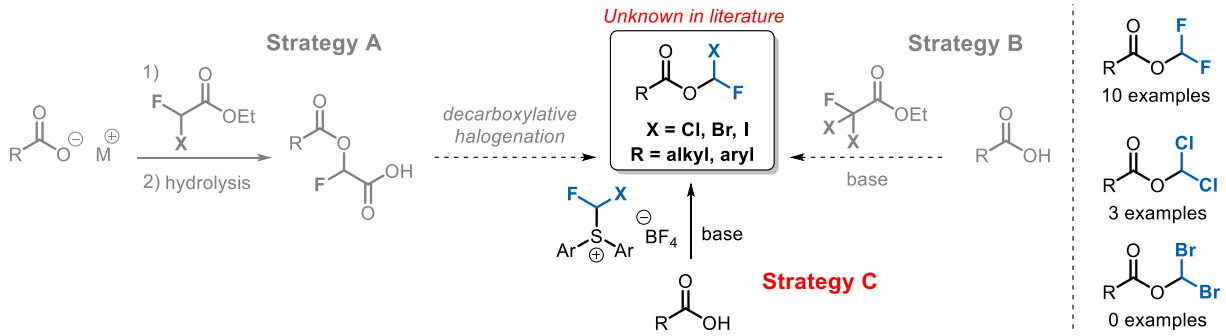
The synthesis of fluorohalomethyl esters has been mainly limited to the preparation of difluoromethyl esters using various difluorocarbene sources – TMSCF2Br[1], difluoromethylene phosphobetaine[2], deuteriodifluoromethyl sulfonium ylides[3] and fluorosulfonyldifluoroacetic acid.[4] However, the preparation of mixed esters, such as fluorochloro-, fluorobromo-, or fluoroiodomethyl esters, has not been reported at all.

Herein, we demonstrate a simple and practical method for the synthesis of various mixed fluorohalomethyl esters via electrophilic fluorohalomethylation of carboxylic acids by exploiting diarylfluorohalomethyl sulfonium salts.[5]



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