Laboratory of Catalysis and Organic Synthesis

Prof. Jérôme Waser

http://isic.epfl.ch/page-21086.html

jerome.waser@epfl.ch

**General area**

Organic Chemistry

**Research goals**

At the laboratory of catalysis and organic synthesis, we work at the development of new reactions in organic chemistry. In the search for unconventional and efficient approaches towards key structural elements of natural products and bioactive substances, we will design new metal- and organo- catalyzed processes for the formation of C-C bonds, which forms the skeleton of organic molecules. These new processes can then be applied in the synthesis of pharmaceutically important targets and will contribute to the establishment of a more sustainable chemistry.

The presented projects are general area of research, and interested students are welcome to discuss the exact details of their future work. For motivated students, opportunities are open for master work and semester projects, but also for undergraduate and summer internship. Master works will be an independent project in one of the three proposed area of research under the supervision of a PhD student. Internship and Semester projects will be in closer collaboration with a PhD student.

**Research themes**

**Project 1: Developing New Reactions for the Synthesis of Alkynes**

Project Manager Metal Catalysis-Double Bond Functionalization: Stefano Nicolai

Project Manager Metal Catalysis-C-H Functionalization: Jonathan Brand

![Figure 1. Acetylene: A Versatile Building Block](image)

Alkynes are versatile functionalities in organic synthesis, as they participate for example in addition reactions to carbonyl compounds, as well as cycloaddition and coupling reactions. These processes have found widespread applications in neighbouring fields, such as...
biochemistry and material sciences (Figure 1).\(^1\) Our goal is to develop new access to this useful class of compounds based on asymmetric catalysis and the functionalization of readily available feedstocks, such as alkenes, hydrocarbons and heterocycles. To reach our goal, we make use of the exceptional reactivity of hypervalent iodine reagents.

Recently, we reported the first Au-catalyzed alkynylation of indole and pyrrole heterocycles,\(^2\) as well as the intramolecular oxyalkynylation of olefins\(^3\) using benziodoxolone-based hypervalent iodine reagents (Figure 2). These new methods for the introduction of acetylenes in heterocycles are expected to find widespread applications in the synthesis of bioactive compounds and organic materials.

**Figure 2.** New catalytic alkynylation reactions using hypervalent iodine.

This project involves the synthesis of organo- or metal-catalysts, the preparation of substrates and intensive optimization of reaction conditions using analytical techniques such as HPLC, GC-MS and NMR.

**Project 2: Cationic Cyclization Reactions for the Synthesis of Polycyclic Compounds**

Project Managers: **Filippo De Simone, Florian de Nanteuil, Dr. Fides Benfatti**

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Figure 3. Anticancer and Antibiotic Compounds with Complex Polycyclic Structures: How Can we Synthesize them?

Polycyclic structures are omnipresent in natural products and bioactive compounds (Figure 3).\(^4\) The generation of cationic reactive intermediates is a well-known method to promote cyclization reactions, but such reactions have traditionally relied on stoichiometric activating agents. The goal of this project is to develop catalytic methods based on cationic intermediates and address the challenge of stereoselectivity in the formation of polycyclic compounds.

Recently, the first catalytic formal homo-Nazarov reaction has been discovered at the LCSO (Figure 4).\(^5\)

![Homo-Nazarov Reaction](image)

Figure 4. The Catalytic Formal Homo-Nazarov Reaction developed at the LCSO

The newly developed methodology was then applied to the synthesis of two natural products, aspidospermidine and goniomitine (Figure 5).\(^6\) Collaboration with the group of Prof. Jürg Gertsch in Bern has been initiated to study the bioactivity of goniomitine. In this project, focus is more on organic multi-step synthesis, with less time dedicated to optimization and catalyst synthesis. Depending on the results in the bioactivity testing, projects in medicinal chemistry will also become possible.

![Synthesis of Alkaloid Natural Products](image)

Figure 5. Synthesis of alkaloid natural products

Project 3: Computational and physical organic studies of reaction mechanisms (in collaboration with the Laboratory of Computational Molecular Design (Prof. Corminboeuf)

During the first three years of research, new reactions have been developed at LCSO. Many of these new processes are not yet well understood. The goal of this project is to study in details the mechanism of the reactions using mostly computational methods. This will be done in collaboration with the group of Prof. Corminboeuf in computational chemistry. In contrast with other projects, no reaction development will be involved and most of the work will be done on the computer. Some physical organic experiments (kinetics, isotopic effects,…) will be also done to compare with the results of the calculations. The master student will get an insight in two different fields of chemistry.

**Methodology of work/special instrumentation**

The students will be involved in a multidisciplinary work, constantly increasing his knowledge and skills in inorganic (synthesis of metal complexes), organic (multi-steps synthesis of small organic molecules) and analytical (HPLC, GC-MS, NMR) chemistry. He will deepen his practical knowledge of organic chemistry and begin the formation of a synthetic chemist, which open good job opportunities in the pharmaceutical industry.

**Recent examples of MSc thesis**
