SCS Division of
Industrial & Applied Chemistry (DIAC)

17th Freiburger Symposium 2025 «Sustainable Chemistry – from R&D to Manufacturing»

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Swiss Chemical
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Chemistry

3-4 April 2025
School of Engineering & Architecture Fribourg

Welcome to the 17th Freiburger Symposium, a Well-Established Platform

The objective of this biennial conference is to regularly provide our members and other interested chemists working in process development and production with opportunities for professional training and networking. The event is organized by the SCS Division of Industrial & Applied Chemistry (DIAC).

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Program Thursday, 3 April 2025

08.30	Opening of the symposium's reception desk Welcome Coffee
09.30	Address of welcome by Dr. Niklaus Künzle, Lonza AG, President of the DIAC, Dipl. Ing. Urban Jenelten, dsm-firmenich Ltd., Dr. Maurus Marty, dsm-fimenich Ltd., Dr. Roger Marti, HEIA-FR
Session 1: R4 (Reduce, Reuse, Repurpose, Recycle) Chair: Dr. Stefan Abele, Pharvaris	
09.45	Dr. Brian Schwegler, Lonza AG «*Carbon Footprint Reduction in the Pharmaceutical Industry Through Innovative Solvent Recovery*»
10.30	Dr. Lynda Si-Ahmed, Metalor Technologies SA and Frank Bühler, Bayer CropScience Schweiz AG «*Circular Economy for Precious Metals Catalyst*»
11.15	Dr. Sebastiano D'Angelo, Syngenta Crop Protection AG «*Syngenta's Early Stage Framework to Quantify Climate Impacts of New Active Ingredients*»
12.00	Exhibitor Talk: Marlies Moser and Finn Steinemann, Fluitec mixing + reaction solutions AG
12.15	Lunch Break, Poster Session and Exhibition
Session 2: Manufacturing Excellence / AI Chair: Dr. Andrea Sting, Syngenta Crop Protection AG	
14.00	Prof. Philippe Schwaller, EPFL Lausanne and Dr. Raphael Bigler, F. Hoffmann-La Roche AG «*Combining HTE and Data Science to Optimize Chemical Processes*»
14.45	Matteo Scalabrino and Raphael Pochard, Syngenta Crop Protection AG «*Synergy Between Manufacturing Excellence and Sustainable Manufacturing at Syngenta*»
15.30	Coffee Break
16.00	Jorge Gamara, Holcim Ltd. «*Optimizing Cement Plant Maintenance with Digital Solutions*»
Keynote Lecture Chair: Dr. Lucie Lovelle, Novartis Pharma AG	
16.45	Jürgen Wieland, Novartis Pharma AG «*Environmental Sustainability in Pharma – Beyond Green Chemistry*»
19.00	Aperitif and Symposium Dinner

Program, Friday, 4 April 2025

08.30 Morning Coffee

Session 3: Sandmeyer Award Lectures
Chair: Dr. Stefan Hildbrand, F. Hoffmann-La Roche Ltd

09.00 Sandmeyer Award Lecture 2024:
Prof. Urs von Gunten and Dr. Christa McArdell as representatives of the Eawag winner team
«*Advanced Wastewater Treatment by Ozonation for Abatement of Micropollutants from Municipal Wastewater Effluents*»

09.45 Sandmeyer Award Lecture 2025:
Dr. Stephan Bachmann, F. Hoffmann-La Roche AG as representative of the winner team
«*A Highly Atroposelective Negishi Coupling enables the Commercial Manufacturing Process of Divarasib*»

10.30 Coffee Break

Session 4: Green Process Chemistry
Chair: Dr. Maurus Marty, dsm-firmenich Ltd

11.00 Prof. Eva Hevia, University of Bern
«*Exploiting Sustainable Polar Organometalllics for Arene Functionalisation and Catalysis*»

11.45 Dr. Tobias Brütsch, Dottikon ES and
Dr. Stephan Rummelt, F. Hoffmann-La Roche AG
«*Development of the Commercial Manufacturing Process for Inavolisib*»

12.30 Lunch Break, Poster Session and Exhibition

14.00 Dr. George Lem, dsm-firmenich Ltd.
«*A Brief Survey of Recent Dry Woody and Ambery Odorants*»

14.45 Prof. Siegfried Waldvogel, Max-Planck-Institut für Chemische Energiekonversion (MPI CEC) in Mülheim an der Ruhr
«*Electrifying Organic Synthesis – an Elegant Way to Oxygenated Products*»

15.30 Best Poster Award Ceremony

15.45 Symposium Closure & Aperitif

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Carbon Footprint Reduction in the pharmaceutical industry through innovative solvent recovery

Brian Schwegler, Niklaus Kuenzle, Marco Müller

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Environmental Sustainability is of upmost importance for Lonza, a leading CDMO in the pharmaceutical industry. The production of API's requires large amounts of energy and typically yields high volumes of waste. Lonza is committed to continuously reducing its carbon footprint through green energy, green solvents, energy integration, waste reduction and solvent recovery. The majority of the process waste is going to a recovery process resulting in the regeneration of over 10,000 Tons of solvent per year. This is an extremely effective method for reducing the carbon footprint in the Small Molecule API production business. The methods of identifying and implementing processes to recover solvents and their effect on carbon reduction in a highly regulated environment are presented.

Circular Economy for precious metals catalyst

L. Si-Ahmed[I], F. Bühler[II]

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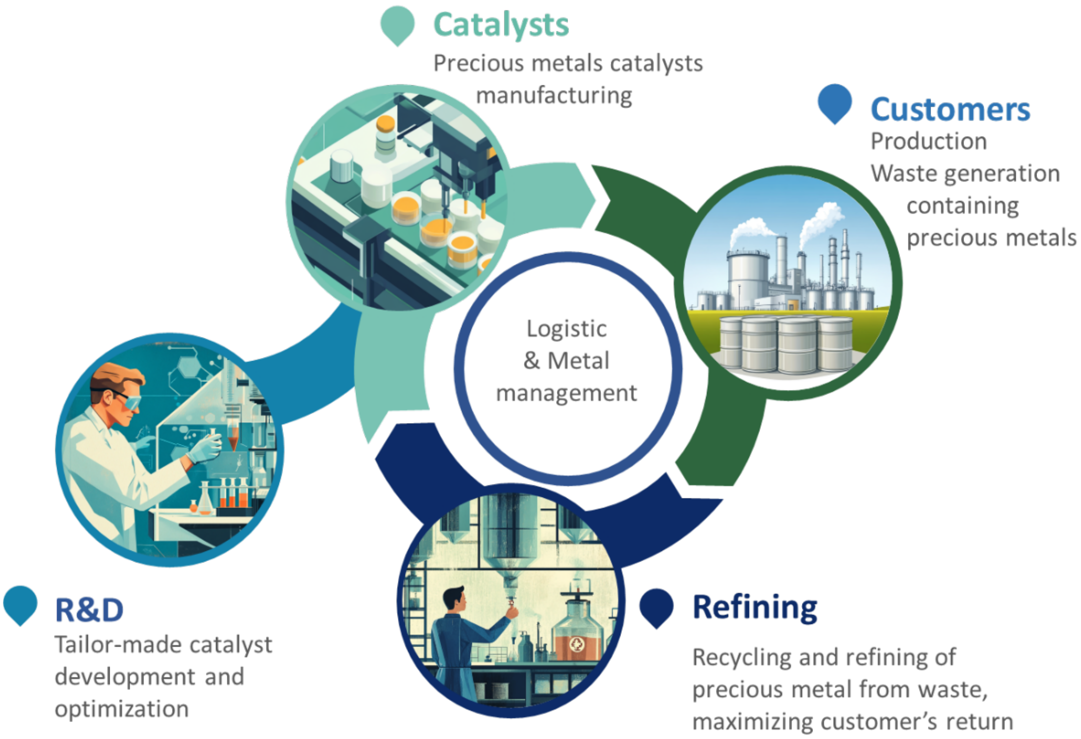

Scheme 1: Metalor full loop (1)

To meet the growing needs of the fine chemical, pharmaceutical, and agrochemical industries in precious metals catalysts and recycling, Metalor technologies has placed its precious metals' expertise at the service of its customers. A dedicated department develops, manufactures precious metal catalysts and elaborate tailor-made recycling methodologies leading to the offering of a full loop service in Switzerland for a more sustainable future (Scheme1). An example of the impact of this offering will be presented.
To reduce operational costs and minimize dependence on precious metal prices, a novel concept for enhancing palladium recycling was developed and implemented as an intermediate step in fungicide production. This initiative built upon an existing setup that achieved approximately 25% palladium recycling, with the goal of closing the recycling loop and significantly increasing the recycling rate.
Throughout the design phase, various challenges were identified and addressed, particularly concerning the entire process and subsequent treatment at Metalor. The results indicate that calculated recycling rates of up to 96% are achievable, highlighting the potential for improved sustainability and cost-effectiveness in production.

Syngenta's early-stage framework to quantify climate impacts of new active ingredients

Sebastiano C. D'Angelo, Sara Bello, Rebecca Steidle

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With the world facing the challenge of climate change and its alarming effects, the chemical industry needs to find reasonable approaches to account for the environmental sustainability of its products. This should be initiated during the early stages of process design, when more degrees of freedom are still available to process chemists and engineers. Accordingly, several approaches were designed in the past years to introduce simplification practices when performing a life cycle assessment.[1]

In Syngenta, a business process and web-based software was created to support early-stage life cycle assessments of our active ingredient portfolio, with the concept of modularity in mind. The core objective designed into the tool is to empower the owners of the technology, *i.e.*, the process chemists and engineers, to model different process design options and then calculate the associated cradle-to-gate climate impact with minimal life cycle assessment expert support. To enable such order-of-magnitude estimates at scale, simplifications were introduced for the impact estimation of raw materials, energy, and waste treatment.

Such a modeling solution enabled Syngenta to obtain the first screening-level estimates of climate impacts for their active ingredients, obtaining insights to hotspots and enabling early-stage decision making for informed chemical process design.

[1] S. Beemsterboer, H. Baumann, H. Wallbaum, *Int J Life Cycle Assess* **2020**, *25*, 2154, DOI: 10.1007/s11367-020-01821-w.

Combining HTE and Data Science to Optimize Chemical Processes

Prof Philippe Schwaller, Raphael Bigler

Laboratory of Artificial Chemical Intelligence | LIAC - Institute of Chemical Sciences and Engineering - School of Basic Sciences - École Polytechnique Fédérale Lausanne EPFL

We present initial results from the collaboration between Roche's High-Throughput Experimentation (HTE) team in Process Chemistry and the Laboratory of Artificial Chemical Intelligence (LIAC) at EPFL. We will showcase the setup of our cutting-edge HTE facility and demonstrate how we improve traditional screening strategies using advanced data science tools. This synergy has led to the development of Minerva, an ML optimization workflow that effectively covers large chemical search spaces, resulting in more informative and enhanced screening designs.

«Synergy between manufacturing excellence and sustainable manufacturing at Syngenta»

Raphaël Pochart, MSc. – Matteo Scalabrino, MSc.

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Syngenta's Global Manufacturing Excellence (ManEx) function aims to enhance the competitiveness of manufacturing assets while promoting sustainable operations. The proposed presentation examines the integration of operational efficiency and environmental sustainability within Syngenta's production processes, focusing on the company's commitment to reducing greenhouse gas emissions in alignment with Science Based Targets initiative (SBTi) goals.

The Syngenta Production System, implemented across 26 global manufacturing sites, provides a framework for continuous improvement and daily performance management. This system is crucial in supporting Syngenta's pledge to reduce Scope 1 and 2 emissions by 38% by 2030 (baseline 2022), as outlined in the 2024 ESG report. The company is also developing targets for Scope 3 emissions reduction for its Crop Protection and Seeds business units. The presentation highlights two primary approaches to emissions reduction: efficiency measures and transformational initiatives.

Efficiency measures focus on optimizing energy consumption, improving material utilization, enhancing process control, and standardizing operations. These short-term, controllable interventions aim to reduce CO2e emissions while simultaneously optimizing manufacturing costs.

Transformational initiatives involve more significant changes, such as transitioning to renewable energy sources, electrifying processes, and implementing carbon capture and storage technologies. While these measures have a more substantial impact on emissions reduction, they often require longer implementation times and higher investments.

The key case study that will be presented examines the optimization of energy (steam) consumption in distillation processes. By leveraging the Syngenta Production System, the company aims to continuously monitor steam consumption and distillation performance, identify parameters causing yield deviations, and implement targeted measures to maintain optimized standards. This approach not only addresses Scope 2 emissions but also enhances overall production efficiency.

The presentation shows how Syngenta's integrated approach to manufacturing excellence and sustainability creates a competitive advantage. By improving operational discipline and implementing data-driven optimization strategies, the company expects to achieve significant improvements in both production performance and environmental impact.

In conclusion, the presentation illustrates the potential for synergy between manufacturing excellence and sustainable practices in the agrochemical industry. Syngenta's approach serves as a model for how companies can align operational efficiency goals with environmental commitments, potentially leading to both cost savings and reduced ecological footprint.

Optimizing Cement Plant Maintenance with Digital Solutions

Jorge Gamarra

Holcim Technology, Switzerland
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In today's fast-paced industrial landscape, the cement industry is undergoing a transformative shift, driven by the power of digitalization. As the demand for higher efficiency and reliability increases, digital technologies are reshaping preventive maintenance strategies, enabling cement plants to proactively address issues before they escalate. By integrating advanced sensors, data analytics, and real-time monitoring, digital tools are enhancing machine performance, reducing downtime, and extending equipment lifespan. In this presentation, we will explore how digitalization is not only elevating maintenance practices but also unlocking new levels of productivity and performance in the cement industry. Let's dive into how this technological revolution is bringing the cement industry into a new era of precision and efficiency.

1. Current Challenges in Cement Plant Maintenance:

Discuss the traditional methods of preventive maintenance, such as scheduled inspections and routine checks, which are often time-consuming and reactive rather than proactive.

Highlight common issues such as unplanned downtime, equipment failure, and costly repairs, and how they impact productivity and profitability.

2. The Role of Digital Technologies:

Introduce key digital solutions like predictive maintenance, Internet of Things (IoT) sensors, artificial intelligence (AI), and machine learning that are being implemented in cement plants to gather real-time data.

Explain how IoT sensors monitor equipment health continuously, allowing for early detection of issues like vibrations, temperature fluctuations, and wear-and-tear.

3. Impact on Preventive Maintenance:

Emphasize how these technologies are shifting from reactive to predictive and prescriptive maintenance, where maintenance actions are based on data-driven insights rather than fixed schedules.
Discuss how digitalization allows for continuous monitoring and remote diagnostics, reducing the need for on-site personnel and minimizing downtime.

4. Improved Machine Performance:

Illustrate how machine performance is enhanced through real-time data analysis, which helps optimize parameters like speed, load, and energy consumption.

Mention how digitalization can also help identify inefficiencies and suggest improvements in machine operations, leading to better output, reduced energy consumption, and lower maintenance costs.

5. Cost Savings and Efficiency Gains:

Provide examples or case studies of cement plants that have seen significant cost reductions in maintenance, energy consumption, and downtime due to the adoption of digital tools.

Discuss the potential for long-term savings by extending the life of expensive equipment, reducing labor costs, and increasing operational efficiency.

6. The Future of Digitalization in Cement Plants:

Touch on future trends like automation, robotics, and advanced data analytics that will further enhance maintenance practices and overall plant performance.

Discuss how digitalization is paving the way for a more sustainable and environmentally-friendly cement industry through better resource management and reduced emissions.

Environmental Sustainability in Pharma – beyond Green Chemistry

Jürgen Wieland

Novartis Pharma AG, CH-Basel
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This keynote aims to zoom out from the various challenges and opportunities around sustainable chemistry and focus on the overall Environmental Sustainability challenges for the pharmaceutical and healthcare sector overall. Having exceeded globally the 1.5°C Paris target first time in 2024, with Switzerland reaching already almost +3°, the time for action is now.

We will present the Novartis approach on Sustainable Product Design supported by environmental Lifecycle Assessments (LCA) and its integrations into the R&D process. On top, we will investigate examples of effective industry collaboration within the Sustainable Markets Initiatives' Health System Task Force, the creation of an environmental LCA standard for pharmaceuticals and how the Sustainable Healthcare Coalition is addressing the carbon footprinting and emissions & waste reduction in clinical trials.

Sandmeyer Award Lecture 2024: Advanced wastewater treatment by ozonation for abatement of micropollutants from municipal wastewater effluents

Urs von Gunten[1,2,3], Christa S. McArdell[1], Juliane Hollender[1,3], Adriano Joss[1], Marc Böhler[1],
Christian Abegglen[4], Hansruedi Siegrist[1,3]

[1]Eawag, Dübendorf, [2]EPFL Lausanne, [3]ETH Zurich, [4]Waste and recycling, City of Zurich
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The contamination of the aquatic environment by synthetic organic compounds is a major problem for the ecosystem and potentially human health if water resources are used for drinking water and food production. Many anthropogenic activities lead to the discharge of organic micropollutants to aquatic systems by point or diffuse sources, including industries, agriculture, traffic and urban water management. The Eawag team has shown early on by a rigorous assessment of fluxes of organic chemicals that municipal wastewaters are an important source of synthetic organic compounds in receiving water bodies with diverse impacts on aquatic organisms. This was the starting point of an Eawag-based research initiative to develop concepts for mitigation of wastewater treatment plant effluents to protect aquatic ecosystems from an important source of contaminants. Based on this research, selected municipal wastewater treatment plants in Switzerland are currently been upgraded with an additional polishing step, either ozonation or activated carbon treatment to reduce the discharge of micropollutants to the aquatic environment. This talk will focus on the options and limitations of ozonation.

There are five factors which need to be considered to assess ozonation processes for micropollutant abatement in wastewaters: (i) reaction kinetics, which control the efficiency of the process, (ii) elucidation of the formation of transformation products by experimental and theoretical approaches, (iii) formation of oxidation by-products from the matrix (e.g., bromate, carbonyl compounds), (iv) biological effects after ozonation, resulting from transformation products and/or oxidation by-products, (v) biodegradability of transformation products during post-treatment.

In this talk, basic chemical principles of ozonation related to micropollutant abatement and result from pilot- and full-scale applications for advanced wastewater treatment will be shown.

A Highly Atroposelective Negishi Coupling Enables the Commercial Manufacturing Process of Divarasib

Stephan Bachmann, Raphael Bigler, Dainis Kaldre, Dominique Kummli, René Lebl, David Linder, Ugo Orcel, Isabelle Prévot, Jörg Sedelmeier

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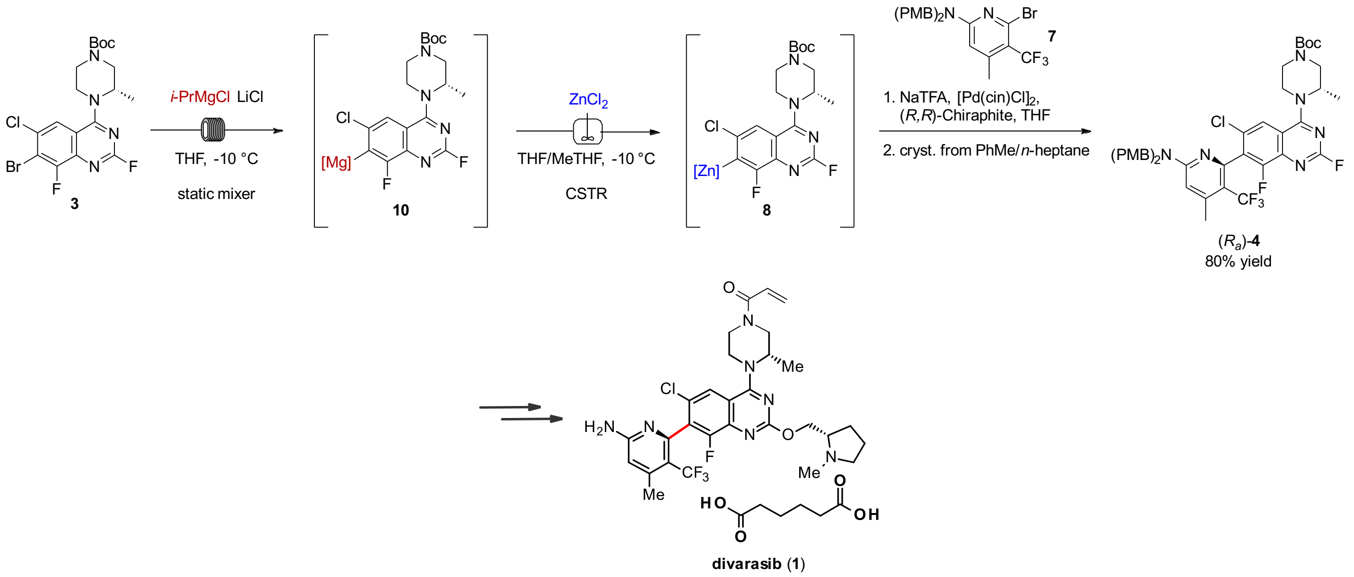
The development efforts that will result in the commercial manufacturing process of divarasib (**1**), a highly potent KRAS G12C inhibitor currently undergoing Ph III clinical trials, will be highlighted. Most prominently, our process landmarks the first example of a highly atroposelective Negishi coupling at manufacturing scale, allowing isolation of the step product (*R*a)-**4** as a single isomer without chromatography.[1] The implementation of a continuous process for the metalation steps of the Negishi coupling allowed for the elimination of the cryogenic reaction conditions from the manufacturing process.[2]



We will also outline improvements to the other key synthesis steps, overall resulting in a 6-fold yield increase and a 29-fold process mass intensity reduction.

[1] J. Xu, L. Ngiap-Kie, J. Timmerman, J. Shen, K. Clagg, U. Orcel, R. Bigler, E. Trachsel, R. Meier, N. A. White, J. Burkhard, L. E. Sirois, Q. Tian, R. Angelaud, S. Bachmann, H. Zhang, F. Gosselin, *Org. Lett.*, **2023**, *25*, 3417-3422.

[2] S. M. Kelly, R. Lebl, T. C. Malig, T. Bass, D. Kummli, D, Kaldre, U. Orcel, L. Tröndlin, D. Linder, J. Sedelmeier, S. Bachmann, C. Han, H. Zhang, F. Gosselin, *Org. Process Res. Dev.* **2024**, *28*, 1546-1555.

Exploiting Sustainable Polar Organometallics for Arene Functionalisation and Catalysis

Eva Hevia

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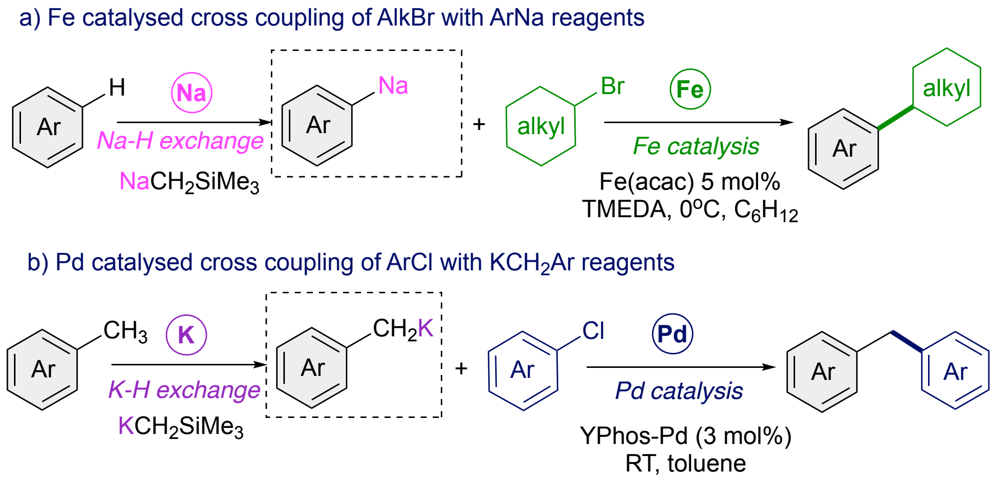
Organolithium and lithium amides such as LDA or LiTMP are commodity reagents in organic synthesis, finding widespread applications in industry and academia.[1] Their versatile reactivity and widespread applications has inevitably led to the commercialisation of both organolithium compounds as well as related commodity lithium amides. In recent years however, whilst addressing the need to promote sustainability issues in chemistry, research into the more richly abundant sodium and potassium analogues has been reinvigorated.[2]

This talk will discuss recent developments from our group on the use of sustainable organosodium and organopotassium reagents for the functionalisation of organic molecules, demonstrating that not only are they a more sustainable alternative to organolithium reagents but that they can also display superior reactivities. This includes their use on selective C-H metalation of synthetically attractive arenes, providing access to the selective functionalization of these scaffolds, including the borylation,[3] and transition-metal catalysed reactions (see Figure).[4] Their use as catalysts to promote deuteration of organic molecules,[5] as well as alkene isomerisation processes[6] will also be discussed.


a) Fe catalysed cross coupling of AlkBr with ArNa reagents

b) Pd catalysed cross coupling of ArCl with KCH_2Ar reagents

[1] Lithium Compounds in Organic Synthesis – From Fundamentals to Applications, (Eds.: R. Luisi, and V. Capriati, Wiley-VCH, Weinheim 2014.

[2] (a) P. B. De, S. Asako, L. Ilies, *Synthesis* **2021**, *53*, 3180–3192. (b) S. Asako, H. Nakajima, K. Takai, N*at Catal* **2019**, *2*, 297–303.

[3] a) L. J. Bole, A. Tortajada, E. Hevia, *Angew. Chem. Int. Ed.* **2022**, *61*, e202204262. b) D. E. Anderson, A. Tortajada, E. Hevia, *Angew. Chem. Int. Ed.* **2024**, *63*, e202313556.

[4] (a) D. Knyszek, J.Löffler, D. E. Anderson, E. Hevia, V. H. Gessner, J. *Am. Chem. Soc.* **2025**, 147, 5417–5425. (b) Nat. Synth. **2025**, *in press*.

[5] (a) Tortajada, A.; Hevia, E.*; J. Am. Chem. Soc.* **2022**, *144*, 20237–20242. (b) M. S. Tschopp, A. Tortajada, E. Hevia, Angew, Chem. Int. Ed. **2025**, 64, e202421736.

[6] A. Tortajada, G. L. Righetti, A.McGinley, M. Mu, M. García-Melchor, E.Hevia, *Angew. Chem. Int. Ed.* **2024**, *63*, e202407262.

Development of the Commercial Manufacturing Process for Inavolisib

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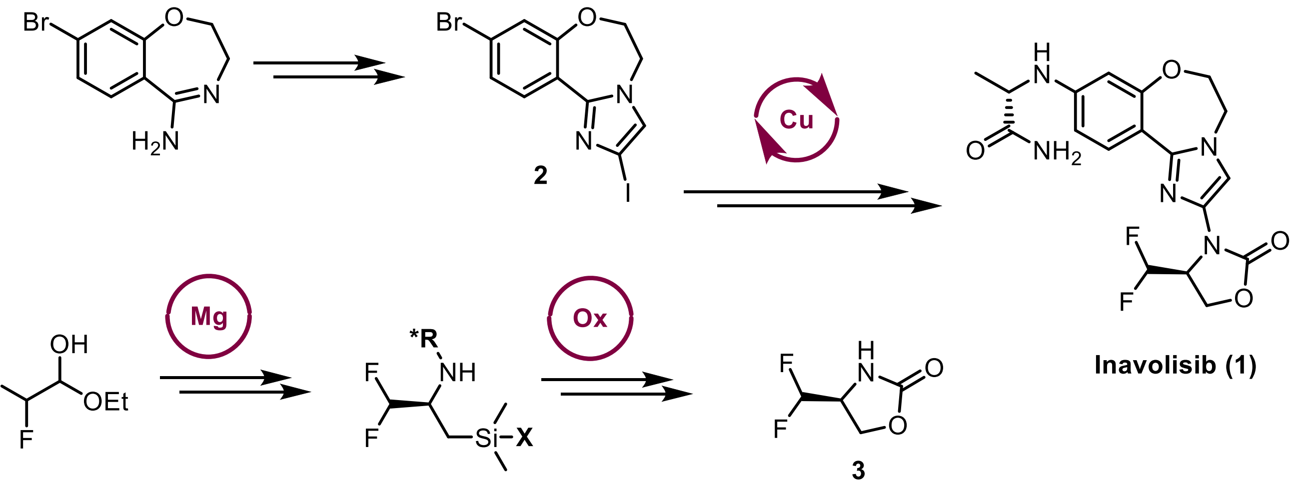

Scheme 1: Synthesis of Inavolisib (1)

Inavolisib (1) is a highly potent and selective PI3Kα inhibitor, which is currently in clinical development for the treatment of HR+, HER2- breast cancer and has recently been approved by the FDA.[1]
Herein we present the development of a robust and scalable manufacturing process for Inavolisib (1). A route scouting case study and process design for the oxazolidinone 3 is presented. The selected route for 3 features a diastereoselective Grignard addition followed by a Tamao-Fleming oxidation.[3] At the core of the synthesis of Inavolisib (1) are two consecutive Cu-catalyzed CN-coupling reactions with one of them connecting the two key building blocks dihalide 2 and oxazolidinone 3 (Scheme 1).[2]

References

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A brief survey of recent dry woody and ambery odorants

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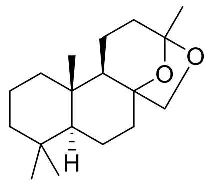
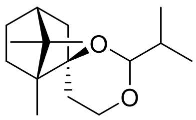
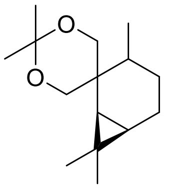
There is an ever-increasing need for maximizing the performance-to-cost ratio in perfumery applications, as well as minimizing the environmental impact in the eventual production of odoriferous molecules. The dry woody and ambery olfactive combination plays a key role in the creation of high impact compositions and the focus of our discovery work has been geared towards the exploitation of terpenes and sesquiterpenes to find increasingly potent molecules possessing extremely low thresholds of detection. The importance of the acetal functionality displaying highly appreciated woody/amber facets has been known from the initial discovery in 1954 by Jeger, Ruzicka, *et al*, of Z-11™ **1.**[1] The syntheses, from renewable carbon feedstocks, of related acetals such as Belambre® **2**,[2] Spirambrene® **3**,[3] Ysamber K® **4**[4] in the subsequent decades were a welcomed addition to the perfumer's palette. The discovery of the ultra-powerful cedrane-based molecules exemplified by Ambrocenide® **5**,[5] Ambrostar®**6**[6] and the dehydro-analog **7**[7] with odor thresholds on the order of 10^{-1} to 10^{-2} ng/L perhaps represents the culmination of a long-term search for woody amber odorants displaying excellent cost-performance advantages in perfumery applications.



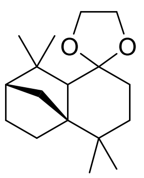
Z-11™
1



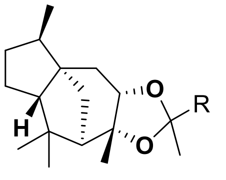
Belambre®
2



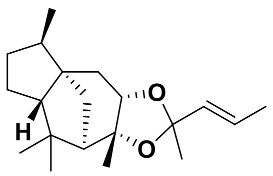
Spirambrene®
3



Ysamber K®
4



R = Me, Ambrocenide® **5**
R = Pr, Ambrostar® **6**



7

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Electrifying Organic Synthesis – An Elegant Way to Oxygenated Products

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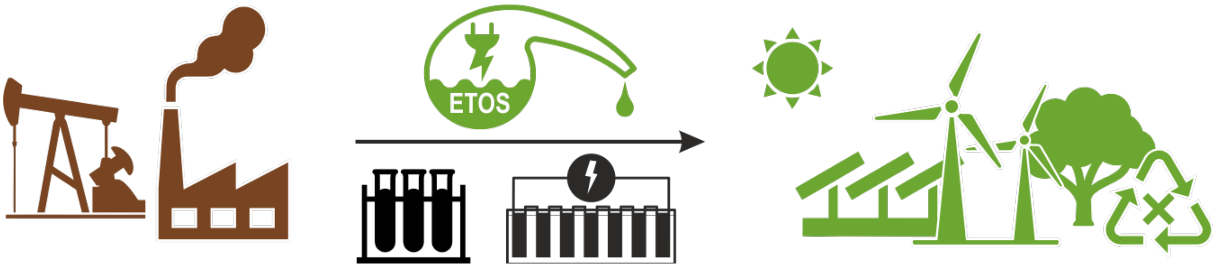
The direct use of electrochemistry for the generation of reactive intermediates can have major advantages towards conventional synthetic strategies. Compared to the action other sustainable approaches such as photochemistry, the overall energetic balance is superior and allows easily scalable conversions. Less or no reagent waste is generated and new reaction pathways are accessible. In order to exploit the electricity driven conversions for synthetic purposes and to install unique selectivity two modern approaches will be outlined:

1) For reaching larger scale in electrochemical conversions, the formation of high-performance oxidizers is an option. By the given versatility a broad applicability is targeted.
2) Several unique molecular entities require for their installation large amounts of reagents, when using electrochemical tools this can be achieved almost waste-free. This is of particular interest when complex molecules are desired.

The working horse to identify suitable electrolytic conditions is the electrosynthetic screening approach. This strategy gives also rise to fast optimization and subsequent scale-up. For technical realization of electrosyntheses carbon electrodes play a crucial role ranging from diamond to highly isostatic graphite carbon allotropes.



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Poster Presentations

Yaser Balmohammadi, University of Bern
«Atoxyl: The journey of a drug from Historical use to interplay between conformation, polarization, and electron density distribution»

Reinhard Berger, ZHAW Winterthur IMPE
«Advancing Chemical Waste Reduction and Recycling through Formulation Science»

Roel Bienenmann, University of Bern
«Nickel catalysed silylation of aryl-ethers: a mechanistic study»

Clara Bovino, Lonza AG
«Electrochemical Fluorination of Organic Compounds using an Hexafluorosilicate Salt as Fluorine Source»

Fabio Casanova, dsm-firmenich
«Sustainable heterogeneous ring opening / addition of epoxides»

Pauline Daul, HEIA Fribourg
«Keratin Based Biosorbent for Chemical Waste Treatment»

Kim-Long Diep, HEIA Fribourg
«A scalable dynamic cascade flow reactor for challenging continuous heterogeneous processes»

Vincent Freiburghaus, University of Zürich
«Novel dipolar, aprotic solvents for SPPS»

Gaetano Geraci, HEIA Fribourg
«Exploiting mechanochemistry for the synthesis of APIs: benzamides synthesis via Beckmann rearrangement»

Roman Goy, dsm-firmenich
«Sustainable Building Blocks to Produce Carotenoids»

Souvik Guha, HEIA Fribourg
«Unlocking Indazole Synthesis from α-diazo-β-ketoesters via Aryne Trapping: A Streamlined Approach»

Sofia Monnard, dsm-firmenich
«Optimizing the Synthesis of a Perfumery Ingredient through Process Intensification and Continuous Processing»

Darryl Nater, Max-Planck Institute for Chemical Energy Conversion
«Flow Electrosynthesis at Scale: Investigations of the Electrochemical Hofmann Rearrangement in Commercial parallel plate reactors»

Tom Nelis, EPFL Lausanne
«Novel dipolar aprotic solvents»

Subrata Patra, University of Bern
«Simplifying Nitration Chemistry: Safe, Sustainable, Selective, Controllable»

Esaïe Reusser, HEIA Fribourg
«Water-based amide coupling with sustainable xylose acetals as co-solvents: A novel organic base-free strategy»

Philippe Roth, WAB Group
«Evaluation of scalability parameters in synthesis using agitator bead mills for mechano-chemistry»

Kevin Simon, RCPE GmbH
«Scalable and Selective Electrochemical Synthesis of Pantoprazole: A Sustainable Approach to Active Pharmaceutical Ingredients»

Jordan Gay, HEIA Fribourg
«Lignin and its derivatives as bio-based alternatives for the plastics industry»

Atoxyl: The journey of a drug from Historical use to interplay between conformation, polarization, and electron density distribution

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One of the important steps in drug design is understanding the fact of how the conformation of your drug will be in the protein or biological environment[1]. In this regard, we look at para-arsanilic acid or atoxyl ($C_6H_8AsNO_3$), an arsenic-based drug. We employed the emerging field of quantum crystallography for our study. We look at different conformations that atoxyl adopts in different environments. The cornerstone of the differences between these conformations is the rotation of arsenite (ASO_3) group. We demonstrated that the rotational barrier for arsenite can be provided by crystal packing and intermolecular interactions since it is less than 5 Kcal/mol. Also, for the first time, we reported here the helical chirality of atoxyl in its single-crystal structure.

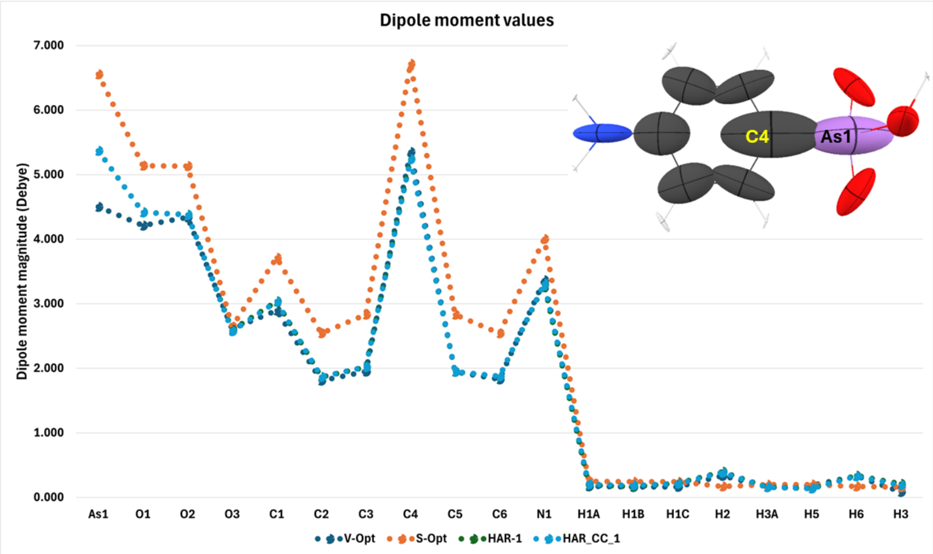

Figure 1. Scatter plot of the atomic dipole moments in 4 different environments. The picture on the top right represents the polarizabilities calculated using polaber.

Then we evaluate the interplay between conformation, polarization, and electron density distribution by two different strategies: **i)** by fixing the conformation and **ii)** by changing the conformation. The first strategy shows that the electron density distribution of the drug will change by changing the environment. We proposed X-ray wave function fitting is a very suitable approach to simulate the biological environment[1]. The second strategy shows us despite changing the conformation, atomic charges and bond distances of atoxyl remain similar but the atomic dipoles are changing (Figure 1). We concluded that despite the similarity of atomic charges and bond distances, the distribution of electron density in each atomic basin changes. Then we showed that the major impact on the atomic dipole moment belongs to arsenic and the carbon atom bonded to it. This prediction aids us in finding a suitable protein for its medical application[2].

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Advancing Chemical Waste Reduction and Recycling through Formulation Science

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Formulation science presents a promising avenue for the advancement of chemical waste reduction and recycling processes. The Laboratory of Process Engineering is dedicated to applying innovative formulation techniques to design and optimize environmentally sustainable processes. These efforts aim to minimize chemical waste generation and enhance resource recovery.

For example, our research explores the integration of solvent and surfactant selection supported by physical or semi-empirical theories with advanced synthetic pathways for micellar chemistry. This comprehensive approach seeks to establish a robust foundation for the systematic reduction of chemical waste and the promotion of effective recycling methods.

Key areas of focus include:

- Carbon dioxide removal
- Development of environmentally friendly solvent replacement strategies
- Utilization of pyrolysis for waste-to-value transformation
- Emulsion Phase Control for Micellar Chemistry

Nickel catalysed silylation of aryl-ethers: a mechanistic study

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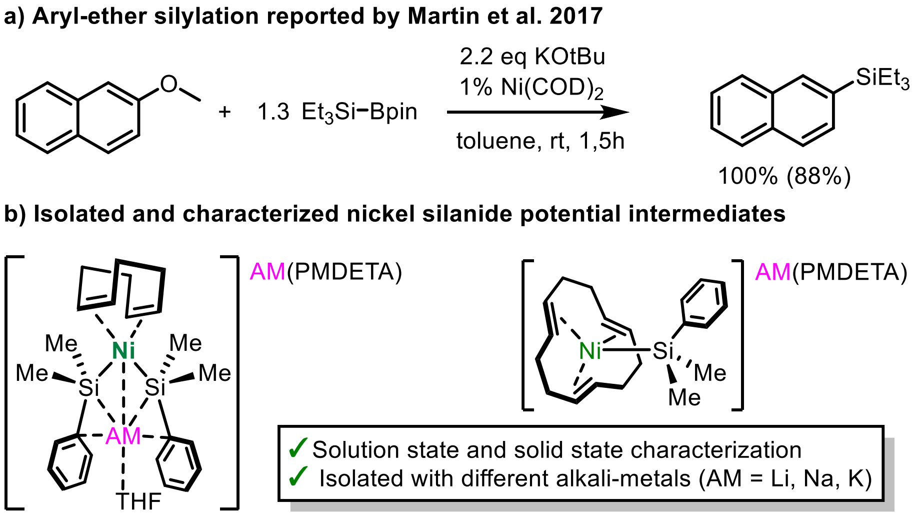
Aryl-ethers have a major potential as sustainable and renewable platform chemicals for the synthesis of aromatic fine chemicals due to their abundance in lignin.[1] However, the bottleneck in their utilization is the cleavage and functionalization of the C–O bond. Current methods for the C–O bond cleavage often depend on harsh reaction conditions and high catalyst loadings, making these impractical for industrial adaptation.[2] In 2017, Martin et al. published the catalytic silylation of aryl-ethers using earth abundant $Ni(COD)_2$ (COD = 1,5-cyclooctadiene) as catalyst under mild conditions and with low catalyst loadings (Figure 1a).[3] Because these mild reaction conditions stand out, it is interesting to study the reaction mechanism. Despite computational efforts, there are many open questions about the role of various components in the reaction and the speciation of the catalyst, such as whether the alkali-metal in these reactions plays an active role in facilitating C–O cleavage.[2] In our work we therefore take an experimental approach demonstrating the involvement of highly reactive anionic nickel silanide complexes that represent potential catalytic intermediates (Figure 1b). By studying the nature and reactivity of these complexes in both stoichiometric and catalytic reactions, we provide insight into the mechanism of the catalytic silylation of aryl-ethers, advancing the understanding on these Ni(ate) mediated transformations.



a) Aryl-ether silylation reported by Martin et al. 2017

b) Isolated and characterized nickel silanide potential intermediates

✓ Solution state and solid state characterization
✓ Isolated with different alkali-metals (AM = Li, Na, K)

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Electrochemical Fluorination of Organic Compounds using an Hexafluorosilicate Salt as Fluorine Source

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Gabriele Laudadio, C. Oliver Kappe, David Cantillo

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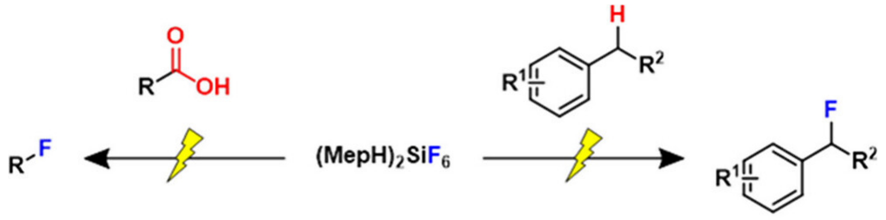
The introduction of fluorine into organic molecules is of the utmost importance in the preparation of active pharmaceutical ingredients (APIs). While a wide range of fluorine sources for organic synthesis have been used over the past decades, the associated safety risks, cost, or environmental impact are still serious limitations. Hexafluorosilicate salts are one of the most inexpensive and readily available sources of nucleophilic fluorine, but they have so far not been used in organic synthesis. Herein we report the first example of the use of a hexafluorosilicate salt as a reagent for the formation of C–F bonds. We have selected as the model reaction an electrochemical decarboxylative fluorination procedure. The synthesis of bis(5-ethyl-2-methylpyridin-1-ium) hexafluorosilicate(IV) was key to obtaining a soluble and reactive hexafluorosilicate salt. This protocol enabled the synthesis of a wide range of primary, secondary, and tertiary aliphatic fluorides (22 examples) in up to 85% yield. The electrochemical method was also successfully transferred to a flow electrolysis cell, demonstrating its robustness and scalability. Finally, we extended the scope of the fluorine source by demonstrating its applicability to electrochemical benzylic C–H fluorination



Economical, abundant, non-toxic and versatile fluoride source
Mep = 2-methyl-5-ethyl-pyridine

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Zeolites-based catalysis for efficient alcoholysis of epoxides for the manufacture perfumery ingredients

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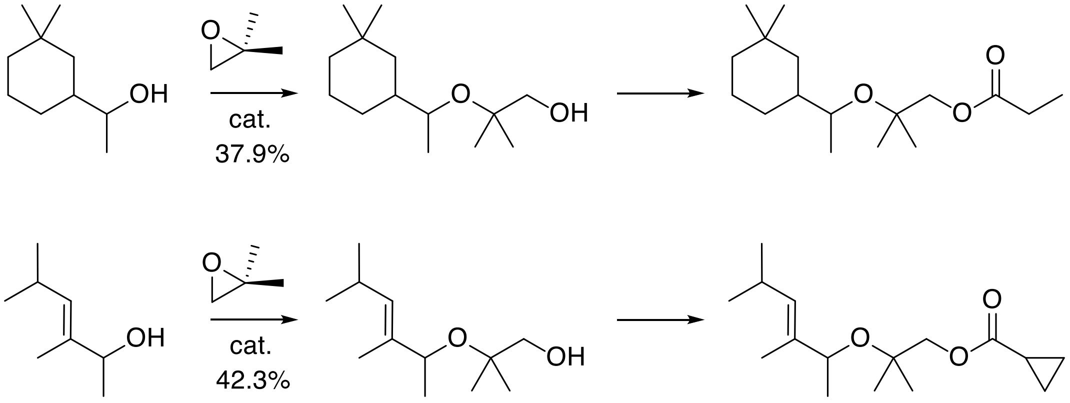
Known for their unique and long-lasting scent profiles that form the base notes in many fragrances, Musks are of paramount importance in perfumery and efforts aiming at improving their synthesis remain critical. In this context, the alcoholysis of epoxide, one of the key steps in Helvetolide®, Alpinolide®, Sylkolide® and Serenolide® synthesis, is herein investigated using heterogeneous catalyst as a more sustainable and productive alternative to the traditional homogeneous catalysts. Remarkably, crystalline aluminosilicates and in particular USY zeolites displaying a hydrophobic character offer bright prospects in this respect being more selective than most of the homogeneous catalysts reported in literature while not requiring extensive washing steps. Overall, a gain in productivity of 40 wt.% could be achieved thus enabling to cope with the increasing market demand for those ingredients while minimizing investments.



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Keratin Based Biosorbent for Chemical Waste Treatment

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The meat industry and animal breeding significantly impact the environment, generating large quantities of by-products such as feathers, wool, and hair, all rich in keratin. Simultaneously, heavy metals pose serious threats to both environmental and human health. This project aims to create a circular process by valorizing these keratin-rich wastes to treat polluted effluents contaminated with heavy metals.

Static tests were conducted to evaluate the efficiency of wool, hair, and feathers in adsorbing copper from aqueous solutions. Various surface treatments were then applied to enhance the adsorption properties of the keratin-based materials. All treated materials outperformed their untreated counterparts, with NaOH-treated wool showing the highest copper adsorption capacity (30.50 mg/g) compared to untreated wool (3.25 mg/g). Additionally, experiments were designed to optimize the environmental friendliness of NaOH treatment and minimize waste generation. Lowering the NaOH concentration reduced the copper adsorption capacity by 10% but decreased adsorbent loss by 33.5%. Moreover, increasing the adsorbent-to-NaOH solution ratio resulted in a 44% improvement in yield without compromising adsorption performance. The reuse of NaOH was also investigated, demonstrating that the treatment solution could be reused at least once without losing efficiency.

Dynamic adsorption experiments, conducted using packed column systems, were employed to assess the scalability of this process for industrial applications. These results indicated that factors such as flow rate and bed height significantly influenced adsorption efficiency. The saturation values obtained from the dynamic system were lower than those from the static system, attributed to particle size reduction during grinding and sieving, as well as mass transfer limitations and inhomogeneities in the packed bed.

When compared to commercial ion exchange resins in terms of environmental impact, cost, and efficiency, the proposed keratin-based system emerges as a competitive and promising alternative for heavy metal removal from contaminated effluents.

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A scalable dynamic cascade flow reactor for challenging continuous heterogeneous processes

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We herein present our work on the development, characterization (residence time distribution, heat transfer) and application tests of a flow reactor equipped with a dynamic mixer (DCR - Dynamic Cascade Reactor), which was designed for continuous processes that require handling of solids/fouling as well as reactions requiring long residence times. The reactor acts as a 12 CSTR cascade and can be used for a wide range processes with a focus on multiphasic reactions.

To illustrate the reactor's ability to handle solids in suspension, Grignard reagents were synthesized in continuous flow from magnesium powder suspended in the reactor. The reactor is particularly well suited for this application as the reactor can be used in batch mode to perform the initial magnesium activation prior to starting the continuous process, thus ensuring that the reaction then takes place smoothly in flow.

Figure 1. *Dynamic Contiplant Reactor from Fluitec mixing + reaction solutions AG*

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Novel bio-based solvents for SPPS

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The increasing demand for therapeutic peptides and peptide-based drugs drives the urgent need for more sustainable synthetic methods.[1] Solid-phase peptide synthesis (SPPS) is the method of choice to reliably synthesize peptides and small proteins.[2] However, the current manufacturing processes compare unfavourably in terms of process mass intensity (PMI) to other modalities such as small molecules and biopharmaceuticals. The main contributor to the unfavourable PMI of SPPS is the excessive solvent usage.[3] *N,N*-dimethylformamide (DMF), the most used solvent in SPPS, is classified as carcinogenic and reprotoxic. Consequently, the European Union has restricted DMF usage as of December 2023, highlighting the need for alternatives.[4]

Here, we present the usage of novel, bio-based solvents for SPPS. The solubilities of Fmoc-protected amino acid building blocks and activators were tested, as were the resin swelling capabilities of the novel solvents. Finally, several peptides have been synthesized without the use of concerning solvents. Amino acid couplings and Fmoc-deprotections were executed in the novel solvents, while the resin was washed with isopropanol and ethyl acetate. Difficult peptides were synthesized and compared to conventional synthesis in DMF. While the challenge of extensive solvent usage is yet to be solved, we show that DMF can be replaced with bio-based solvents, which is a big leap towards more sustainable SPPS.

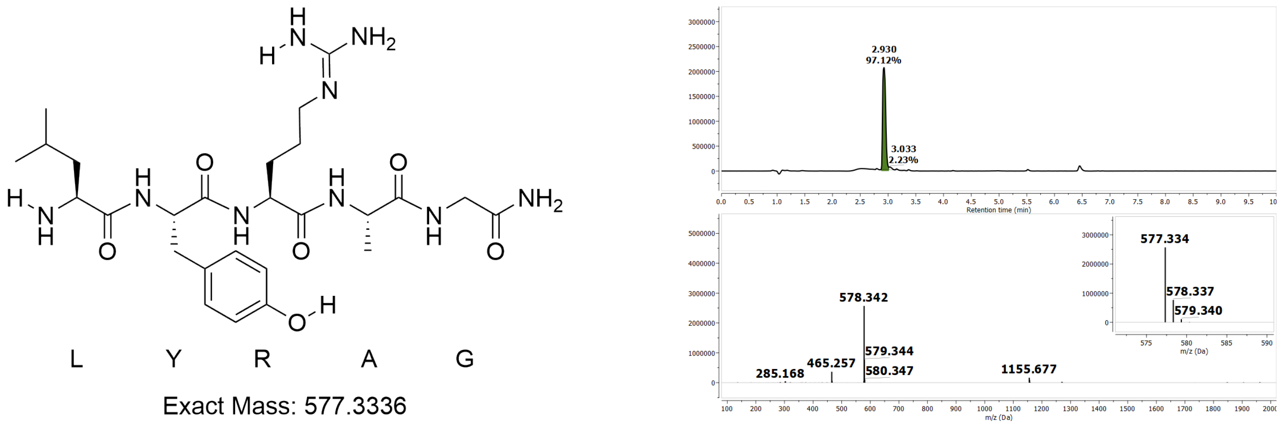

Figure 1. Example synthesis of the peptide LYRAG only using the novel bio-based solvents.

The structures of the solvents are omitted for confidentiality reasons but will be shown on the event.

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Exploiting mechanochemistry for the synthesis of APIs: benzamides synthesis via Beckmann rearrangement

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To tackle the climate emergency which has been emerging for decades, the development of new sustainable chemical processes is required. In 2019, mechanochemistry was named by IUPAC as one of the top ten emerging technologies in chemistry.[1] Also Suschem Switzerland acknowledged mechanochemistry as a technology who can reduce the footprint of chemicals manufacture.[2] The main advantage of this technology is that no solvents are necessary to perform reactions. To show the great potential of mechanochemistry and its applicability in process chemistry, the synthesis of two benzamides APIs (Active Pharmaceutical Ingredients) will be presented. The reactions were performed using bead-mill technology (Dyno®-Mill) and took advantage of the Beckmann rearrangement. For the paracetamol synthesis, the optimized solvent-free method was able to deliver around ten grams on a laboratory scale, and gave better yields and green metrics compared with solvent-based[3]. For the Flutolanil synthesis, preliminary results will be presented.

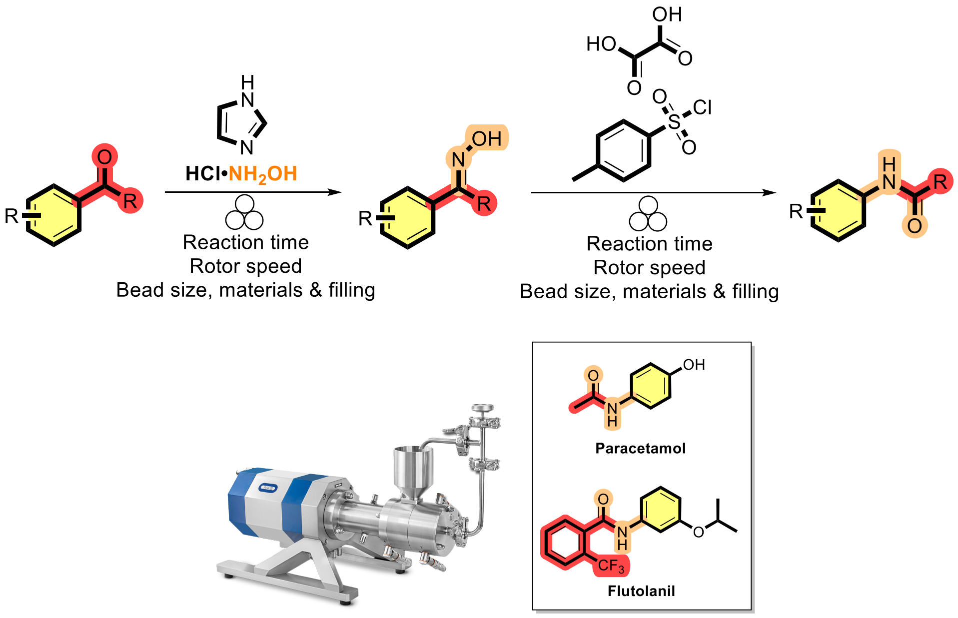

Fig 1: Beckmann rearrangement with the Dyno®-Mill technology (image courtesy of WAB).

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Sustainable Building Blocks to Produce Carotenoids

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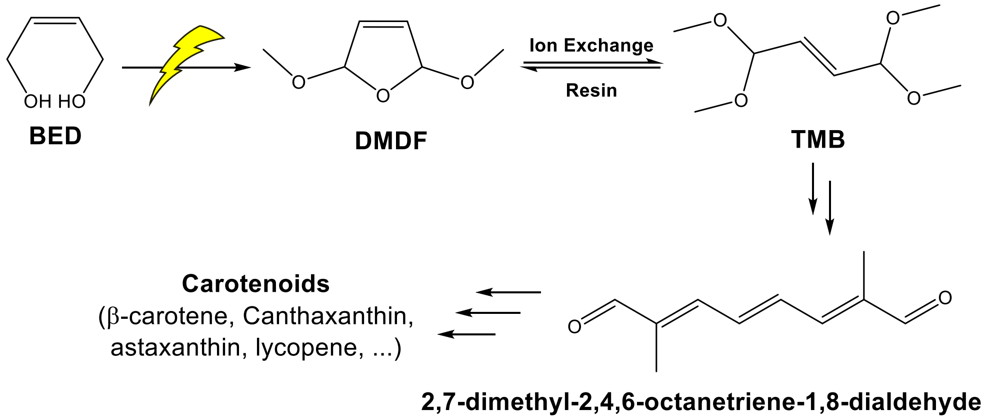
Carotenoids are a group of natural pigments that are vital for human and animal nutrition and health *e.g.*, as source of vitamin A. In addition, carotenoids add color to foods and beverages. The industrial manufacturing of most of the carotenoids is executed through chemical synthesis to manage the need and market demands. A key intermediate for carotenoids synthesis is 2,7-dimethyl-2,4,6-octanetriene-1,8-dialdehyde (see Scheme). [1] An important intermediate is 1,1,4,4-tetramethoxy-2-butene (TMB), which can be synthesized by acid catalyzed ring-opening reaction from 2,5-dimethoxydihydrofuran (DMDF). The current preparation method for TMB and DMDF faces challenges in enhancing reaction performance, managing waste, and avoiding the use of hazardous reagents.



Here we present results of the electrochemical oxidation of *Z*-2-butene-1,4-diol (BED) to DMDF, [2] optimized and scaled-up to 100 cm^2 electrode surface area. A two-stage nanofiltration for >99% recycling of the spent electrolyte and pervaporation for water removal were identified as the best options for further processing of the crude DMDF. [3] A complete process concept was developed. Purified DMDF was successfully converted in presence of an acidic ion exchange resin to TMB in a continuous mode resulting in an excellent selectivity control, while salt waste could be minimized. [4] Unconverted DMDF could easily be recycled and re-used. The new process fulfills the criteria for a green and sustainable production and engineering for the carotenoid building block TMB. The downstreaming produces only minimal amount of wastewater (released during reaction). An LCA showed the significantly improved carbon food print for the new process by a potential decrease of >66% compared to the current process.

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Unlocking Indazole Synthesis from α-diazo-β-ketoesters via Aryne Trapping: A Streamlined Approach

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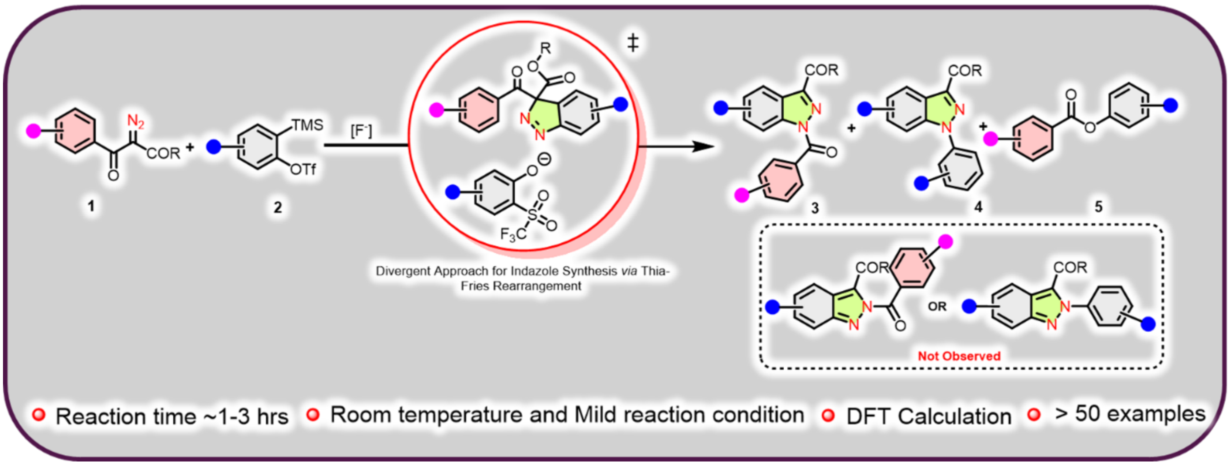
Indazoles are high value chemical building blocks used in medicinal chemistry and materials science for their distinct structural and functional features. This study details a [3+2]-cycloaddition reaction between various aryl-ketodiazoesters and ortho-(trimethylsilyl)aryl triflates under mild conditions, leading predominantly to 1-acyl-1*H*-indazoles. *N*-aryl-1*H*-indazoles and aryl benzoates were also observed as other products. The reaction exhibits broad functional group tolerance and scalability, making it a valuable synthetic approach. Mechanistic insights, derived from control experiments and density functional theory (DFT) calculations, elucidate the cycloaddition pathway and rationalize the formation of the products. Collectively, these findings underscore the method's potential for synthesizing complex indazole derivatives, which hold significant promises for applications in pharmaceutical development and advanced materials research.



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Optimizing the Synthesis of a Perfumery Ingredient through Process Intensification and Continuous Processing

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Across various industries, there is a rising demand to enhance productivity and performance while simultaneously reducing production costs and minimizing environmental impact. In the chemical industry, process intensification can provide an effective solution to meet this demand. Our team was tasked with optimizing a key chemical step in the synthesis of a major perfumery ingredient by implementing an intensified, continuous process. A detailed kinetic model was developed using a mini-CSTR designed by the School of Engineering and Architecture Fribourg (HEIA-FR) [1]. The kinetic model was subsequently used for in-silico reactor selection, which helped us identify a CSTR cascade with staged reagent addition as the most suitable reactor, leading to the highest selectivity. The reaction was then further optimized in an Agitated Cell Reactor (ACR) using DOE methodology. The results obtained were successfully used to scale up the process, resulting in a more robust, efficient, and cost-effective operation.

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Flow Electrosynthesis at Scale: Investigations of the Electrochemical Hofmann Rearrangement in Commercial parallel plate reactors

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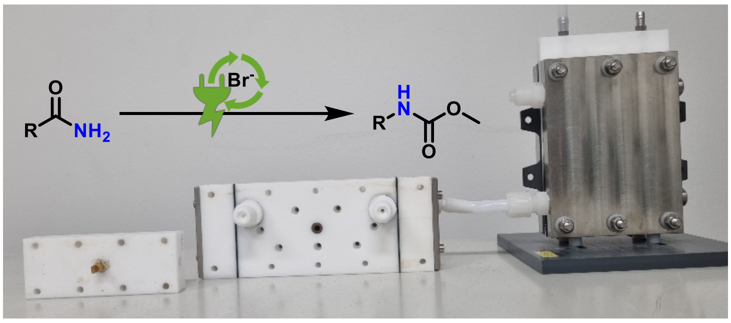
In order to make chemical synthesis more environmentally benign, a reduction of hazardous reagents is of paramount importance.[1] However, many critical processes and their products rely on these reactants. A prominent example of the use of hazardous substances in synthesis is the Hofmann rearrangement,[2] which requires (super-) stoichiometric amounts of caustic halogen or halo-reagents.

Electrosynthesis has garnered increased interest in the past few years[3] as an environmentally benign methodology. In the case of the electrochemical Hofmann rearrangement, the required halo reagent is produced in situ through the oxidation of bromide anions, whereas the other necessary reactant, a base, is produced cathodically with concomitant hydrogen production.[4]



As such, we investigated the electrochemical Hofmann rearrangement in commercial parallel plate reactor. Our investigations started in screening cells with 12cm^2 of anode surface, with up to quantitative yields.[5] We subsequently moved to larger cells with up to 162 cm^2 of anode surface, where we could also achieve excellent yields. Finally, we could illustrate that we could perform the electrochemical Hofmann rearrangement at hectogram scale with 94% yield. This ultimately demonstrates that large scale electrosynthetic reactions can be performed using commercially available reactors with excellent results.

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Sustainable dipolar aprotic solvents

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Dipolar aprotic solvents are widely used in pharmaceutical and medicinal chemistry due to their versatile solvation properties and non-hydrogen-bond-donating nature. However, conventional solvents in this category, such as DMF, NMP and DMAc, pose significant environmental and health risks. Existing bio-based alternatives, including dihydrolevoglucosenone (Cyrene), gamma valero lactone (GVL), and propylene carbonate, suffer from limited versatility due to reactivity issues and / or high boiling points (> 205 °C), restricting their recyclability. Consequently, there is an urgent need for non-toxic, bio-based, stable, recyclable and cost-effective alternatives.

Here we introduce novel dipolar aprotic solvents derived from glycerol, a widely available and underutilized waste product from the biodiesel industry. These solvents green profile is demonstrated by a simple synthesis under mild conditions, employing heterogeneous catalysis and utilizing crude glycerol as a feedstock.

With a boiling point below 190 °C, one of these new solvent candidates is distillable and recyclable, while its high flash point ensures it does not require classification as a flammable substance. To assess its performance, we evaluated its efficacy in pharmaceutically relevant reactions (Menshutkin, amidation and Baylis-Hillman) by comparing reaction rate constants. This new solvent performed comparably or better than conventional dipolar aprotic solvents (Fig 1A), aligning with its charge density profile similarity to DMF (Fig 1B). Toxicological and biodegradability assessments are currently ongoing, while a preliminary techno-economic analysis suggests a minimum selling price of 2.72 USD/kg, which is comparable to existing dipolar aprotic solvents.

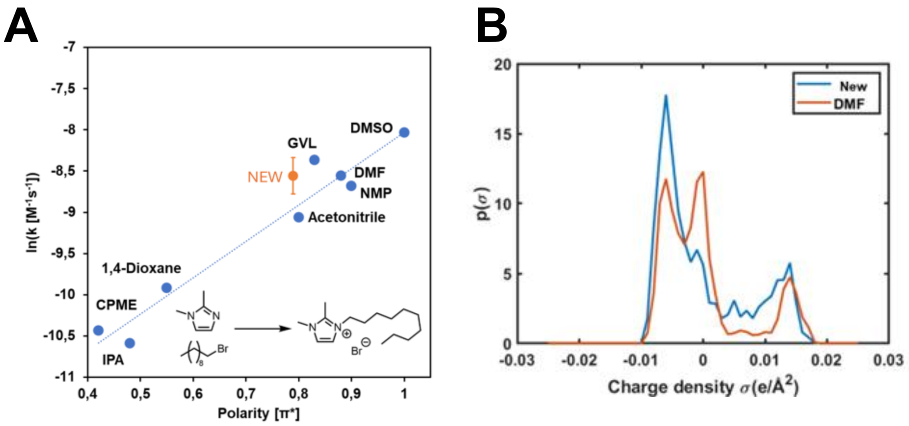

Figure 1: Performance of one new solvent candidate and selected other solvents in Menshutkin alkylation model reaction, against relevant Kamlet-Taft parameter (A) Sigma profiles of charge density of the new solvent compared to DMF (B) (AMS COSMO).

Simplifying Nitration Chemistry: Safe, Sustainable, Selective, Controllable

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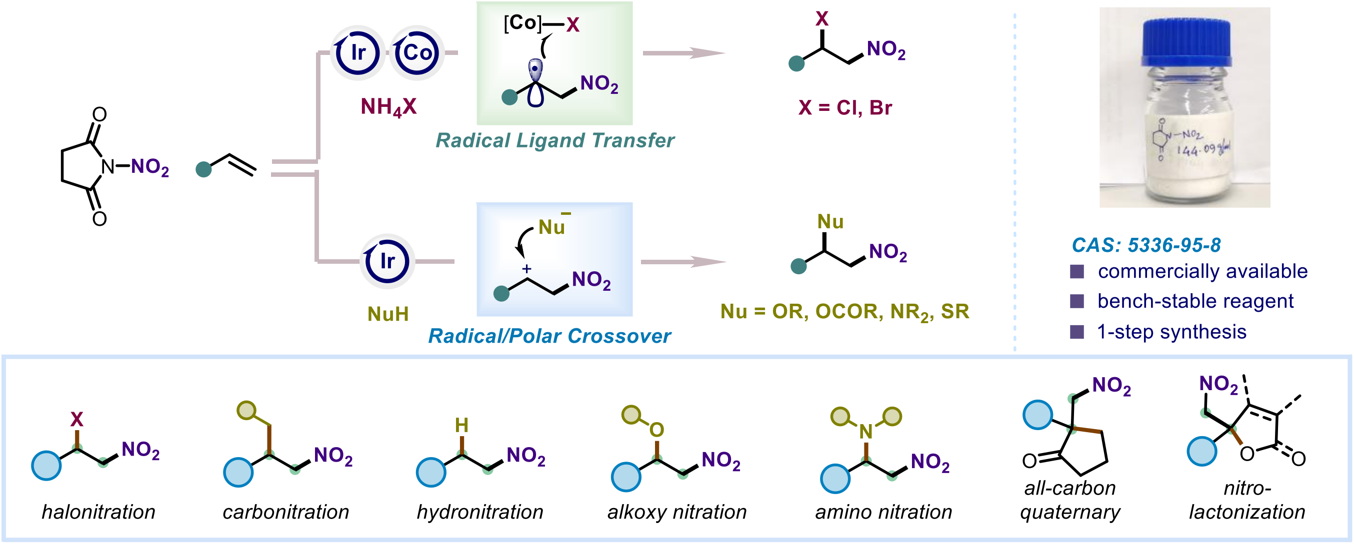
Nitration reactions hold significant importance in organic synthesis and are foundational school topics. While the classical electrophilic nitration method using strong mineral acids prevailed for many years since its discovery in the 19th century, recent decades have shifted towards exploring new reactivity and reagents. Researchers now seek practical and mild reaction conditions for accessing nitro compounds. Organic nitrating reagents have emerged as key players in this endeavour, offering enhanced reactivity and enabling eco-friendly and sustainable nitration processes.[1]

Herein, we present a novel dual photoredox-mediated paradigm for difunctionalization of alkenes, yielding challenging 1,2-halonitroalkane molecules. We employ N-Nitrosuccinimide as a redox-active nitrating reagent to introduce a controlled amount of nitryl radicals into reaction mixture. In contrast, cobalt-mediated radical ligand transfer (RLT) facilitates the transfer of a secondary functionality into the organic scaffold. This synergistic process between photocatalyst and cobalt operates under mild conditions, enabling a one-pot synthesis of 1,2-chloronitro- and 1,2-bromonitroalkanes with excellent chemo- and regioselectivity, demonstrating exceptional functional group tolerance. Detailed mechanistic studies supported the role of cobalt as a radical halogen transfer catalyst. Furthermore, employing a net-neutral radical/polar crossover (RPC) approach under cobalt-free reaction conditions allowed to accommodate a variety of external protic nucleophiles, including thiols, alcohols, acids, and, notably, substituted amines.[2,3] Highly functionalized olefin scaffolds also successfully underwent nitrative difunctionalization, demonstrating the viability of these protocols for the late-stage functionalization of bioactive molecules.



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Water-based amide coupling with sustainable xylose acetals as co-solvents: A novel organic base-free strategy

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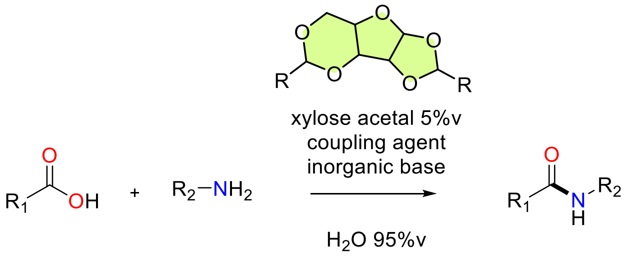
Amide bond formation is one of the most fundamental and widely used chemical transformations, playing a crucial role in the synthesis of pharmaceuticals, agrochemicals, and bulk chemicals. Despite its industrial significance, traditional amide coupling methodologies often require highly polar, petroleum-derived solvents such as N,N-dimethylformamide (DMF), acetonitrile, or N-methyl-2-pyrrolidone (NMP) to efficiently solubilize polar coupling reagents,[1] which are essential for activating carboxylic acids toward nucleophilic attack by amines. These solvents are not only derived from non-renewable resources but are also associated with significant environmental and human health concerns, including reprotoxicity.

To address these issues, aqueous reaction media supplemented with surfactants have been explored as a more sustainable alternative. However, these methodologies still rely on toxic and hazardous non-renewable organic bases such as pyridine, 2,6-lutidine, or triethylamine, which are often used in excess and, in turn, act as co-solvents.[2,3] A major challenge in developing greener alternatives lies in maintaining efficient solubilization of all reagents in a strictly aqueous medium while ensuring high reactivity and selectivity. Inorganic bases offer a more sustainable alternative, yet they often lead to lower reactivity and reduced selectivity in amide bond formation due to their weaker solubilization and buffering capabilities.



This work presents a novel organic base-free amide coupling strategy that leverages biomass-derived xylose acetals as key additives.[4] By utilizing these renewable sugar-based compounds, we aim to improve the solubility and reactivity of coupling agents in aqueous media, thereby reducing reliance on hazardous polar aprotic solvents and organic bases. Additionally, xylose acetals play a crucial role in counterbalancing the intrinsic lower reactivity and selectivity induced by inorganic bases, offering an efficient and more sustainable approach to amide bond formation.

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Evaluation of scalability parameters in synthesis using agitator bead mills for mechano-chemistry

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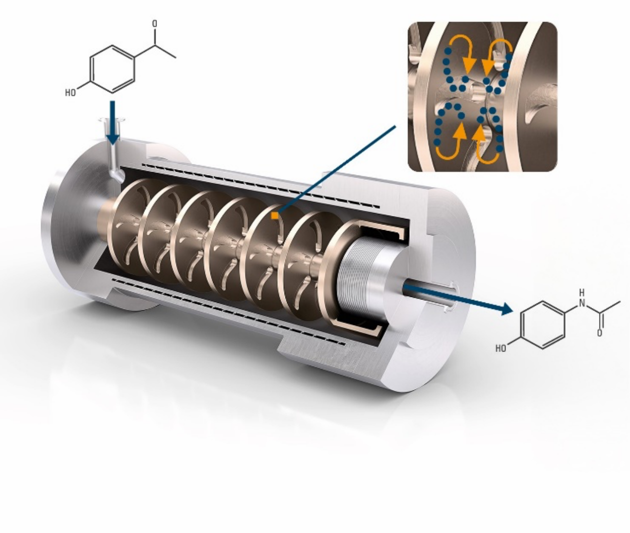
Mechanochemistry, the study of chemical reactions driven by mechanical force, has emerged as a promising approach for more sustainable chemical processes. Unlike conventional methods that rely on heat, solvents, or other energy-intensive techniques, mechanochemistry utilizes mechanical energy to initiate or accelerate reactions, often under milder conditions. This offers significant advantages, including reduced energy consumption, minimized waste, and the re-placement of hazardous solvents with greener alternatives.



The goal of WAB-GROUP® is to develop cutting-edge technologies to provide customers with state-of-the-art solutions (the picture shows the principles of a continuous flow reactor). To as-sess the potential of the existing equipment for mechanochemical processes, a thorough evaluation of key process parameters was conducted, including heat transfer coefficients for various product flows, cooling media, and process settings, as well as residence time distributions under multiple operating conditions, and micro mixing efficiency. These studies aimed to fully characterize WAB mills and identify their properties towards mechanochemical applications.

A particular focus was placed on the WAB IMPA°CT REACTOR®, which integrates both conventional flow chemistry and bead milling technology. Applications on the paracetamol synthesis [1] and the overall benefits of the technology for chemistry and the environment will also be displayed

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Scalable and Selective Electrochemical Synthesis of Pantoprazole: A Sustainable Approach to Active Pharmaceutical Ingredients

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Gastroesophageal reflux disease (GERD) is a common disorder of high incidence rate with its prevalence increasing. GERD is caused by acid reflux, which can be treated by suppressing gastric acid secretion[1]. Key medications for this disease include the members of the prazole family, such as omeprazole, pantoprazole and lansoprazole, which contain a sulfoxide group as the key motif. Usually, the sulfoxide group is generated by oxidation of the corresponding thioether in the last step of the synthetic route.

Traditional approaches carry out this transformation using a variety of oxidizing agents, such as NaOCl, m-CPBA or ^{t}BuOOH. However, they suffer from low selectivity due to overoxidation or side-reaction with other functional groups.[2] To circumvent these undesired reactions, an electrochemical method would highly desirable, as electrolysis often results in milder and more economical processes.

Herein, an electrochemical method for the oxidation of thioethers to sulfoxides is presented. Reaction optimization was carried out in a continuous flow, parallel plate electrolysis cell, not only increasing mass-transfer compared to batch approaches, but also ensuring the reliable scalability of the transformation.[3] Our benchmark oxidation of pantoprazole was developed by employing an electrochemical recirculation platform within a spinning cylindrical electrochemical reactor (SCER) for the sustainable, selective and scalable oxidation of its thioether group, using water as an inexpensive and readily available oxygen source. Scalability proof-of-concept has been carried out employing a 50 mL SCER in recirculation mode (500 mL), providing valuable information regarding the industrial application of this process. Details on the reaction development and implementation of the flow devices, which provided the target compound in 1.8 g/h, will be shown.

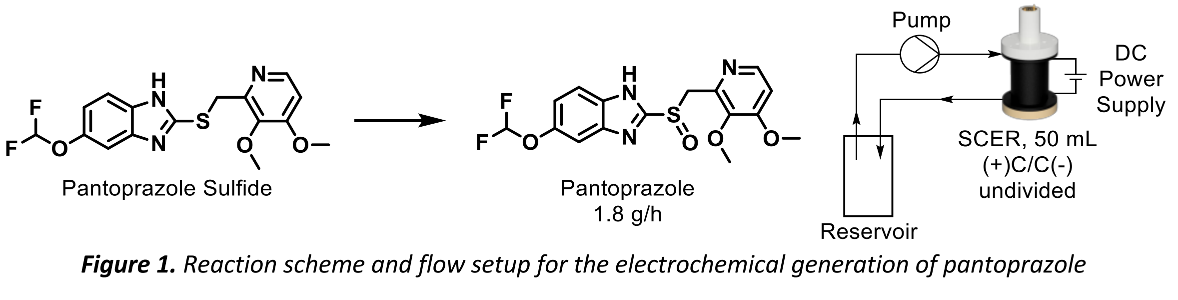

Figure 1. *Reaction scheme and flow setup for the electrochemical generation of pantoprazole*

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Lignin and its derivatives as bio-based alternatives for the plastics industry

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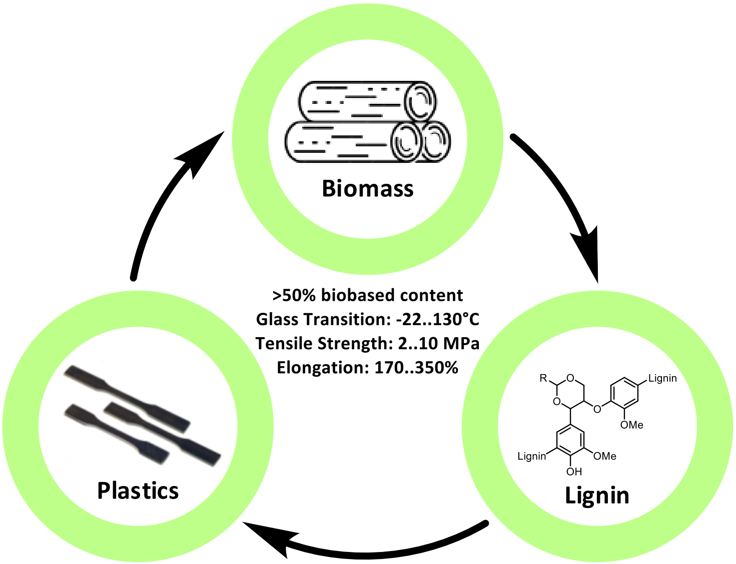

The chemical and plastics industries currently heavily rely on petroleum. 14% of every oil barrel are used to produce chemicals, of which a large fraction flows into the plastics industry. In light of legislation and sustainability targets of companies, sustainable alternatives and solutions are needed before 2030. Lignin and its derivatives (oligomers and various monomers) are valuable sustainable alternatives to replace fossil-based additives, fillers and reagents.[1,2]

Recently a group from EPFL in collaboration with Bloom Biorenewables showed that lignin can be used as a hardener, UV barrier and antioxidant to obtain high-lignin-content thermoset films and coatings with a bio-based content over 50%.[3] Here we report the screening of different epoxy resins, catalysts, chain-extenders and aldehyde-stabilized lignin to produce various elastomers showing a wide range of thermal and mechanical properties. These promising results demonstrate the use of lignin as an ingredient to suit sustainable and scalable applications.

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