SEMINAR
Frontiers in Organic Synthesis

Dedicated to the 70th birthday of Professor Margus Lopp

Friday, 15 Nov 2019

Akadeemia tee 15 TALLINN (Loodusteaduste maja), SCI-109

9:00 Arrival. Coffee

10:00 Introduction

10:10 *Mendoza Abraham*

Group Leader, Stockholm University, Sweden

ASYMMETRIC SYNTHESIS WITH CHIRAL CARBON-ATOM PRECURSORS

11.00 *Mikk Kaasik*

PhD Student, Tallinn University of Technology

TRIAZOLE-BASED XB DONORS IN SOLUTION AND APPLICATIONS IN CATALYSIS

11:25-11:50 Coffee

11:50 *Tomislav Friščić*

Professor, McGill University, Quebec, Canada

MECHANOCHEMISTRY FOR SYNTHESIS

12.40 *Gábor Elek*

PhD student, Tallinn University of Technology

OXIDATIVE RING CLEAVAGE REACTIONS OF CYCLOPROPANOLS AND THEIR SYNTHETIC APPLICATIONS

13:00-14.00 Break

14:00 *Selena Sephton*

Research Scientist, University of Cambridge, UK

POSITRON EMISSION TOMOGRAPHY AS A BRIDGE BETWEEN CHEMISTRY AND NEUROSCIENCE AT THE MOLECULAR IMAGING CHEMISTRY LABORATORY

14.50 *Livia Matt*

PhD student, University of Tartu

NOVEL BIOBASED ALTERNATIVES TO CONVENTIONAL POLYMERS

15:10-15:30 Coffee

15:30 *Zoltán Novák*

Associate Professor, Eötvös Loránd University, Hungary

DEVELOPMENT OF NOVEL COUPLING TECHNOLOGIES FOR THE CONSTRUCTION AND FUNCTIONALIZATION OF AROMATIC AND HETEROAROMATIC SYSTEMS

16:20 Closing

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EESTI KEEMIASELTS

Asymmetric synthesis with chiral carbon-atom precursors

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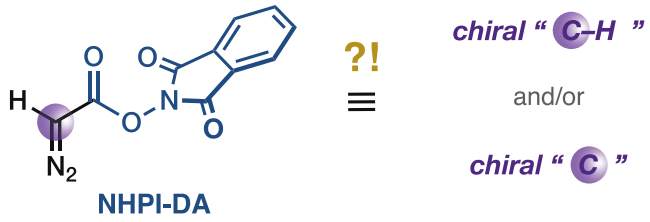
Synthetic strategies to access enantiopure compounds are highly dependent on the final functionalization of the desired product. For example, alkyl- and boryl-cyclopropanes are prepared using different routes from distinct precursors, catalysts, and reagents. While these specific methods will remain relevant in process chemistry, the diversity-oriented synthesis of compound libraries would be accelerated if alternative unified approaches could be realized.

Recently, our group has pioneered the enantioselective transfer of carbenes with redox-active ester handles (Scheme 1), which allow for facile late-stage installation of a wide range of functions. At the core of this comprehensive approach is a universal carbene precursor (NHPI-DA) that can deliver unrelated products through a single strategy and with enantioselectivities that, for the first time, do not depend on the desired decoration.



Scheme 1. Are redox-active carbenes suitable synthetic equivalents of fundamental carbon stereogenic elements**?**

References

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Mechanochemistry for Synthesis

Tomislav Friščić, Department of Chemistry, McGill University, Montreal, Quebec

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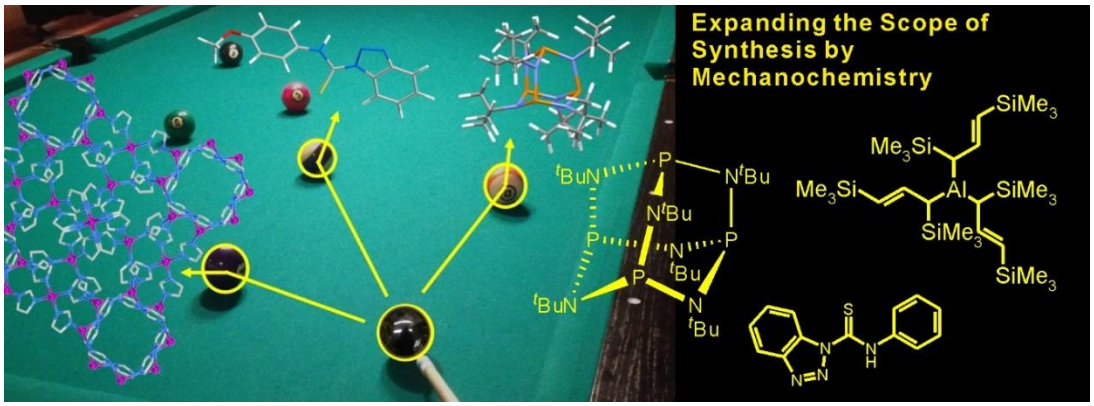
The past two decades have witnessed an explosive development of mechanically-induced (mechanochemical)[1,2] reactions. While such reactivity has been known for millennia,[3] its synthetic potential became fully appreciated by chemists only recently, and its mechanisms are only now being unraveled through cutting-edge methods such as real-time synchrotron diffraction.[4]



This lecture will illustrate the new synthetic opportunities offered by mechanochemistry over a wide range of organic, metal-organic and organometallic systems, including pharmaceuticals and microporous materials (metal-organic frameworks, MOFs). Particular attention will be given to the advantages of solid-state reactivity in making molecules and materials that have previously been difficult or impossible to access.[2]

References

[1] Kaabel *et al. Angew. Chem. Int. Ed.* **2019**, *58*, 6230; [2] Friščić *et al. Angew. Chem. Int. Ed.* **2019**, *58*, doi:10.1002/anie.201906755; [3] Theophrastus "On Stones", translation by E. R. Caley & J. F. C. Richards, Graduate School Monographs, Ohio State University, Columbus, USA (**1956**); [4] Julien *et al. J. Am. Chem. Soc.* **2016**, *138*, 2929.

PET as a bridge between Chemistry and Neuroscience at the MICL

Selena Milicevic Sephton

Molecular Imaging Chemistry Laboratory, Department of Clinical Neurosciences, University of Cambridge, West Forvie Site, Robinson Way, Cambridge, UK

Positron Emission Tomography (PET) is a non-invasive molecular imaging technique which is extensively used both for biomdeical research and in clinical practice. PET technique uses imaging agents which are compounds radiolabelled with short-lived positron emitting radionuclides (e.g., ^{18}F, ^{11}C). The development of PET is heavily dependent on the availability of PET radiotracers as well as novel radiochemical methodology to access these. The driving force behind the new approaches to synthesize PET imaging agents is a continuous need for faster, reliable and reproducible chemicals methods. On the other hand, the clinical demands for more specific biomarkers of disease drive the development of novel imaging agents with better properties.

In our group we are primarily interested in the development of novel PET radiotracers for imaging brain particularly targeting processes of neurodegeneration and their biomarkers (e.g., TSPO receptors, tau fibrils). Our interests extend to quantification of the rate of protein synthesis and is coupled to novel radiochemical methodology.

Some of the examples from our research laboratory will be presented to showcase the requirements for the development of new imaging agents and also novel methods for their preparation.

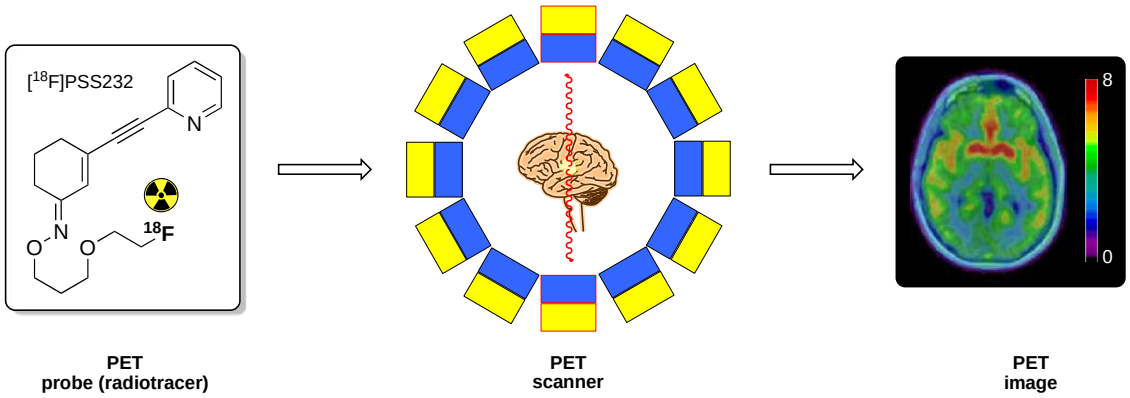


Figure 1. Principle of PET, modified from *Neuromethods 130*, Positron Emission Tomography of Metabotropic Glutamate Receptors, **2018**.

Acknowledgements: Members of the MICL team.

Development of novel coupling technologies for the construction and functionalization of aromatic and heteroaromatic systems

Zoltán Novák[a]

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In our research group, we developed various palladium and copper catalyzed coupling reactions for the functionalization of aromatic and heteroaromatic systems. We used two major approach for the functionalizations: cross-coupling reactions and C-H activation. In the lecture, the developed methods will be summarized, including various C-C and C-O bond forming reactions for the synthesis of alkynes, ethers, ketones and fluoroalkylated scaffolds. Besides the functionalizations, heterocyclic ring construction is also in focus in our laboratory. In the field of oxidative couplings, a novel, highly modular copper-catalyzed ring closure – carboarylation methodology for the construction of different heterocyclic systems from alkyne derivatives with the aid of diaryliodonium salts were developed. Additionally, we designed a novel fluoroalkeny-iodonium salt and used as excellent building block for trifluoromethylated aziridines.

Triazole-based XB donors in solution and applications in catalysis

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The number of applications that utilize the attractive interaction between a Lewis acidic halogen atom and a Lewis base, *i.e.* the halogen bond (XB), is growing.[1] Many of these applications describe the use of XB-based catalysts.[2] As of now, no examples of asymmetric catalysis based solely on XB activation have been reported, although enantiodiscrimination utilizing XBs is possible.[3] We envisioned that asymmetric XB catalysis could be achieved by using chiral halo-triazoles (Figure 1, A), which are readily accessible via a copper-catalysed click reaction between haloalkyne and organic azide.[4] Herein we characterise the XBs formed by these donors in the solid state to the counterion or a second donor molecule (Figure 1, B). Next, association constants in solution to (thio)ureas, amines and imines are described, with values of up to 1.1 x 10^4 M^{-1} in the case of quinuclidine (Figure 1, C).[5] Additionally, the enantiodiscrimination ability of the donors is explored. Finally, the catalytic potential of the triazoles in an aza-Diels-Alder reaction is described with catalyst loading as low as 2 mol% (Figure 1, D).

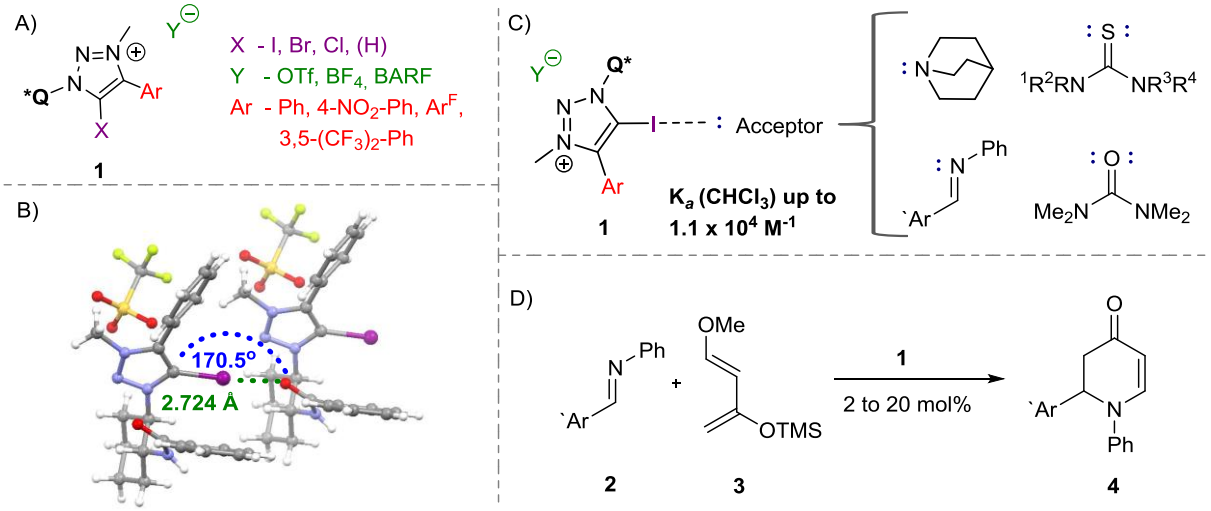

Figure 1: A) Triazole-based XB donors, B) a XB in the solid state, C) studies in solution, D) model reaction under study.

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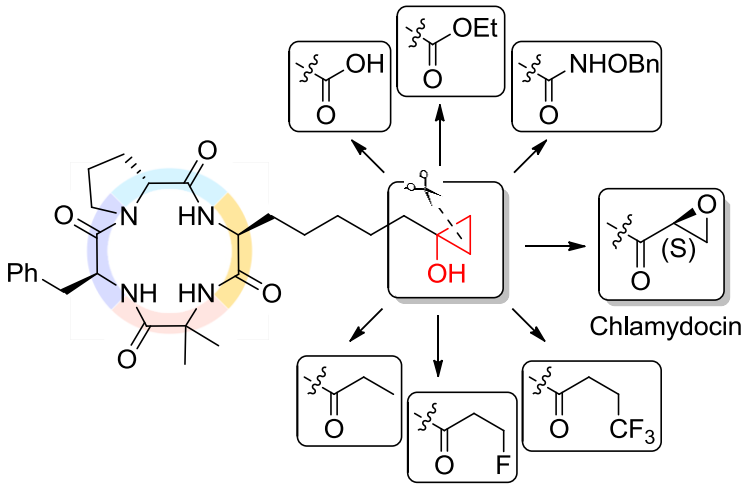
Oxidative ring cleavage reactions of cyclopropanols and their synthetic applications

Gábor Elek, Tallinn University of Technology

Cyclopropanols are easily available starting materials exhibiting versatile transformation possibilities via facilitated cleavage of the strained cyclopropane ring. For oxidative cleavages, concerning one-electron redox pathway processes, aerobic oxygen can be employed as green oxidant in cooperation with transition metal catalysis. These methodologies, besides being high yielding with regards to the obtained value-added products (chiral epoxyketones, versatile β-Michael adducts), are carried out under mild conditions and demonstrate tolerance towards a wide range of functional groups, making them ideal candidates for late-stage modification of peptides and further bioactive targets.[1,2]



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Novel biobased alternatives to conventional polymers

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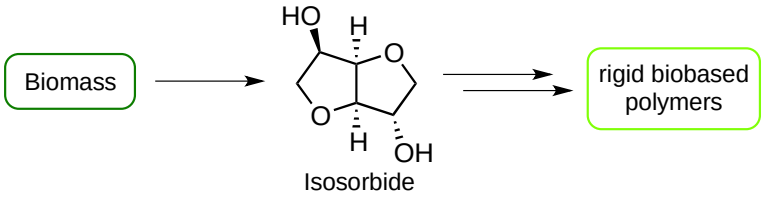
[4]*Lund University, Sweden*

Increasing concerns for the environment and the inevitable depletion of petrol resources have motivated researchers to find sustainable alternatives to fossil-based carbon compounds and materials. Biomass, especially lignocellulosic biomass, is the obvious source for this type of sustainable materials. Various polymers and composites from bioresources have been developed, but the general problem is the lack of sufficient thermostability, strength and other such properties, which would make them competitive with current fossil-based materials.

The goal of our work is to develop novel chemical building blocks from renewable feedstock and prepare corresponding polymers with the aim to fill the gap of rigid biobased plastics that maintain shape and strength at elevated temperatures.



Scheme 1. Rigid biobased polymers from Isosorbide.

Herein we present our work with isosorbide derivatives.[1,2] Isosorbide is a commercially available nontoxic rigid diol derived from D-glucose. We have developed method for novel isosorbide-based polymethacrylates applicable in various areas like paper and cardboard coatings, paints etc.[2,3] In general, polymers are used in most applications in our everyday life and novel sustainable materials are therefore highly awaited.

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