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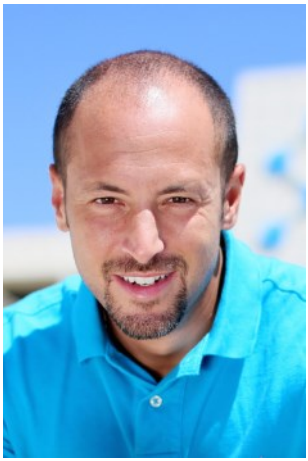

Phil Baran

The Scripps Research Institute, USA

*To download the abstract, please click **here***

Phil Baran was born in 1977 in Denville, New Jersey. He received his B.S. in chemistry from NYU in 1997, his Ph.D. The Scripps Research Institute in 2001, and from 2001-2003 he was an NIH-postdoctoral fellow at Harvard. His independent career began at Scripps in the summer of 2003. Phil has published over 250 scientific articles, several patents, and has been the recipient of several ACS awards such as the Corey (2015), Pure Chemistry (2010), Fresenius (2006), and Nobel Laureate Signature (2003), and several international distinctions such as the Hirata Gold Medal and Mukaiyama Prize (Japan), the RSC award in synthesis (UK), the Sackler Prize (Israel), and the Janssen Prize (Belgium). In 2013 he was named a MacArthur Foundation Fellow, in 2015 he was elected to the American Academy of Arts and Sciences, in 2016 he was awarded the Blavatnik National Award, and in 2017, he was elected to the National Academy of Sciences, USA. He has delivered hundreds of lectures around the world and consults for numerous companies such as Bristol-Myers Squibb and Gilead. He currently serves as a scientific advisory board member for Eisai, Alkermes, Nutcracker, Quanta and AsymChem.From 2016-2020 he served as an Associate Editor for the Journal of the American Chemical Society. He co-founded Sirenas Marine Discovery (2012), Vividion Therapeutics (2016), Elsie Biotechnologies (2021), and Elima Therapeutics (2022). In 2013 he co-authored The Portable Chemist's Consultant, an interactive book published on the iBooks store along with his graduate class in Heterocyclic Chemistry (viewable on YouTube).

The Baran laboratory is committed to identifying areas of chemical synthesis that can have a dramatic impact on the rate of drug discovery and development. This is achieved both through the development of practical total syntheses of complex natural products (such as terpenes, alkaloids, peptides, and oligonucleotides) and by inventing reactions which can dramatically simplify retrosynthesis.

Enhancing the Biocompatibility of Rhodamine Fluorescent Probes by Positional Isomerism Approach

Jonas Bucevičius

Max Planck Institute for Multidisciplinary Sciences, Germany

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Jonas Bucevičius was born in Lithuania in 1987. He received his B.S. and M.S. degrees in chemistry from Vilnius University whilst at the same time he worked in Fine Synthesis Ltd company on custom synthesis projects. In 2015, he obtained a Ph.D. degree in organic chemistry from Vilnius University under the supervision of Prof. Sigitas Tumkevičius. He took a lectureship position at the same university for the 2015-2017 period. In 2017, Jonas moved to Germany as a postdoctoral fellow and joined the Department of Nanobiophotonics at Max Planck Institute for Biophysical Chemistry led by Prof. S. W. Hell. In 2018, he obtained Nobel Laureate Fellowship (awarded by Prof. S. W. Hell) and joined the newly established group of Chromatin Labeling and Imaging at the same institute as a postdoctoral researcher under the supervision of Dr. Gražvydas Lukinavičius. His current research focuses on the synthesis and characterization (by physicochemical and computational means) of fluorescent dyes and probes compatible with various current state-of-the-art super-resolution microscopy techniques.

Transition Metals in Synthesis and Alternatives

Janine Cossy

ESPCI Paris, France

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Janine Cossy did her undergraduate and graduate studies at the University Champagne-Ardenne in Reims (France), working on photochemistry under the supervision of Prof. J.-P. Pète. After a postdoctoral stay with Prof. B. M. Trost at the University of Wisconsin (USA), she came back to Reims as CNRS Associate Researcher. In 1990, she was appointed Professor of Organic Chemistry at the ESPCI in Paris. Janine Cossy's research interests focus on the synthesis of natural products and biologically active molecules and on the development of synthetic methods. Her research efforts have resulted in more than 560 publications and 18 patents. Among the awards, she received the CNRS Silver Medal (France, 1996), the UK Royal Society Rosalyn Franklin International Lecturership awarded to internationally recognized women scientists (UK, 2005); the IUPAC 2019 Distinguished Women in Chemistry or Chemical Engineering (2019). She is a member of the French Academy of Sciences since 2017.

Innovation in the Synthesis of Complex Pharmaceutical Agents

Martin Eastgate

Bristol-Myers Squibb, USA

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Martin obtained his bachelor's degree in Chemistry from the University of Surrey, UK (1999), graduating with first class honors. He received his doctoral degree in Organic Chemistry (2002) from the University of Cambridge, UK, working under the direction of Dr. Stuart Warren. His thesis research involved sulfur participation chemistry, specifically the generation of thiiranium ions under basic conditions and their use in pyrrolidine synthesis. Martin then carried out postdoctoral research with Prof. Scott E. Denmark, at the University of Illinois Urbana-Champaign, working on the Lewis-base activation of Lewis-acids and understanding ligand-field theory in hyper-valent silyl cations.

In 2005 Martin joined Bristol Myers Squibb and is currently Executive Director, Head of Portfolio Chemistry in Chemical Process Development (CPD). Martin has led multiple teams through innovation projects, developing novel approaches to complex molecular systems, and designing commercial approaches to important drug candidates, such as the HIV attachment inhibitor Fostemsavir. Martin is currently accountable for CPDs early portfolio programs, commercial route selection and external development activities. Martin is also the co-lead of the BMS-Biocon Research Center (BBRC), a research institute on the campus of Syngene Inc. in Bangalore India, where Martin is accountable for the Product Development facing team.

Additionally, Martin is on the joint research committee (JRC) of the BMS-Scripps collaboration, is a member of the Scientific Advisory Board (SAB) of Asymchem Life Sciences Inc, the Editorial Advisory Board (EAB) for the ACS journal Organic Process Research and Development (OPRD), the Board of Directors for Organic Reactions, is a member of the Scientific Advisory Board (SAB) of Elsie Biosciences and has been a Fellow of the Royal Society of Chemistry (FRSC) since 2018.

Martin has co-authored over 100 peer reviewed publications, is a co-inventor on multiple patent applications and granted patents and has been invited to give more than 100 lectures at conferences and universities world-wide. Martin has been the recipient of several awards including the GlaxoSmithKline Post-Doctoral Fellowship in Organic Chemistry, was selected as a 2011 ACS Young Investigator, was a 2017 McElvain lecturer at the University of Wisconsin, was the inaugural recipient of the 'Industrial Chemistry Award' from the International Society of Heterocyclic Chemistry (2017), received the 'Organic Industrial Chemistry Award' from the Royal Society of Chemistry (2019), the 'Ondetti & Cushman Award' (a scientific honor presented by Bristol Myers Squibb, 2019), is a winner of the EPA Green Chemistry Challenge award (2021), the 'Industrial Chemistry' Award by the Philadelphia Organic Chemists Club (POCC, 2021) and was part of a team that received the Robert Robinson 'Horizon Award' from the Royal Society of Chemistry (2022).

Application of Innovative Technologies to Advance the Development of Novel Pharmaceutics

Margaret M. Faul

Amgen Inc, USA

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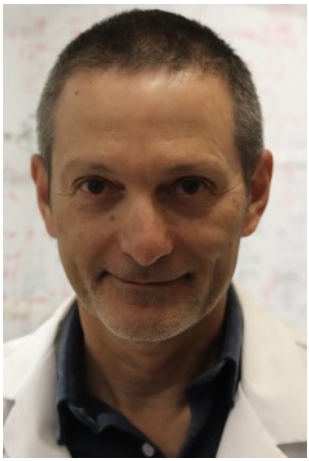
Margaret received her Ph.D. degree in Synthetic Organic Chemistry from Harvard University. She currently works at Amgen Inc, in Thousand Oaks, CA where she is Vice President of Manufacturing and Clinical Supply and the Amgen Thousand Oaks Operations Site Head.

Margaret has supported drug development programs across all phases of clinical and commercial. She has experience working with commercial manufacturing organizations worldwide and has invested significant effort in evolving a green chemistry culture in the workplace. As a result, Amgen was awarded in 2017 the Presidential Green Chemistry Challenge Award for developing an improved green process for commercial manufacture of Parsabiv®. Margaret has a strong external presence. She was chair of the Board of Directors of the International Consortium for Innovation and Quality in the Pharmaceutical Industry and past chair and founder of the Enabling Technologies Consortium.

Margaret has authored/co-authored more than 150 peer reviewed publications, presentations, and patents, and has served as a symposium organizer and session chair for several major process chemistry events. She is an associate editor for *Organic Letters* and is a member of the editorial boards for *Science of Synthesis*, *Organic Syntheses*, *Synthesis and SynLett,* and *Advanced Synthesis and Catalysis.* In partnership with Thiéme and the *Science of Synthesis*, she sponsors the Dr. Margaret Faul Award for Women in the Chemical Sciences

Hybrid Pd-radical Chemistry: New Mechanism, New Possibilities



Vladimir Gevorgyan

University of Texas at Dallas, USA

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Vladimir Gevorgyan received his PhD from the Latvian Institute of Organic Synthesis in 1984. After two years of Postdoctoral research (1992-1994, JSPS- and Ciba-Geigy International Postdoctoral Fellowships) at Tohoku University, Japan, and a visiting professorship (1995) at CNR, Bologna, Italy, he joined faculty at Tohoku University (Assistant Professor, 1996; Associate Professor, 1997-1999). Vladimir Gevorgyan joined UIC as an Associate Professor in 1999. He was promoted to the rank of Full Professor in 2003, and a Distinguished Professor of Liberal Arts and Sciences in 2012. In 2019, Vladimir Gevorgyan moved to Texas to become a Robert A. Welch Distinguished Chair in Chemistry at the University of Texas at Dallas. He also holds a Professor position at the University of Texas Southwestern Medical Center.

Gevorgyan group focuses on the development of novel synthetic methodologies. The emphasis is placed on conceptual novelty and potential application of the newly developed methods in synthetic and medicinal chemistry.

Tailoring Sodium Organometallic Reagents For Arene Functionalisation

Eva Hevia

University of Bern, Switzerland

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Eva Hevia completed her Ph.D. degree, from the Universidad de Oviedo (Spain) in 2003, under the supervision of the late Victor Riera. In 2006, after a three-year appointment at the University of Strathclyde (UK) as a Marie Curie postdoctoral fellow working with Robert Mulvey, she took up a Lectureship at the same institution. Subsequently, she was promoted to Senior Lecturer in 2010, and to full Professor in 2013. In 2019, Eva moved to the University of Bern where she is currently a Professor in Inorganic Chemistry. Research in her group focuses on polar organometallic chemistry at the crossroads of inorganic, organic, and green chemistry.

Eva has published over 180 papers and she is an elected fellow at the European Academy of Sciences and the Royal Society of Edinburgh. Her research has been recognised with several awards, including the RSC Corday-Morgan Prize (2017), GDCh Arfvedson-Schlenk Prize (2021) and the Spanish Royal Society of Chemistry Excellence Award (2021).

Using the Available pK_a Data in Non-Aqueous Solvents

Ivo Leito

University of Tartu, Estonia

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Ivo Leito works as a professor of analytical chemistry at the University of Tartu, leading the analytical chemistry research group involved in a variety of research directions ranging from studies of acids and bases and behaviour of ions to the development of sensors and metrology in chemistry. He coordinates the Estonian Center of Analytical Chemistry, a distributed interdisciplinary scientific research infrastructure for the development and application of modern analytical methods.

Measurements and computations of acidities and basicities as well as ion behavior and solvation effects in different non-aqueous solvents and obtaining new chemical insight into properties of compounds and materials is a key topic of the group. The group has created experimental acidity and basicity scales in several solvents (acetonitrile, tetrahydrofuran, etc) and routinely receives requests for measurement or prediction of different acidity-basicity-related parameters. Recently, the group has opened a new horizon of the acid-base studies with implementing the unified pH scale (pH_{abs} scale), which enables direct comparison of pH between different solvents.

New Synthetic Methods Based on Halogen-Atom Transfer and Photoexcited Nitroarene Chemistry

Daniele Leonori

RWTH Aachen University, Germany

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Daniele started his independent academic career at the University of Manchester in 2014 where he was promoted to Reader in 2018 and Professor in 2020. In 2022 Daniele and his group moved to the RWTH Aachen University, where he is a Chair of Organic Chemistry. Research in the Leonori group focuses on the development of novel methods exploiting the reactivity of radical and photoexcited species.

From Batch to Flow: Advancing Synthetic Organic Chemistry through Technological Innovation

Timothy Noël

University of Amsterdam, The Netherlands

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Timothy Noël is a researcher in the field of synthetic organic chemistry and technology, with a particular interest in the delicate synergy between the two fields.
In 2004, Tim earned his MSc degree in Industrial Chemical Engineering before pursuing his passion for synthetic organic chemistry, which led him to complete his PhD in the field at Ghent University in 2009. Following his PhD, he traveled across the Atlantic as a Fulbright Postdoctoral Fellow to work with Professor Stephen L. Buchwald at the Massachusetts Institute of Technology (MIT), where he gained valuable experience and expertise in flow chemistry. Upon returning to Europe, he joined Eindhoven University of Technology as an Assistant Professor in 2012, and later became an Associate Professor in 2017. In 2020, Tim was promoted to Full Professor at the University of Amsterdam, where he is now the Chair of Flow Chemistry.
His research in the area of flow chemistry was recognized with several awards, including the DECHEMA award (2017), the Hoogewerff Youth Prize (2019), the IUPAC-ThalesNano Flow Chemistry Award (2020), the KNCV Gold Medal (2021) and the ACS Sustainable Chemistry & Engineering Lectureship Award 2022. He is the editor in chief of Journal of Flow Chemistry.

Investing in New Technologies for Current & Future Processes

Rebecca T. Ruck

Merck Research Laboratories, USA

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Rebecca T. Ruck (she/her/hers) is Associate Vice President, MSD Process Research & Development, where she leads the Enabling Technologies group, a role she proposed that has created an innovation incubator of biologists, chemists, engineers and data scientists. Her team is making impressive contributions across all pipeline projects, including the application of an unprecedented biocatalytic cascade sequence to the manufacturing route of islatravir, a pioneering photochemical flow process for belzutifan and an immobilized enzymatic flow reaction for nemtabrutinib. Becky has been actively involved in the external research community through academic collaborations, creation of MSD's university lectureship series and recruiting efforts that have led to an unrivaled increase in the number of women in the Process R&D team. She has expanded her women in chemistry efforts externally through the WCC-Merck Research Award and Empowering Women in Organic Chemistry (EWOC) conference and internally through expanded Diversity, Equity & Inclusion accomplishments, such as a series of D&I-themed TED-style talks that have greatly impacted the department's understanding and appreciation of these important topics.For these efforts, Becky has been recognized with the 2018 ACS Award for Encouraging Women into Careers in the Chemical Sciences and as a 2020 HBA Rising Star and ACS Fellow. In addition, she currently holds positions on the NASEM Board on Chemical Sciences & Technology, ACS Petroleum Research Fund and the MIT Visiting Committee and is a Topic Editor at ACS Catalysis. Becky graduated summa cum laude from Princeton University, obtained her PhD in organic chemistry from Harvard University in the lab of Prof. Eric Jacobsen and conducted NIH-funded post-doctoral research at the University of California-Berkeley with Prof. Robert Bergman.

Total Synthesis of Complex, Bioactive Natural Products

Christopher Vanderwal
University of California, USA

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Christopher Vanderwal received a B.Sc. degree in Biochemistry (1995) and an M.Sc. degree in Chemistry (1998) from the University of Ottawa. He then moved to the Scripps Research Institute for doctoral studies in the group of Professor Erik Sorensen. After obtaining his Ph.D. in 2003, Chris joined the group of Professor Eric Jacobsen at Harvard University as a Jane Coffin Childs postdoctoral associate. In 2005, Chris began his independent academic career at the University of California, Irvine.
In 2011, Chris was promoted with tenure to Associate Professor and was named a UCI Chancellor's Faculty Fellow, and in 2013, he was promoted to Professor of Chemistry, and he was recently appointed Professor of Pharmaceutical Sciences.
Chris's group focuses on the synthesis of complex natural products, including alkaloids, terpenoids, and polyhalogenated secondary metabolites. They develop target-specific but potentially broadly applicable methods en route to the natural product goals, and frequently engage in post-synthesis collaborative experiments to investigate biological activity of the target and synthetic analogs.

Monofluorinated One Carbon Synthons

Janis Veliks

Latvian Institute of Organic Synthesis, Latvia

*To download the abstract, please click **here***

Janis Veliks was born in 1986 in Daugavpils, Latvia. He did his undergraduate studies at Riga Technical University. He received his doctoral degree (2014) in chemistry from the University of Zurich under the supervision of Prof. J. S. Siegel. As a SNSF postdoctoral fellow, he joined the group of Prof. V. Gouverneur to work in the area of fluorine chemistry. In 2016, he moved back to Riga, Latvia and currently, he is a principal researcher and head of laboratory at the Latvian Institute of Organic Synthesis (LIOS).
His current research interests include the development of new reagents and methodologies to advance efficient delivery of one-fluorine one-carbon containing species to a target substrate and finding novel retrosynthetic disconnections in organofluorine chemistry.

Green Chemistry and the Sustainability Pendulum

John C. Warner

The Technology Green House, USA

*To download the abstract, please click **here***

John is a chemistry inventor who works to design and create commercial technologies inspired by nature consistent with the principles of green chemistry. With over 300 patents, he has invented solutions for dozens of multinational corporations. His inventions have also served as the basis for several new companies. Examples include: Collaborative Medicinal Development (ALS therapy), Hairprint (hair color restoration), Collaborative Aggregates (asphalt warm mix rejuvenators), Ambient Photonics (lowlight indoor photovoltaic devices for IoT and BIPV).

He is one of the co-founders of the field of green chemistry, co-authoring the defining text "Green Chemistry: Theory and Practice" and articulating the 12 principles of green chemistry with Paul Anastas. John has over 100 publications providing foundational work in the fields of noncovalent derivatization, polymer photochemistry, metal oxide semiconductors and synthetic organic chemistry. John has received prestigious awards as an academic (Presidential Award for Excellence in Science Mentoring – President G. W. Bush & NSF, 2004) and the August Wilhelm von Hofmann Medal from the German Chemical Society, 2022), industrial chemist (Perkin Medal – Society of Chemical Industry, 2014), inventor (Lemelson Ambassadorship – Lemelson Foundation & AAAS) and for governmental chemicals policy (Reinventing Government National Performance Review – Vice President A. Gore & EPA, 1997). He received the American Institute of Chemistry's Northeast Division's Distinguished Chemist of the Year for 2002 and the Council of Science Society President's 2008 Leadership award. Warner was named by ICI Services as one of the most influential people impacting the global chemical industries. In 2011 he was elected a Fellow of the American Chemical Society and named one of "25 Visionaries Changing the World" by Utne Reader. He serves as Distinguished Professor of Green Chemistry at Monash University in Australia and was named an Honorary Professor at the Technical University of Berlin. He served as the 2020 and 2021 Global Chair for the Center for Sustainable and Circular Technologies at the University of Bath. In 2017 the German Ministry of Economic Affairs and The Technical University of Berlin announced the naming of "The John Warner Center for Green Chemistry Start-Ups" in his honor. He serves as strategic advisor for the Science, Engineering and Health Committee of EPA Victoria in Australia.

John received his BS in Chemistry from UMASS Boston, and his PhD in Chemistry from Princeton University. After working at the Polaroid Corporation for nearly a decade, he then served as tenured full professor at UMASS Boston and Lowell (Chemistry and Plastics Engineering). In 2007 he founded the Warner Babcock Institute for Green Chemistry, with Jim Babcock (a research organization developing green chemistry technologies), and Beyond Benign with Amy Cannon (a non-profit dedicated to sustainability and green chemistry education). John is constantly giving keynote talks and workshops on Green Chemistry, Innovation, The Circular Economy, and Biomimicry. He continues to advise several international organizations.

Asymmetric Catalysis with Peptides

Helma Wennemers
ETH Zurich, Switzerland

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Helma Wennemers is an organic chemist whose research concentrates on asymmetric catalysis, chemical biology, and supramolecular chemistry. Helma received her Ph.D. degree from Columbia University, New York, with Prof. W. Clark Still (1996) and was a postdoctoral fellow with Prof. Hisashi Yamamoto at Nagoya University (1997–1998). She joined Basel University as the Bachem-endowed Assistant Professor in 1999 where she was promoted to Associate Professor. In the fall of 2011, Helma moved to ETH Zurich, where she is a Professor of Organic Chemistry.
Her research has been recognized by numerous named lectureships and awards, including the Leonidas Zervas Award from the European Peptide Society (2010), the Inhoffen Medal from the Helmholtz Center (2017), the Pedler Award from the Royal Society of Chemistry (2016), the Netherlands Scholar Award for Supramolecular Chemistry (2019), the Arthur C. Cope Scholar Award from the American Chemical Society (2021), the Ernesto Scoffone Award from the Italian Peptide Society (2022), and the Vincent du Vigneaud Award from the American Peptide Society (2023).

Discovery and Development of Laquinimod

Johan Wennerberg

Red Glead Discovery, Sweden

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He became interested in chemistry at the age of 12. Of course, different explosives were interesting but quite early organic synthesis, became the main focus.
Undergraduate studies at Umeå University were finished in 1992 with a master thesis under the guidance of Professor Rolf Carlson. This work dealt with regioselective Diels-Alder reactions catalyzed by zeolites.
He then joined the group of Professor Torbjörn Frejd at Lund University and started to work with attempts to synthesize taxol. During this work, a novel rearrangement reaction of allyl benzyl ethers was discovered. The main focus of the thesis, which was disclosed in 1997, was on the rearrangement reaction. After a year as a lecturer, he began as a development chemist at DuPont Chemoswed in Malmö mainly focusing on scale-up and process development. In 2006, he was promoted to Head of Chemistry. Since 2020 he is Head of Science at Red Glead Discovery. He still teaches part time at Lund University in organic chemistry, medicinal chemistry and green chemistry. He was appointed associate professor in organic chemistry in 2009 and adjunct professor 2021 at Lund University. Areas of interest are synthesis of biologically active compounds, development of new synthetic methods, process development, synthesis in water, science history and teaching.

Abstracts Nominated to Present Their Work as Short Talks at a Special Session on July 9		
14:15 – 14:30	**P47**	**Dr. Mikk Kaasik**, Tallinn University of Technology, Estonia *Enantioselective [8+2]-Cycloadditions of Photogenerated Ketenes*
14:30 – 14:45	**P48**	**Dr. Dainis Kaldre**, Roche, Switzerland *Development of a Continuous Flow Grignard Reaction to Manufacture a Key Intermediate of Ipatasertib*
14:45 – 15:00	**P94**	**Mr. Jan Paciorek**, University of Innsbruck, Austria *Total Synthesis of the Dihydrooxepine-Spiroisoxazoline Natural Product Psammaplysin A*
15:00 – 15:15	**P139**	**Mr. Niklāvs Ūdris**, Latvian Institute of Organic Synthesis, Latvia *Total Synthesis of Sitsirkine, Dihydrositsirkine, and Meroquinene via Stereoselective Ireland-Claisen Rearrangement*
15:15 – 15:30	**P153**	**Mr. Jonas Žurauskas**, Vilnius University, Lithuania *Electron-Poor Acridones and Acridiniums As Super Photooxidants in Molecular Photoelectrochemistry by Unusual Mechanisms*

Access to Pentasubstituted Guanidines *via* Common Amide Coupling Reagents

Juhana Aho, Jere Mannisto
University of Helsinki, Finland
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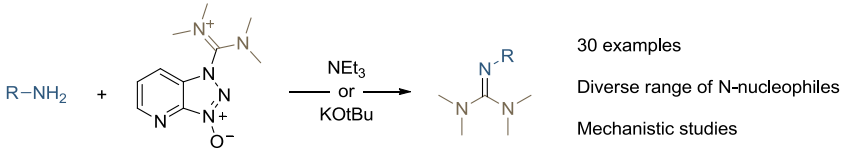
Substituted 1,1,3,3-tetramethylguanidines (TMGs) are sterically hindered superbases. The functional group is utilized in a variety of systems ranging from different organocatalyst roles to polymerization mediators to medicinal chemistry applications. Performing amide couplings with hexafluorophosphate azabenzotriazole tetramethyl uranium (HATU) are known to produce TMGs as byproducts. Yet the mechanistic details of this reactivity have been unclear. In our systematic study, the nature of this reactivity is investigated. The lessons learned were applied on two fronts: minimizing guanlyation in competing amide coupling and utilizing HATU as a guanylation reagent for a variety of amines including for late-stage functionalization of pharmaceuticals.[1]



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Synthesis of Double *peri*-PEG Substituted 1,8-Naphthalimides

Denitsa Anastasova[1], Monika Mutovska[1], Silvia Angelova[2], Yulian Zagranyarski[1]

[1] Sofia University 'St. Kliment Ohridski', Faculty of Chemistry and Pharmacy, 1 James Bourchier Ave., 1164 Sofia, Bulgaria
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1,8-Naphthalimides have found wide application as emissive materials in OLEDs, chemosensors for cations and anions, fluorescent cellular imaging agents and DNA intercalators. The NMI core have proven itself as versatile photoactive structure upon which many fluorescent compounds can be built. The addition of electron donating substituents to the electron acceptor already present in the aromatic ring forms a push-pull system with good photostability and high fluorescence quantum yields.
Here we present the synthesis of double *peri*-PEG substituted naphthalimides containing both hydrophilic and hydrophobic substituents. The substances are highly fluorescent, both in solution (including water) and in the solid state, making them highly suitable for bio application.

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

Untangling the Aggregation of Lithiated Pyridine N-Oxides

Joseph Anslow, Andrei V. Malkov
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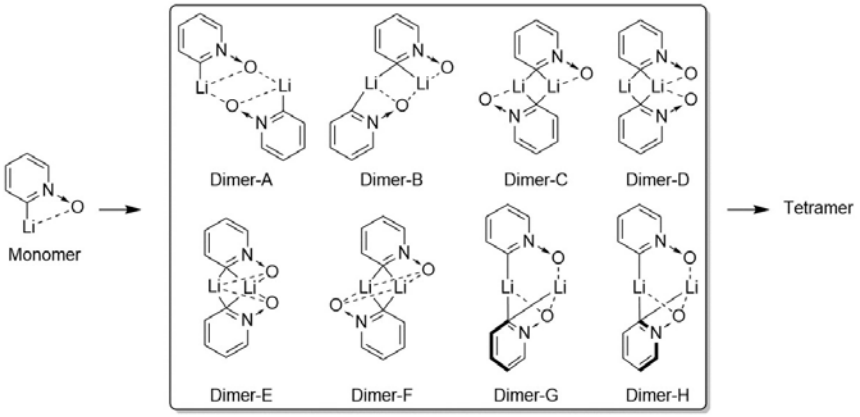
Organolithium species are widely used in a variety of applications due to their diverse reactivity. The polar nature of the Carbon-Lithium bond results in complex aggregation behaviour which is known to dictate reactivity. Despite decades of research there are still large gaps in understanding the way in which aggregation occurs. A greater understanding is vital for controlling reactivity and unlocking new reactions. Oxidative coupling of pyridine N-oxides proceed via lithiated species.[1] The time sensitive nature of this reaction and substrate scope is likely due to aggregation. The first crystal structure of a lithiated pyridine has only recently been published in 2020 and there has been no research into aggregation. Density functional theory was used to probe aggregate structures in many aggregate forms, with special focus on dimers. Strong intramolecular interactions appear to stabilise non-reactive aggregates and aggregation to tetramer species is favourable. These observations aggree with experimental findings. Further investigation with other solvents and ligands is in progress.



Proposed and investigated route of aggregation, including theorised dimer structures A to H

Acknowledgements
Financial support from Loughborough University is acknowledged.

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Synthesis and Biological Investigation of 2*H*-Pyrazolo[4,3-*c*]pyridines

Eglė Arbačiauskienė[1], Vaida Milišiūnaitė[1], Eva Řezníčková[2], Asta Žukauskaitė[2], Vladimír Kryštof[2], Algirdas Šačkus[1]

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Fused polycycles are renowned for their significant biological and pharmacological properties. Pyrazolopyridines, among other fused systems, possess antidepressant, anti-inflammatory, antihyperglycemic, antitumor, antibacterial, anxiolytic activities.[1]
In this study we applied our previously reported synthetic approach[2] to prepare a library of various 6-substituted 2-phenyl-2*H*-pyrazolo[4,3-*c*]pyridines and assessed their biological activity. The strongest antiproliferative activity displaying compound was further evaluated for its biological effects *in vitro*. Flow cytometry analysis of compound-treated K562 cells showed an enrichment of G2/M cell population and increased number of subG1 cells undergoing cell death. Subsequent immunoblotting and BrdU-pulse labelled K562 analyses confirmed that the most active compound induces massive M phase arrest followed by endoreduplication caused by disruption of proper cytokinesis.

Acknowledgements
This work was supported by the Research Council of Lithuania (Project No. S-MIP-23-51).

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2. Milišiūnaitė, V. et al. *Eur. J. Med. Chem.* **2018**, 150, 908.

Building Diverse Hit-Finding Collections through Novel Chemistries

Tomas Baikstis, Allan Jordan
Sygnature Discovery, United Kingdom
t.baikstis@sygnaturediscovery.com

High quality screening collections are critical to the long-term success of projects. Sygnature Discovery **LeadFinder PRISM** library has been designed to afford attractive, lead-like hits that will allow rapid exploration of SAR in good property space and provide the foundation for successful drug discovery programs. Here, we highlight a selection of novel and readily accessible structural scaffolds that we have developed through our compound generation pipeline. Each is synthetically tractable and has been used by our High Throughput Chemistry (HTC) team to generate a large number of lead like chemical compounds.

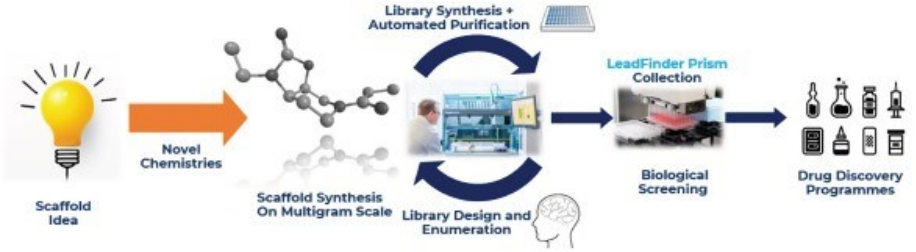

Figure 1. The LeadFinder PRISM workflow.

Combinatorial High-throughput Assembly and Review of Molecular Degraders

Tomas Baikstis, Roland Hjerpe
Sygnature Discovery, United Kingdom
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Sygnature's CHARMED platform delivers rapid synthesis, screening, and characterisation of potential bifunctional lead compounds. Ready-to-couple plates of diverse linkers and popular ligase warheads accelerate the identification of degrader hits for novel targets. Here we report an outline of the platform; its synthetic approach and scope, example screening technologies, including HTRF (Homogeneous Time Resolved Fluorescence) and Jess methods to orthogonally confirm target protein degradation. We demonstrate the platform using SHP2 as a model target. We further demonstrate value of SPR biophysical methods to evaluate binary and ternary complex formation in a SOS1 model system, and CRBN Fluorescence Polarization (FP) competition assays to assess binding cooperativity for both SHP2 and SOS1 examples.

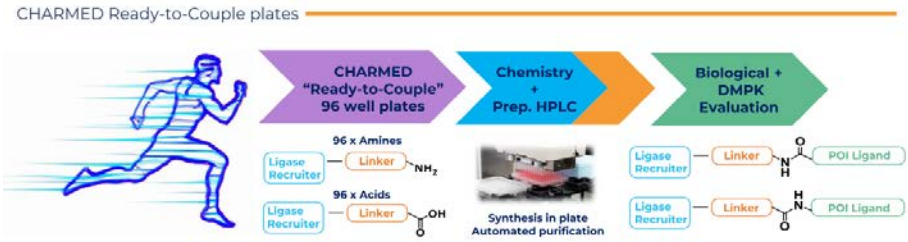

Figure 1. Plate-based degrader synthesis, purification and biological screening triage that composes the Charmed Platform.

Benzoxaphosphepine 2-Oxides – a Novel Class of Carbonic Anhydrase Inhibitors

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The ubiquitous metalloenzymes carbonic anhydrases (CA, EC 4.2.1.1) are an established drug target for a range of diseases, including bacterial infections, malaria, cancer and glaucoma. Our research interests were aimed at development of novel and isoform-selective CA inhibitors, which can potentially serve as anticancer agents. Herein we present the facile synthesis and biological evaluation of benzoxaphosphepine 2-oxides.[1,2] This novel class of CA inhibitors displays excellent water solubility and remarkable inhibitory activity towards cancer-associated CA isoforms IX and XII, rendering them attractive drug-like candidates for further studies.

SAR studies
Solubility >2 mg/mL

Acknowledgements
This project was supported by LIOS student grant IG-2024-05.

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Phosphocumarin Derivatives as Carbonic Anhydrase Inhibitors

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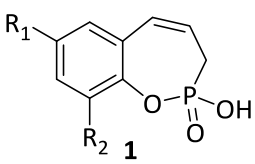
Carbonic anhydrases (CA) are metalloenzymes involved in vital physiological processes, such as pH regulation and CO_2 homeostasis.

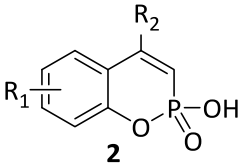
In last two decades, CA have been identified as drug target. CA inhibitors can act as anticancer, antiglaucoma and, as shown in recent years, antibacterial agents.

Previously in our research group, were synthesized organophosphorus compounds **1**, which have been identified to be isoform-selective and effective CA inhibitors.[1]

Extending our research, we decided to develop potential CA inhibitors – 2-hydroxybenzo-1,2-oxaphosphinine 2-oxide **2**, which are considered phosphocoumarin.



1



2

Acknowledgements

This work has received funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement No 951883 within SPRINGBOARD project.

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Synthesis and Evaluation of Optical Properties of New Fluorescent 2-Styryl-3*H*-indole Derivatives

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Synthetic 3*H*-indole derivatives are important in medicinal chemistry and material science due to their great optical properties and vast applicability (e.g. fluorescent probes).[1] Therefore, the synthesis of new 2-styryl-3*H*-indole derivatives was accomplished *via* Fischer indolization, Suzuki cross-coupling and Knoevenagel condensation reactions. The absorption, emission and fluorescence quantum yields of newly synthesized compounds were evaluated in THF. The emission of new 2-styryl-3*H*-indoles was mainly within the visible part of the spectrum.

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Ruthenium Complexes for Olefin Metathesis: Can Cyclic Triel Carbenoids be Used as Their Auxiliary Ligands?

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Not long after the development of stable *N*-heterocyclic carbenes such species dominated the field of olefin metathesis as useful ligands for catalysts.[1] In our studies we reached beyond this trend, substituting carbenes with carbenoids containing a triel atom instead of carbon. We simulated reaction pathway for selected Grubbs and Hoveyda–Grubbs type complexes bearing E(AmIm) ligand[2] with three different alkenes: ethylene (the simplest possible system), styrene (exhibiting steric hindrance) and isobutylene (forming tetrasubstituted alkene). We show that the most promising candidate for efficient catalysis seems to be the Hoveyda–Grubbs type catalyst with Tl(AmIm) ligand.

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Triazole Ring Containing PNA Nucleobases for Enhancing π–π Stacking and Stability of dsRNA-PNA Triplexes

Vladislavs Baškevičs[2], Ilze Kumpiņa[1], Sara Farshineh Saei[1], Dace Katkeviča[2], Ēriks Rozners[1], Mārtiņš Katkevičs[2]

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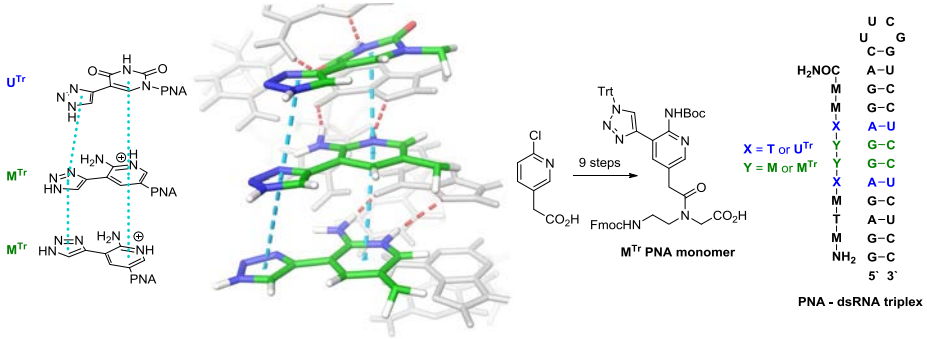
π–π Stacking between base pairs provides a significant contribution to the stability of RNA and DNA double strands.[1] Some examples of triplex-forming PNA nucleobases with extended π system are known to increase the thermal stability of dsRNA-PNA triplexes.[2] Molecular dynamics simulation of dsRNA-PNA triplex system shows that the addition of a triazole ring to **U** (uracil) or **M** (2-aminopyridinyl) PNA nucleobases promotes a continuous stack within the PNA strand and between triazoles, thereby increasing the overall stability of the triplex.



Computational results, synthesis of triazole substituted **M**^{Tr} PNA monomer and stability of dsRNA-PNA complex will be presented.

Acknowledgements
This work was supported by *ANM-OSI-PA-51* grant.

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One-Step Regioselective Synthesis of N-1 Substituted Dihydrouracils: A Motif of Growing Popularity in the Targeted Protein Degradation Field

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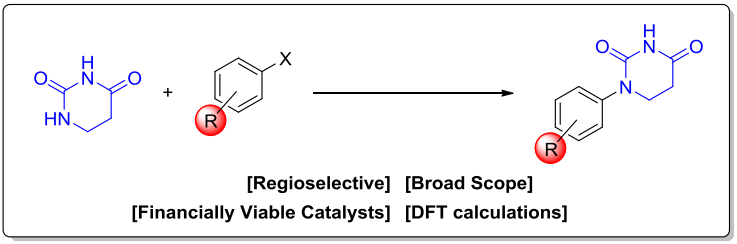
The increasing popularity of the dihydrouracil (DHU) motif in cereblon-recruiting proteolysis targeting chimeras has necessitated the development of a facile, inexpensive and high yielding method for its introduction into molecules. To that end, we have developed an N-1 selective Pd-catalyzed cross-coupling of DHU with aryl electrophiles to provide access to medicinally-relevant scaffolds in a single step. This approach exhibits excellent functional group tolerance, broad applicability to an abundance of readily-available (hetero)aryl halides and triflates, and utilizes commercially-viable catalyst/ligand systems. Thus, our strategy should find broad utility in the arena of PROTAC research, as it obviates the drawbacks of previous methodologies that rely on multi-step synthetic routes and protecting group strategies to achieve N-1 selectivity.



Photocatalytic Generation of Trifluoromethyl Nitrene from Azidotrifluoromethane and Alkene Aziridination

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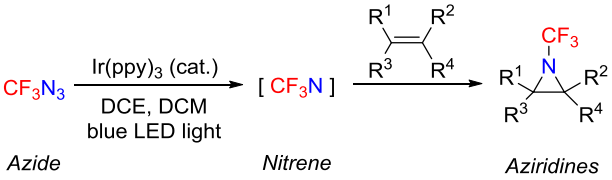
beier@uochb.cas.cz

Here we present photocatalytic generation of trifluoromethyl nitrene from azidotrifluoromethane. This unstable reactive triplet nitrene reacted with structurally diverse alkenes to afford N-trifluoromethylaziridines – new fluorinated nitrogen heterocycles (Figure). The reaction mechanism for the formation of CF_3N and aziridines was investigated by spectroscopic, electrochemical, and quantum chemical methods.



Acknowledgements
This work was financially supported by the Czech Science Foundation (23-04659S) and the Czech Academy of Sciences (RVO: 61388963).

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Dendrimer-Bound Arylmethyl Meldrum's Acids as Radical Scavengers

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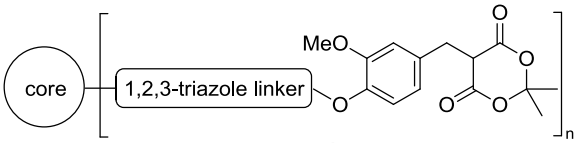
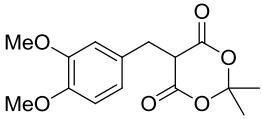
Arylmethyl Meldrum's acids are 1,3-dicarbonyl type antioxidants,[1] which have shown promising antiradical activity.[2] Here we have synthesized dendrimeric structures **1** with arylmethyl Meldrum's acid moieties as surface groups.



1a-d

DPPH inh.(100 μM) = 82-88%,
IC_{50} = 11-18 μM



2

DPPH inh.(100 μM) = 86%,
IC_{50} = 18 μM

The antiradical activity of dendrimers **1** is comparable to the free surface group (compound **2**).

Acknowledgements
This work was supported by Riga Technical university (project no. ZM-2021/15 and C4835.Doc.1028).

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Antiradical Activity of Arylmethyl Meldrum's Acid Salts

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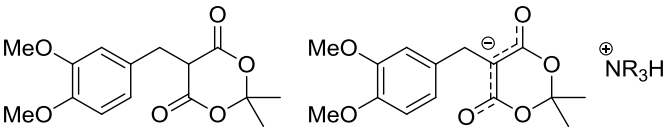
Arylmethyl Meldrum's acids mainly quench radicals through a sequential proton loss – electron transfer (SPLET) mechanism.[1] In this mechanism deprotonation of the antioxidant is typically the rate-determining step, therefore pre-deprotonation (or salt formation) is expected to increase the activity of the compound. Here we have used various amines to deprotonate arylmethyl Meldrum's acid **1** and tracked the changes in radical scavenging ability.



1 **2a-s**

DPPH inh.(100 μM) = 83%,
IC_{50} = 40 μM

DPPH inh.(100 μM) = 32-84%,
IC_{50} = 12->200 μM

We have found that sterically hindered, weakly basic amines lead to salts **2** with higher activity.

Acknowledgements
This work was supported by Riga Technical university (project no. zi-2024/9).

References:
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Design of Hydroxamic Acids as PARP-1 Inhibitors

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Poly(ADP-ribose) polymerase-1 (PARP-1) is a key target in anticancer research due to its role in DNA repair. Hydroxamic acids are known to inhibit metal-dependent enzymes, while the effects on PARP are unclear.

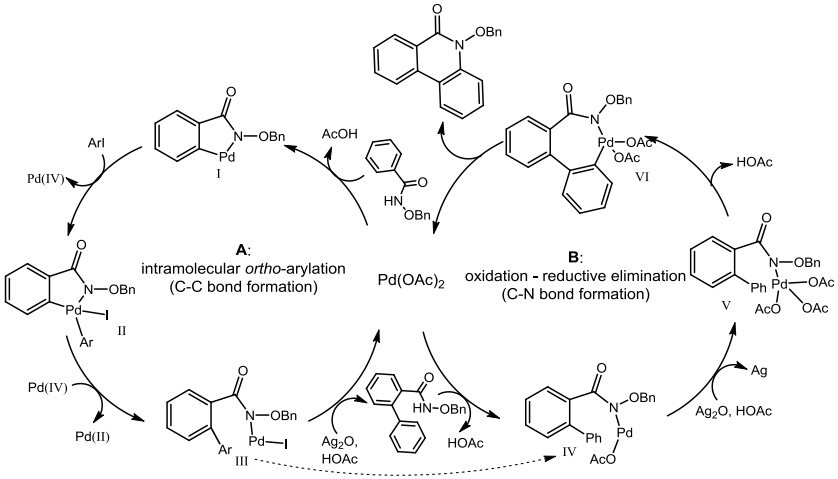

Figure 1. The dual C–H/N–H activation involved in the synthesis.

This study employs molecular docking and dynamics alongside synthetic chemistry to investigate N-O substituted phenanthridinones as PARP-1 inhibitors. These compounds inhibit PARP-1 in the low-nanomolar range and demonstrate reduced toxicity, showing promise as potent inhibitors.

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Dimethilfluromethane Building Blocks for Medicinal Chemistry Purposes

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[1] Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Murmanska Street 5, Kyiv 02660, Ukraine
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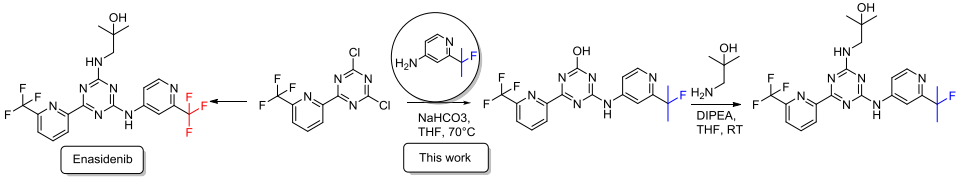
The unique properties of fluorine have facilitated its integration into various realms of academic and industrial research, spanning from pharmaceuticals and agrochemicals to advanced materials and polymers. Notably, the incorporation of fluorine into lead drug candidates has been acknowledged as a potent strategy to enhance their pharmacokinetic and physicochemical attributes by fine-tuning potency, polarity, pKa-value, lipophilicity, and metabolic stability. But last time issue of high metabolic stability has been revised from harmful impact on human body and environment, so agrochemical and pharmaceutical corporation are seeking for a new fluorine containing substituent with aim to decrease its stability. So, goals of this investigation are workout new building blocks where trifluoromethyl was replaced by dialkylfluoro methane recidue for medicinal chemistry purposes and investigate their metabolic stability as well as biological properties. Representative modification of Enasidenib:



Toward the Total Synthesis of Bioactive Prenylated Indole Alkaloids

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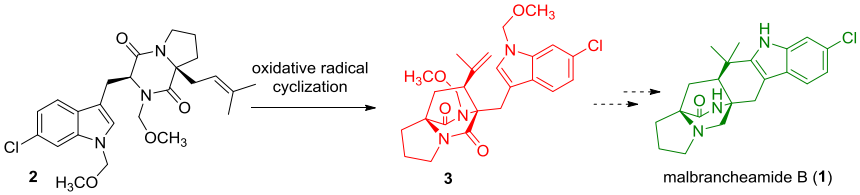
Prenylated indole alkaloids are a broad class of secondary metabolites isolated from different species of terrestrial and marine fungi.[1] These compounds exhibit unique structural features, such as a three-dimensional bridged diketopiperazine system containing a diazabicyclo[2.2.2]octane core. The wide range of biological activities displayed (anthelmintic, cytotoxic, antibacterial, insecticidal etc.) and the challenging structure make prenylated indole alkaloids attractive targets in total synthesis.



In this work, an asymmetric total synthesis toward malbrancheamide B (**1**) will be presented. The key step is an oxidative radical cyclization of diketopiperazine **2,** which is synthesized from enantiopure amino acid derivatives; the resulting olefin **3** will serve as a convenient precursor of **1**. The same method can be employed using other adequately substituted substrates to obtain different bioactive prenylated indole alkaloids.

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Synthesis and Citotoxicity of Novel C-Ring Substituted PBDs

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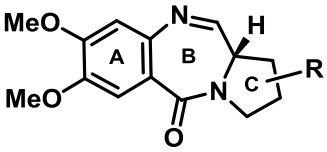
Antibody drug conjugates (ADCs) have seen a lot of success in clinical trials and are one of the fastest growing drug classes in oncology.[1] Among the various ADC payload scaffolds pyrrolobenzodiazepines (PBDs) stand out due to their ability to covalently bind to the minor grove of DNA, leading to potent cytotoxicity. The limited diversity of available payloads for ADC development makes PDBs an attractive target from a medicinal chemistry perspective. By expanding the repertoire of available PBD derivatives, we aim to contribute to the development of more effective and targeted ADC therapies. In this contribution, synthesis of novel C-ring substituted PBDs and evaluation of their cytotoxicity in various cell lines will be presented.



Acknowledgements
Recovery and Resilience Facility (RRF) (5.2.1.1.i.) grant Nr.08/OSI/ZG

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Changing the Mode of Cyclization: Highly Promiscuous Sesquiterpene Cyclase BcBOT2 Promotes 1→6 Cyclizations

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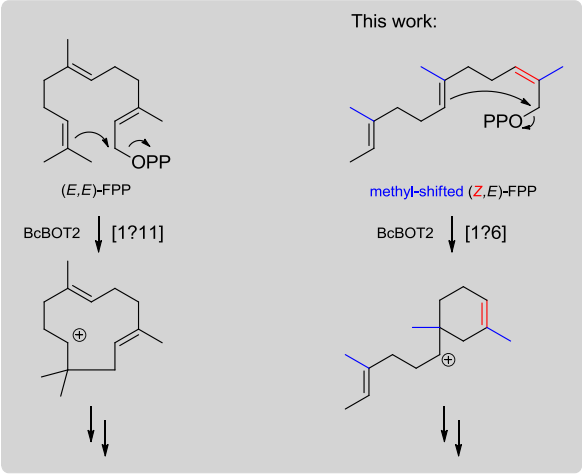
In recent years, terpene cyclases (TCs), unique enzymes that are able to control carbocationic cascade reactions in terpene biosynthesis, have attracted interest in chemobiosynthetic transformations using unnatural substrates to access new terpene backbones. This combinatorial synthesis approach, consisting of chemical synthesis and biotransformation, provides a rapid pathway to diverse cyclized carbon backbone structures in a stereo-selective manner. Prior to this, novel linear terpenes must be synthesized to serve as substrates for the biotransformation.



In this study, both methyl-shifts and double bond isomers of (*E,E*)-FPP are employed to alter the initial cyclization pattern of BcBOT2 from 1→11 to 1→6. Certain synthesized unnatural (Z,E)-FPP derivatives decompose upon exposure to water, resulting in the formation of mono-cyclized alcohols.

Synthesis of 1*H*-Indole Derivatives through Aryl Triazole Ring Opening and Subsequent Cyclization

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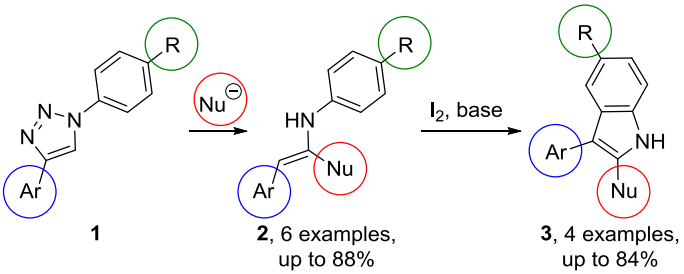
Synthesis of indole derivatives has been an active field of research for over a century, driven by the significant biological activities of these compounds.[1] Accordingly, chemists have continuously developed various methods for the preparation of new indole derivatives.[2]

We present a novel synthetic approach towards 1*H*-indole derivatives **3**. The synthesis begins with the triazole ring opening of compounds **1** using nucleophiles, resulting in the formation of enamines **2** that can be further cyclized into the desired indoles **3**.



1

2, 6 examples, up to 88%

3, 4 examples, up to 84%

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Synthesis of Analogues of Complex Natural Products for Anticancer Application

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[2] Institut Polytechnique de Paris
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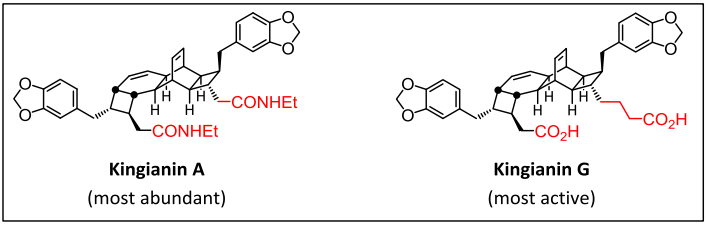
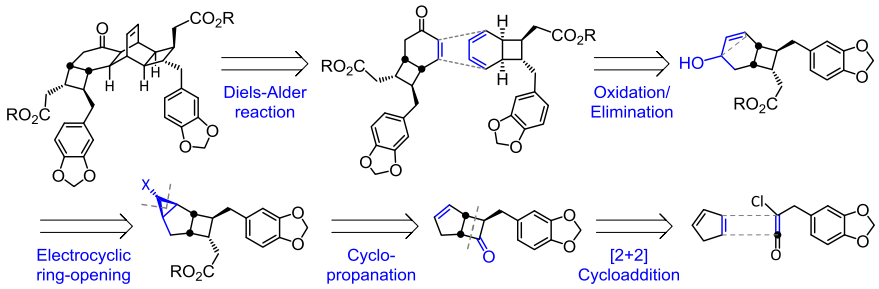
Kingianins are natural products isolated from *Endiandra kingiana*, an endemic tree from Malaysia. These molecules share a highly original and challenging pentacyclic skeleton. Their promising biological activities towards the anti-apoptotic proteins Bcl-xl and Mcl-1 could lead to the development of new anticancer therapies. Our approach addresses challenging selectivity problems, diastereocontrol, and flexibility.



Kingianin A
(most abundant)

Kingianin G
(most active)

Synthetic strategy :



CaC_2 – an Efficient Acetylene Surrogate for the Synthesis of Benzoazepine Derivatives *via* Cobalt Catalysis

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The benzoazepine motif is a common fragment present in naturally occurring alkaloids as well as various biologically active compounds.[1] A straightforward method to access benzoazepines would be C–H bond alkynylation of readily accessible unsaturated phenylalanine derivatives.

C–H bond functionalization using Co(II) salts in combination with bidentate directing group has attracted enormous interest in past decade.[2] Herein we report an efficient method for the synthesis of 3*H*-benzo[*d*]azepine derivatives *via* cobalt-catalyzed C–H alkynylation of α,β-unsaturated phenylalanine derivatives using CaC_2 as an acetylene gas surrogate and picolinamide as a directing group (Fig. 1).

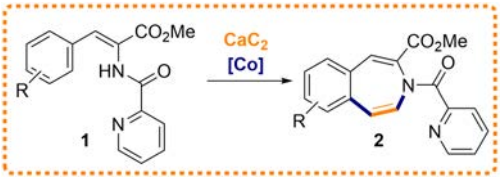

Figure 1. Benzo[d]azepine **2** synthesis *via* cobalt catalysis using CaC_2 as acetylene source.

Supervisor
Dr. Chem. Liene Grigorjeva

Acknowledgements
This research is funded by the Latvian Institute of Organic Synthesis internal grant Nr. IG-2024-03 and ANM_OSI_DG_01 doctoral career grant.

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Electrochemical Formation of Oxazolines by 1,3-Oxyfluorination of Non-Activated Cyclopropanes

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Cleavage of a cyclopropane C–C bond is a convenient way to obtain 1,3-difunctionalized products.[1] Several approaches towards cyclopropane C–C bond cleavage have been investigated, including electrochemical oxidation of cyclopropane. However, this approach is limited to aryl substituted cyclopropanes with sufficiently low oxidation potential to allow selective oxidation in the presence of other functional groups.[2]

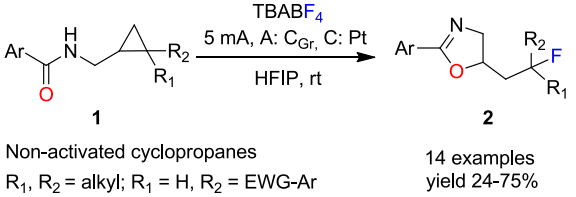

Figure 1. Electrochemical cleavage of cyclopropane C–C bond.

In this work, we have developed a method where anodically oxidized benzamide group in compound **1** induces cleavage of cyclopropane C–C bond, followed by fluorine atom transfer to form the final product **2**.[3] In our case, $TBABF_4$ proved to be an efficient fluoride source.

Acknowledgements
This project has been funded by Recovery and Resilience Facility (RRF) (5.2.1.1.i.) grant Nr. 08/OSI/DG.

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Synthesis of Diazahelicenes *via* Skeletal Editing

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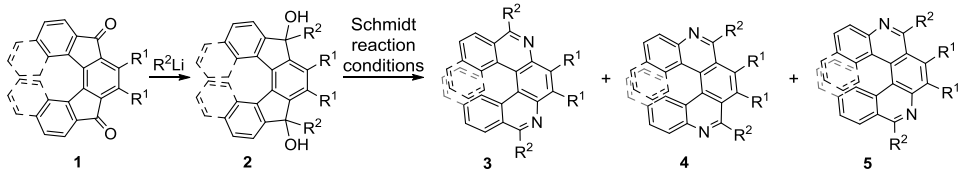
Helicenes are non-planar polycyclic aromatics composed of *ortho*-fused benzene rings. Incorporating heteroatoms in the helicenes scaffold, like nitrogen can significantly modulate their optical, electronic, and supramolecular properties.[1] Despite the importance of azahelicenes, their synthesis remains challenging, and there are currently only a limited number of methods available for producing azahelicene derivatives.

In this work, our attention was focused on developing a methodology for skeletal editing of indeno[2,1-*c*]fluorene-5,8-diones (**1**) to *m,n*-diaza[5]helicenes **3**–**5** using the Schmidt rearrangement,[2] exploring its regioselectivity, and expanding the method for the synthesis of highly enantioenriched *m,n*-diaza[7]helicenes.



Scheme 1. Transformation of diketones to diazahelicenes.

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Iridium-Catalyzed Hydrogenation of Pyridines

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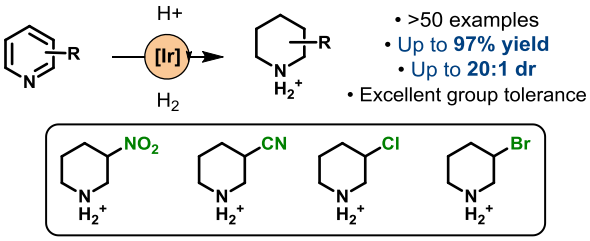
Herein, we report a homogeneous Ir-catalyst capable of performing the mild hydrogenation of a wide range of mono- and multi-substituted pyridines. The reaction proceeds with low catalyst loading using an acid co-catalyst to activate the pyridine. Our method gives access to a wide variety of substituted piperidines in excellent yields and good to excellent diastereoselectivities. Virtually any substitution pattern can be accessed with an unprecedently broad functional group tolerance that provides unique substrates, further proving the relevance of this strategy to access the undeniably valuable piperidine core.



Palladium(II)-Catalyzed Nondirected Late-Stage C(sp^2)–H Deuteration of Heteroarenes Enabled through a Multi-Substrate Screening Approach[1]

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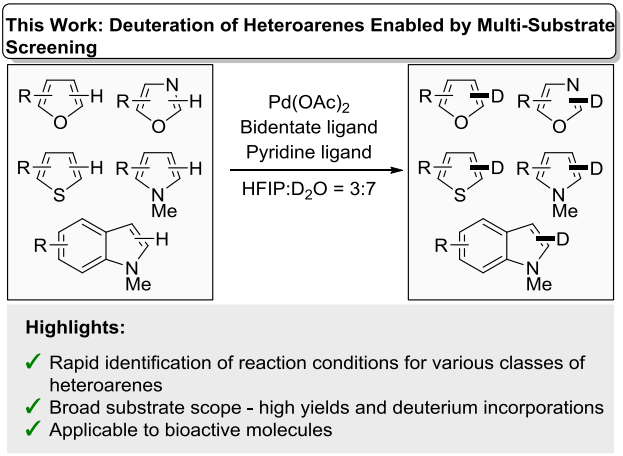
In this study we describe the use of a multi-substrate screening approach to identify optimal reaction conditions for different classes of heteroarenes from a minimal number of screening reactions. Using this approach, four sets of complementary reaction conditions derived from our dual ligand-based palladium catalysts for nondirected C(sp^2)–H activation were identified, that together enable the deuteration of structurally diverse heteroarenes, including bioactive molecules.



Acknowledgements
We thank Kiel University for generous support. This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 946044). S.K. thanks the Studienstiftung des deutschen Volkes for a doctoral fellowship.

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Et_3SiH and KO^tBu – Promote Unprecedented Rearrangements

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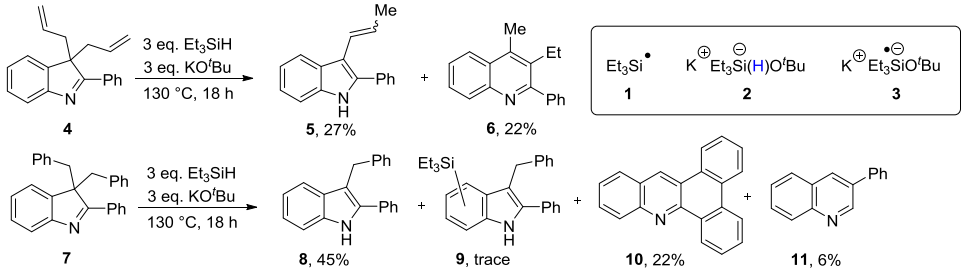
The combination of two simple reagents – Et_3SiH and KO^tBu – produces highly reactive intermediates **1**–**3** that promote a variety of mechanistic pathways resulting in unexpected products. The reagent pair generates the *triethylsilyl radical* **1**, the *silanate complex* **2** (which acts as a hydride donor as well as a hydrogen atom donor source) and the *tert-butoxytriethylsilyl radical anion* **3** (which is a powerful electron donor). Through studying the Et_3SiH and KO^tBu reagent system, we have discovered interesting rearrangements that exemplify the interactions and competitions between intermediates **1**, **2** and **3**. These transformations include the rearrangement of indolenines **4** and **7** to indoles **5** and **8** and quinolines **6**, **10** and **11**. This poster will aim to present and interpret this novel chemistry.[1]



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A Study of the Reactivity of Cyclic Aminomethylammonium Mannich Salts

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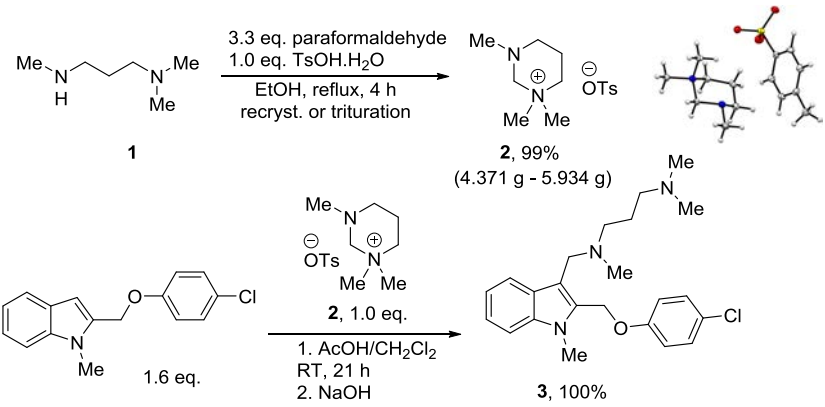
A new approach for the preparation of diamine products was developed utilising novel Mannich-type salts (**2**) featuring a $R_2NCH_2NR_3^+$ moiety.[1] The developed methodology showed good nucleophile scope and was successfully employed in reactions under basic, acidic, and neutral conditions. An array of diamine products was successfully synthesised, including the bioactive neuropeptide Y receptor antagonist (**3**).



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Unlocking Versatile Access to Planar Chiral [2.2]Paracyclophanes through Organocatalytic Desymmetrization

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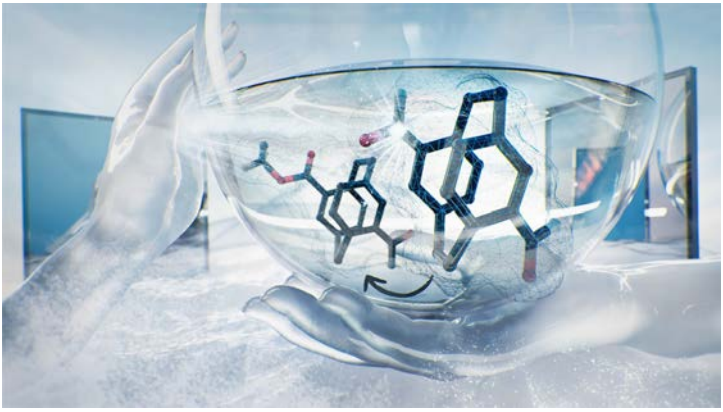
Planar chiral [2.2]paracyclophanes, composed of two functionalized benzene rings connected by two ethylene bridges, have wide-ranging applications in asymmetric synthesis and materials science. However, obtaining both enantiomeric forms currently relies mainly on less efficient chiral separations or kinetic resolutions. Here, we introduce a straightforward, efficient, and metal-free protocol for the organocatalytic desymmetrization of prochiral diformyl[2.2]paracyclophanes. Our detailed experimental mechanistic study, combined with various subsequent applications, demonstrates the versatility of this innovative approach.



Acknowledgements
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Synthesis Development and Comprehensive Study of Thiazol-Orange-Based DNA Chemosensors

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The use of DNA-binding fluorogenic chemosensors, such as the Thiazole Orange (TO) derivatives provides inexpensive and noninvasive means for the detection and quantification of DNA. These DNA-binding dyes are used in several techniques within life sciences (e.g. fluorescent microscopy, flow cytometry, PCR assays), but the choice of the most appropriate DNA dye for a certain application might be challenging.
Our study presents a comprehensive overview of five known and one novel TO-based DNA chemosensors from the aspects of synthetic availability, spectroscopical properties, and PCR applicability, while providing a detailed explanation of their fluorogenic behaviour underpinned by quantum chemical calculations.

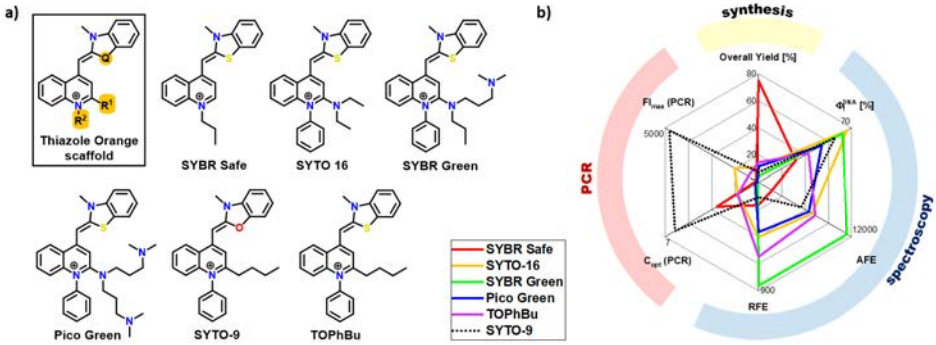

Figure. a) The Thiazole Orange scaffold and its six derivatives included in our study; b) most important characteristics of the selected DNA chemosensors.

Gold-Catalyzed Selective Synthesis of Polycyclic Frameworks Containing Tricyclic Bridgehead Carbon Centers

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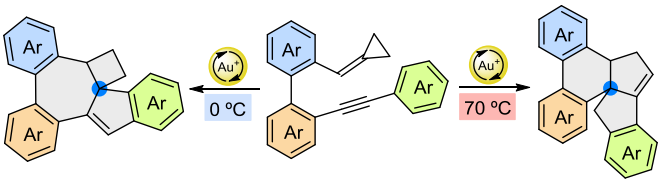
Spirocyclic compounds in which two or more rings are connected by a single quaternary carbon constitute a specific motif which is frequently found in bioactive natural and synthetic products. This kind of structures are in line with the recent interest on incorporating sp^3 carbon atoms in molecules intended for drug discovery.[1]

On the other hand, gold catalysis is currently a powerful tool for organic synthesis with applications in total synthesis and materials science. Specifically, gold catalysts are highly useful for the assembling of cyclic frameworks of different sizes and complexity.[2]

In this work, we report the selective synthesis of two different frameworks that include tricyclic bridgehead carbon centers, based on the gold-catalyzed 7-*exo-dig* cyclization of alkynylbiaryls bearing a methylenecyclopropane unit.



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Metal-Free Borylative Cyclizations of Enynes: Useful Methodologies for the Synthesis of Borylated Polycycles

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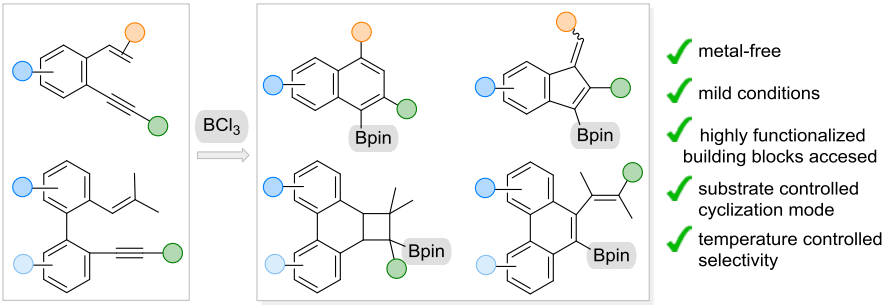
Organoboron compounds are highly useful intermediates for organic synthesis. Borylative cyclizations of enynes offer an interesting alternative to classical methods for their synthesis, as they provide a rapid increase in molecular complexity by the simultaneous formation of a carbocycle and a C–B bond under mild conditions. Metal-free borylative cyclizations are particularly attractive. However, metal-free borylative carbocyclizations have been scarcely described.

Herein we report the selective synthesis of various borylated polycycles by BCl_3-promoted metal-free borylative cyclizations of aryl- and biaryl-embedded enynes.[1]



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Design and Synthesis of Tailored Multisubstituted Cyclopentadienes

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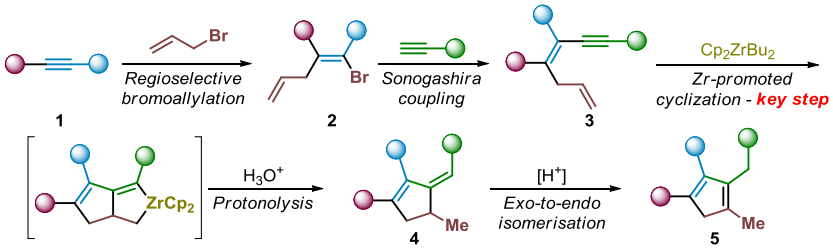
In this work, a methodology for the preparation of multisubstituted cyclopentadienes through several convergent synthesis steps was developed. This strategy allows selective introduction and size-variation of functionalities on the cyclopentadienyl ring. The synthetic pathway begins with the regioselective bromoallylation of disubstituted alkynes **1**, yielding the corresponding bromodienes **2** with a reactive carbon-halogen bond.[1] This is crucial for performing the Sonogashira reaction with terminal acetylenes to generate non-conjugated dienynes **3**. Cyclization of dienynes with low-valent zirconium compound (Negishi reagent) resulted in cyclopentenes **4** with a pendant *exo*-cyclic double bond. In the final step, acid-catalyzed *exo*-to-*endo* double bond isomerisation afforded cyclopentadienes **5** (Scheme 1).



Scheme 1.

Acknowledgements
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Synthesis and Transformation of 3-((4-Acetylphenyl)-(4-(4-substituted phenyl)thiazol-2-yl)amino)propanoic Acids

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The aim of this study is to synthesize potentially biologically active 3-((4-acetylphenyl)(4-(4-substituted phenyl)thiazol-2-yl)amino)propanoic acid derivatives.

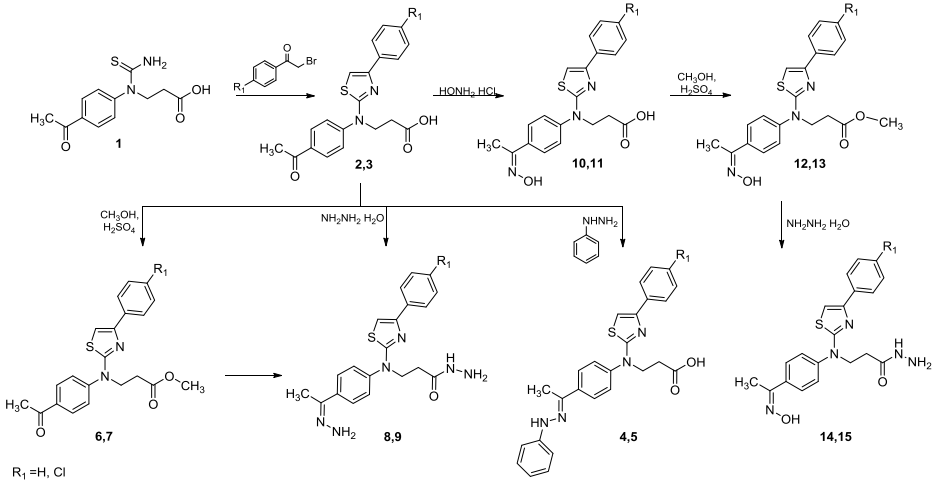

Figure 1. Synthesis of 3-((4-acetylphenyl)(4-(4-substitutedphenyl)thiazol-2-yl)amino)propanoic acid derivatives.

Oximes, esters, hydrazides and hydrazones of compounds **2**, **3** were successfully synthesized, and compounds **2**–**15** are now being tested for anticancer and antimicrobial activity.

Synthesis and Derivatization of Highly Modifiable Pyran-2-ones

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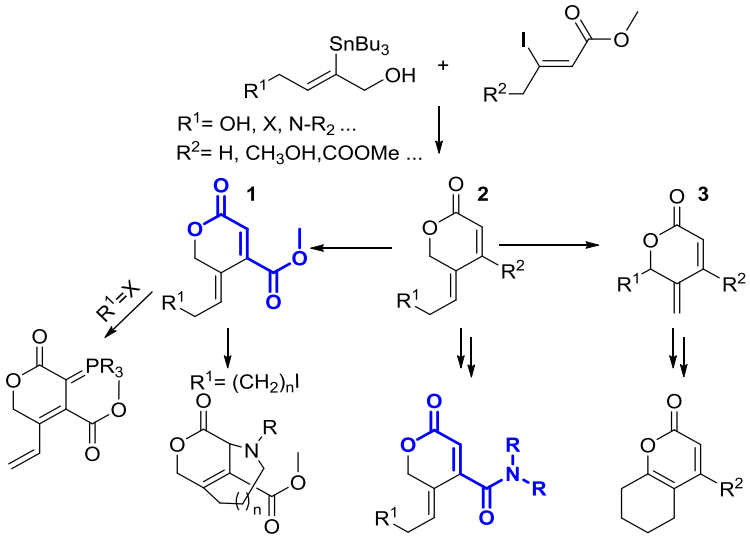
Mehtod utilizing Stille coupling developed by us,[1] leads to an efficient synthesis of highly modifiable pyranones **1**–**3**, some of which contain dimethyl fumarate fragment. DMF, is a naturally occurring compound produced by *Fumaria officinalis* with immunosuppressive properties. Recently, some of its lactone enlocked analogues shown enhanced effects and tolerability by the organism.[2] Derivatization of molecules prepared could also lead to a synthesis of other bioactive natural coupounds, their analogues and various azide carriers.

Scheme 1. Synthesis of pyran-2-ones and their subsequent derivatization



Acknowledgements
This work was supported by Charles University (SVV 260661, GAUK 149124) and Czech Science Foundation (Project No. 22-19209S).

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Modular Synthesis of Arene-Fused Cyclooctadienes *via* Bidentate Lewis Acid-Catalyzed Inverse Electron-Demand Diels-Alder Reaction

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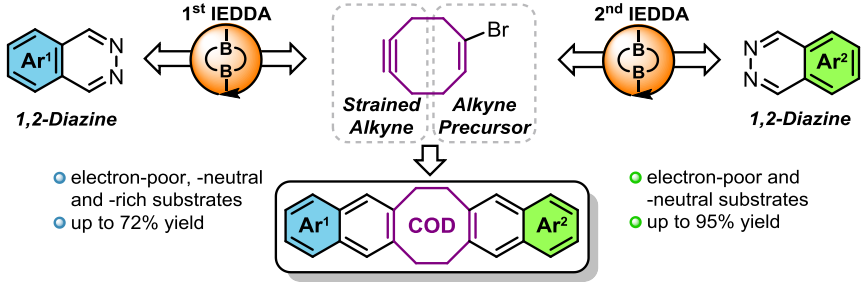
Arenes fused to eight-membered carbocycles have recently received considerable attention in various fields such as photonics,[1] molecular electronics[2] and polymer science.[3] Herein, we report a modular approach for the synthesis of arene-fused cyclooctadienes (CODs) utilizing two sequential inverse electron-demand Diels–Alder (IEDDA) reactions of 1,2-diazines and cyclooct-1-en-5-yne derivatives. By employing a boron-based bidentate Lewis acid catalyst, various readily available phthalazines can be used in this transformation giving rise to diversely functionalized π-systems linked via a flexible COD tether.



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Synthesis and Dynamics of Deuterium Labelled Acylceramides

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Acylceramides (acylCer) are essential components of human skin, necessary for the correct skin barrier function. Despite their importance there is little known about their mobility in skin. To study molecular dynamics using solid state NMR, specific labelling in molecules is required. In this project we focused on synthesis of acylCer with deuteration in their ultralong chain (C2–C16 and C17–C32).

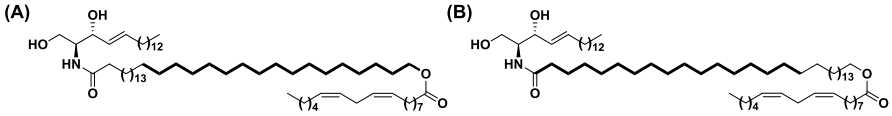

Figure 1. Molecule of acylCer with deuteration in rear (A) and front (B) half.

Synthesis started with perdeuterated γ-butyrolactone and 1,12-dibromododecane which were modified and connected via a Wittig reaction providing 16C deuterated fragment. After modifications, this 16C fragment underwent second Wittig reaction with 16C nondeuterated molecule, providing thirty-two carbon long chain with deuteration in frontal or rear part. This precursor was then esterified with linoleic acid and connected with sphingosine to form the final molecules. Whole synthesis was performed in 17 steps with yield of 2% for acylCer with deuteration in the rear half of ultralong chain (A) and in 12 steps with yield of 0.5% for acylCer with deuteration in front half (B). These modified acylCer were then mixed with other skin lipids and studied in model lipid membranes. Using acylCer with labelling in different positions we found out that: rear half of chain is more mobile (27% of crystalline phase) compared to front part (53% of crystalline phase).

Alkyne-Tagged Imidazolium-Based Membrane Cholesterol Analogs for Raman Imaging Applications

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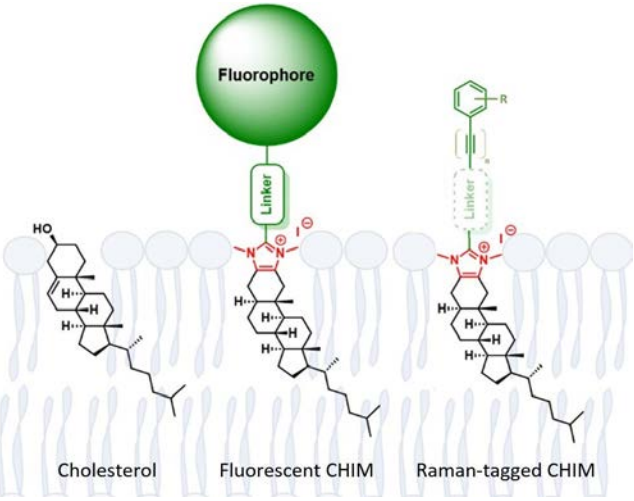
Cholesterol is an important lipid playing a crucial role in mediating essential cellular processes as well as maintaining the basic structural integrity of biological membranes. Due to its vast biological importance, strategies to investigate cholesterol-mediated biological processes are of high interest.
In our work, we report a series of alkyne-tagged imidazolium-based cholesterol analogs (CHIMs). The elaborate design of our analogs allows for – even multiplexed – cellular Raman imaging in HEK cells.



In contrast to other conventionally used fluorescent analogs, our Raman-tagged sterol analogs offer the advantage of being visualizable without the need for a bulky dye that potentially affects natural membrane integration and cellular interactions. Therefore, we envision Raman-tagged CHIM analogs to be a promising tool for the investigation of cholesterol-mediated cellular processes complementary to other established methods, such as the use of fluorescent analogs.

Quantum-Chemical Multiple Ligands Simultaneous Docking to Cholinesterases Using Deep Reinforcement Learning

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Alzheimer's disease is a severe and incurable neurological disease[1] characterized by the loss of an individual's cognitive abilities and presents one of the leading causes of death in the world.[2] According to the cholinergic hypothesis,[1] the concentration of the neurotransmitter acetylcholine, which plays an important role in both the peripheral and the central nervous system, is reduced in the brains of affected individuals. Since cholinesterases hydrolyze acetylcholine, to increase its concentration in the brain of sick people, currently acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitors are used as therapeutics.

This study aims to find the best common inhibitor of AChE and BChE by quantum-chemical multiple ligands simultaneous docking. A newly developed parallelized *Monte Carlo* algorithm for sampling the huge configurational spaces was used for structure generations.[3] The binding energies of docked molecules were calculated by quantum-chemical calculation of the entire target and one or multiple ligands. The potential energy surfaces for the configuration spaces were gradually described by trained deep neural networks using the deep reinforcement learning algorithm and subsequently used to calculate binding energies. This procedure enabled a larger sampling of the configurational space ensuring the proper coverage of the active sites.

Acknowledgements
This work was supported by the Croatian Science Foundation Project IP-2022-10-9525: Target-guided synthesis of cholinesterase inhibitors supported by machine learning.

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Selective Deprotection of Ester Groups in Pyranoses with *Candida Antarctica* Lipase-B

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Natural compounds containing saccharides form glycosidic bonds in specific positions. Generally, several protecting groups are involved for selectively leaving one position in a saccharide unprotected. This strategy relies on the chemical and physical differences of the protecting groups as well as the slight differences in reactivity of the saccharide hydroxyl groups.[1] Enzymes often require an aqueous buffer and work in a narrow range of conditions. However, there are some enzymes like *Candida antarctica* Lipase-B (CAL-B), that work well in organic media and tolerate relatively high temperatures.[2,3] Immobilized CAL-B, Novozyme N435, can be used with high selectivity in transesterification reactions with saccharides. We have shown that glucose-based monosaccharides are deacetylated mainly in the fourth and sixth position.[4] Several new trends have been found, where not only different epimers react differently, but also anomers of the same saccharide.

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Blue-Light Induced 1,2-Chloro-*N*-Cl-amination of Olefins Using *N,N*-Dichloro-*tert*-butylcarbamate Reagents

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Direct amination of olefins has gathered a lot of attention in the recent years, as nearly all modern materials and pharmaceuticals contain nitrogen. Herein we introduce a new functionalization tool allowing the direct installation of nitrogen atoms to olefinic molecules in a streamlined fashion by activation of N–Cl bonds using visible blue light. The mechanistic studies suggest that dichlorocarbamates undergo a photochemical excitation to yield a nitrogen and a chlorine radical which then react with the olefinic double bond.[1]

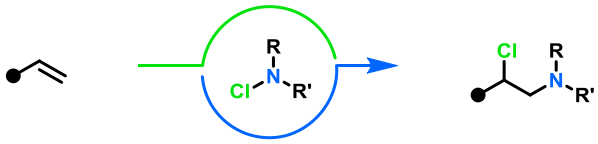

Figure 1. New blue light induced method allows direct installation of nitrogen to olefinic compounds in a streamlined fashion.

Acknowledgements
Academy of Finland, Emil Aaltonen Foundation.

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Constructing of a Tricyclic Substructure of the Phragmalin-Type Natural Compounds

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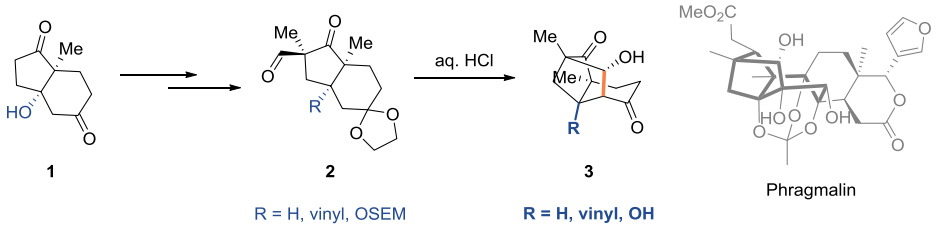
Phragmalin-type limonoids are natural products that demonstrate a wide range of biological effects[1] and possess an unusual octahydro-1*H*-2,4-methanoindene cage structure (Scheme 1, bolded), whose synthetic strategies prior to this work were limited to racemic versions.[2] The Hajos–Parrish ketol (**1**) has been chosen as the starting material for the synthesis of key intermediate **2**. Subsequently, through the aldol reaction (Scheme 1), aldehyde **2** can be converted into the product **3** with distinctive cage framework.[3] In this work, our emphasis was on introducing the hydroxy group or its precursor (vinyl moiety) at the 3a position.



Scheme 1. The new routes toward the methanoindene derivatives.

Acknowledgements
This work was supported by LIOS internal student grant IG-2024-06. We thank Dr. chem. M. Skvorcova for theoretical and practical consultation and Dr. S. Belyakov for the X-ray structure analysis.

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LC-MS Profiling of Dynamic Covalent Library During Mono-Biotinylated Hemicucurbit[8]uril Solid-State Synthesis

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Cyclohexanohemicucurbit[*n*]urils (cycHC[*n*], *n* = 6, 8) are chiral molecular containers, which can be prepared with the aid of mechanochemistry. The new mono-biotinylated hemicucurbit[8]uril (mixHC[8]) is assembled in a multi-component solid-state reaction. The ball-milling step generates a complex dynamic covalent library containing various linear and cyclic oligomers, and is followed by aging to afford the target macrocycles. LC-MS analysis describes the changes in the system depending on the milling duration and aging. Identification and mapping of the intermediates and products provide a mechanistic insight into the self-organization processes occuring in the solid state (Fig. 1).

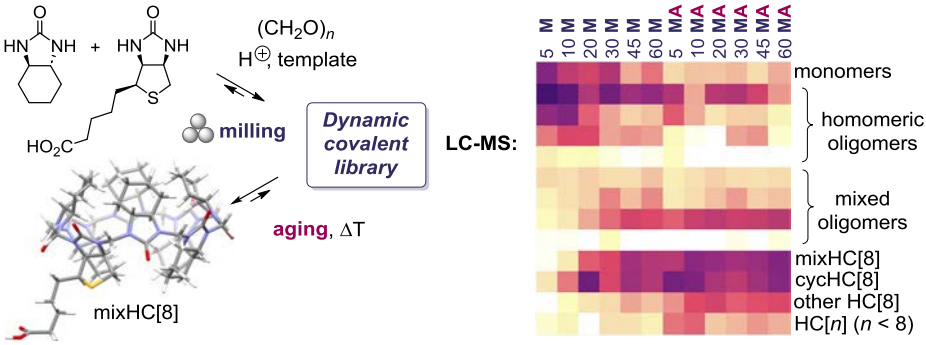

Figure 1. General scheme of mixHC[8] synthesis and heat map describing the reaction mixtures (M – milled; MA – milled and aged samples).

References

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Syntheses of New Antiviral Rocaglates by Modification of Ring A

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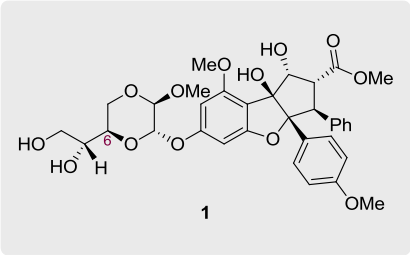
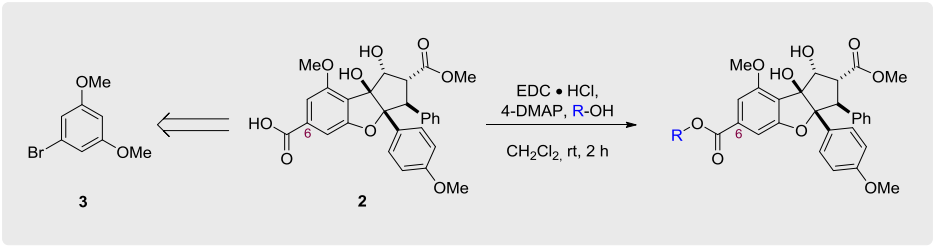
Rocaglates are naturally occurring compounds that belong to the flavaglines. In 2004 (−)-silvestrol (**1**) was isolated from the *Aglaia* plant, which was especially interesting because of its unsusual dioxanyloxy moiety.



1

Our group focuses on the synthesis of new rocaglate derivatives. The synthesis is based on previous work of our group, which included an effective synthetic route towards carboxylic acid **2** starting from 1-bromo-3,5-dimethoxybenzene (**3**). Our aim is to synthesize different esterified rocaglates at position C-6 on ring A of the rocaglate framework. Furthermore we try to mimic the silvestrol substituent at C-6 by attaching different hydrogen bond donors at this position. The biological assays are carried out by cooperation partners at the Ruhr-University Bochum.



3 **2**

Sulfur-Specific Alkylation of Sulfinamides by Zn Carbenoids

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Relatively scarcely represented in chemical research before 2000, sulfoximines have recently experienced an exponential growth in popularity. While remarkable progress has been achieved in asymmetric synthesis of this versatile moiety, the overwhelming majority of current approaches ultimately target only *N*H-sulfoximines. On the other hand, a chiral substituent at the *N*-atom could be obtained *via* *S*-selective alkylation of readily accessible Ellman's sulfinamide derivatives. Although the latter generally undergo *N*-specific alkylation, we serendipitously discovered that Zn carbenoids react exclusively at the *S*-atom. This novel transformation significantly expands the diversity of currently available sulfoximines and offers promising opportunities in drug design.

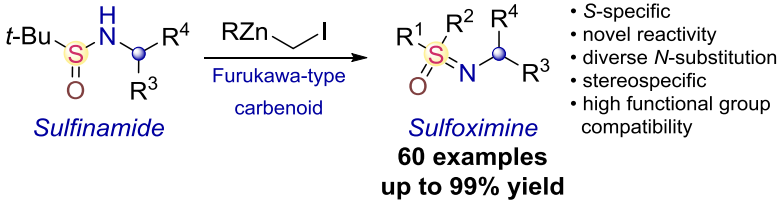

Figure 1. Reagent-controlled *S*-specific alkylation of sulfonamides.

Acknowledgements
This project was funded by the Latvian Council of Science; project LZP-2021/1-0578.

Enantioselective [8+2] Cycloadditions of Photogenerated Ketenes

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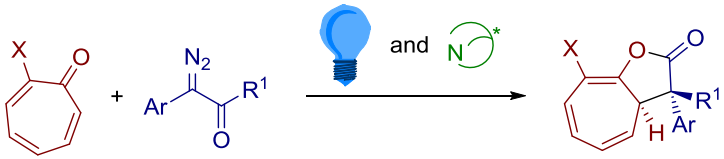
Nominated to present this work as a short talk on July 9, 14:15

Cyclic structures are prevalent in numerous natural products and can efficiently be synthesised via well-developed cycloaddition reactions of alkenes. The application of longer polyenes in corresponding higher-order cycloadditions (HOCs) is more problematic due to a combination of issues with regio-, stereo-, and periselectivity. Gratefully, with the advent of asymmetric organocatalysis great progress has been made in recent years.[1] Herein we wish to demonstrate the use of diazoketones as precursors for photochemically generated ketenes in asymmetric organocatalytic HOCs for the synthesis of 7,5-fused heterocyclic compounds.



Scheme 1. Organocatalytic cycloaddition of photogenerated ketenes.

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Development of a Continuous Flow Grignard Reaction to Manufacture a Key Intermediate of Ipatasertib

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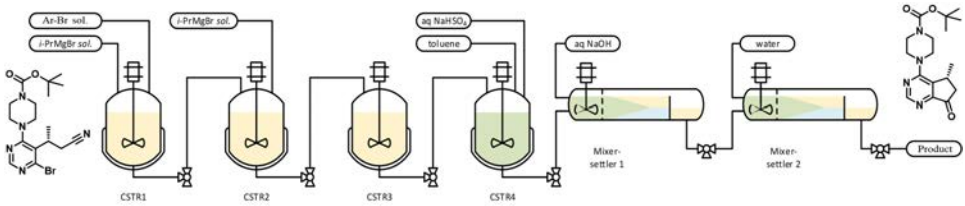
Nominated to present this work as a short talk on July 9, 14:30

This work outlines the development of a continuous flow process for the manufacture of a key intermediate of the active pharmaceutical ingredient ipatasertib for the treatment of metastatic castration-resistant prostate cancer and triple-negative metastatic breast cancer. The reaction sequence incorporates multiple telescoped unit continuous operations, including a Br/Mg exchange reaction leading to intramolecular cyclization of the magnesium species onto a neighboring nitrile group to form a five-membered ring in 5-*exo*-*dig* fashion. The product from the reaction mixture is obtained after continuous aqueous acidic hydrolysis, neutralization/extraction, water wash, and phase separation. Each of these unit operations took place in a cascade of continuous stirred tank reactors. The control strategy was refined via a series of continuous lab studies at 20 g/h using a Design of Experiments approach to define process parameter ranges and to help identify any criticality therein. The learnings from this laboratory study served as a basis for the construction of a suitable pilot-plant facility, where the control strategy was verified at a representative manufacturing scale of about 1.0 kg/h.



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Synthesis of 3-((4-Hydroxyphenyl)amino)propanoic Acid Derivatives as Promising Antimicrobial and Anticancer Candidates

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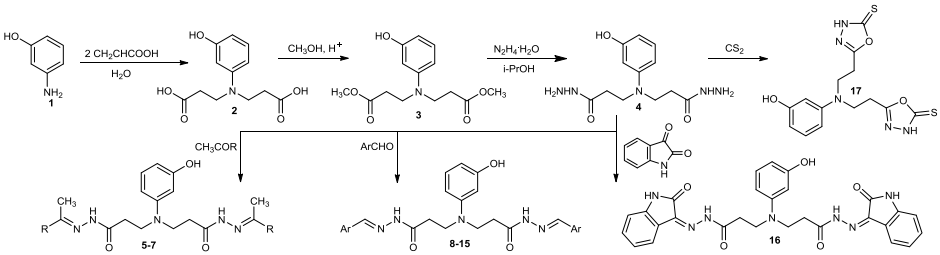
Numerous compounds containing the phenolic (3-hydroxyphenyl) moiety are widely recognized for their potent biological activities.[1]



5 R=CH_3; **6** R=C_2H_5; **7** R=C_6H_5; **8** Ar=C_6H_5; **9** Ar=2,4-F-C_6H_3; **10** Ar=4-NO_2-C_6H_4; **11** Ar=4-Cl-C_6H_4; **12** Ar=4-$(CH_3)_2N$-C_6H_4; **13** Ar=3,4,5-$(OCH_3)_3$-C_6H_2; **14** Ar=1-naphthyl; **15** Ar=2-naphthyl.

Figure 1. Synthesis of β-alanine derivatives.

The reaction of 3-aminophenol (**1**) with acrylic acid in water at reflux afforded diacid **2**. In continuation of our interest in the chemistry of *N*-substituted β-amino acids, dimethyl ester **3** was synthesized through esterification of compound **2**. Dihydrazide **4** was obtained through hydrazinolysis of dimethyl ester **3** in propan-2-ol under reflux. In the next stage of the work, condensation reactions of dihydrazide **4** with various carbonyl compounds were performed, during which a whole series of hydrazones **5**–**16**, as well as oxadiazole **17** were synthesized. The compounds demonstrated promising structure-depended biological activity.

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Development of Reversible Covalent Inhibitors for Plasmodium Serine Protease SUB1

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Malaria is a disease caused by the *Plasmodium* parasite – a unicellular organism which infects and replicates in human erythrocytes. A subtilisin-like serine protease SUB1 is crucial in the parasites escape from the infected cell making it an attractive anti-malarial drug target. Previously we reported that boronic acid **1** acts as an inhibitor of SUB1 by forming a covalent reversible bond with a serine residue in the catalytic site of the enzyme.[1] In this work we decided to depeptidize the $\mathbf{P_1}$-$\mathbf{P_2}$ position to modify the physiological properties of compound **1** (Fig. 1).

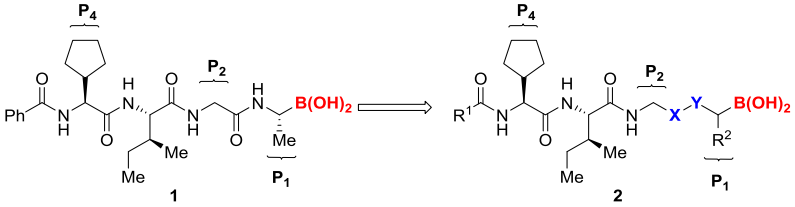

Figure 1. Depeptidization of P_1-P_2 position.

Acknowledgements

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Synthesis of Bipyrazole Derivatives and Evaluation of their Biological Properties

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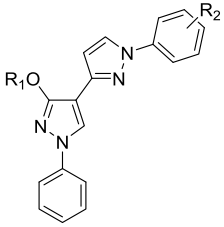
Pyrazole derivatives have many biological properties, including anticancer, antimicrobial, anti-inflammatory, antitubercular, and antioxidant effects.[1] They play a crucial role in drug discovery.[2] In this work, we present the efficient synthesis of bipyrazole derivatives from pyrazole-4-carbaldehyde and their biological activities.



Acknowledgements
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Total Synthesis of Drimentines and their Analogues

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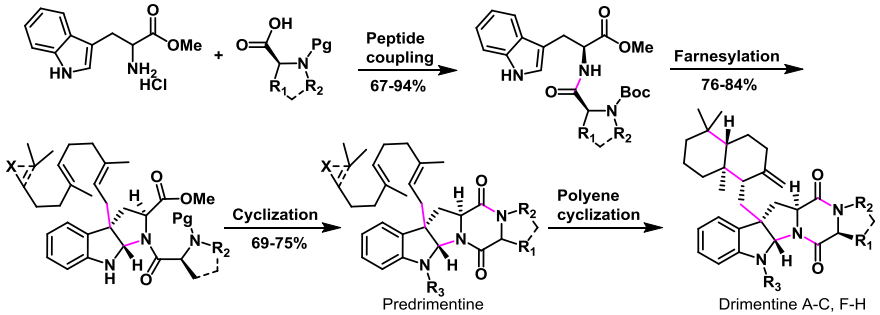
Drimentines are a class of terpenoid containing alkaloids with interesting pharmaceutical properties. These molecules exhibit activity against cancer, parasites, bacteria and fungi. Drimentines are secondary metabolites produced by Actinomycetes.[1]



Published works include an incomplete total synthesis and a tedious ≥12-step synthesis that provided milligram quantities of several drimentines. Our strategy is the total synthesis of all drimentines in as short as 5-steps that also allows for synthesis of non-natural analogues. Investigation into the challenging key step reveals that, depending on the conditions, the polyene cyclization cascade reaction gives products either at a monocyclic stage or as a bicyclized decalin.

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Aquaphotocatalysis Enabled Dearomative [2+2] Cycloaddition to Access Alkyl SuFEx Hubs "on-Water"

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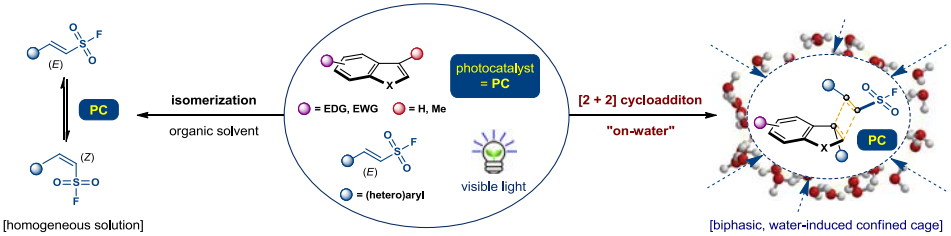
Sulfur(VI) fluoride exchange (SuFEx) has been regarded as a remarkable class in click chemistry during the last decade. Developing organic photocatalysis that allows access to new structures while retaining the sulfonyl fluoride group is of significant interest. In this context, constructing alkylated S(VI) building blocks through sustainable catalytic methods to establish a new SuFExable library will be a crucial approach to satisfying the demands of modern organic chemistry. In this presentation, we report a dearomative [2+2] cycloaddition to access alkyl SuFEx hubs "on-water". The transformation is likely to proceed *via* an energy-transfer mechanism through visible-light mediated aqua photocatalysis, which is accelerated by the high-pressure-like effect of bulk water as a reaction medium. In contrast, conventional organic solvents proved inefficient, resulting in the inevitable photo-isomerization of the starting material.[1]



Acknowledgements
The generous support of the Ministry of Science, ICT and Future Planning of Korea (2020R1C1C1006440, 2019R1A6A1A10073079, RS-2023-00259659, and RS-2023-00219859) is gratefully acknowledged.

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Borylated Cyclobutanes *via* Thermal [2+2] Cycloaddition

K. Prysiazhniuk, O. P. Datsenko, O. Polishchuk, S. Shulha, K.Gudzikevych, O. Kolodiazhna, V. Kubyshkin, P. K. Mykhailiuk

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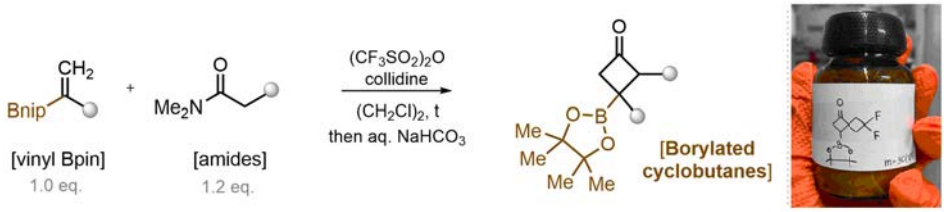
Small aliphatic rings attract a considerable attention in the contemporary research.[1] For example, the cyclobutane ring is common within modern bioactive compounds, and can be found in the structures of at least ten market-approved drugs.[2]
In this work, we elaborated a thermal [2+2] cycloaddition between vinyl boronates and *in situ* generated keteniminium salts. This practical approach allows the preparation of borylated cyclobutanes in one step.



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Towards Reliable pK_a Values of Carboxylic Acids in Non-Aqueous Solutions

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The pK_a values of compounds in various solvents are crucial for rationalizing and predicting numerous chemical processes. The availability of pK_a data differs significantly between solvents.[1] When it comes to the quantity, diversity, and quality of accessible pK_a data, dimethyl sulfoxide (DMSO), dimethyl formamide (DMF), and acetonitrile (MeCN) stand out from most other aprotic non-aqueous solvents.[2] However, the quality of pK_a data for carboxylic acids in these solvents has a room for improvement. There are numerous cases when published pK_a values of carboxylic acids from different groups differ by more than an order of magnitude. The present research aimed to obtain reliable pK_a values for a set of carboxylic acids with a wide range of pK_a values in the polar aprotic solvents: MeCN, DMSO and DMF. Acids with reported pK_a values in these solvents, as well as acids with unpublished pK_a values, will be included in this work.

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Synthetic Development of Locked GFP Chromophore: Excellent Flourophores for Microscopy

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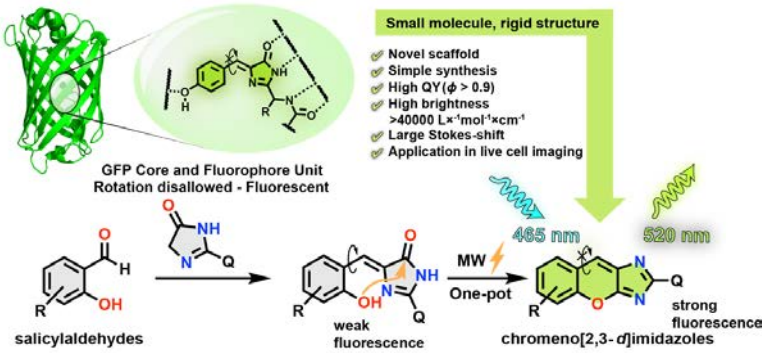
In this work, the synthesis and application of a novel heterocyclic scaffold inspired by the chromophore of the Green Fluorescent Protein was presented. These derivatives have bright fluorescence and a relevant Stokes-shift. The synthesis using a new ring-closure reaction and the detailed spectroscopical characterization and optimization of the probes for 450–480 nm excitation is reported. The utility of the new fluorophore is demonstrated in different biological applications.



Acknowledgements
The research was supported by the 2018-1.3.1-VKE-2018-00032, TKP2021-EGA-42, -NVA-14, 2020-1.1.5-GYORSÍTÓSÁV-2021-00004 and KFI-18-2018-00097 grants.

Application of the Chiral Epoxyimine in Diastereoselective Synthesis

Vadims Kovada, Edgars Suna

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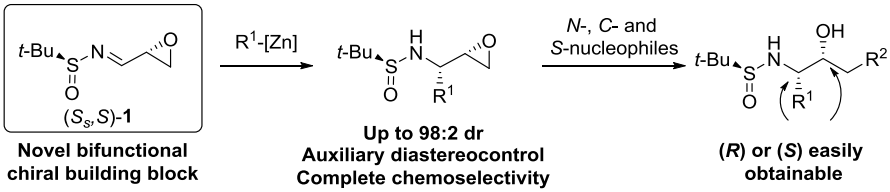
Epoxyimine (S_S,*S*)-**1** is a novel bifunctional building block containing two orthogonal electrophilic fragments. Chemo- and diastereoselective addition of organozinc reagents to the imine of (S_S,*S*)-**1** followed by opening of epoxide ring with *N*-, *C*- and *S*-nucleophiles provides simple access to diverse enantiopure scaffolds. Medicinal relevance of the latter is demonstrated by a rapid synthesis of a clinically used anti-HIV drug darunavir from epoxyimine (S_S,*S*)-**1**.



Acknowledgements

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Total Synthesis of Polyphenolic Compounds: Nostotrebin 6 and Its Analogues

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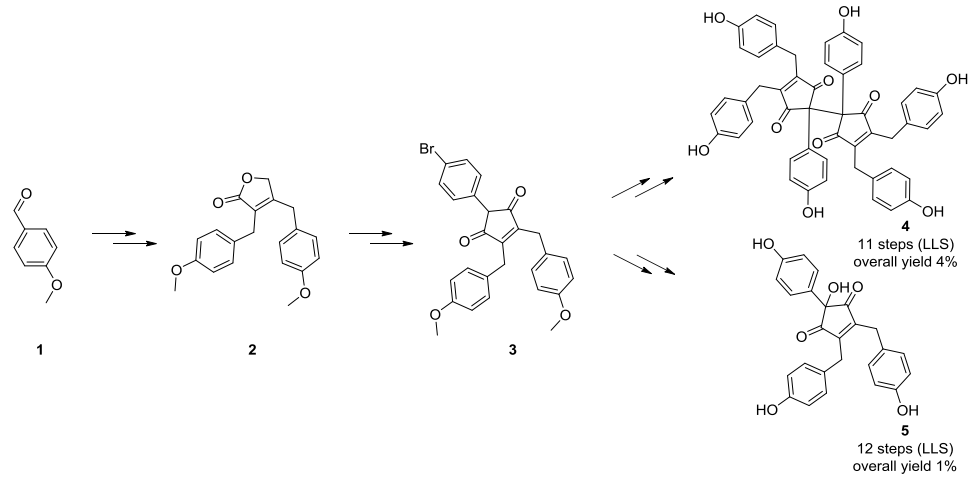
Nostotrebin 6 (Scheme 1; **4**) is a polyphenolic compound isolated from the cyanobacterial strain *Nostoc* sp. It has various biological activities, such as antimycobacterial and antibacterial.[1] We have established robust synthetical procedure starting from anisaldehyde (**1**), therefore, total syntheses of nostotrebin 6 and its monomeric derivative nostotrebinol 3 (**5**) were successfully achieved. Ongoing research includes the evaluation of biological properties of these compounds and their derivatives.

Scheme 1



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The Development of Electro-Organocatalytic Enantioselective Cascade Michael Reaction

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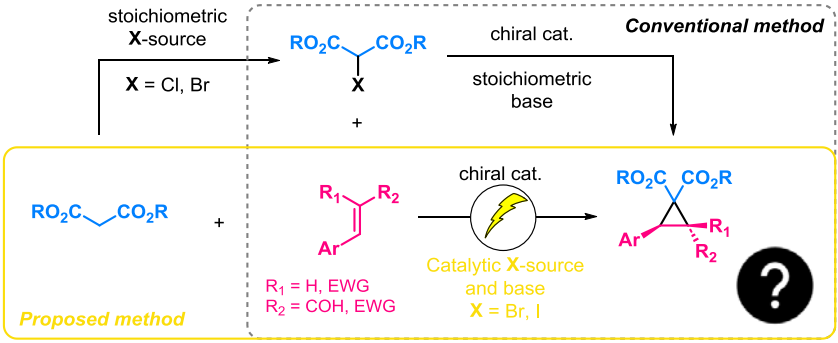
Cyclopropanes are found in natural products, pharmaceuticals, and agrochemicals, and they are valuable as synthetic building blocks. One way to synthesize them is through Michael-alkylation reactions of nucleophilic alkyl halides.[1,2] However, synthesizing alkyl halides requires an additional reaction step. Instead, we propose using electrochemically generated halogenated species *in situ* for the reaction of Michael acceptors with malonates, leading to the formation of a cyclopropane core. High enantio- and diastereoselectivities of the reaction are secured by using chiral organocatalysts, and the use of catalytic amounts of halogen sources significantly increases the atom economy of the reaction.



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Expanding the Possibilities for Heterocycle Synthesis by Propargyl Silane Cyclization *via* the 1,2-Silyl Shift

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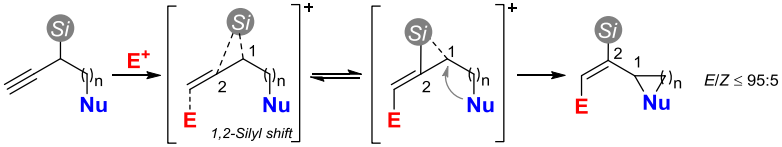
In this work we demonstrate the use propargyl silanes as precursors for various *O*-, *S*-, *N*-heterocycles, containing a highly stereodefined olefin side chain (Scheme 1). Brønsted acids, electrophilic halogen sources and selenyl chloride induce this transformation, providing diverse functionalization for the resulting olefin side chain. Further synthetic utility of the obtained products is demonstrated by electrophilic substitution (C=C-Si → C=C-Hal) and cross-coupling reactions.[1]



Scheme 1. Heterocycle synthesis from propargyl silanes.

Acknowledgements

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Regioselective C–H Amination of Lupane-Type Triterpenoids

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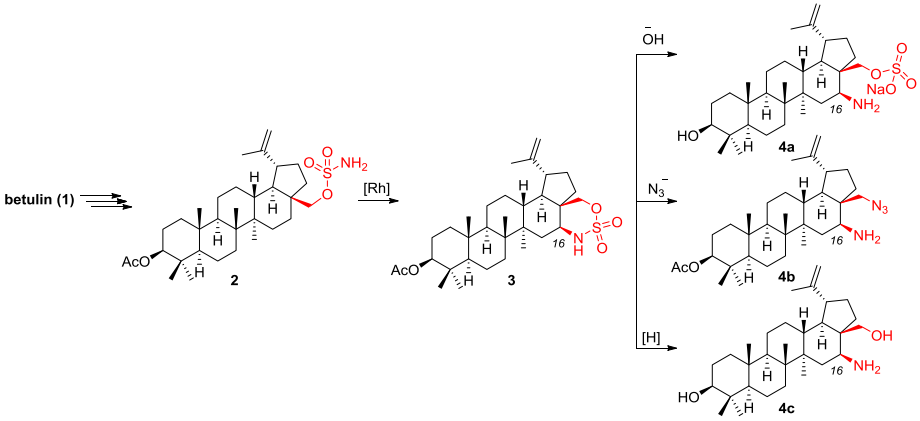
Betulin and betulinic acid are lupane-type secondary metabolites found in birch bark. These triterpenoids and their derivatives are known for their remarkable antitumor, antidiabetic, anti-inflammatory and antiviral properties. Among many possible functionalization possibilities, the C–H activation is underdeveloped in this compound class. Hence, we present here C(16) and C(22) C–H amination followed by functional group transformation that provides heteroatom containing triterpenoid derivatives with better solubility profile.

Sulfamate ester **2** was obtained in few steps from betulin (**1**) and following C-H amination reaction proceeds in the presence of rhodium catalyst, forming oxathiazinane **3**, which is versatile precursor for various ring-opening reactions.



Acknowledgements
The authors acknowledge project VPP-EM-BIOMEDICĪNA-2022/1-0001 (BioMedPharm) for financial support.

Water Soluble Phosphonate Derivatives of Pentacyclic Triterpenoids

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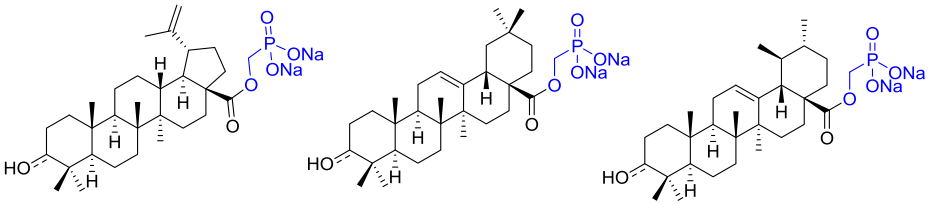
Natural pentacyclic triterpenoids are important secondary metabolites, which have attracted interest due to the wide range of their biological activities. Oleanolic, ursolic acids and betulin, are the most known compounds of this group, which are isolated from various plants. However, the medicinal application of these natural products are hindered by their extremely low water solubility and thus – low bioavailability. One option to overcome this limitation is introduction of polar anionic functional groups such as phosphates and sulfates, which, however, are prone to hydrolysis.

Here we describe the synthesis of novel anionic triterpenoid phosphonates, which bear methylene-bridged anionic phosphonate group side chain and exhibit excellent water solubility.[1]



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Telescoped Synthesis of Vicinal Diamines *via* Ring-Opening of Electrochemically Generated Aziridines in Flow

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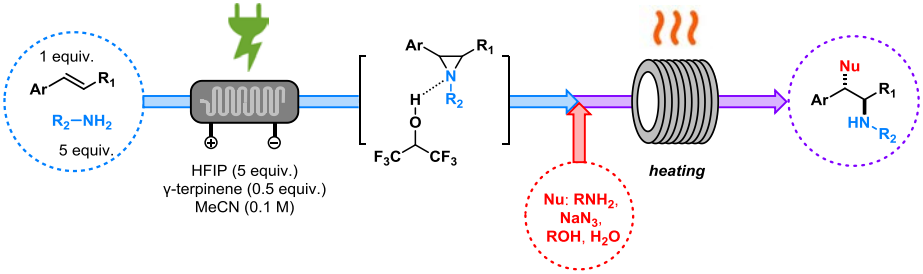
Herein, we present the ring opening of electrochemically generated non-activated aziridines[1] with various nucleophiles in continuous flow, rendering a telescope procedure. The excess of hexafluoroisopropanol used in the initial electrochemical step promotes the ring-opening, while the flow setup enables to perform the ring-opening reactions under pressure at high temperatures providing β-functionalized amines within minutes timeframe. Moreover, we were able to use explosive compounds under controlled conditions, which demonstrated the safety features of flow chemistry.[2]



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Visible Light Photocatalysis for Selective Peptide Modification

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Late-stage modification of peptides is garnering significant interest from medicinal chemists due to its potential to enhance peptide properties. Meanwhile, photocatalysis offers an efficient and sustainable method for achieving chemoselective bioconjugation under mild and biocompatible conditions, making it a promising approach in peptide modification.

Visible light-initiated reaction (LED_{460} or sunlight) has been used to develop an efficient method for the functionalization of selenocystine-containing peptides[1,2] through the generation of a selenium radical in the presence of an organic dye. The selenium radical is subsequently oxidized to an electrophile and trapped by heterocycles such as indoles,[1] coumarins[2] and quinolinones.[2] Notably, intramolecular indole selenylation was successfully performed, resulting in Sec-containing indole-based macrocycles.[1] Furthermore, a facile approach for the synthesis of Se–S bond-containing peptides was established using a visible light-initiated reaction.[3] Unprotected peptides with "sensitive" amino acids exhibited excellent tolerance under the developed conditions.

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Concise Access to PBD Natural Products Oxo-Prothracarcin, Oxo-Tomaymycin, and Boseongasepine B

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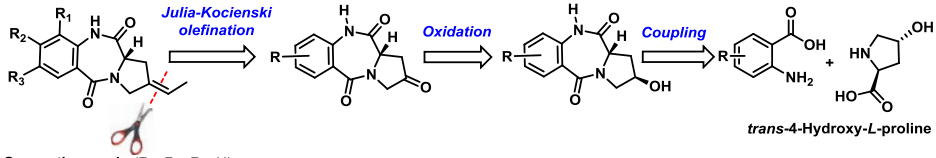
Pyrrolo[1,4]benzodiazepines (PBD) are a broad family of natural products possessing considerable anticancer activity owing to their ability to covalently bond through N-2 of guanine in the minor groove of DNA.[1]

Several PBD members possess an *E*-configured C2 alkylidene group in the pyrrolidine ring, the configuration of which plays a crucial role in the cytotoxic properties of these compounds.[2]

A concise total synthesis of oxo-prothracarcin, oxo-tomaymycin and boseongazepine B will be reported representing the shortest total synthesis of these natural products to date.[3]



Oxoprothracarcin (R_1=R_2=R_3=H)
Boseongazepine B (R_1=OMe, R_2=R_3=H)
Oxotomaymycin (R_1=H, R_2=OH, R_3=OMe)

Acknowledgements

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syn-Selective Difunctionalization of Bicyclobutanes Enabled by Photoredox-Mediated C–S σ-Bond Scission

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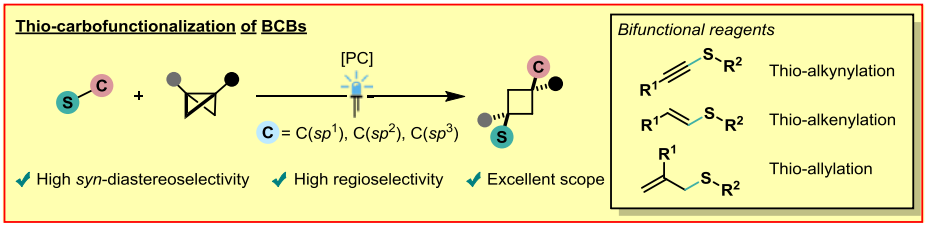
Given the significance of cyclic frameworks in molecular scaffolds and drug discovery, the ability to precisely create and modify ring systems in synthetic chemistry is captivating. In this domain, achieving intermolecular synthesis of densely substituted cyclobutanes with exact diastereocontrol under straightforward reaction conditions poses a challenge. This work presents a photoredox approach for the difunctionalization of bicyclo[1.1.0]butanes (BCBs) with high regio- and *syn*-selectivity. The C–S σ-bond cleavage of partially unsaturated sulfur-containing bifunctional reagents in a strain-release -driven process facilitates the thio-alkynylation, -alkenylation, and -allylation of BCBs under gentle conditions and underscores the versatility of this method. Mechanistic studies suggest that cyclic distonic radical cations may play a crucial role in enabling efficient scission of C–S σ-bonds and in determining the source of diastereoselectivity.



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Design and Synthesis of Functionalized Benzo[*b*]fluorene-based Organic Materials *via* Bidentate Lewis Acid Catalysis

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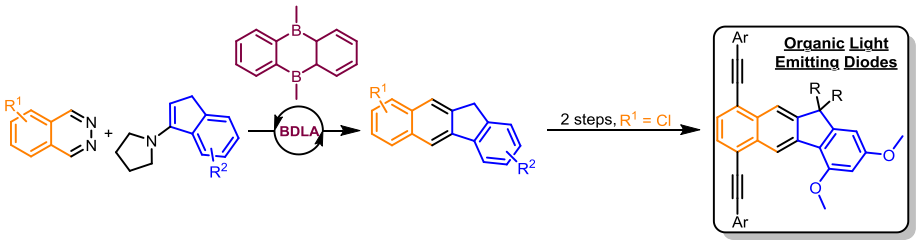
Lewis acids (LAs), especially boron-based ones, are a common tool in the repertoire of synthetic chemists.[1] Despite the outstanding activity achieved with a bidentate mode of activation in such Lewis acids, only few examples are known in the literature.[2] We demonstrated the utility of 1,10-dimethyldiboranthrene as catalyst for inverse electron-demand Diels–Alder reactions via a reactive *o*-quinodimethane intermediate.[3,4] Herein, we present the utilization of the elimination pathway as a modular synthesis of benzo[*b*]-fluorenes. Furthermore, we were able to design and synthesize materials based on this motif with possible applications in organic photovoltaics or organic light emitting diodes.



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Flow Electrolysis of Biomass Derived Furanoics to Obtain Building Blocks for API Synthesis

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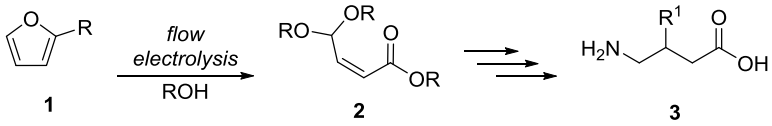
Electrochemical techniques have demonstrated the ability to enhance and improve transformations that were previously challenging with conventional redox reagents. Scaling up electroorganic synthesis can be achieved safely and efficiently with the use of flow electrolysis.

Herein, we present the Torii-type electrosynthesis from biomass-derived furanoics and application of product **2** (scheme 1) as a multifunctional building block to access gabapentinoids (e.g. pregabalin), a class of CNS drugs.



Scheme 1. Torii-type electrosynthesis toward gabapentinoids

Optimization of flow electrolysis conditions for the transformations of furanoics **1** to obtain product **2** and further chemical steps towards gabapentinoids **3** will be demonstrated

Acknowledgements
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Synthesis of Polymer-Bound Redox Mediators for Electrosynthesis

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Redox mediators are widely used as homogeneous electrocatalysts in organic electrosynthesis for improving the chemo-, regio- and stereoselectivity of the reaction and lowering the potential required for the electrochemical reaction.[1] Meanwhile, polymer-bound redox mediators immobilized on electrodes have not been widely explored for applications in electrosynthesis. The properties of redox polymers can be modulated by changing the of monomer nature or their ratio within the polymer, as it significantly impacts the hydrophobicity, hydrophilicity, stability on electrodes, redox potential, swelling properties, and catalytic performance of the redox polymer.
This work demonstrates the design of redox-active polymers containing *N*-oxyl radicals as redox mediators. The electrochemical properties and performance in electrochemical reactions when immobilized on electrodes has been investigated.

Acknowledgements
This project has been funded by Recovery and Resilience Facility (RRF) (5.2.1.1.i.) grant Nr.47/OSI/PG.

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Targeted C2 Modification of Quinazolines Using Azide-Tetrazole Tautomerism

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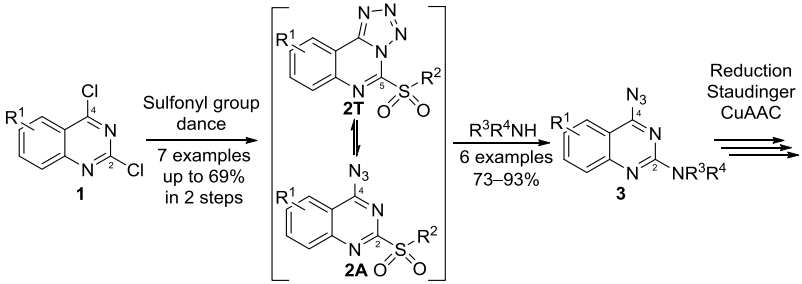
Several methods for the modification of quinazoline C4 position are known, but the modification of the C2 position still poses a challenge.[1]
We report the use of the sulfonyl group dance[2] for the synthesis of 4-azido-2-sulfonylquinazolines **2**, which obey selective C2 substitution in S_NAr reactions. We show further modification of products **3** in Staudinger and CuAAC reactions, as well as in reduction reactions for the synthesis of α_1-blockers terazosin and prazosin.



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Advancing Aldehyde Synthesis from Esters: The Role of Halogenated Triarylborane in Ester Hydrosilylation

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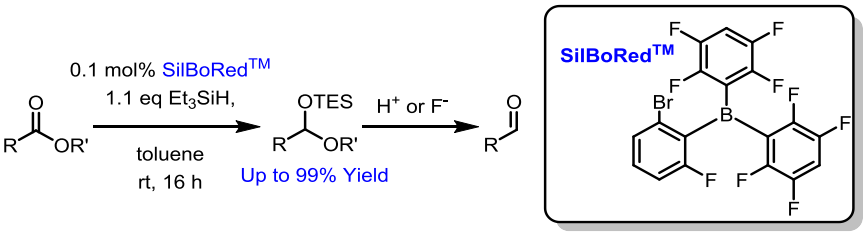
The reduction of an ester functional group to the corresponding aldehyde is a fundamental reaction in organic chemistry. The typically used Al-hydrides have often proved to be nonefficient for this transformation. In 2020, Aldexchem Ltd. patented novel heteroleptic halogenated triarylborane catalysts (brand name SilBoRed™), demonstrating excellent selectivity and conversion in the hydrosilylation of various esters, resulting in nearly quantitative yields of the corresponding silyl acetals.
The application of the SilBoRed™ catalyst in the hydrosilylation of esters as well as in the total synthesis and API intermediate will be presented.



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WO2022129966A1

Catalytic Desymmetrization of [2,2]Paracyclophanes

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

Acknowledgements
Grant PID2019-110008GB-I00 (MICIN/AEI/FEDER, UE) and Grant IT1741-22 (Basque Government). D. Alonso thanks Basque Government for a fellowship.

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Branched Methoxydiphenylamine-Substituted Carbazole Derivatives for Perovskite Solar Cells

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A set of novel branched molecules bearing a different number of 3,6-bis(4,4′-dimethoxydiphenylamino)carbazole-based (Cz-OMeDPA) periphery arms linked together by aliphatic chains (Fig. 1) have been developed and their performance was tested in perovskite solar cells. Electrical and photovoltaic properties have been investigated with respect to the number of the Cz-OMeDPA chromophores and the nature of the linking aliphatic chain.

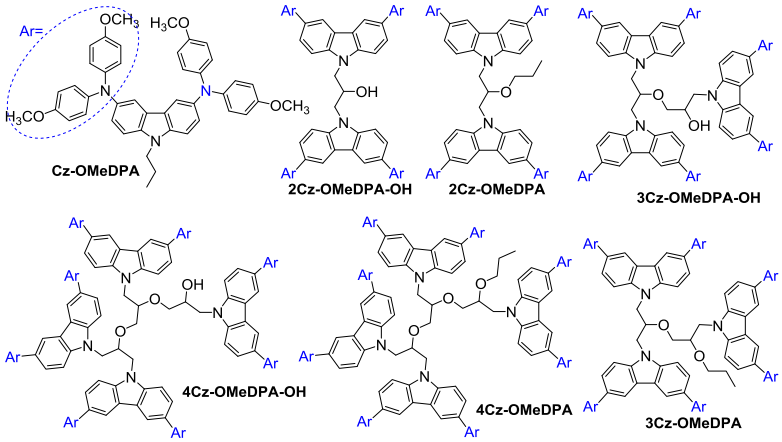

Figure 1. Chemical structures of synthesized organic semiconductors.

The structure of new compounds was confirmed by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy methods. HTMs possess sufficient thermal stability and are amorphous minimizing the risk of direct layer crystallization. Finally, perovskite solar cells employing two new HTMs (2Cz-OMeDPA and 3Cz-OMeDPA-OH) bearing two and three substituted carbazole chromophores, showed a performance of around 20%, which is comparable with devices using spiro-OMeTAD and demonstrate slightly enhanced device stability.

Streamlined Synthetic Strategy and Catalytic Performance of α-Chiral CAAC Ligands

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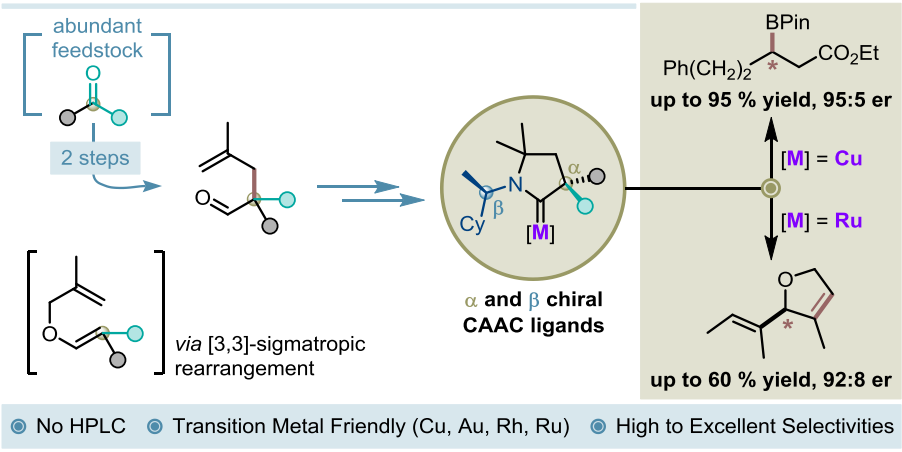
Asymmetric transformations involving CAAC complexes featuring an α-chiral element adjacent to the carbene centre are yet limited to few examples. Herein we describe a streamlined approach to access highly modular carbene precursors featuring chiral α-quaternary centres. A library comprising more than 30 metal complexes was prepared, showcasing unprecedented substitution patterns. Selected copper complexes were benchmarked in an Asymmetric Conjugate Borylation reaction, providing excellent yields and high to excellent enantioselectivities.



Pd-Catalyzed Direct β-C(sp^3)–H Fluorination of Aliphatic Carboxylic Acids

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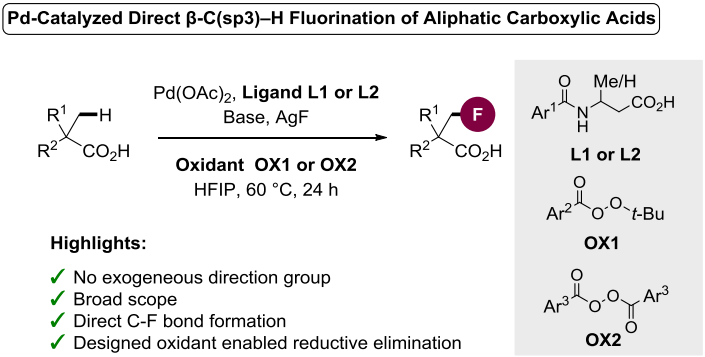
In this study, we have developed a protocol that enables a direct β-C(sp^3)–H fluorination of aliphatic carboxylic acids. The reported protocol uses an operationally simple source of fluoride and a rationally designed external oxidant to provide access to a wide range of fluorinated scaffolds from the respective acids in a single step and without the need for an exogeneous directing group.



Acknowledgements
We thank Kiel University and the Deutsche Forschungsgemeinschaft (DFG, Emmy-Noether-Programme GE 2945/2-1 to MvG and Walter Benjamin Programme HI 2351/1-1to KH) for generous financial support.

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Efficient Synthesis of Tetrazine and Trans-Cyclooctene Derivatives Used in New Generation of Click Chemistry

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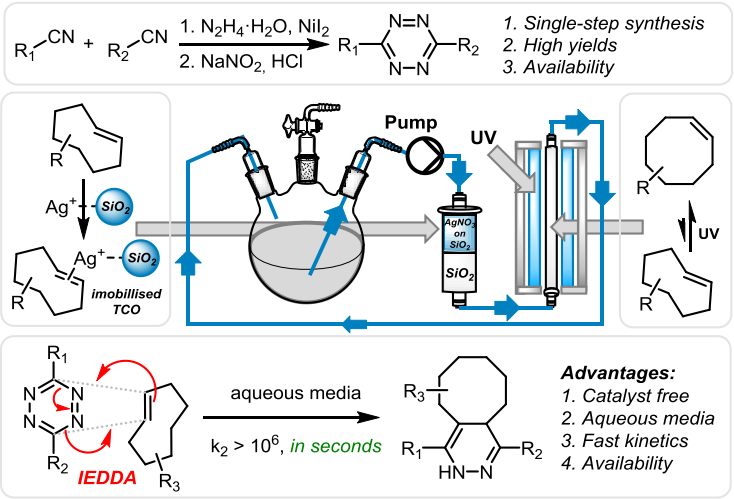
Over the past two decades tetrazine chemistry has garnered attention due to its application in a new generation of click chemistry. Tetrazines react with *trans*-cyclooctenes even at very low concentrations providing fast and reliable bioorthogonal tools for uncovering unexplored biological mechanisms. Unfortunately, the synthesis of tetrazines and TCO's remains challenging and expensive. Herein we report efficient tetrazine synthesis and a simple UV TCO isomerisation flow reactor setup.



Acknowledgements
Funded by the Research Council of Lithuania (S-MIP-23-18).

S-Propargyl-type AdoMet Analogues for Application in Nucleic Acids Labeling

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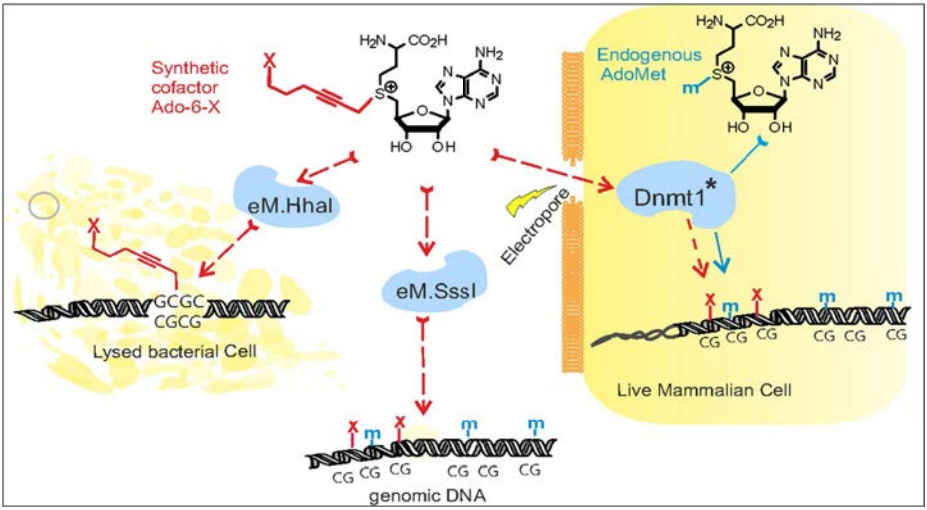
DNA and RNA is the basis of life composed of nucleotides which can be further furnished with biologically important covalent modifications. Among the variety of enzymes involved in modification of NA, AdoMet-dependent methyltransferases (MTases) play important roles in biological signaling, but transferred methyl group is poor physical reporter. Therefore, an obvious strategy to unlock the practical utility of the methyltransferase reactions is to enable the transfer of "prederivatized" (extended) versions of the methyl group.



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2-Aryl-N-(heteroaryl)acetamides: Synthesis and Biotesting

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Artificial intelligence programs are increasingly being used to predict the structure of potential pharmaceutical active ingredients, but their efficiency remains inadequate. The synthesis of new potentially biologically active compounds by combining several fragments that have previously been shown to have similar activity remains relevant. Following preliminary testing of such compounds, further modifications are planned in line with the results from biological testing.

Various 2-arylacetamides[1] and pyridine derivatives[2] are known to exhibit antibacterial effects. In the recent publications benzimidazole phenylacetamides were reported as trypanosomacides.[3]

N-Acylation reaction of various amino-*N*-heterocycles with several 2-(chlorophenyl)acetic acids were performed seeking to prepare a library of 2-aryl-N-heteroarylacetamides.

All compounds were tested for their antibacterial activity against the *E. coli dh5a* bacterial line and *Ciliated protozoa*. The results were used to evaluate the influence of heterocycle size and the position of the chlorine atom on the benzene ring on the biological activity.

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Store it in Small Molecules: from NHC–Silver Complexes to Data Storage

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In our ever-evolving society, technology has emerged as an indispensable cornerstone, a fact emphasized by the exponential surge in human-generated data.[1] In this context, we report the synthesis of silver complexes bearing chelating *N*-heterocyclic carbene ligands.[2] These silver complexes exhibited significant catalytic efficiency in A^3 and KA^2 coupling reactions, successfully transforming a variety of aldehydes (for A^3) or ketones (for KA^2), amines, and alkynes into propargyl amines. The synthesized propargyl amines were investigated for data storage applications due to their tunable physical properties. Surprisingly, they proved to be a suitable and viable option, making the decoding of the stored data both cost-effective and user-friendly.

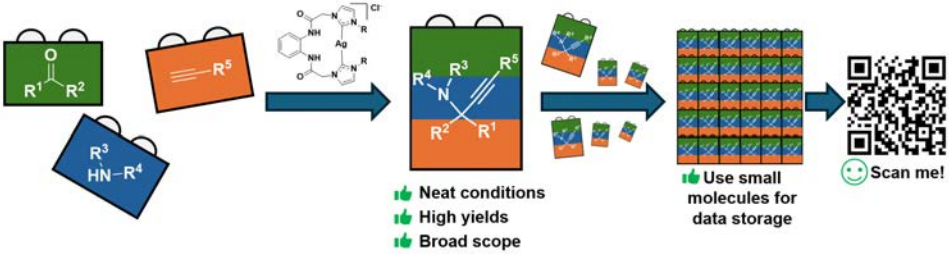

Figure 1. Usage of small molecules for data storage.

Acknowledgements
This work was supported by funding from Charles University (Project PRIMUS/20/SCI/017) and Charles University Research Centre (Program UNCE/SCI/014).

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Synthesis and Reactivity of Substituted Tetrahydropyridines as Masked Cyclic [3]Dendralenes

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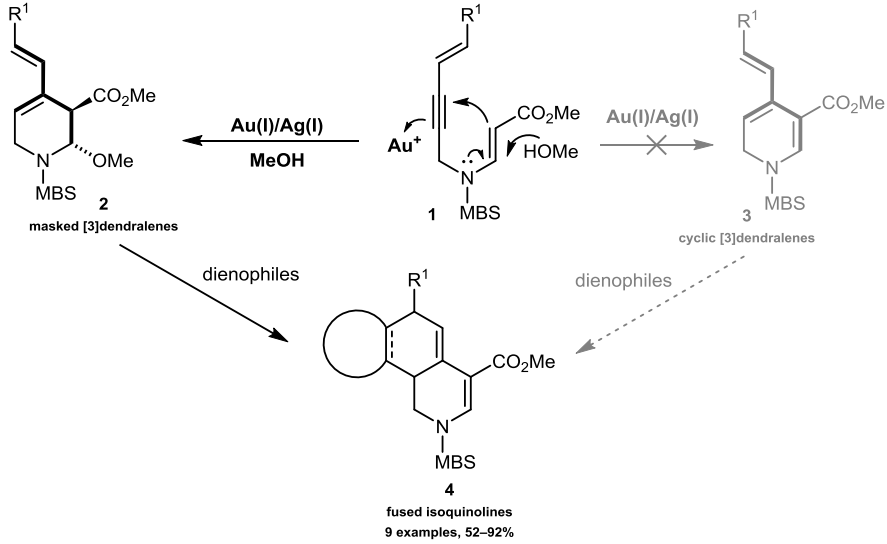
Gold-catalyzed cyclization[1] of the easily available 3-aza-1,5-enynes **1** provided substituted tetrahydropyridines **2** that can be considered masked cyclic [3]dendralenes **3**, whose direct synthesis was not successful. Diels-Alder reaction of **2** with simultaneous elimination of methanol furnished a series of remarkable fused isoquinoline derivatives **4**.



Scheme 1. Synthesis and reactivity of substituted tetrahydropyridines.

Acknowledgements
This work was supported by Charles University (SVV 260661), Czech Science Foundation (Project No. 22-17868S) and The project New Technologies for Translational Research in Pharmaceutical Sciences / NETPHARM, project ID CZ.02.01.01/00/22_008/0004607, that is co-funded by the European Union.

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Extending Phosphorescence Afterglow through Alkyl Group Engineering

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Phosphorescent luminophores (phosphors) have found broad application in data encryption, bioimaging, sensing and other fields.[1] While inorganic and organometallic materials feature high phosphorescence efficiency, their less efficient organic counterparts are becoming a widely studied alternative due to their limitless design possibilities, low cost, and versatility.[2] Although organic phosphors operate through trace impurity mechanism,[3] there are no examples in the literature on the fine-tuning of emission lifetimes for fully characterized bulk material and impurity systems. Herein, we show that alkyl substituent engineering allows to manipulate the phosphorescence emission lifetimes in binary systems of **1a**–**e** and **2a**–**e**. The broader applicability of this alkyl engineering approach is demonstrated by doping common luminophores in crystals of fully aromatic and alkyl-substituted aromatic bulk crystalline materials.

Acknowledgements

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Birch Wood Origin Anhydrosugars as Platform Chemicals

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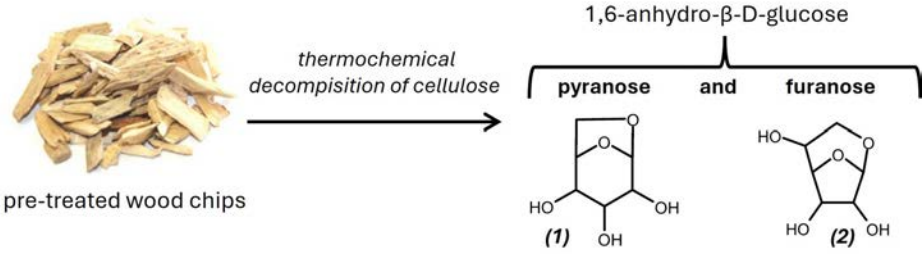
Production of value-added products from biomass, such as wood, is one of the keys for achieving a bioeconomy, where fossil-based commodities are replaced with sustainable ones, obtained from renewable feedstocks.
Pyrolysis is the thermochemical conversion of a material in the absence of oxygen. Depending on the pyrolysis conditions, type and pre-treatment of the raw material, pyrolysis products can significantly vary. We aim to produce 1,6-anhydro-β-D-gluco-pyranose or levoglucosan (**1**), which is known as a potential platform chemical, because of its unique chiral structure.[1] At the same time levoglucosan's isomer 1,6-anhydro-β-D-glucofuranose (**2**) is an underestimated by-product in birch wood pyrolysis, with its own structural merits. Pyrolysis-based anhydrosugars are a valuable source of green feedstocks for chemical synthesis.



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A DFT Study of an Organocatalytic Enantioselective Mannich Reaction Reveals that the Enantiodeterming Step is Associated with the Torsional Degrees of Freedom

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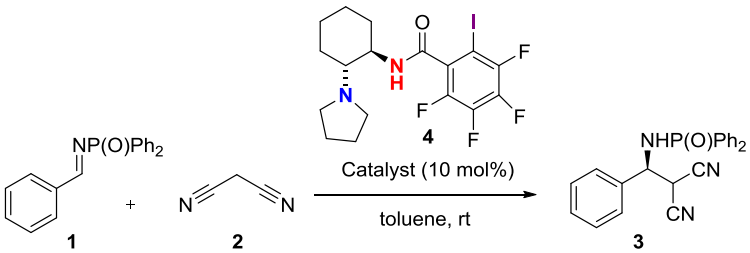
In theoretical organic chemisry the main question is how the reagents and products are connected via transition states (TS) on the potential energy surface (PES); this is known as a reaction path (RP).

A study on an asymmetric Mannich reaction between iminophosphorane and malononitrile, catalysed by a multifunctional organocatalyst was performed using Density Functional Theory (DFT), such as M06-2X functional with a def2-SVP and def2-TZVP basis sets. Three reaction coordinates were modeled:

1. C-C bond-forming reaction coordinate
2. Proton transfer reaction coordinate
3. Torsional reaction coordinate

Interestingly, the study found that the rate-determining and enantiodetermining step (the transition state) was not associated with either the C–C bond-forming reaction coordinate nor the proton transfer coordinate. Instead, the enantiodetermining step was associated with the torsional degrees of freedom and was influenced by the network of non-covalent interactions.



Application of 2-Alkynylthioimidazoles in the Synthesis of Condensed Heterocyclic Systems for Amyloid Aggregation

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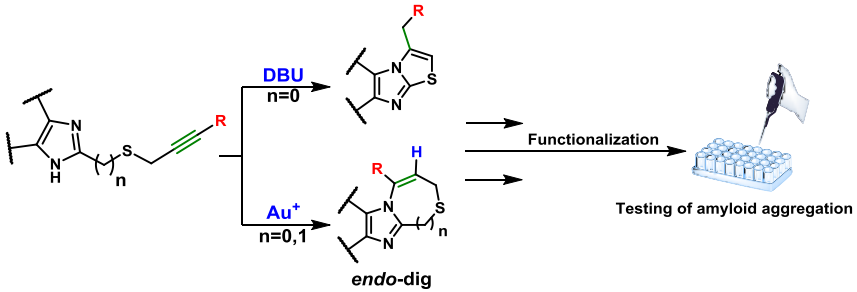
Insoluble amyloid fibrils accumulate in the intercellular spaces of organs and tissues, leading to various amyloidosis-related disorders in the human body. Efforts to prevent and halt the progression of these diseases involve the search for small molecular compounds. Recently, high-throughput screening identified imidazo[2,1-*b*][1,3]thiazines as potential candidates for inhibiting amyloid aggregation. 2-Alkynylthioimidazoles are chosen as precursors in the synthesis of various imidazo[2,1-*b*][1,3]thiazines and their analogues through reactions initiated by bases or Lewis acid in atom-economic way.



Efficient Method for Weak-Nucleophile Functionalization of 1,8-Naphthalimide Core

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1,8-Naphthalimide and its derivatives with a strong electron-withdrawing imide group are a specific series of environmentally sensitive fluorophores, widely utilized in various fields due to their good chemical stability, large Stokes shift, and high fluorescent quantum yield. They have been widely used as biological, biomedical, optical, and electronic materials. 1,8-Naphthalimides have been used with considerable success as intracellular markers in a wide variety of systems.

Here we present the new efficient method for weak-nucleophile derivatization of 1,8-naphthalimide. This method allows to introduce weak nucleophiles, such as water, alcohols and fluoride anions to the 1,8-naphthalimide core. In addition, the method works with short reaction times and high yields in relatively mild conditions. The obtained compounds are highly fluorescent in solution and in solid state which make them very suitable for OLED application.[1]

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

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Merging Visible-Light Photoredox-Catalysis and Iodine(III) Chemistry for Radical Fluoromethylation

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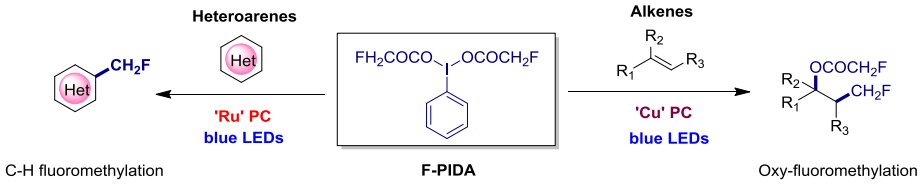
The synthesis of organo-fluorine compounds plays a crucial role in the field of pharmaceuticals; agrochemicals etc., and these compounds have shown enhanced biological and physicochemical properties.[1] Significant synthetic methodologies and reagents has been developed towards making various fluoroalkylated compounds (CF_3, CF_2H, etc.).[2] However, particularly, the syntheses of monofluoromethyl-containing compounds are limited. Therefore, we reported an iodine(III) reagent (F-PIDA) serves as a powerful source of a monofluoromethyl (CH_2F) radical, enabling the step economical synthesis of monofluoromethyl-containing compounds from a broad range of alkenes and heteroarenes under visible-light photoredox catalysis.[3]



Acknowledgements

Postdoc Latvia ERDF project Nr. 1.1.1.2/VIAA/4/20/748 and Recovery and Resilience Facility (RRF) (5.2.1.1.i.) grant Nr.14/OSI/PG/38.

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N-Heterocyclic Carbenes as Versatile Tool for Molecular Surface Modification

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The successful isolation of an N-heterocyclic carbene in 1991 opened up a new class of organic compounds for investigation. From these beginnings as academic curiosities, N-heterocyclic carbenes today rank among the most powerful tools in organic chemistry, with numerous applications in commercially important processes.[1,2] Here we provide a concise overview of on-surface chemistry of N-heterocyclic carbenes, summarizing their general properties, their binding modes and their self-assembly on metal surfaces.[3–5] We give insight into common preparation methods[3] (Fig. 1) and highlight various fields of application (Fig. 2), including surface protection,[1,3] biosensing,[6] (photo) switchable surface properties,[7,8] microelectronics[9,10] and heterogeneous catalysis.

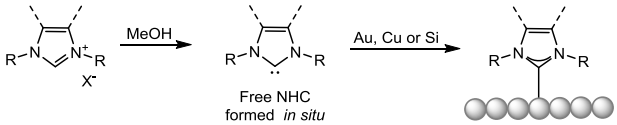
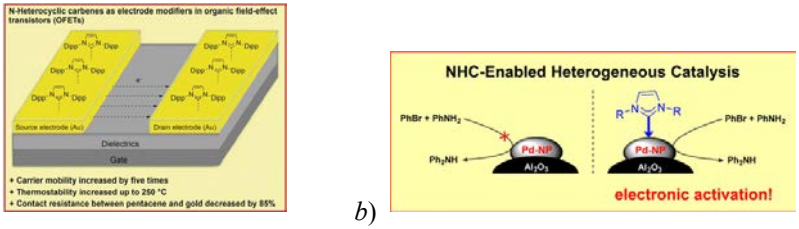


Figure 1. General preparation procedure for N-heterocyclic carbene monolayers on metal surfaces.



a) *b*)

Figure 2. Two exemplary applications for N-heterocyclic carbene monolayers. *a*) Microelectronics, *b*) catalysis.

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Synthesis of a Novel Monofuntionalized Hemicucurbit[8]uril

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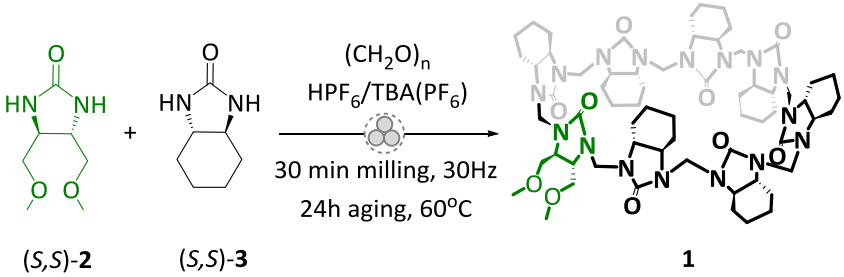
Monofunctionalization of macrocyclic receptors is vital for tuning the binding properties and physicochemical characteristics of parent compounds. It is also essential for derivatization and immobilization, necessary for applications in sensing devices. Monofunctionalized derivatives can be obtained in one step through chemical editing of parent structures or controlled self-assembly of different building blocks. However, both approaches are challenging and require precise control over product selectivity by choosing proper reaction conditions. Herein, we present the mechanochemical synthesis of a new 8-membered methoxy-functionalized cyclohexanohemicucurbituril **1**. This compound was synthesized by acid-catalyzed polycondensation of urea monomers (*S,S*)-**2** and (*S,S*)-**3** with formaldehyde, followed by anion-templated self-assembly of **1** in the solid state. After chromatographic purification, the structure and binding properties of **1** were elucidated by spectroscopic techniques.



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Lewis Acid-Catalyzed Annulation of Strained Rings with (Aza)Dienes for the Synthesis of Medium-Sized (Hetero)Cycles

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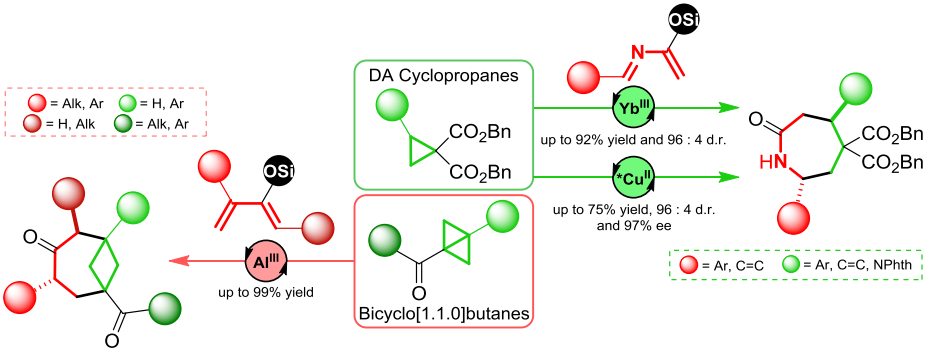
Seven-membered hetero- and carbocycles are important frameworks that are present in a number of both natural and bioactive compounds.[1] Lewis acid-catalyzed strain-releasing annulations of small rings represent a concise and efficient approach to the synthesis of these valuable scaffolds. We herein report the highly diastereoselective synthesis of azepane derivatives through the formal (4+3) cycloaddition of donor-acceptor cyclopropanes with azadienes under Yb^{III} catalysis.[2] An asymmetric version of this reaction was also realized, using a Cu^{II} catalyst with a chiral ligand. Next, an Al^{III} catalyst enabled a complementary [4+2] annulation of bicycle[1.1.0]butanes with carbodienes to provide an expedient access to bridged bicycle[4.1.1]octanes.[3] The latter have recently gained attention as potential bioisosteres of aromatic rings.[4]



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Design and Synthesis of Transmembrane Transporters for Phosphate

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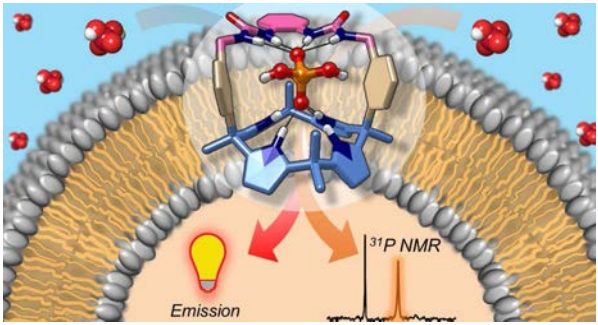
Until recently, no synthetic transporters for inorganic phosphate were reported. However, in this report, we show a strapped calix[4]pyrrole with 8 H-bond donors that allows the extraction of strongly hydrated $H_2PO_4^-$ into the lipid bilayer while shielding its charges from the lipophilic bilayer interior and transferring this anion through the membrane.[1] Phosphate transport was monitored by emission spectroscopy using an encapsulated phosphate sensitive europium(III) probe.[2] Furthermore, ^{31}P-NMR spectroscopy was used to confirm and identify the transported phosphate species.



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Enantioselective Lewis Base Catalysed N-Allylation of Halogenated Amides in Synthesis of β-Amino Acid Derivatives

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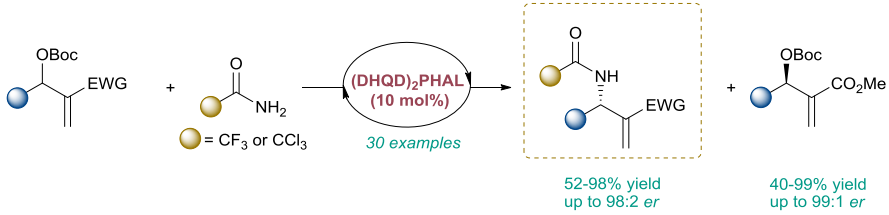
Trifluoro- and trichloroacetamides undergo enantioselective Lewis base catalyzed *N*-allylation with Morita–Baylis–Hillman carbonates to produce enantioenriched β-amino acid derivatives and highly enantioenriched allylic carbonates through a kinetic resolution. We introduced halogenated acetamides as suitable pronucleophile surrogates of ammonia where the electron-withdrawing group lowers the nucleophilicity of the parent nucleophile and sufficiently lowers the acidity of the N-H protons which allows for nucleophile activation via deprotonation during the course of the reactions.



The approach features a broad substrate scope, good enantioselectivity and mild reaction conditions. The obtained products are used to produce a library of spiro-isoxazoline lactams via deprotection – cyclization – diastereoselective cycloaddition sequence.[1]

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Study of Triazolyl Purine Derivatives as Sensors for Metal Ions

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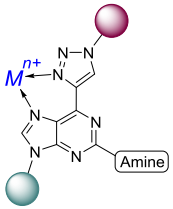
Fluorescent purine derivatives can be used as metal ion sensors in analytical applications.[1] In this work, we synthesized 2-piperidinyl-6-triazolyl purine derivatives, performed their spectrophotometric and NMR titration experiments with Ca^{2+}, Mg^{2+}, Cu^{2+}, Fe^{2+}, Zn^{2+}, Pb^{2+} and Hg^{2+} ions, and determined possible complexation sites and equivalency points of these complexes.



Acknowledgements
This work is supported by MEPS co-project LV-LT-TW/2024/5.

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Predictive Model for the Regioselectivity of Cyclopropyl Carbinyl, Cyclobutyl, and Homoallyl Rearrangements

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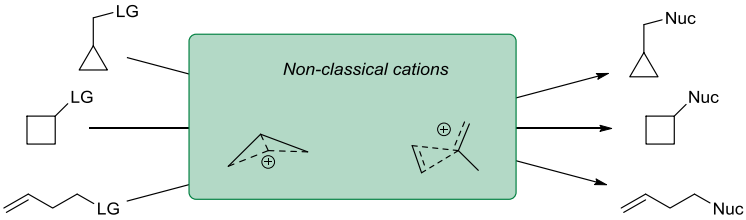
Even after decades of research in the field on non-classical carbocations, there is no general model that predicts and explains the regioselectivity in the cyclopropyl carbinyl, cyclobutyl, and homoallyl rearrangements. We proposed a straightforward model that can predict the major product of these complex rearrangements according to the substitution pattern and the nature of the substituents. The prediction is based on a simple scoring of the key parameters of the transformation.



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Total Synthesis of the Dihydrooxepine-Spiroisoxazoline Natural Product Psammaplysin A

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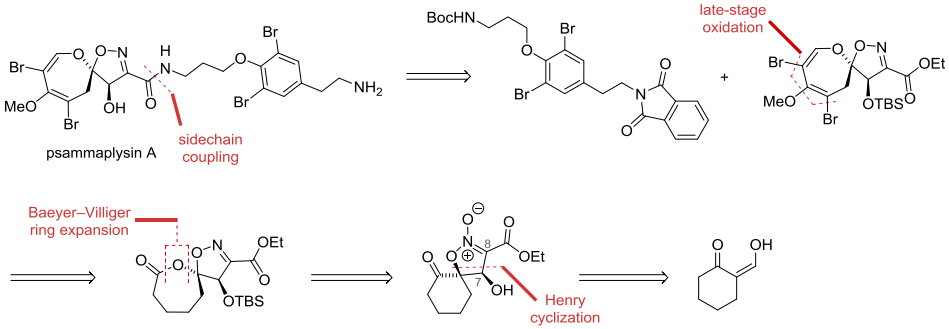
Nominated to present this work as a short talk on July 9, 14:45

We report a general synthetic entry to dihydrooxepine-spiroisoxazoline natural products that culminated in the first total synthesis of psammaplysin A. The strategy featured two key transformations: (1) a diastereoselective Henry reaction/cyclization sequence to access the C7 hydroxylated isoxazoline scaffold and (2) a regioselective Baeyer−Villiger ring expansion that allowed the installation of the fully substituted dihydrooxepine and avoided the risk of a previously observed oxepine-arene oxide rearrangement.



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Radical-Mediated Azidofunctionalization of Alkenes

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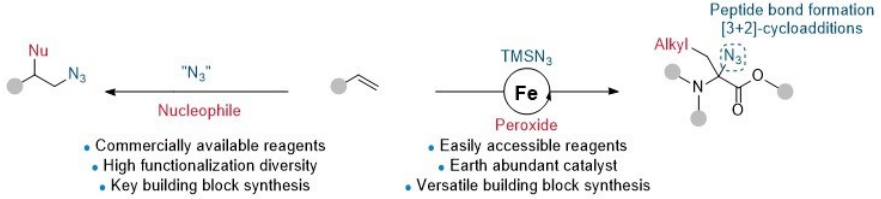
The difunctionalization of alkene is among the most efficient methods for introducing diverse functional groups. Azides, in particular, are recognized highly versatile and have found broad applications in synthetic chemistry and the pharmaceutical industry. In chemical sciences, non-proteinogenic amino acids (NPAAs) show great potential for the optimization of various biological properties of peptide drugs. However, the use of α-nitrogen substituted amino acids has been scarce due to their challenging synthesis. In this context, we developed an easy access to *α*-azido amino acids from dehydroamino acids as alkyl radical acceptors using iron catalysis. Additionally, we developed a method for the functionalization of other types of $C(sp^2)$–$C(sp^2)$ bonds such as styrenes, enols or enamides enabling the introduction of both an azide moiety and a wide variety of different nucleophiles.



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Total Synthesis of (±)-Lappaceolides A and B

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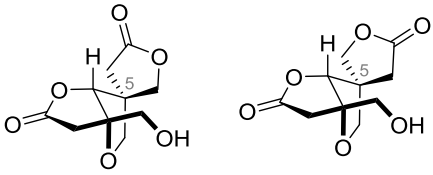
Lappaceolides A and B, isolated from seeds of Rambutan (*Nephelium lappaceum*) in 2005, share a unique monoterpene skeleton. Despite its discovery two decades ago, there was no synthetic attention to the molecules which prompted us to establish a synthetic route and probe the plausible biosynthetic origins. Herein we present a rapid assembly of lappaceolides A and B using a biomimetic dimerization approach.



Lappaceolide A **Lappaceolide B**

Figure 1. Isolated natural products from seeds of *Nephelium lappaceum*.

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The Synthesis of *S*-Adenosylhomocysteine (SAH) Analogue: Methylene Fluoride Moiety as Isostere of Carboxyl Group

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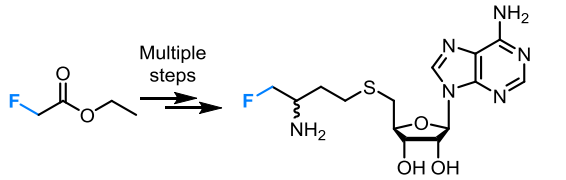
Methyltransferase (Mtase)-directed transfer of activated groups (mTAG) from synthetic *S*-adenosyl-L-methionine (SAM) analogues is an effective tool for DNA derivatization. Wider application of SAM analogs for *in vivo* labeling of nucleic acids is limited due to their low stability in physiological conditions and higher affinity of MTases towards native cofactor. Structural modifications of SAM analogues enhance their stability and selectivity towards engineered DNA methyltransferases. The strategic deployment of fluorine atoms in biologically active molecules is a common tactic in enhancing their physico-chemical properties.

Herein we report the synthesis protocol for the SAH analogue bearing isosteric methylene fluoride moiety instead of carboxyl group starting from ethyl fluoroacetate. These SAH analogues will be applied in the synthesis of the potentially more stable SAM analogues.



Ethyl fluoroacetate **_S_-adenosylhomocysteine (SAH) analogue**

Synthesis of Amino Acids Containing *N*-Heterocycles

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The global COVID-19 pandemic has revealed a deficit in therapeutic treatment options against coronaviruses. To develop new antiviral drugs, SARS-CoV-2 nsp10/nsp16 2′-O-methyltransferase (MTase) complex was selected as the drug target. Development of potential inhibitors of this enzyme complex was based on *N,N*-dimethyl-1H-pyrazole-4-sulfonamide (**1**) originating from crystallographic fragment screening and the natural substrate *S*-adenosylmethionine (SAM) (Fig. 1). Computer assisted drug design studies have sugested merging the two structures into 5-membered *N*-heterocycle-containing amino acids which were selected as synthesis targets. The project also aims to develop approaches for applying AI in the design of new drug compounds.[1]

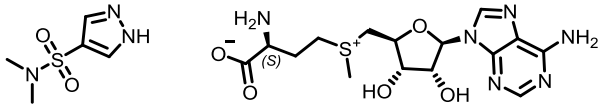

Figure 1. Fragment **1** and SAM structures.

Acknowledgements
HORIZON.1.3.3 – The innovation potential of European Research Infrastructures and activities for Innovation and Training (Grant Agreement ID 101094131).

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Uncertainty Due to Sampling in the Quantitative NMR Analysis of Lignin

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Lignin is the second most abundant biopolymer. It's an aromatic heteropolymer generated from the polymerization of three primary monolignol units, which are p-coumaryl alcohol (H), coniferyl alcohol (G), and sinapyl alcohol (S).[1]

QNMR is a widely used for the quantitative analysis of lignin. In the quantitative analysis, attention has been devoted to uncertainties arising from different sources, however sampling was mostly overlooked. Only a couple of reports have discussed sampling uncertainties. However, lignin as a solid natural product, inherently exhibits some inhomogeneity. Thus, subsamples from the lignin bulk sample may have slightly different compositions, meaning different NMR spectra.

This work has the aim of estimating sampling uncertainty of qNMR analysis of lignin. We used 15 samples collected from 1 kg of lignin container. We collected 5 samples from the top, 5 from the middle, and 5 from the bottom of the container.

Our experiment demonstrated that sample-to-sample variations account for roughly half of the total variability in qNMR measurements. The relative standard deviation (RSD) for sample-to-sample variability was 2.4%. By comparison, other sources of variability in qNMR, including measurement errors, baseline irregularities, and partial peak overlap, resulted in an RSD of 4.4%. The overall variability RSD was 5.0%.

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Transition-Metal-Free Alkylation of N-Heterocycles with Nitriles *via* Heteroarylphosphonium Intermediates

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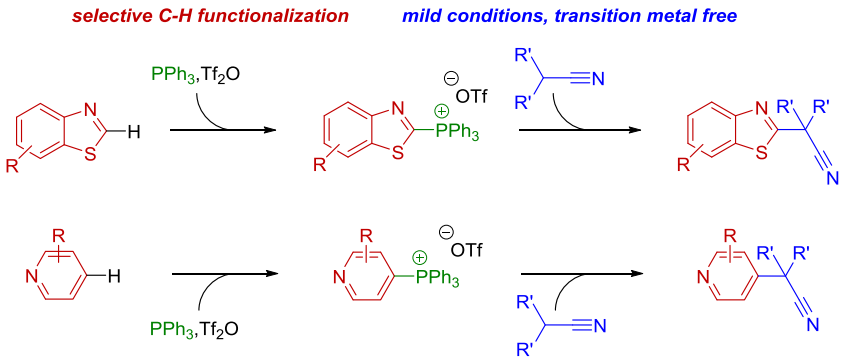
Heteroarylphosphonium salts are easily accessible, versatile intermediates in functionalization of N-heterocycles. Direct C–C bond formation by net substitution of the phosphine has so far required transition metal catalysts, the use of strongly basic reagents or redox catalysis. Here we describe a C–C bond formation in direct reactions of benzothiazol-2-yl-phosphonium and pyridin-4-yl-phosphonium salts and nitrile anions which together with the direct synthesis of phosphonium salts from benzothiazoles and pyridines constitute an efficient and simple two-step protocol for C–H functionalization of these heterocycles under mild conditions.



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One-Pot Photoredox-Organocatalysis Approach for the Synthesis of Chiral N-(cyano(aryl)methyl)acetamides Form Simple Bulding Block

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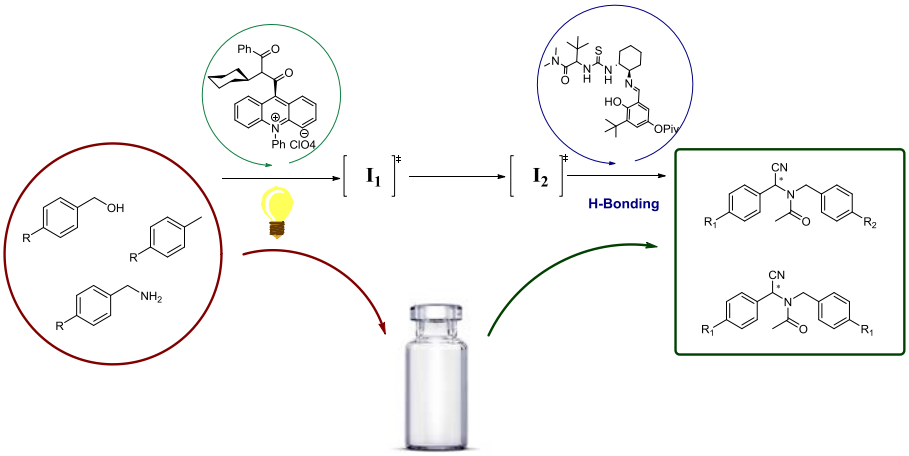
Nowadays synthetic chemistry is dealing with a constant demand of more efficient and greener techniques to minimize efforts on intermediates isolation, energy consumption and amount of waste. In this context, we herein report a one-pot approach starting from simple, readily available and cheap starting materials such as toluenes, benzylic alcohols and amines involving an oxidative photocatalytic step and an enantioselective hydrogen bonding catalytic step to build highly decorated chiral N-cyano(aryl)methyl acetamides



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Synthesis of a New Generation of Bifunctional Resorcinol-Benzimidazole HSP90 Inhibitors

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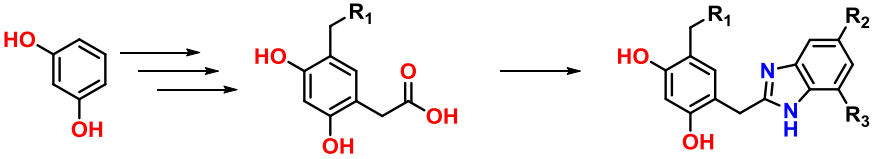
HSP90 (*Heat Shock Protein 90*) is a chaperone protein that is responsible for proper protein folding, their stabilization during heat stress conditions and assistance during degradation.[1] The chaperone has been the subject of numerous studies as a target for anti-cancer and anti-neurodegenerative medications and it has been shown that a resorcinol moiety is crucial for the inhibition of the ATP binding pocket found in the N-terminal domain of the protein.[2] The objective of this work is to synthesize various arylacetic acids and use them in the synthesis of potential resorcinol-based HSP90 inhibitors.



R_1 = -C_6H_5, -(*p*-OMe-C_6H_4), -(3,4-$(OMe)_2$-C_6H_3), -C_5H_9
R_2 = -H, -Cl, -F, -CN, -Me, -COOMe, -COC_6H_5
R_3 = -H, -Cl

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Synthesis of Unsymmetric Perinone/Carboxylic Anhydride-Based Derivatives as Electron Transporting Materials

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Recently, non-fullerene *n*-type organic semiconductors have been attracting considerable attention from the scientific community because these materials can be obtained *via* straightforward synthesis. In this study, unsymmetric perinone/carboxylic anhydride-based molecules derived from 1,4,5,8-naphthalenetetra-carboxylic dianhydride (NTDA) were designed and synthesized (Fig. 1) in a simple two or three step synthesis procedures. As in the synthetic routes of traditional perinone derivatives, the first step of the synthesis leading to these compounds was accomplished via condensation reaction of dianhydride NTDA and o-phenylenediamine derivatives. Subsequently, the perinone-based intermediate was heated under reflux with corresponding amino phosphonate to form the target compounds **V1647-V1653** and **V1655**. Accordingly, the phosphonate esters were hydrolysed to the corresponding acids under reflux with concentrated HCl.

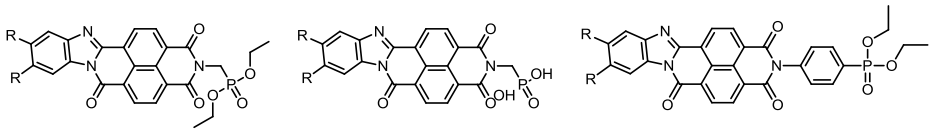

Figure 1. Perinone/carboxylic anhydride-based derivatives.

The thermal, optical and electric properties of these molecules were investigated.

The Development of P-Chiral Biarylphosphine Ligands in Enantioselective Gold(I)-Catalyzed Cylization of 1,6-Enynes

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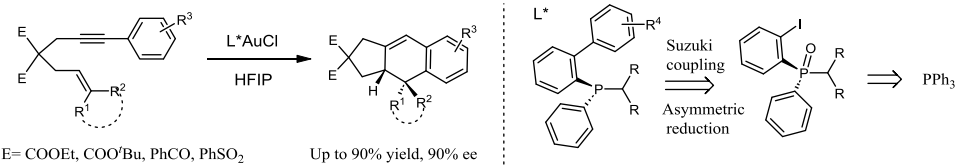
Phosphine ligands have been tremendously explored in the field of catalysis to facilitate the synthesis of organic compounds.[1] Despite the development of bidentate axial and planar chiral phosphine ligands, P-chiral monodentate phosphine ligands have been much less explored.[2] Herein, we report the synthesis of monodentate P-chiral biarylphosphine ligands, which were synthesized by desymmetrization of simple branched alkyl(diphenyl) phosphine oxides via directed ortho metalation using (+)-sparteine as ligand. The asymmetric reduction of P-chiral phosphine oxides was carried out under $Ti(OiPr)_4$/ hydrosilane-mediated conditions to generate highly enriched P-stereogenic monophosphine ligands, which easily form stable gold(I) complexes. These catalysts display high catalytic activity and asymmetric induction in gold(I)-catalyzed 1,6-enyne cyclization reactions.



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Total Synthesis of *ent*-Pimaranes and Indole Sesquiterpenes

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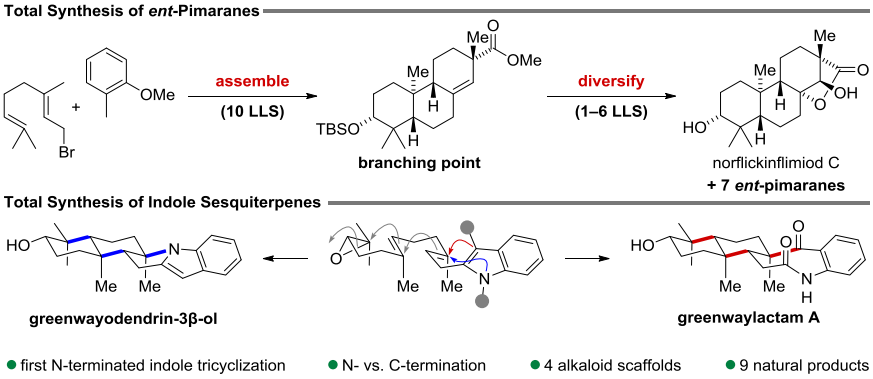
We present the enantioselective total syntheses of several *ent*-pimaranes and sesquiterpenoid alkaloids. Key features of our divergent synthetic strategies involve (1) Sharpless asymmetric dihydroxylation for chirality introduction and (2) bioinspired Brønsted/Lewis acid catalyzed polyene cyclization for rapid access to the requisite polycyclic carbon scaffolds.



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Synthetic Application of 2-Fluorocyclopropyl-1-sulfinate

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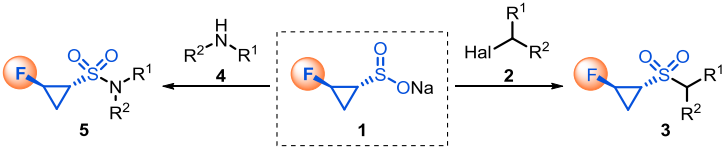
Fluoroalkyl-containing compounds are of high significance in the research of pharmaceuticals,[1] agrochemicals,[2] and advanced materials,[3] as fluoroalkyl groups can alter their physicochemical properties.[4] Fluorocyclopropyl group is an intriguing moiety with potential application in medicinal chemistry, therefore, fluorocyclopropylsulfinate **1**, being similar to *Langlois* reagent,[5] could be an attractive, yet little explored, source of fluorocyclopropyl moiety in fluorine chemistry.

Herein, we demonstrate application of fluorocyclopropylsufinate **1** to access fluorocyclopropylsulfones **3** *via* reaction with primary or secondary alkyl halides **2** and fluorocyclopropylsulfonamides **5** via reaction with secondary alkyl amines **4**.



Acknowledgements

This work has been supported by the Latvian Council of Science project lzp-2022/1-0335.

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The Design and Synthesis of Conjugated Organic Compounds for Electronic and Thermoelectric Applications

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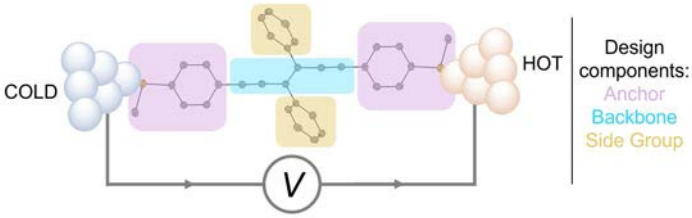
Loss of energy through waste heat has become of increasing concern in the drive for a sustainable future. Thermoelectric materials have been highlighted as a potential route for the efficient recovery of waste heat. To achieve efficient conversion of heat to electricity, thermoelectric materials require a high electrical conductance and high Seebeck coefficient, in addition to a low thermal conductance. Molecular materials have shown potential in minimizing the interdependence of electrical and thermal conductance, while maximising the value of the Seebeck coefficient. Linear polyynes have been proposed as potential thermoelectric molecular materials, and hexa-3-ene-1,5-diyne compounds provide an interesting scaffold for introducing side group functionalisation, allowing for tuning of thermoelectric properties while maintaining a conductive central (backbone) pathway. Herein, we present an overview of synthetic strategies in the production of linear α,ω-functionalised oligoynes and functionalised hexa-3-ene-1,5-diyne compounds, and preliminary results towards the investigation of their thermoelectric properties.



Photoredox-Catalyzed Amination Reactions of Alkanes, Ethers, Sulfides, Arenes, and Alkenes with Nonaflyl Azide

Chiranan Pramthaisong[1], Ameneh Tatar[1], Anna Poryvai[1], Ján Tarábek[1], Radek Pohl[1], Jan Zelenka[2], Jana Roithová[2], Ullrich Jahn[1]

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[2] Institute for Molecules and Materials, Radboud University, The Netherlands
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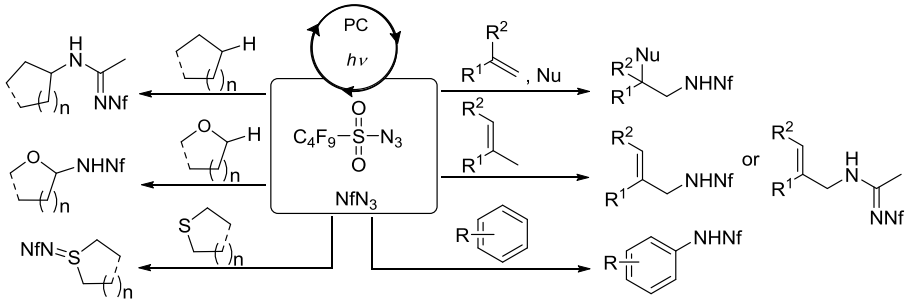
C–H amination reaction of non-functionalized compounds enables both natural product, and pharmaceutical compound modifications. Transition metal-catalyzed C–N bond formation through nitrene transfer was commonly applied to introduce amino functional groups into hydrocarbons.[1] Recently, visible light-induced protocols have become an important synthetic platform due to their mild reaction conditions.[2] However, amination methods of hydrocarbons remain a challenge and the nitrene sources are not atom economic or hard-to-handle. Therefore, in this study, we present the photoredox-catalyzed amination reactions of alkanes, ethers, sulfides, arenes, and alkenes with self-stable nonaflyl azide to provide amidines, amides, *N–O* acetals, sulfilimines, or sulfonamides products under our optimal conditions.



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Target-Guided Synthesis of Novel α-Acylamino Amides

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Target-guided approach to synthesis uses the macromolecule of interest as a template to step up the making of its own inhibitors.[1] This methodology engages the direct participation of the target, usually via the catalytic active site of enzymes in the preliminary screening, evolution, and selection of potential hits. For example, using the target-guided approach Sharpless' team designing and synthesizing inhibitors of acetylcholinesterase (AChE) by click-chemistry.[2] Since then, several studies of AChE-guided synthesis have been done by *in situ* click-chemistry, and the one thio-Michael addition cascade route to AChE inhibitors was described as well.[3] In this work, we used a four-component Ugi reaction for a target-guided synthesis to identify novel butyrylcholinesterase (BChE) inhibitors in the development of new potential drugs for Alzheimer's disease. α-Acylamino amide products were produced in one step and a novel diverse library of peptidomimetics that has not been yet described in the literature was created. New protocols for preparations of Ugi products including the use of mechanochemistry (with or without solvent) and microwave synthesis were developed. The conditions were varied systematically and ease of the isolation and yields of the reactions were compared. α-Acylamino amide conformers in the solution were determined experimentally and studied by quantum-chemical calculations.

Acknowledgements
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Design and Synthesis of Molecular Building Blocks for Modular Supramolecular Cavitands

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Our current research is based around a system that enables the modular synthesis of various different-sized cavitands from a small selection of molecular building blocks through cyclocondensation reactions. The system is centered around derivatives of bicyclo [3.3.1]nonane-2,6-dione **1**. Macrocyclization with aromatic 'wall fragments' would allow for synthesis of rectangular cavitands, while incorporation of both enantiomers of the bicyclic compound could be used to create even more complex cavitands, having both positive and negative internal curvature (e.g. **4**). Introducing ureidopyrimidinone moieties would allow for synthesis of dynamic supramolecular cavitands, the formation of which could be modulated by changing various properties of the solution (e.g. pH, polarity, temperature).

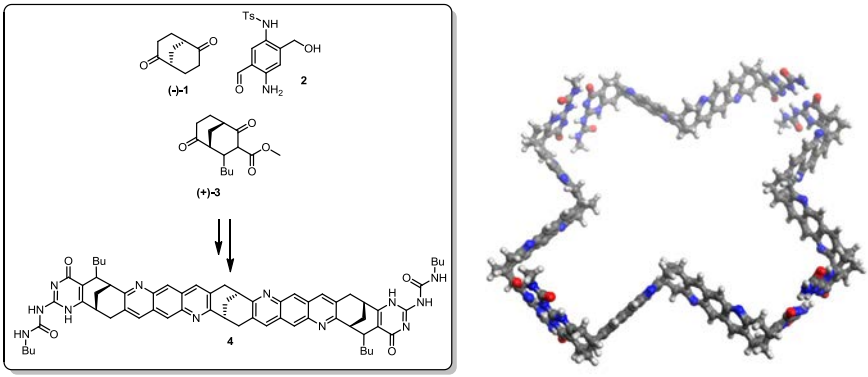

Figure 1. Simplified synthesis scheme of monomer **4** (left); Modelled structure of tetrameric **4** in solution (right).

Organo-Photoredox Catalyzed Radical Fluoromethylation – Cascade Cyclization of Aryl *N*-Acrylamides

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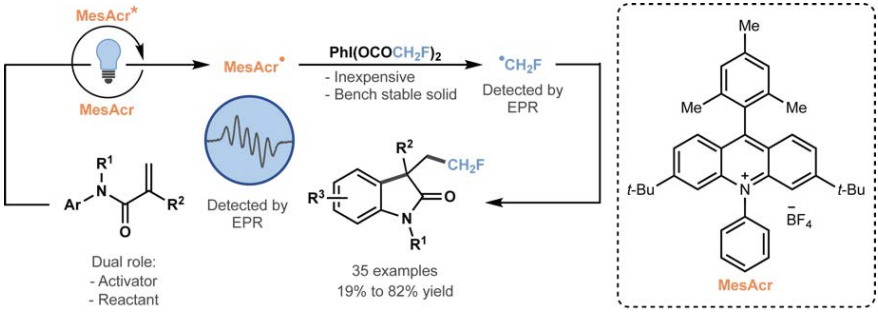
Inclusion of fluorine atoms has been shown to improve physiochemical and biological properties of bioactive compounds.[1] While introduction of trifluoromethyl group is well developed, further development of monofluoromethylation strategies is needed. We report a method for accessing monofluoromethylated 2-indolones using an iodine (III) reagent as a fuoromethyl radical source under visible-light photoredox catalysis.[2] Contrasting previous works,[3,4] our method is mild, transition metal free and no additives are required as aryl *N*-acrylamides display dual role both as an activator and reactant of the reaction.



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Biginelli Dihydropyrimidines: A Tunable Class of Heterocyclic Electroauxiliaries for Alkyl Radical Delivery *via* C–C Bond Activation

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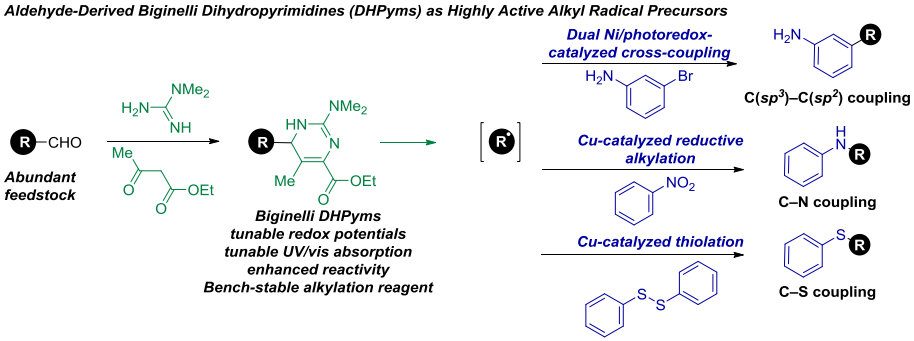
We identified alkyl-substituted dihydropyrimidines (DHPyms), synthesized via the Biginelli reaction, as tunable alternatives to 4-alkyl Hantzsch esters in radical chemistry. Our study explores their redox properties, UV/vis absorption, and synthetic potential, demonstrating DHPyms as versatile alkyl radical precursors. DHPyms with lower oxidation potentials showed enhanced reactivity in Ni/Photoredox dual catalytic cross-coupling reactions, outperforming traditional Hantzsch esters.



Acknowledgements
This work was supported by the Fonds der Chemischen Industrie (scholarships to D. J.-M. and S. R.). Prof. Dr. Lutz Ackermann is greatly acknowledged for his continuous support.

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Design and Aapplication of NHC-Metal Ssurfaces as Catalyst

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Recent progress in NHC on metal catalysis was predominantly focused on the preparation and characterization of NHC coated metal surfaces to understand chemical information and dynamics at the molecular level.[1] However, researchers have shown significant interest in the design strategies of heterogeneous systems with NHC-modified surfaces and their applications in catalysis for tuning key catalytic parameters. The establishment of the structure-property relationship of such heterogeneous systems is still in its early stages.[2] By modifying the molecular structures, it is possible to control the activity, stability, and solubility of the nanoparticles.[3,4] Chiral NHCs, which are relatively unexplored, offer the opportunity to induce an asymmetric environment that enables enantioselective chemical transformations.[5] Therefore, the development of various heterogeneous surfaces using NHCs as molecular modifiers may achieve alternative activity and selectivity for challenging yet rewarding chemical reactions that cannot be achieved using homogeneous systems.

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New 4H-Bonding Motif

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Hydrogen bonding is a highly adaptable non-covalent molecular interaction that is extensively employed by nature to fulfill crucial life functions such as maintaining structural integrity, facilitating catalytic processes, and enabling replication. The term "hydrogen bonding motifs" pertains to particular configurations of hydrogen bonds inside molecular structures, serving as fundamental units for the construction of modular assemblies of hydrogen-bonded dynamic structures. The association strength of an array is determined by the overall number and arrangement of individual hydrogen bonds. In order to form supramolecular polymers, it is necessary to have quadruply bonding motifs to ensure adequate aggregation. In this study, we introduce a novel molecular structure, present its synthesis, and aggregation properties.

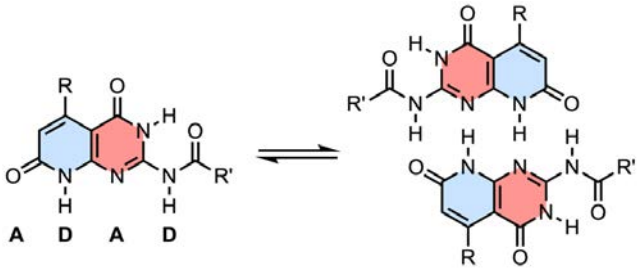

Figure 1. A. Chemical structure of the 4H-bonding motif.

Formal Synthesis of 9,11-Secosterols

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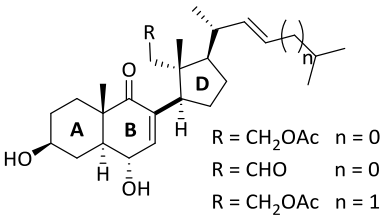
9,11-Secosterols are a class of modified steroids that are well known for both their complicated chemical structures and their various biological activities. Many semisynthetic pathways are known for synthesizing these steroids, however, the very first total synthesis pathways have begun to appear only recently. Our group has been involved in elucidating a total synthesis pathway to 9,11-secosterols for many years and while we have not reached a complete total synthesis pathway yet, with the recent developments in the field, we are closer than ever.

Herein we present two formal synthesis pathways for obtaining one of the 9,11-secosterols first isolated from the cold-water coral *Gersemia Fruticosa* in 1998.[1]



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Novel Synthesis of Seco-Pseodopterosin Aglycon

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Seco-pseudopterosin, a biologically active diterpene with significant anti-inflammatory and anticancer properties, has attracted the attention of many synthetic organic chemists. However, its complex molecular structure poses significant challenges for synthesis.[3] Herein, we report a novel and efficient synthesis of seco-pseudopterosin, employing a strategic sequence of reactions that enhance yield and stereoselectivity. Our approach integrates a stereoselective allylation,[2] followed by an innovative stereocontrolled oxy-Cope rearrangement[1] and a regioselective cyclisation, culminating in the formation of the target molecule. Our method presents a significant advancement in the synthetic accessibility of seco-pseudopterosin, paving the way for further pharmacological studies and potential therapeutic applications.

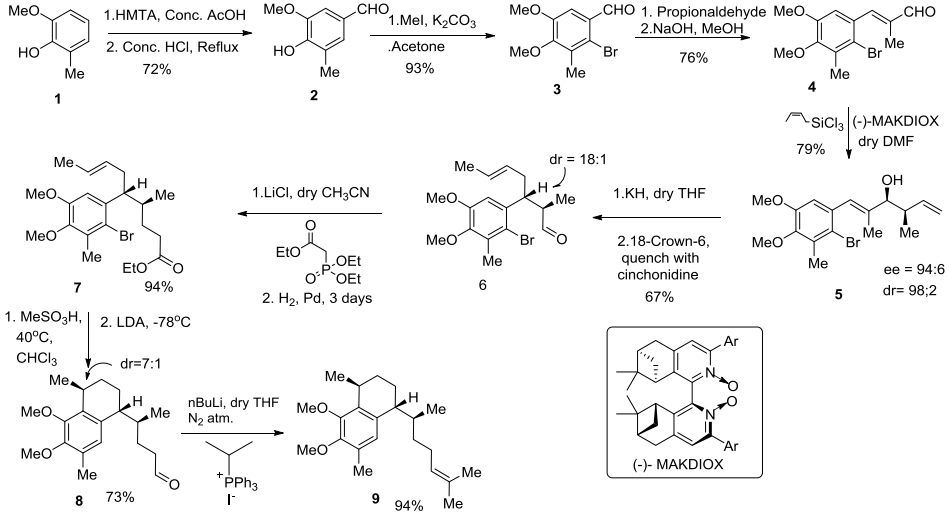

Figure 1. Novel and efficient synthesis of seco-pseudopterosin.

Acknowledgements
This work was supported by NOS fellowship, India and Loughborough University, UK.

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Mechanochemical Birch Reduction with Low Reactive Alkaline Earth Metals

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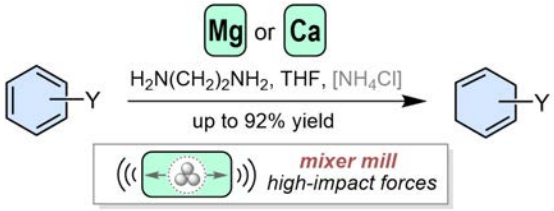
Birch reduction is a powerful dearomatization method that converts arenes into unconjugated cyclohexadienes. The classic approach uses alkali metals (Li, Na, K) dissolved in liquid ammonia at cryogenic temperatures as reductants. In our study, we demonstrate that largely neglected, low-reactive alkaline earth metals (Ca and Mg) can become powerful and affordable reductants when used in a mixer mill under essentially solvent-free conditions, in the presence of ethylenediamine and THF as liquid additives. The mechanochemical approach is operationally simple, employs safe-to-handle metals, features fast reaction rates and high product yields comparable to those of classic Birch reduction. Additionally, Mg metal enables chemoselective reductions, serving as a mild reductant. Our protocol is also applicable to other dissolved metal-type reductive transformations, including reductive amination, deoxygenation, dehalogenation, and alkene and alkyne reductions.



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Access to Novel Biheterocyclic Compounds *via* Multicomponent Reactions of 3-Alkoxy-1*H*-Pyrazole-4-Carbaldehydes

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Multicomponent reactions have attracted significant interest due to their atomic economy, and increased productivity resulting from fewer intermediate purification steps, which enhances the yield of desired products, complies with the principles of green chemistry, and serve as an attractive alternative to gradual linear synthesis.[1,2]

A number of new biheterocyclic compounds have been synthesized starting with 3-alkoxy-1*H*-pyrazole-4-carbaldehydes, employing various multicomponent reactions. The structures of the obtained 4-(pyrazol-4-yl)pyrano[2,3-c]pyrazole, 4-(pyrazol-4-yl)pyrazolo[4',3':5,6]-pyrano[2,3-*b*]quinoline, 4-(pyrazol-4-yl)pyridine, and 4-[(pyrazol-4-yl)methylidene]-1,2-oxazole derivatives were thoroughly characterized and confirmed using detailed nuclear NMR, HRMS, IR, and X-ray analysis.[3]

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Synthesis of Cyclic Biaryl λ^3-Bromanes *via* Electrochemical Oxidation of 2,2'-Dibromobiphenyls

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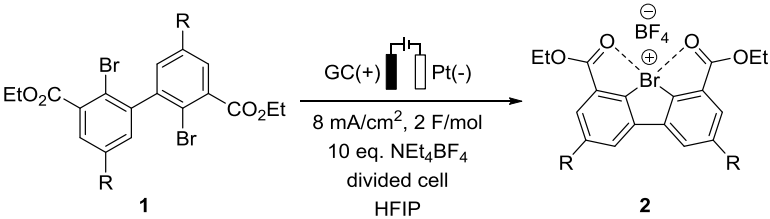
The synthesis of hypervalent bromine(III) compounds is much less studied and developed than their iodine(III) counterparts. Despite offering stronger oxidizing power, bromine(III) reagents are known for their lower stability and the need for toxic and highly reactive BrF_3 as a precursor in their synthesis. We have found that cyclic biaryl λ^3-bromanes **2** can be obtained by the anodic oxidation of 2,2'-dibromobiphenyls **1** (Scheme 1). X-ray analysis of **2** shows that the bromane molecule exists in the form of an ionic pair and that the bromine(III) atom is stabilized by *ortho* carbonyl groups. Current progress in elucidation of the reaction mechanism and the substrate scope will be demonstrated.



Scheme 1. Electochemical synthesis of λ^3-bromane **2**.

Acknowledgements
This research is funded by the Latvian Science Council grant LZP-2021/1-0595.

Copper-Catalyzed Arylation of Propargyl Silanes with Consequent Internal Cyclization

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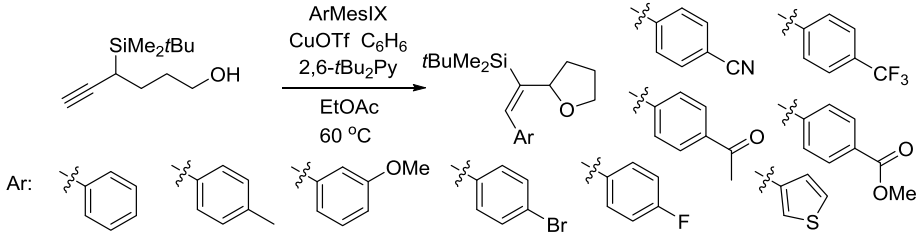
Recently we have published synthesis methods for propargyl silane 1,3-difunctionalization with concomitant silyl shift.[1] The concept involves propargylsilane activation with an electrophile, followed by a 1,2-silyl shift. This creates an electrophilic carbon center that can react with a nucleophile. This work presents a formal carbon electrophile to activate the propargylsilane. In this case aryl cuprate, generated from diaryliodane, activates the propargylsilane, which undergoes a 1,2-silyl shift. This generates a carbenium ion or its equivalent, which is trapped by the alcohol. Aromatic groups with electron donating and electron withdrawing substituents and some heteroaromatic groups can be used.



Acknowledgements
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Progress in Total Synthesis of Nostolactone 4

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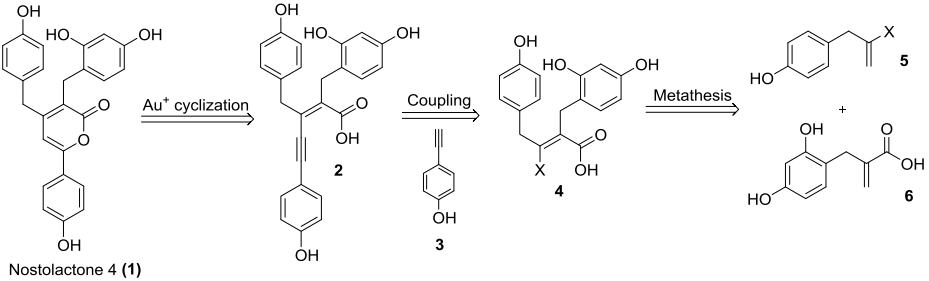
Nostolactone 4 is a polyphenolic compound isolated from the cyanobacterial strain *Nostoc* sp. with biological activity against some Gram-positive bacteria.[1] Its skeleton is composed of 2,3,5-trisubstituted δ-lactone ring and it has not been synthesized yet. Our aim is to develop and optimize the synthesis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

Scheme 1. Retrosynthetic approach to synthesis of nostolactone 4



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Ring-Opening of Arylbicyclobutanes with Silyllithium Reagents

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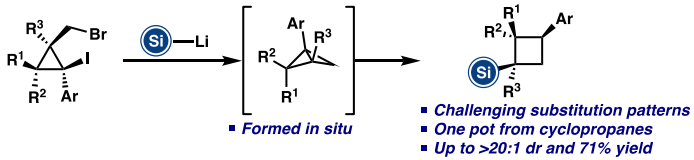
Bicyclobutanes are versatile and reactive synthetic intermediates commonly used to access cyclobutanes and aryl bioisosteres by functionalization of their strained bridging bond.[1] However, reported nucleophilic ring openings of bicyclobutanes are generally limited to substrates bearing electron-withdrawing groups and 1-2 substituents. We disclose the in-situ formation and ring opening of arylbicyclobutanes with silyllithium reagents to provide polysubstituted cyclobutylsilanes with high diastereoselectivity. This reaction, enabled by the high ring strain of bicyclobutanes and the exceptional nucleophilicity of silyllithium reagents, represents the first nucleophilic ring opening of bicyclobutanes lacking an electron-withdrawing group. We also demonstrate further derivatization of the reaction products.



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Development and Biological Evaluation of Novel *S*-Substituted 1,2,4-Triazole-3-thiones Containing a Heterocyclic Moiety in their Structure

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Tumors are abnormal tissue masses resulting from uncontrolled cell growth. This condition poses challenges for healthcare due to its widespread occurrence and limited treatment efficacy. Developing new, precise anticancer drugs is crucial for improving patient outcomes and minimizing side effects. This study reports the synthesis and evaluation of the anticancer properties of substituted 1,2,4-triazole-3-yl thioaceto-hydrazides. The target compounds were prepared through a series of reactions and characterized using spectroscopic techniques. Their effectiveness was tested against various cancer cell lines, showing promising results, particularly for derivatives containing specific fragments (pyrrole, 2-hydroxybenzene, and 2-hydroxy-5-nitrobenzene). These findings highlight the potential of these compounds as anticancer agents and warrant further investigation.

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An Effective Method for Preparation of Ethyl 2,5-Dimethyl-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidine-6-carboxylate as a Key Step to the Human Adenosine A_{2A} Receptor Antagonists

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Istradefylline is a new drug that was recently approved by the FDA for use as adjunctive treatment to L/C in adult patients with PD experiencing "off" episodes. In this research we assembled the molecules with similar shape containing thieno[2,3-*d*]pyrimidine core. The effective procedure for preparation of 2,5-dimethyl-4-oxo-3,4-dihydrothieno[2,3-d] pyrimidine-6-carboxylate based on application of N,N-dimethylacetamide dimethyl acetal was suggested. At the cyclization step ammonium acetate application gave high yields of the intermediate ester for further alkylation with chloroacetamides. The results of docking studies revealed that all of the obtained target amides are capable of binding to the active site of human adenosine A_{2A} receptor and in general well fit its shape.

Acknowledgements
Authors acknowledge The Ministry of Health Care of Ukraine for the State Budget grant on the topic "Molecular modeling and synthesis of innovative pyrimidine derivatives as promising agents for the treatment of neurodegenerative diseases" (State registration number: 0124U002006). The authors acknowledge Enamine Ltd. for the chemical research opportunities.

N-Benzylpiperidine-Based Schiff Bases are Cholinesterase Inhibitors – Design, Synthesis and Biological Evaluation

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The chemical structure of donepezil, a clinically used acetylcholinesterase (AChE) inhibitor for Alzheimer's disease (AD) treatment, includes an *N*-benzylpiperidine component (N-BP) that is important for its interaction with the peripheral anionic site within the AChE pocket.[1]
A novel series of Schiff base compounds also containing the N-BP component were designed, synthetized, and evaluated for their *in vitro* cholinesterase inhibitory activity against AChE and butyrylcholinesterase using Ellman's spectrophotometric method to determine their IC_{50} values. Additionally, their antimicrobial properties were also evaluated. Encouraged by promising results in terms of cholinesterase inhibition, another series of Schiff bases were synthesized. The modification concerned for example the usage of isomeric amines or the reduction of selected Schiff bases to corresponding amines.
In this work, the overall design of this series, as well as the synthetic process and the results of the biological evaluation will be discussed.

Acknowledgements
This work was supported by Charles University (SVV 260661) and National Institute of virology and bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) – Funded by the European Union – Next Generation EU.

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Methylation of Phenols

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Alkylation of aromatic compounds, a crucial reaction in organic chemistry, is extensively utilised in the production of petrochemicals, fine chemicals, and pharmaceuticals. Common reagents for methylation include methyl halides, dimethyl sulfate, and diazomethane. Named reagents are toxic and environmentally hazardous. Given the environmental impact of named chemicals, it is important to develop more environmentally friendly methods for producing methyl ethers. Dimethyl carbonate is an environmentally benign alternative to the traditionally used methylating agents.[1,2] This study optimises the conditions for methylating 5-methylresorcinol using dimethyl carbonate.

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C–H Functionalization of Benzoic Acids Controled by Non-Covalent Interactions

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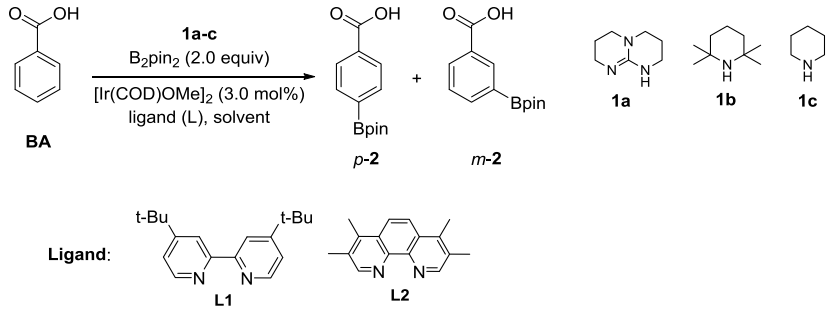
Among other transition metal catalyzed C–H transformations the Ir-catalyzed borylation emerged as one of the most exploited reactions due to its mild conditions that allow facile entry into highly valuable synthons.[1] The regioselectivity issues of this transformation are perhaps one of the best articulated ones due to the low regiocontrol of the non-directed Ir-catalysis. Herein we report a concept for para-selective borylation of carboxylic acids that relies on an unreported to date carboxylate-guanidinium noncovalent interaction (Scheme 1). Our strategy is based on the simultaneous non-covalent protecting of the free acid accompanied by steric guidance of the catalyst in a proximity to the *para* position. Up to 80% yield and *para/meta* selectivity of 6:1 have been achieved.

Scheme 1. Ir-catalyzed borylation of benzoic acid in presence of different organic bases



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Metal-Catalyzed Fluoroacetyl Carbene Transfer from Sulfonium Salts

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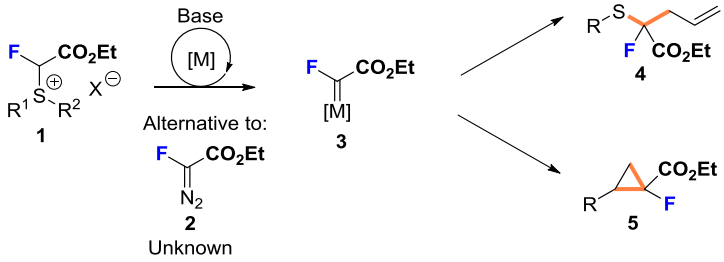
Fluorinated carbene transfer is an effective strategy to create new carbon-carbon or carbon -heteroatom bonds while simultaneously delivering a fluorine atom into the target structure.[1,2] The metal-catalyzed fluorocarbene transfer mostly relies on the use of diazo compounds. Herein, we present newly developed sulfonium salt **1** as an alternative to currently unknown ethyl diazofluoroacetate **2** for fluoroacetyl carbene transfer reactions in Doyle-Kirmse and cyclopropanation reactions to obtain valuable monofluorinated products **4**-**5** (Scheme 1).

Scheme 1. Metal catalyzed fluoroacetyl carbene transfer.



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Synthesis and Structure Revisions of Linariophyllenes A–C

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Linariophyllenes A–C **3**–**5** are terpenoids, which were isolated from *Evolvulus linaroides*, and possess anti-inflammatory activity.[1] Herein, we present a stereoselective semi-synthetic route (Fig. 1) towards linariophyllenes A–C **3**–**5** based on the structural similarity with commercially available β-caryophyllene (**1**) and its oxide (**2**). These starting materials are readily available in bulk quantities and were used previously in our studies.[2] Whereas the structure of linariophyllene B (**4**) was confirmed, the structures of linariophyllenes A and C **3** and **5** were revised to be the epimers of previously elucidated structures.[1]

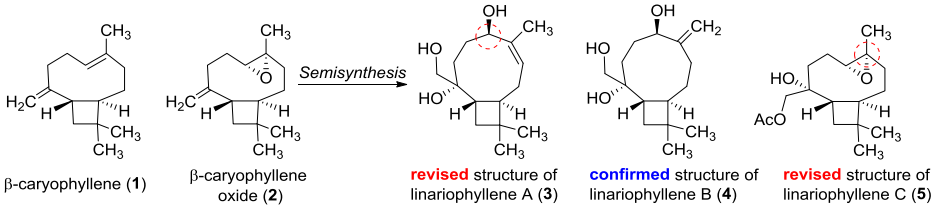

Figure 1. Semisynthesis of linariophyllenes A–C.

Acknowledgements
This work was funded by LIOS internal student grant IG-2024-01 and by Recovery and Resilience Facility (5.2.1.1.i.) grant Nr. ANM_OSI_DG_10.

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Exploring the Reactivity of Thiofumarates in Amino-Mefloquine Catalyzed [4+2] Cycloaddition

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New bicyclo[2.2.1]heptanone derivatives were synthesized in [4+2] cycloaddition reactions of cyclopentenones with thiofumarates using 13-methyl-11-aminomefloquine as an organocatalyst. Products were obtained with good yields and high optical purity (up to 91% ee). DFT-D calculations were performed along with experimental trials to establish the reaction mechanism and rationalize the reactivity of the reagents.

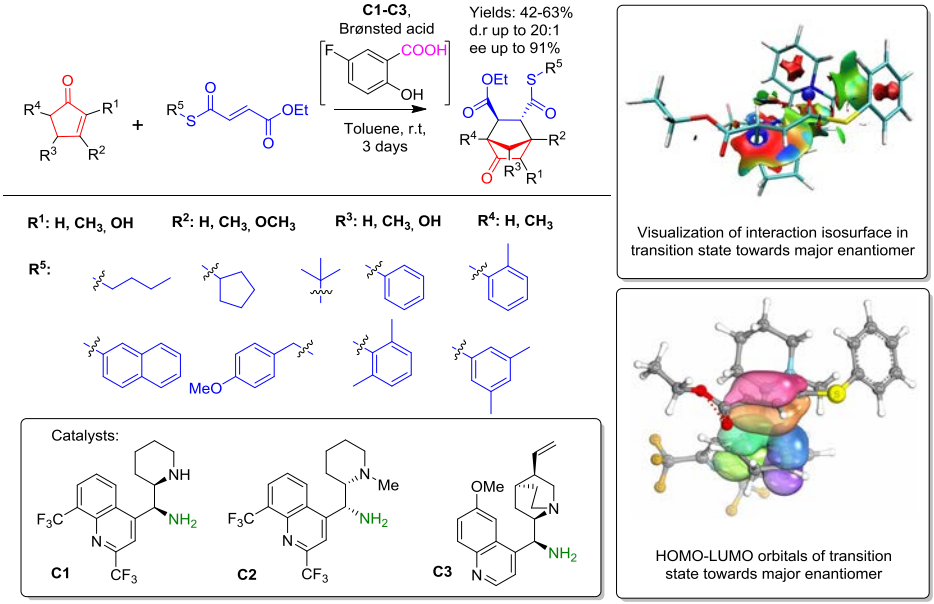

Figure 1. General reaction scheme, visualization of HOMO-LUMO orbitals as well as interaction isosurface in transition state towards major enantiomer.

Acknowledgements
NCN 2018/30/E/ST5/00242 funding.

Methylenecyclopropane Ring-Expansion With SO_2: Synthesis and Applications of Novel γ-Sultines

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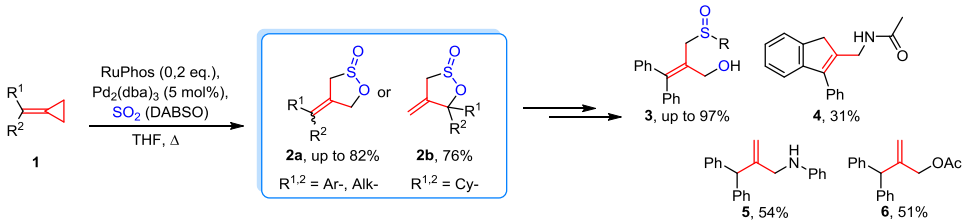
Sultines, cyclic esters of sulfinic acid, are employed in fragrance industry,[1] are known lactone bioisosters[2] and are versatile sulfur-containing intermediates for synthesis of various biologically active substances.[3] Herein we describe novel γ-sultine **2a**,**b** synthesis method through palladium-catalysed methylenecyclopropane **1** ring expansion with sulfur dioxide. Obtained γ-sultines can be derivatized to sulfoxides **3** and they undergo novel reactions yielding indenes **4**, allylamines **5** and allylacetates **6**.



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This work was supported by Riga Technical University grant ZM-2024/19.

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Organocatalytic Glycosylation Reactions with Phosphate Donor

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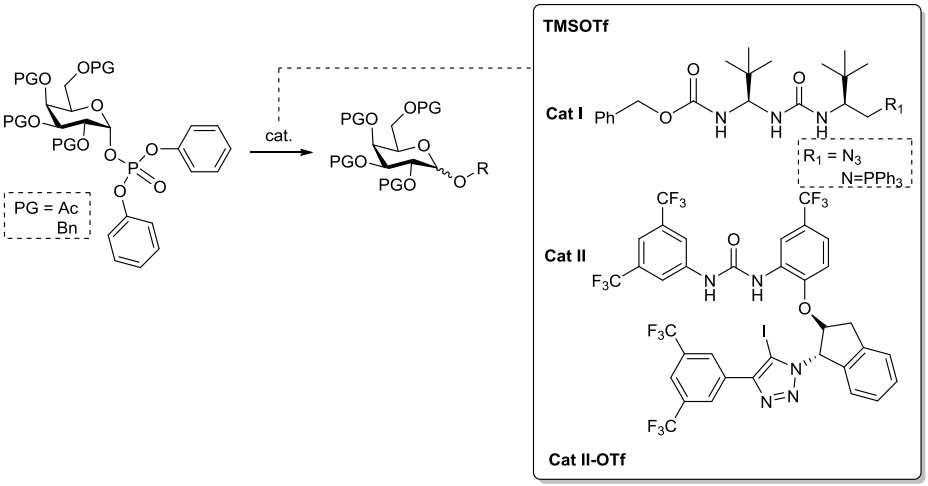
A number of different leaving groups are used in glycosylation reactions. Even though phosphate donors offer several advantages such as being native substrates for enzymatic reactions and being good XB acceptors, there are still a limited number of examples in the literature for their use.[1–3] Here, different thiourea and halogen bond organocatalysts were synthesized and applied to the glycosylation reaction with phosphate donor to assess the reactivity and anomeric selectivity.



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Promiscuity of Sesquiterpene Cyclases towards Cycloylidene Farnesyl Pyrophosphate Derivatives

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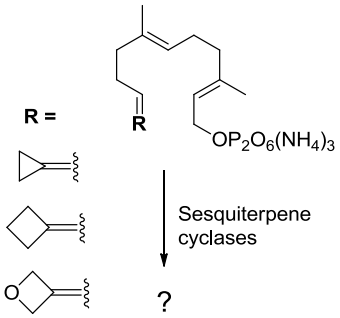
With over 80.000 known compounds terpenes constitute the largest class of natural products – in nature they act as repellents or attractans – in industry they are widespread in the perfume industry and in foodstuff.
Biosynthetically, terpenes are derived from elongated isoprenoid units (C_{5n}), which are cyclised by terpene cyclases and if need be further functionalised. Via sophisticated cascade reactions, the simple, linear, achiral C_{5n}-pyrophosphate precursor is efficiently modified into a highly complex, cyclic, chiral structure by these enzymes.
Our group concentrates on the synthetic potential these enzymes offer, to generate complex molecules from synthetically derived precursors – more specifically to form sesquiterpenoids (C_{15}) via sesquiterpene cyclases (STCs).
In the presented study farnesyl pyrophosphate derivatives with strained ring structures are investigated to showcase the synthetic potential of enzymatic transformations in the generation of intricate organic molecules. Complex cyclised products were isolated in the process.



Synthesis and Metabolism of Methylated Heterocyclic Bases

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Ribonucleic acid is central to many life processes and, to fulfil its function, it has a wide chemical variety in all RNA species. Major cellular source of modified nucleosides is tRNA, where >150 modified nucleotide species are found. The modifications are important for tRNA metabolism, structure, stability, localization and transport. Despite the huge progress in discovery of genes that introduce chemical modifications into tRNA and the investigation of the role of them in cell physiology and disease, it is much less known about the break down and return to the metabolism of the modified nucleosides and corresponding heterocyclic bases.

In this study, *N*,*O*,*S*-methylated pyrimidine and purine heterocyclic bases were synthesized and used for selection of genes involved in the catabolism of the modified heterocyclic bases. The uracil or purine auxotrophy based selection screening systems, similar to previously described ones,[1] allows the selection of enzymes converting the modified pyrimidines and purines into unmodified counterparts. Also, new metagenomic libraries created by isolating DNA from the environmental samples, sharing and cloning into multicopy cloning vectors, were used for selection of DNA fragments involved in metabolism of modified heterocyclic bases.

Acknowledgements
This project has received funding from the Research Council of Lithuania (LMTLT), agreement No [S-MIP-22-71].

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Synthesis of Modified PNA Nucleobases for Triple-Helical Recognition of RNA

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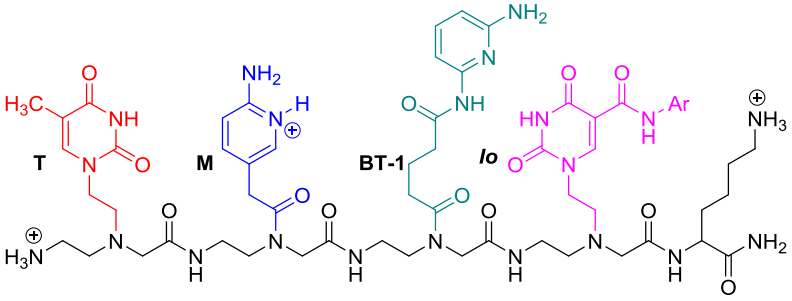
The central dogma of molecular biology highlights the importance of nucleic acids for sustaining life. The past several decades has brought to light the increased complexity of RNA and nucleic acids. Specifically, RNA has been observed to play a role in catalysis of biochemical reactions, gene regulation, and a variety of other processes. This has prompted much interest in oligonucleotide therapies for recognizing specific nucleic acid structures. One tool suited exceptionally well for recognition of complex biomedically relevant RNAs is peptide nucleic acids (PNAs). This work focuses on the synthesis and novel modified nucleobases for the incorporation into PNA. The recognition of the AU base pair in double helical RNA was accomplished using PNA with isoorotamide containing nucleobases. Isothermal titration calorimetry and UV-thermal melting were used to assess stability and specificity of PNA/RNA2 triplexes. Additionally, an analog of a previously designed nucleobase (V-base) was synthesized and incorporated into PNA for the recognition of the CG base pair in double helical RNA. Initial results demonstrate lower affinity for the CG pair when compared to the previously designed V-base. Future work is focused on synthesizing new analogs of V-base for the selective recognition of the CG pair in double helical RNA.



Influence of Terminal Chiral Information in Tetrakis Triazole Anion-Binding Catalysts for the Dearomatization of *N*-Heteroarenes

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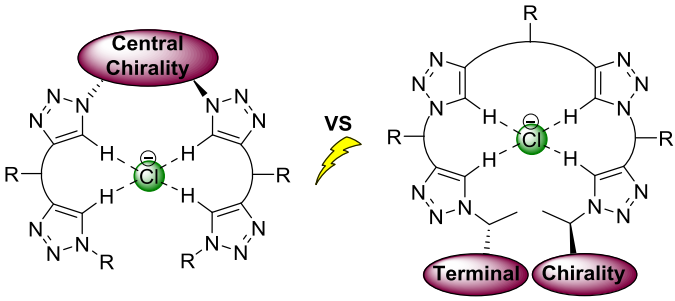
In the past decade, chiral tetra-triazole foldamers have been established as potent anion-binding catalysts for the dearomatisation of quinolines, isoquinolines, quinazolines and pyridines.[1] While these systems are based on a chiral 1,2-diaminocyclohexyl central skeleton to enforced the formation of a defined helical complex upon anion binding, the effect of implementing the chirality at the side ends of the backbone has not been explored. In this work, we addressed this until now untouched structural information on similar tetra-triazole based catalyst structures and tested them towards the Reissert-type dearomatisation of quinolines.[2]



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One, Two, Three, Go: Novel Applications of 1,2-Silyl Shift for 1,3-Difunctionalization of Propargyl Silanes

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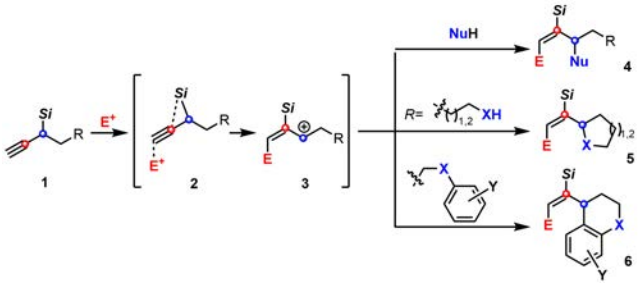
Propargyl silanes can act as precursors of 1,3-dipols, if their electrophilic activation is followed by 1,2-silyl shift.[1] Herein, we report propargyl silane **1** activation by electrophiles (H^+, X^+, RSe^+, R-Cu(III)) that results in allyl cation **3** formation. The latter is trapped with various *N*-, *O*-, *S*-, *C*-nucleophiles in either intramolecular or intermolecular fassion.[2] This provides higly 1,2,3-functionalized systems **4**, **5**, **6** with possibilities for further derivatization.



Acknowledgements
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Synthesis of Fused Heterocycles *via* Cascade 1,2-Silyl Shift – Friedel–Crafts Cyclization

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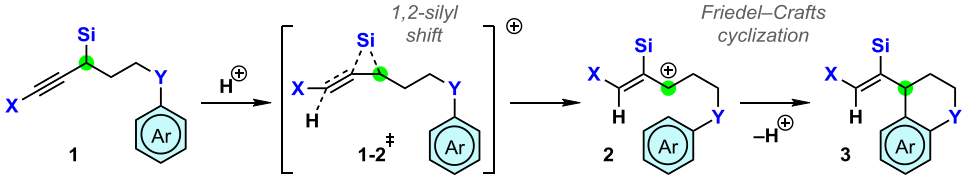
Herein we report a new synthetic pathway to fused heterocycles. The key synthetic step involves tandem 1,2-silyl shift – Friedel–Crafts cyclization. First, propargyl silane **1** undergoes an electrophilic attack, which induces silyl group migration in an *anti*-fashion. This provides a relatively stable allylic cation **2**, which can further react with the internal nucleophile. Previously, our scientific group successfully applied this concept by affording 5-membered carbocycles[1] or heterocycles.[2] In this work, we expand our method to the synthesis of 6-membered heterocycles **3**.



Acknowledgements
The authors thank the Latvian Council of Science Grant No. LZP-2023/1-0576 and Riga Technical University Master Research Grant No. ZM-2024/6 for financial support.

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Total Synthesis Of Sitsirkine, Dihydrositsirkine, and Meroquinene *via* Stereoselective Ireland–Claisen Rearrangement

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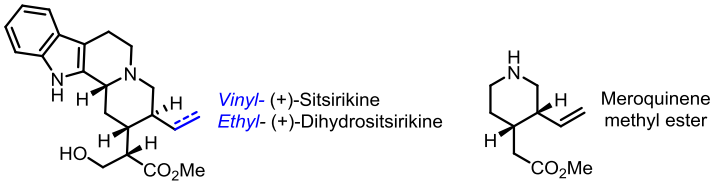
Nominated to present this work as a short talk on July 9, 15:00

Sitsirikine and Dihydrositsirikine are monoterpenoid indole alkaloids isolated from the leaves of *Vinca rosea* Linn.[1] the structure of which was fully assigned by Kutney[2] and Leonard.[3] These alkaloids exhibit vasorelaxant activity against phenylephrine-induced contraction of rat mesenteric arteries, with EC_{50} values less than 10 μM.[4]
The first total synthesis of Sitsirikine and Dihydrositsirikine as well as a simpler piperidine natural product – Meroquinene will be reported employing a stereoselective Ireland–Claisen rearrangement as the key step.



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Individual fellowship project of the Latvian Council of Science Nr. lzp-2020/2-0045.

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Synthesis of New N-Substituted 3-Aminobenzenesulfonamides

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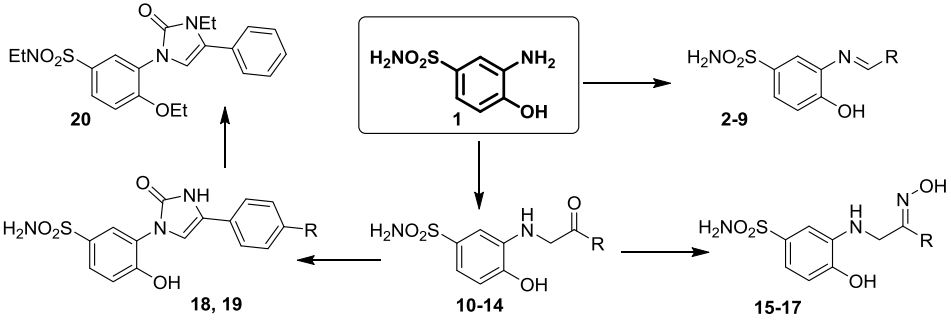
Benzenesulfonamide motif is widely explored in medicinal chemistry due to its vast variety of pharmacological properties. In the present study, Schiff bases **2**–**9** were synthesized by the standard procedure starting from 3-amino-4-hydroxybenzene-sulfonamide (**1**), which was condensed with the appropriate aromatic aldehyde in propan-2-ol at reflux for 1 h. Starting from readily available primary amine **1**, its reaction with the corresponding bromoacetophenone afforded target compounds **10**–**14**. To obtain ketoximes **15**–**17** the corresponding compounds **10**, **12** and **13** were treated with hydroxylamine hydrochloride in methanol at reflux in the presence of sodium acetate in the mixtures.



2, 10, 15, 18 R = Ph; **3** R = 4-FPh; **4, 12, 17** R = 4-ClPh; **5** R = 4-Me oph; **6, 14** R = 1-naphthyl; **7** R = 2-naphthyl; **8** R = thien-2-yl; **9** R = 5-NO_2-thien-2-yl; **11** R = 2,4-diFPh; **13, 16, 19** R = 4-HOPh.

To obtain the imidazol-2-one derivatives **18**, **19**, the corresponding precursors **10** and **13** were cyclized with carbamide in glacial acetic acid. Compound **18** was alkylated with large amount of ethyl iodide.

Design and Synthesis of Structurally Simple Supramolecular Capsule

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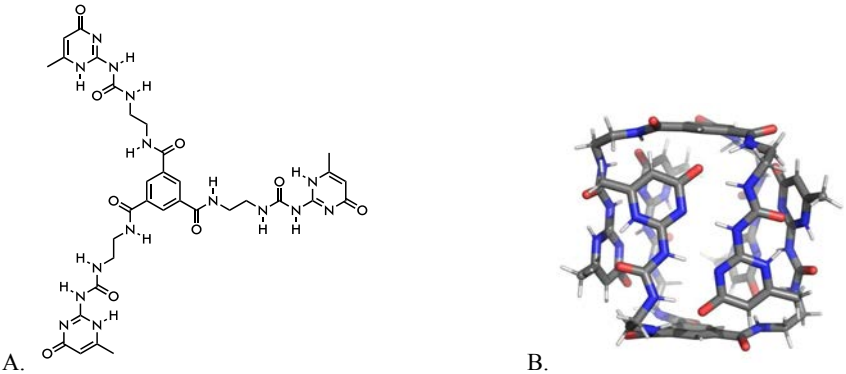
The molecular capsules, typically assembled using coordination or hydrogen bonds (H-bonds), are extremely well suited to interrogate the complexation phenomena and gain fundamental insights into the nature of non-covalent interactions.[1] In order to form capsular aggregates, large degree of preorganization is required which is achieved by introducing rigid molecular scaffold usually by employing complicated synthesis. In our report, we present a new approach toward molecular capsules using simple tripoidal monomer, containing three ureidopyrimidinone (UPy) 4H-bonding units connected to a central trimesic acid core (Fig.1). We have shown that such monomer quantitatively forms dimeric molecular capsules ensured by the secondary H-bonding.



A. B.

Figure 1. A. Supramolecular monomer. B. 3D model of capsule.

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Synthesis and Physical Properties of Polyazido Purine and Homopurine

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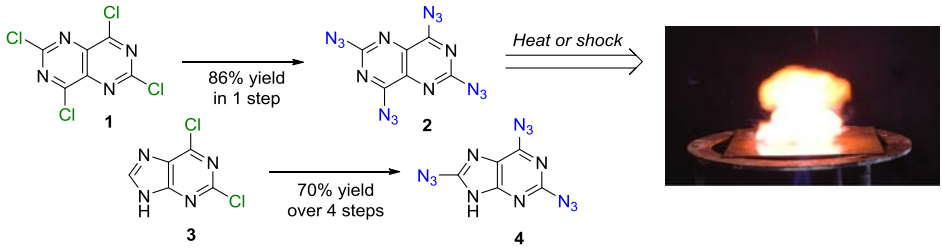
Binary C_xN_y organic compounds are impact-sensitive and possess explosive properties due to the high nitrogen content. The performance of nitrogen-rich compounds is attributed to the high heat of formation. Moreover, the main combustion product of such nitrogen-rich compounds is non-toxic nitrogen gas rather than the CO_2 from oxidation of a carbon backbone. Hence, nitrogen-rich compounds are currently the most promising candidates for the next-generation "green" explosives.

To the best of our knowledge, purine and its homologue – pyrimido[5,4-*d*]pyrimidine have not been used in the synthesis of energetic materials before. However, the nitrogen-rich backbone presents excellent features for application as high energy density materials. Recently, we have designed an approach towards binary C_6N_{16} compound **2** and triazidopurine (**4**) and tested their energetic properties.



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Synthesis and Investigation of New Pyrazole–Benzazole and Pyrazole–Indole Hybrids

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In this work, we report the synthesis of new pyrazole-benzothiazole, pyrazole-benzoxazole, pyrazole-indole hybrids, and investigation of their optical and biological properties. Easily accessible substituted 4-ethenyl-1*H*-pyrazoles, 6-bromo-2-benzothiazoles/benzoxazoles, 5-bromo-3*H*-indoles were utilized as Heck reaction substrates to give the target hybrids in 30–73% yields. UV-Vis absorption and fluorescence properties of the pyrazole hybrids were investigated in water and tetrahydrofuran. Pyrazole-indole hybrids showed anticancer activities in melanoma G361 and breast cancer MCF-7 cells within submicromolar range upon 414 nm light irradiation.

Acknowledgements
This work was supported by the Research Council of Lithuania (No. S-MIP-23-51), European Union (program EXCELES, No. LX22NPO5102), Doctoral Fund of Kaunas University of Technology (No. A-410) and Internal Grant Agency of Palacký University Olomouc (IGA_PrF_2024_005).

Development of Potent Microtubule Targeting Agent by Structural Simplification of Natural Diazonamide

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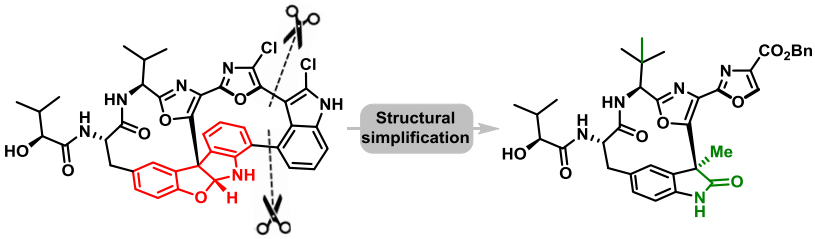
The marine metabolite diazonamide A exerts low nanomolar cytotoxicity against a range of tumor cell lines; however, its highly complex molecular architecture undermines the therapeutic potential of the natural product. We demonstrate that structural simplification leads to considerably less complex analogues with improved drug-like properties and nanomolar antiproliferative potency. The structurally simplified macrocycles are accessible in 12 steps with excellent diastereoselectivity (99:1) in the key macrocyclization step. The most potent macrocycle acts as a tubulin assembly inhibitor and exerts similar effects on A2058 cell cycle progression and induction of apoptosis.



Diazonamide A

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Synthesis of Fluorinated Benzenesulfonamides as Covalent Carbonic Anhydrase Inhibitors

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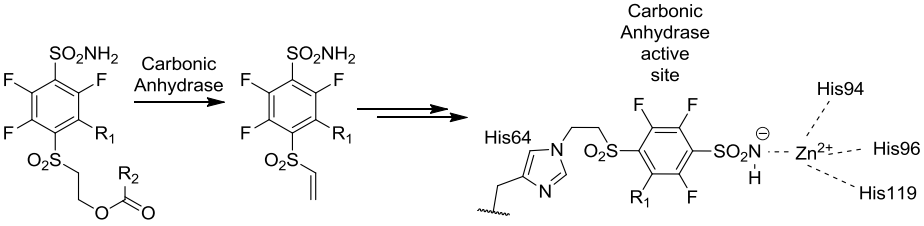
Carbonic anhydrases (CAs, EC 4.2.1.1) are enzymes responsible for reversible CO_2 hydration reaction catalysis to HCO_3^- and H^+. Overexpression of different CA isoforms is related to various diseases: glaucoma (CAII), epilepsy (CAVI), cancer (CAIX and CAXII) etc. Thus by selectively inhibiting specific CA isoform it is possible to treat respective diseases.

Using sulfonamide as a guiding group we have developed fluorinated benznesulfonamide prodrug which after binding to zinc in CA active site rearrange to vinylsulfone and react with catalitically important His64 residue. This new prodrug may have great potential for cancer treatment due to lower necessary dosage for complete inhibition of cancer associated CA IX.



Design and Synthesis of D-Glucose Based Glycoclusters for Enhanced Multivalent Binding

Andrea Vopálenská, Michaela Hovorková, David Vrbata, Vladimír Křen, Pavla Bojarová

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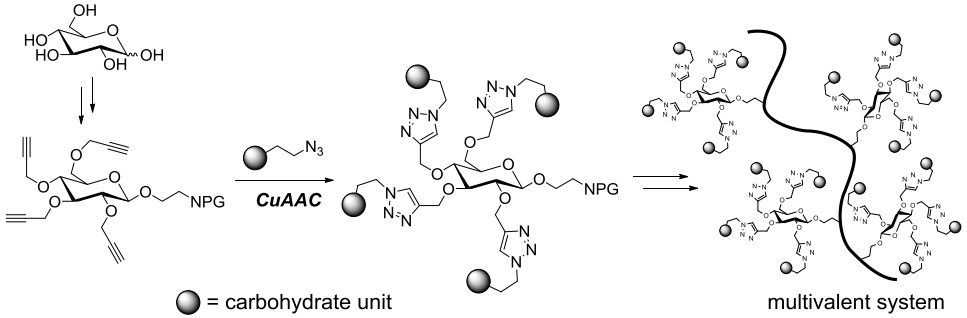
Glycoclusters bind/inhibit strongly biomedically important lectins, e.g., human galectins, by enhancing interactions *via* multivalent presentation.[1]
In this work, we have focused on the design of a multivalent glycocluster suitable as a potential inhibitor of Gal-3 and -4. We have synthesized two types of glycoclusters containing a D-glucose-based subcarrier, using Cu(I)-catalyzed azide-alkyne cyclo-addition (CuAAC). We performed an ELISA assay that showed affinity for Gal-3 and -4. In addition, these glycoclusters will be attached to a hydrophilic polymer scaffold.



Acknowledgements
This work was supported by the Czech Science Foundation (project 22-00197K), and by the mobility project LUC23148 of the Ministry of Education, Youth and Sports of the Czech Republic.

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Synthesis and Characterization of 2-[(Piperidin-4-yl)methyl]-3-(*N*-heterocycl-1-yl)propionic Acid Derivatives

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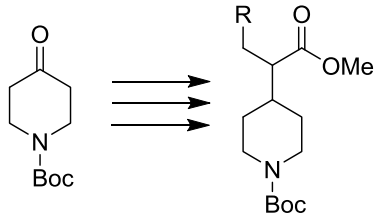
Heterocyclic amino acids are essential in drug discovery. For example, D-nipecotic acid, a building block for (*R*)-1-[4,4-bis(3-methyl-2-thienyl)-3-butenyl]-3-piperidine carboxylic acid, which amplifies neurotransmission of GABA, the predominant inhibitory neurotransmitter in the brain.[1] Recently, we reported a protocol providing easy access to chiral 2-(azetidin-3-yl)-2-alkylpropanoic acids as novel GABA derivatives.[2]



Herein, we report the efficient synthesis of 2-[(piperidin-4-yl)methyl]-3-(*N*-heterocycl-1-yl)propionic acid derivatives as a novel methylene homologue of GABA for novel scaffolds and building blocks from *N*-Boc-4-piperidinone.

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Catalytic Asymmetric Vinylogous Addition of Butenolides to Chromones

Takumi Watanabe, Jin Cui, Sadhanendu Samanta, Raphael Oriez, Yasunari Otsuka, Hidetoshi Noda, Masakatsu Shibasaki

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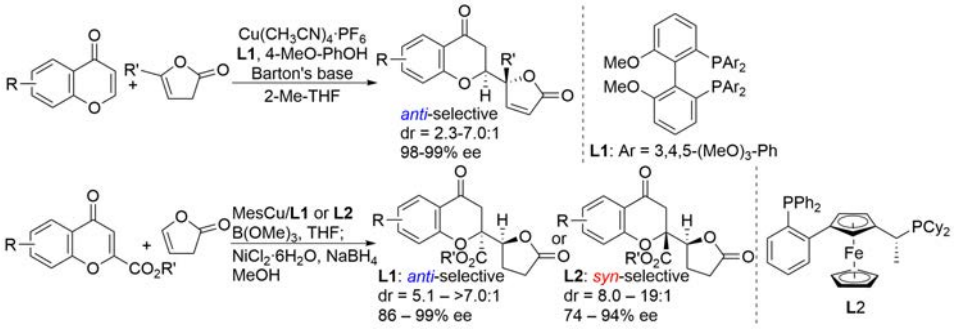
Chiral chromanone lactones are widely seen among biologically active natural products. This presentation shows two types of direct catalytic asymmetric vinylogous Michael-type reactions of chromones and β,γ-butenolides to construct the privileged structure as shown below. Applications of these methodologies to synthesis of natural products will be also discussed.



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Modular Synthesis of Teraryl-based alpha-Helix Mimetics

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The inhibition of protein-protein-interactions (PPIs) with small molecules has become a new paradigm in Chemical Biology. Hamilton and co-workers have shown that trisubstituted linear terphenyls can function as α-helix mimetics, displaying the *i*, *i*+4 and *i*+7 amino acid residues. To address solubility issues, our group has developed a modified design, in which pyridine nitrogen atoms are introduced at the water-exposed face distal to the protein binding site. Most recently, we have achieved comprehensive coverage of the protein sequence space by assembling teraryls from a library of readily available building blocks decorated with the side chains of all proteinogenic amino acids relevant for PPIs (Fig. 1).

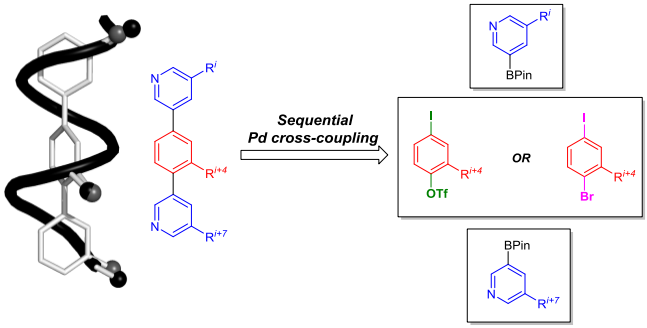

Figure 1. Assembly of teraryl-based alpha-helix mimetics.

Synthesis of Multi-Substituted Anilines *via* Cobalt-Catalyzed C–H Bond Functionalization

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Substituted aniline is a common fragment in many organic synthesis building blocks, pharmaceutically valuable compounds and agrochemicals.[1] Therefore development of novel methods for the synthesis of highly substituted anilines is desirable.
Cobalt catalysts for the C–H bond functionalization have been widely studied in the last decade due to their earth-abundance and relatively low toxicity. Herein we report a method development and optimization studies for the synthesis of substituted anilines via cobalt-catalyzed, picolinamide-directed C–H bond alkynylation of α,β-unsaturated amino acid derivatives (Fig. 1).

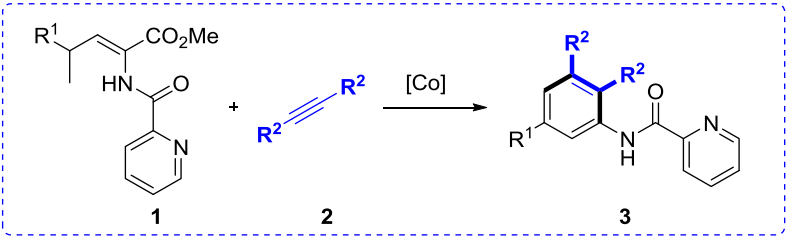

Figure 1. Cobalt catalyzed synthesis of multi-substituted anilines **3**.

Supervisor
Dr. Chem. Liene Grigorjeva

Acknowledgements
This research is funded by the ANM_OSI_ZG_04 academic career grant.

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New Powerful Building Block Molecules in 1,8-Naphthalimide Chemistry

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In recent years, much attention has been paid to the design and preparation of new substituted 1,8-naphthalimide architectures and the studies on the properties of materials. Wide possibilities of changing the optical and fluorescence, thermal, electrochemical, electroluminescent, and photoelectrical properties of 1,8-naphthalimide compounds can be materialized by introducing different electron-donating or electron-accepting moieties at the 1,8-naphthalimide core. At the same time, derivatives of substituted 1,8-naphthalimide have found application in other optoelectronic devices, such as organic light emitting diodes, organic solar cells, as well as in memory devices.

In our laboratory we have developed several new building block molecules[1] that have found wide application for the synthesis of various naphthalene based fluorophores and chromophores. The new dyes are promising candidates for high-tech applications such as OLEDs, OFET, visualization of cellular organelles[1], bimodal diagnostic imaging, etc.

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

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Design and Synthesis of Carbonic Anhydrase Inhibitors

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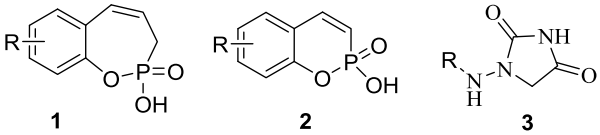
Carbonic anhydrases (CA) are enzymes containing metals that play essential roles in physiological processes like regulating pH and maintaining CO_2 levels. Recent advancements have marked CA as targets for drug interventions, with CA inhibitors showing potential in cancer treatment, glaucoma therapy, and even combating bacterial infections. In prior studies, we successfully synthesized selective CA inhibitors, including organophosphorus compounds. Expanding on this work, we are now focusing on developing a new class of CA inhibitors known as 2-hydroxybenzo-1,2-oxaphosphinines **1**, phosphacoumarins **2** as well as aminohydantoin derivatives **3**.



Acknowledgements
This work has received funding from Recovery and Resilience Facility (RRF) (5.2.1.1.i.) grant Nr.40/OSI/ZG.

Electron-Poor Acridones and Acridiniums as Super Photooxidants in Molecularp Hotoelectrochemistry by Unusual Mechanisms

Jonas Žurauskas[1], Soňa Boháčová[2], Shangze Wu[2], Valeria Butera[2], Simon Schmid[2], Michał Domański[2], Tomáš Slanina[2], Joshua P. Barham[2], Edvinas Orentas[2]

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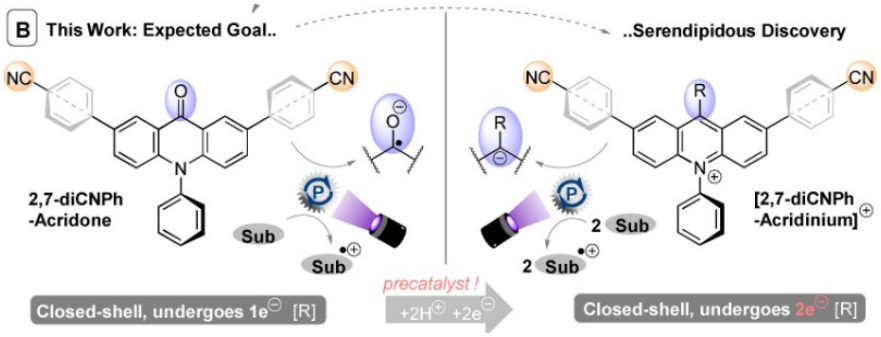
Nominated to present this work as a short talk on July 9, 15:15

Electron-deficient acridones and in situ generated acridinium salts are reported as potent, closed-shell photooxidants that undergo surprising mechanisms. Brønsted acid activation of acridones dramatically increases excited state oxidation power (by +0.8 V). Upon reduction of protonated acridones, they transform to electron-deficient acridinium salts as even more potent photooxidants ($*E_{1/2}$ = +2.56–3.05 V *vs* SCE). These oxidize even electron deficient arenes where conventional acridinium salt photooxidants have thusfar been limited to electron-rich arenes. Critically, this study illustrates how redox active chromophoric molecules initially considered photocatalysts can transform during the reaction to catalytically active species with completely different redox and spectroscopic properties.[1]



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High-Affinity Infrared-Fluorescent Probes for Cancer Imaging *via* Carbonic Anhydrase IX

Gediminas Žvinys[1], A. Petrosiute[2], A. Zakšauskas[2], A. Zubrienė[2], E. Čapkauskaitė[2], V. Juozapaitienė[2], A. Mickevičiūtė[2], Š. Grincevičienė[2], J. Matulienė[2], A. Ščerbavičienė[2], S. Raišys[3], Z. Kalnina[4], K. Tars[4], K. Shubin[5], D. Matulis[2]

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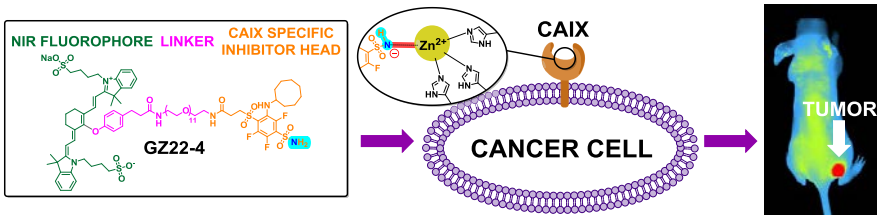
Metalloenzyme carbonic anhydrase (CA) IX is involved in cancer progression and persistence. CAIX is overexpressed in many hypoxic solid tumors and therefore, may be used as a tumor cell-expressing biomarker for cancer identification, imaging and delivery of therapeutic agents.



A series of benzenesulfonamide compounds bearing a CAIX-recognizing, high-affinity, and high-selectivity group conjugated via a PEG linker to infrared fluorescent moieties was synthesized. The data of compound binding to CAs were obtained using thermal shift assay and showed high affinity and selectivity to CAIX compared to other human CAs. Matching results were acquired with CAIX expressed on the cancer cell surface in live HeLa cell cultures. Compounds showed excellent fluorescent characteristics to visualize CAIX-positive tumors, but the CAIX-negative knockout tumors showed no response in a nude mice xenograft model

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Glycosylation Donors and Their Reactivities

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Glycosylation reactions have a 140-year history with many of the original procedures for saccharide synthesis still in use today.[1] There are many well-established catalytical procedures for performing glycosylation reactions – acid catalysis, hydrogen bond catalysis, organocatalysis, enzyme catalysis. Still, the complexity of the glycosylation reaction itself, with its plethora of side reactions and capricious starting materials, infers that there is yet no general method in glycosylation chemistry. Although the aforementioned synthesis strategies allow access to many products, there is still plenty of ground to be covered when it comes to easier, more efficient access to anomerically pure products. In this work, a range of glycosylation donors, many of them phosphorous based, were synthesized and subjected to the enzyme CAL-B with surprising results. Many examples represent a more efficient route to deacetylation of sugars than previously reported.

Supervisor
Prof. Tõnis Kanger

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