BALTICUM ORGANICUM SYNTHETICUM 2022

In memory of Prof. Victor Sniečkus

July 3-6, 2022
Vilnius, Lithuania

PROGRAM AND ABSTRACT BOOK

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WELCOME

Dear BOS participants,

Welcome to Balticum Organicum Syntheticum known as the **BOS** conference which follows the tradition of previous conferences held biennially in the Baltic capitals since the year 2000. Unfortunately, the COVID pandemic forced us to postpone BOS2020 to 2022. This time the conference will proceed as a hybrid event, some talks and posters will be presented virtually.

Prof. Victor Sniečkus

During the interim, we suffered the monumental loss of **our founder, Prof. Victor Sniečkus, who** in 1998 raised the idea to organize a conference in the Baltics. Having both Lithuanian and Estonian roots, he shared this idea with fellow Balts Drs. Jaan Pesti and John Dunčia and Prof. Eugenijus Butkus. And together with the organic chemists of the three Baltic countries, **BOS** was born. The first inaugural BOS was organized in Vilnius in 2000 hosting next year's Nobel laureate Professor Ryoji Noyori. Since inception, BOS has continued to maintain the highest standards, attracting 10 Nobel laureates and many other distinguished speakers. BOS also conveyed to its international attendees from over 30 countries, the warmth, culture, and unique flavor of the Baltics. We dedicate BOS2022 to the memory of Victor to mark his contributions to the field of organic chemistry and to BOS.

After over twenty years, the excitement of sharing the latest discoveries in organic chemistry by the international community at **BOS** remains ever so strong. The **BOS** conferences are renown for their balance of academic and industrial talks, presenting the fundamental and practical aspects of organic chemistry. We are grateful to the Plenary Speakers for endowing us with an exciting program. Since its inception, the **BOS** conference program and format consists of 1) plenary lectures by distinguished international speakers and three Baltic speakers and 2) poster sessions held in a most congenial and discussion-stimulating atmosphere. **BOS 2022** for the first time will include 15 min short talks by young scientists.

We are grateful for the financial support of companies and institutions listed on the cover of the booklet, especially to our historic sponsors Thieme, Chemical Abstracts Service (CAS), and ACS/OPRD, and also to Go Vilnius and the Research Council of Lithuania. Their contributions were key to helping make the conference possible and to realize a dream in these complicated times.

We welcome you most warmly. We believe you will have an exciting experience and a most memorable conference.

BOS 2022 Organizing Committee

ORGANIZATION

Conference Organizing Committee:
- † Prof. Viktoras A. Sniečkus, Queen's University, Canada
- Prof. Eugenijus Butkus, Vilnius University, Lithuania
- Dr. Jaan Pesti, EnginZyme AB, USA
- Dr. John Duncia, Bristol-Myers Squibb Co., Princeton, USA

Local Organizing Committee:
- Prof. Edvinas Orentas, chairman, Vilnius University, Lithuania
- Tomas Javorskis
- Augustina Jozeliūnaitė
- Barbara Chatinovska

Conference Secretariat
Jurgita Jurkonė
Conference & Event Management Agency

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ABOUT THE CONFERENCE

Conference Venue:
Radisson Blu hotel Lietuva:
Konstitucijos av. 20, Vilnius

Registration and Hospitality Desk
Location: lobby of the conference center of Radisson Blu Hotel Lietuva (2nd floor of the hotel)

Opening hours (local time):
Sunday, July 3, 2022, 12:00–17:00
Monday, July 4, 2022, 08:00–19:00
Tuesday, July 5, 2022, 08:00–19:00
Wednesday, July 6, 2022, 08:00-14:00

Participants’ Name Badges
Name badges will be provided together with conference material at the registration and hospitality desk. They are required to enter Scientific sessions of the conference as well to join Welcome reception and/or Vilnius city tour.

Abstracts
Companies and participants may copy abstracts for their personal use, but further copying for sale or any further commercial purpose is prohibited without prior permission of the Organizing Committee.

POSTER SESSIONS:
There will be 2 poster sessions during the conference:

Poster Session 1: from 17:30 to 19:00 on July 4, 2022
Set-up: from 08:30 to 10:00 on July 4, 2022
Dismantling: from 19:00 to 19:30 on July 4, 2022

Poster Session 2: from 17:30 to 19:00 on July 5, 2022
Set-up: from 08:30 to 10:00 on July 5, 2022
Dismantling: from 19:00 to 19:30 on July 5, 2022

Both sessions will take place in the lobby of the conference center. Authors shall be present at their posters during the designated poster session date and time. Beer, wine and other soft drinks will be served during the sessions.

If posters will not be removed by the end of dismantling time, they will be taken off and discarded by the organizers.

SOCIAL PROGRAM

Welcome Reception
Date: July 3, 2022
Time: 17:30-19:30
Venue: The Gallery Restaurant in National Gallery of Art
Location: Konstitucijos av. 22, Vilnius (7-10 min walk from the conference venue)
Fee: free of charge for registered participants
Entrance with badges only

Vilnius City Walking Tour
Date: July 5, 2022 (Tuesday)
Time of departure: 19:00
Duration: 1,5-2 hours
Meeting point: lobby of Radisson Blu hotel Lietuva on the first floor
Fee: free of charge to all registered participants and accompanying persons

FINAL PROGRAM

SUNDAY | JULY 3, 2022		
12:00 - 17:00	REGISTRATION & HOSPITALITY DESK	
15:00 - 16:00	**Shuttle Catalysis – a Conceptual Blueprint for Reversible Functional Group Transfer** Bill Morandi ETH Zürich, Switzerland	
16:00 - 17:00	**Expanding the Borders of Chemical Reactivity** Karl Anker Jørgensen Aarhus University, Denmark Molecules Plenary Speaker	
17:30 - 19:30	WELCOME RECEPTION The Gallery Restaurant in National Gallery of Art (free of charge for conference participants), Konstitucijos av. 22, Vilnius	

MONDAY | JULY 4, 2022

08:00 - 19:00 **REGISTRATION & HOSPITALITY DESK**

08:45 - 09:00 **Conference Opening: "Victor Sniečkus and BOS"**
Thomas Krimmer
Thieme, Germany

09:00 - 10:00 **C(sp³)–Si Cross-Coupling**
Martin Oestreich
Technische Universität Berlin, Germany
Thieme Plenary Lecture

10:00 - 11:00 **Decarboxylative Catalytic Construction of Quaternary Carbon Centres**
Vilius Franckevičius
Lancaster University, UK

11:00 - 11:30 **COFFEE BREAK**

11:30 - 12:30 **A Second-Generation Process for the Small Molecule Drug Substance Intermediate for BDC-1001 and Implementation in Downstream Bioconjugation**
Diane E. Carrera
Bolt Biotherapeutics, USA

12:30 - 14:00 **LUNCH BREAK | GROUP PHOTO**

14:00 - 15:00 **Process Enablement of COVID-19 Oral Inhibitor PF-07321332 at Unprecedented Speed: from mg to MT in 18 months**
Christophe Allais
Pfizer Inc., USA

15:00 - 16:00 **Regioselective Preparation and Functionalization of Azoles for the Synthesis of Active Pharmaceutical Ingredients**
Sébastien Lemaire
Janssen, Belgium

16:00 - 16:30 **COFFEE BREAK**

16:30 - 17:30 **Innovations in Synthetic Chemistry at Merck: New Methods for the Functionalization of Complex Molecules**
Patrick S. Fier
Merck & Co., Inc., USA

17:30 - 19:00 **POSTER SESSION 1**

19:30 - 22:00 **THIEME DINNER**
(with invitations only)

TUESDAY | JULY 5, 2022

08:00 - 19:00 **REGISTRATION & HOSPITALITY DESK**

08:45 - 09:00 **Welcome and BOS updates**

09:00 - 10:00 **Functional Supramolecular Chemistry**

Stefan Matile
University of Geneva, Switzerland

10:00 - 11:00 **New Methods for Carbon-Hydrogen Bond Functionalization**

Olafs Daugulis
University of Houston, USA

11:00 - 11:30 **COFFEE BREAK**

11:30 - 12:30 **Exploring the Chemical Composition of Immune Modulators and Their Conjugates: How Targeted Delivery Creates Anti-Tumor Immunity**

Romas Kudirka
Bolt Biotherapeutics, USA

12:30 - 14:00 **LUNCH BREAK & CAS PRESENTATION "CAS SCIFINDER-N UPDATE"**

14:00 - 15:00 **Late-Stage Functionalizations**

Tobias Ritter
Max-Planck-Institut für Kohlenforschung, Germany

15:00 - 16:00 **Stereocontrolled Photochemical Synthesis**

Tehshik P. Yoon
University of Wisconsin, USA

16:00 - 16:30 **COFFEE BREAK**

16:30 - 17:30 **SHORT ORAL PRESENTATIONS**

- **Phenanthrenequinone-Sensitized Photocatalytic Synthesis of Polysubstituted Quinolines from 2-Vinylarylimines**
  Juulia Talvitie, University of Helsinki, Finland
- **Novel Trasformations of Nitroarenes**
  Michał Barbasiewicz, University of Warsaw, Poland
- **Sustainable Synthesis of Useful Building Blocks Enabled by Electrolysis in Continuous-Flow**
  Maksim Ošeka, Tallinn University of Technology, Estonia
- **Enantiomerically Pure Azabicyclo[3.3.1]nonanes for the Synthesis of Sarpagine Family Alkaloids**
  Barbara Chatinovska, Vilnius University, Lithuania

17:30 - 19:00 **POSTER SESSION 2**

19:30 - 22:00 **VILNIUS CITY TOUR**
(free of charge for conference participants)
Meeting point - Radisson Blu Hotel Lietuva lobby

WEDNESDAY | JULY 6, 2022

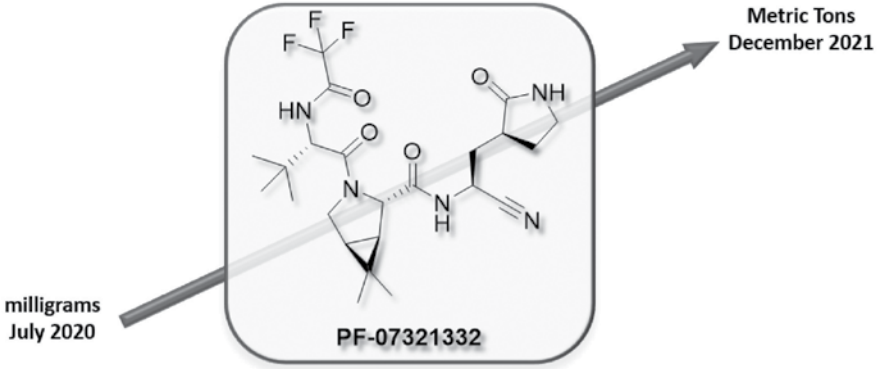
08:00 - 14:00	**REGISTRATION & HOSPITALITY DESK**	
08:45 - 09:00	**Welcome and BOS updates**	
09:00 - 10:00	**Ring Construction via Palladium(0)-Catalyzed C–H Activation** Olivier Baudoin University of Basel, Switzerland	
10:00 - 11:00	**Organization, Activities and Inhibitors of Viral RNA Synthesis Apparatus** Andres Merits University of Tartu, Estonia	
11:00 - 11:30	**COFFEE BREAK**	
11:30 - 12:30	**C–H Functionalization – From Academic Collaborations to Industry Applications** Antonia F. Stepan F. Hoffmann-La Roche Ltd, Germany	
12:30 - 13:30	**Oxalic Diamides: A New Generation of Ligands for Cu-Catalyzed Arylation of Nucleophiles (video presentation)** Dawei Ma State Key Laboratory of Bioorganic & Natural Products Chemistry, China Molecules Plenary Speaker	
13:30 - 14:00	**CONFERENCE CLOSING & PRIZES**	

INVITED SPEAKERS' ABSTRACTS

PROCESS ENABLEMENT OF COVID-19 ORAL INHIBITOR PF-07321332 AT UNPRECEDENTED SPEED: FROM MG TO MT IN 18 MONTHS

Chris Allais
Pfizer, Chemical Research and Development
Groton, United States

Shortly after the COVID-19 pandemic was declared in March 2020 by the WHO, Pfizer initiated a multi-front approach to combat the virus, which included the vaccine but also recognized very early the need for an orally dosed treatment able to help infected patients. This initiative resulted in the discovery of PF-07321332 from the Groton labs, the first SARS-CoV-2-specific protease inhibitor treatment available under emergency use by the FDA. I will share the story of this API, from its initial milligram quantities in Summer 2020 to metric tons supplied in late 2021 and into 2022. The presentation will disclose the different routes we developed to manufacture clinical lots as well as the design of the final commercial process. How the team managed to dramatically accelerate to deliver this new therapy at unprecedented speed, along with the challenges encountered along the way will also be discussed.



RING CONSTRUCTION VIA PALLADIUM(0)-CATALYZED C–H ACTIVATION

Olivier Baudoin
University of Basel, Department of Chemistry, Basel, Switzerland

Intense research efforts from our group in the past couple of decades have been dedicated to the functionalization of non-activated C(sp^3)-H and C(sp^2)-H bonds using catalysis by palladium(0) complexes.[1]

This lecture will present some of the most recent aspects of this chemistry, for instance enantioselective reactions using different types of chiral catalysts,[2] remote bond formation using the 1,4-Pd shift strategy,[3] and applications in natural product synthesis.[4]

References:

[1] O. Baudoin, *Acc. Chem. Res*. 2017, 50, 1114.
[2] a) L. Yang, R. Melot, M. Neuburger, O. Baudoin, *Chem. Sci*. 2017, 8, 1344; b) D. Dailler, R. Rocaboy, O. Baudoin, *Angew. Chem. Int. Ed.* 2017, 56, 7218; c) D. Savary, O. Baudoin, *Angew. Chem. Int. Ed.* 2021, 60, 5136; d) R. Melot, M. Zuccarello, D. Cavalli, N. Niggli, M. Devereux, T. Bürgi, O. Baudoin, *Angew. Chem. Int. Ed.* 2021, 60, 7245.
[3] a) R. Rocaboy, I. Anastasiou, O. Baudoin, *Angew. Chem. Int. Ed.* 2019, 58, 14625; b) A. Clemenceau, P. Thesmar, M. Gicquel, A. Le Flohic, O. Baudoin, *J. Am. Chem. Soc.* 2020, 142, 15355; c) T. Čarný, R. Rocaboy, A. Clemenceau, O. Baudoin, *Angew. Chem. Int. Ed.* 2020, 59, 18980;
[4] a) D. Dailler, G. Danoun, O. Baudoin, *Angew. Chem. Int. Ed.* 2015, 54, 4919; b) R. Melot, M. V. Craveiro, T. Bürgi, O. Baudoin, *Org. Lett.* 2019, 21, 812; c) P. Thesmar, O. Baudoin, *J. Am. Chem. Soc.* 2019, 141, 15779.

DEVELOPMENT OF A SECOND GENERATION PROCESS FOR BELVARAFENIB, A PAN-RAF INHIBITOR

Carrera, D. E.[1] *Dalziel, M. D.*,[1] *Zell, D.*,[1] *Mercado-Marin, E. V.*,[1]
Bachmann, S.,[2] *Zhang, H.1 and Gosselin, F.*[1]
[1]*Department of Small Molecule Process Chemistry, Genentech, Inc., South San Francisco, USA*
[2]*Process Chemistry and Catalysis, CoE Catalysis, Basel, Switzerland*

This lecture will describe the discovery and development of a proposed late stage and commercial route to pan-RAF inhibitor belvarafenib, a small molecule treatment for solid tumors. Key features of this route include a novel heterocyclic starting material synthesis and a catalytic nitro group hydrogenation. Significant development work was required to successfully develop and implement a production scale synthesis of the heterocyclic starting material. A regulatory strategy for the control of genotoxic and potentially genotoxic impurities in this route will also be discussed.

NEW METHODS FOR CARBON-HYDROGEN BOND FUNCTIONALIZATION

Olafs Daugulis
University of Houston, Houston, TX, USA

In last decade, C-H bond functionalization has matured from an academic curiosity to widespread applications in synthesis of complex natural products and drugs.[1] Carbon-hydrogen bonds are the most abundant functionality in organic molecule and their use as a functional group for further conversions allows shortening of synthetic pathways saving reagents, solvents, and decreasing labor costs. Since the amount of generated chemical waste is decreased, positive impact of this chemistry on environment is achieved as well. This talk will describe the development of new copper catalysts for directed and non-directed C-H bond functionalization reactions. Furthermore, we will report on recent developments showing that monodentate pyridine ylide auxiliaries rival efficiency of aminoquinoline directing group in C-H functionalization of sp^2 and sp^3 C-H bonds.

References:

[1] Daugulis, O.; Roane, J.; Tran, L. D. *Acc. Chem. Res.* 2015, 48, 1053-1064.

INNOVATIONS IN SYNTHETIC CHEMISTRY AT MERCK: NEW METHODS FOR THE FUNCTIONALIZATION OF COMPLEX MOLECULES

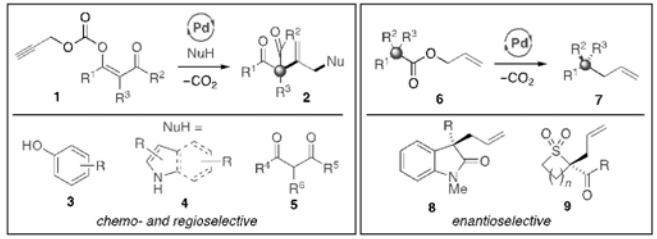
Patrick S. Fier
Merck & Co., Inc.Rahway, NJ, United States

In drug discovery and development, it is often realized that classic reactions requiring harsh conditions are not suitable for the functionalization and diversification of complex, drug-like molecules. To overcome such limitations, a series of rationally-designed reagents and reactions have been invented that now allow for previously difficult-to-access compounds to be accessed in a single step. We have also developed reactions that enable late-stage functionalization of common, typically inert, functional groups common in drugs and drug-like molecules, opening new avenues in drug discovery. In all cases, the reactions we developed occur under mild conditions with readily available reagents, generate minimal waste, and can be used on complex substrates without the need for protecting groups.

DECARBOXYLATIVE CATALYTIC CONSTRUCTION OF QUATERNARY CARBON CENTRES

Atkinson, B.; Bowen, E. P.; Jackson, P.; Kenny, M.; Kitson, D. J.; Laidlaw G.; McArdle-Ismaguilov, T.; Schröder, S. P.; Taylor, N. J.; Franckevičius, V.
Department of Chemistry, Lancaster University, United Kingdom

The construction of quaternary carbon centres, particularly in enantioselective form, remains to be a formidable task to organic chemists.[1] Our research focuses on the development of new metal-catalysed approaches to the chemo-, regio- and stereoselective assembly of congested carbon centres. We have developed the first Pd-catalysed intermolecular coupling of nucleophiles with propargylic enol carbonates **1** that proceeds with high levels of *chemo*- and *regioselectivity* due to the decarboxylative nature of the reaction. This process installs two new bonds and an all-carbon quaternary centre in **2**, and enables the coupling of enolates with a range of nucleophiles derived from phenols **3**,[2] pyrroles and indoles **4**,[3] and 1,3-dicarbonyls **5**.[4] The analogous allylic electrophiles **6** can result in the *enantioselective* decarboxylative allylic alkylation of nucleophiles (**7**), and we have developed stereoselective routes to novel heterocyclic products for medicinal chemistry, including indoles **8**,[5] and cyclic sulfones **9**.[6]



References:
1. Franckevičius, V. *Tetrahedron Lett*. 2016, 57, 3586.
2. Schröder, S. P.; Taylor, N. J.; Jackson, P.; Franckevičius, V. *Org. Lett*. 2013, 15, 3778.
3. Kenny, M.; Kitson, D. J.; Franckevičius, V. J. *Org. Chem*. 2016, 81, 5162.
4. Kenny, M.; Christensen, J.; Coles, S. J.; Franckevičius, V. *Org. Lett.* 2015, 17, 3926.
5. Franckevičius, V.; Cuthbertson, J. D.; Pickworth, M.; Pugh, D. S.; Taylor, R. J. K. *Org. Lett.* 2011, 13, 4264.
6. Laidlaw, G.; Bowen, E. P.; Atkinson, B.; McArdle-Ismaguilov, T.; Franckevičius, V. 2020, *manuscript in preparation*.

EXPANDING THE BORDERS OF CHEMICAL REACTIVITY

Karl Anker Jørgensen
Department of Chemistry, Aarhus University, Denmark

The lecture will demonstrate how organocatalysis has made it possible to expand the classical cycloadditions involving 6π-electrons, to now being able to control peri-, diastereo- and enantioselectivity for cycloadditions involving more than 6π-electrons – higher-order cycloadditions. The expanding of chemical reactivity will be extended to novel concepts for organocatalytic oxidative coupling reactions.

EXPLORING THE CHEMICAL COMPOSITION OF IMMUNE MODULATORS AND THEIR CONJUGATES: HOW TARGETED DELIVERY CREATES ANTI-TUMOR IMMUNITY

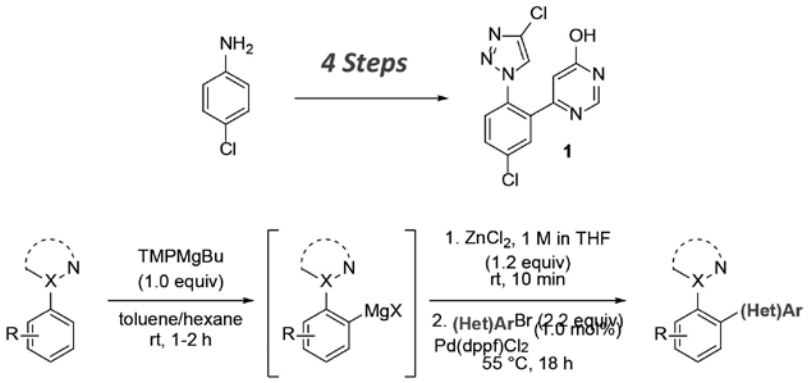
Kudirka, R.A., Zhou, M., Lee, A., Sarma, G., Deol, S., Huber, M., Henning, K., Mallet, B., Bradley, E., Alonso, M., Chapin, S., Pearson, C., Luo, A., Luo, A., Ackerman, S.E., Melrose, J., Nolin, J., Blum, L., Kowanetz, M., and Safina, B.S
Bolt Biotherapeutics, 900 Chesapeake Dr. Redwood City, CA, USA

Immune-stimulating antibody conjugates (ISACs) represent a promising new therapeutic option for oncology. By harnessing mechanisms of the innate immune response, treatment with ISACs can lead to prolonged adaptive immune responses, effectively “teaching” the immune system to recognize and eliminate cancer cells. The innate immune system, which is governed by the interaction of chemical agonists with Toll-like receptors (TLRs) helps distinguish self from non-self. Antigen presenting cells (APCs), serve as the bridge between the innate and adaptive immune system. Activation of TLRs leads to activation of APCs, which in turn stimulate T cells, part of the adaptive immune response. By conjugating powerful TLR 7/8 small molecule agonists to tumor targeted antibodies, ISACs activate tumor resident APCs, driving uptake, processing and presentation of tumor neoantigens to T cells that mediate anti-tumor immunity. In this presentation, we will present structure activity relationships (SAR) for the chemical components of ISACs, such as conjugation chemistry, linker, and small molecule TLR agonist. We shall demonstrate how the use of ISACs leads to tumor clearance and the development of anti-tumor immunologic memory, providing strong rationale for this technology as a platform for cancer immunotherapy.

REGIOSELECTIVE PREPARATION AND FUNCTIONALIZATION OF AZOLES FOR THE SYNTHESIS OF ACTIVE PHARMACEUTICAL INGREDIENTS

Sébastien Lemaire
Discovery Product Development and Supply, Janssen Pharmaceutica, Beerse, Belgium

Beyond the incredible challenge of inventing any new medicine, Process Chemists are tasked with designing the best chemical process for every product in the pipeline. Chemistry alone can make all the difference between an unviable product and a drug that is affordable and accessible to every patient that needs it. In many cases, a completely redesigned novel synthetic route is needed to meet this objective. Chemists at Janssen working on the development of the novel antithrombotic agent Milvexian[1] discovered a 4-step process to intermediate **1**, drastically simplifying the synthesis of this compound. New chemistry developed to enable the preparation of differently substituted triazoles found application in Discovery chemistry to expand the understanding of this chemical space.[2]



References:
[1] A. K. Dilger *et al. J. Med. Chem.* 2021, in press.
[2] a) F. H. Lutter, L. Grokenberger, L. A. Perego, D. Broggini, S. Lemaire, S. Wagschal, P. Knochel, Nature Comm. 2020, 11, 4443. b) A. Hess, S. B. Doerrich, F. Trauner, F. H. Lutter, S. Lemaire, S. Wagschal, K. Karaghiosoff, P. Knochel *Chem. Sci.* 2021, 12, 8424.

OXALIC DIAMIDES: A NEW GENERATION OF LIGANDS FOR CU-CATALYZED ARYLATION OF NUCLEOPHILES

Dawei Ma
State Key Laboratory of Bio-Organic & Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, P. R. China

During the past two decades we have witnessed great progress in ligand-promoted copper-catalyzed arylation of nucleophiles.1 However, there still remain a lot of problems in this field. The most challenging problem is that less expensive aryl chlorides are inert for almost all Cu/ligand-catalyzed coupling reactions.1 Additionally, the catalytic loadings are still high in most cases. Recently, we found that some *N,N'*-diaryl, *N*-aryl-*N'*-alkyl or *N,N'*-dialkyl substituted oxalamides are very powerful ligands for copper-catalyzed arylation of nucleophiles.[1] These ligands not only make Cu-catalyzed coupling of (hetero)aryl chlorides with nucleophiles proceed smoothly under relatively mind conditions, but also lead to Cu-catalyzed coupling reactions with aryl bromides and iodides being conducted at low catalytic loadings and reaction temperatures.[2] In this lecture, we wish to describe these results.

References:
1. For a recent review, see: Bhunia, S.; Pawar, G, G.; Kumar, S. V.; Jiang Y.; Ma, D. *Angew. Chem. Int. Ed.* 2017, 56, 16136.
2. (a) Zhou, W.; Fan, M.; Yin, J.; Jiang, Y.; Ma, D. *J. Am. Chem. Soc.* 2015, 137, 11942. (b) Fan, M.; Zhou, W.; Jiang, Y.; Ma, D. *Org. Lett.* 2015, 17, 5934. (c) Fan, M.; Zhou, W.; Jiang, Y.; Ma, D. *Angew. Chem. Int. Ed.* 2016, 55, 6211. (d) S. Xia, L Gan, K. Wang, Z. Li, D. Ma. *J. Am. Chem. Soc.* 2016, 138, 13492. (e) Gao, J.; Bhunia, S.; Wang, K.; Gan, L.; Xia, S.; Ma, D. *Org. Lett.* 2017, 19, 2809. (f) De, S.; Yin, J.; Ma, D. *Org. Lett.* 2017, 19, 4864. (g) Pawar, G. G.; Wu, H.; De, S.; Ma, D. *Adv. Synth. Catal.* 2017, 359, 1631. (h) Kumar, S. V.; Ma, D. *J. Org. Chem.* 2018, 83, 2706. (i) Chen, Z.; Jiang, Y.; Zhang, L.; Guo, Y.; Ma, D. *J. Am. Chem. Soc.* 2019, 141, 3541.

FUNCTIONAL SUPRAMOLECULAR CHEMISTRY

Matile, Stefan
Department of Organic Chemistry, University of Geneva, Switzerland

This lecture will focus on synthetic organic, molecular and supramolecular systems with significant activities. Emphasis is on the integration of underrecognized or even new concepts to get into contact on the molecular level, in the hope that fundamentally new approaches to create function will ultimately allow us to tackle challenges that are otherwise beyond reach. One topic of interest concerns catalysis with unorthodox interactions. This was realized first with anion-π interactions and then expanded to chalcogen, pnictogen and tetrel bonds. Today, several reactions have been realized, including enolate, enamine, iminium and Diels-Alder chemistry. The most recent natural product inspired polyether cascade cyclizations are particularly attractive for autocatalysis on π-acidic surfaces, to show the pnictogen-bonding catalysts are more than just weak Lewis acids, and to develop lipid bilayer membranes as unique environment for catalysis. Other catalytic systems explored in this context include small molecules but also foldamers, carbon nanotubes, artificial enzymes, and even electric fields.
The same chalcogen bonds are also the key to build mechanosensitive fluorescent probes that change color like lobsters during cooking. The imaging of physical forces in living cells is a central challenge in biology, and the resulting “flipper probes” have been shown to provide the chemistry tools needed to image to membrane tension by FLIM. Examples will move from design and synthesis to intracellular targeting by empirical tracking, genetic engineering, and photocaging, with illustration of pertinent biological questions related to tension-induced microdomain assembly, mitochondrial division, plasma membrane asymmetry, endocytosis and the secretory pathway. As a final topic, dynamic covalent exchange chemistry will be introduced as the key to find new ways to enter cells. Thiol-mediated uptake will the covered as the emerging method of choice to deliver directly into the cytosol, explain the mystery of cell-penetrating oligonucleotide phosphorothioates, and develop new strategies to inhibit viral entry. This growing significance of thiol-mediated uptake calls for “walker-like” dynamic covalent cascade chemistry with bioinspired epidithiodiketopiperazines, benzopolysulfanes, cyclic thiosulfonates, pnictogen relays and tetrel-centered Michael and thiolactone exchangers.

ORGANIZATION, ACTIVITIES AND INHIBITORS OF VIRAL RNA SYNTHESIS APPARATUS

Merits, A.; Lello, L.S., Wang, S., Utt, A.; Žusinaite, E.
Institute of Technology, University of Tartu, Tartu, Estonia

RNA viruses (realm Ribovira) are the only biological objects capable for efficient synthesis of RNAs on the RNA templates. This is carried out by RNA-dependent RNA polymerase assisted by other virus- and host derived factors which together form replicase complex (RC). In eukaryotic cells the RC is anchored to cellular membrane and is capable of multiple enzymatic reactions including methylation, polymerization and ATP hydrolysis. As these activities must occur in coordinated manner the RC has defined structure. RC of alphaviruses consist from four viral subunits while RC of coronaviruses has sixteen subunits. Using reverse genetics, synthetic and structural biology methods we have demonstrated that: i) binding of RC to the cellular membranes is triggered by palmitoylation of viral methyltransferase and its subsequent interaction with cholesterol; ii) binding of specific RNAs by RC of alphaviruses is based on recognition of RNA secondary structures by viral polymerase; iii) RNA binding is assisted by viral helicase/protease. The interaction involves hydrophobic stacking between RNA bases and aromatic amino acid residues and regulates protease activity of the enzyme; iv) virus encoded enzyme with mono(ADP-ribosyl)hydrolase activity is covalently modified by phosphorylation of serine/threonine residues; v) viral polymerase can form catalytically active RCs with other RC subunits originating form heterologous viruses. All these activities and interactions can be specifically inhibited by chemical compounds. In some cases, the inhibition of viral activities is straight forwarded: binding of RC to membranes is sensitive to drugs inducing cholesterol sequestration, protease activity can be inhibited by compounds that interact with active site of the enzyme, and viral polymerase can be inhibited by nucleotide analogues. However, due to plasticity of viral genomes resistance to these inhibitors is rapidly developed, though often this adaptation is associated with fitness cost. Other type of inhibitors, such as hyper-mutagenic nucleoside analogues, are active against numerous viruses and have high barriers for development of resistance; however, they suffer from potential side effects. Therefore, the compounds targeting higher-order processes such as specific interactions between viral and host components would be valuable as novel drug leads as well as tools for studies of molecular biology of RNA viruses.

SHUTTLE CATALYSIS – A CONCEPTUAL BLUEPRINT FOR REVERSIBLE FUNCTIONAL GROUP TRANSFER

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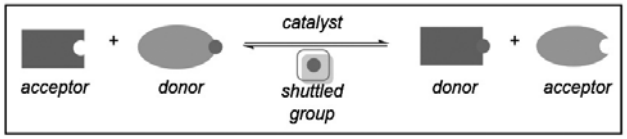
Catalytic reversible reactions, such as alkene metathesis and transfer hydrogenation, have had an auspicious impact on the molecular sciences. This presentation will describe our eff¬orts to develop related "shuttle catalysis" reactions for the functionalization and defunctionalization of organic compounds.[1-6] These reactions avoid the use of toxic reagents (e.g. HCN, CO) through the reversible transfer of chemical moieties between organic molecules. Shuttle catalysis has further been employed in the development of novel single bond metathesis reactions that can help to address significant synthetic challenges across the molecular sciences.



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C(sp³)–SI CROSS-COUPLING

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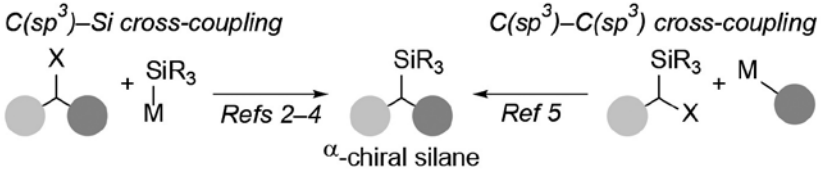
The combination of silicon (pro)nucleophiles and alkyl electrophiles is an obvious approach toward the formation of C(sp³)–Si bonds.[1] Regioselectivity issues are avoided as the locus of bond formation is set in the prefunctionalized alkyl coupling partner. However, synthetically useful protocols only evolved in recent years, closing an important gap in silicon chemistry. We present here our efforts for the construction of C(sp³)–Si bonds by radical cross-coup-lings,[2] enantiospecific nucleophilic substitution,[3] and cross-electrophile coupling reactions.[4] An alternative way to access such α-chiral silanes enantioselectively is by radical C(sp³)–C(sp³) cross coupling.[5]



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LATE-STAGE FUNCTIONALIZATIONS

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Late-stage functionalization reactions should reliably functionalize already complex molecules to quickly access value-added molecular diversity. Late-stage functionalization is desirable in many areas of discovery such as in drug or agrochemical development and a requirement in other areas such as the synthesis of positron-emission tomography (PET) tracers. I will describe the development of novel, modern highly selective reactions in late-stage functionalization, as well as their application in transition-metal-catalyzed and photoredox reactions, with a focus on the synthesis of ^{18}F and ^{19}F containing complex small molecules. In particular, I will describe the development of a broadly useful new C-H functionalization reaction to create molecular complexity for applications in catalysis, drug discovery, and medicine.

C–H FUNCTIONALIZATION - FROM ACADEMIC COLLABORATIONS TO INDUSTRY APPLICATIONS

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Synthesis is a key driver for innovative medicinal chemistry and often remains the rate-limiting step towards accessing the vast small molecule chemical space. C–H functionalization methodologies applied to the late-stage diversification of complex molecules can rapidly explore novel analogs and has therefore the potential to significantly accelerate the identification of drug candidates. In this presentation, we will explore how different types of collaborations, such as between academia and industry, can catalyse the development of C–H functionalization reactions relevant to small molecule drug discovery, culminating in the application of a late-stage oxidation protocol to a phosphodiesterase 2 inhibitor project that resulted in a significantly reduced cycle time.

STEREOCONTROLLED PHOTOCHEMICAL SYNTHESIS

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Photochemistry is intriguing as a synthetic tool because the absorption of light by an organic molecule results in the formation of exceptionally energetic reactive intermediates that can react in ways that are inaccessible to ground-state molecules. However, this high reactivity is also a challenge for stereoselective synthesis: control over the stereochemistry of photochemical reactions, particularly using enantioselective catalysts, has been a long-standing challenging synthetic problem with few general solutions. One solution developed in our laboratory involves the use of chiral visible-light-aborsbing transition metal complexes, the photophysical and chemical properties of which facilitate the discovery of a wide range of highly enantioselective excited-state organic transformations.

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PHOTOACTIVATED ALCOHOL OXIDATION WITH PHENANTHRENEQUINONE DERIVATIVES

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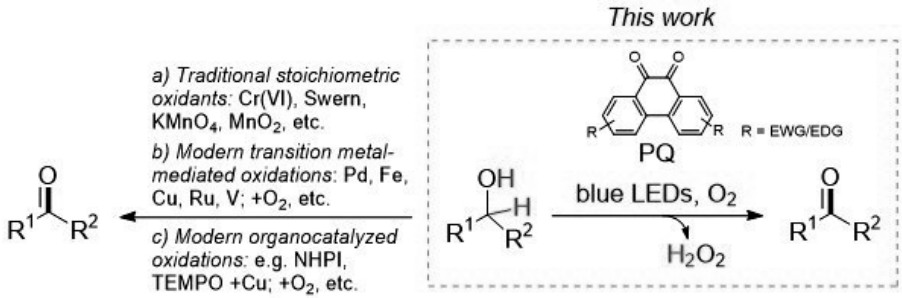
Oxidation of alcohols is one of the fundamental transformations in organic chemistry, and therefore a plethora of metal-mediated and metal-free stoichiometric and catalytic protocols exist to facilitate this transformation. Amongst milder strategies, photoredox chemistry provides an interesting and greener protocol. As 9,10-phenanthrenequinone (PQ) is known to act as a photoactivated oxidant,[1] we have developed a mild, fast and effective method for alcohol oxidation using PQ as an organophotocatalyst and oxygen atmosphere as terminal oxidant. Structural modification of PQ allowed to adjust its oxidation power resulting in smoother oxidation of electron-deficient substrates.



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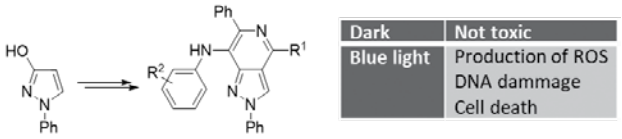
SYNTHESIS OF *N*-ARYL-2,6-DIPHENYL-2*H*-PYRAZOLO[4,3-C]PYRIDIN-7-AMINES WITH PHOTODYNAMIC PROPERTIES AGAINST HUMAN SKIN MELANOMA CELL LINE G361

Eglė Arbačiauskienė[1], Beatričė Razmienė[1], Veronika Vojáčková[2], Eva Řezníčková[2], Lukáš Malina[2], Vaida Dambrauskienė[1], Martin Kubala[2], Robert Bajgar[2], Hana Kolářová[2], Asta Žukauskaitė[2], Algirdas Šačkus[2], Vladimír Kryštof[2]*

[1]Kaunas University of Technology, Kaunas, Lithuania

[2]Palacký University, Olomouc, Czech Republic

Photodynamic therapy is a promising treatment for various diseases. It uses a non-toxic medication – photosensitizer, which upon activation by specific light within target cells produces reactive oxygen species and causes cell destruction. Here we present series of *N*-aryl-2,6-diphenyl-2*H*-pyrazolo[4,3-c]pyridin-7-amines, which were synthesized from easily accessible 1-phenyl-1*H*-pyrazol-3-ol. The compounds were evaluated for their potential use in photodynamic therapy revealing that while compounds are not toxic to melanoma G361 cells in the dark, their cytotoxicity can be induced by irradiation with visible blue light (414 nm) [1].



Scheme 1. *Synthesis and photodynamic properties of N-aryl-2,6-diphenyl-2H-pyrazolo[4,3-c]pyridin-7-amines.*

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1,2,6-THIADIAZINONES AS NOVEL NARROW SPECTRUM CALCIUM/CALMODULIN-DEPENDENT PROTIEN KINASE KINASE 2 (CAMKK2) INHIBTIORS

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[2]University of Eastern Finland, Finland

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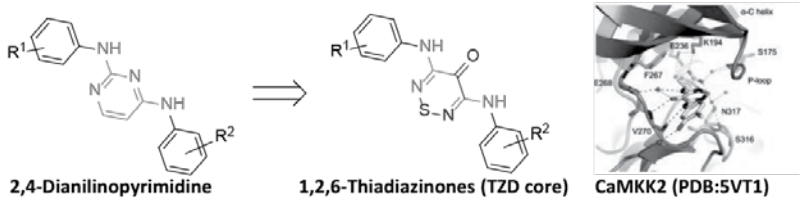
[4]University of Cyprus, Cyprus

We have demonstrated that 1,2,6-thiadiazin-4-one (TDZ) scaffold can function as a novel chemotype for the design of ATP-competitive kinase inhibitors. The TDZ core can be used as an electronic isostere for the more common 2,4-dianilinopyrimidine kinase inhibitor scaffold. The resulting analogues showed reduced kinome promiscuity compared to their 2,4-dianilinopyrimidine counterparts and using this screening we identified calcium/calmodulin-dependent protein kinase kinase 2 (CaMKK2), as a promising target. We solved a co-crystal structure of a 3,5-bis(arylamino)-4H-1,2,6-thiadiazin-4-one bound to CaMKK2 and several analogues were identified with micromolar activity through targeted displacement of bound water molecules in the active site. The TZD scaffold represents an exciting starting point for development of highly selective kinase inhibitors.



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SYNTHESIS OF NOVEL SUPRAMOLECULAR IMIDAZOLE DERIVATIVES AND INVESTIGATION OF THEIR PHOTOPHYSICAL PROPERTIES

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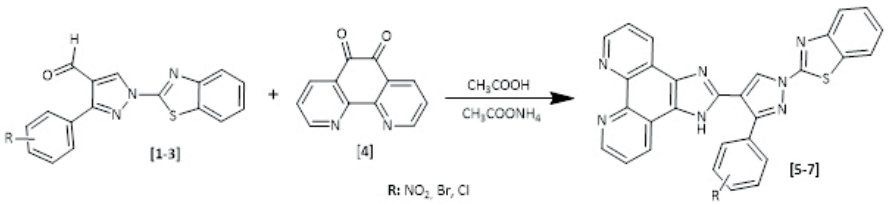
Pyrazole molecules have become a common motif for many pharmaceutically active compounds. Furthermore, carbaldehyde derived from thiazole and pyrazole are also known for their antitubercular and antimicrobial activity. On the other hand, tricyclic heterocyclic 1,10-phenanthroline has received considerable attention in material chemistry due to its large conjugated area, broad-spectrum antibacterial property and electron-deficient properties.

In this study we aimed to obtain biologically active pyrazole-4-carbaldehyde derivatives (1-3) by Vilsmeier–Haack reaction and combine them with 1,10-phenanthroline to synthesize new supramolecular imidazole derivatives (5-7) by condensation reaction, investigate their photophysical properties by UV-Vis spectroscopy, characterize by the spectroscopic methods (FT-IR, 1H-NMR, 13C-NMR and MS).



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SYNTHESIS AND INVESTIGATION OF BENZENESULFONAMIDES BEARING DIHYDRAZONES AS HUMAN CARBONIC ANHYDRASE INHIBITORS

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Inhibitors of human carbonic anhydrase (CA) isoforms have the potential in a range of therapeutic areas. In this study we synthesized benzenesulfonamides bearing dihydrazones and evaluated their binding towards 12 human catalytically active CA isoforms. Dihydrazides **2a,b** were synthesized by the nucleophilic ring opening of 2-pyrrolidinones **1a,b** with hydrazine monohydrate (Fig. 1). Dihydrazides **2a,b** reactions with corresponding ketones yielded hydrazones **3–5a,b,** whereas the ones with corresponding benzaldehydes provided hydrazones **6–12a,b**.

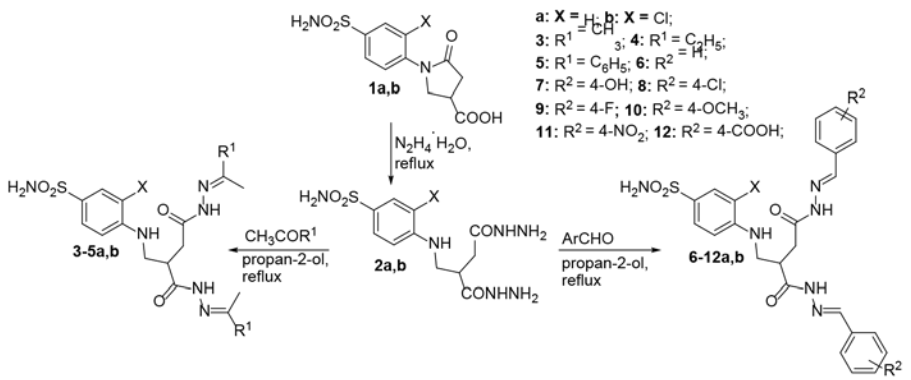

Fig. 1. *Synthesis of benzenesulfonamide-bearing dihydrazones*

BENZOXAPHOSPHEPINE 2-OXIDES AS POTENTIAL CARBONIC ANHYDRASE INHIBITORS

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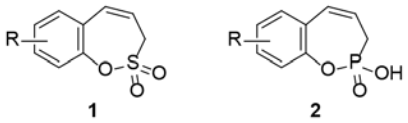
Carbonic anhydrases (CAs) are a superfamily of metalloenzymes present across all kingdoms of life, as they catalyze reversible carbon dioxide hydration.[1] Inhibition of the CAs has pharmacological applications in many fields, such as anticancer agents, antiglaucoma, antibacterial, and anti-infectives. Previously, in our research group, benzoxathiepine 2,2-dioxides **1** were designed and synthesized.[2] They demonstrated good inhibitory activities and selectivity of tumor-associated hCA IX and hCA XII. Extending our research, we decided to synthesize potential benzoxathiepine 2,2-dioxide **1** bioisosteres – benzoxaphosphepine 2-oxides **2**.



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BIS-CYCLOMETALLATED IRIDIUM COMPLEXES FOR C-H BORYLATION

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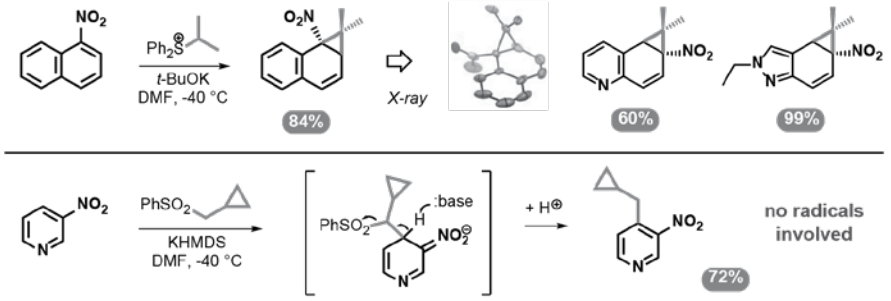
Although nitroarenes are known for more than a century, their chemistry still inspires a search of new and unique transformations. We demonstrate **Corey-Chaykovsky cyclopropanation** of nitronaphthalenes and related heterocycles, which react as Michael-type acceptors, giving e.g. *gem*-dimethylcyclopropanes.[1] In turn electrophilic **nitropyridines can be alkylated** with sulfonyl-stabilized carbanions via Vicarious Nucleophilic Substitution (VNS). [2] Mechanistic studies reveal effect of the carbanion branching on the reaction course.[3]



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SYNTHESIS OF TRISUBSTITUTED VINYL SILANES FROM PROPARGYL SILANES VIA 1,2-SILYL MIGRATION

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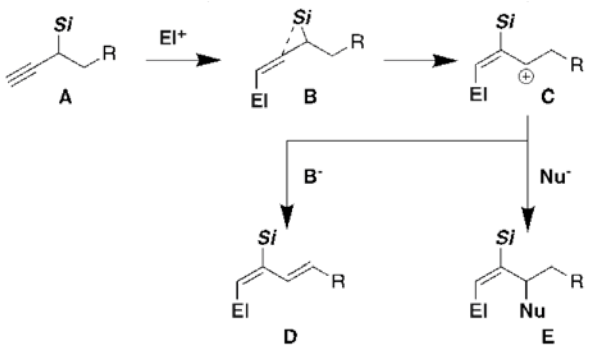
Stabilizing properties of ß-silicon effect has been known to increase the rate of the reactions for unsaturated systems that proceed via the formation of ß-silyl carbenium ion. The formation of the latter in the combination with other stabilizing effects can lead the reactions to proceed via 1,2-silyl migration [1,2].
Herein, we report the synthesis of highly functionalized alkenes by the activation of propargylsilane with various electrophyles. The obtained allyl cation then reacts with various nucleophiles to obtain alkenes or dienes. Functionalized alkenes **E** are prearranged for the cross-coupling chemistry, which further increases the molecular complexity. Our findings on synthesis and further transformations of products **D** and **E** will be reported in detail.



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DENDRIMER ANTIOXIDANTS WITH MELDRUM'S ACID AS SURFACE GROUP

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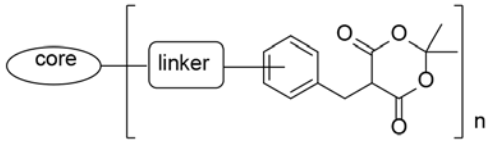
Institute of Technology of Organic Chemistry, Faculty of Materials Science and Applied Chemistry, Riga Technical University, Latvia

Oxidation processes cause the degradation of various products[1] and can lead to oxidative stress, which causes conditions like Parkinson's disease, Alzheimer's disease, and cancer.[2] To regulate oxidation processes, antioxidants can be used. However, their effectiveness is often limited by low solubility, bioavailability etc.[3] One of the ways to solve these issues is binding the active molecules to dendrimers. Dendrimers are highly branched polymers with a very precise structure. Besides modified physical properties, they have also shown improved antiradical activity in some cases.[4,5]
Arylmethyl Meldrum's acids previously demonstrated significant antioxidant and antiradical activity.[6] Herein, we present dendrimeric antioxidants **1** with Meldrum's acid as surface groups. The impact of aromatic and aliphatic cores and aliphatic and heterogenic linkers is studied.



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VISIBLE-LIGHT-INDUCED REDUCTION OF EPOXIDES WITH ALKYLTITANIUM ALKOXIDES

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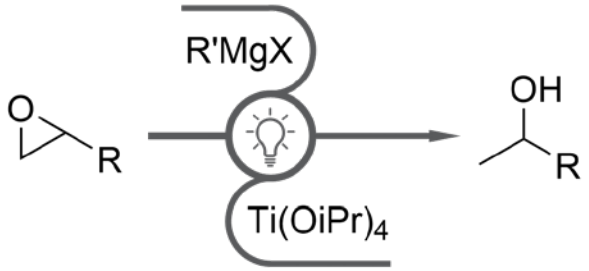
Ti-based organometallic compounds have been used for a long time as versatile tools in synthetic chemistry.[1,2] Recently, we found that under the visible light irradiation, organotitanium compounds undergo nickel-catalyzed cross-coupling with organic halides.[3] Here, we report that alkyltitanium alkoxides generated in situ from a Grignard reagent and $Ti(OiPr)_4$ serve as a reducing reagent in the reaction with epoxides when irradiated with blue LEDs. The discovered transformation proceeds in the absence of a photocatalyst through the direct photoexcitation of the organometallic reagent, which leads to the formation of low-valent titanium species capable of the epoxide reduction. The regioselectivity of the ring-opening depends on type of alkylmagnesium halide used.



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NMR-BASED STRUCTURE ELUCIDATION OF NOVEL METHYL 5-(N-BOC-CYCLOAMINYL)-1,2-OXAZOLE-4-CARBOXYLATES

Aurimas Bieliauskas[1], *Greta Račkauskienė*[1], *Miglė Dagilienė*[1], *Vaida Milišiūnaitė*[1], *Gita Matulevičiūtė*[1,2], *Jolita Bruzgulienė*[1,2], *Algirdas Šačkus*[1,2]
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A convenient and efficient synthesis of novel achiral and chiral heterocyclic amino acid-like building blocks was developed. Regioisomeric methyl 5-(*N*-Boc-cycloaminyl)-1,2-oxazole-4-carboxylates were prepared by the reaction of ß-enamino ketoesters (including azetidine, pyrrolidine or piperidine enamines) with hydroxylamine hydrochloride. Unambiguous structural assignments were based on chiral HPLC analysis, ^{1}H, ^{13}C, and ^{15}N-NMR spectroscopy, including spectral data of ^{15}N-labeled derivative (Figure 1, a).
In the NMR spectra of chiral 1,2-oxazoles, two sets of signals with different intensities were observed due to the existence of two Boc-group rotational conformers (Figure 1, b). This was confirmed via chemical exchange NMR experiments such as saturation transfer e.g., 1D selective NOESY [1].

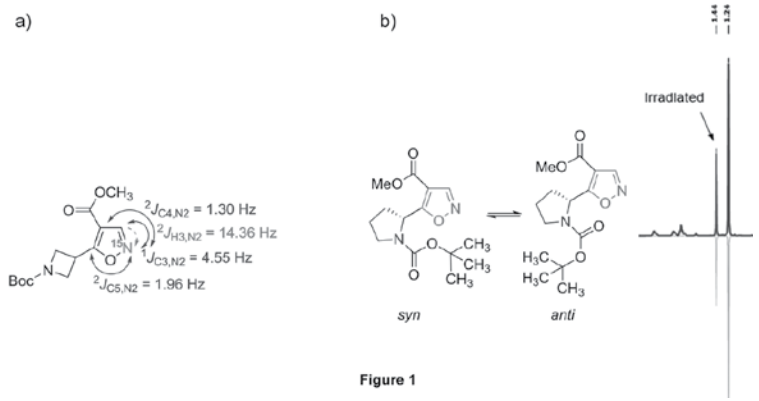

Figure 1

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CONTROLLABLE ACCESS TO FURANS AND DIHYDROFURANS THROUGH TANDEM CYCLIZATION/COUPLING REACTION

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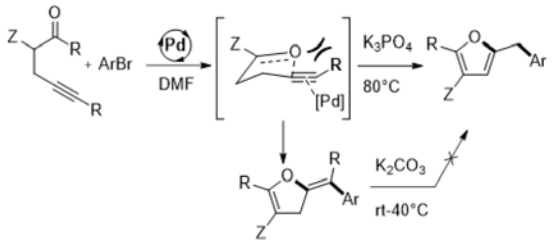
[1]*Institute of Organic Chemistry PAS, Poland*

Five-membered oxygen-heterocyclic system is a common structural motif present in a variety of molecules, often exhibiting interesting biological activity. Since works of Paal and Knorr, a plethora of methods providing access to furans were developed. Arcadi showed that 2,3,5-substituted furans can be synthesized from acetylenic ß-ketoesters and aryl iodides or triflates via a Pd-catalyzed tandem process encompassing 5-exo-dig cyclization, coupling and isomerization[1]. Recently, we disclosed a protocol applicable for cheaper and more readily available, but considerably less reactive aryl bromides[2]. On further research we developed reaction conditions suitable for synthesizing furans from internal alkynes and, to our delight, we were able to accommodate it for the purpose of obtaining dihydrofurans, elusive precursors, whose occurrence was postulated, yet not previously isolated within catalytic cycle.



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TANDEM PD-CATALYZED ANNULATION/ COUPLING OF ACETYLENIC ENAMINES

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In modern organic synthesis, palladium complexes are one of the most versatile catalysts. Ability to promote various mechanistically distinct transformations makes them a useful tool for design of tandem reactions, often featuring broad functional group tolerance. Herein we present a novel method, in which enamines undergoes intramolecular nucleophilic addition to a tethered alkyne moiety followed by coupling with (hetero)aryl triflate. Presented method is characterized by wide scope for electronically varied triflates, as well as a range of sterically hindered enamines.

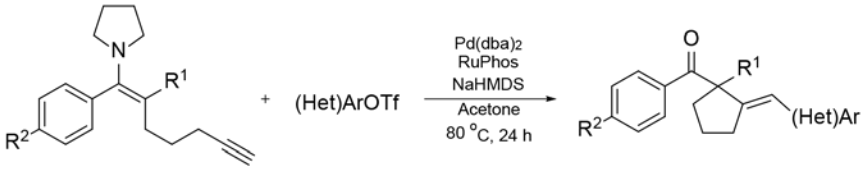

Fig. 1. *General reaction scheme.*

Acknowledgements: Financial support from the Polish National Science Centre (Grant decision DEC-2016/22/E/ST5/00537) is gratefully acknowledged.

SYNTHETIC APPROACHES TOWARD C-C BONDED TRIAZOLYLPURINES FOR USE IN MATERIALS SCIENCE

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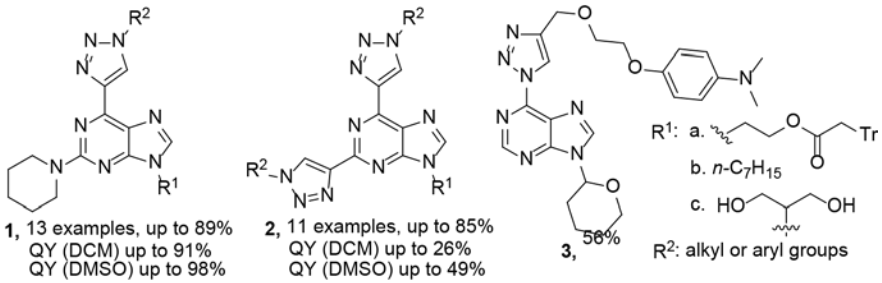
Faculty of Materials Science and Applied Chemistry,
Riga Technical University, Riga, Latvia

Purine-triazole conjugates belong to the push-pull systems and possess fluorescent properties which can be potentially used in OLED technology and in cell imaging.[1,2] Our group synthesized C-C bonded triazolylpurine derivatives **1-2** from 2,6-dichloropurine, using the sequence of Mitsunobu, Sonogashira, CuAAC and S_NAr reactions and studied their photophysical properties. Quantum yields reached up to 91% in DCM and 98% in DMSO solutions. Recently C-N bonded triazolylpurine **3** was designed. Further THP group can be substituted with various alkyl groups.



Acknowledgements: The authors thank MEPS co-project LV-LT-TW/2022/9 for financial support. A.B. thanks Riga Technical University for doctoral student research grant DOK.OĶTI/21.

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ENANTIOMERICALLY PURE AZABICYCLO[3.3.1] NONANES FOR THE SYNTHESIS OF SARPAGINE FAMILY ALKALOIDS

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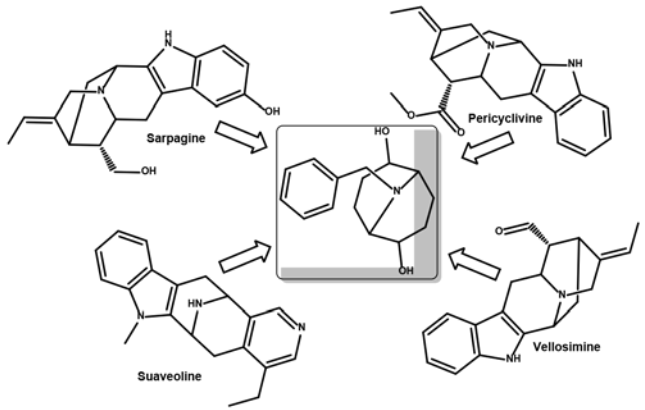
The sarpagine family of alkaloids, traditionally known for their phytochemical applications, constitute a group of monoterpenoid indole alkaloids in great demand for their potential pharmaceutical activity. While naturally very scarce, these alkaloids have been synthesized by Cook's group in the late 1990s - early 2000s employing Pictet – Spengler type chemistry[1].
We suggest a different approach towards the total synthesis of sarpagine family alkaloids from enantiomerically pure azabicyclo[3.3.1] nonanes (Fig. 1). The proposed synthetic approach opens up the way for the large scale synthesis of both enantiomers of sarpagine family alkaloids and enables their further developments for pharmaceutical applications.



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SYNTHETIC STRATEGIES TOWARDS THE TOTAL SYNTHESIS OF ANTHOGORGIENE P

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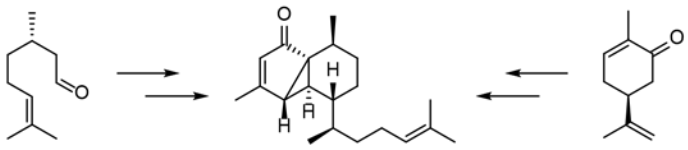
Department of chemistry, Loughborough University, Loughborough, Leicestershire, UK

Herein we report synthetic strategies towards Anthogorgiene P (**1**), a natural Diterpinoid isolated from *Euplexaura sp*, a soft coral located in the South China Sea. Anthogorgiene P has shown to exhibit cytotoxic effects towards the human laryngeal carcinoma (Hep-2) cell line.[1] The tricyclo[4.4.0.0^{1,5}]dec-3-en-2-one, cubebene-like ring system exhibits an interesting synthetic challenge along with the 6 chiral centres. Our trialled strategies have started with abundant monoterpenoids, and the key synthetic steps have proceeded through Michael promoted cascades, lithium amide-induced cyclopropanation of trishomoallylic epoxides, cyclopropanations through metallocarbenes from diazocompunds and, gold catalysed oxidative cyclopropanations of 1,5-enynes. The most promising results will be presented.



Anthogorgiene P (1)

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USE OF WASTE BIOMASS AFTER PHYTOREMEDIATION FOR THE PREPARATION OF POLYMETALLIC CATALYSTS AND APPLICATION IN C-P BOND FORMATION

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[1]Wroclaw University of Science and Technology, Poland

One of the effects of global industrialization is contamination of soils with heavy metals, therefore the decontamination is very important to reduce the associated risks. Phytoremediation as a new technology of soil purification, is based on the implementation of green plants. It stands out from other techniques thanks to its cost-effectiveness and environmental friendliness. The purifying aspect of phytoextraction has some limitations due to the production of metal-contaminated biomass, which must be properly disposed of.
On the other hand, there is a problem in the management of metal resources. Metals necessary for harmonious technological progress and at the same time characterized by a limited raw material base are classified as critical raw materials.
An innovative idea that addresses these problems is the use of metal-contaminated biomass from the plants used in the phytoremediation as an alternative source of metals used for catalysts. The polymetallic catalysts obtained in this way are suitable for use in organic synthesis and for the preparation of various heteroorganic compounds, including phosphorus-containing derivatives

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ISOLATION, IDENTIFICATION AND INVESTIGATION OF MICROORGANISMS GROWING ON COFFEE GROUNDS AND INSTANT COFFEE

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Caffeine (1,3,7-trimethylxanthine) is a purine alkaloid found in coffee, tea [1]. The major catabolic pathway of caffeine is: caffeine → theobromine/theophylline → 3-methylxanthine → xanthine → uric acid → allantoin → allantoic acid → CO_2 + NH_3 [2]. It is known that microorganisms such as fungi and bacteria can grow on the coffee bean fruit. Bacteria are able to use caffeine as a sole carbon and nitrogen source. There are two bacterial mechanisms for caffeine degradation: *N*-demethylation and C-8 oxidation [3].
In this study, two types of fungi (*Geotrichum silvicola* and *Penicillium crustosum*) and eight types of bacteria, some of them are Klebsiella species were investigated. These microorganisms were isolated from coffee bean grounds or instant coffee, and identified by DNA sequencing. Minimal media with caffeine was used to determine the growth of microorganisms in a caffeine environment. The ability of bacteria to degrade caffeine was investigated by high-performance liquid chromatography (HPLC) to identify newly formed caffeine metabolites.

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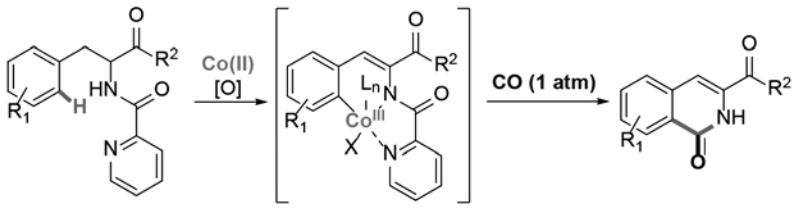
COBALT-CATALYZED, PICOLINAMIDE-DIRECTED C(sp²)-H CARBONYLATION OF PHENYLALANINE DERIVATIVES

Aleksandrs Cizikovs, Lukass Lukasevics, Liene Grigorjeva
Latvian Institute of Organic Synthesis, Riga, Latvia

Over the past few decades, transition metal-catalyzed C-H functionalization reactions have been immensely investigated due to their ability to functionalize relatively unreactive C-H bonds. Majority of the results have been achieved using third row transition metals (Pd, Ru, Rh).[1] Cobalt being cheaper and less toxic in combination with directing group and oxidant have shown the great potential in C-H functionalization methodology. Our work is dedicated to the development of cobalt-catalyzed, traceless picolinamide-directed C-H carbonylation of amino acid derivatives.



Acknowledgements: This research is funded by the Latvian Council of Science, project No. lzp-2019/1-0220.

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SYNTHESIS OF NEW POLYCYCLIC NITROGEN HETEROCYCLE COMPOUNDS VIA MULTICOMPONENT REACTIONS FROM 3-ALKOXY-1*H*-PYRAZOLE-4-CARBALDEHYDES

Viktorija Dargytė[1,2], *Eglė Arbačiauskienė*[1], *Aurimas Bieliauskas*[2], *Algirdas Šačkus*[1,2].
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[2]*Institute of Synthetic Chemistry, Kaunas University of Technology, Kaunas, Lithuania*

In multicomponent reactions (MCRs) three or more reagents have their atoms incorporated into the final product in a single reaction pot [1]. MCRs are considered as an alternative to sequential multistep synthesis due to the atom economy and reduced waste generation.
In continuation of our interest in the efficient synthesis and investigation of pyrazole-containing polycyclic systems from easily accessible starting materials [2-4] we report herein the synthesis of novel pyrazole-containing polycyclic compounds via various multicomponent reactions.
Starting from 3-substituted 1*H*-pyrazole-4-carbaldehydes and employing one-stage four-component reaction a series of 4-(pyrazol-4-yl)dihydropyrano[2,3-c]pyrazoles was obtained, while Hantzsch MCR conditions [5] and further oxidation were applied for the synthesis of 4-(1*H*-pyrazol-4-yl)pyridines. Furthermore, 4-((pyrazol-4-yl)methylene)isoxazolones were successfully synthesized in one-pot three-component reaction under ultrasound irradiation [6].
The structures of the synthesized compounds were confirmed by ^{1}H, ^{13}C and ^{15}N NMR spectroscopy.

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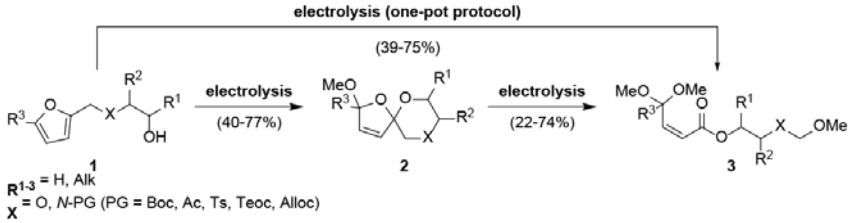
ELECTROSYNTHESIS OF *α,β*-UNSATURATED ESTERS FROM FURFURYLATED ETHYLENE GLYCOLS AND AMINO ALCOHOLS

Madara Darzina, *Anna Lielpetere*, *Aigars Jirgensons*
Latvian Institute of Organic synthesis, Latvia

Biomass derived furanoics are versatile starting materials to obtain a range of chemicals with an application in material science, drug discovery and agriculture[1]. Among others, electrochemical methods have been explored as a means of converting furanoics into value-added products[2]. Furan derivatives are suitable substrates for electrochemical transformations due to the relatively low oxidation potential of the furan ring which allows selective oxidation in the presence of other functional groups.



Scheme 1. *Electrochemical transformations of alcohols* **1**.

In this work we have developed a method to transform furfurylated ethylene glycols and amino alcohols **1** into spirocycles **2** and unsaturated esters **3** (Scheme 1)[3].

Acknowledgements: This work was supported by student grants from Latvian Institute of Organic Synthesis (IG-2020-05, IG-2021-03, IG-2022-06).

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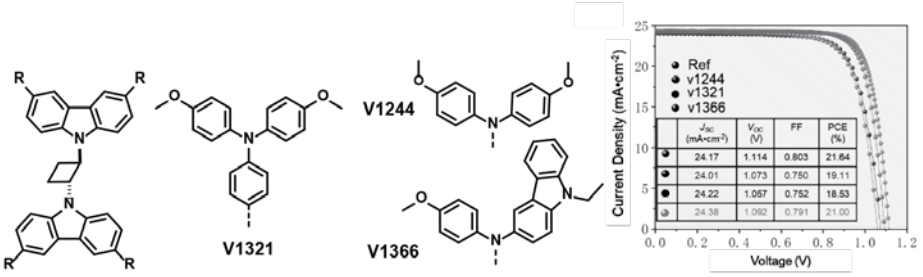
HIGH EFFICIENCY OF PEROVSKITE SOLAR CELLS AND MODULES VIA GREEN CHEMISTRY INSPIRED HOLE SELECTIVE MATERIALS

Šarūnė Daškevičiūtė-Gegužienė[1], Yi Zhang[2], Kasparas Rakštys[1], Marytė Daškevičienė[1], Vygintas Jankauskas[3], Mohammad Khaja Nazeeruddin[2], Vytautas Getautis[1]
[1]Kaunas University of Technology, Lithuania
[2]École Polytechnique Fédérale de Lausanne, Sion, Switzerland
[3]Institution of Chemical Physics, Vilnius University, Lithuania

It's known that photodimerized carbazole is an attractive building block due to the simple, elegant and green synthesis [1]. Novel cyclobutane-based HTMs have been successfully applied in PSCs showing PCE up to 21%. Most importantly, to obtain novel HTMs we have applied protocols inspired by green chemistry, for the first time presenting that HTMs for PSCs could be synthesized eliminating the use of hazardous substances in order to reduce the adverse environmental impact without sacrificing the efficiency.



	J_{SC} (mA•cm^{-2})	V_{OC} (V)	FF	PCE (%)
●	24.17	1.114	0.803	21.64
●	24.01	1.073	0.750	19.11
●	24.22	1.057	0.752	18.53
●	24.38	1.092	0.791	21.00

Figure 1. *J-V curves (reverse-scan) of the PSCs based on **V1244**, **V1321**, and **V1366** as HTMs and spiro-OMeTAD as the reference.*

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SEMI-TARGETED SEQUENCING OF FUSION TRANSCRIPTS IN PROSTATE CANCER ENABLED BY OLIGONUCLEOTIDE-MODIFIED DIDEOXYNUCLEOTIDES

Ugne Drazdauskiene[1], Zana Kapustina[2], Justina Medziune[1,3], Varvara Dubovskaja[1], Rasa Sabaliauskaite[4], and Arvydas Lubys[1]
[1]Thermo Fisher Scientific Baltics UAB, Vilnius, Lithuania
[2]Droplet Genomics UAB, Vilnius, Lithuania
[3]Faculty of Chemistry and Geosciences, Vilnius University, Vilnius, Lithuania
[4]National Cancer Institute, Vilnius, Lithuania

We developed efficient and straightforward synthesis strategy of oligonucleotide-tethered dideoxynucleotides (OTDDNs) to capture unknown sequences downstream of the target site. Modified OTDDNs, upon random incorporation during primer extension reaction, create DNA fragments of a desired average length, with simultaneous labeling of a corresponding DNA strand with sequencing adapter. Oligonucleotide modification then serves as a priming site for subsequent synthesis of cDNA strand. We applied method termed fusion sequencing via terminator-assisted synthesis (FTAS-seq) to study *TMPRSS2-ERG* fusion transcripts in prostate cancer cell line NCI-H660 and in clinical prostate cancer RNA samples. We identified 3 previously described chimeric transcripts in NCI-H660 RNA as well as one new possible variant. Analysis of clinical samples showed that FTAS-seq is more sensitive approach than conventional PCR-based methods: 3 TMERG fusion transcripts, which were previously detected with amplification-based methods, and 10 other possible variants were detected. It is a good alternative to amplicon sequencing as it has greater discovery potential at the same level of cost-effectiveness.

CARBAZOLE BASED PHOSPHONIC ACIDS WITH DIFFERENT LENGTH OF ALIPHATIC LINKER FOR PEROVSKITE SOLAR CELLS: SYNTHESIS AND INVESTIGATION

Aida Drevilkauskaite[1], Artiom Magomedov[1], Amran Al-Ashouri[2], Steve Albrecht[2], Vytautas Getautis[1]
[1]Department of Organic Chemistry, Kaunas University of Technology, Kaunas, Lithuania
[2]Young Investigator Group Perovskite Tandem Solar Cells, Helmholtz-Zentrum Berlin, Germany

Perovskite solar cells (PSCs) over the last decade have reached competitive efficiencies, however, the stability of the devices remains a big challenge. One of the reasons behind reduced stability is the extensive use of dopants in organic hole-transporting materials (HTMs) [1].
Recently, as an alternative to the traditional doped HTMs, hole-selective monolayers were introduced into PSCs as a dopant-free alternative [2]. The highest efficiency of 20.8% was achieved for the carbazole based phosphonic acid, called **2PACz** (Fig. 1. n=2). Seeing a high potential of monolayer HTMs, further structure optimization was performed.

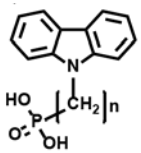

Fig. 1. *The general structure of the **nPACz** materials, where n = 2, 3, 4, 5, 6.*

In this work, a series of new carbazole based phosphonic acids with different length of aliphatic linkers were synthesized (Fig. 1.) It is expected, that longer chains could improve the ordering of the monolayer film, however, at the cost of reduced ability to transport charges. Materials were tested in photovoltaic devices and the results show that performance deacreases due to increased length of the aliphatic chain.

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SHORT SYNTHESIS OF N-ACETYLCOLCHINOL USING ELECTROCHEMISTRY

Yi Du, Andrei. V. Malkov
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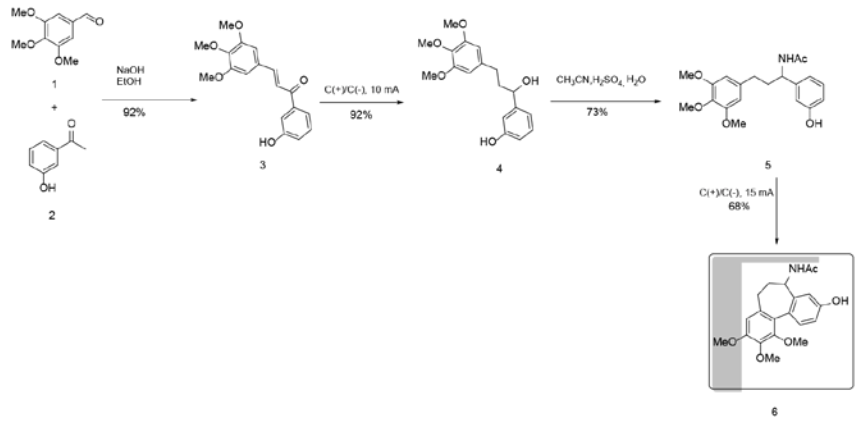
Colchicine is a natural alkaloid that in clinical trials by Amorosoi in 1935 showed antitumor activity but high toxicity. N-Acetycochinol 6 attracted attention of researchers due to the similar biological activity but lower toxicity than many other colchicine analogues. Following this, several groups developed synthetic routes of around 8 chemical steps using metal reagents. Herein we report a green and highly efficient route to N-acetylcochinol. The novel 4-step synthesis shown in the Scheme commences by aldol condensation of 3-hydraoyacetophenone with 3,4,5-trimethoxybenz-aldehyde and deploys two electrochemical steps.



DESIGN AND SYNTHESIS OF GRADUALLY AUGMENTED HYDROPHOBIC LIGANDS AS AN APPROACH TO ENZYME ACTIVE SITE EXPLORATION

Virginija Dudutienė[1], Asta Zubrienė[1], Visvaldas Kairys[2], Alexey Smirnov[1], Daumantas Matulis[1]
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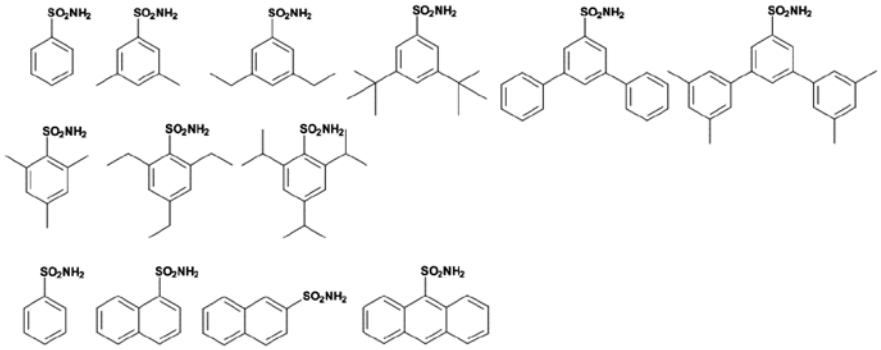
We varied the length and bulkiness of hydrophobic substituents of benzenesulfonamides by three approaches: substituting 3,5-positions; substituting 2,4,6-positions, and extending the condensed ring system.



The gradual augmentation of the inhibitor size led to exploration of active site cavities giving new insights into the rational design of isoenzyme-selective inhibitors of carbonic anhydrases that are involved in numerous physiological and pathological processes and are considered as important therapeutic targets (*Dudutiene et al, Biophys J. 2020*).

ACCESS TO 2-PYRIDYL KETONES VIA ACYLATION OF 2-(TRIMETHYLSILYL)PYRIDINE

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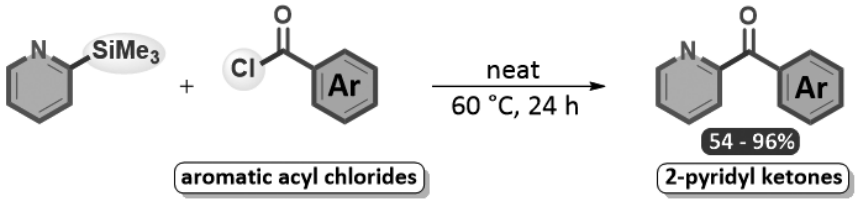
Many years ago Pinkerton and Thames reported that 2-(trimethylsilyl) pyridine can react with a variety of carbonyl compounds, such as benzaldehyde,[1] benzoyl chloride, ethyl chloroformate and phthalic anhydride,[2] yielding 2-substitued pyridines. Inspired by the early examples, we demonstrate that acylation of 2-(trimethylsilyl)pyridine with a number of acyl chlorides occurs under mild conditions giving 2-pyridyl ketones in good to excellent yields.[3]



Acknowledgements: The project was financed from NCN, Poland (grant DEC-2018/31/B/ST5/01118).

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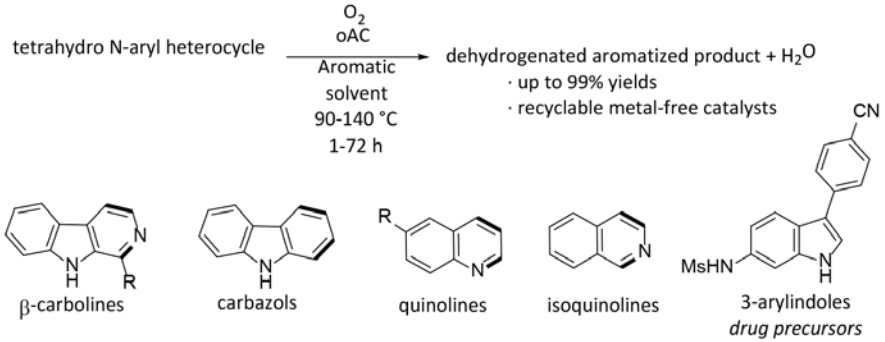
AIR OXIDIZED ACTIVATED CARBON CATALYST FOR AEROBIC OXIDATIVE AROMATIZATIONS OF N-HETEROCYCLES

Lukas Enders, David Casadio, Santeri Aikonen, Anna Lenarda, Tom Wirtanen, Juho Helaja
University of Helsinki

Various (nano)carbon materials are known to dehydrogenate hydrocarbons catalytically.[1] We have discovered that oxidized active carbon (oAC) materials are able to oxidatively dehydrogenate (ODH) nitrogen containing 1,2,3,4-tetrahydroaromatic compounds utilizing oxygen as terminal oxidant with a remarkable activity.[2] The oAC catalysts are prepared via thermal treatment under air atmosphere from inexpensive and environmentally benign starting materials. The developed OHD methodology gives convenient, metal-free catalytic access to various aromatic N-heterocyclic structures.



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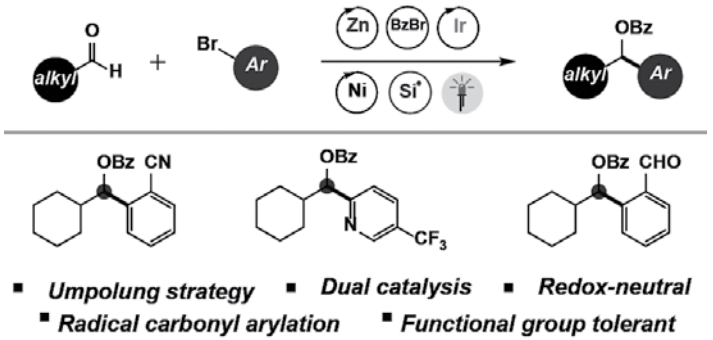
RADICAL CARBONYL UMPOLUNG ARYLATION VIA DUAL NICKEL CATALYSIS

Huan-Ming Huang, Peter Bellotti*, Johannes Eike Erchinger, Tiffany Olivia Paulisch, Frank Glorius*
Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Münster, Germany

We have demonstrated that 1,2,6-thiadiazin-4-one (TDZ) scaffold can function as a novel chemotype for the design of ATP-competitive kinase inhibitors. The TDZ core can be used as an electronic isostere for the more common 2,4-dianilinopyrimidine kinase inhibitor scaffold. The resulting analogues showed reduced kinome promiscuity compared to their 2,4-dianilinopyrimidine counterparts and using this screening we identified calcium/calmodulin-dependent protein kinase kinase 2 (CaMKK2), as a promising target. We solved a co-crystal structure of a 3,5-bis(arylamino)-4H-1,2,6-thiadiazin-4-one bound to CaMKK2 and several analogues were identified with micromolar activity through targeted displacement of bound water molecules in the active site. The TZD scaffold represents an exciting starting point for development of highly selective kinase inhibitors.



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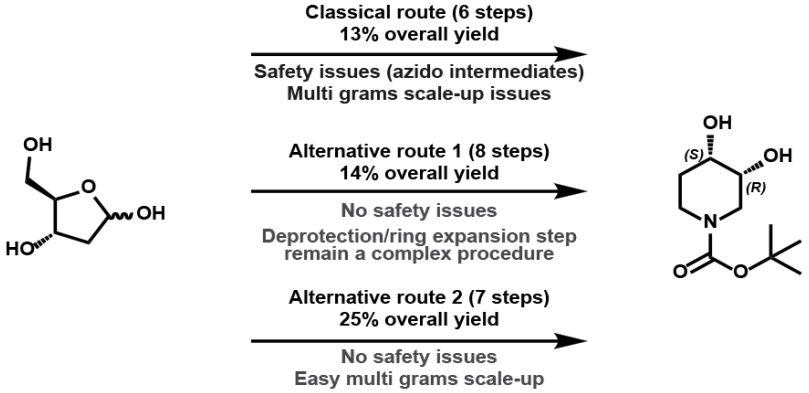
*H.-M. H. and P. B. contributed equally.

AZIDE-FREE SYNTHESIS OF BOC-PROTECTED (3*R*,4*S*)-3,4-DIHYDROXYPIPERIDINE

Danilo Fabbrini, Paola Fezzardi, Nicola Relitti, Federica Ferrigno, Ilaria Rossetti, Alessio Sferrazza, Alessia Petrocchi, Christian Montalbetti
IRBM S.p.A., Department of Medicinal Chemistry, Via Pontina Pomezia, Italy

Boc-protected (3*R*,4*S*)-3,4-dihydroxypiperidine diol **1** is an enantiomerically pure, highly valuable synthetic intermediate. Herein we report the development of two scalable synthetic strategies avoiding the use of hazardous sodium azide, as well as the formation of azido intermediates. Starting from the readily available 2-deoxy-D-ribose, it was possible to produce a substantial amount of diol **1** following two distinct routes, without a significant decrease in performance when scaling up from 1- to 230-mmol.



SYNTHESIS AND THERMALLY ACTIVATED DELAYED FLUORESCENCE PROPERTIES OF 4,6-DI(HETARYL)-5-METHYLPYRIMIDINES

Irina Fiodorova,[1] Tomas Serevicius,[2] Rokas Skaisgiris,[2] Dovydas Banevicius,[2] Saulius Jursenas,[2] Sigitas Tumkevicius[1]
[1]Institute of Chemistry, Vilnius University, Lithuania
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The interest in organic materials exhibiting thermally activated delayed fluorescence (TADF) has been significantly increased in recent years owing to their potential application as emitters in highly efficient organic light emitting diodes (OLEDs). Recently, compounds containing pyrimidine heterocycle as an electron acceptor unit have been demonstrated to be promising TADF emitters for applications in organic optoelectronics. Here, we performed the design, synthesis, and photophysical characterization of some pyrimidine-based emitters in which electron donating carbazole, acridane or phenoxazine moieties are directly bonded with the acceptor unit (Fig. 1).

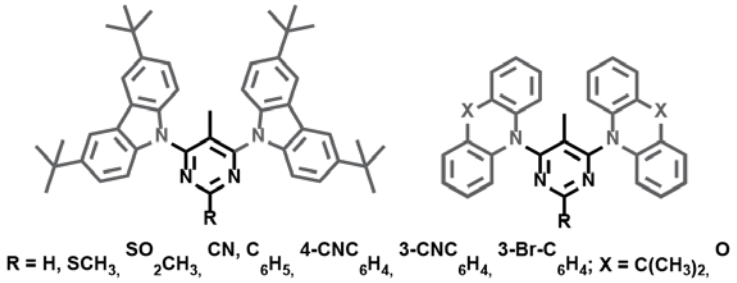

Fig. 1. *Structures of pyrimidine-based fluorophores.*

Influence of structure modifications of the synthesized emitters on their electronic and photophysical characteristics as well as application of some optimized compounds in OLED devices will be demonstrated.

CHIRAL H-P REAGENTS DERIVED FROM ALCOHOL, AN EFFECTIVE TOOL FOR THE ASYMMETRIC SYNTHESIS OF C-STEREOGENIC ORGANOPHOSPHORUS COMPOUNDS

Joseph Gbubele, Tomasz Olszewski
Wrocław University of Science and Technology, Faculty of Chemistry, Wrocław, Poland

Organophosphorus compounds are class of compounds with extraordinary biological activity due to their unique physical and chemical properties and found wide range of applications that span from medicinal chemistry to enantioselective catalysis. The chemistry of these compounds continuously to attract the attention of the organic and medicinal chemists but however, their synthesis is still a challenging task, especially with precise stereochemistry control at the chiral carbon atoms. In respect to that, the nucleophilic addition of H-P reagent bearing chiral alcohol moiety attached to the phosphorus atom to carbon heteroatom bond gives an interesting pathway in inducing stereochemistry in the desired product [1].
During our presentation, we will report the recent results from our laboratory on the application of such chiral H-P reagents which serve as chiral auxiliary in the synthesis of substituted phosphonates and phosphonic acids.

Acknowledgements:
The authors acknowledge the funding from the Polish Ministry of Education and Science.

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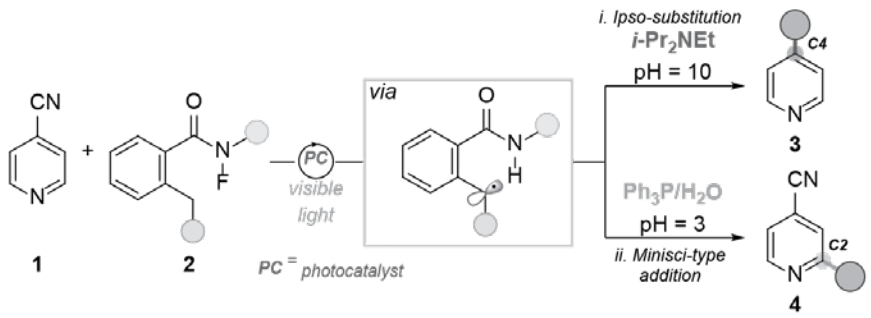
PHOTOCHEMICAL CHEMODIVERGENT BENZYLATION OF CYANOPYRIDINES

Eleni Georgiou[1], Davide Spinnato[1], Kang Chen[1], Kilian Muñiz[1,2], Paolo Melchiorre[1,2]
[1]ICIQ – Institute of Chemical Research of Catalonia, Spain
[2]ICREA, Spain

We report a photoredox system for the chemodivergent benzylation of 4-cyanopyridines **1** using N-fluorobenzamides **2** as radical precursors. Key for the chemoselective switch between C4 or C2 benzylated pyridines (**3** or **4**, respectively) is the nature of the chosen photochemical quencher, which channels the radical process towards two distinct mechanistic pathways: i) an ipso-substitution path, proceeding via radical-radical coupling, and ii) a Minisci-type addition to cyanopyridines. The protocol grants access, at will, to orthogonal substitution patterns on the pyridine core. Mechanistic investigation, by means of pH measurements, Stern-Volmer quenching experiments and reaction profile analysis, allowed us to rationalize the chemoselectivity switch.



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DESIGN, SYNTHESIS AND BIOLOGICAL ACTIVITIES OF NEW PURINES AND AZAPURINES

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Faculty of Pharmacy and Food Sciences. University of Barcelona, Barcelona, Spain

We are interested in the synthesis of compounds that interfere with key enzymes by allosteric mechanism.[2]
The activity of several purines and deazapurines (pyrrolo[2,3-*d*] pyrimidine) considered analogues of purine bases (6-mercaptopurine, 6-thioguanine) against cancer diseases such as pancreas and sarcoma lends support to the view that purines-derivatives might be expected to be useful against divers neoplastic diseases and as considered as being worthy of the broadest range of modification.[1] Some time ago, purine-derivatives have been involved in the inhibition of cyclin-dependent kinases (CDKs), which set the cell signaling pathways in motion.
The functionalization of the 2-, 3-, 5-, and 6- positions of the purine and azapurine nucleus, formation of the heterocyclic system and *N*-arylation of *N*-7 position were among the structural modifications carried out. Organic chemistry classical methods are used for the preparation of these substituted azapurines. Also, cross-coupling optimized conditions have been useful for the C- and *N*-arylation. Finally, the antitumor activity of the synthesized compounds was evaluated using MTT assay. Some compounds have demonstrated great inhibition of the growth of tumor cells. Molecular Modeling Studies were applied for the design and selection of structures to synthesize.
Several compounds containing purine or deazapurine scaffold have been prepared and the design, synthesis and the biological activities should be discussed in the presentation of this research work.

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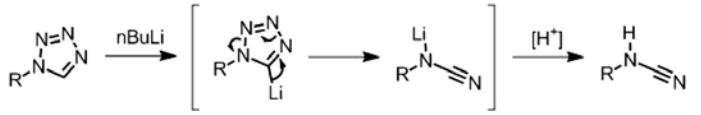
SYNTHESIS AND APPLICATIONS OF METALLATED 1*H*-TETRAZOLES

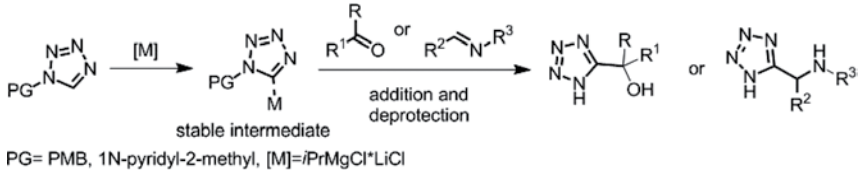
Konstantinos Grammatoglou, Madara Dārziņa, Aigars Jirgensons
Latvian Institute of Organic Synthesis, Latvia

Tetrazoles have a wide range of applications in pharmacology and materials science. Therefore, efficient methods for their synthesis are of great need.[1] Tetrazole can be derivatized via metallated intermediate at relatively acidic 5-CH position. However, the decomposition of metallated tetrazole is fast process which significantly limits the application of this approach (Scheme 1).[2,3]



Scheme 1.

We propose the functionalization of tetrazoles by C-H deprotonation using the turbo-Grignard reagent which provides a stable organomagnesium intermediate (Scheme 2).[4] Tetrazole derivatives with 1*N* protection such as acid/hydrogenolysis/oxidation labile PMB group or electrochemically cleavable pyridyl-2-methyl group can be used as substrates.



Scheme 2.

The newly developed approach significantly broadens tetrazole functionalization options including the reactions with aldehydes, ketones and imines.

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SYNTHESIS AND BIOLOGICAL ACTIVITY OF N-HYDROXYPHENYL SUBSTITUTED ß-ALANINE DERIVATIVES

Birutė Grybaitė[1], Povilas Kavaliauskas[1,2], Birutė Sapijanskaitė-Banevič[1], Vytautas Mickevičius[1]
[1]Kaunas University of Technology, Lithuania
[2]Weill Cornell Medicine of Cornell University, United States

ß-Amino acids are promising intermediates in organic, bioorganic, medicinal and peptide chemistry [1].

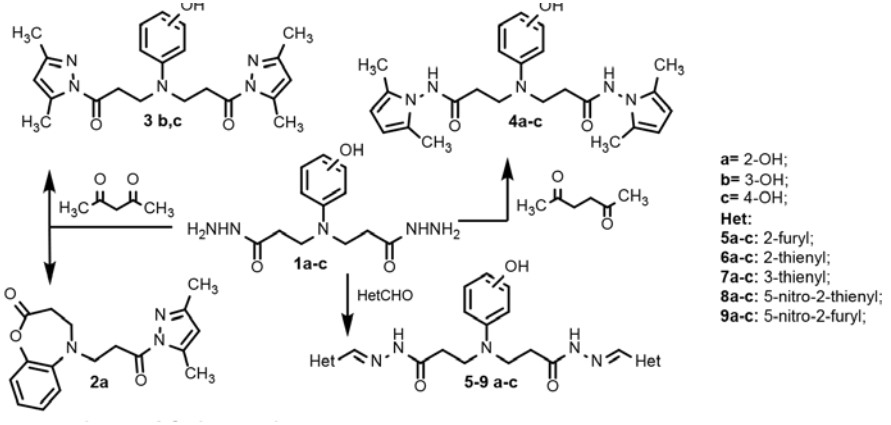

Fig. *Synthesis of ß-alanine derivatives*

The reaction with 2,4-pentanedione in 2-propanol in the presence of a catalytic amount of hydrochloric acid provided pyrazoles **2a**, **3 b**, **c**. Condensation of dihydrazides **1a-c** with 2,5-hexanedione gave pyrrole compounds **4a-c**. Hydrazones **5-9 a-c** were prepared by the reaction of corresponding dihydrazides **1a-c** and heterocyclic aldehydes in 2-propanol. The resulting compounds demonstrated favorable antimicrobial activity against panel of and multidrug resistant bacterial and fungal pathogens at micromolar range.

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SYNTHESIS AND PURIFICATION OF ENANTIOMERICALLY PURE 2-(N-BOC-AZETIDIN-3-YL) ACIDS

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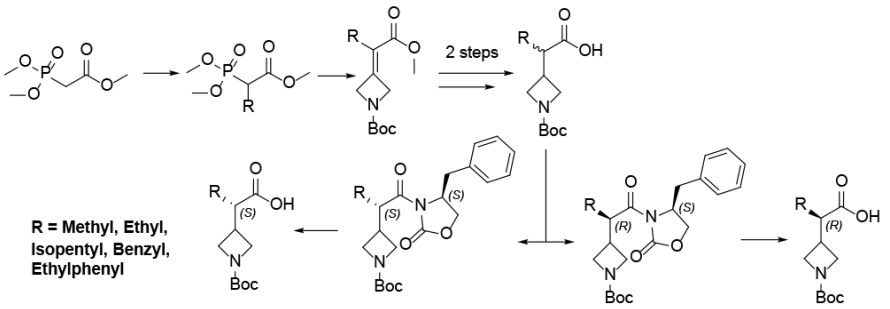
[3]Vipergen ApS, Copenhagen, Denmark

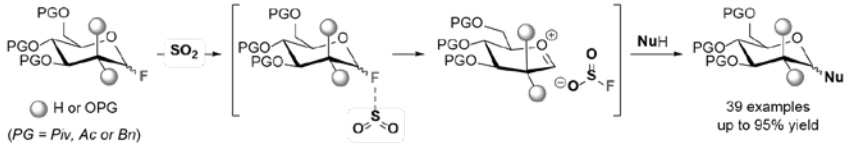
Pure single enantiomers can be obtained via the selective synthesis of one enantiomer or the separation of racemic mixtures. Stereoselective syntheses are rarely selected for large scale separations, particularly at the early stages of development of new drugs in the pharmaceutical industry because they are both expensive and time-consuming. In this work we have developed an inexpensive and effective method to prepare pure enantiomers of 2-(*N*-Boc-azetidin-3-yl) acids via separation of the racemic mixture.
The multi-step process involves preparation of 2-(*N*-Boc-azetidin-3-yl) acids racemate, which with an optimized optically pure derivatizing agent affords diastereomeric (*S*)-4-Benzyl-2-oxazolidinone, which was separated by conventional method preparative chromatography. After separation the pure enantiomers was recovered by elimination of the derivatizing agent. The absolute configuration of chiral compounds was proven by x-ray crystallography and the proton nuclear magnetic resonance (NMR) methods.



SO2-ASSISTED GLYCOSIDIC BOND FORMATION

Krista Gulbe[1], Jevgeņija Lugiņina[1], Edijs Jansons[1], Artis Kinēns[2,3], Māris Turks[1]
[1]Institute of Technology of Organic Chemistry, Riga Technical University, Latvia
[2]Latvian Institute of Organic Synthesis, Latvia
[3]Department of Chemistry, University of Latvia, Latvia

Being one of the few polar solvents that possess Lewis acid properties, liquid SO_2 facilitates Lewis acid promoted and/or carbenium ion mediated chemical transformations.[1] Furthermore, SO_2 has an affinity towards fluoride ion that leads to covalent bonding in the form of fluorosulfite anion.[2]
Based on the aforementioned physico-chemical properties of SO_2, we have developed SO_2-assisted glycosylation with glycosyl fluorides as glycosyl donors in liquid SO_2 without an external promoter.[3] The novel synthetic method was demonstrated with variously protected mannosyl and glucosyl fluorides, and series of O-, S- and C-glycosides were obtained in moderate to excellent yields. The α/ß-selectivity of glycosylation was proposed to be substrate-controlled presenting thermodynamic equilibrium. The formation of fluorosulfite species during the glycosylation in the presence of SO_2 was proved by both ^{19}F NMR spectroscopy and DFT calculations.



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TRANSITION METAL COMPLEXES OF ARYLAZOPYRAZOLE INCORPORATED FLEXIBLE LIGAND SYSTEMS

Debapriya Gupta[1], Ankit Kumar Gaur[1], Deepanshu Chauhan[2], Sandeep Kumar Thakur[1], Vaitheesh Jeyapalan[1], Sanjay Singh[1], Gopalan Rajaraman[2], Sugumar Venkataramani[1]
[1]Indian Institute of Science, Education and Research (IISER) Mohali, India
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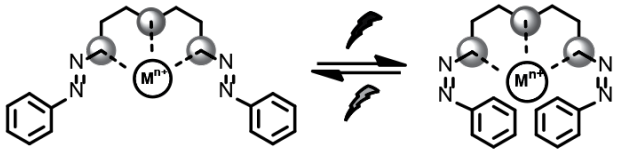
Photo-responsive transition metal complexes are useful in different optomechanical devices, light-induced ligand driven spin-crossover (LD-LISC) and logics and memories, etc.[1] Such applications require compounds to photoisomerize efficiently in both solution and solid state. However, most of the reported compounds exhibit restricted photoswitching in solid-state. In this regard, we have prepared three photoactive azopyrazole-based ligands, as the phenylazo-3,5-dimethyl-pyrazole photoswitches are known for their excellent photoswitching characteristics.[2] We have investigated the complexation properties of these ligands with a number of transition metal ions and also explored their photoswitching properties in solution phase and solid-state. The studies were supported by DFT calculations. Through this contribution, we present the photophysical studies of solid-state photochromic ligands and their transition metal complexes.[3]



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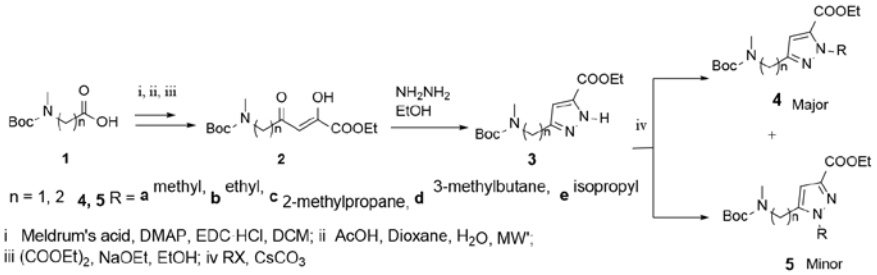
N-ALKYNYL-1-H-PYRAZOLECARBOXYLATES SYNTHESIS FROM N-METHYLGLYCINE AND N-METHYL-ß-ALANINE SCAFFOLDS

Rokas Jankauskas[1], Emilis Gudelis[2], Neringa Kleizienė[1], Urtė Šachlevičiūtė[1], Gabrielė Kliučinskaitė[1], Frank A. Sløk[3], Algirdas Šačkus[1]
[1]Institute of Synthetic Chemistry, Kaunas University of Technology, Lithuania
[2]Department of Organic Chemistry, Kaunas University of Technology, Lithuania
[3]Vipergen ApS, Copenhagen, Denmark

In the present work N-methyl-ß-alanine and N-methylglycine were applied for the preparation of new pyrazole derivatives as building blocks for the preparation of peptides, or in combinatorial chemistry for the screening of new potential drugs.
The enolic form of 2,4-diketo esters **2**, available in three- steps from Boc-N-methyl-ß-alanine and Boc-N-methylglycine, was treated with hydrazine hydrate to afford the desired pyrazole **3**. The N-alkyl group (R) is then introduced by N-alkylation with alkyl halides to give a mixture of regioisomers **4a-e** and **5a-e** which were identified by ^{1}H, ^{13}C-HMBC and ^{1}H, ^{15}N-HMBC NMR spectroscopy.



SOLID-PHASE SYNTHESIS OF COMBINATORIAL DNA-ENCODED CHEMICAL LIBRARY FOR MICROFLUIDICS ASSISTED ACTIVITY ASSAY

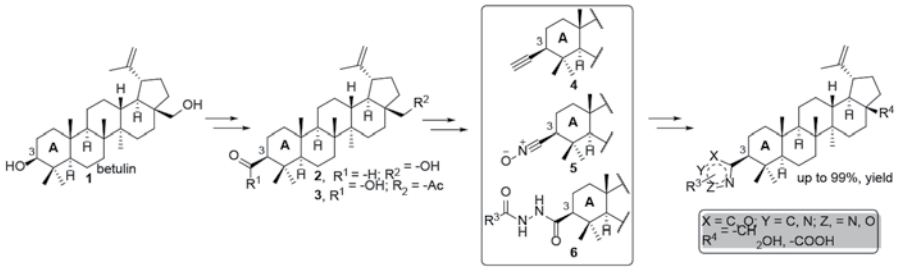
Alberta Jankūnaitė, Domantas Naruševičiu[1], Edvinas Orenta[1]
Department of Organic Chemistry, Vilnius University, Vilnius, Lithuania

DNA-encoded chemical libraries (DELs) – platform used in medicinal chemistry to synthesize and screen considerable collections of small molecule compounds. Each compound is covalently linked to a DNA fragment that encodes information about the structural peculiarity of each library member. Combinatorial solid-phase synthesis method used here produces resin-bound libraries in the one-bead-one-compound (OBOC) format, where each bead carries multiple copies of a single compound encoded with a unique DNA sequence. Herein we present primary OBOC library synthesis for inhibitors of the main protease of the coronavirus (SARS-CoV-2 MPro). Using droplet microfluidics technology assisted assay library members are screened directly for antiviral activity.

SYNTHESIS OF NOVEL C(3)-LINKED LUPANE-AZOLE CONJUGATES

Edijs Jansons, Elīna Peipiņa, Rūdolfs Beļaunieks, Jevgeņija Lugiņina, Māris Turks
Institute of Technology of Organic Chemistry, Riga Technical University, Latvia

Betulin and betulinic acid are lupane type triterpenoids, that possesses variety anticancer and antiviral properties. Theraputical properties can be enhanced by linking lupane to azole type heterocycles.1 Traditionally C(3) lupane-heterocycle conjugates are linked via ether or ester linker.2 In this work we explore the synthesis of novel, carbon-carbon bonded, lupane-azole conjugates and their biological activity. We converted betulin **1** to corresponding homologous aldehyde **2** and carboxylic acid **3** at lupane **A** ring C(3) position. Next, aldehyde group was transformed into alkyne **4** and nitrile oxide 5 derivatives that were used to construct disubstituted 1,2,3-triazole and isoxazole heterocycles correspondingly. Acid **3** was converted to hydrazide **6** and cyclized to afford disubstituted 1,3,4-oxadiazoles.



Acknowledgements: This work is supported by Riga Technical University grant ZM-2021/10

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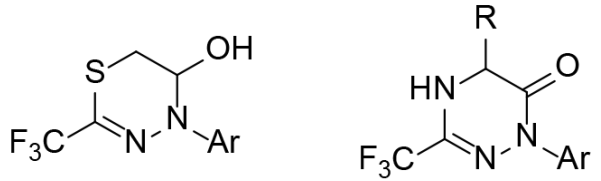
SIX-MEMBERED HETEROCYCLES THROUGH (3+3)-ANNULATIONS OF TRIFLUOROACETONITRILE IMINES

Marcin Jasiński, Anna Kowalczyk, Kamil Świątek, Greta Utecht-Jarzyńsk
Faculty of Chemistry, University of Lodz, Łódź, Poland

In recent work we have demonstrated CF_3-nitrile imines as useful building blocks for preparation of diverse 5-membered systems available via formal (3+2)-cycloadditions.[1,2] Taking into account dual electronic character of title 1,3-dipolar agents we paid attention to (3+3)-annulations with appropriate bifunctional partners such as α-mercapto- and α-aminocarbonyls.[3] Syntheses and properties of trifluoromethylated 1,3,4-thiadiazine- and 1,2,4-triazine derivatives (below) will be presented.



Acknowledgements: Authors thank the University of Lodz for financial support in the framework of IDUB grant #3/IDUB/DOS/2021.

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TRIFLUOROMETHYLATED PYRAZOLES THROUGH CYCLOADDITIONS OF THE CF_3-NITRILE IMINES

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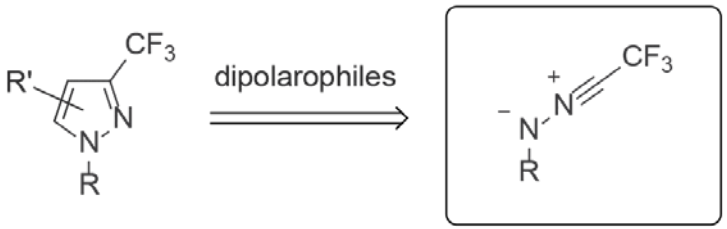
Trifluoromethylated pyrazoles are considered privileged structural motifs for drug discovery and for this reason they received great attention in the last two decades.[1] In this context, we turned attention to trifluoroacetonitrile imines as 1,3-dipolar CF_3-synthons potentially useful for the synthesis of title heterocycles.[2] Our recent results related to exploration of the mentioned nitrile imines for preparation of 3-trifluoromethylpyrazoles and mechanisms of the studied reactions will be summarized.[3]



Acknowledgements: Financial support by the University of Lodz (IDUB grant no. 3/IDUB/DOS/2021) is gratefully acknowledged.

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ASYMMETRIC EPOXIDATION OF ENONES PROMOTED BY DINUCLEAR MAGNESIUM CATALYST

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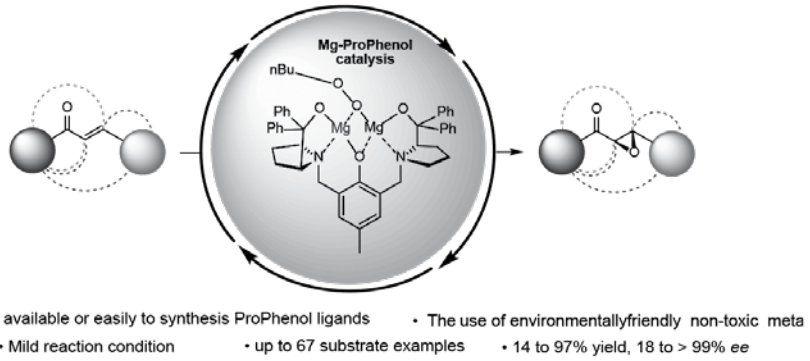
Institute of Organic Chemistry Polish Academy of Sciences, Warsaw, Poland

Asymmetric synthesis with cheaper and non-toxic alkaline earth metal catalysts is becoming an important and sustainable alternative to conventional catalytic methodologies mostly relying on precious metals. In spite of some sustainable methods for enantioselective epoxidation of enones, the development of a well-defined and efficient catalyst based on magnesium complexes for these reactions is still a challenging task. In this perspective, we present the application of chiral dinuclear magnesium complexes for asymmetric epoxidation of a broad range of electron-deficient enones. We demonstrate that the in situ generated magnesium-ProPhenol complex affords enantioenriched oxiranes in high yields and with excellent enantioselectivities (up to 99% *ee*). Our extensive study verifies the literature data in this area and provides a step forward to better understand the factors controlling the oxygenation process. Elaborated catalyst offers mild reaction conditions and a truly wide substrate scope.



Financial support from the Polish National Science Centre (OPUS Grant No. NCN 2017/27/B/ST5/01111)

FLUORENE - TERMINATED MATERIALS FOR EFFICIENT PEROVSKITE SOLAR CELLS

Aistė Jegorovė[1], Cristina Maria Rincón Momblona[2], Marytė Daškevičienė[1], Vygintas Jankauskas[3], Egidijus Kamarauskas[3], Mohammad Khaja Nazeeruddin[2], Vytautas Getautis[1]
[1]Kaunas University of Technology, Lithuania
[2]École Polytechnique Fédérale de Lausanne, Switzerland
[3]Institute of Chemical Physics, Lithuania

In this work we synthesized Spiro-OMeTAD analogues and simpler „half" structures, containing carbazolyl- and methoxyphenyl-chromophores, that have been obtained by a simple synthetic method. Thermal and photoelectrical properties were investigated and compared with Spiro-OMeTAD.

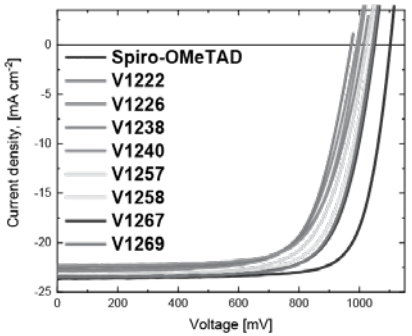


Figure 1. *J-V curves of the most efficient solar cells containing Spiro-OMeTAD and new HTMs.*

All synthesized HTMs exhibit good thermal stability (up to 400 °C). Almost all new HTMs showed T_g significantly exceeding 100 °C. The ionization potential (I_p) of target materials is in range of 4.85–5.02 eV. The PCE of the most efficient n-i-p PSCs perovskite device containing carbazolyl-terminated Spiro-OMeTAD analogue V1267 have reached 18.3 %. Furthermore, "half" structures with methoxyphenyl/carbazolyl fragments show good long-term stability and outperform Spiro-OMeTAD.

SYNTHETIC APPROACH TOWARDS ENANTIOPURE CYCLIC SULFINAMIDES

Glebs Jersovs, Edgars Suna, Pavel Donets
Latvian Institute of Organic Synthesis, Latvia

N-Alkylation of readily accessible Ellman's sulfinamide derivatives has become a routine step in preparation of enantiopure amines.[1] On the other hand, rarely exploited nucleophilic character of the S-atom in tert-butyl sulfinamides can be revealed in a serendipitously discovered intramolecular alkylation. High regio- and stereoselectivity of this transformation allows for facile preparation of diverse cyclic sulfinamides **3**. The latter are convenient enantiopure building blocks for medicinal chemistry owing to ample opportunities for diversification at the asymmetric S-atom and at the olefin.

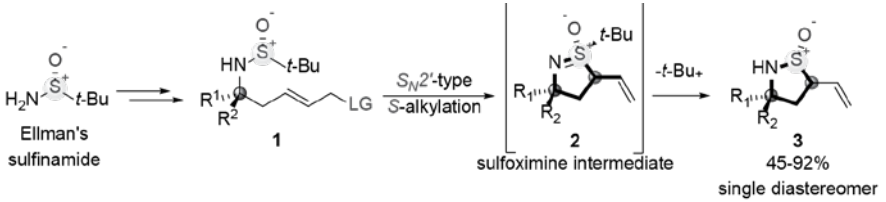


Figure 1. *Intramolecular S-cyclization of tert-butyl sulfinamides **1**.*

Acknowledgements: This project was funded by Latvian Institute of Organic Synthesis internal student grant IG-2021-04 and by the Latvian Council of Science; project LZP-2021/1-0578.

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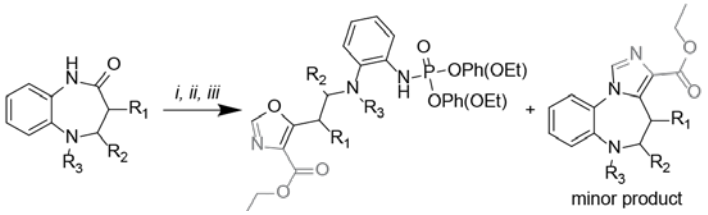
STUDY OF UNEXPECTED REARRANGEMENT OF 1,5-BENZODIAZEPIN-2-ONE DERIVATIVES UNDER MODIFIED WITTIG- HORNER REACTION CONDITIONS

Simona Jonušienė[1], Dalia Vektarytė[1], Mantas Jonušis[1], Aušra Vektarienė[2], Regina Jančienė[1]
[1]Vilnius University, Life Sciences Center
[2]Vilnius University, Institute of Theoretical Physics and Astronomy

During ongoing research on 1,5-benzodiazepin-2-one (BD) based polycyclic compounds we have applied modified Wittig-Horner methodology on 4,5-substituted 1,5-BD in order to synthesize new imidazo[1,5-a][1,5]benzodiazepine derivatives. Unexpectedly, reaction led to ethyl 5-substituted-1,3-oxazole-4-carboxylates as the main products.



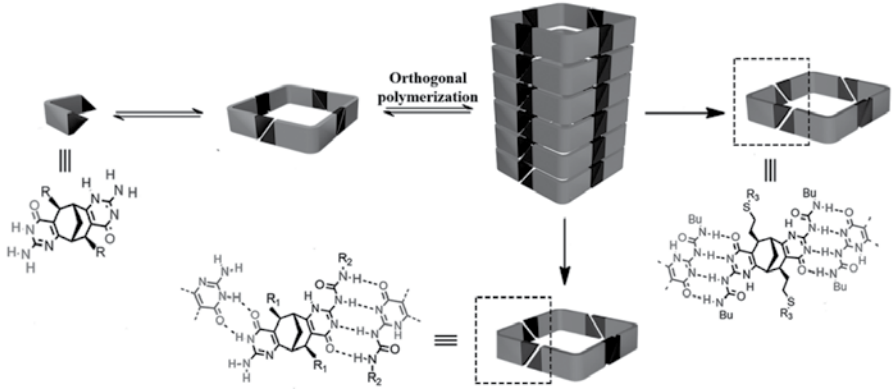
R_1=H, CH_3; R_2=H, CH_3, Ph; R_3=H, $COCH_3$, CH_2Ph
Reagents and conditions: (i)KOtBu, THF, N_2, -40°C, 1h r.t.; (ii)$ClPO(OPh)_2$ THF, N_2, -40°C , 2h r.t.; (iii)$CNCH_2COOEt$, KOtBu, THF, N_2, -40°C, 20h r.t.

In order to investigate the rearrangement process of the 1,5-BD and to confirm the structure of oxazole derivatives the Natural bond orbital and delocalized Molecular orbital (MO) computational modeling techniques were used. Optimized geometries at DFT/B3LYP/311+G (d,p) level of theory of target models were further used to get insight into the electronic structure of the molecules. The Klopman–Salem principle of charge and MO controlled reactions were also taken into account to explain the course of the reaction. It was found that the high level of nucleophilicity of the N(1) atom in the ambident nucleophilic center of 1,5-BD determinates a unique course of the reaction, controlled by an increased p_z-electrons population density of the highest occupied MO, while the course of the reaction of 1,4-BD depends mainly from the negatively charged oxygen atom.

AN ENANTIOPURE HYDROGEN-BONDED AGGREGATES: FROM DISCRETE TETRAMER TO TUBULAR POLYMER

Augustina Jozeliūnaitė, Edvinas Orentas
Department of Organic Chemistry, Vilnius University, Lithuania

Evolution of supramolecular chemistry as a concept of pre-organized smallest entities held together by weak intermolecular forces has established possibilities for the so-called “bottom-up” approach to create various smart materials at molecular level. The building blocks have to be encoded with essential information required for spontaneous self-assembly. Hence, the synthesis of monomers often can be quite challenging and time consuming. A new level of elegance and simplicity has to be achieved to develop starting building blocks. Herein, chiral C_2-symmetric bicyclo[3.3.1.]nonane framework encompassing self-complementary moieties was used as synthon for self-assembly. We introduce a strategy how manipulation of size and spatial arrangement of substituents can provide the means to control orthogonal stacking from discrete tetrameric cycles into tubular polymers and vice versa.



REACTIVITY AND SELECTIVITY OF FORMYL CYCLOHEPTATRIENES

Mikk Kaasik, Karl Anker Jørgensen
Department of Chemistry, Aarhus University, Denmark

Numerous bioactive compounds contain chiral cyclic skeletons. Therefore, much effort has gone into devising synthetic routes for these compounds or their analogues in pharmaceutical applications. Cycloadditions such as the highly regio- and stereoselective Diels–Alder reaction have found extensive use in the synthesis of cyclic systems. The Woodward-Hoffmann rules are used to explain the outcome of a thermal or a photochemical pericyclic process. However, when poly-conjugated systems are used then several reaction paths are allowed and the issue of periselectivity enters the forefront. This is one of the major issues that has hindered the development of cycloadditions involving more than 6π-electrons, termed „higher-order“ cycloadditions.
This presentation will focus on how the location of the formyl group influences the reactivity of the cycloheptatriene system in rearrangement reactions and asymmetric organocatalytic cycloaddition reactions.

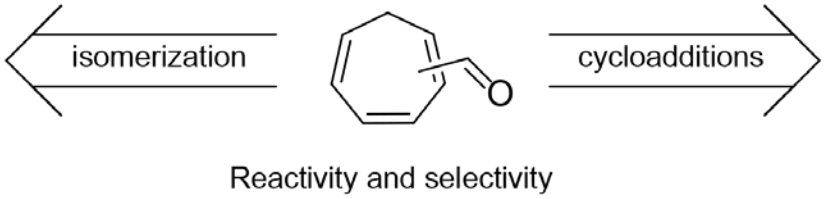
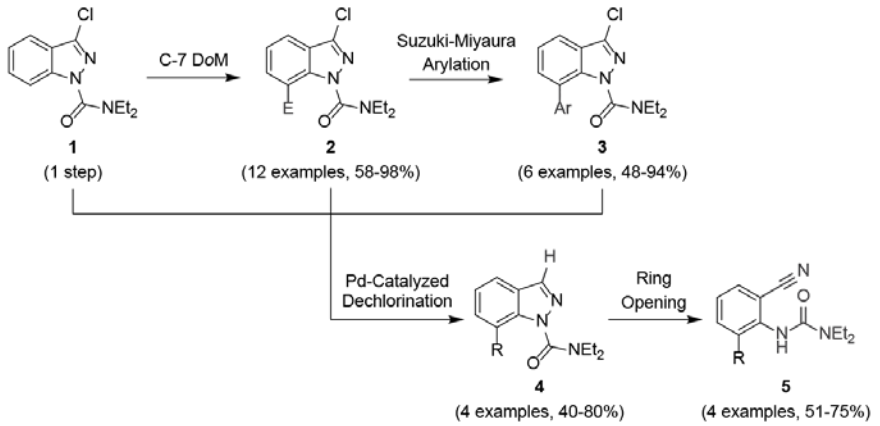


Figure 1. *Reactivity of formyl cycloheptatrienes.*

ADVANCES IN THE DIRECTED *ORTHO* METALATION, SUZUKI-MIYAURA CROSS-COUPLING, AND RING-OPENING REACTIONS OF INDAZOLES

Lucas Kapeniak, John F. Cullen, Jignesh J. Patel, Victor Snieckus
Queen's University, Department of Chemistry, Canada

The Directed ortho Metalation (DoM) reaction is a ubiquitous tool in the synthesis of polyfunctionalized aromatic and heteroaromatic molecules. Previously established metalation chemistry in the Snieckus group has stimulated our interest in applying the DoM reaction to the indazole motif. Using chemistry developed for related classes of heteroaromatic compounds, it was shown that indazole **1** bearing an N-1 Directed Metalation Group (DMG) undergoes C-7 deprotonation using an alkyllithium base. We wish to report a general synthetic methodology for the C-7 functionalization of indazoles through the use of this new reaction. Arylation of the C-7 iodinated indazole **2** establishes a new DoM – transition metal catalysed cross-coupling connection. We then coupled these methods with the traditionally undesirable ring-opening of N-1 functionalized indazoles **4** towards the synthesis of 6-substituted *N*-(2-cyanophenyl)ureas **5**, molecules difficult to access by conventional means.



REACTION OF OXIDIZED SPIRO-MEOTAD WITH PEROVSKITE SOLAR CELL COMPONENTS

E. Kasparavičius, I. Skendelytė, V. Getautis, T. Malinauskas
Faculty of Chemical Technology, Kaunas University of Technology, Kaunas, Lithuania

World energy consumption has been gradually increasing past 50 years and it grows every year. Alternative energy sources can supply the growing demand for energy and one of the most promising ones is photovoltaic systems [1]. Due to simple manufacturing and good performance prospects perovskite solar cells received growing interest from research community. As a result of rapid development in this field, perovskite photovoltaic systems have reached efficiency of 25.7%. Perovskite solar cell technology is rapidly approaching commercialization, but for this new technology there is lack of data on the stability of the devices and the reactivity of the perovskite with other components in the device. One of them charge-transporting materials has been developed for use in perovskite solar cells and vast majority of them require the use of chemical doping as an essential step for preparation of efficient devices. Oxidized 2,2´,7,7´-tetrakis(N,N-di-p-methoxyphenylamine)-9-9´-spirobifluorene (Spiro-MeOTAD) could be one of the potential weak links in the perovskite solar cell composition. Interestingly, very little investigation is done concerning stability of the oxidized materials applied in photovoltaics.[2]
In this work oxidized spiro-OMeTAD, has been investigated under various conditions in order to estimate influence of temperature, different additives and ion migration from perovskite surface on sensitivity of oxidized spiro-OMeTAD.

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SYNTHESIS OF N-(4-HYDROXYPHENYL)-ß-ALANINE DERIVATIVES AS PROMISING NEW CANDIDATES TARGETING MULTIDRUG-RESISTANT PATHOGENS

Povilas Kavaliauskas[1,2], Birutė Grybaitė[1], Vytautas Mickevičius[1]
[1]Kaunas University of Technology, Lithuania
[2]Weill Cornell Medicine of Cornell University United States

In view of the promising pharmacological potential of highly functionalized carbocyclic ß-amino acids bearing hydroxy, azido, amino or fluoro groups can be as building blocks in the synthesis of novel bioactive compounds [1].

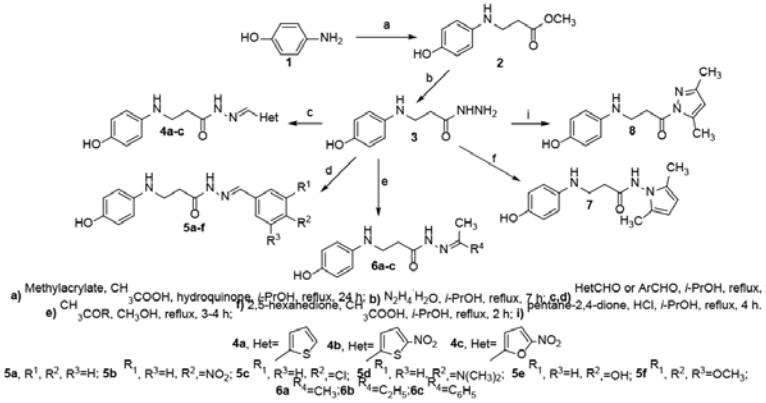

Fig. 1. *Synthesis of ß-alanine derivatives 2-8.*

Hydrazones **4a-c** and **5a-f** were prepared by the reaction of hydrazide **3** and heterocyclic or aromatic aldehydes in 2-propanol. The reaction with acetone, ethyl methyl ketone or acetophenone in the presence of a catalytic amount of acetic acid provided hydrazones **6a-c**. Condensation of hydrazide **3** with 2,5-hexanedione gave pyrrole compounds **7**. The reaction with 2,4-pentanedione in 2-propanol in the presence of a catalytic amount of hydrochloric acid provided pyrazole **8**. The compounds showed structure depended antimicrobial activity against Gram-negative and Gram-positive pathogens. Furthermore, compounds exhibited good in silico predicted ADMET properties, making them attractive candidates for further hit to lead optimization.

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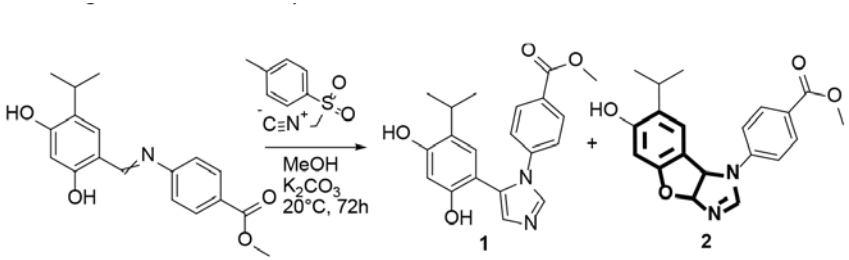
VAN LEUSEN REACTION APPLICATION AND INVESTIGATION IN THE SYNTHESIS OF POTENTIAL HSP90 INHIBITORS

Paulina Kaziukonytė[1], Vilius Petraška[1], Kamilė Venskūnaitė[1], Tomas Venslauskas[2], Algirdas Brukštus[1]
[1]Faculty of Chemistry and Geosciences, Vilnius University, Lithuania
[2]Faculty of Medicine, Vilnius University, Lithuania

Continuing our previous research on 5-aryl-4-(2,4-dihydroxyphenyl)-1,2,3-thiadiazoles as potential Hsp90 (Heat Shock Protein) inhibitors [1], we decided to assess the effect of binding affinity in compounds with an imidazole fragment. A series of 4-isopropyl-6-(1-substituted-1*H*-imidazol-5-yl)benzene-1,3-diols were synthesized.
In our pursuit to obtain imidazole 1, an unexpected compound 2 was isolated as a side product. Therefore, the formation of a 3a,8b-dihydro-1*H*-benzofuro[3,2-*d*]imidazole fragment in various reaction conditions was investigated and the impact of different substituents was evaluated.



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SYNTHESIS AND BIO-INVESTIGATION OF NOVEL BIPIRAZOLE DERIVATIVES

Vilija Kederienė[1], Julija Mickevičiūtė[1], Ieva Bartkevičiūtė[1], Paulius Ruzgys[2]
[1]Department of Organic Chemistry, Faculty of Chemical Technology, Kaunas University of Technology, Kaunas, Lithuania
[2]Faculty of Natural Sciences, Vytautas Magnus University, Kaunas, Lithuania

The progress of the pharmaceutical industry depends on new biologically active substances availability. Despite the widespread interest in pyrazole chemistry, many unresolved challenges remain, such as the synthesis and biotesting of polycyclic pyrazole derivatives. Based on this, the concept of current work was formulated: the development of novel bipyrazole derivatives synthetic procedures and their applicability in anticancer therapy.
Pyrazole and hydrazone derivatives possess broad spectra of biological characteristics ranging from antioxidant, anti-inflammatory, antiviral effects activity and other [1-2]. The bipyrazole system could not only improve the biological effects of compounds already possessing a pyrazole ring but also provide a new asset of pharmacologically desired properties [3].
In search of a condensation reaction for the bipyrazole system, various methods were tested. It was found, that sodium nitrite catalyzed cyclization of pyrazole-hydrazones proved to provide the highest yield of the target bipyrazole. The effect of synthesized bipyrazole derivatives on cell viability was investigated.

Acknowledgements: This research was funded by grant (BiPyCellDeath) from funds of Kaunas University of Technology and Vytautas Magnus University.

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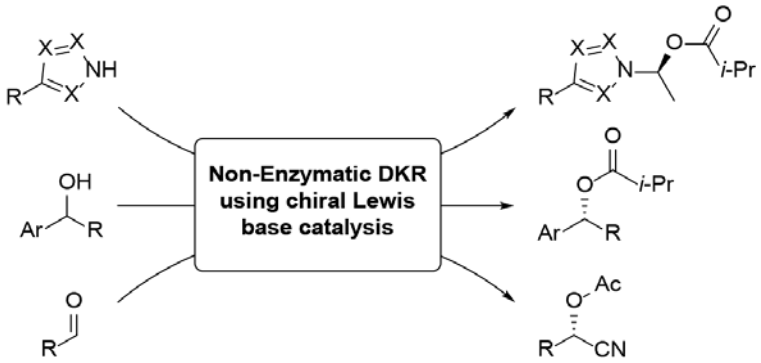
NON-ENZYMATIC DYNAMIC KINETIC RESOLUTION USING CHIRAL LEWIS BASE CATALYSIS

Artis Kinens[1,2]
[1]*Latvian Institute of Organic Synthesis, Riga, Latvia*
[2]*University of Latvia, Riga, Latvia*

The need for enantiomerically pure building blocks in medicinal and organic chemistry has stimulated the development of methods of asymmetrical synthesis. Among them, the dynamic kinetic resolution (DKR) is especially attractive since it allows for the direct conversion of a racemate into a single enantiomer.
Herein we report on the development of enantioselective DKR of azole hemiaminals[1], secondary alcohols[2] and cyanohydrins by chiral-Lewis base catalyzed enantioselective *O*-acylation. Racemization of the substrate was achieved either through transition metal catalysis or inherent disassociation-association equilibrium of the substrate.



Acknowledgements: Financial support from ERDF project No. 1.1.1.2/ VIAA/3/19/589 is acknowledged.

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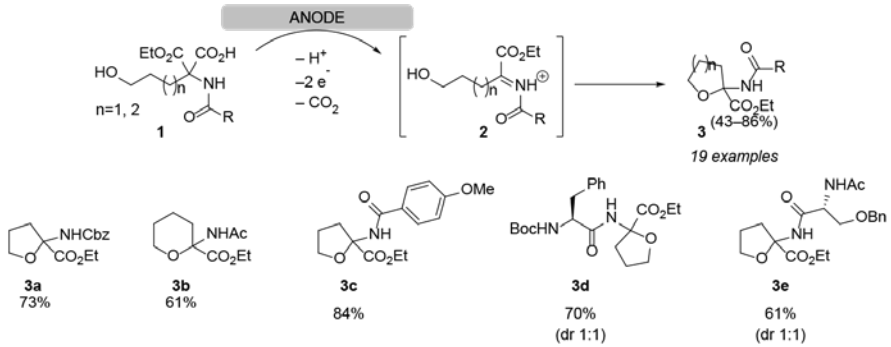
ELECTROCHEMICAL DECARBOXYLATION OF *N*-SUBSTITUTED 2-AMINOMALONIC ACID MONOESTERS IN INTRAMOLECULAR HOFER-MOEST REACTION

Olesja Koleda, Katrina Prane, Edgars Suna
Latvian Institute of Organic Synthesis, Riga, Latvia

Malonic acid is an inexpensive and readily available substrate that can be easily functionalized, e.g. by alkylation reactions. Highly functionalized substrates can be obtained even after decarboxylation of the malonate. Hence, malonic acid derivatives are well suited for electrochemical decarboxylation. Herein we report a previously unreported intramolecular Hofer-Moest reaction of *N*-substituted 2-aminomalonic acid monoesters (Scheme 1). A stabilized cation **2** is formed after anodic decarboxylation of a malonic acid monoester **1**. Subsequent cyclization affords quaternary carbon-containing tetrahydrofuranes and tetrahydropyranes in high yields.

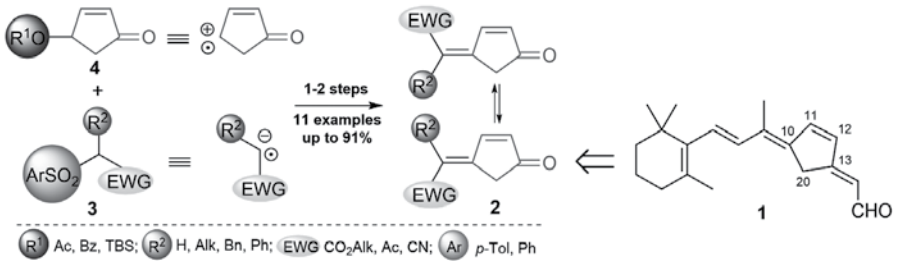


Scheme 1. *Intramolecular Hofer-Moest reaction of N-substituted 2-aminomalonic acid monoesters.*

OLEFINATION WITH α-CARBONYL AND α-CYANO ALKYL SULFONES: FACILE ACCESS TO ELECTRON-DEFICIENT ALKYLIDENE CYCLOPENT-2-EN-4-ONES

Edward E. Korshin, Lena Trifonov, Ayelet Rothstein, Arie Gruzman
Department of Chemistry, Bar-Ilan University, Ramat-Gan, Israel

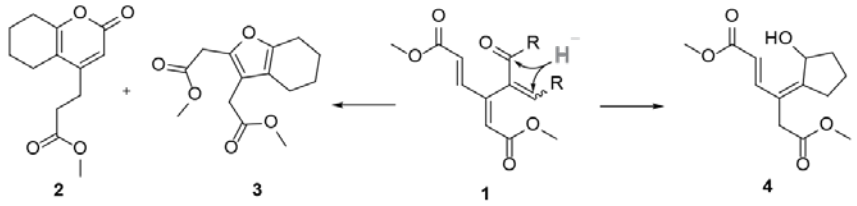
Toward more efficient access to 11-cis-locked 5-membered retinal **1** as pharmaceutically relevant substitute of natural 11-*cis*-retinal, we elaborated a straightforward synthesis of scarcely explored, terminally disubstituted electron-poor alkylidene cyclopent-2-en-4-ones **2** through uncommon olefination with secondary α-carbonyl and α-cyano alkylsulfones **3**. Base-promoted couplings of activated secondary sulfones 3 with 4-acyloxy- or -*tert*-butyldimethylsilyloxy-cyclopent-2-en-1-ones **4** gave alkylidene cyclopent-2-en-4-ones 2 (up to 91%). The base-promoted reactions lead initially to C-allylation of **3** with formation of diastereomeric γ,δ-unsaturated ε-ketosulfones, which can often be isolated. Subsequent vinylogous dehydrosulfinylation resulted in alkylidene cyclopentenones **2**. Depending on the nature of substituents the overall processes could proceed sequentially or tandemly. In this olefination, 4-RO-substituted cyclopentenones **4** serve as cyclopent-2-en-4-one cation-radical synthons, whereas the activated secondary sulfones **3** play a role of alkylidene anion-radicals surrogates. The scope and limitations, a plausible mechanism as well as some extensions of the elaborated olefination to acyclic systems will be briefly discussed.



REDUCTION OF ELECTRON-DEFICIENT [3] DENDRALENES BY HYDRIDE REAGENTS

Ondřej Kratochvíl, Rastislav Antal, Stefanie M. Perdomo, Milan Pour
Department of Organic and Bioorganic Chemistry, Faculty of Pharmacy in Hradec Králové, Charles University, Hradec Králové

The synthesis of electron-deficient [3]dendralenes[1] containing electron withdrawing groups, such as carbonyl and ester functionalities, is based on the palladium-catalyzed Migita-Stille coupling between stannylated diene and iodinated alkene (cycloalkene).
Subsequent reaction of substituted [3]dendralenes **1** with sodium borohydride led to 1,2- or 1,4-addition of hydride anion to the α,ß-unsaturated ketone, resulting in the formation of the corresponding enolate or alcoholate, which were further transformed to various products **(2–4)** depending on the substitution of the starting [3] dendralene (Scheme 1).



Scheme 1. *General scheme of [3] dendralenes reductions.*

Acknowledgements: This work was supported by Charles University (SVV 260547, GAUK 362421) and Czech Science Foundation (Project No. 18-17868S).

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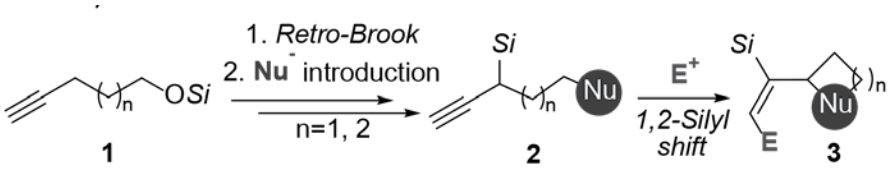
HETEROCYCLIZATION OF TERMINALLY FUNCTIONALIZED PROPARGYL SILANES VIA 1,2-SILYL SHIFT

Rasma Kroņkalne, Artem Ubaidullaev, Rūdolfs Beļaunieks, Māris Turks
Institute of Technology of Organic Chemistry, Faculty of Materials Science and Applied Chemistry, Riga Technical University, Latvia

Electrophilic activation of propargyl silanes has been known to induce the 1,2-silyl shift, generating allylic carbenium ions, stabilized by the ß-silicon effect. In the absence of reactive nucleophiles silyl dienes as reaction products are obtained. Intramolecular Friedel–Crafts reactions in aryl-substituted propargylic systems, when activated by Brønsted acids, give access to silyl indenes.[1,2]
In this work we investigate the 1,2-silyl shift in propargyl silanes containing intramolecular O-, N- or S-nucleophile **2** and subsequent cyclization as a novel synthesis pathway towards 2-(1-trialkylsilyl) vinyl-substituted heterocycles **3**.



Acknowledgements: R. Kroņkalne thanks Riga Technical University Master's student research grant ZM-2021/19 for funding.

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C-H AMINATION OF PENTACYLIC TRITERPENOIDS

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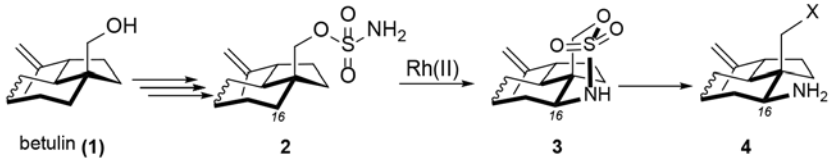
Betulin, erythrodiol and uvaol are pentacyclic triterpenoid natural products that are observed as secondary metabolites in many plants. These triterpenoids and their semi-synthetic analogs exhibit several important pharmacological properties such as antitumor, anti-inflammatory, antiparasitic, and anti-viral activities [1]. The aim of this work is to develop syntetical approach towards unexplored introduction of amino functionality at triterpenoid C(16).



For this purpose, precursors **2** bearing sulfamate ester moiety were obtained, and converted to oxathiazinanes **3** via Du Bois γ-C-H bond amination [2]. Key intermediates **3** are further converted into variously functionalized compounds **4** through the ring opening reactions.

Acknowledgements: This work has been supported by the European Social Fund within the project «Support for the implementation of doctoral studies at Riga Technical University».

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MECHANOCHEMICAL C–N BOND FORMING REACTIONS IN THE SYNTHESIS OF ACTIVE PHARMACEUTICAL INGREDIENTS

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Mechanochemical organic synthesis has emerged as a green and operationally simple technique which allows to perform organic reactions without a bulk solvent. This offers several advantages over the conventional solution chemistry, such as fast reaction rates, superior safety profile and low amount of waste.[1] C–N bond forming reactions prevail in the synthesis of active pharmaceutical ingredients (APIs).[2] Here we present application of mechanochemical amide[3] and amine[4] forming reactions developed in our group for preparation of APIs. Thus, essentially solvent-free synthesis of anticancer drug Imatinib was implemented from carboxylic acid **1** by using two consecutive and chemoselective C–N bond forming reactions (Fig. 1).

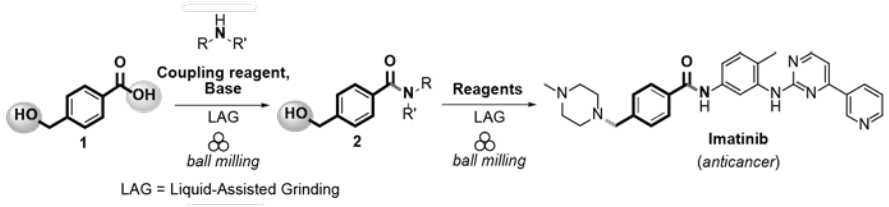

Figure 1. *Mechanochemical synthesis of Imatinib.*

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SELAGIBENZOPHENONES A-C AND UNNATURAL DERIVATIVES: SYNTHESIS, STRUCTURE REVISION AND BIOLOGICAL EVALUATION

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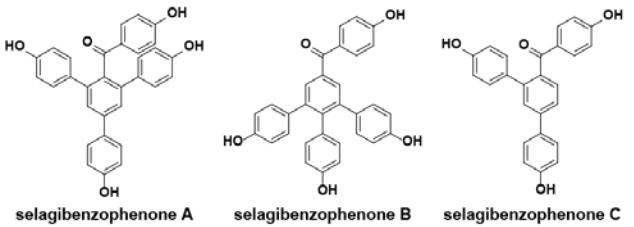
Selaginella genus has been a source for structurally diverse natural products with various biological activities. Selagibenzophenones A, B and C were isolated recently.[1] We accomplished first total synthesis of these compounds, which allowed us to correct the misassigned structures.[2] In addition, we were able to identify unnatural derivatives with a promising anticancer activity.



Acknowledgements: Research was funded by Charles University program PRIMUS/20/SCI/017.

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LATE-STAGE OLEFINATION IN PBD NATURAL PRODUCT TOTAL SYNTHESES

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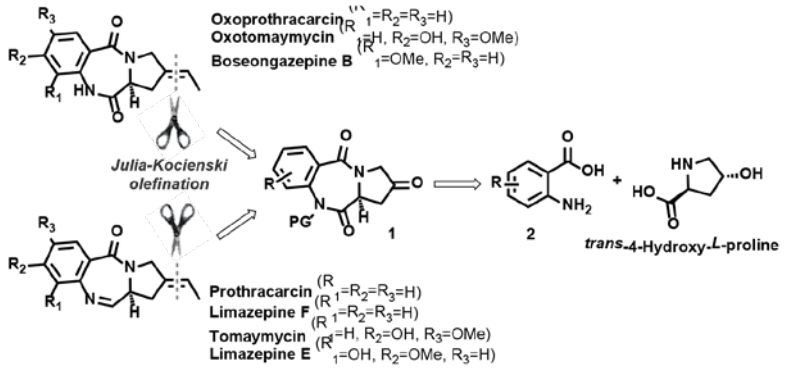
Latvian Institute of Organic Synthesis, Riga, Latvia

Pyrrolo[1,4]benzodiazepines (PBD) are a broad family of natural products possessing considerable anticancer activity owing to their ability to covalently bind to minor grove 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] Although several total syntheses of these natural products have been published, a stereoselective introduction of the alkylidene substituent still possesses a considerable challenge. Within our preliminary studies,[3] we have shown that a late-stage olefination is a convenient approach to synthesize these natural products.

Herein we report our studies on the Julia – Kocienski olefination of PBD triones **1**, including the development of novel reagents, optimization of reaction conditions, and determining the olefination stereochemistry determining factors. The necessary triones **1** can be easily accessed starting from readily available *trans*-4-hydroxy-L-proline and the corresponding anthranilic acids **2**.



Scheme 1. *Retrosynthetic analysis of PBD natural products.*

Acknowledgements: We acknowledge the ERDF (PostDoc Latvia) project No.1.1.1.2/VIAA/4/20/751.

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AZIDOAZOMETHINE-TETRAZOLE TAUTOMERISM IN PYRIDOPYRIMIDINES

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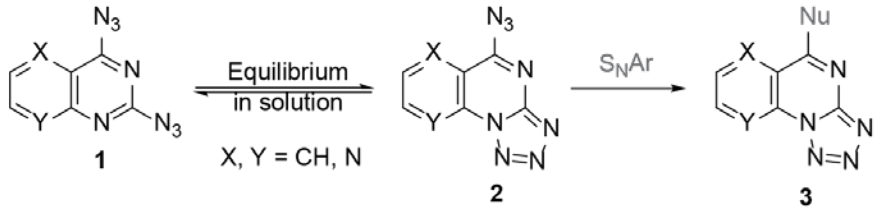
[2]Latvian Institute of Organic Synthesis, Riga, Latvia

Heterocycles with azido-azomethine structural entity undergo dynamic azide tetrazole equilibrium in solution phase. The equilibrium can be shifted towards one or other tautomer by altering ambient conditions such as solvent polarity and temperature. Thus, azide tetrazole ring-chain tautomerism is known to influence S_NAr reactivity and regioselectivity.

We have synthesized a new class of tetrazolopyridopyrimidines **3** and characterized azidoazomethine-tetrazole tautomerism thereof. FT-IR and X ray analysis of **3** reveals tetrazole to be the major tautomeric form present in the solid state. Thermodynamic heats of tautomerization in solutions were calculated using variable temperature NMR and DFT.



Acknowledgements: The authors thank the Latvian Council of Science Grant LZP 2020/1 0348 for financial support. K.L. thanks the European Social fund within project Nr. 8.2.2.0/20/I/008.

PHOTOCHEMICAL NICKEL-CATALYZED CROSS-COUPLING OF ALKYLTITANIUM ALKOXIDES WITH ARYL AND ALKENYL HALIDES

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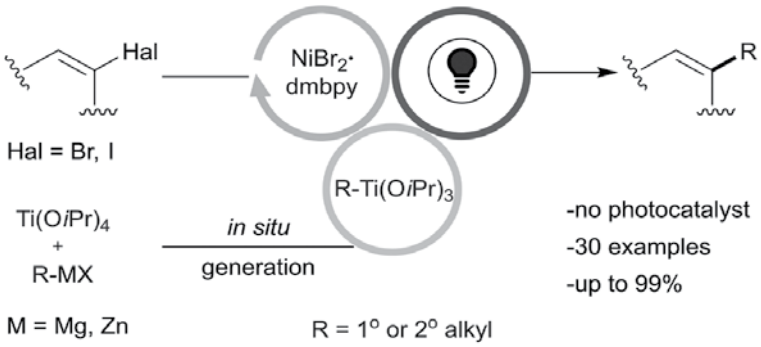
Metallaphotocatalytic transformations have recently emerged as a novel tool for the C-C and C-heteroatom bond construction. [1] Here, we report that alkyltitanium reagents, generated in situ from Grignard reagents or alkylzinc halides and titanium (IV) isopropoxide, undergo a visible-light-promoted photocatalyst-free nickel-catalyzed cross-coupling with organic halides[2]. The reaction tolerates a variety of functional groups and hindered substituents in (het)aryl bromides/iodides and alkenyl bromides. Our mechanistic studies proved, that the reaction proceeds through photoactivation of organotitanium species and its further decomposition leading to formation of alkyl radicals.



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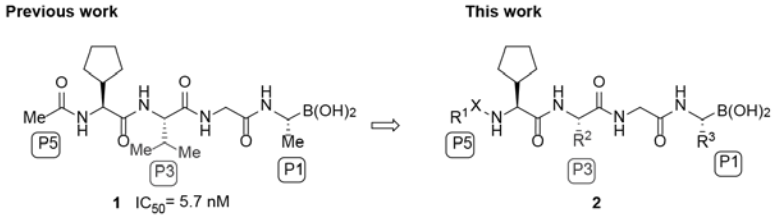
NEW PEPTIDIC BORONIC ACID CONTAINING INHIBITORS OF MALARIAL SUBTILISIN-LIKE SERINE PROTEASE (SUB1)

Elina Lidumniece[1], Chrislaine Withers-Martinez[2], Michael J. Blackman[2], Aigars Jirgensons[1]
[1]Latvian Institute of Organic Synthesis, Riga, Latvia
[2]Malaria Biochemistry Laboratory, The Francis Crick Institute, London United Kingdom

Malarial subtilisin-like serine protease (SUB1) is a multifunctional processing protease with a significant role in egress of merozoites by activation of a cascade of proteolytic events, leading to rupture of human red blood cell (RBC)[1]. Therefore, an inhibition of this enzyme can prevent from parasite replication and disease progression. Our previous research led to boronic acid based inhibitor **1** with nanomolar PfSUB1 inhibitory potency and remarkable inhibition of parasite egress in RBC assay[2] (scheme 1).



Scheme 1. *Development of peptidic boronic acid containing inhibitors*

Herein we present SAR studies of boronic acid based inhibitors **2** depending on the amino acid side chains at P1 and P3 positions, as well as *N*-capping groups (P5 position). These compounds were synthesised and evaluated for their PfSUB1 inhibitory activity compared to the parent inhibitor **1** (scheme 1).

Acknowledgements: This work is funded by FLPP lzp-2020/1-0327.

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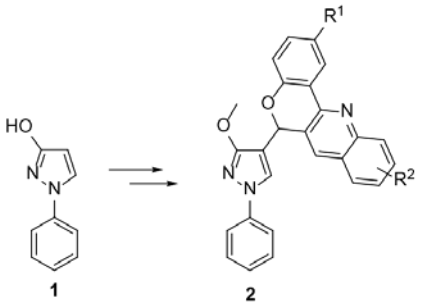
SYNTHESIS OF 6-(3-METHOXY-1-PHENYL-1*H*-PYRAZOL-4-YL)-6*H*-CHROMENO[4,3-*b*] QUINOLINE DERIVATIVES

Agnė Lisauskaitė, Eglė Arbačiauskienė
Kaunas University of Technology, Lithuania

Derivatives containing pyrazole, chromene or quinoline fragments exhibit significant biological activities and are widely used in medicinal chemistry. All three heterocycles belong to the group of privileged structures for drug development.
In continuation of our interest on developing synthesis of novel polycyclic pyrazole-containing compounds, herein we present an access to yet unknown 6-(3-methoxy-1-phenyl-1*H*-pyrazol-4-yl)-6*H*-chromeno[4,3-*b*]quinolone derivatives (**2**) (**Scheme 1**) starting from easily accessible 1-phenyl-1*H*-pyrazol-3-ol **1**.



Scheme 1. *Synthesis of 6-(3-methoxy-1-phenyl-1H-pyrazol-4-yl)-6H-chromeno[4,3-b]quinoline derivatives*

The structures of products were confirmed by data of nuclear magnetic resonance spectroscopy, infrared spectroscopy, and mass spectrometry.

Acknowledgements: This work was funded by the European Social Fund under the “Development of scientific competence of researchers, other researchers, students through practical scientific activities” under measure (09.3.3-LMT-K-712-25-0020).

SYNTHESIS OF ENANTIOPURE PIPERIDINES VIA IRELAND-CLAISEN REARRANGEMENT

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Piperidine ring is a common structural motif in a vast number of biologically important natural products and pharmaceuticals.[1] Despite considerable progress towards the development of synthetic methods providing access to piperidine fragments, the development of a convenient and stereoselective method for straight-forward preparation of piperidines remains highly desired.
Herein we report our preliminary results on the development of a chiral version of the Ireland – Claisen rearrangement of 10-membered lactones for the stereoselective synthesis of enantiopure piperidine motifs. The synthesis of starting materials as well as the rearrangement transition states will be discussed.

Acknowledgements: The authors acknowledge the individual fellowship project of the Latvian Council of Science Nr. lzp-2020/2-0045 for the financial support.

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ALKYLATION OF PHENOLS AND RESORCINOLS

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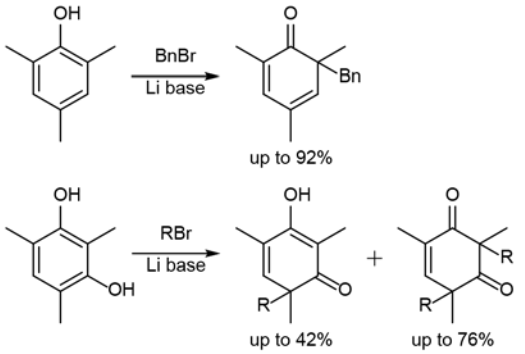
Phenol and resorcinol core structure appears in various natural compounds, such as flavonoids, chalcones, etc. Various biological activities including antioxidant and anti-inflammatory activities have been found for these structures.[1] Easily available phenols and resorcinols are good starting materials for the synthesis of abovementioned complex molecules and natural products.



In this study, differently substituted phenols and resorcinols were used for direct alkylation with electrophiles in order to get selectively the addition products.[2] The addition result depends considerably on the used conditions.

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PALLADIUM-CATALYZED C-H ACTIVATION OF TRITERPENOIDS

Jevgeņija Lugiņina[1], Vladislavs Kroškins[1], Anatoly Mishnev[2] and Māris Turks[1]
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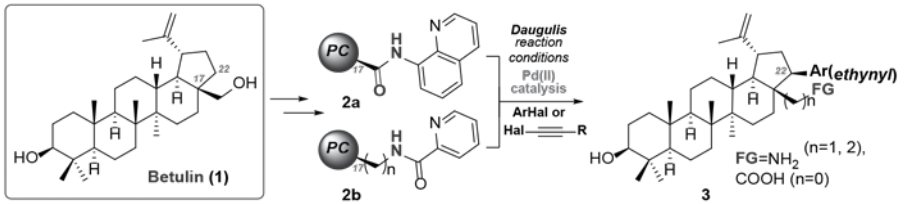
[2]Latvian Institute of Organic Synthesis, Riga, Latvia

Triterpenoids are numerous and structurally diverse natural products that are widely distributed in plants and possess a wide range of biological functions. The interest in these natural compounds and their semisynthetic analogues is reflected in more than 6000 articles in the last decade [1]. Here, we present a method for the preparation of C(22)-modified triterpenoids using Pd-catalyzed C-H activation reactions. Different pentacyclic cores (PC) such as betulin (illustrated below), ursolic and oleanolic acids were transformed into corresponding 8-aminoquinoline and picolinic acid derived amides, 2a and 2b, respectively. Our investigation revealed that using Pd(II)/Cu(II) catalytic system amides successfully combine with various aryl halogenides and haloalkynes under the Daugulis C-H activation conditions [2]. To date, this is an exclusive example of C-C bond formation at position C(22) of triterpenoids.



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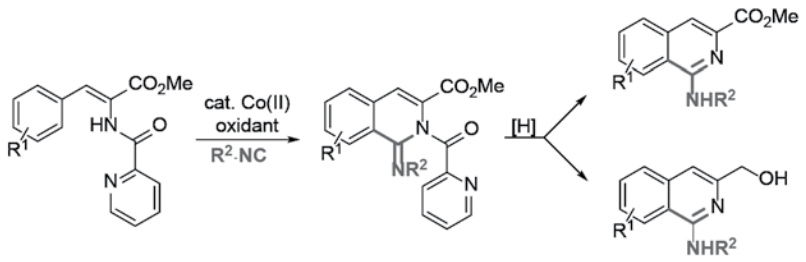
SYNTHESIS OF 1-AMINOISOQUINOLINES VIA COBALT-CATALYZED, PICOLINAMIDE-DIRECTED C(SP²)-H FUNCTIONALIZATION OF PHENYLALANINE DERIVATIVES

Lukass Lukasevics, Aleksandrs Cizikovs, Liene Grigorjeva
Latvian Institute of Organic Synthesis

1-Aminoisoquinolines are important class of compounds due to their potential applications in medicinal chemistry.[1] Accordingly, the development of methodologies for the synthesis of such moiety is of great interest among organic chemists. More recently, a direct C-H functionalization has proven to be very effective approach to obtain 1-aminoisoquinolines in a very step-economical fashion.[1] Herein we report the first example of cobalt-catalyzed, picolinamide-directed C-H imination protocol of phenylalanine derivatives using $Co(dpm)_2$ as a catalyst. The obtained imine products can easily be transformed 1-aminoisoquinoline derivatives under reductive conditions, providing an attractive alternative to already existing methodology.



Acknowledgements: This research is funded by the Latvian Council of Science, project No. lzp-2019/1-0220

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SYNTHESIS OF 2-HETEROARYL-1,3,4-OXADIAZOLES AND THEIR PROTECTIVE ACTIVITY AGAINST OXIDATIVE STRESS

Vida Malinauskienė[1], Jiří Voller[2], Selvina Bezaraitė[1], Vytenis Markevičius[1], Emilija Jonušaitė[1], Gintarė Garlaitė[1], Meda Veličkienė[1], Monika Iškauskienė[1], Alena Kadlecova[2], Asta Žukauskaitė[2], Algirdas Šačkus[1]
[1]Kaunas University of Technology, Lithuania
[2]Palacký University, Czech Republic

Oxidative stress is a hallmark of age-related or hereditary diseases, including cancer, diabetes, neurodegenerative disorders, etc. Compounds that can reduce the oxidative stress are promising as potentially pharmaceutically active ingredients. Several 1,3,4-oxadiazole derivatives are known as antioxidants. Combining 1,3,4-oxadiazole motif with low molecular mass *N*-heterocycles into one molecule is expected to result in compounds with enhanced biological properties.

In this work we present a fast and effective synthetic route towards a collection of new sulfur bridge-containing 2-heteroaryl-1,3,4-oxadiazole hybrids starting from various heterocyclic carboxylates as well as an assessment of their protective activity against chemically induced oxidative stress in a model nematode *Caenorhabditis elegans* and in fibroblasts derived from patients suffering from Friedreich's ataxia.

Acknowledgements: This work was supported by the Ministry of Education, Youth, and Sports of the Czech Republic (program INTER-COST, grant numbers LTC18078 and LTC19030), by the European Regional Development Fund (Project ENOCH, No. CZ.02.1.01/0.0/0.0/16_019/0000868) and by the European Social Fund (Development of Competences of Scientists, other Researchers and Students through Practical research Activities No 09.3.3-LMT-K-712-25-0043 and No 09.3.3-LMT-K-712-22-0115). The strains used in this study were provided by the Caenorhabditis Genetics Center (CGC).

ELECTROCHEMICAL SYNTHESIS: HYDROCARBOXYLATION OF UNSATURATED COMPOUNDS

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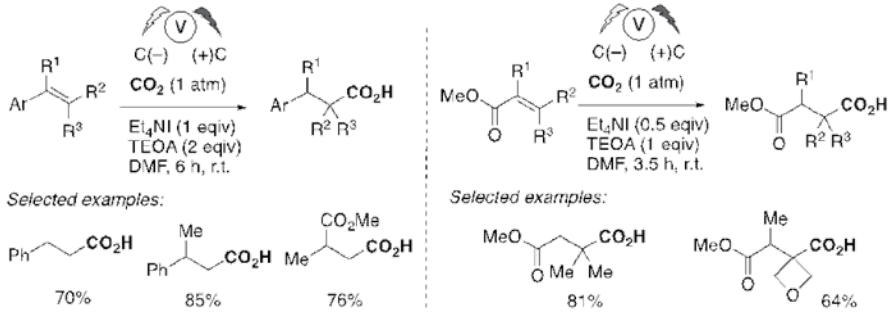
Department of Chemistry, School of Science, Loughborough University, Loughborough, Leicestershire

Electrosynthesis has been widely studied within the electrochemical community, but represents an underused tool, with great potential for synthesis.[1] Currently, there are currently only a few processes at the industrial or pilot-plant scale for the electrosynthesis of organic molecules. Herein we report a new electrosynthetic approach to the selective hydrocarboxylation of alkenes,[2] dienes,[3] and esters.[4] The method allows direct access to carboxylic acids derived from terminal, *di*- and *tri*-substituted alkenes, as well as conjugated dienes and unsaturated esters, in a highly regioselective manner. A plausible reaction mechanism will be discussed.



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ORGANIC SEMICONDUCTORS WITH REACTIVE FUNCTIONAL GROUPS FOR APPLICATION IN OPTOELECTRONICS

Mantas Marcinskas, Elzbieta Pocobut, Tadas Malinauskas
Kaunas University of Technology, Faculty of Chemical Technology, Lithuania

Organic semiconductors are integral to modern technologies and are commonly used in various devices, such as sensors, electronics, or photovoltaics. Usually, organic semiconductors benefit from synthesis versatility or solution-processing methods and can be successfully applied in thin-film optoelectronics. So far, a big number of different hole or electron transporting materials were introduced for application in organic solar cells, perovskite solar cells and other photovoltaics. Every photovoltaic system needs suitable charge transporting semiconductors and search for the optimal ones often leads to the performance increase as well as improvement of the other photovoltaic characteristics.

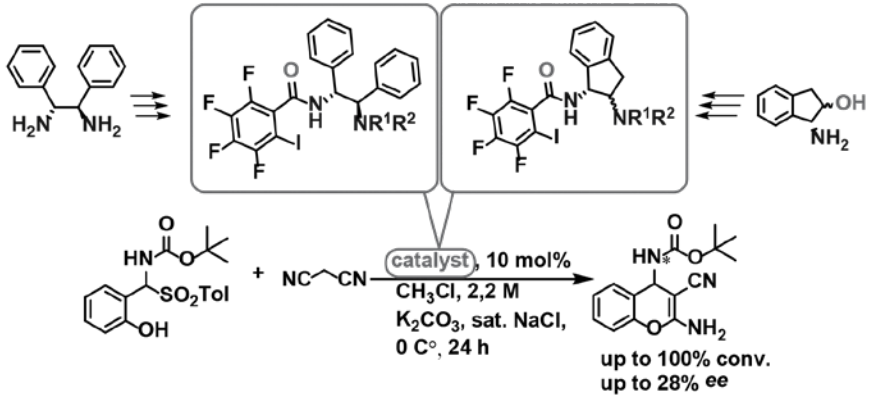
Promising strategy for further photovoltaics development is modification of organic semiconductors by incorporating specific reactive functional groups, which can provide additional benefits or properties. Few groups can be highlighted, such as „anchoring" groups, which can be used for surface modification, modifying surface energetics and/or hydrophobicity. Another important class of reactive functional groups is vinylenes or alkynes, which can be used for material cross-linking.

In this research several materials with different reactive functional groups were synthesized and studied. Materials containing phosphonic acid „anchoring" groups for surface modification, as well as materials containing reactive alkyne groups for light initiated cross-linking have been investigated.

SYNTHESIS OF CHIRAL BIFUNCTIONAL HALOGEN BOND DONOR CATALYSTS AND THEIR APPLICATION IN ASYMMETRIC CASCADE REACTION

Harry Martõnov, Kadri Kriis, Tõnis Kanger
Tallinn University of Technology, Estonia

Several enantiomerically pure bifunctional halogen bond donor catalysts consisting of either diphenylethylenediamine or indane-1,2-diamine and tetrafluoro-iodophenyl carboxamide moieties were synthesised. The catalysts were evaluated in the asymmetric synthesis of *tert*-butyl (2-amino-3-cyano-4*H*-chromene-4-yl) carbamate. The best enantiomeric excess (28%) was achieved using a *cis*-indane-1,2-diamine halogen bond donor catalyst. The hydrogen analogue of the *cis*-indane-1,2-diamine halogen bond donor gave very poor enantiomeric excess (6%), demonstrating the importance of the catalyst's halogen bond donor ability in determining the enantioselectivity.



SYNTHESIS AND CRYSTALLOGRAPHIC STUDIES OF HALOGEN-BONDED COMPLEXES

Jevgenija Martõnova[1], Jas S. Ward[2], Riina Aav[1], Kari Rissanen[2]
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[2]Department of Chemistry, University of Jyvaskyla, Jyväskylä, Finland

Halogen bonding has gained attention as it complements hydrogen bonding, and benefits from advantages such as highly linear interactions. In particular, it has been used for the development of various functional materials, as well as coordination polymers.[1] Neutral halogen-bonded systems have been widely investigated as they are easy to synthesize from suitable pairings of halogen bond donors and acceptors.[2] However, instances of halogen atoms, X (X = I, Br, Cl), being fully ionised to a formally cationic state and stabilised by a pair of suitable Lewis bases, are less explored.[3]
In this study, halogen-bonded iodine(I) complexes were straightforwardly synthesised from a number of silver(I) carboxylate salts upon reaction with pyridine-based compounds and elemental iodine (**Figure 1**). Single crystal XRD studies of the halogen-bonded iodine(I) compounds provided insight into the nature of the O–I–N bonds via study of their respective bond lengths and angles.

Figure 1. *The general synthetic procedure for the synthesis of the halogen-bonded compounds.*

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NOVEL SYNTHESIS OF TETRAZINE BEARING ADOMET ANALOGUES FOR BIOORTHAGONAL LABELING

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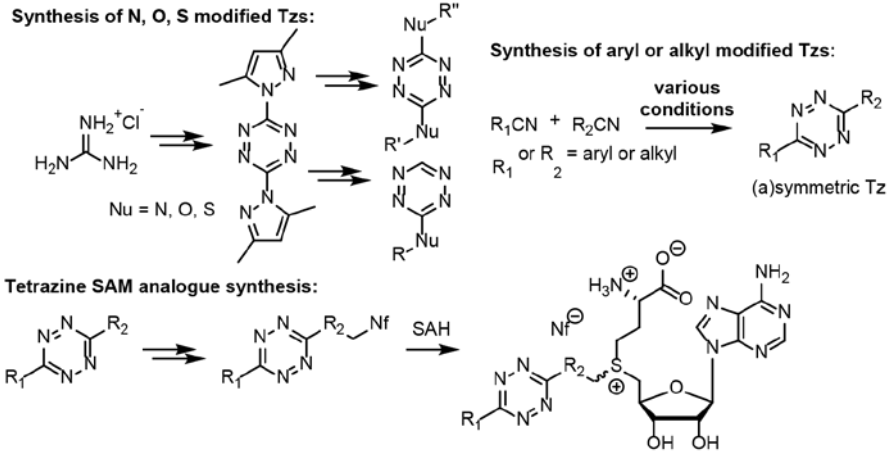
Vilnius University, Institute of Chemistry, Department of Organic Chemistry, Lithuania

The emerging inverse electron demand Diels-Alder (IEDDA) reaction is gaining widespread application in bioorthagonal chemistry owing to its unparalleled kinetics, excellent orthogonality, and biocompatibility[1]. With recent developments in novel dienophiles and optimal tetrazine coupling partners the attention has now been shifted to *in vivo* applications. Currently employed bioorthagonal reactions in DNA labelling are either slow or toxic to the living cell, therefore the transfer of tetrazine moieties onto various biomolecular targets mediated by methyltransferases is an outstanding new possibility to advance the field of research.
Herein we report the different syntheses approaches to tetrazines and SAM tetrazine analogues.



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A RAPID CONSTRUCTION OF TETRAHYDROPYRIDINES AND THEIR FUSED DERIVATIVES VIA NUCLEOPHILE-ASSISTED GOLD(I) CYCLIZATIONS

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[2]Freie Universität Berlin, Germany
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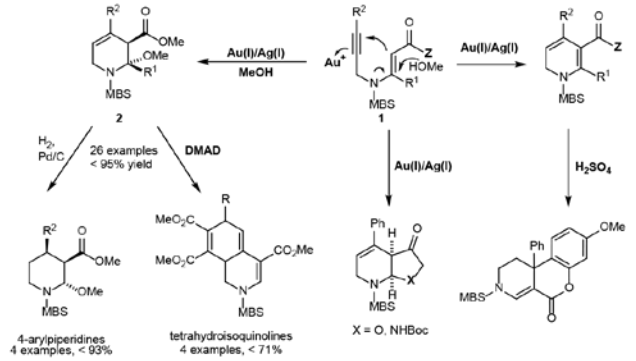
Easily available enynes can serve as precursor for the synthesis of several types of biologically important nitrogen heterocycles. Thus, cyclization of 3 aza-1,5-enynes **1**, carried out in the presence of methanol, afforded tetrahydropyridines **2** in high isolated yields. An intramolecular version, using substrates with OH, NHBoc and 3-$MeOC_6H_4$ pendant groups as internal O-, N-, and C-nucleophiles, yielded the corresponding orthofused cyclic derivatives. Synthetic utilization of tetrahydropyridines **2** has been demonstrated by their conversion into substances with privileged pharmacophore scaffold.[1]



Scheme 1.

Acknowledgements: This work was supported by Charles University (SVV 260547), Czech Science Foundation (Project No. 22-17868S) and EFSA-CDN project (reg. No. CZ.02.1.01/0.0/0.0/16_019/0000841)

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SYNTHESIS AND CHARACTERISATION OF ANALOGUES OF PIPECOLIC, NIPECOTIC AND ISONIPECOTIC ACIDS

Gita Matulevičiūtė[1,2], Eglė Arbačiauskienė[2], Neringa Kleizienė[1], Vilija Kederienė[2], Greta Račkauskienė[1], Miglė Dagilienė[1], Aurimas Bieliauskas[1], Vaida Milišiūnaitė[1], Frank A. Sløk[3], Algirdas Šačkus[1,2]
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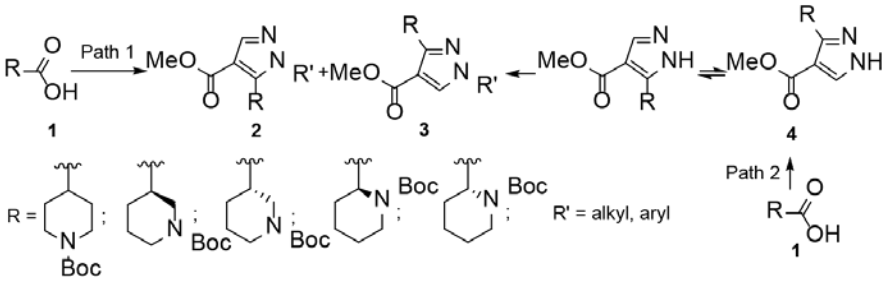
[2]Department of Organic Chemistry, Kaunas University of Technology, Kaunas Lithuania;
[3]Vipergen ApS, Copenhagen, Denmark

Heterocyclic amino acids are extensively applied as molecular scaffolds in medicinal chemistry. The efficient protocol for the regio-controlled synthesis of novel 3- or 5-(*N*-Boc-piperidinyl)-1*H*-pyrazole-4-carboxylate derivatives from *N*-Boc protected pipecolic, nipecotic and isonipecotic acids (**1**) was developed (Scheme 1). By following path 1, methyl 5-(*N*-Boc-piperidinyl)-1*H*-pyrazole-4-carboxylates (**2**) were obtained as the main products from *N*-Boc protected piperidine carboxylic acids **1** and various substituted hydrazines. However, by following path 2, *N*-Boc protected piperidine carboxylic acids **1** were first treated with hydrazine hydrate and obtained tautomeric pyrazole **4** was further *N*-alkylated with various alkylhalides to give 3-(*N*-Boc-piperidinyl)-1*H*-pyrazole-4-carboxylates (3) as major products. Regioisomeric ratio was determined by NMR analysis.

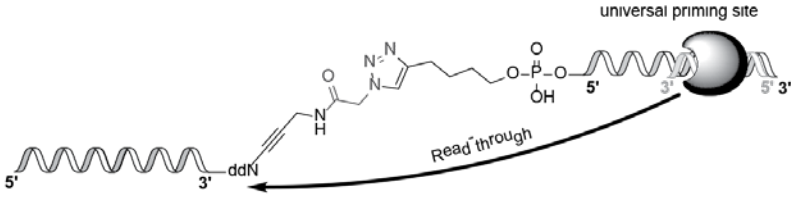


Scheme 1. *Synthesis of 3(5)-(N-Boc-piperidinyl)-1H-pyrazole-4-carboxylate derivatives*

ADVANCED PREPARATION OF FRAGMENT LIBRARIES ENABLED BY OLIGONUCLEOTIDE-MODIFIED 2',3'-DIDEOXYNUCLEOTIDES

Justina Medžiūnė[1,2], Žana Kapustina[1], Simona Žeimytė[1], Jevgenija Jakubovska[1], Rūta Sindikevičienė[1], Inga Čikotienė[1], Arvydas Lubys[1]
[1]Thermo Fisher Scientific Baltics UAB, Department of Research and Development, Lithuania
[2]Vilnius University, Faculty of Chemistry and Geosciences, Lithuania

The ever-growing demand for inexpensive, rapid, and accurate exploration of genome revealed the mandatory refinement of existing sequencing techniques. Development of next generation sequencing (NGS) induced the revolutionary alteration in genome analysis across the global scientific communities. Modified nucleotides are inherent tools in sequencing and imaging. Development of properly designed modified (d)dNTP subunits enables the expansion of even more diverse applications. Herein we sought to synthesize the uniquely designed oligonucleotide-tethered 2',3'-dideoxynucleotide (dd^{ON}NTP) terminators bearing universal priming sites attached to the nucleobase, followed by their enzymatic evaluation by means of incorporation during primer extension reaction (PEX) and read-through assays. Furthermore, tested representatives of polymerase families A, B, X and RT displayed incorporation and read-through ability via PEX.



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SYNTHESIS OF FLUOROCYCLOPROPYLIDENES VIA JULIA-KOCIENSKI OLEFINATION

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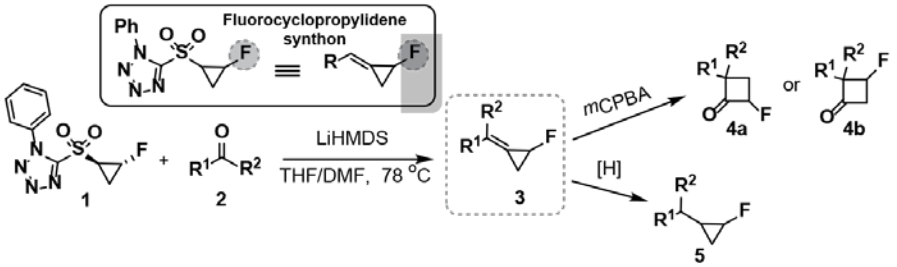
Latvian Institute of Organic Synthesis, Latvia

The fluorocyclopropyl group presented in the drug molecule plays on important role as a bioisostere which possesses the ability to increase its activity and bioavailability.[1] There is proof that the presence of a fluorocyclopropyl group in a known drug molecule indeed enhances its activity parameters in comparison to the original drug.[2]
Herein we demonstrate synthesis and application of less studied[3] compounds – monofluorocyclopropylidenes (Scheme 1) – which gives opportunity to introduce fluorocyclopropyl moiety into carbonyl group containing substrates – aldehydes, ketones – potential drug molecules.



Scheme 1. *Synthesis and application of CPD*

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QUANTUM CHEMICAL CALCULATION PROCEDURE FOR THE C-C BOND FORMING REACTIONS

Andrus Metsala, Mikk Kaasik, Kadri Kriis, Tõnis Kanger, Mariliis Kimm
Taltech

In theoretical organic chemistry 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).
Quantum chemical modelling of the C-C bond forming reaction mechanism was performed. This was done with the help M062x density functional theory with Def2SVP and Def2TZVP basis sets.
The main focus is shed to the development of the forming C-C bond, (characteristic to the very many reaction mechanisms), and performing conformational analysis on each RP point. From these sets the minimum energy (<25 kcal/mol) structures were selected., and several RP's were constructed. It appears that some of these (RP) are reactive, but some other ones are not. Some appropriate selection rules were determined.

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SALTS OF ARYLMETHYL MELDRUM`S ACIDS AS PROMISING ANTIOXIDANT PLATFORMS

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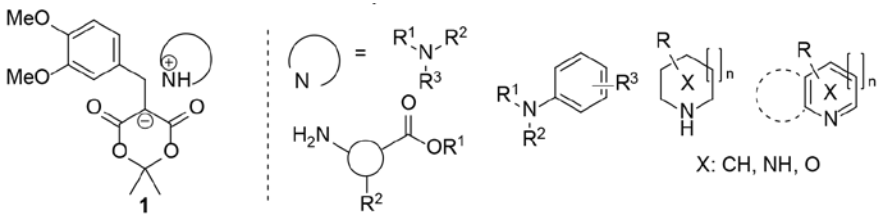
Faculty of Materials Science and Applied Chemistry
Riga Technical University, Latvia

Due to the presence of 1,3-dicarbonyl moiety arylmethyl Meldrum`s acids are excellent antiradical and antioxidant agents [1]. The free radical scavenging activity of them were increased when alkylamino moiety was introduced in the structure [1a]. Such moiety facilitated deprotonation of the α-position in the 1,3-dioxane-4,6-dione, besides such compounds exist as zwitterions in crystalline state [2]. On the other hand, Amorati et al. has demonstrated that *aza*-analogues of phenol-type antioxidants lead to effective co-antioxidant systems [3]. Inspired on these findings, herein our first attempts to develop carrier-enhanced antioxidant systems **1** are presented. The effect of the counter cation on the antiradical activity and structure both in solution and crystalline state is discussed.



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APPLICATION OF CHIRAL BIFUNCTIONAL HALOGEN BOND CATALYSTS IN GLYCOSYLATION REACTIONS

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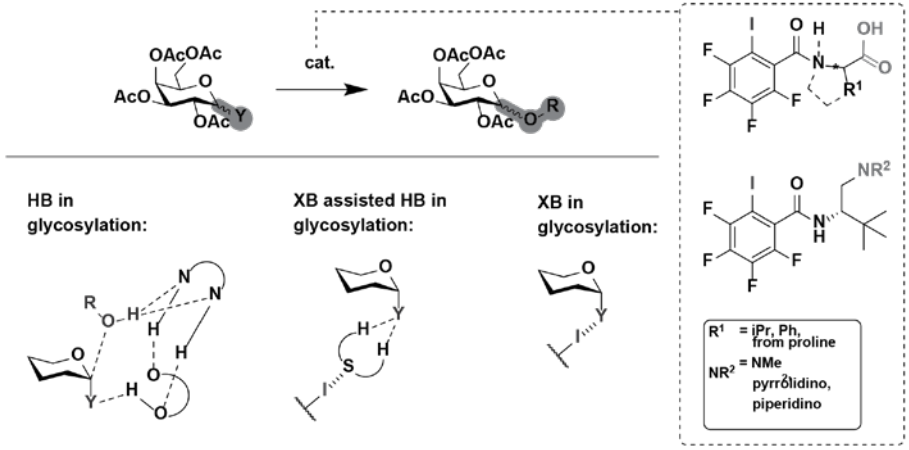
Tallinn University of Technology

Glycosylation reactions have a 140-year history with many of the original procedures for saccharide synthesis still in use today.[1] Although acid catalysis, hydrogen bond catalysis and organocatalysis are all well-established methods for catalytic glycosylation reactions, halogen bond (XB) catalysis has yet to have been systematically adopted for this type of reaction, outside of a few singular examples.[2] Here, a wide range of chiral bifunctional XB catalysts and organocatalysts were applied to a glycosylation reaction with the aim of attaining anomerically pure sugars utilizing different donor groups Y. Additionally, the significance of the role of the XB in the formation of the products was analyzed.



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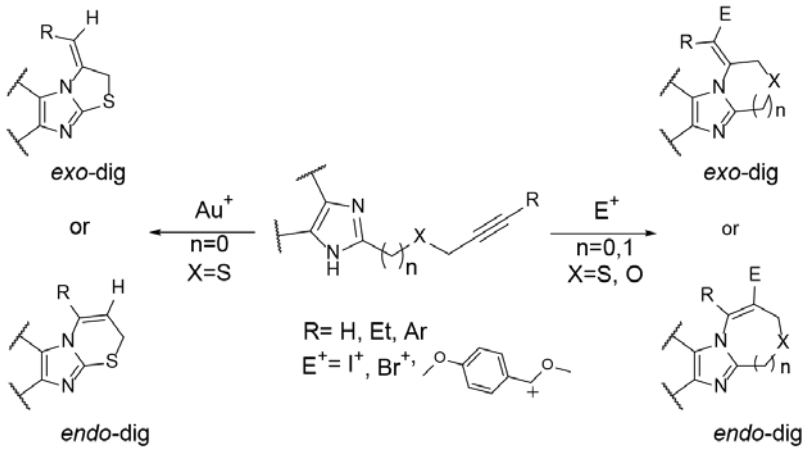
ELECTROPHILE PROMOTED NUCLEOPHILIC CYCLIZATION OF 2-ALKYNYLTHIOBENZIMIDAZOLES AND IMIDAZOLES

Indrė Misiūnaitė, Karolis Žigas, Raminta Bajarūnaitė, Ieva Žutautė, Algirdas Brukštus
Faculty of Chemistry and Geosciences, Vilnius University, Vilnius, Lithuania

One of the best ways to obtain heterocycles from alkynes is via cyclization reaction using electrophiles such as halogens [1], carbocations [1] or transition metals as catalysts [2]. In recent years electrophile promoted cyclization reactions of functionalized alkynes containing O, N, S heteroatoms are becoming increasingly popular [1,3]. Intrigued by the possibility to synthesize imidazothiazine and imidazothiazepine compounds, we carried out cyclizations of 2-alkynylthioimidazoles / 2-alkynylthiobenzimidazoles to investigate their reaction pathway.



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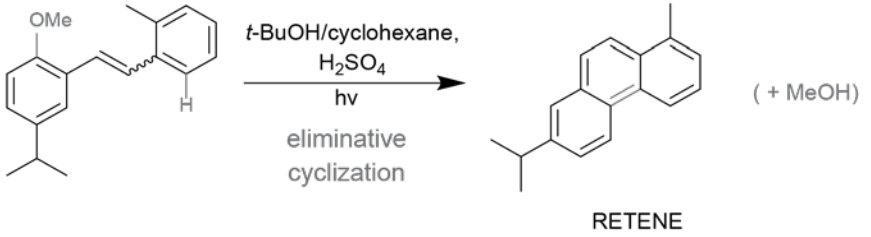
PHOTOCHEMICAL SYNTHESIS OF RETENE

Monika Moreń, Helene Grøtting, Erling Berge Monsen, Kåre Bredeli Jørgensen
Department of Chemistry, Bioscience and Environmental Engineering, University of Stavanger, Stavanger, Norway

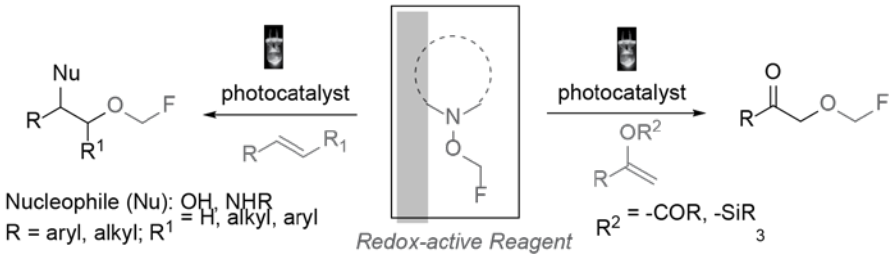
Retene (7-isopropyl-1-methyl-phenantrene) is an alkylated phenanthrene which genotoxic and cardiotoxic to fish. It is also cytotoxic to human lung cell line and may increase the risk of carcinogenesis. Collected data indicate that exposure to retene might pose a serious threat to people and the environment. Further thorough studies of retene's toxic properties are crucial but hampered by lack of available compound by synthesis nor extraction from natural sources. We have developed a simple and efficient 4-step synthesis of 7-isopropyl-1-methylphenanthrene with eliminative photocyclization as the key step (Scheme).



VISIBLE LIGHT PHOTOREDOX CATALYSIS FOR RADICAL FLUOROMETHOXYLATION

Ram Kumar Nagarajan[1], *Janis Veliks*[2]
Latvian Institute of Organic Synthesis, Riga, Latvia

Incorporation of the mono-fluoromethyl group can profoundly influence the physicochemical properties of organic molecules, offering a promising strategy for the discovery of novel pharmaceutical agents.[1] We have developed nitrogen based redox active reagents for the generation of fluoromethoxy radical under photoredox catalysis.[2] Direct fluoromethoxylation of unfunctionalized C(sp^2) centres is achieved for the synthesis of complex ß-fluoromethoxy alcohols/amides and α-fluoromethoxy ketones. These complex fluoromethoxylated products which are inaccessible until now, may serve as useful building blocks or fragments in synthetic and medicinal chemistry both in academia and industry.



Acknowledgements: This study was supported by PostDoc Latvia ERDF project Nr.1.1.1.2/VIAA/4/20/748, ja ir vieta, var pielikt arī nosaukumu “Development of new reagents and synthetic methodologies to access monofluorinated compounds for drug discovery”.

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MECHANOCHEMICAL BARBIER-TYPE GRIGNARD ADDITION REACTIONS OF ORGANIC HALIDES

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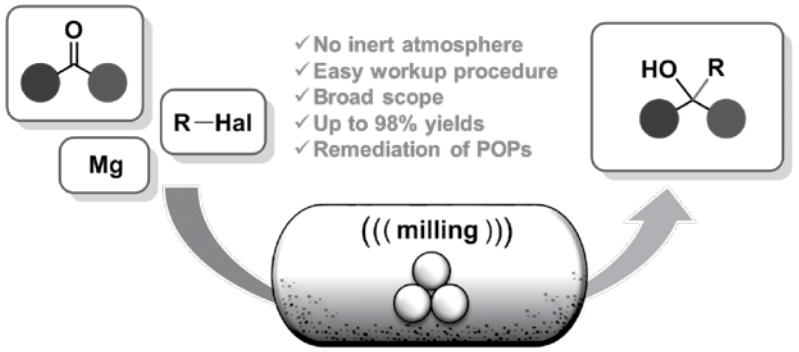
Department of chemistry and Biotechnology, Tallinn University of Technology, Tallinn, Estonia

Discovered more than a century ago, Grignard reaction remains one of the most fundamental transformations in organic chemistry. A number of step-wise protocols for mechanochemical generation and use of Grignard reagents have been reported [1–3]. However, more convenient single-step method (Barbier variant) remains unexplored. Here, we present the first one-step protocol for mechanosynthesis of Grignard addition products by milling an organic halide, magnesium powder and a carbonyl compound in a shaker mill. The method features short reaction times, easy workup procedure and suitable for a broad range of carbonyl and halide substrates. No inert atmosphere is required. Moreover, some Brønsted acid additives can be used for decomplexation of the products, with minimal protonation of in situ generated organomagnesium halides. The developed protocol is also suitable for remediation of some halogenated persistent organic pollutants (POPs).



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SYNTHESIS OF OXEPANE DERIVATIVES BASED ON ENOLATE ADDITION TO ALKENE

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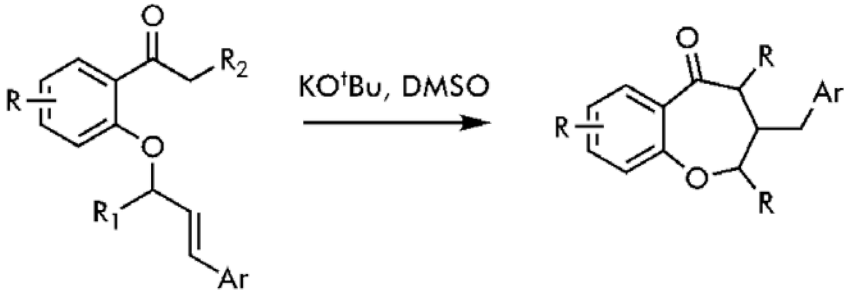
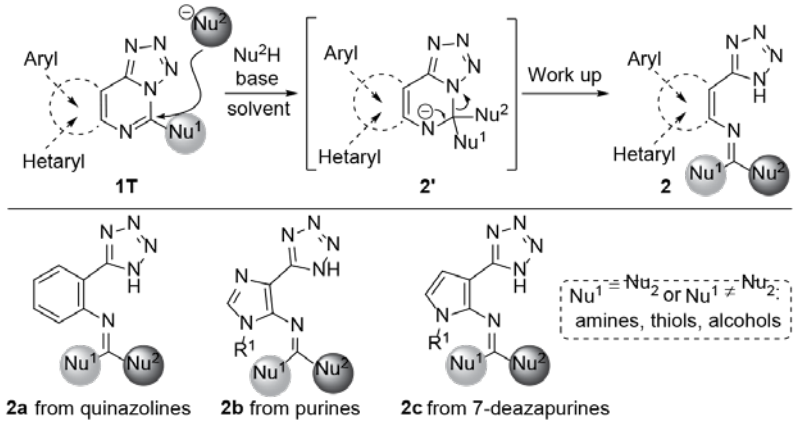
Oxepane heterocyclic system is often found in the structure of many natural products and pharmaceutical agents. The currently known synthetic methods used for the assembly of these seven-membered heterocycles often rely on multi-step procedures, especially in cases of heavily functionalized scaffolds, where multiple stereocenters have to be introduced with high stereoselectivity. Herein we report a novel one-step procedure for the formation of oxygen containing seven-membered rings using enolate addition to non-activated double bonds. The procedure utilizes affordable 2-hydroxyacetophenone derivatives appended with styrene functionalities as starting materials. These reactions proceed under very mild conditions using potassium tert-butoxide as a base, yielding products with good diastereoselectivities and yields.



RING OPENING REACTIONS OF FUSED TETRAZOLOPYRIMIDINES

Jānis Miķelis Zaķis[1], Zigfrīds Kapilinskis[1], Dinesh Kumar[1], Anna Dozorina[1], Jurijs Renārs Vērdiņš[1], Anatoly Mishnev[2], Irina Novosjolova[1], Māris Turks[1]
[1]Faculty of Materials Science and Applied Chemistry, Riga Technical University, Riga, Latvia
[2]Latvian Institute of Organic Synthesis, Riga, Latvia

Purine derivatives can be opened at both pyrimidine and imidazole rings.[1] In our research we focused on investigation and optimization of ring opening reactions in fused pyrimidines based on azido-tetrazole equilibrium. Under nucleophile attack the pyrimidine ring opened, forming tetrazolyl derivatives **2a-c**. The structures were proved by X-ray analysis.



Acknowledgements: This work is supported by the Latvian Council of Science grant No LZP-2020/1-0348.

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THE SELENYLATION OF PURINE DERIVATIVES

Agnija Ritere, Andris Jeminejs, Erika Bizdena, Irina Novosjolova, Maris Turks
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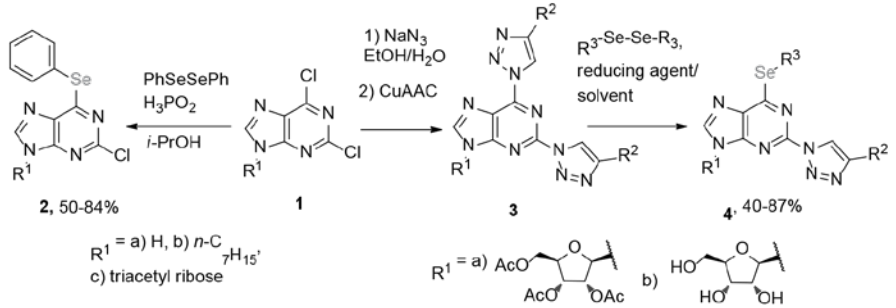
Earlier we demonstrated that 1,2,3-triazole moiety at C(6) position of purine is a good leaving group in S_NAr reactions with *N, S, O, C* and *P*-nucleophiles [1,2]. In this study we extended the range of nucleophiles with selenols. The synthetic routes to 6-selanyl-2-triazolylpurine nucleosides (**4**) and 2-chloro-6-selanylpurines (**2**) were developed and will be discussed.



Acknowledgements: This work was supported by the Latvian Council of Science grant No LZP-2020/1-0348.

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SUSTAINABLE SYNTHESIS OF USEFUL BUILDING BLOCKS ENABLED BY ELECTROLYSIS IN CONTINUOUS-FLOW

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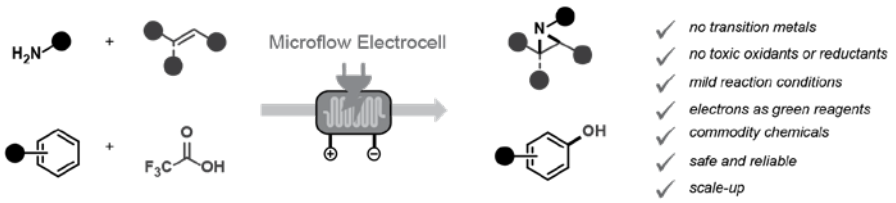
Tallinn University of Technology, Estonia

Electrochemistry has recently witnessed a renaissance in modern organic chemistry. This approach uses electrons as traceless and green reagents to generate highly reactive radical species under mild reaction conditions avoiding the utilization of hazardous oxidants or reductants and metal catalysts. Combining electrochemistry with the continuous-flow technology, we managed to obtain highly valuable building block, such as aziridines and electron-rich phenols, starting from common and broadly available starting materials.[1,2] In flow microreactors, high electrode surface-to-volume ratio and effective mixing significantly reduce reaction time, which helps to prevent degradation of sensitive products under the electrochemical conditions and increases reaction selectivity. The continuous nature of the process readily allowed to scale-up the reactions safely and efficiently.



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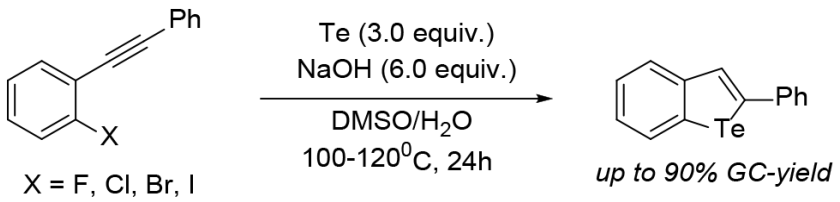
SIMPLE ACCESS TO BENZO[*b*]TELLUROPHENES

Edgars Paegle, Pavel Arsenyan
Latvian Institute of Organic Synthesis, Latvia

The scope of tellurium application so far has been quite diverse as it has been employed in various fields ranging from metallurgy to electronics.[1] There are several major methodologies for the construction of benzo[*b*]tellurophene's (BT's) heterocyclic system. Although all of these protocols provide desired BTs in moderate yields, each of these methods have some disadvantages like tediousness, requires inert and dry conditions, regioselectivity problems, pregeneration of key intermediates is mandatory, functional group intolerance, and perhaps some less significant downsides. Therefore, development of improved methodologies is highly desirable. Herein we present new variation of Takimiya's type synthesis, which is arguably the simplest methodology so far for the preparation of BTs as all the necessary and readily available reagents can be simply mixed together and heated overnight to provide 2-phenylbenzo[*b*] tellurophene in up to 90 % GC-yield and moderate isolated yields. Investigation of the substrate scope is currently in progress.



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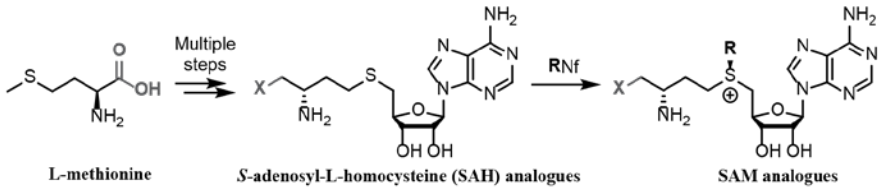
THE SYNTHESIS OF S-ADENOSYL-L-METHIONINE ANALOGUES WITH THE MODIFICATION ON AMINOACID MOIETY

Edvin Parafjanovič, Martynas Malikėnas, Gražina Petraitytė, Viktoras Masevičius
Vilnius University, Institute of Chemistry, Department of Organic Chemistry, Vilnius, Lithuania

S-adenosyl-L-methionine (SAM) analogues containing allylic or propargylic moiety directly bound to sulfonium is an effective tool to manipulate DNA in a selective and unique way [1]. However, these synthetic cofactors suffer from short lifetimes in physiological buffers, competing methylation by endogenous SAM and lower acceptance by DNA methyltransferases compared to the native cofactor. Structural modifications of SAM analogues enhance their stability and selectivity towards engineered DNA methyltransferases. Herein we report the synthesis protocol for the SAM analogues bearing other moieties instead of carboxyl group starting from L-methionine.



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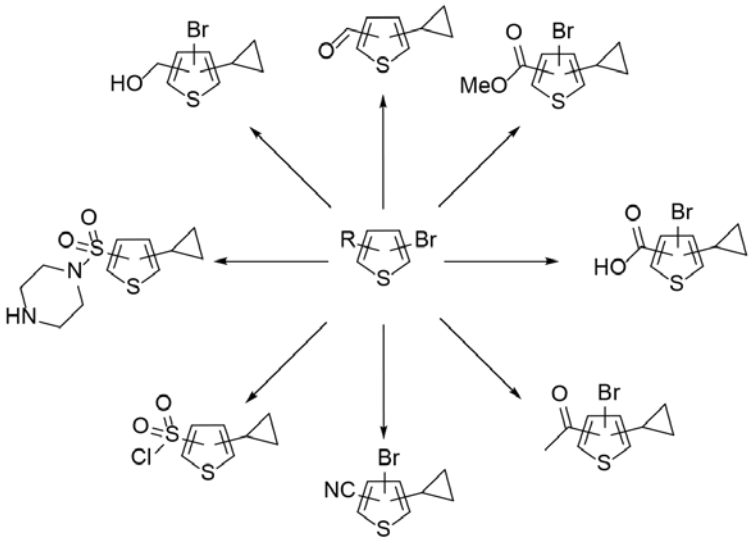
OPTIMIZATION OF SYNTHETIC METHODS FOR CYCLOPROPYLTHIOPHENE DERIVATIVES

Tomas Paškevičius, Linas Labanauskas
Center for Physical Sciences and Technology, Lithuania

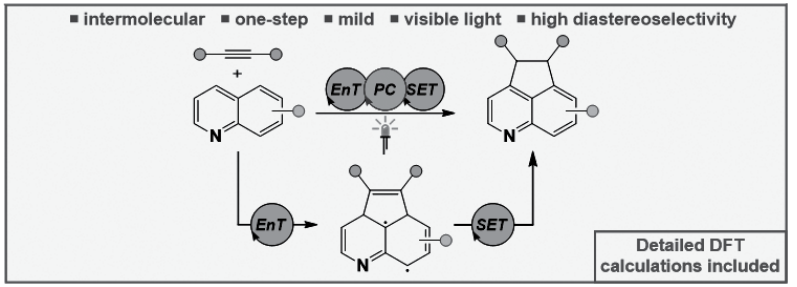
The synthetic procedure for functionalized cyclopropylthiophenes via the Suzuki cross-coupling reaction with cyclopropylboronic acid was optimized to work with low catalyst loadings. Improved methods for bromination of cylopropylthiophenes facilitated further functionalization of the thiophene ring. Synthetic method for preparation of cyclopropylthiophenesulfonyl chlorides was developed and successfully applied to large scale synthesis of the aforementioned compounds. In most cases the synthetic paths and means were successfully simplified, the yields of target molecules were significantly improved. Synthetic procedures were optimized keeping accessibility of starting materials and applicability to larger scale synthesis in mind.



VISIBLE-LIGHT PHOTOCATALYZED *peri*-[3+2] CYCLOADDITION OF AZAARENES.

Peter Bellotti[1], Fritz Paulus[1], Torben Rogge[2], Jiajia Ma[1], Ranjini Laskar[1], Nils Rendel[1], Kendall Houk[2], Frank Glorius[1]
[1]Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Münster, Germany.
[2]Department of Chemistry and Biochemistry, University of California, Los Angeles, USA.

Azaacenaphthenes are relevant structural motives found in several natural products and pharmaceuticals yet are challenging to access. Currently, the preparation of these compounds is achieved by step-intensive de-novo synthesis or intramolecular cyclization of prefunctionalized substrates. Herein we present a visible-light photocatalyzed, highly diastereoselective *peri*-[3+2] cycloaddition between alkynes and azaarenes forming azaacenaphthenes in a single reaction step. This unprecedented reaction takes place at two different cycles of the aromatic system requiring transient dearomatization of both rings. The dual role of the photocatalyst as both a triplet sensitizer and a photoredox catalyst is crucial to enable this demanding transformation. Detailed DFT calculations and experimental studies support the proposed reaction mechanism.



SYNTHESIS OF NEW ACRAB-TOLC EFFLUX PUMP INHIBITORS

Laura Pauniņa,[1] Marina Madre,[1] Aigars Jirgensons,[1] Björn Windshügel,[2] Jānis Veliks[1]
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Bacterial resistance to the existing classes of antibiotics is one of the most important challenges for the future healthcare system and bacterial cells efflux pumps play an important role for this internal drug resistance. To reduce the ability of the efflux pumps binding to medication substrates, the molecules called efflux pump inhibitors are used to rejuvenate the antibiotics activity by binding to the efflux pump protein.[1]
In the framework of the project, it was hypothesized that AcrAB-TolC efflux pump outer membrane protein TolC in Gram-negative *E.Coli* bacteria cells could represent an attractive drug target. Therefore, analogues of a new class of TolC inhibitors have been synthesized to identify structure-activity relationships. In addition, a synthetic pathway has been developed for the preparation of known AcrA inhibitor useful as a standard for further studies of biological activities.

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FLUORENE DERIVATIVES AS HOLES AND ELECTRONS TRANSPORTING MATERIALS

Julius Petrulevičius[1], Marytė Daškevičienė[1] Vytautas Getautis[1], Egidijus Kamarauskas[2], Vygintas Jankauskas[2]
[1]Department of Organic Chemistry, Kaunas University of Technology, Lithuania
[2]Institute of Chemical Physics, Vilnius University, Lithuania

Holes transporting material (HTM) is one of the main constituents of perovskite solar cells (PSC), determining the cost, energy conversion efficiency and longevity of the device [1]. The main disadvantage of majority of organic HTMs is the low mobility of the holes. To overcome this shortcoming, HTM additives, which reduce the stability of the PSC are often used. Therefore, organic semiconductors that do not require additives have been receiving increasing attention. One of such organic semiconductors is bipolar organic semiconductors [2].
The aim of this work was to synthesize fluorene derivatives with hole- and electron-transporting ability and to investigate the semiconducting properties of new semiconductors **V1374**, **V1383**, **V1384** and **V1416** (**Fig. 1.**).

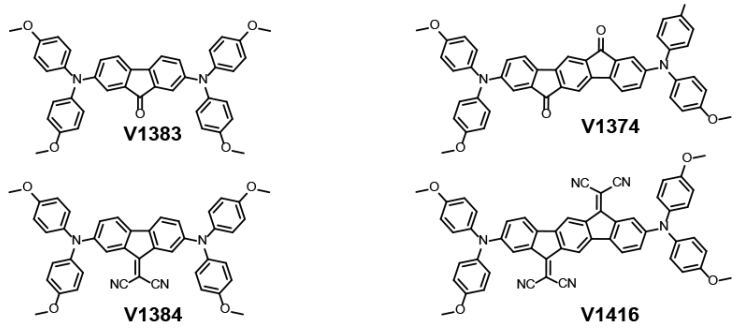

Fig. 1. *Bipolar fluorene derivatives*

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DIASTEREODIVERGENT ASYMMETRIC ALLYLIC ALKYLATION OF CYCLOBUTENES: A CHALLENGING MECHANISTIC PUZZLE

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Technical University of Darmstadt, Darmstadt, Germany

Transition metal catalyzed allylic alkylation has emerged as a powerful synthetic tool for asymmetric organic synthesis, enabling the formation of C-C bonds in an enantio- and diastereoselective fashion.[1] A specially remarkable variant, using racemic cyclobutene substrates, allows for controlling diastereo- and enantioselectivity only by the choice of ligand and independent of the configuration of substrate, thus displaying the characteristics of a diastereodivergent deracemization and de-epimerization.[2]
Aiming to shine light on the driving forces for the unusual stereoselectivity, we started a systematic mechanistic investigation. By synthesizing various putative reaction intermediates and performing a deuterium labeling study to capture the intermediates under reactive conditions, we could establish the reaction to include an extended Curtin-Hammett-type equilibrium of different isomeric intermediates, which exhibit different reactivity towards the nucleophile.
To get further information about the turnover-limiting and stereodetermining step, a detailed kinetic analysis was conducted, including extraction of rate orders and kinetic isotope effects. Our results suggest this step to proceed via two competing mechanisms, with the ligand controlling which path is preferred. As each of these paths leads to different product diastereomers, diastereodivergence seems to be achieved by a mechanistic dichotomy that is to the best of our knowledge unprecedented in allylic alkylation chemistry.

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CARBONIC ANHYDRASES: INHIBITOR SYNTHESIS

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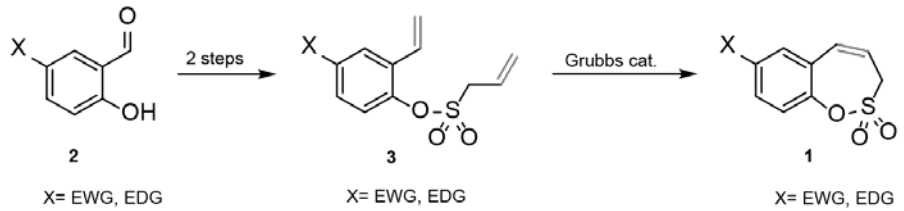
[2]Institute of Technology of Organic Chemistry, Faculty of Materials Science and Applied Chemistry, Riga Technical University, Riga, Latvia

Carbonic anhydrases (CAs) are metalloenzymes witch catalyze reversible carbon dioxide hydratation. In many organisms, the CAs are involved in vital physiological processes – such as pH regulation and providing of CO2 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 as antibacterial agents.
Our research group focuses on selective and effective CA inhibitor design and synthesis. Recently we have developed benzoxatiepine dioxides **1**, which proved to be effective and selective inhibitors.

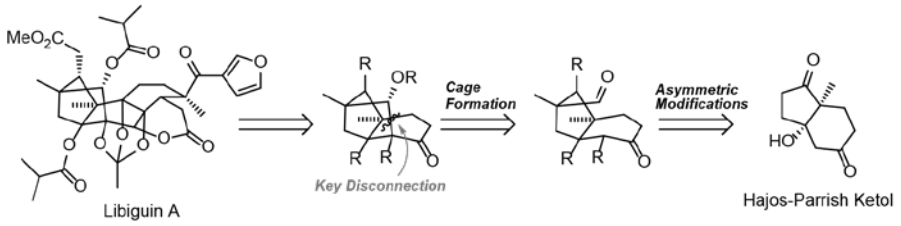


Acknowledgements: The SPRINGBOARD project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement No 951883.

APPROACHES TO THE TOTAL SYNTHESIS OF PHRAGMALIN-TYPE NATURAL PRODUCTS: SYNTHESIS OF A FUNCTIONALIZED METHANOINDENE CAGE

Olavs Rāciņš, Joseph Becica, Aigars Jirgensons
Latvian Institute of Organic Synthesis, Latvia

Phragmalin-type compounds are triterpenoid natural products of the limonoid family, and are typified by the presence of an octahydro-1*H*-2,4-methanoindene cage. Limonoid natural products exhibit a wide range of pharmacological properties, including anti-HIV, antibiotic, anti-cancer, anti-malarial, and anti-viral activities[1], therefore, are of high synthetic interest. Due to the high level of complexity, phragmalins have eluded total synthesis, however, Libiguin A, as developed in our group, can be prepared by semisynthesis from the more abundant Phragmalin itself[2]. Recently, we have developed strategies to approach the total synthesis of Phragmalin-type limonoids by focusing on routes to the functionalized methanoindene cage. Asymmetric modifications of the Hajos-Parrish ketone are demonstrated, including a diastereoselective α-methylation, which primes the bicyclic scaffold to engage in a cage-forming acid-catalyzed aldol reaction. Further functionalization of the cage, including a Reformatsky reaction, late-stage C-H oxidation, and elaboration of methods for C-ring and D-ring formation will also be discussed.



Acknowledgements: Project is supported by ESIF project Nr.1.1.1.2/ VIAA/4/20/752.

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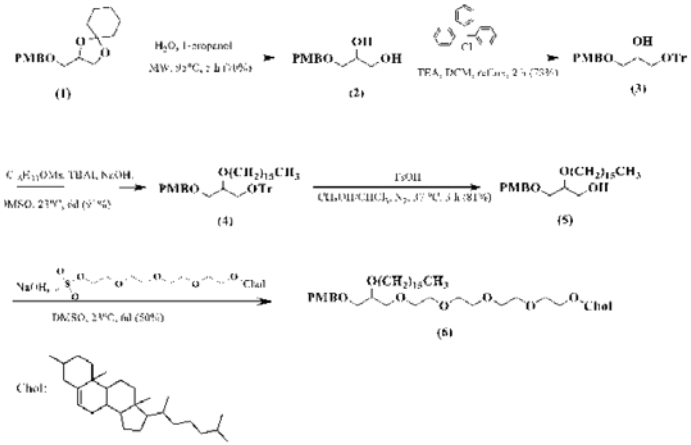
SYNTHESIS OF TRISUBSTITUTED GLYCEROL DERIVATIVES FOR ARTIFICIAL MEMBRANES RESEARCH

Greta Olimpija Remeikytė[1,2], Tatjana Charkova[2], Zenonas Kuodis[2], Olegas Eicher-Lorka[2]
[1]Faculty of Chemistry and Geosciences, Vilnius University, Lithuania
[2]Department of Organic Chemistry, Center for Physical sciences and technology, Lithuania

The main objective of this work is to synthesize glycerol derivative with three different substituents. Same alkyl disubstituted glycerol derivatives frequently used for tethered bilayer membranes creation and investigation. This kind of compounds with different type of alkyl substituents have never been used for this purpose, that's why we synthesized glycerol derivative with long alkyl chain and with tetraethylenglycol cholesterol ether. We successfully found a new hydrolysis way of cyclohexylidene ring (Scheme 1, compound 1): shorter reaction time and only water used for hydrolysis with assistance of microwave irradiation. After tritylation (compound 3) synthesis of monoalkyl glycerol ether (compound 4) is initiated. Selective deprotection and alkylation of primary OH group with mesylated TEG-cholesterol leads to glycerol with three different substitutes (compound 6).



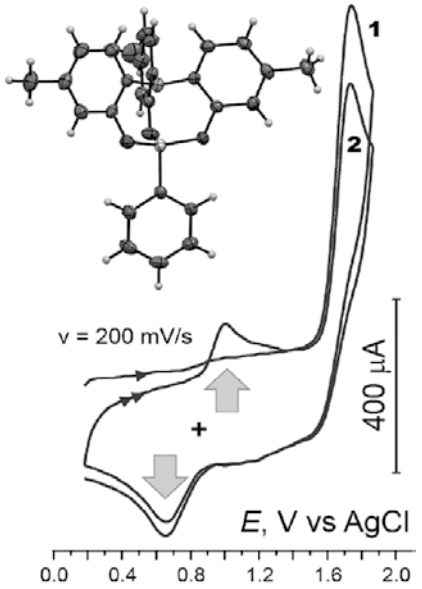
Scheme 1. *Synthesis of trisubstututed glycerol*

TRI(*p*-R-benz)SILATRANES: NOVEL 3c-4e SYSTEMS WITH PERSISTENT CATION RADICALS

Vitalijs Romanovs[1], *Edvins Kulins*[1], *Viatcheslav Jouikov*[2]
[1]*Latvian Institute of Organic Synthesis, Latvia*
[2]*UMR 6226 ISCR, University of Rennes, France*

Novel Si-substituted tribenzsilatranes with the increased stability of their cation radical states, required for spin-switching applications [1], were theoretically designed (B3LYP/Lanl2DZ and B3PW91/6-311G(d,p)) and synthesized. First representatives of this new family have been prepared from organotriacetoxysilanes (R = CH_2CH_2CN, *t*-Bu, Ph, Tol,) and the *p*-R' (R' = F, CH_3) nitrilo tris(o-phenol) preliminary prepared by Ullmann condensation of the corresponding p-R'-o-anizidine and p-R'-o-iodoanisole.

Spectroelectrochemical (UV-Vis and EPR) study of persistent cation radicals of these silatranes revealed spin localization on N atom which is flip-flopping between its stable endo- and exo-forms which accounts for the quasi-reversible character of ET ($E^{o}_{app} \approx 0.85$ V) in these 3c-4e systems. The new tri(p-R-benz) silatranes thus offer a new core for bistable molecular devices; their electro commutation is more advantageous compared to photoisomerization in e.g. diazene-based systems which is dependent on the overlap of λmax of their E/Z forms and on their thermolability.



Acknowledgements: Author is grateful to European PostDoc Latvia (#1.1.1.2/VIAA/3/19/577) for the financial support.

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CONNECTING THE A,B- AND D-RINGS OF 9,11-SECOSTEROLS

Kristi Rõuk, Marek Kõllo, Margus Lopp
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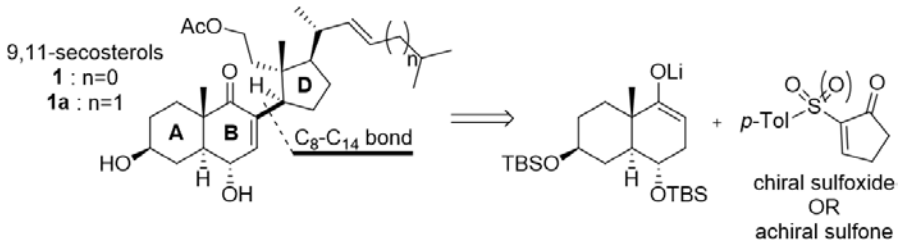
9,11-secosterols are of great interest due to their anticancer properties [1]. Our general approach to these compounds comprised separate synthesis of the A,B-ring [2] and D-ring [3] fragments and building the secosterol skeleton by connecting these fragments. Finding an appropriate reaction for that has been a challenge for quite some time.

Herein we present the formation of the secosterol skeleton by creating the C8-C14 bond via conjugate addition of ketone enolate to cyclopentenones activated by sulfoxide and sulfone groups. Synthesis of the necessary Michael acceptors is also presented.



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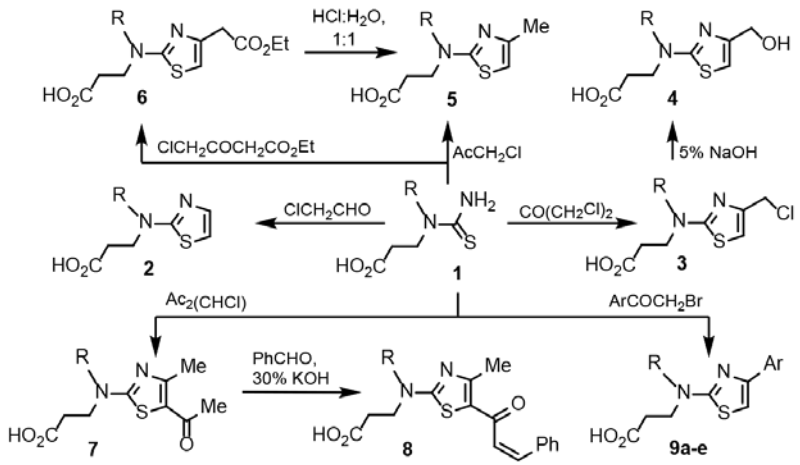
SYNTHESIS OF NEW FUNCTIONALIZED N-(9-ETHYLCARBAZOL-3-YL)AMINOTHIAZOLES

B. Sapijanskaitė-Banevič, V. Plečkaitytė, B. Grybaitė, R. Vaickelionienė
Kaunas University of Technology, Lithuania

In this work, N-(9-ethylcarbazol-3yl)-N-thiocarbamoyl-ß-alanine 1 was used in the synthesis of aminothiazole derivatives according to the Hantsch reaction. The reaction of thioureido acid 1 with chloroacetaldehyde in water in the presence of sodium acetate in the mixture gave compound 2, while the reaction with 1,3-dichloroacetone provided thiazole 3, which under alkaline hydrolysis conditions was converted to hydroxymethyl derivative 4. The 4-methylthiazole 5 was obtained directly from compound 1 by refluxing it with chloroacetone in water or by two-step procedure involving the reaction of 1 with ethyl 4-chloroacetoacetate to form thiazole 6 and then acidic hydrolysis and decarboxylation to obtain compound 5. The reflux of compound 1 with 3-chloro-2,4-pentanedione in acetone gave 5-acetyl-4-methylthiazole 7, which in the reaction with benzaldehyde in the presence of a base catalyst form compound 8, containing chalcone functional group in the structure. The condensation of compound 1 with various 2-bromoacetophenones provided derivatives 9a—e.

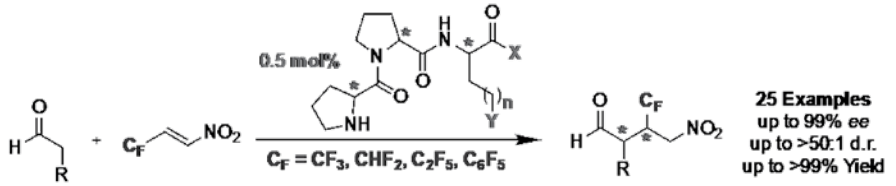


R = 9-ethylcarbazol-3-yl; **9**: **a** Ar = Ph, **b** Ar = 4-ClPh, **c** Ar = 4-BrPh, **d** Ar = 4-FPh, **e** Ar = 4-O_2NPh

OVERCOMING CATALYST DEACTIVATION: ACCESS TO FLUORINATED γ-NITROALDEHYDES BY PEPTIDE CATALYSIS

Martin Schnurr, Prof. Helma Wennemers
ETH Zurich, D-CHAB, Laboratory of Organic Chemistry, Switzerland

Tripeptides of the H-Pro-Pro-Xaa type are highly reactive and stereoselective catalysts for asymmetric aldol reactions and conjugate addition reactions of carbonyl compounds to nitroolefins, dicyanoolefins and maleimide.[1] For example, as little as 0.05 mol% H DPro Pro-Glu-NH_2 suffices to catalyze conjugate addition reactions of aldehydes to nitroolefins in high yields and excellent stereoselectivities.[2]
Herein we present the stereoselective conjugate addition of aldehydes to ß-fluorinated nitroolefins, a highly reactive class of electrophiles which usually deactivate secondary amine based organocatalysts by *N*-alkylation. By using peptide catalysts, we were able to overcome this deactivation and perform the reaction with only 0.5 mol% catalyst, while maintaining high yield and stereoselectivity.



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NEW SYNTHETIC PATHWAY TO 7-ARYLPURINES

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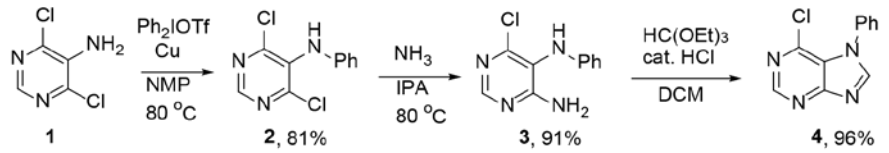
Arylation on the purine ring usually proceeds almost selectively at N(9) position where most often used methods are Cu catalyzed Chan-Lam reaction[1] and arylation with iodanes.[2] The few existing methods for purine N(7) arylation are not selective and are substrate dependent.[3] We have developed a pathway to 7-arylpurines using substituted pyrimidines.
The synthetic path depicted in the scheme below provided the best results. Modifications of compound **1**, diaryliodane reagent and ring closing reagent resulted in the formation of differently substituted 7-arylpurines **4**.



Acknowledgements: This work was supported by the Latvian Council of Science grant No LZP-2020/1-0348.

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SYNTHESIS OF 2-AMINOQUINAZOLINES AND INDAZOLES FROM 2-FORMYLPHENYLBORONIC ACIDS

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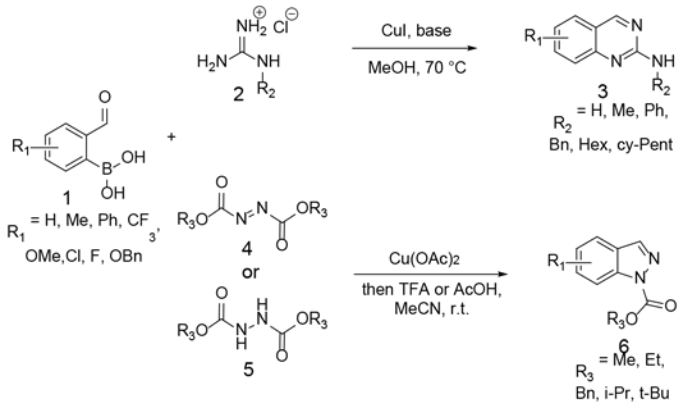
[2]Faculty of Materials Science and Applied Chemistry, Riga

New methods for the synthesis of indazole and 2-aminoquinazoline which are relevant for the development of a new antimicrobials, has been studied and developed. Using discovered technique, 2-formylphenylboronic acids (1) can be converted to the target heterocycles in a mild conditions.
For 2-aminoquinazoline synthesis (3), variously substituted guanidines (2) has been used. Reaction proceeds in alcoholic media with Cu (I) iodide as a catalyst (Chan-Evans-Lam reaction conditions adaptation).
With dialkyl azodicarboxylates (4) and dialkyl hydrazinedicarboxylates (5) N-protected indazoles (6) can be obtained. Protocol involves coupling stage, mediated by Cu (II) acetate, with subsequent one-pot conversion of formed semi-product to indazole in acidic media.



Acknowledgements: research work supported by CARTNET project (H2020 grant agreement № 765147). Special thanks for SPRINGBOARD project mobility support (H2020 grant agreement ID № 951883)

EXPLORING THE POTENTIAL OF METAL CATALYZED FLOUROMETHYLSULFONIUM SALT REACTIONS

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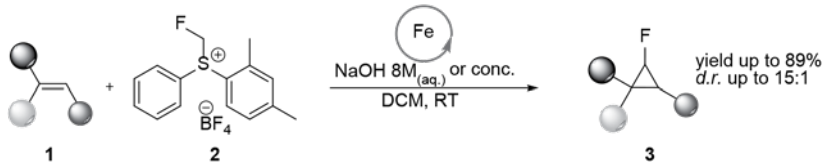
Synthesis of fluorine containing molecules is of great interest due to its unique properties and vast application in pharmaceuticals, agrochemicals and materials[1]
Fluoromethylsulfonium salts are emerging as synthetic equivalents of flouromethylene synthon.[2] However, their reactivity in transition metal catalyzed reactions is unexplored. Therefore, it is important to research the potential of metal catalyzed fluoromethylsulfonium salt reactions in order to obtain highly valuable fluorinated molecules.
Herein, we wish to report first fluoromethylene transfer to unactivated alkenes **1** by employing sulfonium salt **2** and earth abundant Fe catalyst (Scheme 1).



Scheme 1. *Fluorocylopropanation of unactivated alkenes*

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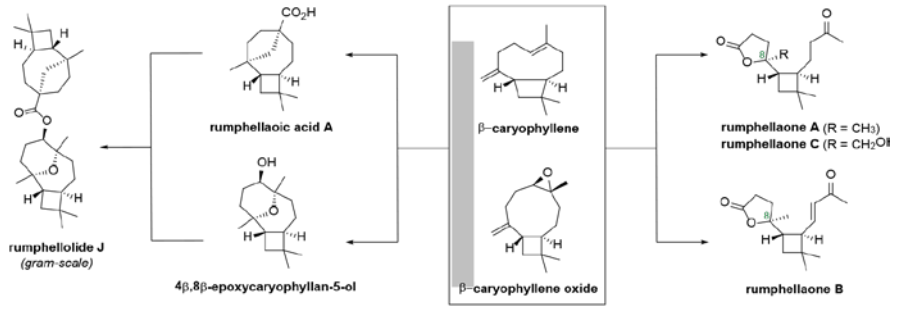
SEMISYNTHESIS OF NATURAL PRODUCTS FROM (–)-B-CARYOPHYLLENE

Georgijs Stakanovs, Dace Rasina
Latvian Institute of Organic Synthesis, Latvia

β-Caryophyllene is one of the most abundant sesquiterpenes found in nature, therefore it is available at low price from several commercial sources. The unusual structure of β-caryophyllene with two stereodefined chiral centers renders this terpene as an attractive renewable starting material to access diverse high value compounds. Our research of chemoselective transformations of β caryophyllene opened an opportunity to develop a concise semisynthetic routes towards biologically active sesquiterpene lactones (rumphellaones A-C and their C-8 epimers)[1] as well as disesquiterpenoid rumphellolide J using esterification of rumphellaoic acid A via acyl fluoride[2]. Structures of final products were unambiguously confirmed by single crystal X-ray analysis.



Acknowledgements: This work was supported by ERDF Project no. 1.1.1.2./VIAA/2/18/380 and by LIOS student grant IG-2022-03.

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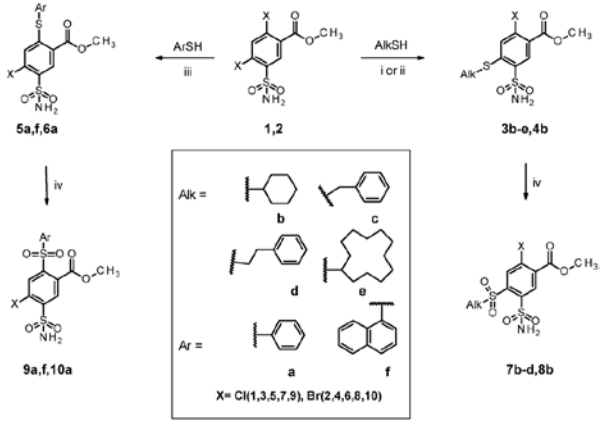
METHYL 2-HALO-4-SUBSTITUTED-5-SULFAMOYL-BENZOATES AS HIGH AFFINITY AND SELECTIVE INHIBITORS OF CARBONIC ANHYDRASE IX

L. Stančaitis[1,2], E. Čapkauskaitė[2], A. Zakšauskas[2], V. Paketurytė-Latvė[2], D. Matulis[2]
[1]Vilnius University, Faculty of Chemistry and Geosciences, Vilnius, Lithuania
[2]Vilnius University, Institute of Biotechnology, Life Sciences Center, Vilnius, Lithuania

Among the twelve active carbonic anhydrase (CA) isozymes in the human body, the CAIX is overexpressed in tumors. Therefore, many attempts have been made to design compounds that would exhibit high affinity and selective binding to CAIX over the remaining CA isozymes. We have designed a series of compounds and determined their affinities for all twelve CA isozymes by thermal shift assay. Variations of substituents on the benzenesulfonamide ring led to compound **4b**, which exhibited high observed binding affinity to CAIX; the Kd was 0.12 nM.[1]



References:
[1] Zakšauskas, A.; Čapkauskaitė, E.; Paketurytė-Latvė, V.; Smirnov, A.; Leitans, J.; Kazaks, A.; Dvinskis, E.; Stančaitis, L.; Mickevičiūtė, A.; Jachno, J.; Jezepčikas, L.; Linkuvienė, V.; Sakalauskas, A.; Manakova, E.; Gražulis, S.; Matulienė, J.; Tars, K.; Matulis, D. *Int. J. Mol. Sci.* 2022, 23, 130.

MECHANOCHEMICAL SYNTHESIS OF NEW MONO-FUNCTIONALIZED CYCLOHEXANOHEMICUCURBIT[8]URIL

Elina Suut, Tatsiana Shalima, Dzmitry Kananovich, Riina Aav
Department of Chemistry and Biotechnology, Tallinn University of Technology, Tallinn, Estonia

Design of novel supramolecular receptors is of great interest due to their host-guest chemistry and synthetic versatility, which allows to construct new structures possessing peculiar molecular recognition properties. Nevertheless, the formation of the target product (Figure 1) can be challenging due to reactivity and selectivity obstacles. Our group recently reported synthesis of new macrocycles using mechanochemistry,[1,2] perceived as a more sustainable and greener solvent-free approach.[3]

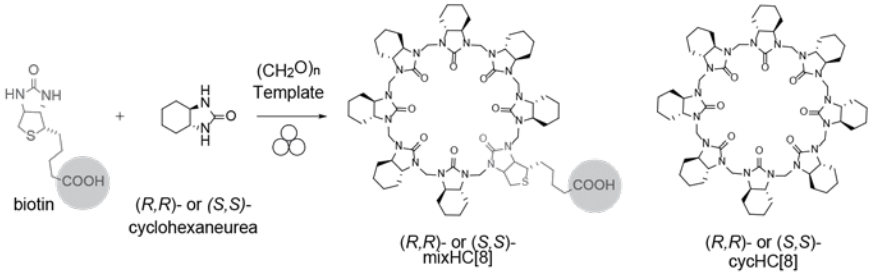


Figure 1. *Mechanochemical synthesis of mixHC[8].*

Herein we present the mechanochemical protocol for the synthesis of chiral (*R,R*)- and (S,S)-mixHC[8] via combination of 7 cyclohexaneurea and 1 biotin monomers. The impact of various synthetic parameters was evaluated throughout optimization experiments. The developed methodology allows to obtain pure diastereomeric products with up to 16% yield.

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SELF-ASSEMBLED MONOLAYERS BASED ON 1,8-NAPHTHALIMIDE AND 1,4,5,8,-NAPHTALENETETRACARBOXYLIC DIIMIDE DERIVATES

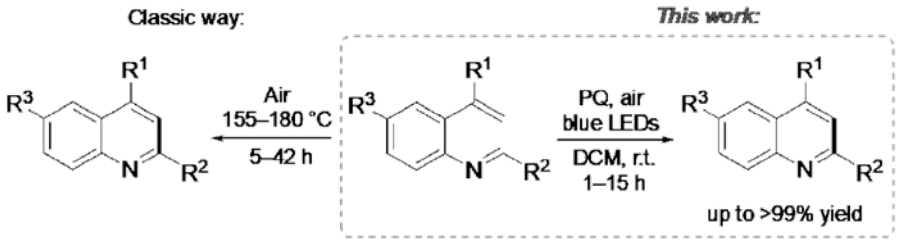
Lauryna Monika Svirskaitė, Tadas Malinauskas
Faculty of Chemical Technology, Kaunas University of Technology, Lithuania

High costs and insufficient conversion efficiencies are the major issues in the development of the photovoltaic devices to become a primary source of energy. Development of new organic semiconductors for solar cells construction is necessary to reach high performance and longevity. Innovative way to increase device efficiency is application of self-assembled monolayers (SAM). SAMs can form ordered one-atom thick layer with well-defined orientation on the surface. The layout of directed organic semiconductors molecules maintain constant dipole moment, which influences charge transporting efficiency and the alignment of energy levels at the layers interface.
Naphthalenetetracarboxylic diimide (NDI) and naphthalimide (NI) derivatives are widely used as electron transporting materials. NDI and NI solubility, photophysical and electronic behavior can be controlled by the incorporation of different functional groups on the core structure, which overall influences device photovoltaic properties.
In this work *n*-type semiconductors containing 1,4,5,8,-naphtalenetetracarboxylic diimide or 1,8-naphthalimide central fragment along with functionalized anchoring groups were synthesized. These materials could be promising candidates for further photovoltaics development.

PHENANTHRENEQUINONE-SENSITIZED PHOTOCATALYTIC SYNTHESIS OF POLYSUBSTITUTED QUINOLINES FROM 2-VINYLARYLIMINES

Juulia Talvitie, Iida Alanko, Juho Helaja
Department of Chemistry, University of Helsinki, Helsinki, Finland

One traditional way to synthesize polysubstituted quinolines is via thermal electrocyclization. However, it requires harsh reaction conditions, such as high temperatures or pressures[1], or strong Lewis acid catalysts[2]. By using visible-light-excited 9,10-phenanthrenequinone (PQ*) as a photocatalyst, we received up to quantitative yields of polysubstituted quinolines even after 1 h of excitation with blue LEDs at room temperature when MgCO3 n-hydrate was used as an additive in DCM.[3] On the basis of experimental and DFT studies, we propose that PQ* induces one-electron oxidation of the imine substrate that triggers the electrocyclization mechanism.



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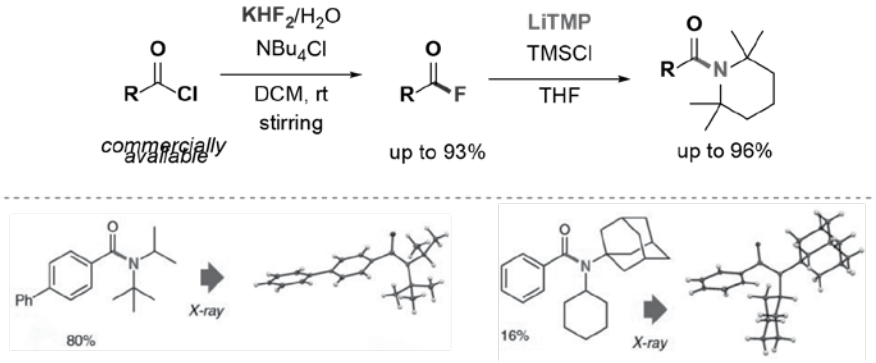
SYNTHESIS OF ACYL FLUORIDES AND BULKY AMIDES

Michał Tryniszewski, Michał Barbasiewicz
Faculty of Chemistry, University of Warsaw, Warsaw, Poland

Carbonyl group in acyl fluorides displays properties intermediate between acyl chlorides and aldehydes. Thus, sterically hindered lithium amides like LiTMP could react as nucleophile with COF group rather than as a base in directed ortho-metalation of aromatic rings. In result, a series of bulky amides was synthetized under mild conditions with good yield. Acyl fluorides used for these transformations were prepared using new protocol of phase-transfer catalyzed halogen exchange reaction at 100 mmol scale.



Acknowledgements: The project was financed from NCN, Poland (grant DEC-2018/31/B/ST5/01118).

References:

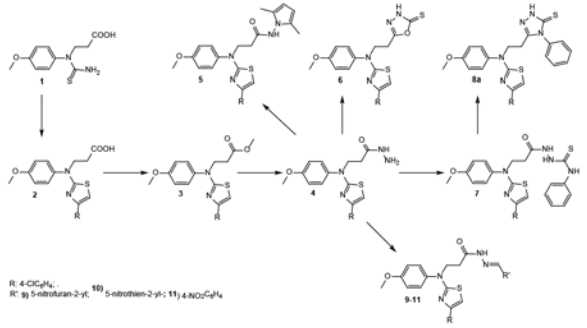
M. Tryniszewski, M. Barbasiewicz, *Synthesis* 2022, 54, 1446-1460.

SYNTHESIS AND ANTIOXIDANT ACTIVITY OF NOVEL DISUBSTITUTED THIAZOLE DERIVATIVES

Ingrida Tumosienė[1], Ilona Jonuškienė[1], Kristina Kantminienė[2], Aida Šermukšnytė[1], Vytautas Mickevičius[1]
[1]Department of Organic Chemistry, Kaunas University of Technology, Lithuania
[2]Department of Physical and Inorganic Chemistry, Kaunas University of Technology, Lithuania

Thiazole scaffold has been identified in a number of natural biologically active compounds. Its synthetic derivatives also possess a broad spectrum of biological activities, including antioxidant and antimicrobial ones.

1,3-Thiazole derivative **2** was obtained from thioureido acid **1** in the reaction with 2-bromo-4'-acetophenone. Propanehydrazide **4** was synthesized from acid **2** *via* ester **3** by usual synthesis procedure.



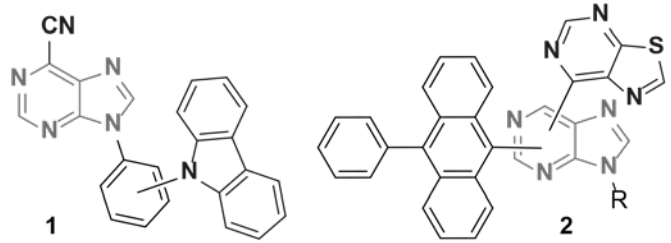
Condensation reaction of **4** with hexane-2,5-dione gave pyrrole derivative **5**. Compound **6** bearing 1,3,4-oxadiazole moiety was synthesized in the reaction of **4** with CS_2 in EtOH in the presence of KOH. Thiosemicarbazide **7** and hydrazones **9–11** were synthesized by condensation reactions of **4** with phenyl isothiocyanate or corresponding heterocyclic aldehydes.

Compounds **5** and **7** have been shown to possess high DPPH free radical scavenging acitivity, 81.8% and 78.6%, respectively.

FUNCTIONALIZED PURINES FOR MATERIALS SCIENCE APPLICATIONS

Armands Sebris, Zigfrīds Kapilinskis, Kārlis Ēriks Kriķis, Kaspars Traskovskis, Irina Novosjolova, Māris Turks
Faculty of Materials Science and Applied Chemistry, Riga Technical University, Riga, Latvia

Fluorescent purine derivatives are well known as probes for nucleic acid and enzymatic research [1], but their applications in materials science are less known [2,3]. We have recently reported synthesis and photophysical studies of novel fluorescent purine push-pull systems [4,5].
Here we report design of novel 6-cyanopurine-carbazole (**1**) [6] and purine-thiazolopyrimidine (**2**) conjugates, which act as exciplex systems exhibiting thermally activated delayed fluorescence (TADF). Their synthesis and photophysical studies will be reported in detail.



Acknowledgements: Financial support by Latvia-Lithuania-Taiwan co-project MEPS is kindly acknowledged.

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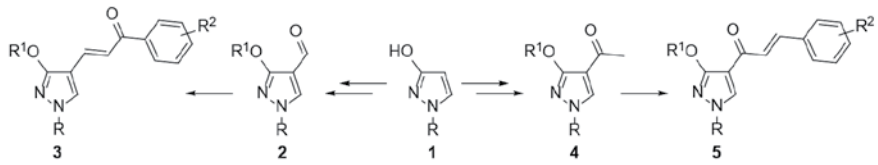
SYNTHESIS OF NOVEL HETEROCYCLIC CHALCONE DERIVATIVES FROM 1-PHENYL-1H-PYRAZOL-3-OL

Arminas Urbonavičius[1], Graziana Fortunato[1,2], Emilija Ambrazaitytė[1], Vaida Milišiūnaitė[3], Aurimas Bieliauskas[3], Renzo Luisi[2], Eglė Arbačiauskienė[1], Sonata Krikštolaitytė[1], Algirdas Šačkus[1,3]
[1]Department of Organic Chemistry, Kaunas University of Technology, Kaunas, Lithuania
[2]Department of Pharmacy - Drug Sciences, University of Bari Aldo Moro, Bari, Italy
[3]Institute of Synthetic Chemistry, Kaunas University of Technology, Kaunas, Lithuania

Chalcones constitute an important group of natural products and synthetic compounds. Some of them exhibit a wide range of therapeutic activities, such as anticancer, antioxidant, antibacterial, antiviral, anti-inflammatory. Nitrogen heterocycles bearing a chalcone fragment have been recently reported to be active against lung adenocarcinoma and brain glioma cells, as well as against some of the Gram-positive and Gram-negative bacteria.



Herein we report the synthesis and structure elucidation of either a 3-hydroxy- or 3-alkoxy-1H-pyrazole moiety containing chalcones. The synthetic strategy for the synthesis of novel chalcone derivatives 3 and 5 starting from 1-phenyl-1H-pyrazol-3-ol 1 is outlined in Scheme 1. The structure assignments of the synthesized compounds were based on, DEPT, COSY, gs-HSQC, gs-HMBC and NOESY NMR spectroscopic data.

CYCLOHEXANOHEMICUCURBIT[*n*]URIL MACROCYCLES: SUPRAMOLECULAR INTERACTIONS

Lukas Ustrnul, Riina Aav
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Chiral macrocyclic hosts cyclohexanohemicucurbit[*n*]urils (cycHC[*n*], see Figure) were reported to bind anions[1] and neutral heterocycles[2] in methanol. Also, cycHC[*n*] form complex with Lewis acids and organic acids in chloroform[3-5]. This presentation is focused on a recent study, which examined interactions of cycHC[*n*] with large scope of organic guests to clarify the binding sites, stoichiometry and general trends in the stability of supramolecular bonds[6]. In addition, an overview of up to date known complexes of cycHC[*n*] in various media is provided.

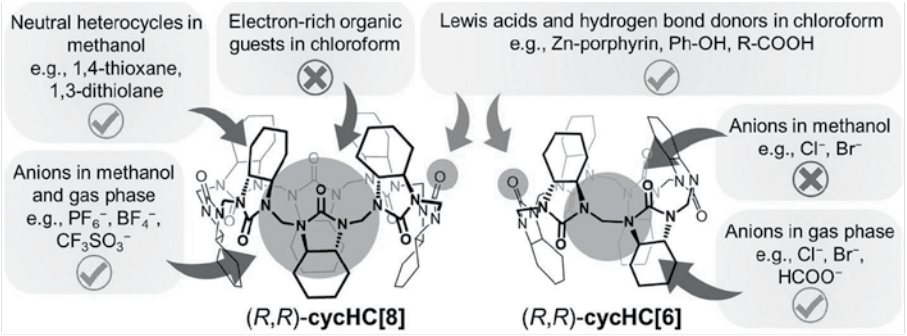

Figure: *Examples of interactions studied in the recent and previous studies.*

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6. Ustrnul, L. et al., *Front. Chem.* 2021, 9, 468.

AMBIPOLAR CHARGE TRANSPORT IN ANTHRAQUINONE-BASED SEMICONDUCTORS

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[1]Department of Organic Chemistry, Kaunas University of Technology, Lithuania
[2]Institute of Chemical Physics, Vilnius University, Lithuania

Nowadays, growing attention is directed to the synthesis of organic semiconductors, which are known for a relatively low-cost and solution processable films. Moreover, an increase in charge transport properties, especially both hole and electron mobilities, shows their potential for application in semiconducting devices.

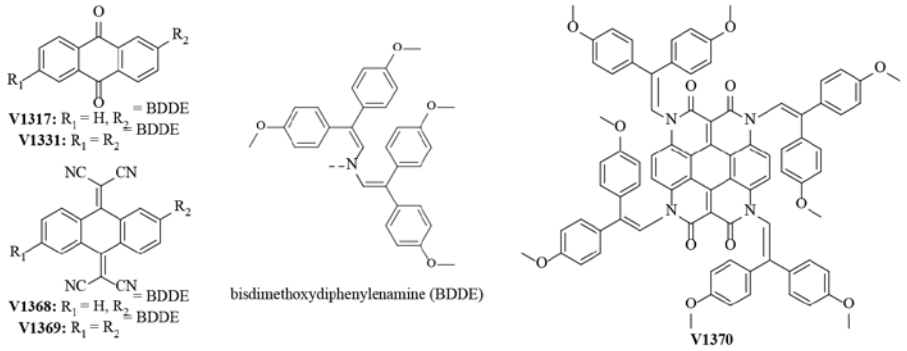

Fig. 1. *Structures of anthraquinone-based semiconductors.*

Here, a new series of deeply coloured anthraquinone derivatives is presented. Enamines containing dicyanovinyl acceptors were synthesized by Knoevenagel condensation, mediated by the Lehnert reagent ($TiCl_4$/pyridine). In addition, heterocoronene-based enamide was obtained for the first time by the same Knoevenagel reaction using diethyl malonate. Xerographic time of flight (XTOF) measurements were used to determine the charge mobility of synthesized compounds. The results demonstrate that anthraquinone-based compounds show ambipolar charge transport behavior.

ARYLATION AND ALKENYLATION OF CYCLOPROPANOLS VIA NICKEL/PHOTOREDOX CATALYSIS

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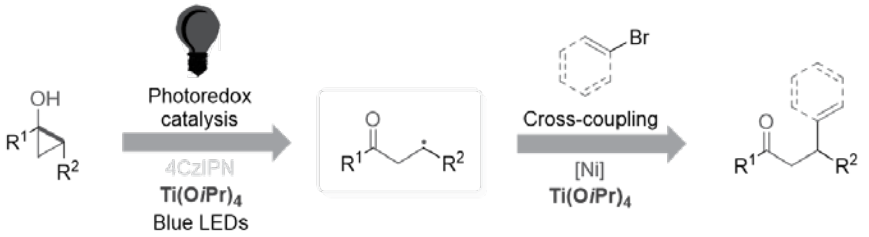
[1]Department of Chemistry, Belarusian State University, Republic of Belarus
[2]Institute of Bioorganic Chemistry of the National Academy of Sciences of Belarus, Republic of Belarus

Over the past 8 years, dual nickel and photoredox catalysis has become a powerful tool for constructing new C–C and C–heteroatom bonds [1]. In these reactions, photochemically generated radical species undergo further cross-coupling with an organic halide. Although cyclopropanols are known radical sources, their use in dual nickel and photoredox catalysis remains extremely limited [2]. In this work, we present a new general $Ti(OiPr)_4$-enabled protocol for the arylation and alkenylation of mono- and disubstituted cyclopropanols with a wide range of functional groups in the side chain [3].



Acknowledgements: The authors are grateful for the financial support from the Belarusian Foundation for Fundamental Research (Projects X20M-036 and X20PTI-008).

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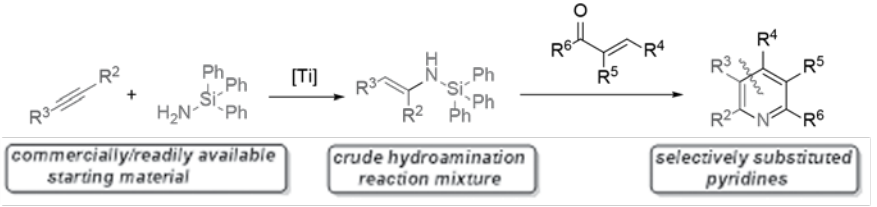
TOWARD THE SYNTHESIS OF JULANDINE AND CRYPTOPLEURINE. ONE-POT SEQUENTIAL HYDROAMINATION TO SELECTIVELY ACCESS TRI-, TETRA-, AND PENTA-SUBSTITUTED PYRIDINES

Vani Verma, Laurel L. Schafer
Department of Chemistry, University of British Columbia, Vancouver, British Columbia, Canada

Functionalized pyridines have long been known as biologically active compounds. Owing to their prevalence in natural products, pharmaceuticals, and agrochemicals, new and improved synthetic methods are important in the field of medicinal chemistry and drug design. Herein we report a one-pot protocol for the assembly of selectively substituted and less explored tri-, tetra- and penta-substitution patterns for pyridines. Titanium-catalyzed hydroamination of alkynes with commercially available N-triphenylsilylamine selectively generates N-silylenamines. One of the advantages of using *N*-silylamine as a substrate is the selective formation of the enamine product, with no tautomerization to the imine form. The in situ generated *N*-silylenamines upon reaction with an *α,β*-unsaturated carbonyl compounds followed by oxidation furnish 32 examples of selectively substituted tri-, tetra- and penta-substituted pyridines in isolated yields of up to 78%. This modular reaction features a high functional group compatibility providing an expeditious approach for the construction of a diverse range of less investigated pyridine derivatives. The expandability of this approach is under investigation in the total syntheses of Julandine and Cryptopleurine which belong to the class of phenanthroizidine alkaloids.



DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF A NOVEL CLASS OF N-ALKYLATED BENZO[B]THIOPHENE DERIVATIVES

Paulina Voznikaitė[1], Vilija Kederienė[1], Indrė Jaglinskaitė[1], Algirdas Šačkus[1], Arnaud Tatibouët[2]
[1]Department of Organic Chemistry, Kaunas University of Technology, Kaunas, Lithuania
[2]Institut de Chimie Organique et Analytique (ICOA), Université d'Orléans et CNRS, Orléans, France

Benzo[*b*]thiophene ring containing compounds are important derivatives in drug discovery and biotechnological process investigation. Previous studies have shown that sulfur atom containing heterocycles demonstrated impressive anti-oxidant and anti-bacterial results which greatly extends the limits of these compounds in chemistry, medicine, and recently medication design [1,2]. In addition, benzothiophene-based derivatives as clinical drugs have been valuated as candidates for the treatment of human cancer which has led to their large-scale developments [3].
Due to such a wide range of applicability, in this work the synthesis and biological evaluation of benzo[*b*]thiophenes were developed. A new library of different functional group substituted aromatic iodides were based on 3-aminobenzo[*b*]thiophene-2-carboxylate skeleton using inexpensive and air-stable catalyst systems, including copper iodide salt and structurally simple L-proline ligand [2].
The synthesized heterocyclic compounds indicated that Ullman-type cross-coupling reactions is an efficient and affordable way to produce highly pharmacologically potential heterocyclic amines in a good yield using mild copper-catalyzed C-N coupling procedures.

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2. Kederienė, V., et. al. *Mol.* 2021, 26, 6822.
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2-AZANORBORNANE VS. BRIDGED AZEPANE: VARIOUS EFFECTS OF RING EXPANSION

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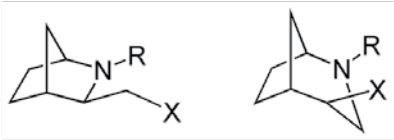
2-Azanorbornane (2-azabicyclo[2.2.1]heptane) has proven its versatility as the easily available, intrinsically chiral platform for the construction of ligands and catalysts used in various asymmetric transformations and as a precursor of various biologically active compounds.[1] A stereoselective conversion to bridged azepane (2-azabicyclo[3.2.1]octane) derivatives opens the route to a series of chiral compounds with an expanded bicyclic system.[2]
In the presentation, a comparison of catalytic performance and activities of isomeric bicyclic systems bearing various functionalities (amines, amides, sulfonamides, triazoles, thioureas) will be discussed.



Acknowledgements: National Science Center (NCN) Poland, grant number 2018/30/M/ST5/00401 is kindly acknowledged.

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COPPER-CATALYZED TANDEM HALOGEN EXCHANGE/C-P CROSS-COUPLING OF (CYCLO) ALKENYL/ARYL BROMIDES AND SECONDARY PHOSPHINE OXIDES

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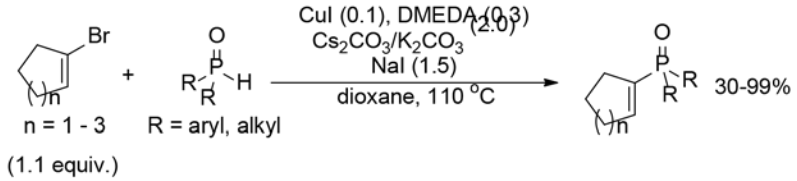
We report on a protocol for copper-catalyzed tandem halogen exchange/C-P cross-coupling between cycloalkenyl bromides and secondary phosphine oxides[1] The method utilizes the catalytic system based on CuI and DMEDA, and NaI additive. The use of the iodide salt reduces the required amount of organic bromides to near-stoichiometric by promoting *in situ* halogen exchange which was shown in a kinetic study to be faster than the cross-coupling. The method shows good efficacy for diarylphosphine oxides including sterically hindered ones, lower efficacy was observed with the introduction of an alkyl or electron-deficient aryl substituents at phosphorus atom (Scheme 1). The procedure can also be used for acyclic alkenyl bromides and aryl bromides albeit with lower generality.



Scheme 1.

Acknowledgements: We thank the Polish Ministry of Science and Higher Education for financial support (Grant no. DI 2017 012247).

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USE OF TOSYLATED 1,2-GLYCEROL CARBONATE TO GIVE PYRAZOLE COMPOUNDS

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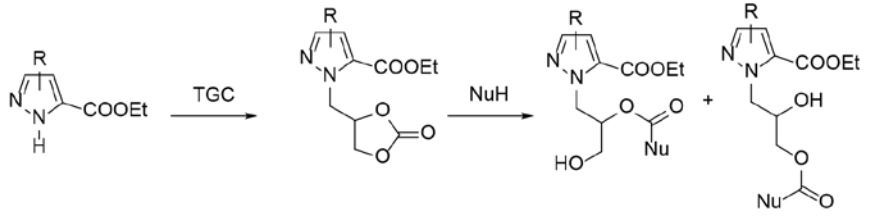
Glycerol carbonate (GC), a product of glycerol valorization, is renewable and versatile building block for sustainable organic synthesis. GC is highly investigated as a desirable green reagent, mainly of its wide reactivity due to both nucleophilic and electrophilic sites [1].
In continuation of our interest in application of tosylated 1,2-glycerol carbonate (TGC) for the functionalization of heterocyclic compounds [2,3] we report herein *N*-glycerylation of NH-pyrazoles using TGC and further ring opening of glycerol carbonate using various nucleophiles (Scheme 1).



Scheme 1. *N-glycerylation of pyrazole-5-carboxylates and nucleophilic ring opening of glycerol carbonate*

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BIS-CYCLOMETALLATED IRIDIUM COMPLEXES FOR C-H BORYLATION

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[2]Process Chemistry Research, Syngenta Crop Protection AG, Switzerland

Cyclometallated complexes are emerging as a new class of stable catalysts for C-H functionalization including Late-stage functionalization (LSF) of complex molecules.[1] Recently a new class of cyclometallated Iridium complexes bearing Pyrido-thiophene ligand have been reported for the directed C-H borylation.[2]

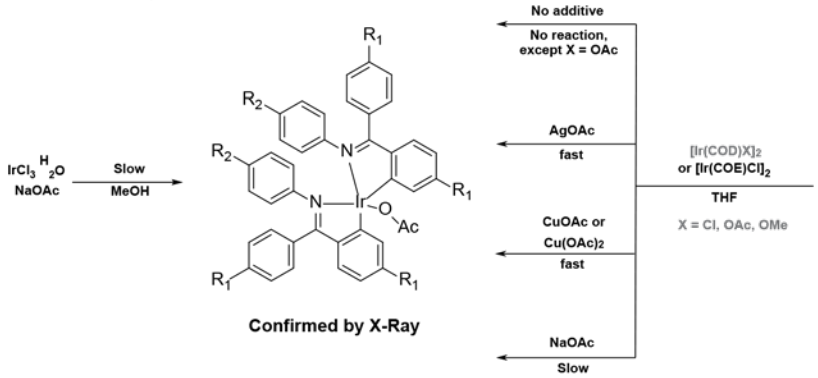

Figure 1. *Synthesis of bis-cyclometallated Iridium catalyst.*

Herein we report the synthesis and application of novel bis-cyclometallated imine-Ir catalysts. These catalysts can be prepared from different Iridium sources and are soluble in a wide range of organic solvents. We are currently exploring their potential for highly selective ***ortho*** **directed C-H borylation**.

Acknowledgements: This project has received funding from the EU's Horizon 2020 R&I programme under the MSCA, GA No 860762.

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SYNTHESIS OF FLUORINATED BENZENSULFONAMIDES AND THEIR DERIVATIVES CONJUGATED WITH FLUORESCEIN FOR VISUALIZATION OF CARBONIC ANHYDRASES EXPRESSED IN CELLS

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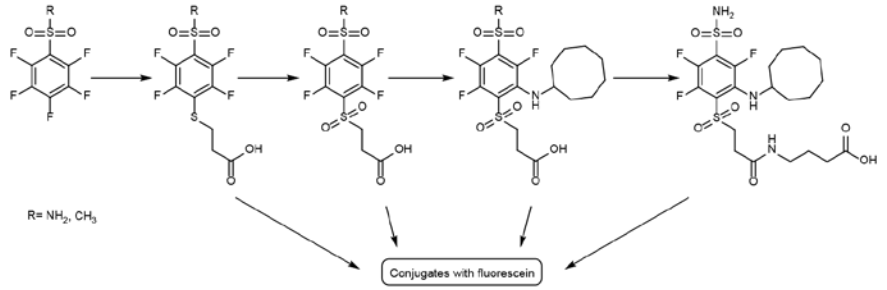
Metalloenzymes carbonic anhydrases are human protein family involved in various physiological and pathological processes. Isoenzyme CAIX is involved in cancerous processes and its overexpression is observed in a variety of cancerous tissues, whereas CAIX is almost undetectable in healthy tissues. Therefore, CAIX has been identified as good anti-cancer target and also as an important biological marker in cancer identification. Selective fluorescence imaging is an emerging cancer imaging technique that uses CAIX as one of its targets.



A series of fluorinated benzenesulfonamides and their derivatives, bearing modified sulfonamide group, conjugated with fluorescein were synthesized. Binding activities of synthesized compounds were determined by the fluorescent thermal shift assay (FTSA), fluorescent imaging was performed on HeLa cells.

NOTES