HRSMC Organic Synthesis Summer School



July 7-10, 2025

Hotel Willibrordhaeghe, Deurne

The Netherlands

PROGRAMME AND ABSTRACT BOOK

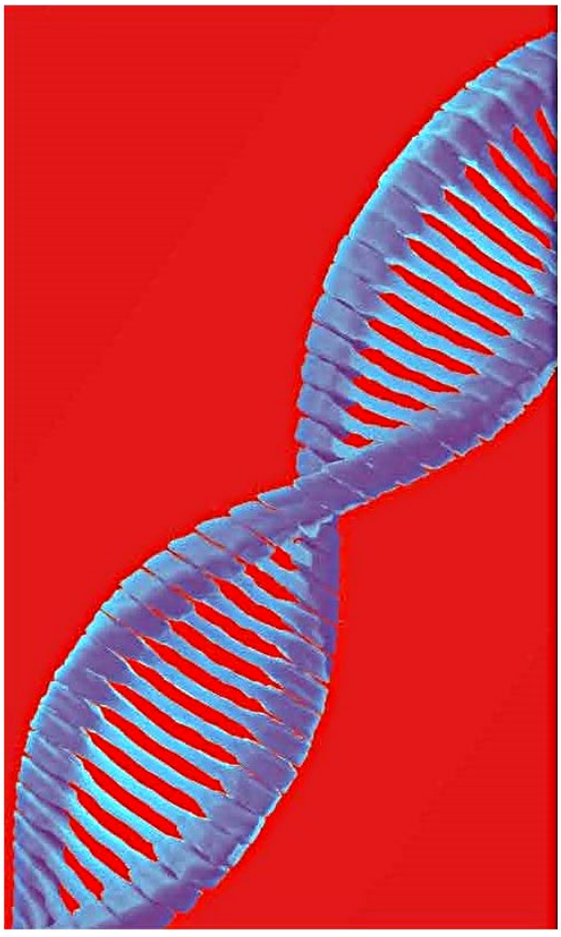
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Welcome

On behalf of the Organising Committee and the Holland Research School of Molecular Chemistry (HRSMC), it is my great pleasure to welcome you to Kloosterhotel Willibordhaeghe for the seventh HRSMC Organic Synthesis Summer School. Since 2001, this event has played a key role in postgraduate training in synthetic organic chemistry in the HRSMC.

The programme features six three-hour lectures by renowned scientists in synthetic organic chemistry and related fields, including a one-hour interactive session with each lecturer. The programme is complemented by two evening lectures by industrial scientists, as well as a poster competition. The aim of the School is to inspire young chemists to address synthetic challenges from diverse perspectives in order to advance science and technology.

The combination of the excellent scientific programme and the stimulating surroundings of Fletcher Kloosterhotel Willibrordhaeghe set the stage for an atmosphere of active knowledge exchange and scientific as well as social interaction. I hope that the School will not only bring you lots of new chemical knowledge, but also many new contacts and new perspectives on scientific problems.

I wish you all a week full of inspiring science and productive interaction here at Fletcher Kloosterhotel Willibrordhaeghe.

On behalf of the organising committee,

Prof. dr. E. Ruijter
Chair, Organising Committee 2025

Organising Committee 2025
Prof. dr. E. Ruijter (VU Amsterdam)
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Programme

Monday July 7

11:30 Registration Summer School & Welcome Coffee/Tea
Luggage drop-off at registration and hang poster

12:30 Lunch

13:25 Opening by Eelco Ruijter
Chair Eelco Ruijter

13:30 José Luis Mascareñas
From flasks to living systems: A Journey Through Transition Metal Catalysis (*Part 1*)

14:30 Coffee/Tea

14:45 José Luis Mascareñas
From flasks to living systems: A Journey Through Transition Metal Catalysis (*Part 2*)

15:45 Coffee/Tea
Check in to hotel rooms

16:15 José Luis Mascareñas (*interactive session*)

17:15 Welcome drinks & Poster session 1

18:45 Dinner
Chair Eelco Ruijter

20:30 Peter Buijnsters (J&J Innovative Medicine)

Tuesday July 8

07:30 Breakfast
Chair Tati Fernández Ibáñez

09:00 Bill Morandi
New Concepts for Atom and Functional Group Transfer (Part 1)

10:00 Coffee/Tea

10:15 Bill Morandi
New Concepts for Atom and Functional Group Transfer (Part 2)

11:15 Ehider Polanco (Account Manager R&D, Busch Group)

11:20 Coffee/Tea

11:30 Bill Morandi (*interactive session*)

12:30 Group picture and lunch

13:30 Social Event (different location)

18:00 BBQ Dinner (different location)

Wednesday July 9

07:30 Breakfast

Chair Eelco Ruijter

09:00 Armido Studer
Pyridine C–H Functionalization and Radical Hydrogen Atom Transfer to π-Systems (Part 1)

10:00 Coffee/Tea

10:15 Armido Studer
Pyridine C–H Functionalization and Radical Hydrogen Atom Transfer to π-Systems (Part 2)

11:15 Coffee/Tea

11:30 Armido Studer (*interactive session*)

12:30 Lunch

Chair Tati Fernández Ibáñez

13:30 Cristina Nevado
Radical approaches in catalysis (Part 1)

14:30 Coffee/Tea

14:45 Cristina Nevado
Radical approaches in catalysis (Part 2)

15:45 Coffee/Tea

16:00 Cristina Nevado (*interactive session*)

17:00 Drinks & Poster session 2

Removal of posters at the end of the session

18:30 Dinner

Chair Jan van Maarseveen

20:30 Tjeerd Barf (Artica Therapeutics & Covalution BioSciences)

Thursday July 10

07:30 Breakfast

Check out of hotel rooms by 10:00 AM. Please hand in the key at the HRSMC

Chair Jan van Maarseveen

08:30 Corinna Schindler
Azetidines, Azetines, and Oxetanes: New Cycloadditions of Imines and Carbonyls (Part 1)

09:30 Coffee/Tea

09:45 Corinna Schindler
Azetidines, Azetines, and Oxetanes: New Cycloadditions of Imines and Carbonyls (Part 2)

10:45 Coffee/Tea

11:00 Corinna Schindler (*interactive session*)

12:00 Lunch

Chair Jan van Maarseveen

13:30 Siegfried Waldvogel
Electrifying Organic Synthesis (Part 1)

14:30 Coffee/Tea

14:45 Siegfried Waldvogel
Electrifying Organic Synthesis (Part 2)

15:45 Coffee/Tea

16:00 Siegfried Waldvogel (*interactive session*)

17.00 Poster Awards & Closure

17:30 Departure

CV's and abstracts of invited lectures (in alphabetical order)

Dr. Tjeerd Barf

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Summary

Tjeerd is co-founder and CEO of Artica Therapeutics. He has extensive experience in pharmaceutical Research and Development and contributed to the delivery of several clinical candidates in the metabolic disease, autoimmune and oncology space. He successfully exploited the covalent binding paradigm for kinases and other protein families, resulting for instance in the discovery and approval of covalent BTK inhibitor Calquence.

Since Tjeerd joined the pharmaceutical industry early 1997, he served in various project and line management roles at Pharmacia & Upjohn, Biovitrum, Organon, Schering-Plough and MSD. Tjeerd co-founded Acerta Pharma and served as the EVP of Chemistry since its inception in 2013. Tjeerd has been a member of the Board of Directors or Scientific Advisory Board for several oncology startup companies, including Cytura Therapeutics, PearlBio and Acerta Pharma.

Tjeerd holds a PhD in Medicinal Chemistry and MSc in Organic Chemistry from the University of Groningen, The Netherlands.

Covalent Drug Journeys

Tjeerd Barf[1]

[1]*Artica Therapeutics B.V., Leiden, The Netherlands*

Covalent drug have served patients for more than a century. While initially discovered by serendipity, more recently researchers and pharma companies go after these drugs deliberately. Covalent drugs, which form a bond with their target protein, offer several advantages over non-covalent drugs. These include enhanced potency, prolonged duration of action, and the ability to target previously undruggable proteins. They can also be less sensitive to pharmacokinetic parameters and may reduce the risk of drug resistance. While non-covalent inhibitors associate and dissociate freely from proteins, covalent inhibitors form strong, lasting bonds with their targets. This means they can effectively shut down the target protein's activity for an extended period, leading to more sustained therapeutic effects. Covalent drugs can also bind to unintended proteins, leading to off-target effects and potential toxicity. And paradoxically, covalent drugs may be subject to increased risk of drug resistance.

Every quest for a covalent drug is different, and I will share some of my personal experiences from a medicinal chemistry and entrepreneurial perspective.

Dr. Peter Buijnsters



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Summary

Peter Buijnsters obtained his Master's degree from the University of Nijmegen in 1993. Following the completion of his military service with the Royal Netherlands Marechaussee, he furthered his academic credentials by earning a Ph.D. from the same institution in 1999. His doctoral research, conducted under the supervision of Professors R.J.M. Nolte and B. Zwanenburg, concentrated on supramolecular chemistry and synthesis, culminating in his dissertation titled "Chemical Studies on Functional Amphiphiles."

In 1999, he joined Johnson & Johnson Innovative Medicine, where he assumed the position of team leader, responsible for overseeing both early and late-stage projects within the therapeutic areas of oncology and neuroscience. Over the years, he has taken on increasingly significant responsibilities in leading internal chemistry teams and from contract research organizations (CROs), successfully managing projects that led to the identification of critical tool compounds as well as preclinical and clinical candidates in the neuroscience therapeutic domain.

Currently, Peter leads the parallel medicinal chemistry group in Beerse, Belgium. He employs artificial intelligence/machine learning (AIML)-enhanced library design, High Throughput Screening (HTE) and parallel chemistry to facilitate data-driven scientific decision-making, thereby advancing drug discovery projects.

Automated High Throughput Chemistry and Machine Learning for Synthesis at J&J

Peter Buijnsters[1]

[1]Global Discovery Chemistry, Johnson & Johnson Research and Development, Turnhoutseweg 30, 2340 Beerse, Belgium

Inventing a new drug and introducing it to the market is estimated to cost approximately 2.6 billion $ and take 10-15 years.[1] Only 10% of experimental drugs which begin clinical testing are ultimately approved for patients, and the major causes of attrition include inadequate or inaccurate target validation and clinical toxicity.[2] The high failure rate, coupled with the increased complexity of disease biology targeted by contemporary drug discovery programs, compels the development of innovations across spectrum of discovery. Substantial increases in the speed and effectiveness of design-make-test-analyse (DMTA) cycles in early drug discovery have been realized at Johnson & Johnson and across the industry.

Automation of chemical synthesis via high throughput experimentation (HTE), parallel medicinal chemistry (PMC) and high throughput purification (HTP) decreases timelines of the DMTA cycle. The increased throughput enables program acceleration since larger datasets are generated in each cycle; an added benefit is that these datasets train artificial intelligence and machine learning models, which augment medicinal chemistry designs.

This evening's lecture will cover the state-of-the-art high-throughput parallel chemistry capabilities at Johnson & Johnson. It will emphasize the importance of automated, rapid, and high-quality data generation in building models that accelerate solving synthetic challenges and maximize insights from drug discovery data. Examples will demonstrate the integration of machine learning predictions into the library design process to enhance sampling of virtual chemical space and, ultimately, accelerate programs.

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Summary

José Luis Mascareñas is full Professor in Chemistry at the University of Santiago de Compostela (USC, Galicia, Spain) since 2005, and has been the scientific director of the Center for research in biological chemistry and molecular materials (CiQUS) since February 2014 until April 2025. He completed his PhD at the University of Santiago and carried out postdoctoral studies in Stanford University (USA, 1989-1991). He has been visiting scholar in Harvard University (USA) in the summers of 1992 and 1995, and visiting scientist in the University of Cambridge (UK, 2009) and the MIT (USA, 2013). He has supervised 47 PhD theses, published over 250 articles in peer reviewed journals and wrote 23 patent applications.

Some awards and honors: Organic Chemistry award of the Spanish Royal Society of Chemistry (RSEQ, 2009), Advanced grant of the ERC (2014), Galician of the year "Grupo Correo Gallego" (2014), Gold medal of the University of Santiago (2014), Gold Medal of the Spanish Royal Society of Chemistry (2015), award of the Galicia Critic (2018), Research Medal of the Royal Galician Academy of Sciences (2019), Proof-of-Concept grant of the ERC (2020), member of the European Academy of sciences (EURASC, since 2017), founder/first president of the Spanish group of Chemical Biology of the RSEQ and, since 2021, vicepresident of the RSEQ. He has been appointed as member of the Spanish Royal Academy of Sciences in march 2025, and has been the President of the prestigious Bürgenstock conference in 2025. He has been recently awarded with a EIC transition grant for the preclinical development of a new type of anticancer agents, and received the Jaume I award for basic research in Spain in June 2025.

From flasks to living systems: A Journey Through Transition Metal Catalysis

José Luis Mascareñas[1]

[1]*Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CiQUS) and Departamento de Química Orgánica, Universidade de Santiago de Compostela, Santiago de Compostela, Spain*

Transition metal complexes have proven invaluable across a broad spectrum of scientific disciplines, including catalysis, synthesis, photophysics, and supramolecular chemistry. Their diverse coordination geometries and redox properties, combined with the ability to fine-tune these characteristics through ligand modification, offer extensive opportunities for developing novel reactivities and tailored physicochemical responses.

Building on these unique features, our research has focused on leveraging transition metal complexes in catalysis, synthesis, and chemical biology. In recent years, we have explored the feasibility of adapting organometallic catalysis to function in biological environments, including within living mammalian cells. This endeavor poses significant challenges, particularly due to the sensitivity of many metal-catalyzed reactions to air and water, as well as the stringent demands for orthogonality and biocompatibility. Nonetheless, we have successfully developed several intracellular reactions promoted by palladium, ruthenium, and gold complexes.

In this course, we will highlight our contributions to transition metal catalysis, with a particular emphasis on bond-forming reactions initiated through metal-mediated C–H activation. In the second part, we will turn our focus to recent efforts aimed at deploying these metal-based catalysts in biological systems and living organisms.

References

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Prof. dr. Bill Morandi



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Summary

Professor Bill Morandi studied at ETH Zürich (2003–2008), receiving a BSc in Biology and a MSc in Chemical Biology. From 2008 to 2012, he pursued his PhD in organic synthesis at the same institution in the labs of Professor Erick M. Carreira. Afterwards, he moved to the California Institute of Technology (Pasadena, CA) for a postdoctoral stay with Professor Robert H. Grubbs. From 2014 to 2018, he was an independent Max Planck Research Group Leader at the Max-Planck-Institut für Kohlenforschung (Mülheim, Germany), before subsequently returning to ETH Zürich as a Professor in 2018. He is currently Full Professor of Synthetic Organic Chemistry (Laboratorium für Organische Chemie) at ETH Zürich. He was the Head of the Institute of Organic Chemistry (Laboratorium für Organische Chemie) at ETH Zürich from 2022-2023.

His research program targets the design and development of new catalytic reactions for the synthesis of small molecules and materials, as well as the valorization of renewable feedstocks and waste material. He has received numerous awards, among them the Tetrahedron Young Investigator Award, a Novartis Early Career Award in Organic Chemistry, the Carl Duisberg Memorial Prize from the German Chemical Society and a selection as a C&EN's Talented 12. He is currently an Associate Editor for Organic Chemistry Frontiers, a journal from the Royal Society of Chemistry.

New Concepts for Atom and Functional Group Transfer

Bill Morandi[1]

[1]*ETH Zürich, Department of Chemistry and Applied Biosciences, Zürich, Switzerland*

In this presentation, recent developments in synthetic methodology from our group will be discussed. First, progress in the area of molecular editing, including single nitrogen atom insertions, will be presented. New developments in the area of shuttle catalysis, including applications to feedstock and waste valorization, will also be discussed. This will be complemented by a discussion on further methods recently developed in our group, as well as accompanying mechanistic studies.

Prof. dr. Cristina Nevado Blazquez

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Summary

Cristina Nevado graduated in Chemistry at the Autónoma University in 2000. In October 2004 she received her PhD from the same university working with Prof. Antonio M. Echavarren thereafter joining the group of Prof. Alois Fürstner at the Max-Planck-Institut für Kohlenforschung (Germany) as a post doctoral associate. In May 2007 she started her independent career as an Assistant Professor of Organic Chemistry at the University of Zürich. In 2012 she received an ERC Junior Investigator grant and in 2013 was awarded the Werner Prize of the Swiss Chemical Society and was directly promoted to Full Professor. In 2019, she received the Royal Society of Chemistry Award in Organometallic Chemistry and in 2020 the Excellence Research Trajectory Award of the Royal Spanish Chemical Society (RSEQ) as well as the Margaret Faul Women in Chemistry Award in 2021. Among her many contributing roles to the community, Cristina has served as Senior Associate Editor for ACS Central Science, Organic Syntheses and now Science of Synthesis. Rooted in the wide area of organic chemistry, her research program is at the interface of complex chemical synthesis, new organometallic reactions and medicinal chemistry.

Radical Approaches in Catalysis-Part I & Part II

Cristina Nevado[1]

[1]*University of Zürich / Department of Chemistry, Zürich, Switzerland*

Our group has recently explored the reactivity of C and N centered radicals, in combination with transition metals, to streamline the functionalization of π-systems.
Here, we will present our efforts to generate and harvest these valuable intermediates in synthetically relevant contexts, including recent results towards their application in asymmetric transformations.[1]

Further, examples of Nickel catalyzed dicarbofunctionalizations of alkenes and alkynes in a chemo-, regio- and stereoselective manner utilizing radicals as well as studies on the mechanistic features underlying these transformations will be presented in this lecture.[2]

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Summary

Corinna was born and raised in Schwäbisch Hall, Germany. As an undergraduate at the Technical University of Munich, she worked in the area of organometallic chemistry. Upon completion of her Diploma Thesis at the Scripps Research Institute in La Jolla in the laboratory of K.C. Nicolaou, she joined the research group of Erick M. Carreira at the ETH Zurich in Switzerland for her graduate studies. During her time in the Carreira group Corinna worked on developing novel synthetic methodologies as well as successful synthetic strategies to access Banyaside A and Microcin SF608. For her postdoctoral studies, Corinna joined the laboratory of Eric N. Jacobsen at Harvard University as a Feodor Lynen Postdoctoral Fellow to work in the field of asymmetric catalysis. In 2013, she started her independent career at the University of Michigan, Ann Arbor. She was promoted to Associate Professor in 2019 and to Professor in 2021. In 2024, she accepted a position as Canada Research Chair at the University of British Columbia in Vancouver. Her research laboratory is interested in the development of new synthetic transformations and the synthesis of biologically important complex molecules.

Azetidines, Azetines, and Oxetanes: New Cycloadditions of Imines and Carbonyls

Corinna S. Schindler[1]

[1]*University of British Columbia, BC Cancer, Vancouver, British Columbia, Canada*

Four-membered nitrogen heterocycles such as azetidines possess unique properties that make them desirable for drug discovery and synthesis applications. However, synthesis of these compounds is challenging, limiting their applicability. While oxetanes and cyclobutanes are commonly synthesized by highly atom-economical light-mediated [2+2] reactions, this powerful methodology remains limited for the synthesis of azetidines via the aza Paternò-Büchi reaction. Herein we report the development of visible-light mediated intermolecular aza Paternò-Buchi reactions, harnessing the triplet state of unique cyclic oximes, specifically 2-isoxazoline-3-carboxylates, as imine equivalents for the synthesis of unique azetidine and azetine products. Following energy transfer from an iridium photocatalyst, these cyclic oximes initiate [2+2] reactions with unactivated alkenes and alkynes, allowing access to a broad range of azetidines and azetines with excellent yield. This method is mild, operationally simple, and broadly applicable. Importantly, these products can be easily converted to free monocyclic azetidines, offering a new approach to these desirable targets.

References

[1] C.H. Ng, E.R. Wearing, D.E. Blackmun, G.G. Terrones, J. Toigo, K.-M. Tong, K.C. Harper, J.C. Donovan, M. A. Gonley, E.A. Voight, B.D. Bergstrom, M.O. Wolf, H.J. Kulik, C. S. Schindler, *J. Am. Chem. Soc.* **2025**, *accepted*.
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Catalytic Carbonyl-Olefin Metathesis and Oxygen Atom Transfer

Corinna Schindler[1]

[1]*University of Michigan, Department of Chemistry, Willard-Henry-Dow Laboratory, Ann Arbor, Michigan, USA*

The olefin-olefin metathesis reaction is a revolutionary industrial process that utilizes precious metal complexes to enable direct carbon-carbon bond formation from simple olefin starting materials. The carbonyl-olefin metathesis reaction similarly enables the construction of carbon-carbon bonds and has the potential to have an analogous impact on synthetic strategy. However, currently available synthetic procedures are significantly less advanced. My research laboratory has developed a Lewis acid-catalyzed ***carbonyl-olefin metathesis*** that represents a new reactivity mode between carbonyl and olefin functionalities. Our design principle fundamentally differs from stoichiometric carbonyl-olefin metathesis protocols proceeding via intermediate oxametallacycles. It is instead based on the *in situ* formation of oxetanes as reactive intermediates via an asynchronous, concerted [2+2]-cycloaddition of a carbonyl and an olefin upon activation with $FeCl_3$ as Lewis acid catalyst. This distinct reactive intermediate no longer limits the process to precious metals, enables catalytic turnover, and prevents the formation of stoichiometric waste. A first report of our work was published in *Nature* and we have since been able to demonstrate the generality of our approach in the synthesis of a variety of challenging structural motifs. We have since been able to develop a fourth reactivity mode between carbonyls and olefins that proceeds under Brønsted acid catalysis but also relies on oxetanes as reactive intermediates. Under protic conditions oxetanes undergo distinct fragmentation via ***oxygen-atom-transfer*** from the carbonyl to the olefin component to result in the formation of carbocation intermediates. This enables a new strategy for facile carbon-carbon bond formation between two ubiquitous functional groups, carbonyls and olefins.

References

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Summary

Armido Studer received his PhD in 1995 (ETH Zürich, Dieter Seebach). He continued as a Postdoc at the University of Pittsburgh (Dennis P. Curran). In 1996 he started his independent career at the ETH. In 2000, he was appointed as Associate Professor in Marburg and in 2004 as Full Professor in Münster. His current research interests focus on the development of new synthetic methods, living radical polymerization, the preparation of functional polymers, and the development of methods for the chemical modification of surfaces.

Pyridine C–H Functionalization and Radical Hydrogen Atom Transfer to π-Systems

Armido Studer[1]

[1]*Institute of Organic Chemistry, University of Münster, Münster, Germany*

Pyridines belong to the most abundant heteroarenes in medicinal chemistry and in agrochemical industry. In the lecture, highly regioselective pyridine C–H functionalization through a dearomatization/rearomatization sequence will be discussed. The dearomatized oxazino pyridines can be easily prepared on a large scale, and meta-functionalization becomes achievable through light-initiated radical alkylation and ionic transformations.[1] As example, *meta*-fluorinated pyridines are readily accessible.[2] The same intermediates upon protonation to give the corresponding pyridinium salts also allow the regioselective radical Minisci *para*-alkylation.[3,4] In addition, Cu-catalyzed *meta*-arylation[5] and switchable radical *para/meta*-difluoromethylation[6] will be presented. Radical *meta*-nitration[7] and ionic *meta*-hydroxylation[8] work equally well. Finally, it will be shown that this dearomatization concept is also applicable to pyridine skeletal editing.[9]

In the second part of the lecture, we demonstrate a water activation strategy enabled by a photocatalytic phosphine-mediated radical process under mild conditions, generating a metal-free PR_3-H_2O radical cation intermediate, where both hydrogen atoms are used in the following chemical transformation through sequential heterolytic (H+) and homolytic (H•) cleavage of the two O-H bonds.[10] We will show how such phosphoranyl radicals can be turned into ground state super electron donors.[11] Moreover, phosphine radical cations can also be used for activation of nitroarenes under very mild condition[12] and it will be discussed that nitroarenes are highly efficient radical oxygenation reagents for Fe-catalyzed alkene hydrations.[13] Building on this finding a new type of radical amidation reagent is introduced and first applications for the hydroamidation of complex alkenes will be demonstrated.[14] Along these lines, Fe-catalyzed radical hydrohalogenations of alkenes are also discussed.[15]

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Summary

Since 2023- Director at the MPI for Chemical Energy Conversion, Germany

Since 2023- Speaker of Cluster4Future ETOS – Electrifying Technical Organic Synthesis

2010- Full professor at Johannes Gutenberg University Mainz, Germany

2004- Associate professor at Bonn University, Germany

1998- Assistant professor at Münster University, Germany

1997- Post-doctoral fellow at The Scripps Research Institute La Jolla, CA, USA

1996- PhD at the MPI for Coal Research, Mülheim, Germany

Research field

His research interests are novel electro-organic transformations including bio-based feedstock and the upcycling of pollutants to value added chemicals. The research covers all aspects ranging from screening of electrosynthetic methods, automated optimization and scale-up to technical electrolyses. In 2018, he co-founded ESy-Labs GmbH, which provides custom electrosynthesis and contract R&D.

Electrifying Organic Synthesis

Siegfried R. Waldvogel[1]

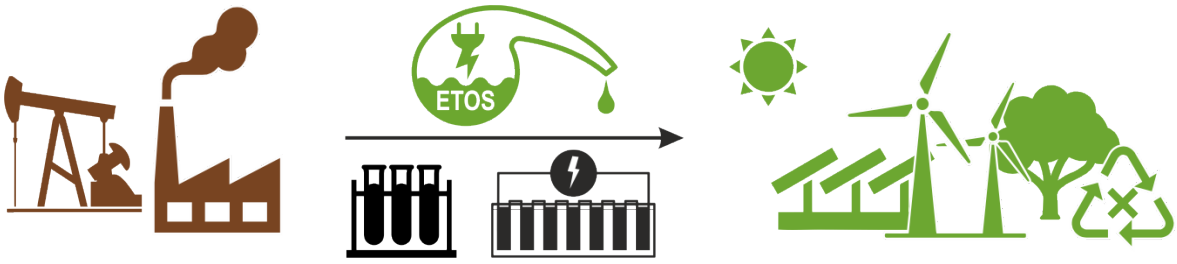
[1]Max-Planck-Institute for Chemical Energy Conversion, Department of Electrosynthesis, Mülheim an der Ruhr, Germany

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. The contribution consists of two parts. First, a tutorial part to circumvent the obstacle of electrosynthesis and get started. Secondly, some cutting-edge examples will be presented underlining the power of this method. 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. The electrosynthesis will change the chemical industry and makes it greener, sustainable and opens up the way to circular economies by electrochemically driven recycling and upcycling.



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Overview poster sessions

Session 1: Monday, July 7th, 17:15–18:45

Poster No.	Presenter Name
1	Theodora Athanasiadou
3	Kathleen Cheasty
5	Jonas Djossou
7	Helena Ehren
9	Jay Hanssens
11	Cassandra Henderson
13	Diego Meneses Sánchez
15	Aryaman Pattanaik
17	Soma Rudi
19	Sebastian Strähler
21	Arezoo Tanbakoochian
23	Stefano Di Ciolo

Session 2: Wednesday, July 9th, 17:00–18:30

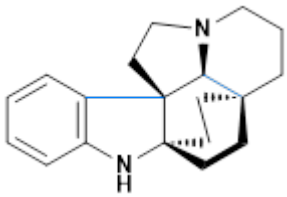
Poster No.	Presenter Name
2	Kamilé Butkuté
4	Frank de Kleijne
6	Zezhong Dong
8	Ekaterina Frantsuzova
10	Jaap Harteveld
12	Brendan Horst
14	Vasilis Papadopoulos
16	Thomas Reszka
18	Sunaina Sardana
20	Luuk Stringer
22	Minghui Wu

Abstracts of Posters

Palladium catalyzed cascade cyclization towards the enantioselective total synthesis of (+)-Aspidofractinine

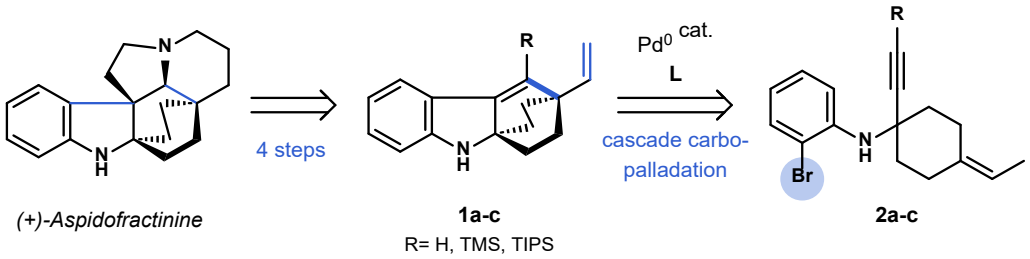
Theodora Athanasiadou[1], Cristiano Cassinera[1], Eelco Ruijter[1]

[1]*Department of Chemistry & Pharmaceutical Sciences, Amsterdam Institute for Molecular and Life Sciences, Vrije Universiteit Amsterdam, The Netherlands*



The monoterpene indole alkaloid (+)-Aspidofractinine was first isolated in 1964 from the leaves of Pleiocarpa tubicina of the family of Apocynacae by Schmid and coworkers[1]. Many monoterpene indole alkaloids have proven to be an important source of drugs in the modern medicine, such as treatment of cardiovascular diseases, malaria, diabetes, fever and rheumatism[2]. (+)-Aspidofractinine bears a bicyclo[2.2.2]octane motif with three all-carbon quaternary stereogenic centers that has proved a challenging synthetic puzzle.

In this poster, we present our synthetic plan towards the enantioselective total synthesis of this hexacyclic indole alkaloid through a carbopalladation of an alkyne followed by a cascade cyclization. The advantages of this plan include that enantioselectivity can be implemented in the later stages of the synthesis providing possibly higher enantioselective ratio and diversification towards different scaffolds. For our retrosynthesis plan, we envisioned an efficient asymmetric total synthesis of (+)-Aspidofractinine from an achiral late-stage intermediate(**1**) which in turn can result from a cascade cyclization of a simple precursor(**2**) (*Scheme 1*).



Scheme 1: Retrosynthetic plan of (+)-Aspidofractinine from simple precursors **2**

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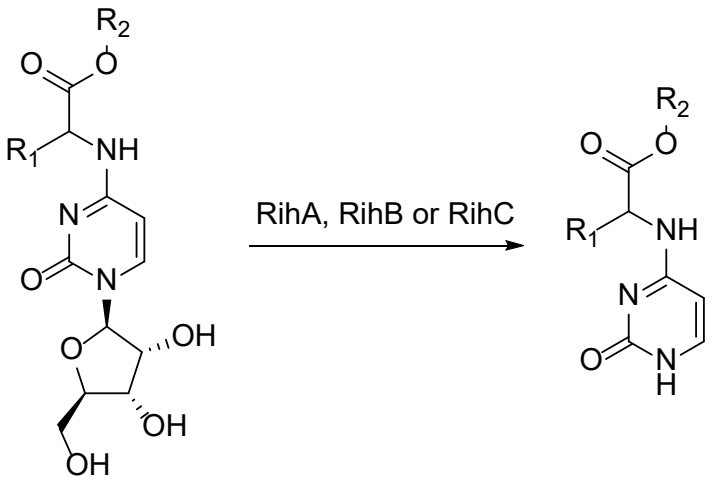
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Rih-type *N*-glucosidases for the synthesis of N^4-amino acid esters substituted cytosines

Kamilė Butkutė[1], Rasa Rutkienė[1], Rolandas Meškys[1]

[1]*Department of Molecular Microbiology and Biotechnology, Institute of Biochemistry, Life Sciences Center, Vilnius University, Vilnius, Lithuania*

Pyrimidinyl amino acids are naturally occurring compounds, that function as antibiotics and serve as intermediates in the biosynthesis. They may also exhibit potential therapeutical activity as antiviral and anticancer agents. *N*-(4-pyrimidinyl) amino acids are synthesized through reaction of 4-methylthio-2-pyrimidinone with the corresponding amino acid [1]. However, this method requires basic pH for catalysis and is unsuitable for amino acid esters, as they undergo hydrolysis under these conditions [2]. In this study, we developed a novel procedure for synthesis of *N*-(4-pyrimidinyl) amino acid esters through reaction of 1,2,4-triazole activated 2',3',5'-tri-*O*-acetyl-uridine and the corresponding amino acid ester. Actually, during the synthesis, nucleoside ribose functioned as a protecting group, which is later removed via enzymatic hydrolysis by the Rih-type *N*-glucosidases. We showed that these hydrolases efficiently convert targeted substrates to *N*-(4-pyrimidinyl) amino acid esters under mild conditions. In summary, we demonstrated the chemoenzymatic synthesis of N^4-modified cytosines. Such approach could be further extended for preparation of other pyrimidines harbouring labile groups.



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Towards a Library of Tethered Arene Ru(0) Complexes with π-Arene/σ-Phosphine Coordination

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Due to their high electron density, Ru(0) complexes show notable reactivity towards C-H bonds. However, development of Ru(0) catalyzed C-H bond activation reactions relies on the development of effective strategies to stabilize the low-valent metal center. Using $[Ru(cymene)(Cl_2)]_2$ as a Ru(II) precursor, we synthesized different Ru(0) complexes using a series of phosphine ligands featuring σ-P/π-arene coordination. Based on their reactivity towards different substrates, novel reactions to forge fine chemicals are being developed. Due to the stabilizing effect of the σ-P/π-arene coordination mode of the phosphorus arene ligand, these ligands show high thermal stability and a lack of intramolecular C-H activation.

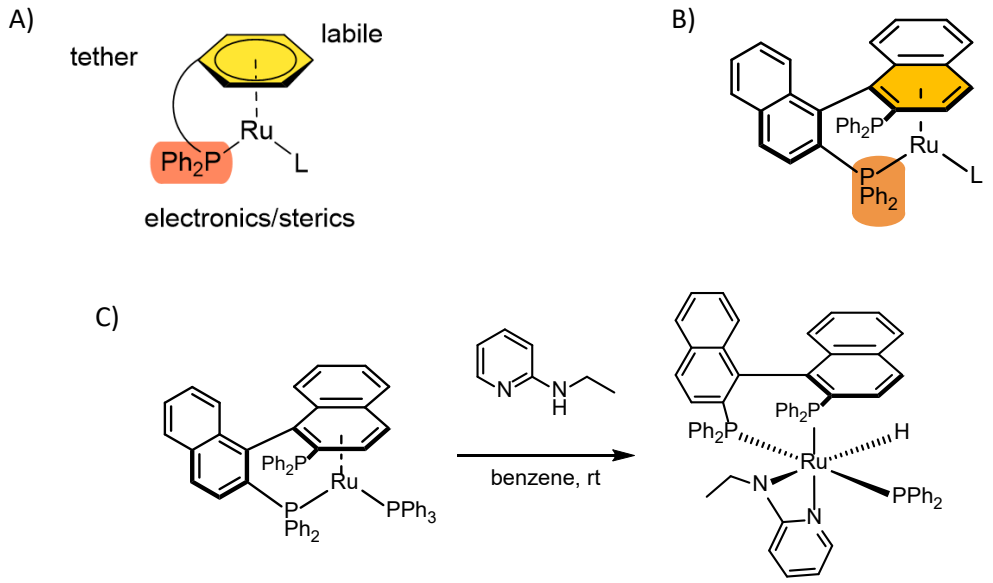


Fig 1: A) general structure of Ru(0) complexes that can be varied in I) the electronics and sterics of the phosphine, II) the flexibility of the tether and III) the π-coordinated arene to result in a different sliding effect. B) Structure of Ru(0)BINAP complex, featuring various counter ligands. C) example reaction that Ru(0)BINAP(PPh_3) undergoes.

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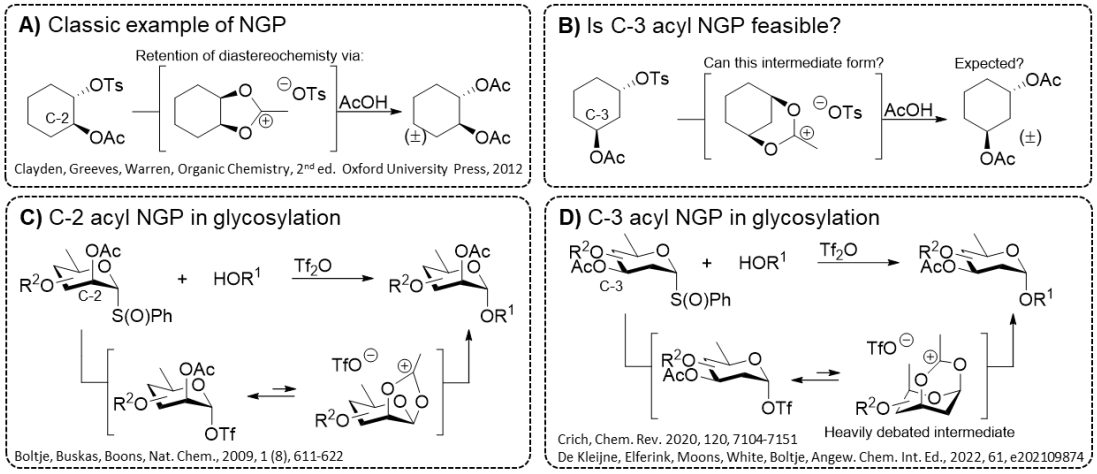
Anchimeric assistance of 'remote' acyl neighboring groups as stereodirecting strategy in synthesis: What can we learn from glycoscience?

Frank F. J. de Kleijne[1], Thomas J. Boltje[1]

[1]*Institute for molecules and materials, Radboud University Nijmegen, The Netherlands*

Neighboring group participation (NGP) is a well-known concept in organic synthesis to modulate the reactivity of a molecule.[1] A famous example of a molecule that experiences high reactivity due to NGP is mustard gas. Another example of NGP is acyl participation (Figure panel A). This type of NGP is useful for stereoselective synthesis. Typically, acyl NGP implies having a 1,2-relationship from participating to electrophilic side leading to transient five membered ring intermediates. In this work we ask ourselves the question: would participation from more remote positions such as in a 1,3-relationship be feasible to afford six membered ring intermediates (Figure panel B)?

To answer this questions we turn our attention to glycoscience where C-2 acyl participation is commonly employed to prepare 1,2-*trans* glycosidic linkages (Figure panel C).[2] For decades participation of acyl groups at C-3, C-4, and C-6 has been proposed but its existence remained heavily debated (Figure panel D).[3] Only recently has direct experimental evidence become available for this phenomenon.[4,5] Herein we present our findings and report factors that enable 'remote' acyl NGP in order to predict if 'remote' acyl NGP would be feasible beyond the realm of glycoscience.



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Rapid Methylation of Aryl Bromides Using Air-Stable DABCO-Bis(Trimethylaluminum) via Nickel Metallaphotoredox Catalysis

Jonas Djossou[1], Andrea Aloia[1,2], Luca Capaldo[3], Demi D. Snabilié[4], Morgan Regnier[1], Jasper H.A. Schuurmans[1], Antonio Monopoli[2], Bas de Bruin[4], Timothy Noël*[1]

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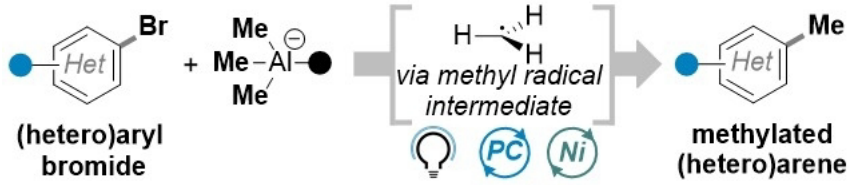
[2]Chemistry Department, University of Bari Aldo Moro, Bari, Italy

SynCat Lab, Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy

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We report a metallaphotocatalytic strategy for the selective methylation of (hetero)aryl bromides via nickel-catalyzed cross-coupling with bis(trimethylaluminum)-1,4-diazabicyclo[2.2.2]octane (DABAl-Me_3), as a commercially available, air-stable, and non-pyrophoric aluminum-based reagent. The method enables a fast, robust, and scalable methylation protocol that broadly accommodates various functional groups while preventing protodehalogenation. Mechanistic studies confirm the unprecedented generation of methyl radicals from an organo-aluminum precursor under photoredox conditions, bypassing the limitations of conventional two-electron pathways. This work expands the toolbox of practical radical precursors and provides a streamlined approach for selective C(sp^2)–CH_3 bond formation.

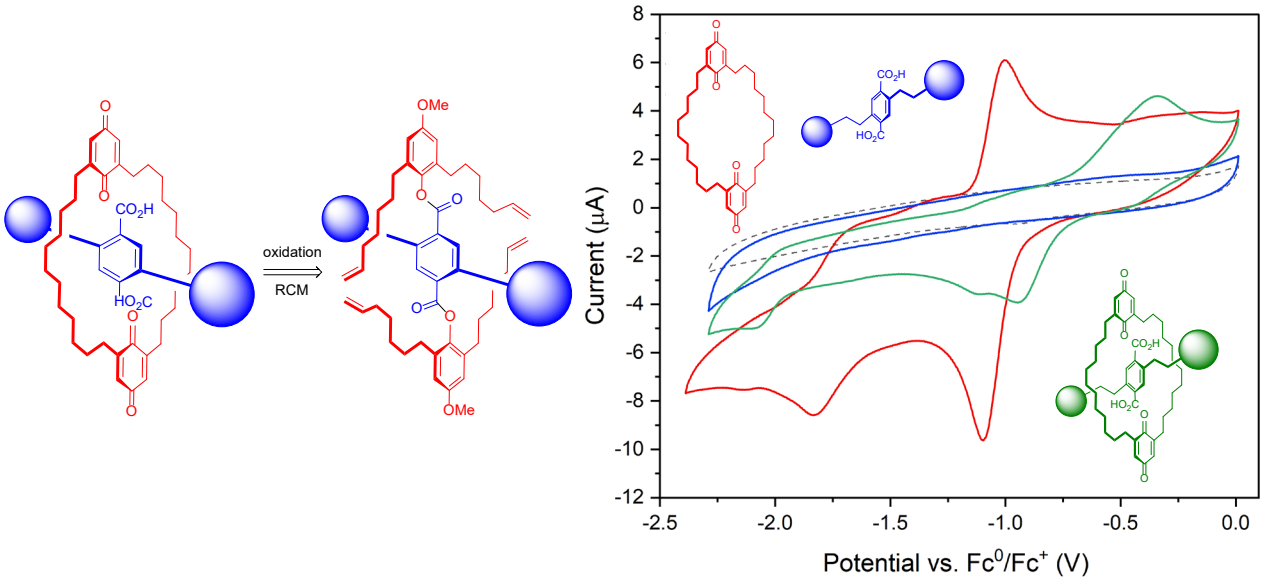


Covalent synthesis and electrochemical characterization of rotaxanes featuring threaded macrocyclic quinones

Zezhong Dong[1], Milo D. Cornelissen[1], Joost J. N. Koning[1], Nick Westerveld[1], Simon Mathew[1], Maartje C. van Rijn[1], Sonja Pullen[1], Jan H. van Maarseveen[1]

[1]*Van 't Hoff Institute for Molecular Sciences, University of Amsterdam, Amsterdam, The Netherlands*

The rotaxane motif has progressed from a structural curiosity to demonstration as an electrochemically-active functional component within molecular motors, switches and redox mediators [1]. Nature employs electrochemically-active p-benzoquinones as redox mediators *pur sang* [2]. Herein, we disclose the synthesis of rotaxanes employing benzoquinone motifs integrated within the macrocycle moiety. The rotaxane–quinones were accessed via prerotaxanes, featuring covalent connection via ester bonds between the 4-methoxyphenol moiety of the macrocycle and the terephthalic carboxylic acid functionality of the thread fragment. Target rotaxanes were liberated oxidatively from these prerotaxanes with concomitant quinone formation. Synthetic refinement to a two-step approach was developed, starting with ester cleavage via amidation after which the liberated 4-methoxyphenols were oxidized to p-benzoquinones. The resulting rotaxane–quinones and hydroquinones demonstrated redox cyclability. Finally, robust all-C alkyl-backbone macrocycle and thread analogs were synthesized, with their cyclic voltammetry demonstrating potential as redox mediators in future devices.



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Electroorganic synthesis of canonical and non-canonical amino acids

Helena Leona Ehren[1], Tati Fernàndez-Ibàñez[1], Amanda Garcia[1]

[1]*Van 't Hoff Institute for Molecular Sciences, University of Amsterdam, Amsterdam, The Netherlands*

Amino acids are essential building blocks of life and as such involved in critical physiological functions and widely used in pharmaceuticals [1–3], nutrition, and biotechnology [4–6]. Current production methods, such as fermentation, protein hydrolysis, and chemical synthesis, are limited by high energy demands, hazardous reagents, low selectivity, and scalability issues. [7-9] This project explores an electrocatalytic strategy for the sustainable, enantioselective synthesis of canonical and non-canonical amino acids from inexpensive starting materials. The approach involves electrochemical oxidation of glycine followed by a *Petasis* reaction to introduce diverse side chains. Optimization will focus on yield, catalyst efficiency, and selectivity, offering a scalable and eco-friendly alternative to conventional methods.

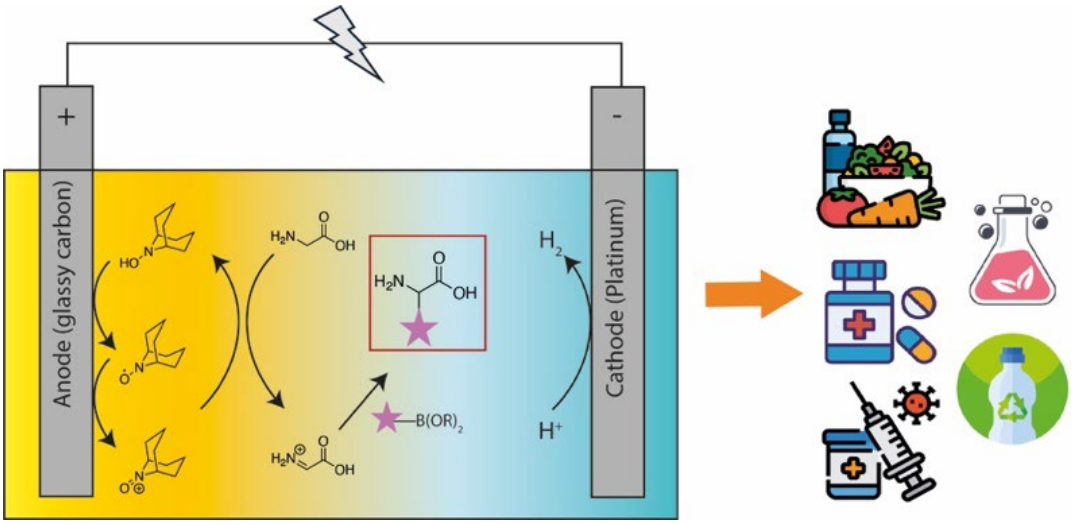


Figure 1. Working hypothesis for the electrocatalytic production of amino acids as important building blocks for food production, drug and vaccine development, fine chemicals and recyclable packaging.

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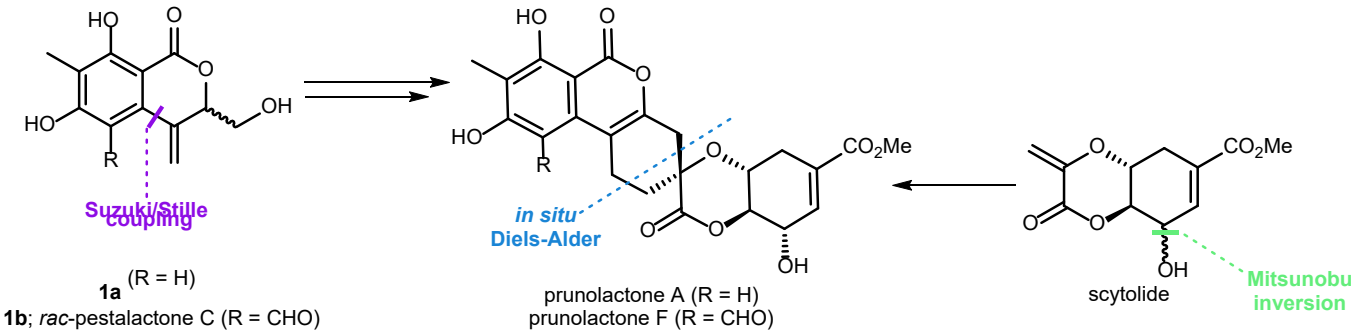
Proangiogenic Agents Unveiled: Synthetic Pathways and Challenges in Prunolactone Chemistry

Ekaterina Frantsuzova [1], Michal Kadaník [1], Milan Pour [1]

[1]*Department of Organic and Bioorganic Chemistry, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic*

Over the past decade, *Phomopsis* fungi have produced over 250 bioactive compounds, several of which show interesting drug development potential. Among these, prunolactones A–G, isolated in 2023 from *Phomopsis prunorum*, stand out due to their rare 6/6/6/6/6 spiropentacyclic skeleton and notable proangiogenic activity[1]. Their biosynthesis is proposed to proceed *via* a Diels-Alder reaction between scytolide (Scheme 1), derived from the shikimate pathway, and a 3,4-bis(methylene)isocoumarin diene, generated by the dehydration of isocoumarin **1** (R = H or CHO)[1].

This work is focused on the preparation of prunolactone F. The naturally occurring isocoumarin, rac-pestalactone C (**1b**), is employed as a key starting material, synthesized *via* multiple routes, including green chemistry methodologies[2]. Finally, the total synthesis of the novel proangiogenic agent is accomplished in a concise 10-step sequence from (–)-shikimic acid, including a pivotal biomimetic Diels-Alder cycloaddition, which underscores the efficiency and elegance of the approach.



Scheme 1

This work was supported by Charles University (SVV reg. No. 260 661 and GAUK No. 443925).

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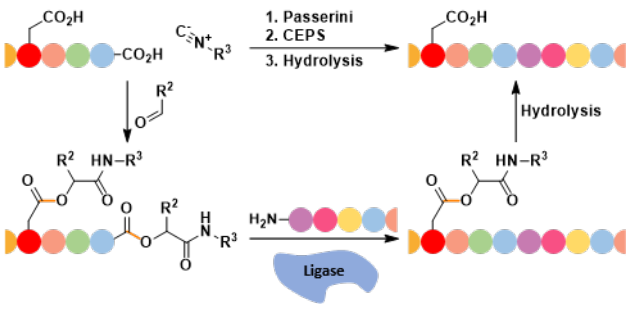
C-Terminal Peptide Modification: Merging the Passerini Reaction with Chemo-Enzymatic Synthesis

Jay Hanssens[1], Sam van Dun[2], Tessa H.G. Lokate[1], Vincent Reinartz[1], Leendert J. van den Bos[2], Romano V.A. Orru[1], Jordy M. Saya*[1]

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Investigating protein materials is key to overcoming sustainability issues from fossil fuel-derived polymers. Natural biopolymers present an eco-friendly alternative, offering performance that is comparable to or even exceeds that of their synthetic counterparts, along with the benefit of non-harmful degradation products. However, the study of protein materials necessitates synthetic access to large quantities of high-purity proteins, a task that remains challenging despite years of research. While synthetic biology offers a route to protein production, chemical synthesis provides a unique advantage by enabling the incorporation of non-natural amino acids. This significantly enhances the diversity of protein structures and functionalities accessible for study. However, traditional methods like Solid Phase Peptide Synthesis (SPPS) are restricted to creating relatively short peptide chains, up to about 60 amino acids in length. In our research, we developed a novel ligation approach that combines the Passerini multicomponent reaction and chemo-enzymatic peptide synthesis (CEPS), facilitating the extension of peptide chains obtained via chemical synthesis.1,2 The Passerini reaction utilizes aqueous acidic buffer conditions to establish chemoselectivity for the carboxylic acids, while the subsequent enzymatic ligation selectively targets the formed C-terminal substrates. We functionalized a diverse set of pentapeptides utilizing numerous isocyanide and carbonyl compounds and successfully performed subsequent ligations. This combined multicomponent chemoenzymatic method therefore represents a valuable novel technology for future research requiring site-selective C-terminal modification of peptides/proteins. We intend to apply this fundamental methodology to the synthesis of peptide and protein materials, providing a more versatile and sustainable approach to protein production.



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Toward a total synthesis of (+)-perophoramidine through a carbopalladation approach

Jaap Harteveld[1], Rutger de Haas[1], Eelco Ruijter[1]

[1]*Amsterdam Institute of Molecular and Life Sciences, VU Amsterdam, Amsterdam, The Netherlands*

Perophoramidine is a complex polycyclic alkaloid isolated from the marine ascidian *Perophora namei* showing promising anticancer activity. These medicinal properties, together with its two vicinal quaternary spiro stereocenters, make it a popular target for total synthesis.

Here, we report a novel synthetic strategy toward the regio- and stereoselective construction of (+)-(dehalo)perophoramidine through an asymmetric carbopalladation approach. In the key step, we envision a Heck – Suzuki coupling cascade to construct the two required vicinal quaternary stereocenters of (+)- (dehalo)perophoramidine. We report our progress in synthesizing suitable substrates and investigating conditions for the envisioned cascade cyclization.

In-Flow Strategy to Safely Generate and Employ Reactive Formyl Fluoride Gas

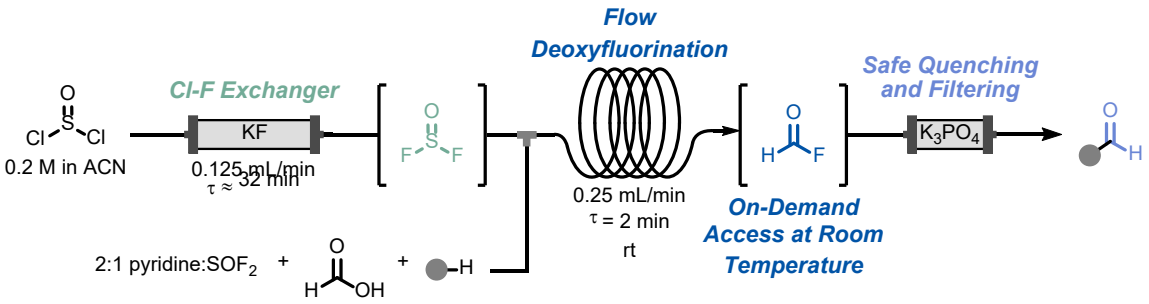
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A new method has been used to generate and utilize reactive formyl fluoride gas at room temperature by using a flow setup. The design comprises first the in-flow generation of thionyl fluoride as per our previously reported methodology[1] using a packed-bed reactor containing fluoride salt, then subsequent reaction with formic acid and pyridine to give a stable, dosable acetonitrile solution of formyl fluoride for synthetic purposes. The presence of formyl fluoride was verified using in-flow NMR analysis, and its utility demonstrated by performing a series of N-, O-, and S-formylation reactions. This flow setup allows for safe, on-demand access to a largely unexplored reactive C1 building block using inexpensive equipment.



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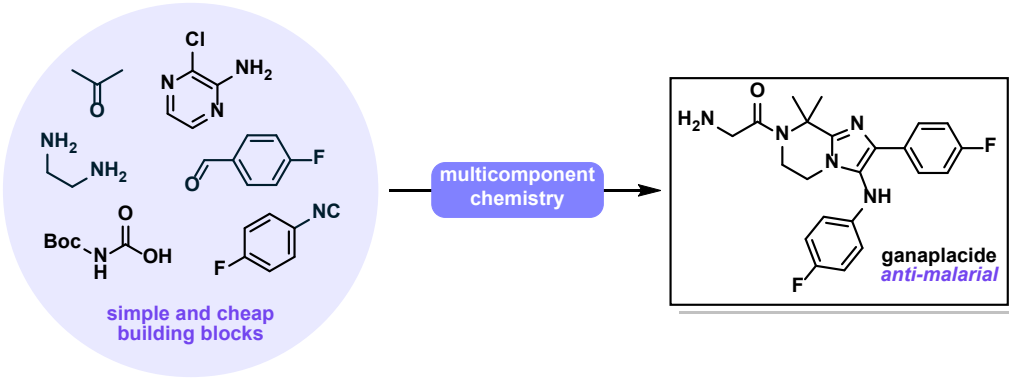
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New Synthetic Approaches towards the Anti-Malarial Drug Ganaplacide

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Malaria is a neglected tropical disease that cause about 600 000 deaths each year, mainly on the African continent.[1] As the effective treatment of malaria has stagnated in the past years due to drug resistance, the discovery of new drugs has high urgency. Developed by Novartis, KAF156 (also known as *ganaplacide*) is a new type of anti-malarial of the imidazolepiperazine class that successfully completed phase II clinical trials recently.[2]



The current route to ganaplacide counts 9 linear steps and it is our goal to scout new short and efficient routes towards this drug. We show that the imidazolopiperazine core of ganaplacide can be formed very quickly and efficiently using multicomponent chemistry.[3] This process uses only simple and cheap building blocks and produces minimal waste. We are exploring various routes involving multicomponent chemistry and we currently are working on the final steps to obtain the desired product.

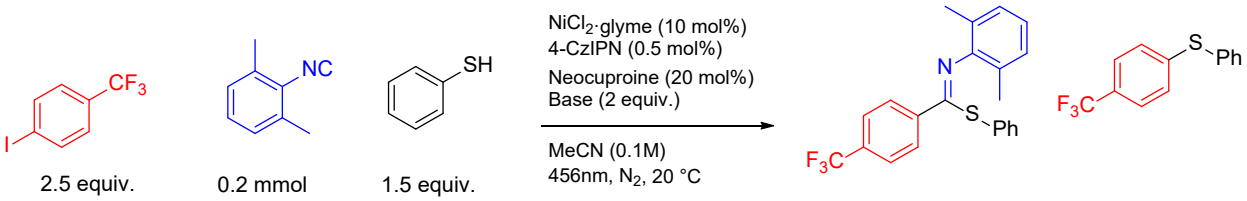
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Isocyanide Insertion via Dual Nickel and Photoredox Catalysis: A Platform for Multicomponent Synthesis

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Isocyanides are versatile C1 building blocks due to their ability to react with nucleophiles, electrophiles, and radicals. They are valuable inputs for multicomponent reactions (MCRs) and one-pot cascade processes. In organometallic chemistry, isocyanides often act as ligands for transition metals, altering the electronic distribution of the isocyano moiety and enabling unique reaction pathways. Palladium-catalyzed isocyanide insertion processes have gained prominence in recent years, but the use of earth-abundant and inexpensive base metals in these reactions is underexplored.[1] On the other hand, cross-coupling reactions are essential in organic synthesis, but diverse reaction conditions often require individual optimization. In this context, we want to merge homogeneous catalysis with nickel, under visible-light-driven redox conditions, to address this challenge.[2]



2.5 equiv. 0.2 mmol 1.5 equiv.

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Utilizing hardwood residues and polycotton textile waste as feedstocks towards furan-2,5-dicarboxylic acid (FDCA)

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In the pursuit of sustainable materials, transitioning from poly(ethylene terephthalate) (PET) to bio-based poly(ethylene furanoate) (PEF) is gaining momentum, with contributions from Avantium and the Industrial Sustainable Chemistry group at the UvA. Furan-2,5-dicarboxylic acid (FDCA) is the key monomer of PEF. Unlike the fossil-derived PET, PEF is 100% plant based and exhibits improved barrier properties.[1] Avantium is currently commissioning the world's first FDCA flagship plant, using high-fructose syrup as feedstock, which is converted into 5-(methoxymethyl)furfural (MMF) and then oxidized to FDCA. Exploring next-generation feedstocks, hardwood wood chip residues and polycotton textile waste provide promising alternatives. Using Avantium's DAWN™ and YUKON technologies, which are based on the principles developed by Bergius in the 1930's, the cellulose fraction is hydrolysed to monomeric glucose using oversaturated hydrochloric acid.[2] The resulting acid-sugar mixture contains mainly C6 carbohydrates and can be thermochemically converted to 5-(chloromethyl)furfural (CMF) in a biphasic system with an immiscible organic solvent.[3,4] This CMF can subsequently be converted to MMF or other furanic derivatives, or even oxidized directly to FDCA. The conversion of these C6 carbohydrates to CMF and its subsequent treatment will be presented.

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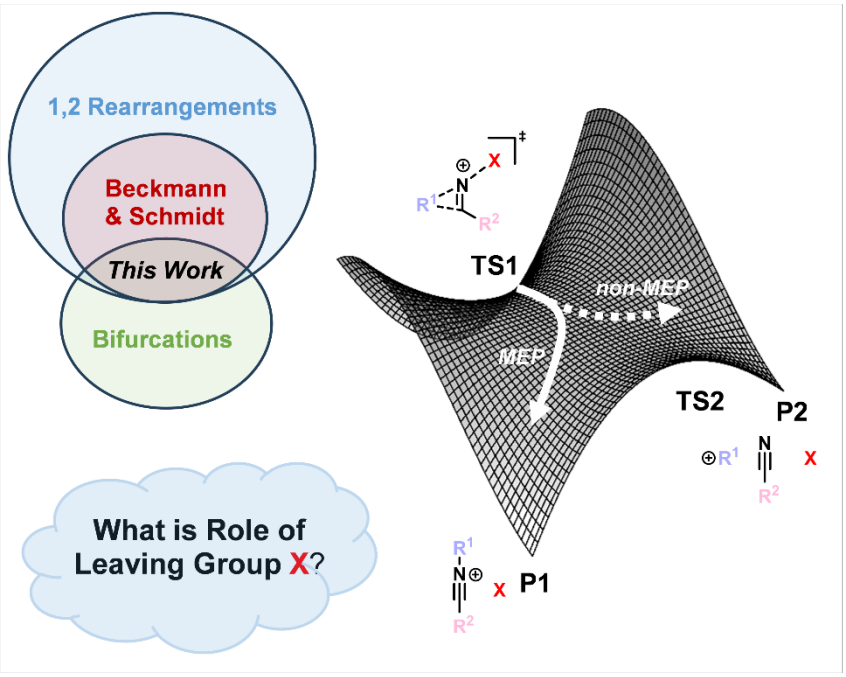
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Leaving Groups: Determinants and Not Participants in Dynamic Selectivity

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Controlling product selectivity in rearrangement reactions is particularly challenging on bifurcating potential energy surfaces, where traditional transition state models fall short.[1] While migratory aptitudes are well studied, the influence of leaving groups has remained largely overlooked. Here, we present the first detailed study on how leaving groups dynamically control product selectivity in Beckmann and Schmidt rearrangements.[2] Using a combination of stationary point analysis and quasi classical dynamics simulations, we show that leaving groups actively shape the bifurcating landscape, steering reaction trajectories toward normal or abnormal products. Experimental trends across four molecular systems confirm that selectivity is highly sensitive to the nature of the leaving group. Our findings reveal that leaving groups are not passive participants but active determinants of selectivity in dynamically complex reactions. This work introduces leaving group engineering as a powerful, underused strategy for tuning selectivity, offering new opportunities for synthetic chemists designing rearrangement pathways.



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Homogeneous Oxidative Cleaving of C—F bonds

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Perfluoroalkyl substances (PFAS) are a class of man-made molecules that are resistant to water, oil, heat, and biological degradation. These properties are useful in various applications such as fire extinguishers and waterproof clothing, but the same properties cause these compounds to accumulate in the environment, which leads to bioaccumulation and biomagnification[1].

Heterogeneous photocatalysis[2] and electrochemical oxidation[3] have been proven to efficiently break down long PFAS chains, but diminish in efficiency with shorter chains due to higher bond energies and higher solubility.

Herein we propose a system where a combination of homogeneous complexes and light irradiation break down PFAS molecules by oxidizing the polar head groups of common contaminants, as well as short chain PFAS such as trifluoracetic acid (TFA).

Through mechanistic studies we have shown that the PFAS substrate binds to the complex and can subsequently undergo Ligand to Metal Charge Transfer (LMCT) upon visible light irradiation. This LMCT breaks the C—C bond to release CO_2 and carbon centered radicals. The Kolbe-decarboxylation pathway is very favorable after the initial difficult 1-electron oxidation, where atmospheric O_2 and water are used to oxidize the perfluorinated radicals and subsequently hydrolyze the acyl fluorides all the way to CO_2 and HF.

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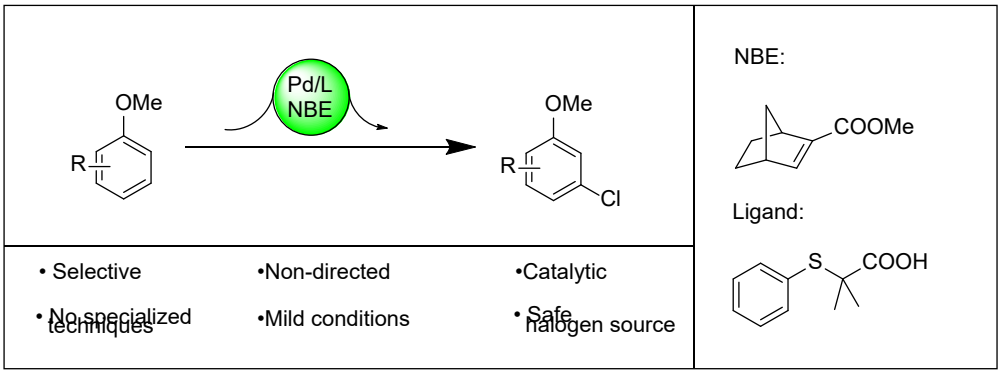
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Dark magic: meta C-H halogenation of ortho/para directed arenes via Palladium/norbornene catalysis

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The electrophilic halogenation of electron rich aryls is a staple in every organic chemists toolbox. To date a plethora of sophisticated methods has been developed for the selective halogenation of the activated *ortho* and *para* positions of electron rich aromatics; many of them operating under mild conditions, and with a high functional group tolerance. In contrast, halogenation of the electronically disfavoured *meta* position is usually achieved via synthetic workarounds, and there are only a handful of direct *meta* C-H halogenation procedures. These methods generally rely on exogenous chelating directing groups that need to be installed and later removed from the molecules turning these 'direct' methods into a multistep synthetic adventure.



This research focuses on the development of a non-directed palladium catalysed chlorination method using a norbornene mediator a safe and affordable halogen source, and mild reaction conditions. Palladium/norbornene cooperative catalysis based on the Catellani reaction has been used in a number of C-H functionalization strategies including arylations, olefinations, and various di-functionalizations. Yet, the scope of these reactions remains limited, and not all functionalities can be installed directly via *meta* C-H functionalization strategies. By halogenating the *meta* position, a wide array of further transformations can be made possible in a more step economic manner, and under conditions that are compatible with highly functionalized substrates. Lastly, chlorinated moieties are omnipresent in pharmaceuticals where a single chlorine atom can enhance the activity of the compound with up to 100 000 fold, similar to the well-known 'magic methyl' effect.

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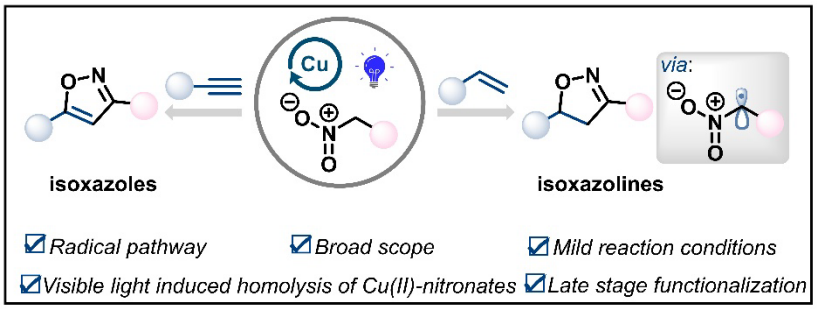
Copper(II)-Photocatalyzed Radical Anellation of Nitroalkanes with Alkenes or Alkynes for the Synthesis of Isoxazolines and Isoxazoles

Sunaina Sardana[1], Aryaman Pattanaik[1], Julia Rehbein[1], Oliver Reiser*[1]

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Isoxazolines and isoxazoles are valuable heterocyclic scaffolds with broad biological relevance, traditionally accessed via [3+2] cycloadditions of oximes and alkenes under harsh conditions.[1-3] Herein, we report a visible light-mediated, copper(II)-catalyzed one-step synthesis of isoxazolines and isoxazoles from readily available nitroalkanes, such as ethyl nitroacetate and phenyl nitromethane. Key to this transformation is the generation of α-nitro radicals[4] via photoinduced ligand-to-metal charge transfer (LMCT) homolysis of Cu(II)-coordinated nitronate complexes. These radicals undergo efficient radical addition and subsequent cyclization with a broad range of alkenes and alkynes. The method furnishes isoxazolines from alkenes and selectively yields isoxazoles in reactions with alkynes, offering a mild and operationally simple alternative to classical cycloaddition approaches.

Detailed DFT calculations revealed that the radical pathway is favoured for both styrenes and electron-deficient alkenes, such as Michael acceptors.



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Sequential Cu-Ir Catalysis For The Stereoselective Synthesis of Fused Rings and Axanes Natural Products

Sebastian Strähler[1,2], Rens Clijnk[1], Anthony Kromodimedjo[1], Olivier Riant[2], Eelco Ruijter[1]

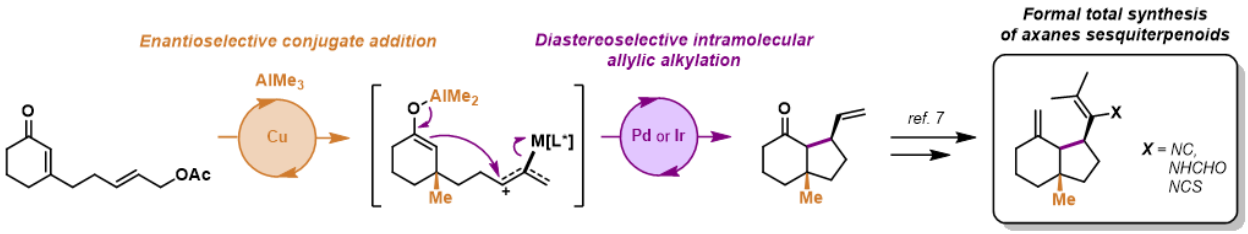
[1] *Amsterdam Institute of Molecular and Life Sciences, VU Amsterdam, Amsterdam, The Netherlands*

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One-pot sequential catalysis refers to catalytic transformations in which the catalysts for each step are added sequentially into the same reaction vessel. Each catalytic step produces an intermediate that serves as the substrate for the next one, allowing for the efficient formation of multiple bonds and stereogenic centers in one single synthetic operation, without the need for costly and tedious isolations of potentially unstable intermediates.[1,2]

Cu-catalyzed conjugate addition of nucleophiles to cyclic enones generates a metal enolate intermediate that can subsequently participate as a nucleophile in Pd-catalyzed asymmetric allylic alkylation.[3] While the amalgamation of these two independent reactions in an intermolecular fashion has already been reported, no example of an intramolecular version has yet been developed.[4–6]

Our strategy is based on the enantioselective Cu-catalyzed conjugate addition of organoaluminium reagents to cyclic enones bearing a tethered allylic group for subsequent intramolecular asymmetric Pd or Ir-catalyzed allylic alkylation. Depending on the position and the length of the tethered chain, bridged, fused, and spirocyclic scaffolds of different ring sizes can be obtained. Many of these bicyclic scaffolds being present in nature, the strategy can be applied to the synthesis of biologically active marine natural products such as axanes.[7]



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Reversible metal binding with the flick of a light switch

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The recovery of valuable metals from end-of-life electronics has garnered growing attention in recent years. Traditionally, industrial processes have relied on pyrometallurgy and hydrometallurgy.[1,2] While effective, these methods require high temperatures or strong acids, leading to significant energy consumption and large volumes of chemical waste.

Chelation extraction has emerged as a promising milder method.[3] This technique uses strong chelating agents like EDTA to extract metal ions from discarded electronic devices under mildly basic conditions, forming stable metal-EDTA complexes. To recover the metal ions from these complexes, however, strong acids are needed, generating chemical waste and decomposing part of the chelating ligand.

We hypothesized that an alternative way to recover metal ions from chelating ligands could be inducing a large configurational change in the ligand using an external stimulus such as light. We will demonstrate how incorporating a photoswitch in the backbone of the chelating ligand enables using different wavelengths of light to go back and forth between strong and weak binding modes (Figure 1). In addition to the synthesis, photoisomerization properties, and metal-binding interactions of photoswitchable chelating ligands, the potential of photoswitchable chelation extraction for recovery of metals from e-waste will discussed.

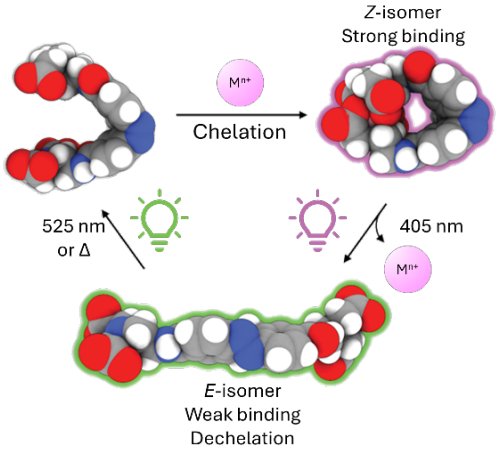


Figure 1: Schematic depiction of a photoswitchable chelator with strong and weak binding modes.

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Iron-photocatalyzed Desaturation of Heterocycles

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Desaturation, the elimination of a hydrogen molecule adjacent to a carbonyl compound, stands as a fundamental organic oxidation reaction with wide-ranging applications in the synthesis of natural products, pharmaceutical compounds, and industrial chemicals[1]. Traditional methods involve indirect α-functionalization pathways via halide, sulfur, and selenium derivatives[2–5]. Alternatively, direct desaturation of carbonyl compounds can be achieved using metal-based catalysts like platinum, palladium, copper[1], and Iron[6], or under metal-free conditions utilizing 2-Iodoxybenzoic acid (IBX)[7] or catalytic iodine[8]. In this study, we present an Iron (III) catalyzed desaturation method for diverse carbonyl compounds, enabling the synthesis of α-β unsaturated compounds and heterocycles (Figure 1). Utilizing iron as a photocatalyst represents a significant step towards sustainable chemical synthesis. Our protocol demonstrates the efficacy of iron (III) photocatalysts in facilitating the desaturation of both aromatic and aliphatic carbonyl compounds, offering a promising pathway for greener and more economically viable desaturation methods.

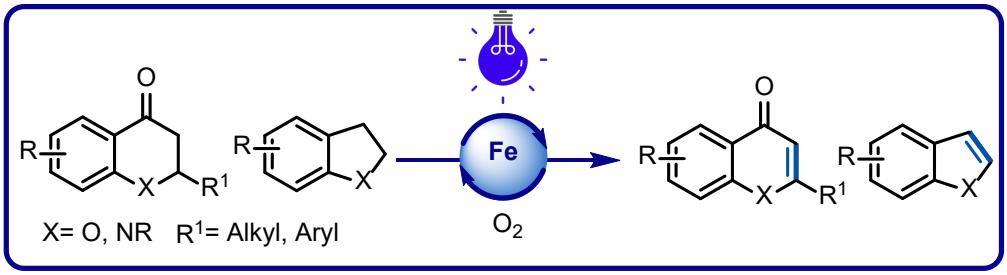


Figure 1: desaturation of Heterocycles

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Non-Innocent Behavior of Aromatic Isocyanides under Visible Light: A Pathway to Thioformimidates

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Thioformimidates play an important role in peptide modifications as the protection group [1]. The most common method for the synthesis of thioformimidates involves S-alkylation of thioformamides with aryl or alkyl halides. However, these processes often suffer from several limitations and purification problems due to the instability of thioformamides and limited substrate scope. Alternatively, thioformimidates can also be synthesized from isocyanides and thiols triggered by UV-light or AIBN initiator [2]. Generally, this reaction proceeds with the formation of a thiyl radical in the presence of UV-light or AIBN followed by thiyl radical addition on the isocyanide to generate an α-thioimidoyl radical [3]. This radical can then undergo H-abstraction from thiols to form the final thioformimidates product. Despite the convenience of this method, less attention has been directed to this pathway due to the following reasons: a) the requirement of UV-light; b) poor reaction efficiency; c) the formation of unwanted side products such as 1,1-bisthiolation; d) C-S bond scission of the intermediate α-thioimidoyl radical, leading to the generation of isothiocyanates.

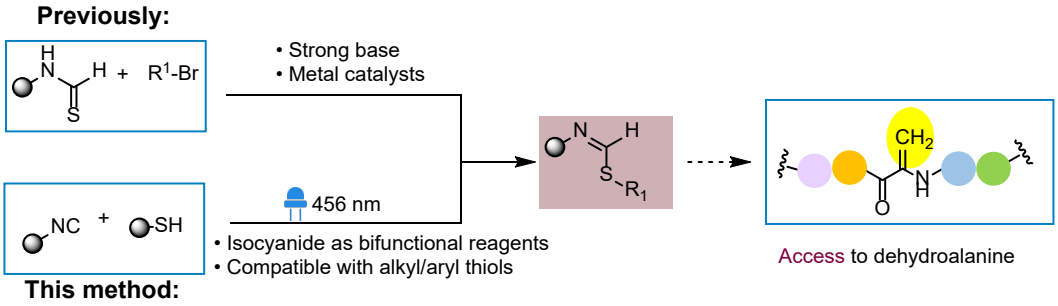


Figure 1: Visible light-mediated synthesis of thioformimidates

Previously, we desighed a photocatalyst-free pathwy to spirocyclic scaffolds from tryptamine-derived isocyanides by employing blue light [4]. Given the significance of thioformimidates and the current limitations in versatile, sustainable synthetic methods, we focused on developing an innovative, photocatalyst-free, visible-light-driven approach for their synthesis. This study marks a significant advance in the field, as it not only improves existing methods for accessing thioformimidates but also reveals a previously camouflaged role of isocyanides in generation of thiyl radicals.

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Towards the Total Synthesis of Ormosianine A

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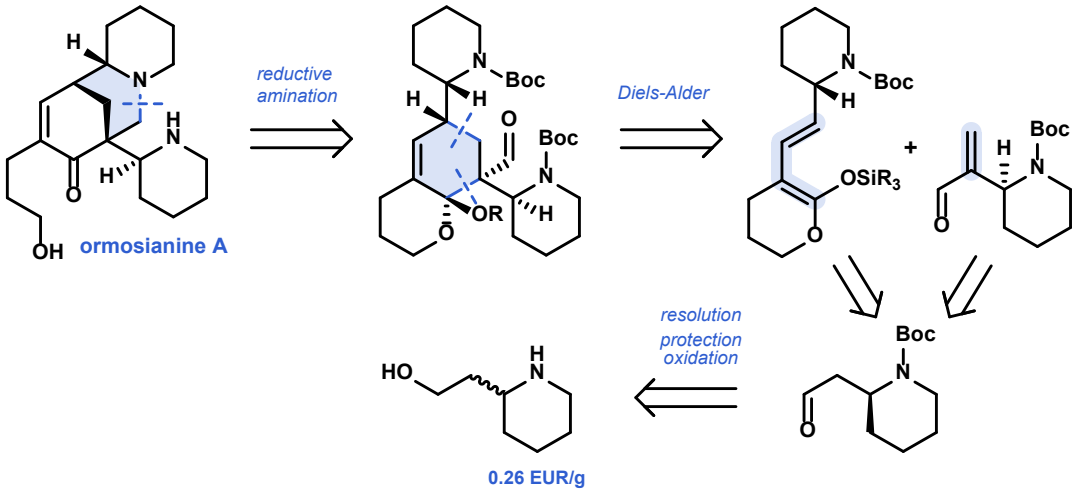
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Ormosianine A is a novel quinolizidine alkaloid isolated from *Ormosia yunnanensis* with potent inhibitory activity against acetylcholinesterase, making it of considerable interest for both drug discovery and agrochemistry.[1] In addition, its polycyclic structure with multiple stereocenters makes it an attractive target for total synthesis.

We recognized that a retrosynthetic disconnection of ormosianine A at the tertiary amine by reductive amination would afford a cyclohexanecarboxaldehyde derivative, which in turn would result from a Diels-Alder cycloaddition. Advantageously, both the diene and dienophile could be derived from the same known chiral amino aldehyde, which is accessible via resolution of inexpensive 2-(2-hydroyethyl)piperidine with CSA.[2] The project encountered and overcame various challenges, including issues related to reagent reactivity and product isolation. Through careful optimization, we were able to access the crucial dienophile and diene. Currently, we are investigating the feasibility of the key Diels-Alder cycloaddition.

Overall, this research contributes to the understanding and accessibility of bioactive quinolizidine alkaloids, highlighting the importance of total synthesis in advancing potential agricultural and medicinal applications.



References

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[2] H.-Y. Cheng, D.-R. Hou, *Tetrahedron* **2007**, *63*, 3000–3005.