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Assembly of Molecular Daisy Chains in Water

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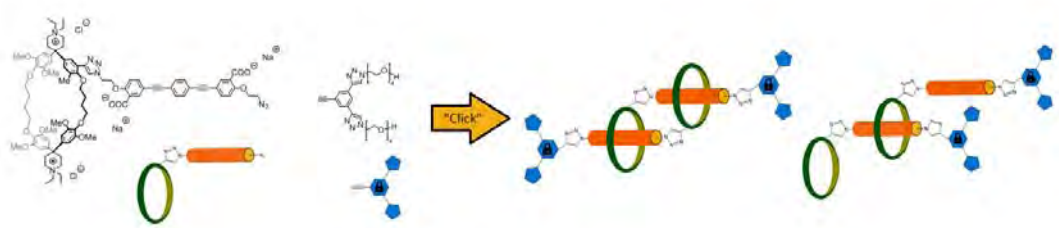
Construction of supramolecular nanosystems based on molecular daisy chains is an appealing option as their monomers are self-complementary and allow to access cyclic or linear oligomers by changing monomer concentration or solvent polarity[1]. Our cyclophane-based approach for the synthesis of daisy chains relies on association driven by a hydrophobic effect combined with electrostatically complementary subunits. The zwitterionic monomer was found to assemble to linear and cyclic daisy chains in aqueous media, which could be characterized by ^{1}H-NMR after interlocking with bulky stoppers via a CuAAC-“click”-reaction. Introduction of redox-active chromophores into the monomer is expected to give daisy chains with switchable dimensions, which could be integrated into molecular muscles. Synthetic investigations towards this goal are currently in progress.



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Laterally Stretched Polycyclic Aromatic Hydrocarbons: Synthesis of Dibenzophenanthroheptaphene and Tetrabenzotriphenylenopyranthrene Derivatives

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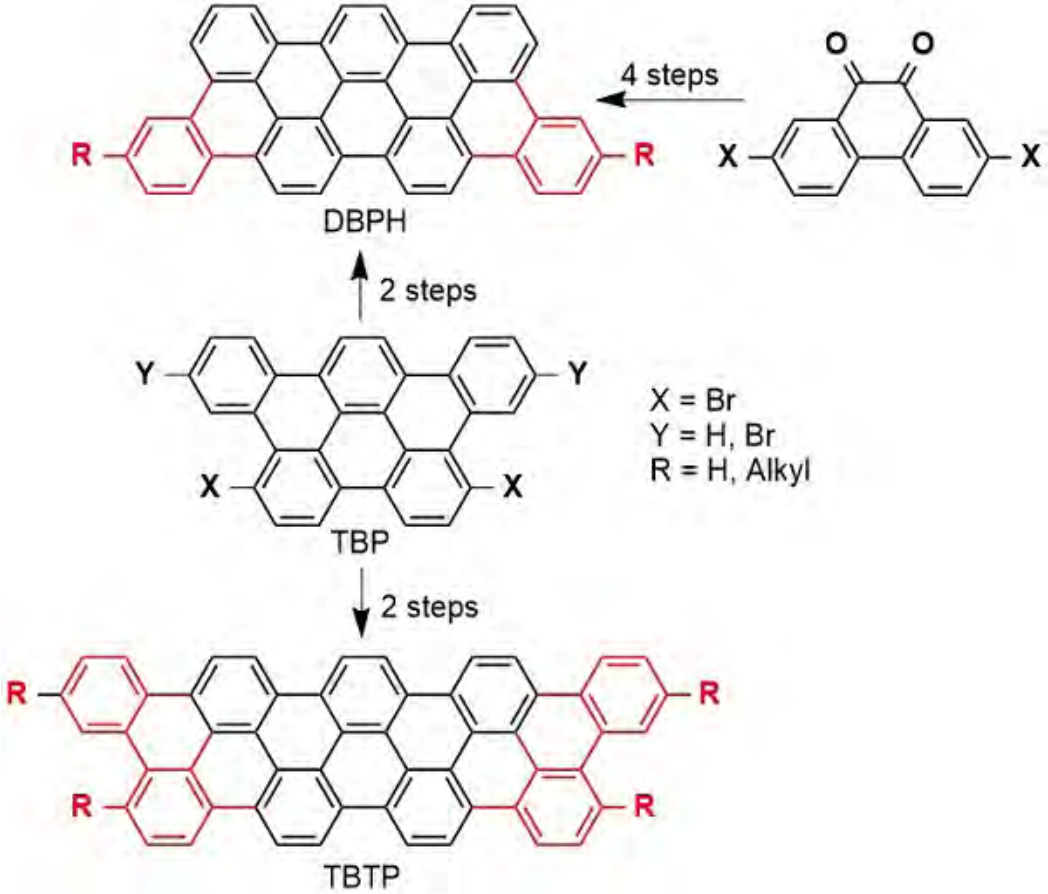
Efficient methods for the synthesis of dibenzophenanthroheptaphene (DBPH) and tetrabenzotriphenylenopyranthrene (TBTP) were developed. As a result, a series of unprecedented derivatives of DBPH (1a-c) and TBTP (2a-b) were conventionally obtained from the Scholl cyclodehydrogenation reaction of their respective tribenzopentaphene synthons. An alternative convergent synthesis of DBPH is also shown herein. The novel compounds were fully characterized by high-resolution matrix-assisted laser desorption ionization time of flight mass spectrometry (HR-MALDI-TOF-MS), nuclear magnetic resonance (NMR), UV-Vis absorption and emission spectroscopy. In addition, density functional calculations were carried out to get insight into the structure and electronic properties of these novel molecules, which corroborates the experimental observations.



General Access to 1,1 and 1,2 Azidolactones from Alkenes using Hypervalent Iodine Reagents

S. Alazet[1], F. Le Vaillant[1], S. Nicolai[1], J. Waser[1]*

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Amino lactones[1] and amino alcohols[2] represent important classes of compounds, which have crucial applications in natural products synthesis and in medicinal chemistry. In recent years, neutral cyclic hypervalent iodine reagents benziodoXoles have emerged as privileged tools in group-transfer chemistry. In addition, being stable crystalline compounds, they are easy to handle and user friendly.[3] In particular, AzidoBenziodoXolones (ABX) and AzidoDimethylBenziodoXoles (ADBX) have demonstrated high efficiency in the transfer of azido group onto organic molecules using metal catalysis. [3] Herein, we describe a versatile synthesis of azidolactones through the cyclization of carboxylic acids onto alkenes, based on photoredox and palladium catalysis. (1,1) and (1,2) azido lactones can be selectively synthesized. Modulating the properties of the catalyst and the benziodoxol(on)e reagent serving as azide source led to either a radical or Lewis Acid mediated process and favored formation of only one of the possible regioisomers starting from the same starting material. These transformations have been carried out under mild conditions using a low catalyst loading and gave access to a large scope of azido lactones.[4]

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Tailor-Made Phthalocyanine with Photocleavable Tags for Interferometry Experiments

D. Alfredo[1], M. Mayor[1]*

[1]University of Basel

Since the dissertation of Louis de Broglie in 1924, where he proposed the wave-matter duality of small particles, such as electrons or neutrons, the study of this phenomenon gained great interest by the scientific community.[1] However, it was never explored in heavier particles and thus, the frontiers between quantum and classical physics could not be established. In the past years, the interference of heavier particles such as fullerenes and phthalocyanines-based compounds has been described[2], pushing the mass limitation to 10`000 amu. However, the studies become more challenging when heavier particles are tested and new approaches are required.

To this aim, the attachment of a photocleavable tag to large objects, such as nanoparticles or biomolecules, is proposed, whose release during the experiment is expected to improve the signal intensity at the detector level. This innovative approach should be tested and optimized first for smaller particles with new optical grids in the interferometry device.[3]

Here we present our new strategy to introduce nitro-aryl protected groups to a phthalocyanine based molecule, to improve the interferometry measurements for the study of massive molecules and to confirm that the photocleavable tag can be split by some new optical grids in the gas phase.

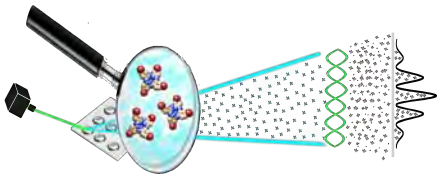

Figure 1: Concept picture of interferometer experiment with nitro-aryl PPG tag (red circles) attached to a phthalocyanine based molecule and the final compound.

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Synthesis of a Diacetylene Bridged Geländer-Type Oligomer

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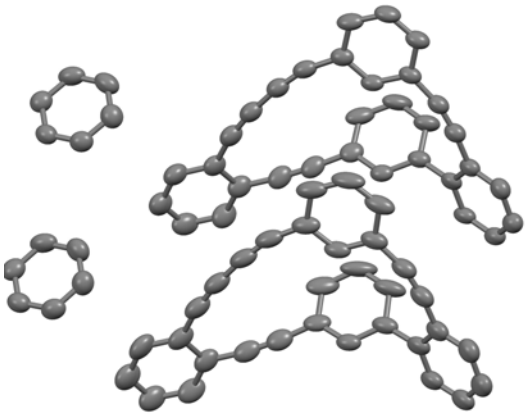
[1]University of Basel

Atropisomers are chiral compounds that do not contain stereogenic centres, but a stereogenic axis. For example, the configuration around a biphenyl axis is an important factor to control the pharmacological properties of bioactive compounds and their usefulness as catalysts in asymmetric synthesis. A new class of atropisomers was introduced in 1998 by Fritz Vögtle and his team: the Geländer-Oligomers[1]. However, his bridged terphenyls are able to rotate around the terphenyl axis. In the classical Geländer oligomers the optically inactive *meso* form is more stable than its enantiomers. Recently, our group reported a novel type of Geländer oligomers that cannot exist as a *meso* form, but still undergo fast racemization. [2-4] To enhance the stability of our new Geländer oligomers, we designed a series of more rigid bridged biphenyls. Consequently, the racemisation process in these atropisomers molecules should be significantly slower. All of our molecules consists of conjugated bridges and aromatic subunits such as benzene, diacetylenes or thiophenes.



X-ray of the diacetylene bridged biphenyl.

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Synthetic Approach to Protein Organophosphorous Chemical Warfare Agent Bioadducts

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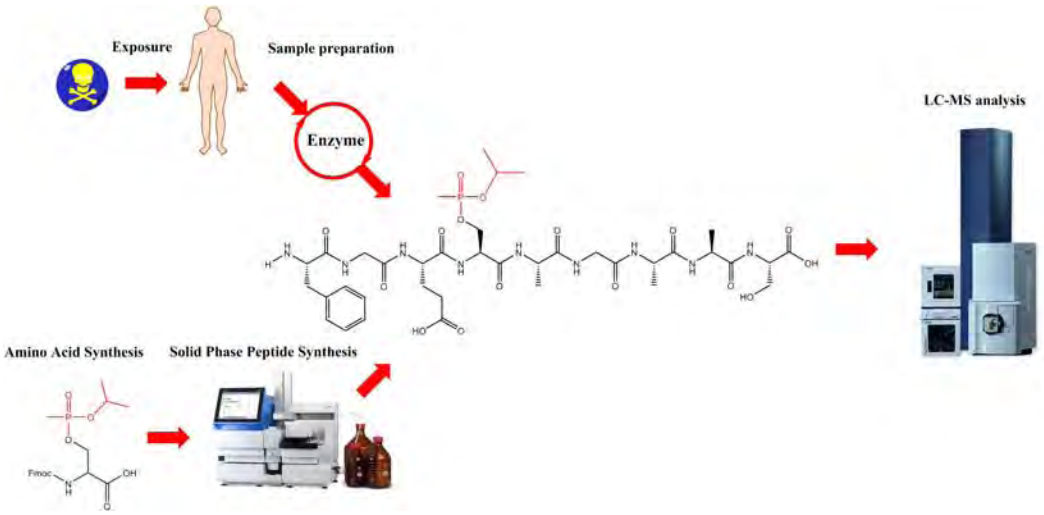
Organophosphorous nerve agents are very potent acetyl- and butyrylcholinesterase inhibitors and their development, production, stockpiling and use is prohibited by the Chemical Weapons Convention. Developed in the 1930s, nerve agent chemical weapons still pose a threat nowadays as recent events in Syria and Malaysia have shown. They react with biomolecules in the body and these bioadducts have an extended half-life compared to the unreacted, degraded and metabolized nerve agents in biological samples. This makes them very attractive as biomarkers, which can be detected using HPLC-MS/MS. Cholinesterase nerve agent adducts can age by losing the *P*-*O*-alkyl chain. The aged adduct is of special relevance since after a certain time it is the major marker found in biomedical samples.



In this work we successfully developed a method, based on a building block approach, to synthesize nonapeptide nerve agent adducts, which are relevant compounds for the analytical verification. Amino acids are phosphylated with nerve agent chloridates and further used in solid-phase peptide synthesis (SPPS). We also developed and investigated two pathways for the synthesis of the aged adduct. Different protecting group strategies were used and an optimized SPPS protocol was developed which takes into account the lability of phosphylated amino acids. In the search for a purificationless preparation of the peptides we identified several side products and solutions to circumvent them were found. Further we synthesized isotope labeled nerve-agent-peptide adducts for their increased value as standards in analysis.

The synthesized adducts can be used as reference standards in the search for evidence of exposure to nerve agents and are successfully in use in the development of biomedical analysis methods at Spiez Laboratory.

Synthesis of Lipid Linked Oligosaccharide Substrates and Inhibitors of a eukaryotic Oligosaccharyl transferase

J. Boilevin[1], A. Ramirez[2], T. Darbre[1], K. Locher[2], J. L. Reymond[1]*

[1]Bern University, [2]ETH Zürich

Here we report the preparation of various synthetic lipid-linked oligosaccharides (LLOs) and their phosphonate analogs. These LLOs act as glycosyl donors in biochemical studies of enzymes involved in protein glycosylation, such as oligosaccharyl flippases (PglK)[1] and oligosaccharyl transferases (OSTs),[2,3] while their phosphonate analogs can be used as inhibitors of the same enzymes. The LLOs were obtained in 16 to 31 steps in a convergent synthesis involving the coupling of a lipid phosphate with a glycosyl phosphate or phosphonate. Inspired by known procedures,[4] we designed an accelerated synthesis of novel α-saturated chiral C_{20}- and C_{25}-polyprenyl phosphates, essential to obtain LLOs reacting with eurakyotic OSTs, using a stereoselective olefination as the key step.[5] Furthermore, we established the synthesis of chitobiose phosphonates from N-acetyl-D-glucosamine involving as key steps C_1-allylation, β-1,4 glycosylation, condensation with diethyl phosphite and deoxygenation.[6] The final products were obtained in 20-50 mg scale in pure form suitable for biochemical and structural studies.

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Highly resolved pure shift NMR experiments for fast spectral assignment

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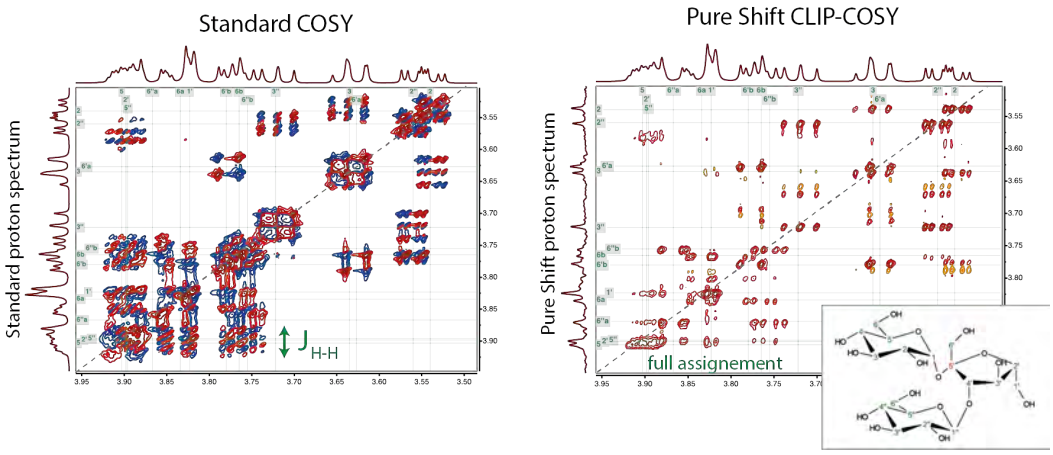
[1]University of Geneva

The analysis of complex NMR spectra poses a real challenge for an organic chemist. Simplification and improved resolution of 1D and 2D proton spectra is highly desired to facilitate the spectral analysis hampered by severe signal overlap over a narrow range of chemical shifts. Recent developments in the NMR methodology provide an easily applicable solution that should facilitate the efforts of chemists seeking to structurally characterize their compounds.

Broadband homonuclear decoupling applied in the indirect dimension of a homonuclear 2D NMR spectrum leads to highly resolved pure shift proton spectra by collapsing the multiplets into singlets [1].

We present here a series of such experiments (2D DIAG [2], CLIP-COSY [3] and TOCSY [4]) with a singlet structure in F1 and multiplets containing the J-coupling information in the F2 dimension. The greatly increased information content of the spectra, relative to standard ^{1}H 2D experiments such as DQF-COSY will be demonstrated in the case of a mixture of carbohydrates.

The great interest in the development of the Pure Shift NMR methodology should equally impact the chemical community as it supplies modern, powerful tool, indispensable for structure elucidation of organic molecules and their mixtures.



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CpRu-Catalyzed Pyridine Dearomatization Through Double Carbene Insertions

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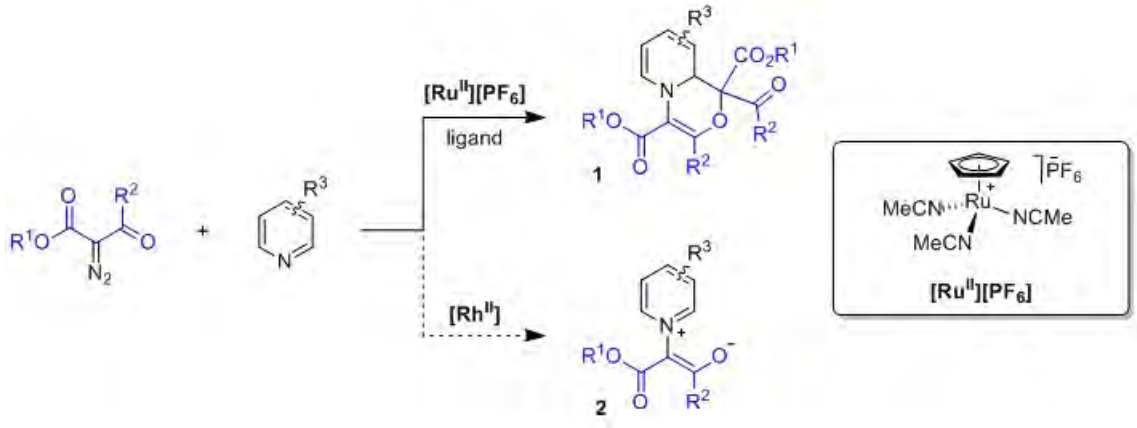
[1]Department of Organic Chemistry, University of Geneva, [2]Department of Quantum Matter Physics, University of Geneva

CpRu complexes are interesting alternatives to copper and dirhodium species for the metal-catalyzed decomposition of diazo compounds.[1] In this context, it has been shown that combinations of $[CpRu(CH_3CN)_3][PF_6]$ and diimine ligands react catalytically with α-diazo-β-ketoesters and allow subsequent condensation, OH and 1,3-CH insertion reactions.[2] Recently, using this catalytic combination, new dioxene motifs were synthetized by enantiospecific *syn* -opening of epoxides.[3]

In a new development that uses electron-poor pyridines and quinolines as substrates, the direct formation of original oxazine moieties **1** is described. Reactions proceed by tandem (double) additions of carbenes and a dearomatization of the azaaromatics. Such a process occurs primarily *via* ruthenium cyclopentadienyle catalysis since, under Rh(II)-mediated reactions, pyridinium ylides **2** are the major adducts.[4] Mechanistic insights will be also presented.



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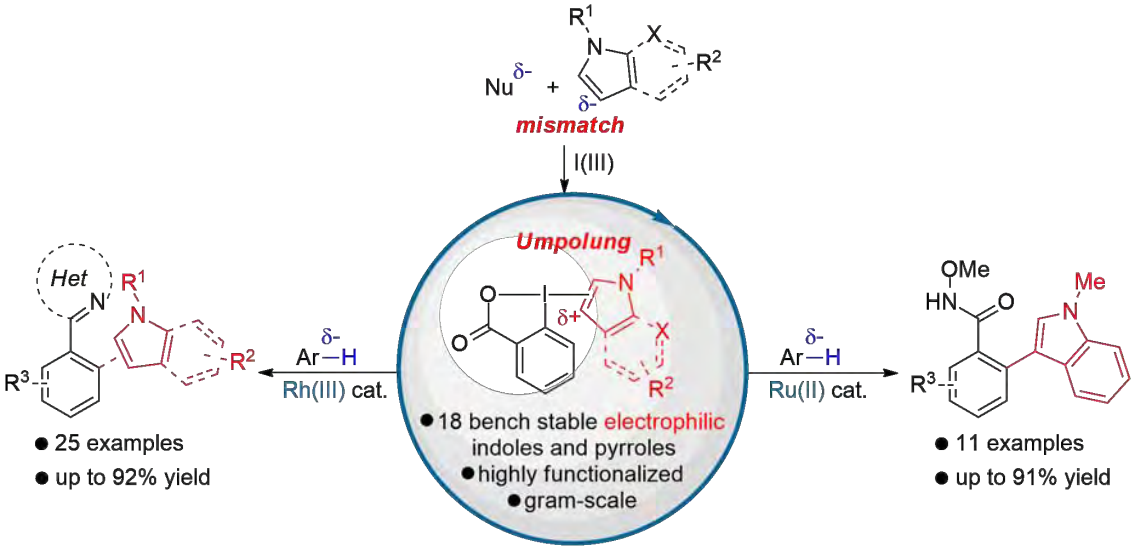
Bench-stable Electrophilic Indole and Pyrrole Benziodoxolone Reagents for C-H functionalization

P. Caramenti[1], S. Nicolai[1], J. Waser[1]*

[1]EPF Lausanne

Amongst all the azoles present in nature, electron-rich pyrroles and indoles are the most ubiquitous.[1] Their application as pharmaceuticals, fragrances and agrochemicals, as well as their relevance as natural bioactive compounds, led to the development of countless methods for both their synthesis[1] and functionalization.[2] While the nucleophilic properties of indoles and pyrroles have been intensively exploited, their "umpolung" into electrophilic synthons remained largely unexplored, although it would be of high interest for the development of new synthetic disconnections. Up to now, few groups reported the synthesis of unstable hypervalent indoles iodonium salts; however the number of applications was limited.[3] We present herein the first synthesis of 18 new bench stable electrophilic indole and pyrrole[4] benziodoxolone[5] reagents. Using these new reagents, rhodium(III) and ruthenium(II) catalyzed C-H "indolization" of nucleophilic arenes were developed to furnish the desired products with complete regioselectivity. The obtained functionalized indoles and pyrroles could not be synthesized using existing metal catalyzed C-H arylation processes and are expected to be useful intermediates for the synthesis of optoelectronical devices and bioactive compounds.



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Fully Substituted α-Aminonitriles as Versatile Intermediates Toward the Synthesis of Alkaloids

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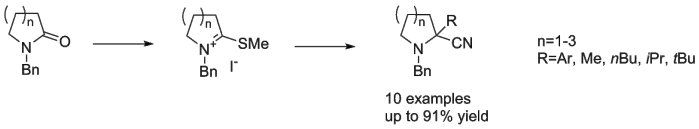
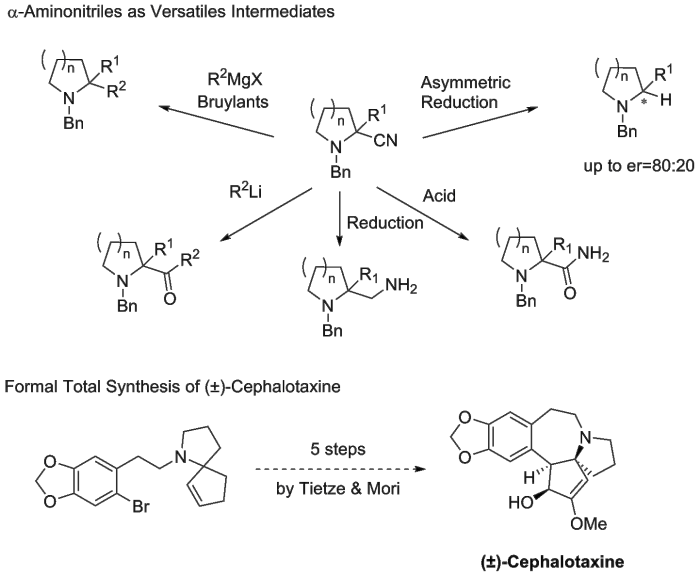
[1]University of Berne

An efficient and robust route toward fully substitued cyclic α-aminonitriles *via* thioiminium ions obtained from cyclic lactams was recently developed in our group. Quaternary α-aminonitriles were obtained in good yields after sequential alkylation-cyanation process.[1]



Nitrile groups are interesting moieties since they can be converted in one step into a variety of other functional groups, including primary amines, ketones, carboxylic acids (or esters), and amides. They are also stable precursors of iminium ions and enamines. Our work focused on the use of those later versatile intermediates and especially their asymmetric reduction.[2] The results are presented herein. This strategy was successfully applied in the formal total synthesis of (±)-Cephalotaxine *via* the preparation of Tietze' s intermediate.[3]



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Isocyanide Insertion of α,α-Disubstituted α-Isocyanoacetate: Development of Multicomponent Reactions for the Synthesis of 5,5-Disubstituted Imidazolones and 5,5,2-Trisubstituted Imidazolones

A. Clemenceau[1]

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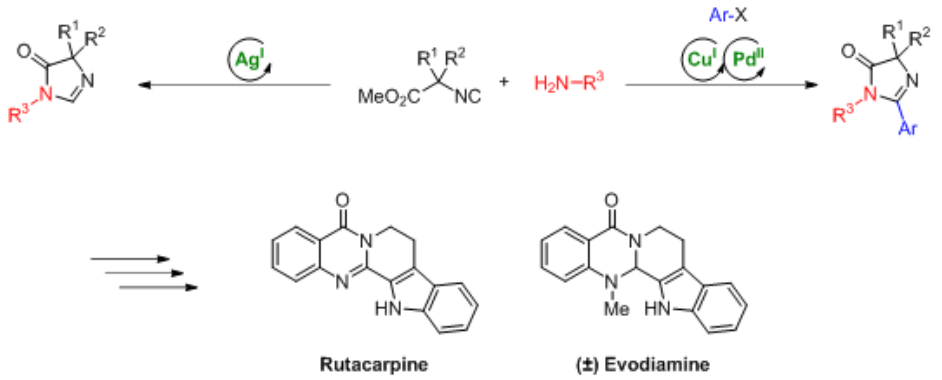
Abstract: The synthesis of various 5,5-disubstituted imidazolones and 5,5,2-trisubstituted imidazolones has been achieved. Two different methodologies have been developed by taking advantage of the rich reactivity of the isocyanide group. The reaction of α,α-disubstituted isocyanoacetate, primary amines in the presence of a catalytic amount of $AgNO_3$ afforded 5,5-disubstituted imidazolones in good to excellent yields. On the other hand, a bimetallic Cu^{I}/Pd^{II} catalyzed reaction of α,α-disubstituted isocyanoacetate, primary amines and aryl halide afforded 5,5,2-trisubstituted imidazolone in moderated to good yield. Finally, total synthesis of Rutacarpine and (±) Evodiamine featuring this methodology have been accomplished.



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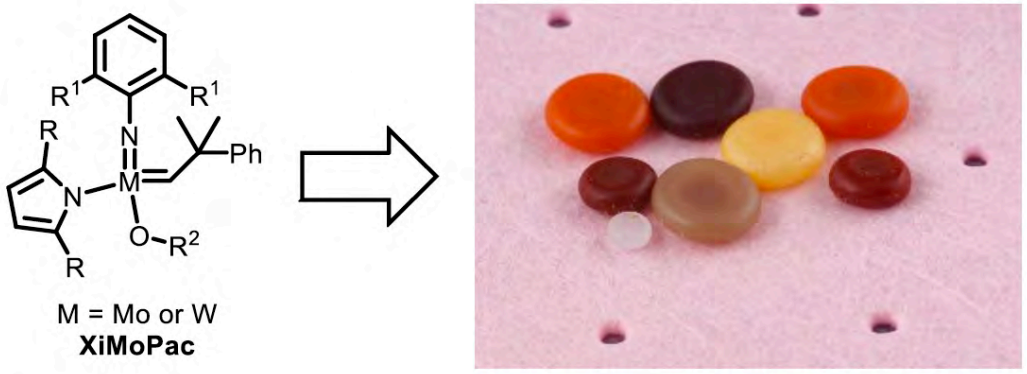
Easy-to-use bench stable preweighed pellets with Mo- / W- metathesis catalysts

J. B. Czirok[1,2], A. Bucsai[1,2], L. Ondi[1,2], G. Frater[1,2]

[1]XiMo AG, Horw, Lucerne, Switzerland, [2]XiMo Hungary Ltd, Budapest, Hungary

XiMo Hungary Ltd and XiMo AG were established in 2011. Our mission is to demonstrate[1,2] that the Mo-/W-catalyzed olefin metathesis is an expedient tool when combination of effectiveness, selectivity, affordability and sustainability is required in research, development or industrial production.

To this end, XiMo in collaboration with its Hungarian partner developed industrial technology for the multi kilogram-scale synthesis of Mo- and W-based metathesis catalysts. Moreover to facilitate their use and make them readily available for the entire chemical community, XiMo invented a physical stabilization for these often moisture sensitive organometallic complexes.



Formulation of the catalysts into easy-to-use paraffin pellets made Mo-/W-catalyzed olefin metathesis a readily accessible technology which can be carried out on the benchtop of every laboratory. Versatility of these newly developed reagents called XiMoPacs is illustrated by various reactions e.g. bifunctionalization of renewables, stereoselective transformations carried out outside the glovebox.[3,4] The improved air stability of the catalysts results from the advanced formulation allows synthetic chemists to carry out high-throughput discovery effortless.

The approach chosen to target the catalysts moisture sensitivity turned out to be broadly applicable which allows the transformation of divers sensitive reagents into their stable user-friendly alternatives as it is demonstrated by the formulation of the highly reactive and pyrophoric triethylaluminum or the highly air sensitive palladium based cross coupling catalysts.

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Trinorbornane: Expanding the Chemical Space

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[1]University of Basel

One of the challenges of synthetic organic chemistry is structural diversity, in particular, at the level of small molecular building blocks.[1] New compounds and compound classes in the size range of small molecules (less than 500 g/mol) are of interest since they may display unforeseen properties and lead to new structural motifs.[2] The computer-assisted enumeration of the chemical space addresses this challenge by generating all possible molecules for a give number of atoms (excluding hydrogen) under consideration of specific rules.[3] One particular example found in the chemical universe database (GDB-11) is the tetracyclic hydrocarbon **1**. This esthetically pleasing, *C*2-symmetrical, chiral molecule is comprised of three partially superposed norbornyl units. It is surprising that this unstrained molecule has not yet been synthesized in over 100 years of norbornane chemistry.[4] The goal of this project is to synthesize and study the properties of hydrocarbon **1**. The total synthesis of this compound as well as the crystal structure of the dimer will be presented.

1

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Natural Non-Canonical Strigolactones - New Efficient Syntheses

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Strigolactones are phytohormones playing pleiotropic roles in plant growth and development.[1] Canonical strigolactones contain a tricyclic ring system and several synthetic approaches have been disclosed. In contrast, non-canonical strigolactones do not contain this tricyclic structural motive and their synthetic access has been so far limited. We report an efficient synthetic access to this novel class of strigolactones.

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Enantioselective Ni(0)-Catalyzed Annulation of Pyridones

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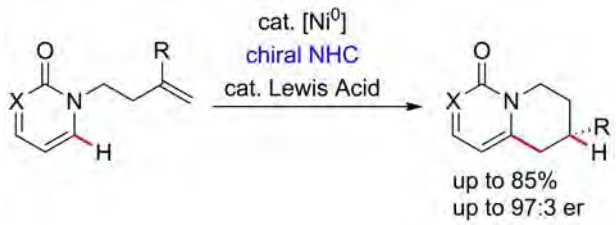
[1] EPF Lausanne

Pyridones are common structural motifs in natural products exhibiting diverse biological activity and hence the pyridine core is found in a variety of pharmacologically potent compounds.[1] In particular 1,6-carboannulated pyridones are found in several biologically active natural products and furthermore annulated 2-pyridones can serve as access to valuable bioactive indolizidine and quinolizidine alkaloids.[2]

Based on the work of Nakao and Hiyama our group has developed a Nickel catalyzed *endo*-selective annulation protocol of *N*-alkenyl-2-pyridones.[3,4] Cooperative Lewis Acid/Ni(0)-catalysis and application of *N*-heterocyclic carbene ligands enabled C-H activation and subsequent regioselective cyclization under formation of a stereocenter. A variety of known chiral NHCs failed to achieve a highly enantioselective transformation, highlighting the need for further ligand development in this area.

We have developed a class of chiral NHCs which enable the formation of valuable 1,6-annulated 2-pyridones in high enantioselectivity.



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Synthesis and Characterization of Assorted Heterocycles Based 6H-indolo[2,3-b] quinoxaline

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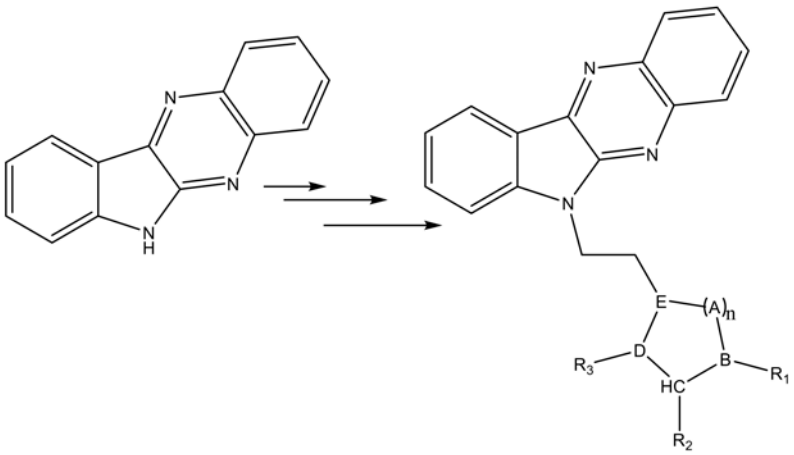
Efficient methodology for the synthesis of unrecorded series of heterocycles based indolo[2,3-*b*] quinoxaline sub-structure is reported. Indolo[2,3-*b]* quinoxaline heterocycles have been synthesized by employing ethyl 3-(6H-indolo[2,3-*b*]quinoxalin-6-yl)propanoate as starting material. The precursor -H-indolo[2,3-*b*]quinoxalin-6-yl)propanehydrazide 3 was synthesized by reaction of ethyl 3-(6H-indolo[2,3-*b*]quinoxalin-6-yl)propanoate with hydrazine in refluxing ethanol.

The structures of synthesized compounds were confirmed on the basis of their elemental analyses and spectral results (IR, MS, 1H and 13C NMR).



A, B, C, D = C, O, N, S
R1, R2, R3 = aliphatic, aromatic, heterocyclic

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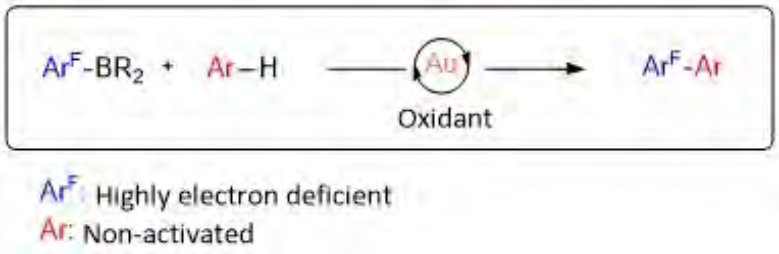
Gold-Catalyzed Oxidative C-H Arylation with Organoboron Reagents

A. Genoux[1], M. Hofer[1], R. Kumar[1], C. Nevado[1]

[1]University of Zurich

Direct C(sp^2)-H functionalization/arylation has attracted increasing interest since the substrates do not need to be functionalized in contrast to classical cross-coupling reactions.[1] Despite significant progress,[2] multiple challenges including low reactivity, lack of selectivity in the activation of an specific C(sp^2)-H bonds and formation of homocoupling products (Ar^1Ar^1, Ar^2Ar^2) are still difficult to master.[3] Herein, we report an efficient synthesis of biaryl compounds through a gold-catalyzed oxidative cross-coupling of arenes with strong electron-deprived aryl boronates. Non-symmetric biaryls can be synthesized with high levels of regio- and chemoselectivity under additives and directing groups-free conditions.[4] This methodology shows orthogonal reactivity and complementary scope with respect to already existing methods.[5]



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Alleno-Acetylenic Cage (AAC) Receptors: Chiroptical Switching and Enantioselective Complexation

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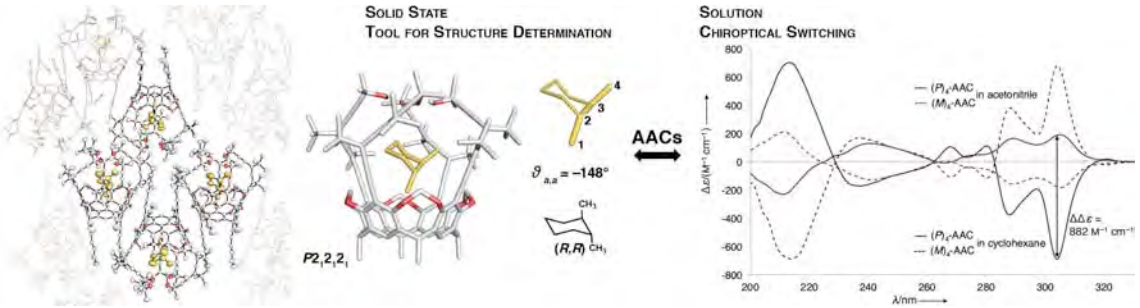
[1]ETH Zurich

Molecular recognition in its modern definition implies that two molecules interact with each other in a specific way, with the result that their pairwise potential energy decreases more significantly than in any other interaction mode.[1] Studies on model systems have greatly helped to decipher and quantify interactions that drive enantioselective binding of chiral guests by natural and artificial host systems, establishing fundamental concepts, such as Fischer's shape complementarity and the three point interaction model.[2]

Herein, we present enantiomerically pure alleno-acetylenic cage (AAC) receptors which undergo solvent-dependent binary conformational switching in solution between a closed cage form, stabilized by a fourfold H-bonding array, and an open form.[3] Controlled switching between the open and closed state, combined with strong conformational dependence of the chiroptical properties allows for selective complexation and quantification of small molecule complexation. The highly confined chiral cavity of the closed conformation renders AACs an ideal model system to study the subtle interplay between space occupancy, conformation and chiral recognition. This system enabled the first enantioselective inclusion complex of a chiral alicyclic hydrocarbon based purely on dispersive interactions and optimal space filling, confirming the validity of the 55 % occupancy rule.[4]

AACs assemble in the solid state to a porous network forming inclusion complexes with otherwise non-crystalline small molecules allowing for the first time the structural elucidation of 1,2-substituted cyclohexanes in their (di)axial conformation in the solid state. In combination with solution studies and computational studies this allows for the investigation and quantification of interaction and conformation at the molecular level [5].



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Ligand-Enabled Pd(0)-Catalyzed Enantioselective C−H Functionalization of Ketene Aminal Phosphates

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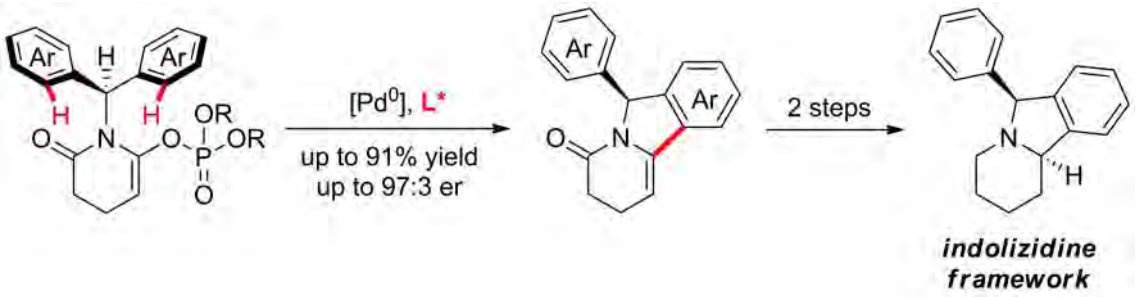
[1]EPF Lausanne

Catalytic C–H functionalizations have emerged as a central theme within organic chemistry.[1] In particular, the stereocontrolled functionalization of C–H bonds is a promising field, as it allows for the rapid generation of structural complexity from simple precursors.[2] Enantioselective Pd(0)-catalyzed C–H arylations and alkenylations have been one of the main focuses in our research group.[3] Whilst aryl and alkenyl triflates have been successfully employed as electrophiles, attempts at using the more elaborate ketene aminal triflates have proven futile due to their instability. In contrast, the corresponding ketene aminal phosphates are readily accessible from cheap and less toxic reagents, exhibit enhanced stability and therefore qualify as potentially suitable starting materials.

Herein, we present Pd(0)-catalyzed enantioselective C–H functionalizations of ketene aminal phosphates toward chiral *N*-heterocycles. A new class of electron-rich phosphine ligands designed for this transformation enabled the synthesis of the desired products in good yields and enantioselectivities. Overall the present reaction allows access to the indolizidine scaffold via a new disconnection.



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Development of an Esterase-Targeted, Cell-Trappable and Photoactivatable Diazoindanone Rhodol for Live Cell Imaging and Stochastic Optical Reconstruction Microscopy

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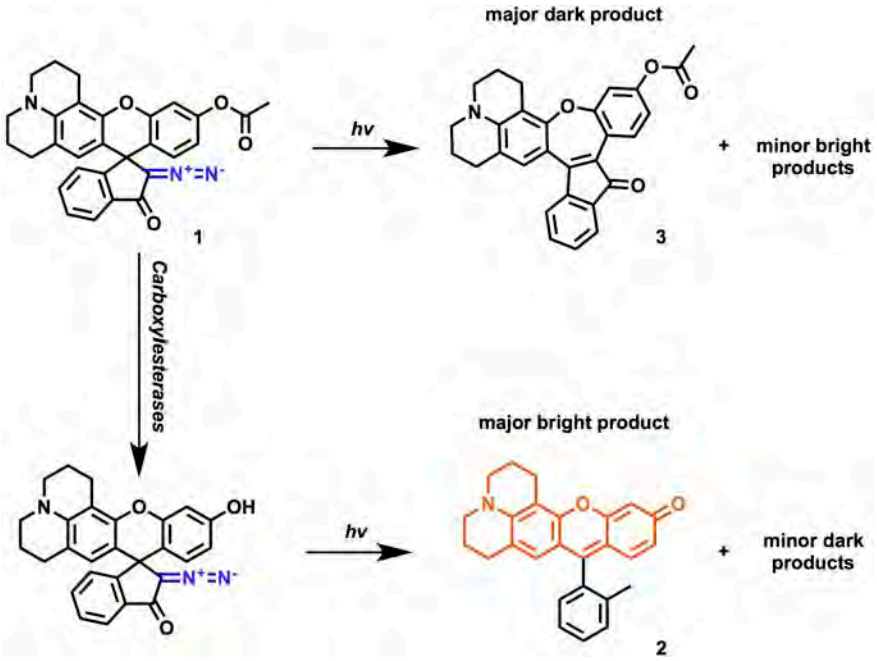
In this study, we discuss the photochemical properties and applications of a double-activatable fluorophore **1**, which is based on a previously reported scaffold.[1] Upon enzymatic deacetylation and subsequent irradiation with 405 nm laser, **1** yields a major fluorescent photoproduct **2**. In the absence of the preceding enzymatic deacetylation, however, mostly non-fluorescent compound **3** is obtained. A bright signal can thus only be attained after photoactivation of **1** in the presence of intracellular carboxylesterases. Moreover, under constant light irradiation, we expect fast photoconversion of **1** immediately after deacetylation. This mechanism is useful for *in situ* mapping of enzymatic reactions and tracking of carboxylesterases with stochastic optical reconstruction microscopy (STORM). In this talk, we will furthermore discuss the development of a *steady state* technique for STORM that allows acquisition of a large number of images without intensity decay, by constantly replenishing the intracellular reserves of **1**. With this novel technique, we aim to obtain higher labeling densities and record super-resolution time-lapse sequences of slow cellular processes.



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Copper-Catalyzed Enantioselective Oxy and Amino-Alkynylations of Diazo Compounds

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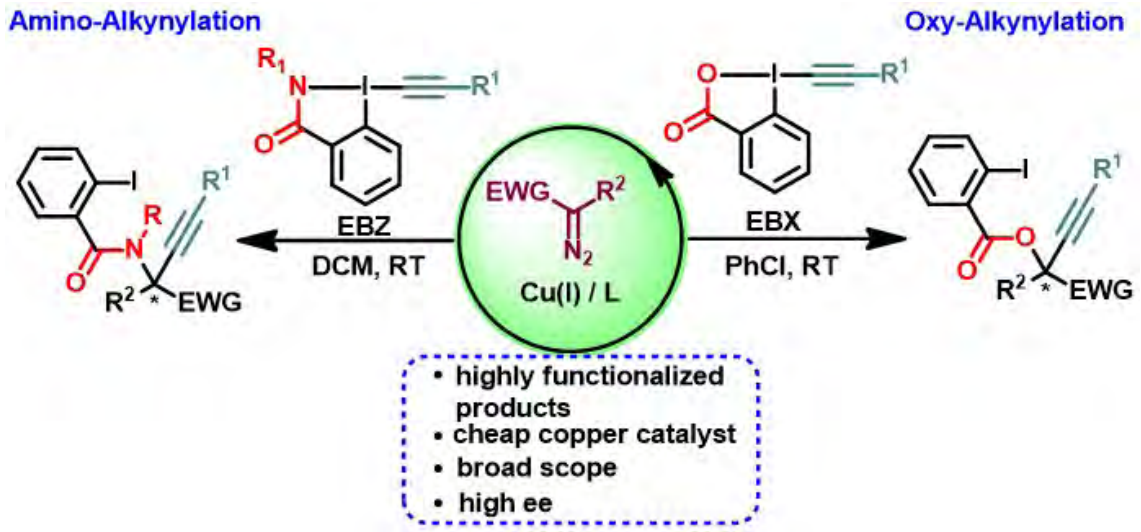
[1]EPF Lausanne

Alkynes are ubiquitous in both naturally occurring and synthetic organic compounds, which have found widespread applications in biology and materials sciences.[1a] Consequently, their synthesis is of fundamental interest in organic chemistry. One of the most often used methods for the synthesis of alkynes consists in the addition of acetylides on electrophilic positions in molecules. In contrast, the Umpolung-based alkynylations, the addition of alkynes onto nucleophiles, have been less investigated. In this context, hypervalent iodine reagents have been used for electrophilic alkynylations due to their exceptional reactivity.[1b,1c] However, alkynylations using hypervalent reagents generates one equivalent of an iodoarene as a side-product, leading to low atom economy. In 2016, our group developed an unprecedented copper-catalyzed oxy-alkynylation of diazo compounds based on the use of EthynylBenziodoXolones (EBX) reagents.[2a] This reaction is highly practical and proceeds under mild conditions for a broad range of substrates with high atom economy. Herein, we report the successful development of an enantioselective variation of this transformation, which represents the first example of asymmetric copper-catalyzed addition of both a nucleophile and an electrophile onto a carbenoid intermediate.[2b] The reaction exhibits broad scope towards both diazo compounds and hypervalent iodine reagents. The functional groups introduced during the transformation served as easy handles to access useful building blocks for synthetic and medicinal chemistry, such as α-hydroxy propargylic esters and vicinal diols, without loss of enantioselectivity. Furthermore, we have developed an enantioselective copper-catalyzed amino-alkynylation of diazo compounds using Ethynylbenziodazalone (EBZ) under mild conditions, giving access to unnatural amino acids.[2c]



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Towards an Excited State Hammond Postulate

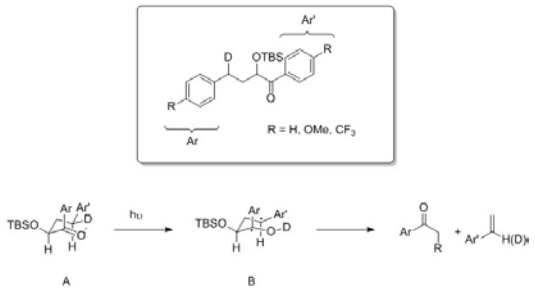
F. Harvey[1], C. G. Bochet[1]*

[1]University of Fribourg

Classical thermal reactions can be studied by estimating the location of the transition state along the reaction coordinate using Hammond's postulate. Photochemical reactions, however, lack simple qualitative tools to determine the location of the conical intersections (CI) on the potential energy surfaces leading to the products, and complex quantum mechanics calculations are necessary in order to predict the outcome of a reaction.

In previous experimental work on photolysis of *o*-nitrobenzyl derivatives[1,2], it was observed that the Bell-Evans-Polanyi principle was followed, and the position of the CI varied with the substituents. This suggests that Hammond's postulate may be applicable to CIs in the excited state.

In order to probe the influence of the position of the CI with respect to the energy level of the reactants and products, the following reaction system was designed:



A reactant-like CI should be stereochemically biased (A), whereas a product-like CI should be stereochemically unbiased (B). Ar and Ar' influence both the energy level of the reactant and the position of the CI.

The above substrates will be synthesised then submitted to a series of photolyses, and the ratio of styrene/styrene-*d*1 will be analysed as a function of the substituent Ar'. The reaction will be performed for both isomers in order to take into account the isotope effect.

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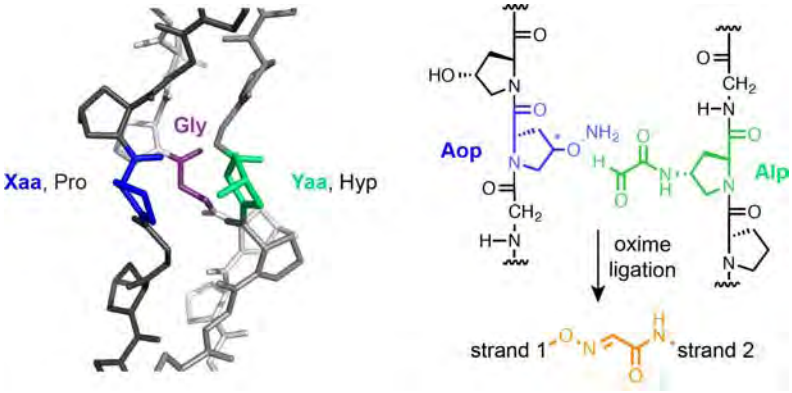
Cross-Linked Collagen Triple Helices by Oxime Ligation

N. B. Hentzen[1], L. E. Smeenk[1], J. Witek[2], S. Riniker[2], H. Wennemers[1]*

[1]Laboratorium für Organische Chemie, ETH Zürich, CH-8093 Zürich, [2]Laboratorium für Physikalische Chemie, ETH Zürich, CH-8093 Zürich

Collagen is the most abundant protein in mammals and the main component of their extracellular matrix.[1,2] The chemical synthesis of collagen is attractive for medical and nanotechnological applications[3] since it can provide access to structurally defined and functionalizable materials.[4,5] However, the bottom-up design of materials mimicking the fibrous structures of natural collagen is hampered by the entropically unfavorable assembly of short single strands into triple helices.[1,2] To lay the foundation for higher-ordered assemblies of collagen model peptides (CMPs), we covalently connected CMPs by oxime linkages between aminooxyproline (Aop)[6] and 2-oxoacetamidoproline (Alp) derivatives placed in neighboring strands. The cross-linked strands folded into collagen triple helices with remarkably high thermal stabilities (T_m ~80°C). The design of the cross-links was guided by an analysis of the conformational properties of Aop, studies on the stability and functionalization of Aop-containing collagen triple helices, and molecular dynamics calculations. Our findings open new opportunities for the design of functional collagen-based materials forming by the sticky-ended assembly of structurally well-defined triple helices.



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Homochiral recognition and excellent atroposelectivity in the oxidative coupling of cationic [4]helicenes

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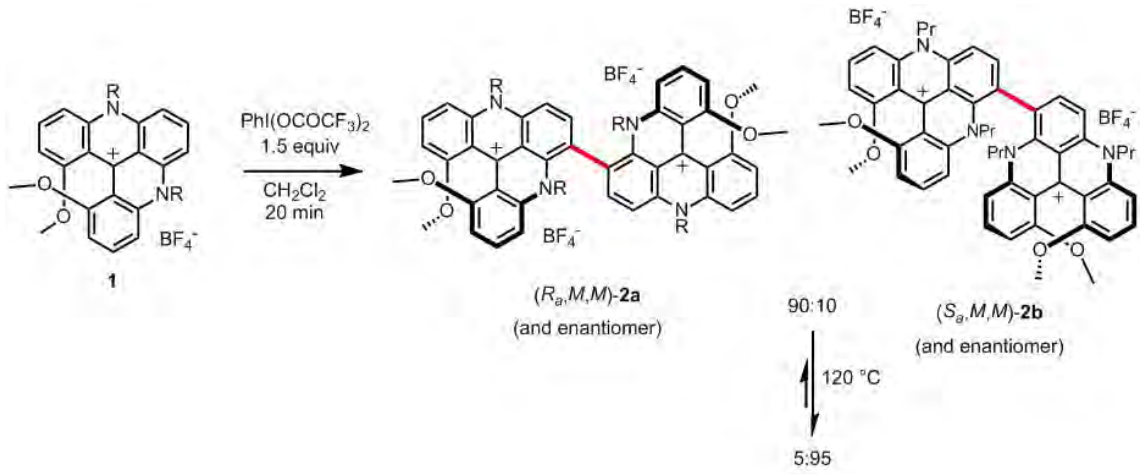
[1]Department of Organic Chemistry, University of Geneva, [2]Departement of Molecular Design and Engineering, Nagoya University, Japan, [3]Departement of Analytical Chemistry, University of Geneva

Homochiral recognition by non-covalent interactions is a rather common phenomenon in helical structures.[1] However, this asymmetric trend has been hardly exploited for the formation of covalent bonds between helicenes.[2] Herein, we report the oxidative coupling of the cationic [4]helicenes **1,** which proceeds with a quasi exclusive homochiral recognition (96% selectivity) to yield chiral (racemic) dimers of type **2**. The lack of *meso* isomers is established by HRMS cross-over experiments. Moreover, this reaction is highly atroposelective forming preferentially (R_a,*M*,*M*)-**2a** over (S_a,*M*,*M*)-**2b** (and enantiomers) (ratio 90:10). The interconversion barrier from **2a** to **2b** is 26.4 kcal/mol at 60 °C in dmso-d_6. Strong chiroptical properties are observed, for both **2a** and **2b**, in the red visible region.



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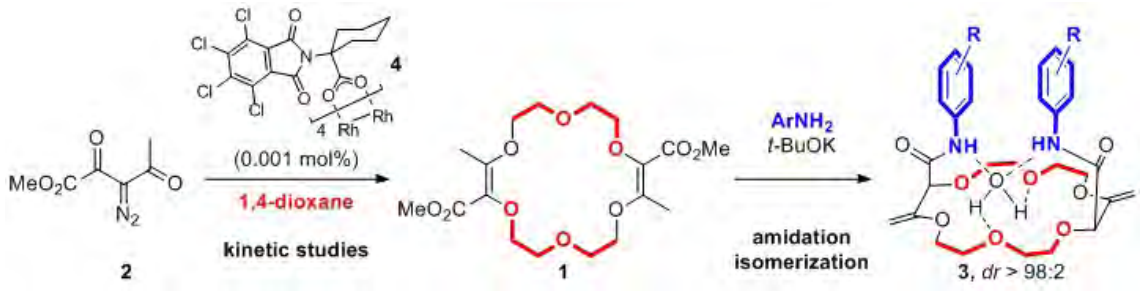
Kinetics of Rh(II)-Catalyzed α-Diazo-β-Ketoester Decomposition for Polyether Macrocycle Synthesis and Straightforward Access to Ditopic Cryptands

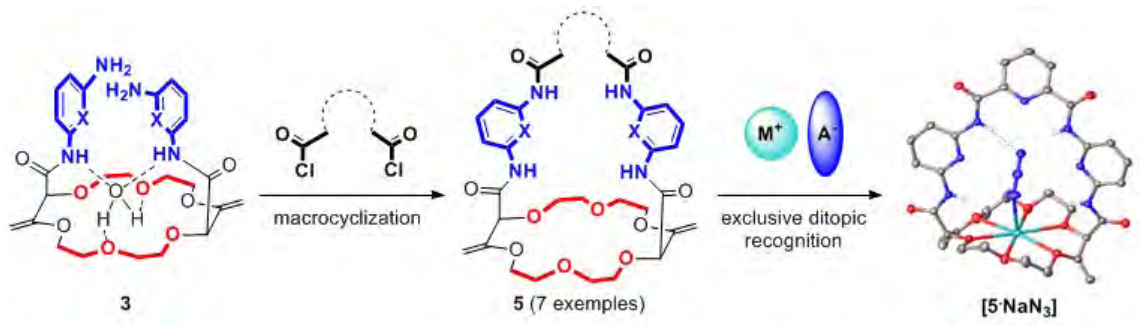
A. Homberg[1], D. Poggiali[1], S. K. Ray[1], J. Lacour[1]*

[1]Department of Organic Chemistry, University of Geneva

Previously, our group reported the synthesis of polyether macrocycles **1** by [3+6+3+6] condensations of α-diazo-β-ketoesters **2** and 1,4-dioxane under dirhodium catalysis at 1 *M* concentration.[1] By reactions of **1** with aromatic amines under basic conditions, chiral crown ethers **3** can then be obtained in a single step by tandem amidation / olefin transposition.[2] These compounds **3** are effective pH-insensitive nanosensors and ratiometric luminescent switches.[3] For these and other applications, preparation of **1** in large quantities was required. Kinetics of decomposition of diazo **2** with various rhodium(II) catalysts and different amounts of dioxane were studied by *in situ* FT-IR monitoring. These mechanistic results showed the superior activity of Hashimoto-Ikegami-like catalyst **4**. Reaction conditions were optimized leading to a decrease of catalyst loading (down to 0.001 mol%) and a scale-up of the reaction up to 20 grams of **1** in a single batch.[4]



Herein, we present in addition a new family of cryptands **5** readily synthesized in two steps from compounds **1**. Hosts **5** display a ditopic character towards sodium salts of linear anions in particular as demonstrated by ^{1}H NMR spectroscopic and solid state structural analysis.



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Molecular Recognition of Cyclohexanes Derivatives by Alleno-Acetylenic Cages

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Monosubstituted and *trans*-1,2-disubstituted cyclohexane derivatives can be selectively cocrystallized in a (di)axial conformation within alleno-acetylenic cage receptors [1,2]. Remarkably, the dihedral angle between the two axial substituents shows a substantial deviation (by up to 40°) from an idealized dihedral angle of 180°. Similarly large deviations from the idealized dihedral angle were detected in theoretically optimized *isolated* cyclohexane derivatives. A comparison of these structures to structures of cyclohexane derivatives optimized within the receptor revealed that encapsulation hardly affects the structure of the guest molecules. The electron densities of the host-guest complexes were qualitatively analyzed [3] to uncover the nature of the interactions between the guest and the host. The analysis revealed that no major steric clashes between the guest and the receptor are present, further illustrating the perfect shape complementarity between the ensemble. The guest instead exhibits allover enveloping dispersive interactions with the receptor. Mono- and dihalocyclohexanes additionally exhibit halogen bonding interactions to the receptors. A recent study by Riley *et al.* [4] revealed that C-X···π interactions such as those present between the guest and the resorcine[4]arene core of the receptor have low geometrical requirements. We additionally studied the geometrical requirements of C-X···||| interactions to quantify the strength of the halogen bonding interactions between the guest and the alleno-acetylenic arms of the receptor. The arrangement of the halocyclohexanes within the receptor allows for a significant amount of halogen bonding to the resorcine[4]arene core as well as to the alleno acetylenic arms of the receptors. Hereby, the halogen bond strength decreases with the atomic number of the halogen substituent. Altogether, this study presents the first example of a chiral recognition study purely based on weak halogen bonding and dispersive interactions between the guest and the receptor.

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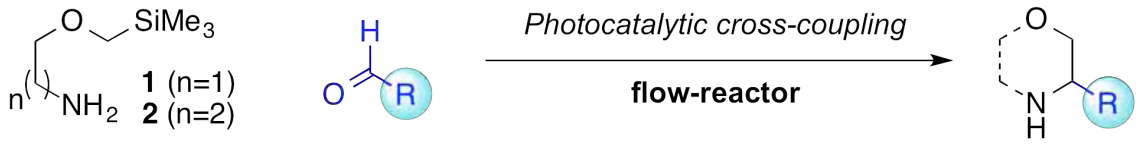
Continuos Flow Synthesis of Morpholines and Oxazepanes with Silicon Amine Protocol (SLAP) Reagents and Photoredox Catalysis

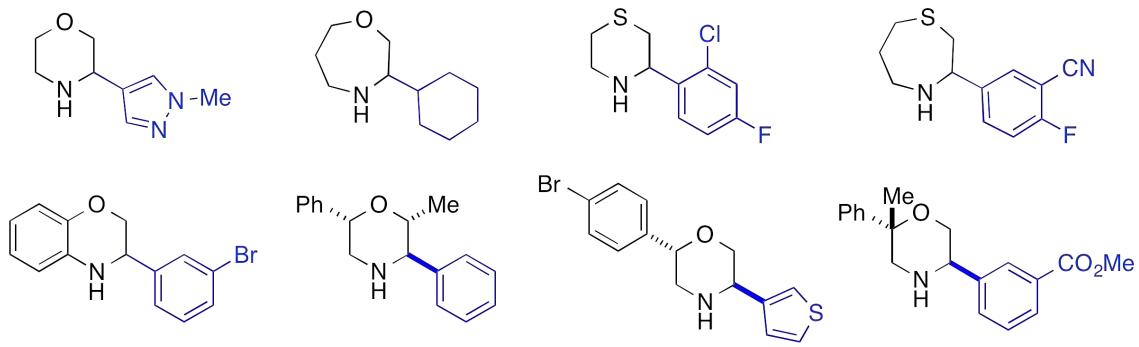
M. K. Jackl[1]

[1]ETH Zürich

A protocol for the synthesis of various substituted morpholines, oxazepanes, thiomorpholines and thiazepanes has been developed by photocatalytic cross-coupling of easily accessible silicon amine protocol (SLAP) reagents and commercially available aldehydes under continuous flow conditions. This reaction tolerates a variety of functional groups and gives access to a tin-free alternative to the related SnAP (tin amine protocol) chemistry.



To establish the utility of this method, a total of 32 examples with different substitution patterns and a variety of functional groups were prepared. The advantage of the continuous flow setup for reaction scale up was demonstrated by reaction on a 5.0 g scale simply by expanding the reaction time.



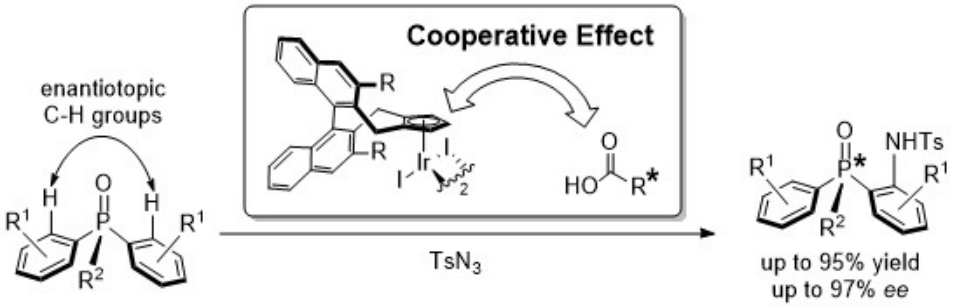
Chiral Cp^XIr(III) Catalyzed C-H Amidation Leading to P-Chiral Arylphosphine Oxides

Y. Jang[1], M. C. Dieckmann[1], N. Cramer[1]*

[1]Laboratory of Asymmetric Catalysis and Synthesis, EPF Lausanne

Organophosphorus compounds with *P*-stereogenic centers are valuable motifs in pharmaceuticals, agrochemicals, organocatalysts and ligands.[1] Only a limited number of catalytic enantioselective approaches have been developed to access molecules with a *P*-stereogenic center.[2]

Chang *et al.* reported an Ir(III) catalyzed amidation of arylphosphine oxides that proceeds in modest enantioselectivities.[3] We report that our recently developed chiral Cp^XIr(III) complex,[4] in combination with a chiral carboxylic acid, provides a highly selective C-H amidation process. A very strong cooperative effect between the chiral Cp^XIr(III) complex and the carboxylic acid was discovered. This proved to be pivotal for high enantioselectivities and yields.



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A Photochemical Amplifier Based on Self-Immolative Spacer

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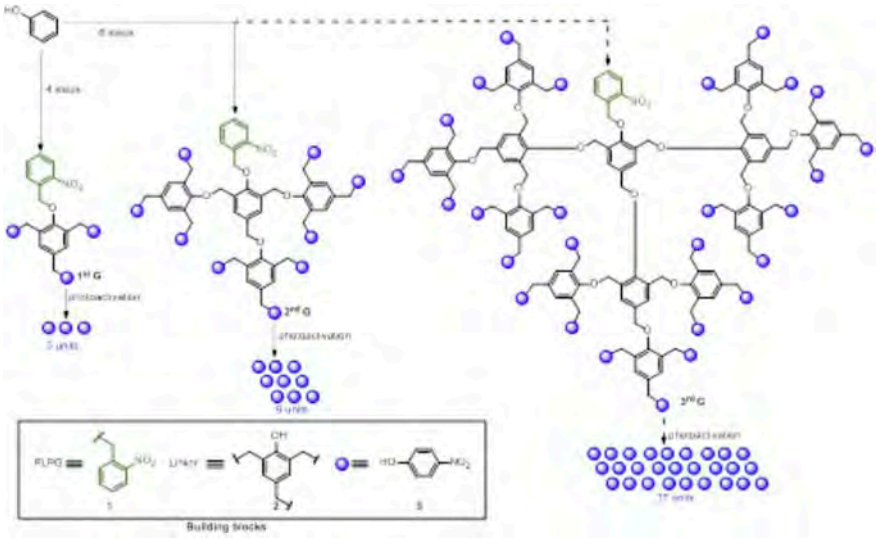
[1]University of Fribourg

A molecular amplifier could be defined as a device capable of transforming a weak chemical (physical) input into a large chemical output. In this work, we will present a molecular amplifier capable of releasing multiple chemical entities upon activation by a single photochemical event (scheme 1).



Our system could be used as 1) indicator 2) solubilizing agent and 3) as controlled drug delivery system, and is based on readily available building blocks, such as 1) a photolabile protecting group (2-nitrobenzyl) to induce an increase of the stability in the system, 2) a self immolative linker to connect two or more entities and be able to fragment upon activation and 3) nitrophenol, a colored releasable group.

Magnesium-Catalyzed Electrophilic Trifluoromethylation: Facile Access to All-Carbon Quaternary Centers in Oxindoles

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[1]Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology, ETH Zurich

3,3-Difunctionalized oxindoles are widely recognized as valuable synthetic intermediates which form the core of many natural products and synthetic analogues. As part of ongoing research in our laboratory towards the development of novel methodologies to access organofluorine compounds via electrophilic trifluoromethylation [1,2], we anticipate that the introduction of fluoroalkyl groups into the oxindole moiety will provide access to new drug candidates with unique biological properties.

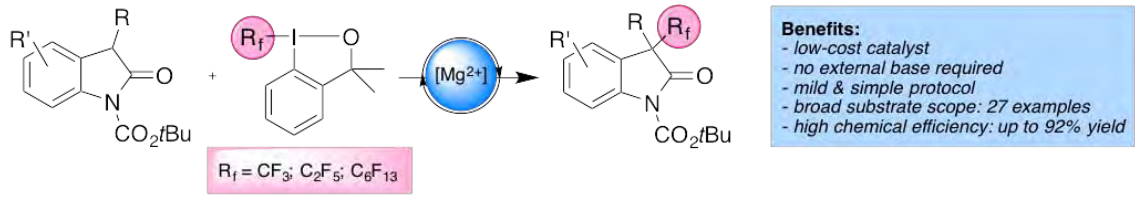

Figure 1. Magnesium-catalyzed perfluoroalkylation of 3-substituted oxindoles.

Herein we describe the first example of direct electrophilic trifluoromethylation of 3-substituted oxindoles under $MgBr_2 \bullet Et_2O$ catalysis using hypervalent iodine reagents as the source of the fluoroalkyl group (Figure 1) [3]. $MgBr_2 \bullet Et_2O$ plays a dual activation role, activating both the trifluoromethylation reagents and the oxindole substrates. Furthermore, this Lewis acid is commercially available, inexpensive, and generates non-toxic by-products. We have also demonstrated an asymmetric variant of the reaction through the use of a chiral ligand, and in addition to trifluoromethylation, other perfluoroalkyl groups could be introduced with a similar level of efficacy. An investigation of the reaction mechanism points towards the involvement of radical species as the likely reactive intermediates. This synthetically valuable transformation constructs challenging perfluoroalkylated quaternary carbon centers under very mild reaction conditions and demonstrates excellent functional group tolerance. The discovery that simple magnesium salts can effectively activate hypervalent iodine-based compounds provides new routes towards the realization of novel perfluoroalkylation methodologies. The introduction of other functional groups through the use of hypervalent iodine reagents in combination with Lewis acid catalysis is currently under investigation.

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Radical Reaction of Sulfonyl Chloride in Access to Vinyl Sulfones

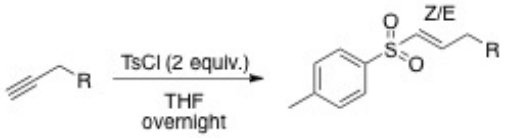
I. Kovalova[1], C. S. Gloor[1], F. Denes[2], P. Renaud[1]*

[1]University of Bern, [2]University of Nantes

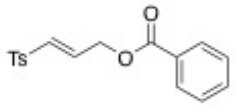
Vinyl sulfones are extensively used as a building blocks for total synthesis of natural products[1]. They can be prepared by olefination reactions[2], elimination from *α*- or *β*-substituted sulfones[3], oxidation of vinyl sulfides[4] or others.

Their preparation from terminal alkynes is highly attractive. However, such transformations have only been reported *via* hydrometallation process[5].

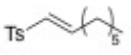
Herein we describe selective introduction of vinyl sulfones. We generate the sulfonyl radical from *p*-toluenesulfonyl chloride and add it onto alkyne.



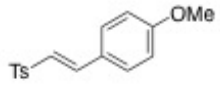
Method A: reflux, DLP (0.5 equiv)
Method B: light irradiation (45-48˚C)



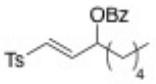
Method A: 83%, Z:E = 2.4:1
Method B: 90%, Z:E = 1.5:1



Method A: 97%, Z:E = 1.2:1
Method B: 80%, Z:E = 2.2:1



Method A: 35%, Z:E = 1:1.0
Method B :23%, Z:E = 1:1.1



Method A: 90%, Z:E = 2.6:1
Method B: 80%, Z:E = 2.9:1

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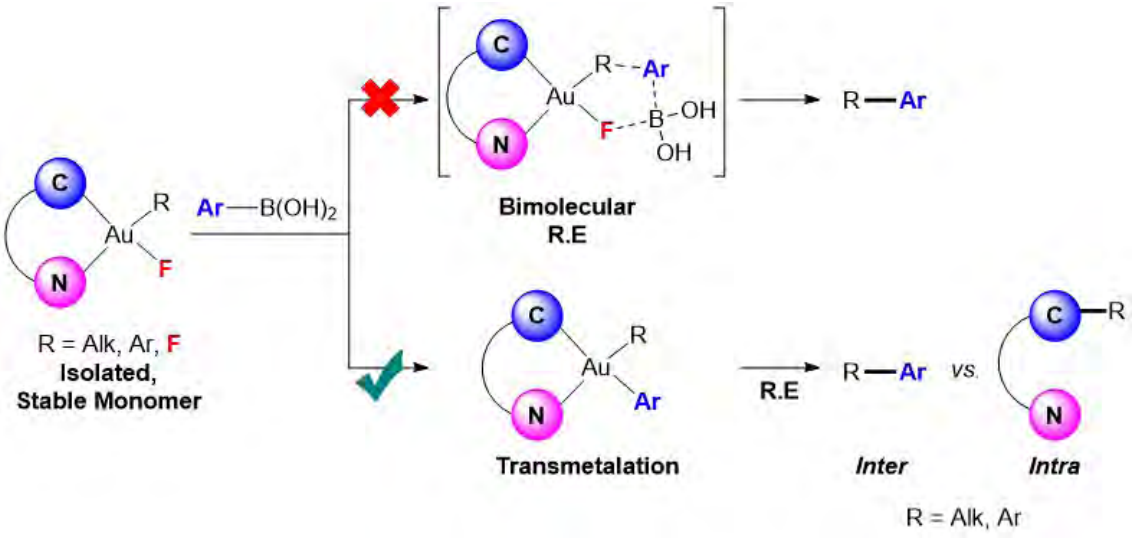
How Boronic Acids Interact with Gold(III)-Fluorides: A Mechanistic Investigation

R. Kumar[1], C. Nevado[1]*

[1]University of Zurich

In the past decade numerous Au^{I}/Au^{III} catalyzed transformations have been developed in order to construct C-C, C-X and C-F bonds.[1] Many of these reactions use Selectfluor (an electrophilic fluorinating reagent) as a sacrificial oxidant and aryl boronic acids as coupling partners. In these processes, it has been proposed that gold(III) fluorides intermediates react with boronic acids via a bimolecular reductive elimination pathway or transmetalation followed by reductive elimination to deliver the product.[2-3] However, due to highly reactive nature of Au^{III}-F species, these mechanistic proposals still lack experimental support. Here, we present our results on the preparation and characterization of a series of novel (C^C^N) and (C^N)-stabilized gold(III) fluorides in monomeric form and an in depth study on their reactivity with aryl boronic acids where we observe and isolate the transmetalation product.[4-5] Importantly, this novel (C^C^N) pincer type gold(III) framework enable the synthesis of first stable gold(III) formate complex which open a way towards homogeneous gold catalyzed dehydrogenation of formic acid.[6]



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B-Alkylpinacolboranes as Precursors for C-Centered Radicals

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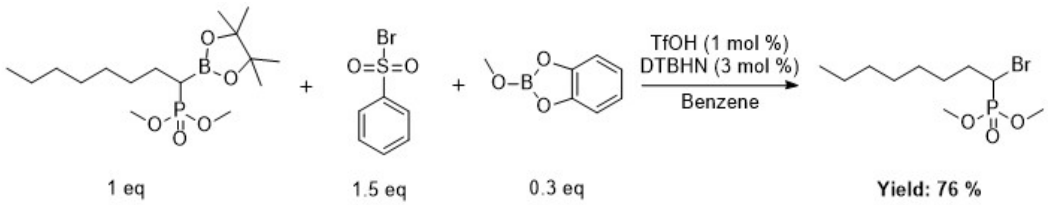
[1]University of Bern

Organoboranes, commercially available or easily prepared via hydroboration of olefins, represent a very attractive source of alkyl radicals [1]. The *B*-alkylpinacolboranes are easy to handle since they are moisture- and air-stable. For instance, they can be readily purified by flash chromatography [2]. The generation of radicals from *B*-alkylpinacolboranes requires formation of ate complex followed by treatment with a strong oxidant [3]. We report here that *B*-alkylpinacolboranes can be used as radical precursors in the absence of oxidizing agent, using *in situ* transesterification process. Highly efficient chain reactions, leading to the products of allylation, bromination as well as hydrogen atom transfer, are reported. Substrate, obtained by hydroboration of unactivated or activated by both EWG or ERG, can be successfully modified by suggested method. Even *α*-chloro, *α*-iodo and *α*-phosphonato radicals provided high yields.



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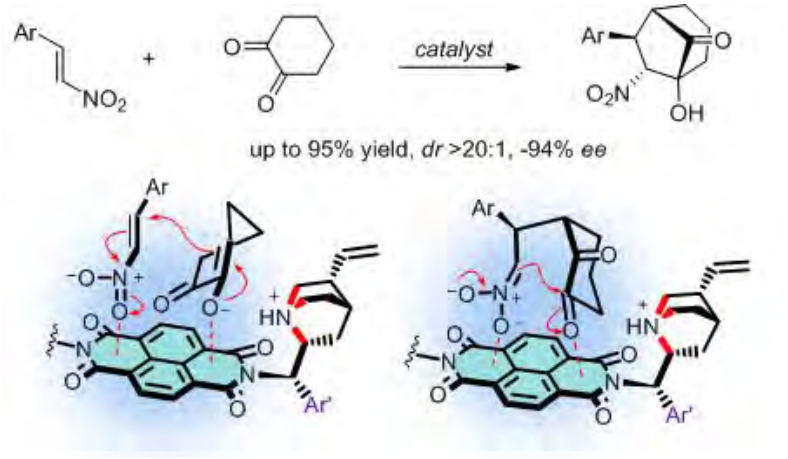
Asymmetric Anion-π Catalysis: Diastereospecific Michael/Henry Reactions for Bicyclic Prodcuts with Quarternary Chiral Centers on NDI Surfaces

L. Liu[1], Y. Cotelle[1], N. Sakai[1], S. Matile[1]*

[1]University of Geneva

The functional relevance of anion-π interactions has been integrated into viarious systems including anion recongnition, binding, transport and catalysis.[1] The general ideal to use anion-π interactions in catalysis is to stabilize negatively charged intermediates and transition states on π-acidic surfaces. The concept has been explicitly proved validate[2] first in 2013 and later on realized also for complex reaction systems including asymmetric enamine activation,[3] iminium cascade processes[4] and the first anion-π enzyme.[5] As a new step forward, we are now extending anion-π catalysis to a more complicated cascade system to prepare bicyclic compounds with four stereogenic centers including one quaternary carbon center from achiral substrates. Hybridization of cinchona alcaloids with naphthalenediimides (NDI) affords a new anion-π cinchona fusion catalyst which results in much improved diastereoselectivity and enantioselectivity compared to previous catalysts and controls. Moreover, the cascade transformation was also realized by artificial anion-π enzyme in neutral water. Evidence in support of the relevance of anion-π interactions in catalyzing the cascade process include increasing stereoselectivities and velocities in the presence of π-acidic surfaces and inhibition with anions in order of NO_3^-, Br^-, BF_4^-, PF_6^-.



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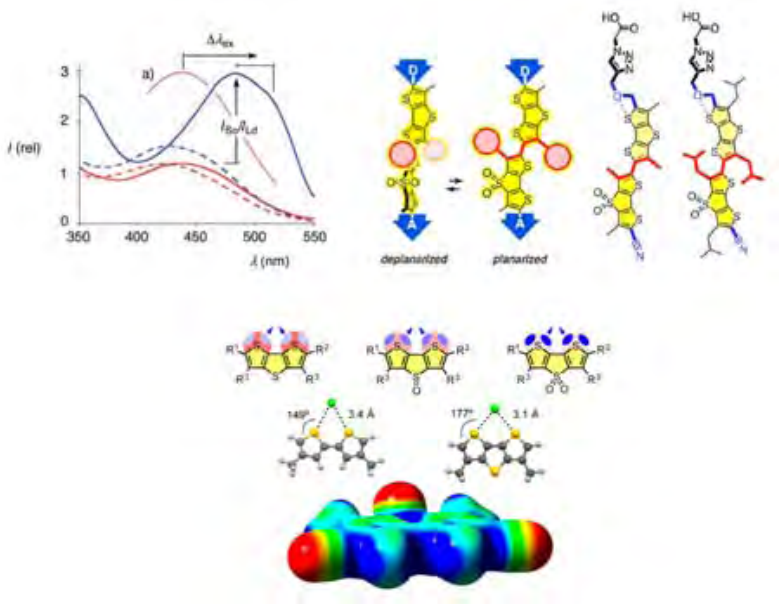
Mechanosensitive Membrane Probes and Beyond

M. Macchione[1], S. Soleimanpour[1], A. Goujon[1], N. Sakai[1], S. Matile[1]*

[1]University of Geneva

To understand the behaviour and the features of biological cellular membranes, mechanosensitive[1] fluorescent “flipper” probes have been developed. Combining the chromophore polarization and ground state planarization is the key to determine and visualize the lateral organization.[2] Improvement on chemical stability have been fully achieved through head group engineering using copper-catalyzed alkyne–azide cycloaddition (CuAAC) approach in a way to have probes ready for use in biology.[3] Introducing “bulky” lateral chains on dithienothiophene (DTT) moyeties that affects the molecule’s twisted state, such as isobutyl groups, strongly hinders the planarization in the first excited state producing a probe that fails to respond to changes in membrane order.[4] However the new more effective synthetic approach introduced, has been highly useful to develop DTT units as privileged motif to study anion transport[5] and catalysis[6] with chalcogen bonding. Expanding the length of the current flipper to “trimer” and “tetramer” units is now in progress with the aim to create a new generation of fluorescent membrane probes.



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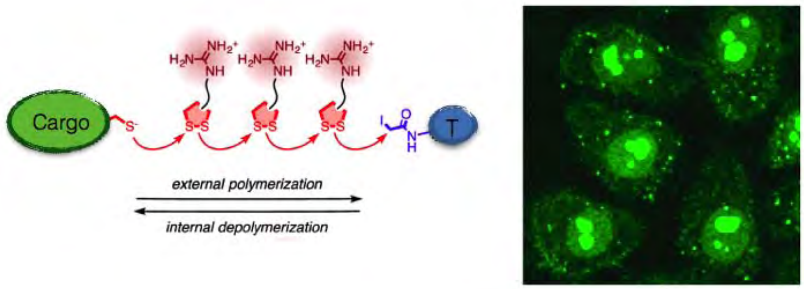
Cell-Penetrating Poly(disulfide)s

P. Morelli[1], E. Bartolami[1], S. Soleimanpour[1], L. Zong[1], N. Sakai[1], S. Matile[1]*

[1]University of Geneva

Substrate-initiated cell-penetrating poly(disulfide)s (si-CPDs) are emerging as innovative molecular transporters due to their ability to deliver cargoes without cytotoxicity, through a proposed novel counterion thiol-mediated uptake mechanism [1]. Inspired by surface-initiated polymerization, we developed a conceptually new approach to grow CPDs on a variety of substrates through ring-opening disulfide exchange polymerization, in solution and under mild conditions. Thiolated fluorescent probes are commonly used as initiators, cyclic disulfides as monomers and iodoacetamides are used as terminators. Like cell-penetrating peptides (CPPs), CPDs are enriched with guanidinium groups which help the delivery of the cargo through the formation of micellar pores in the membrane. However, CPDs also contain a poly(disulfide) backbone which, through dynamic covalent disulfide-exchange, helps to increase uptake and, most importantly, eliminates the cytotoxicity which is common to many CPPs. Due to this dual uptake mechanism, our best performing CPDs were able to reach the nucleus of HeLa cells in 15 minutes and at nM concentration. Once internalized, the poly(disulfide)s are readily depolymerized thanks to the high concentration of glutathione in the cytosol. Recently, CPDs were used to achieve protein delivery through biotin-streptavidin technology [2], leading to the development of a general method to deliver other types of cargoes such as monobodies. CPD sidechain functionalization [3] is used to introduce more solubilizing groups such as sugars is currently undergoing to prevent aggregation during protein delivery.



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Ketenimines from Isocyanides and Allyl Carbonates: Palladium-Catalyzed Synthesis of β,γ-Unsaturated Amides and Tetrazoles

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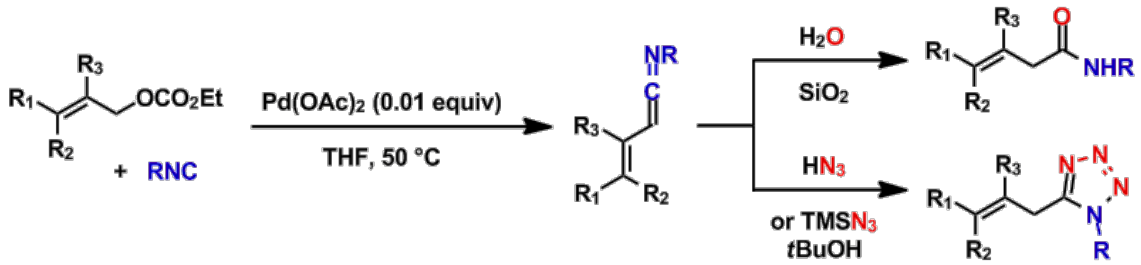
The reaction of allyl ethyl carbonates with isocyanides in the presence of a catalytic amount of $Pd(OAc)_2$ provided ketenimines through β-hydride elimination of the allyl imidoylpalladium intermediates. The insertion of the isocyanide into the π-allyl Pd complex proceeded via an unusual η^1-allyl Pd species. The resulting ketenimines were hydrolyzed to β,γ-unsaturated carboxamides during purification by flash column chromatography on silica gel or converted in situ into 1,5-disubstituted tetrazoles by [3+2] cycloaddition with hydrazoic acid or trimethylsilyl azide.



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† These authors contributed equally.

Helical Oligophenyl Geländer Molecules

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[1]University of Basel

Polycyclic aromatic compounds (PACs) have been of interest to fundamental researchers and material scientists since the concept of molecular chemistry was born. Particularly, chiral PACs have attracted much attention for material applications due to their unique physical properties (e.g. UV absorbance, semiconductance). In addition, their structural beauty brings an exciting and interesting challenge for chemists [1]. Recently, our group succeeded in synthesising a novel type of Geländer molecule with a terphenyl backbone and a bannister oligomer [2,3]. The success of this synthesis inspired us to further investigate this unique structure by extending our research into three new pathways. The first, is the synthesis of longer oligomers (Figure 1a), in order to achieve one full turnover of the helical structure and to determine, if the chiral information is further transferred to the next phenyl unit. Secondly, we designed a fully hydrogen-carbon Geländer oligomer (Figure 1b), to obtain a closer-packed system, we expect this to prohibit racemisation and allow the separation of enantiomers with a chiral packed HPLC column. Our ultimate goal and third pathway is to introduce a molecular platform. For instance a 9,9′-spirobifluorene group would provide the Geländer system with an anchoring group capable of immobilizing the helical Geländer molecule onto a metal surface (Figure 1c). This would lead to surface functionalization and investigations using scanning tunneling microscopy (STM).

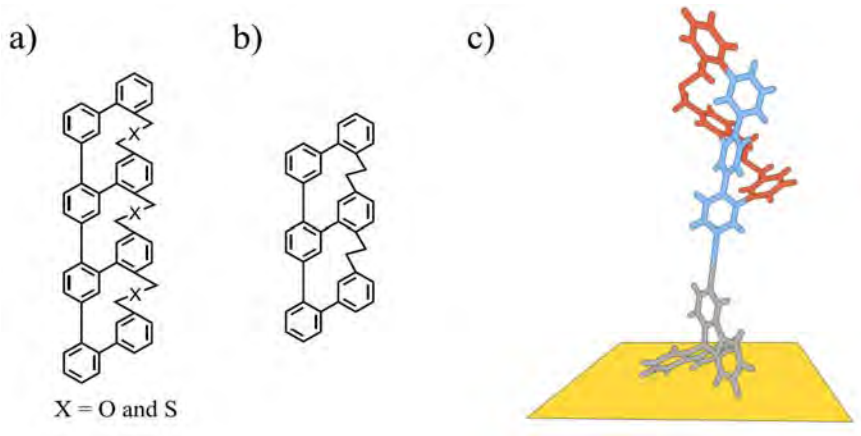

Figure 1: Three novel systems to investigate properties of chiral polycyclic aromatic compounds. a) Design of the higher-order oligomer species. b) Helical Geländer system containing only hydrogen and carbon atoms. c) 3D illustration of the immobilized Geländer molecule on a metal surface.

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Process Optimization for the Scale-Up of a Ribose-Derivative

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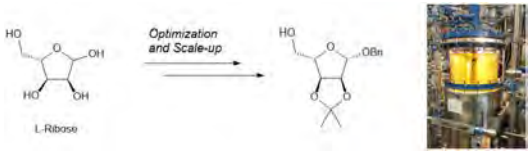
Lysosomal storage diseases constitute a group of inherited metabolic disorders caused by the deficiency of lysosomal functions. Over time, accumulation of lysosomal enzyme substrate is observed in patient's tissues and organs causing irreversible damages like rapid nerve degeneration and short life expectancy. Dorphan SA is developing an iminosugar derivative as a treatment for a subset of the lysosomal storage diseases.



Here, we present our work, which consists in enabling and optimizing the first reactions out of the 11 chemical steps in the synthetic route leading to the active pharmaceutical ingredient. In the course of this work, a DoE was performed to increase the yield of the reactions and get a robust and efficient process. The reactions were further evaluated regarding thermal safety, analytical characterization and costs. A preliminary scale-up run is discussed as well.

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Free-radical transformations involving organoboranes and hydrazones

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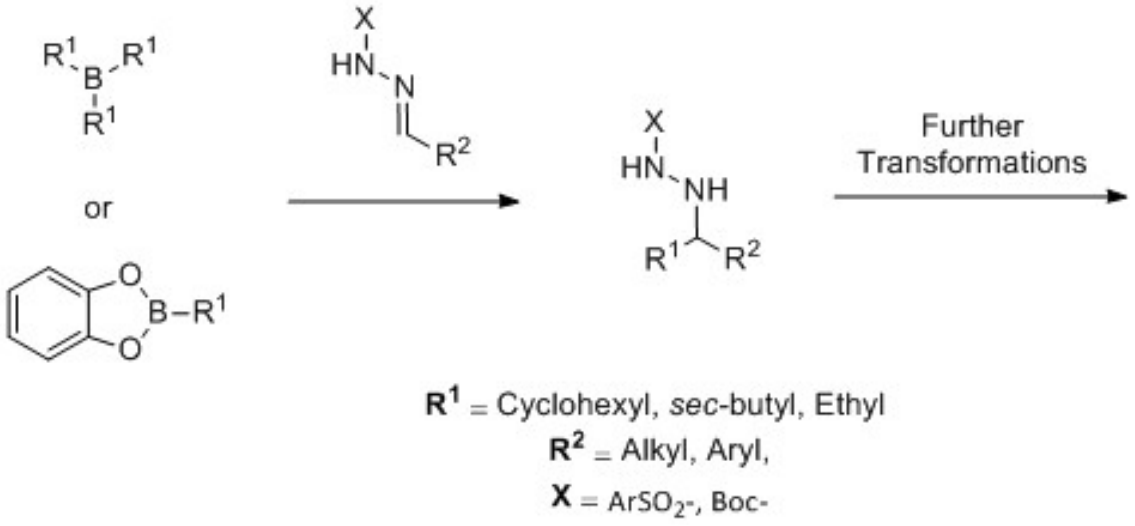
[1]University of Bern

Trialkylboranes and alkyl-catecholboranes (commercially available or prepared by hydroboration of olefins) represent a versatile source of alkyl radicals which can be used in different synthetic transformations.[1] The nucleophilic character of the radicals generated makes possible their addition to suitable electrophilic traps.[2] In this work we describe the addition of alkyl radicals to hydrazones which by turn can serve as a method for the functionalization of olefins. Additionally, we present insights about how the corresponding products can be further transformed into compounds of synthetic value.



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Bioinspired Electro-Photoswitchable Grippers: Radical Control of Molecular Machinery

J. Milic[1], M. Zalibera[2,6], J. Nomrowski[3], D. Neshchadin[4], L. Ruhlmann[5], C. Boudon[5], O. S. Wenger[3], A. Savitsky[2], W. Lubitz[2], G. Gescheidt[4]*, F. Diederich[1]*

[1]ETH Zurich, [2]Max Planck Institute for Chemical Energy Conversion, [3]University of Basel, [4]TU Graz, [5]University of Strasbourg, [6]Institute of Physical Chemistry and Chemical Physics, FCHPT STU

Molecular grippers feature a binary conformational switch in response to external stimuli that results in reversible encapsulation of smaller molecules. This behavior makes them applicable as delivery systems, sensors, elements in nanorobotics, and memory devices.[1,2] However, the control of molecular machinery by physical stimuli, such as voltage or light, is a prerequisite to their application.[2] We therefore developed electro-photoswitchable molecular grippers based on resorcin[4]arene cavitand platforms equipped with quinone (Q) walls that were inspired by the role of semiquinones (SQ) in natural photosynthesis (Figure 1).[2,3] The SQ state was generated electrochemically, via cyclic voltammetry, and photochemically, by using $[Ru(bpy)_3]^{2+}$ as a photocatalyst. The properties were studied by UV-Vis spectroelectrochemistry, EPR, and transient absorption spectroscopy, in conjunction with DFT calculations.[2,3] It was shown that these systems adopt an open conformation in the oxidized Q state until redox interconversion to the paramagnetic SQ radical anion provides the stabilization of the closed form through hydrogen bonding.[3] Their tunable magnetic properties and enhanced binding affinities, along with remarkable reversibility and responsiveness to electrical and electromagnetic stimuli, set the stage for a new generation of artificial molecular machines and devices based on this switching concept in the future.

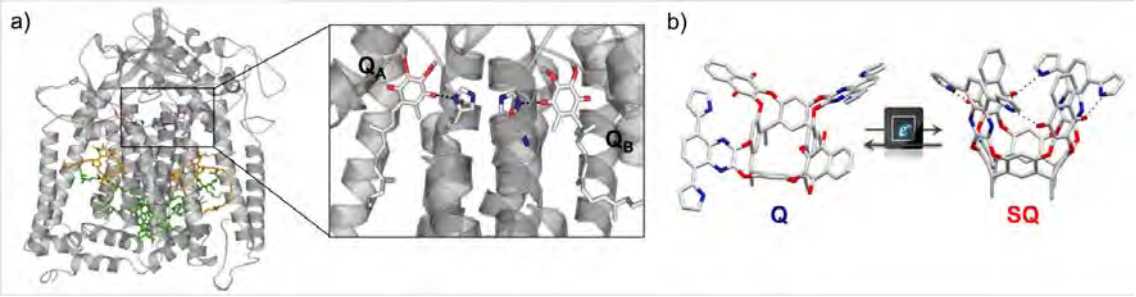

Figure 1. Schematic representation of the (a) photosynthetic reaction center of *Rb. sphaeroides* (PDB 1DV3) that inspired the design of (b) electro-photoswitchable molecular grippers.

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Membrane-assisted Processing of Organometallic Catalysed Reactions: From Down-Stream to Continuous Processing

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Homogeneous organometallic catalysis is a technique that has achieved a high level of maturity, and is often an indispensable and reliable method of synthesizing molecular entities produced within several chemical industry sectors. [1] These complexes, however efficient as they are, can be expensive and difficult to remove after reaction. This naturally urged the industry to place emphasis on increasing catalyst turnover numbers (TON) and catalyst recovery. [2]

In this context, recent decades have witnessed a significant growth in industrial interest in solvent based separations using membranes stable to organic solvents,[3] due in part to the non-thermal, hence mild and energy efficient nature of the technique. Recent membrane developments include ceramic membranes with modified top-layers designed to effect separation not simply on size exclusion alone, but by also making use of solvent – membrane – solute interactions. These membranes open up the possibility of designing the membrane surface and the catalyst ligands to achieve the desired rejection profile and reaction performance. The mild nature of membrane separations makes them particularly suited to integration within reaction systems in which reaction and separation occur simultaneously, a particularly salient example being catalyst recycling.[4]

This contribution will highlight the ongoing research aimed at separating efficiently catalysts under different OSN processing methods namely, online, at-line and off-line.[5] The separation of readily available N-heterocyclic carbene Pd complexes from reaction mixtures with highly stable ceramic membranes will be presented using down-stream processing and continuous-flow synthesis methodologies but also the implementation of new specifically designed N-heterocyclic carbene Pd complexes in a continuous synthesis-separation process (on-line) in which the membrane by efficiently retaining the catalyst is recycling it into the model Suzuki cross-coupling reaction used to demonstrate the principle, resulting in significantly enhanced catalyst TON’s.

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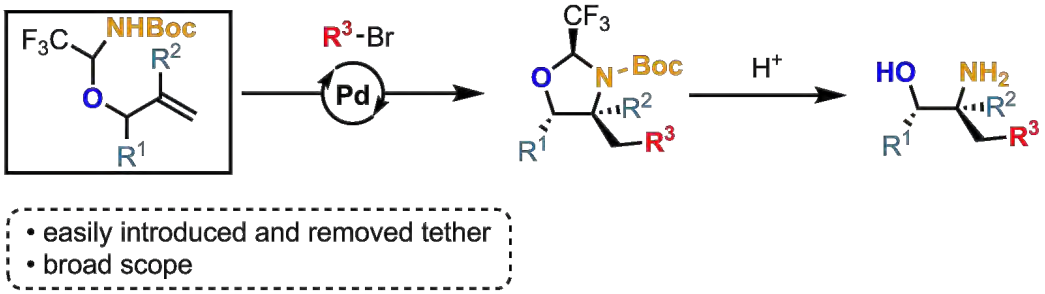
A Tethering Strategy for the Synthesis of Vicinal Aminoalcohols

B. Muriel[1], U. Orcel[1], J. Waser[1]*

[1]EPF Lausanne

Vicinal amino-alcohols are a common structural motif that can be found in a wide array of biologically active natural compounds, ligands, catalysts and chiral auxiliaries.[1] Therefore, efficient methods for their synthesis are necessary. The use of removable tethers combined with Pd-catalyzed olefin functionalization has known intense developments in recent years and has proved to be an efficient strategy for the installation of new functionalities on an alkene in a 1,2 relationship.[2] Recently, our group has introduced (hemi)aminal tethers derived from trifluoroacetaldehyde for the carboetherification and carboamination of allylic amines to give aminoalcohols and diamines.[3] Herein, we would like to report the successful implementation of this strategy to allylic alcohols. The synthesis of a stable hemiaminal could be achieved, followed by a Pd-catalyzed carboamination that could install concomitantly a C-N bond and a highly valuable C-C bond.[4] A wide variety of groups could be introduced to form functionalized oxazolidines that could then deliver the free amino alcohols under acidic hydrolysis.



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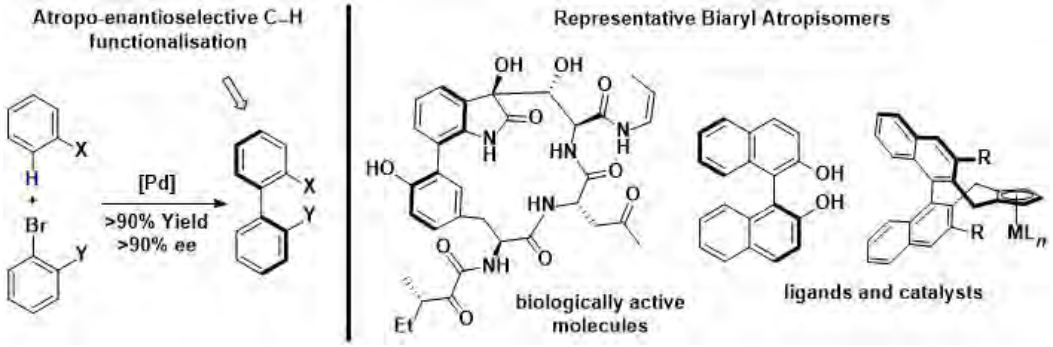
Axially Chiral Biaryl Atropisomers via a Pd–Catalyzed Atropo-enantioselective C–H Arylation

C. Newton[1], E. Braconi[1], N. Cramer[1]*

[1]EPF Lausanne

Most pharmaceuticals and agrochemicals, as well as many valuable material and commercial products are synthesized in organic chemistry laboratories, thus the development of new reactions, strategies, techniques, or improvements in reaction selectivity, efficiency and economy are of great importance. The development of new methods for the direct functionalization of unactivated C–H bonds is ushering in a paradigm shift in the field of retrosynthetic analysis. In particular, the catalytic enantioselective functionalization of C–H bonds represents a highly atom- and step-economic approach toward the generation of structural complexity. However, as a result of their ubiquity and low reactivity, controlling both the chemo- and stereoselectivity of such processes constitutes a significant challenge.[1]

The biaryl atropisomer motif is present in a number of biologically important molecules,[2] and acts as the stereochemical controlling element in many ligand scaffolds.[3] Herein we report the first highly atropo-enantioselective transition-metal catalyzed C−H arylation reaction. This demonstrates, for the first time, that biaryl axial chirality can be controlled in this setting.



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Functionalizable oligoprolines as a platform for the development of extended self-assemblies with tunable morphologies

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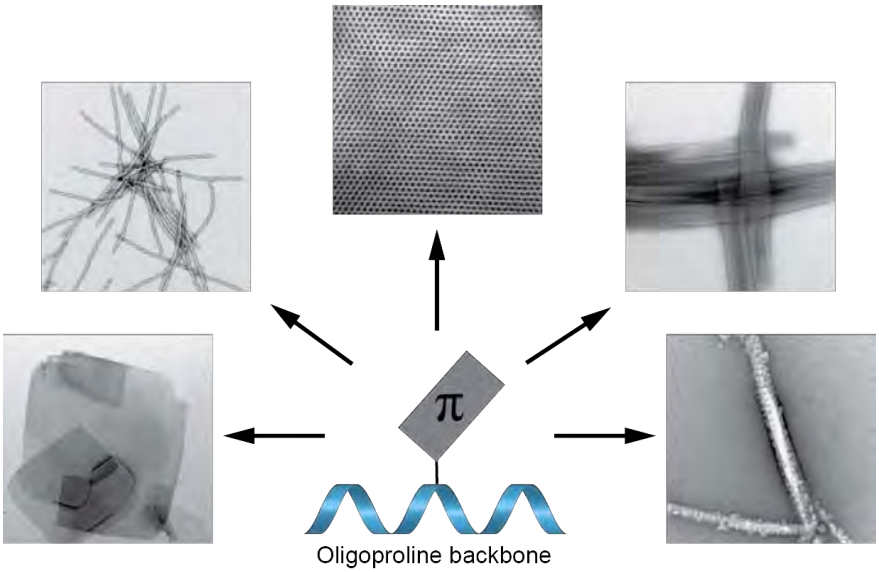
[1]ETH Zurich

Self-assembly of π-conjugated building blocks has become increasingly important for the fabrication of functional nanostructures. Towards this goal, peptides, which readily adopt well-defined secondary structures and are highly modular, have been used to direct chromophore self-assembly into well-organized, chiral nanostructures.[1] The assembly of these conjugates has been controlled by exploiting hydrogen-bonding networks within the peptides. Here we will present the formation of highly ordered supramolecular structures built on non-self-assembling peptidic scaffolds.



Using oligoprolines as scaffolds to direct the self-assembly of conjugated systems, we achieved the hierarchical self-assembly[2,3] of various types of chromophores into fibrils, sheets, and advanced, novel topologies. Variation in length of the oligoproline and choice of chromophore and linker has allowed for facile access to a variety of supramolecular structures that do not rely on H-bonding between peptides. Thus, oligoproline π-system conjugates constitute novel and efficient tools for self-assembly towards functional nanostructures.

+ This work was performed in collaboration with Prof. K. Müllen (Max Planck Institute, Mainz) and Prof. Peter Bäuerle (University of Ulm)

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Heterobimetallic d^8-d^{10} complexes as intermediates, transition states, and transition state analogs for the transmetalation step in Sonogashira and Negishi coupling reactions

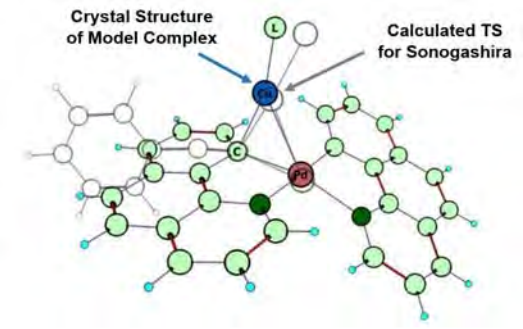
R. J. Oeschger[1], P. Chen[1]*

[1]ETH Zürich

Pd-catalyzed cross-coupling reactions have become one of the key processes for carbon-carbon bond formations. Even though their organometallic coupling partners vary, it is understood that they all follow a common general catalytic cycle in which a transmetalation reaction is one of the key steps. The mechanism of transmetalation reactions has been most thoroughly studied for the Stille reaction and for the Suzuki-Miyaura coupling, and it has been proposed that the reaction proceeds via either an open (S_N2 like) or closed transition state. Gas phase and computational studies on the mechanisms of the Sonogashira (Pd/Cu) and Negishi (Pd/Zn) transmetalations suggest that these reactions proceed somewhat different. [1] The main difference is the existence of direct metal-metal (d^8-d^{10}) interactions in calculated structures of transition states and intermediates.

To study the crucial Pd(II)-Cu(I) [2] and Pd(II)-Zn(II) [3] interactions experimentally we have prepared isolable heterobimetallic d^8-d^{10} complexes. The crystal structures resemble computed transition states for the Sonogashira and Negishi transmetalation steps and we have investigated the bonding qualitatively and quantitatively by X-ray, NMR, mass spectrometry (ESI-MS/MS) and calculations (DFT).

Structural and thermochemical work on the isolable model complexes will be used to predict and optimize substrates, ligands, and reaction conditions for cross-coupling reactions, especially the Negishi coupling, so as to suppress undesired side reactions, e.g. homocoupling, by rational design.



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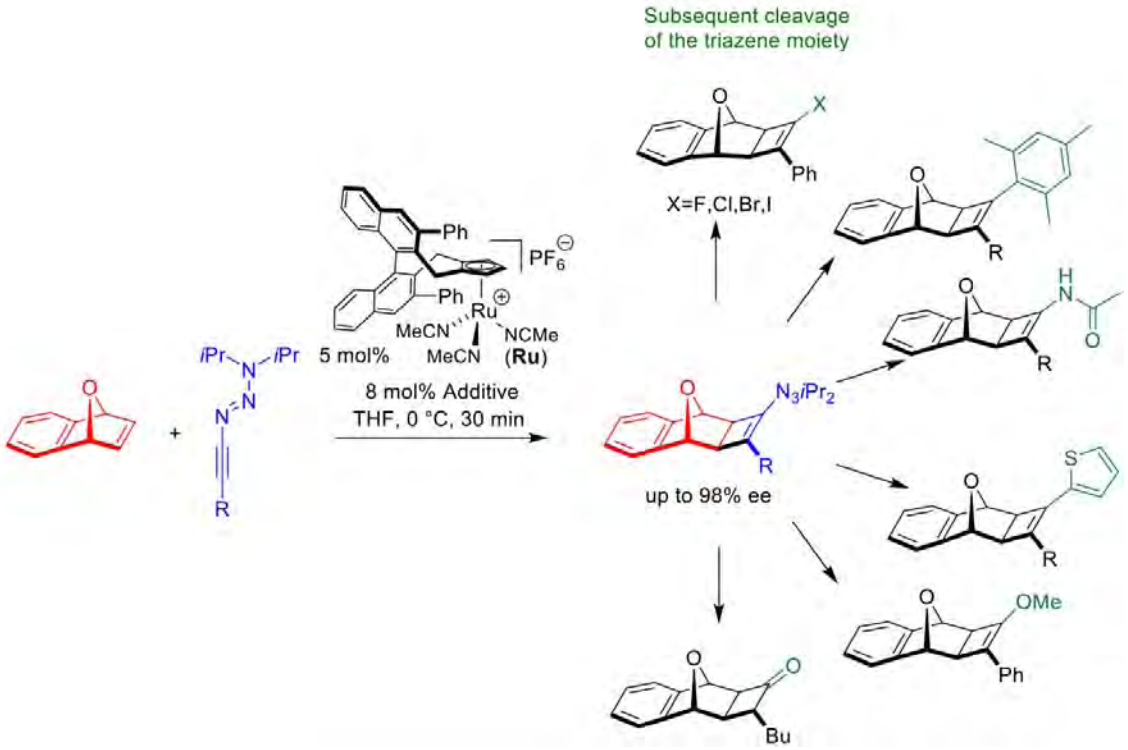
Divergent Asymmetric Synthesis of Polycyclic Compounds via Vinyl Triazenes

F. G. Perrin[1], D. Kossler[1], N. Cramer[1]*, K. Severin[1]*

[1]EPF Lausanne

Recently, our group reported a procedure which allows preparing 1-alkynyltriazenes by a simple one-pot-reaction using nitrous oxide.[1] Subsequently, we have shown that 1-alkynyltriazenes react as activated alkynes with a reactivity profile similar to ynamides.[2] In continuation of these studies, we have used 1 alkynyltriazenes in Ru-catalyzed [2+2] cycloadditions reactions with bicyclic alkenes. In collaboration with the group of Prof. N. Cramer, we have shown that 1-alkynyl triazenes are highly reactive substrates for enantioselective CpxRuII-catalyzed [2+2] cycloaddition reactions with bicyclic alkenes. High yields and enantioselectivities were obtained giving access to a broad range of cyclobutenyl triazenes. A salient feature of the vinyl triazenes is the behavior as divergent platform intermediates.



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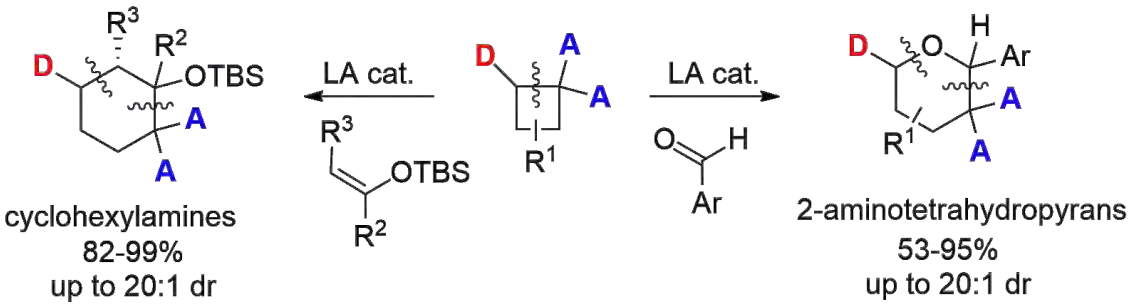
[4+2]-Annulations of Aminocyclobutanes

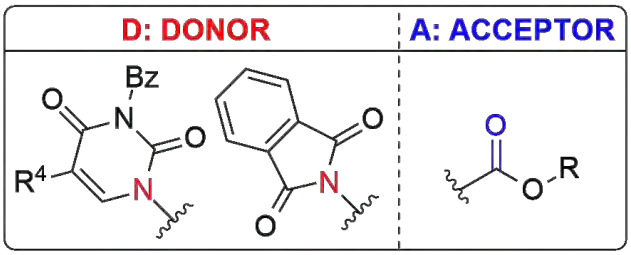
D. Perrotta[1], S. Racine[1], J. Vuilleumier[1], F. de Nanteuil[1], J. Waser[1]*

[1]EPF Lausanne

In the domain of small rings chemistry, donor-acceptor cyclopropanes have been widely used in annulations to generate complex cyclic structures. However, the use of their analogues 4-membered rings have been less investigated up to now. Herein we report for the first time the use of donor-acceptor aminocyclobutanes in [4+2]-annulations with aldehydes and silyl-enol ethers.[1] The 2-aminotetrahydropyrans and cyclohexylamines obtained are recurring motifs in biologically active molecules. [4+2]-annulation of substituted aminocyclobutanes with aldehydes delivered products bearing three stereocenters, using scandium triflate or iron trichloride as catalyst. The use of thymine- or fluorouracil-substituted cyclobutanes gave direct access to six-membered ring nucleoside analogues. Finally, the [4+2]-annulation between aminocyclobutanes and silyl enol ethers led to the corresponding cyclohexylamines. In addition, new results will be presented.



22 examples, up to **three stereocenters**



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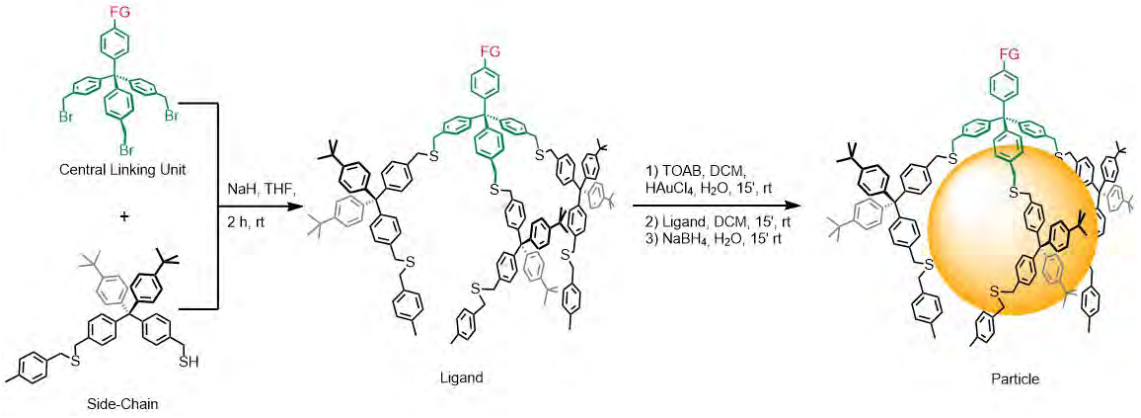
Gold Nanoparticles Reaching out for Molecular Electronics via Tailor-Made Ligands

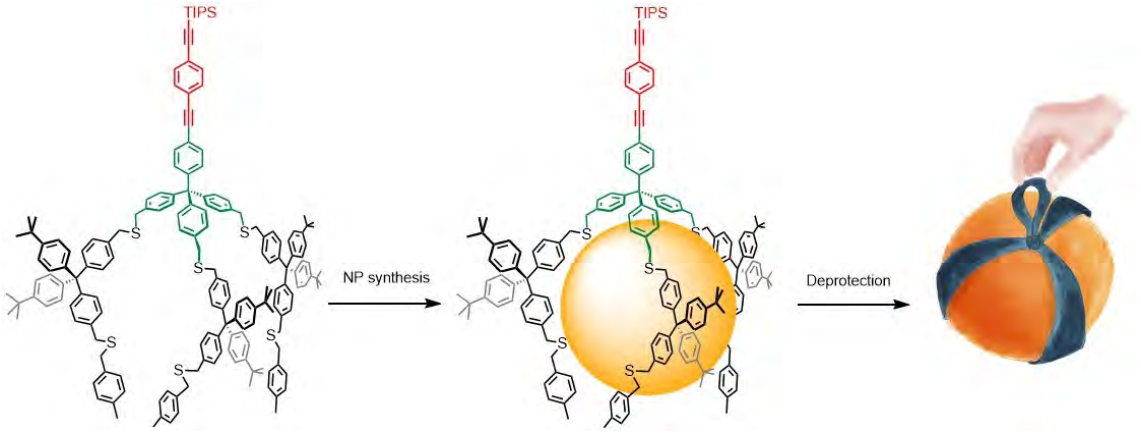
E. H. Peters[1], M. Lehmann[1], M. Mayor[1]*

[1]University of Basel

Due to their unique properties [1], gold nanoparticles (Au NPs) are of major interest In the growing field of molecular electronics [2,3]. A novel, central tripodal subunit has been synthesized, as well as a range of easily attachable, thioether-based side-chain elongations, enabling dendritic coverage of Au NPs. By variation of the side-chain length, monofunctionalized Au NPs exhibiting long-term bench stability and tolerance towards heat stress up to 110 °C were found. Further, the central linking unit offers a perpendicular free site for the introduction of a functional group.



Further work will comprise the introduction of an electronically addressable moiety at the central linking unit, as well as cage-like ligand architectures based on our existing molecules.



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Synthesis of Hypervalent CF_3 Tellurium Compounds

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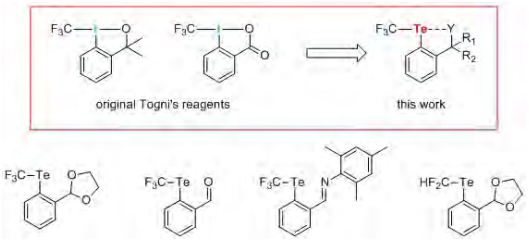
[1]ETH Zürich

Hypervalent iodine (III) reagents are electrophilic trifluoromethylating agents commonly applied in organic syntheses. Since their introduction in 2006,[1,2] the parent structures have been subjected to numerous modifications. However to date, the central iodine atom has been retained in each instance.[3–5] Herein, we report for the first time a synthesis of unique compounds in which the iodine atom has formally been exchanged for tellurium. Thus, a series of CF_3 tellurium (II) species differing in the functional group coordinated to the central atom has been obtained. All products have been fully characterized using HRMS and NMR spectroscopy, including advanced $^{1}H^{125}Te$ and $^{19}F^{125}Te$ correlation measurements. Furthermore, selected modifications performed after installing the CF_3 group on the tellurium atom have been successfully carried out.[6]



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Indolizidine Formation through Dearomative [3+2] Annulation Reactions of N-Heterocycles with Aminocyclopropanes

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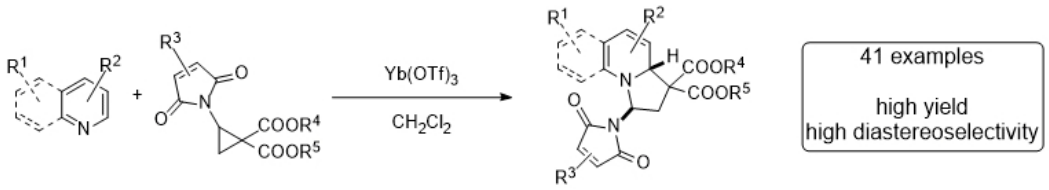
[1]EPF Lausanne

Many natural abundant and highly bioactive alkaloids contain an indolizidine skeleton.[1] We developed a straightforward, high yielding methodology to synthesize this scaffold from simple planar *N*-heterocycles. A wide range of pyridines, quinolines, and isoquinolines react with 2-amino cyclopropane-1,1-dicarboxylates via an ytterbium catalyzed [3+2] annulation reaction to the desired products. They are generally obtained with high diastereoselectivities as *trans*-isomers. Additionally, we show that the aminal in the products can be easily converted into secondary and tertiary amines through intermediary imine formation followed by reduction or nucleophile addition.



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Reductive Transformations Under 1,3,2-Diazaphospholene Catalysis

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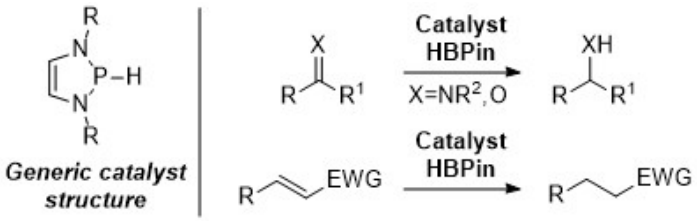
[1]Laboratory of Asymmetric Catalysis and Synthesis, EPF Lausanne

Organocatalysts offer complementary reactivity to transition metal based catalysts, while still addressing the fundamental issues of reaction efficiency and stereoselectivity. We have investigated a nascent class of organocatalysts, namely, the 1,3,2-diazaphospholenes and found that they enable a variety of reductive transformations.[1,2]



By varying the exocyclic substituents on these catalysts, the reactivity can be modulated.[3] Furthermore, by introducing chiral groups onto these positions, we have shown that these reactions can be rendered enantioselective.

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Triangular Donor—Acceptor Systems

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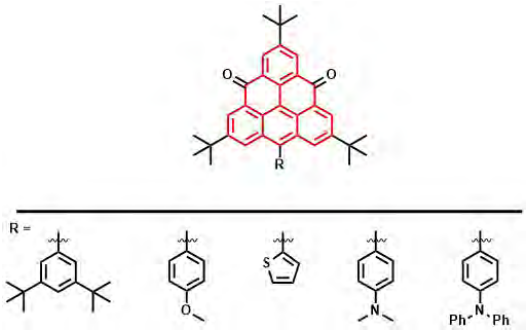
[1]Department of Chemistry, University of Basel, [2]Northwestern University, Department of Chemistry and ANSERC, [3]Department of Chemistry, University of Zurich

Organic molecules that absorb or emit visible light play an important role in many areas of research, including renewable energy production, material science, or biological imaging. Their optoelectronic properties arise from the presence of chromophoric unit, a metal or π-conjugated core, that is embedded in the structure of these molecules. Most of the known π-conjugated chromophores have shapes reminiscent of a square, a rectangle, or a sphere. Chromophores with triangular shapes are far less common and rather unique.

Recently, we synthesized and studied optoelectronic properties of five triangularly shaped donor−acceptor molecules containing triangulene-4,8-dione as an electron-acceptor unit and various electron-donor units. To favor electron communication between the donor and the acceptor units, the electron-donor unit was installed at position 12, at which triangulene-4,8-dione displays the highest coefficient in the LUMO. These molecular triangles were synthesized in eight steps such that the electron-donor substituents were installed in the last step by means of the Suzuki cross-coupling reaction. All molecules absorb and emit light in the region of around 450−650 and 550−850 nm, respectively, exhibit solvatochromism, and possess up to four redox states. On account of the rare triangular shape, these compounds display unprecedented packing modes in the solid state, which is of interest for design of optoelectronic devices.



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Synthesis of Alkylated Pyridine Derivatives via S_HAr of N-Methoxypyridinium Salts

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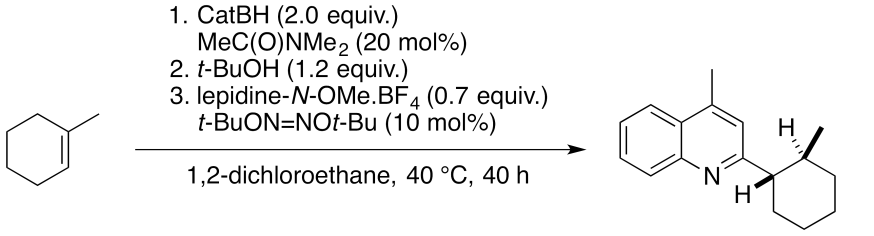
[1]Universität Bern

The homolytic aromatic substitution of nitrogen containing heterocycles is a versatile and well-studied class of transformations and is a viable reaction for late-stage functionalization of organic compounds.

The alkylation or acylation of a protonated, electron-poor heteroaromatic base using a nucleophilic carbon-centered radical was extensively studied by Minisci. Due to polar effects, the reaction shows selectivities that would be impossible to obtain under Friedel-Crafts reaction conditions.[1]

However, the reaction suffers from drawbacks such as use of a stoichiometric amount of oxidant, low regioselectivity and polyalkylation. Due to its viability in natural product synthesis and -functionalization, it is of great interest to overcome this reaction's limitations.

Herein, we describe a method that uses non-protic activation of the substrate. Alkylboranes (RBCat[2,3], R_3B) react with N-methoxypyridinium salts in the presence of a radical initiator to afford substituted pyridines. Interestingly, no external oxidizing agent is required to run this reaction. The scope and limitation of this reaction will be discussed.



86% (dr >97:3, trans/cis)

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Parallel π–π Stacking Interactions: Substituent Effects at Different Displacement

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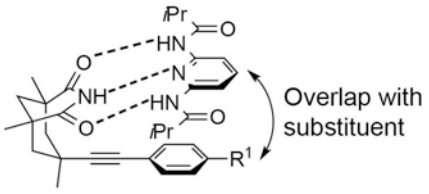
[1]ETH Zurich

Parallel-displaced π–π stacking interactions were investigated experimentally using two different host–guest model systems with Rebek imide-type receptors **1** or **2** and 2,6-di(isobutyramido)pyridine ligand **3** (Figure 1).[1,2]

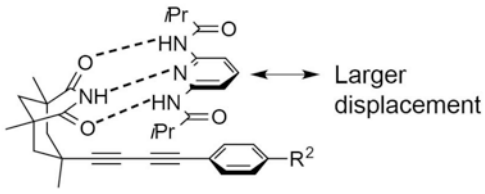
Guest **3** forms a triple H-bonding array to the imide moieties of receptors **1** or **2**. This allows for a parallel stacking geometry between the pyridine ring in **3** and the aromatic platform of **1** or **2** at different displacement, as confirmed by comprehensive structural analysis in solution and in solid state. In complex **1·3**, partial overlap between the pyridine core of **3** and the *para*-substituent R^1 is generated by a short ethyne-1,2-diyl spacer and enables direct, through space interactions. Any substituent had a stabilizing effect on the stacking interaction, independent of its electronic nature. In complex **2·3**, the elongated buta-1,3-diyne-1,4-diyl spacer prevents local, direct interactions between guest **3** and *para*-substituent R^2. Here, the electronic influence of the substituent on the aromatic platform affected the stacking strength crucially.

Changing the distance between substituent and intermolecularly interacting aromatic ring results in a fundamentally different substituent effect on parallel π–π stacking interactions.



1·3

R^1 = NO_2, CF_3, Br, F, H, Me, OMe, NMe_2



2·3

R^2 = NO_2, CN, CF_3, CHO, Br, F, H, Me, OMe, NMe_2

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Synthesis of β-Lactams by Palladium(0)-Catalyzed C(sp^3)-H Carbamoylation

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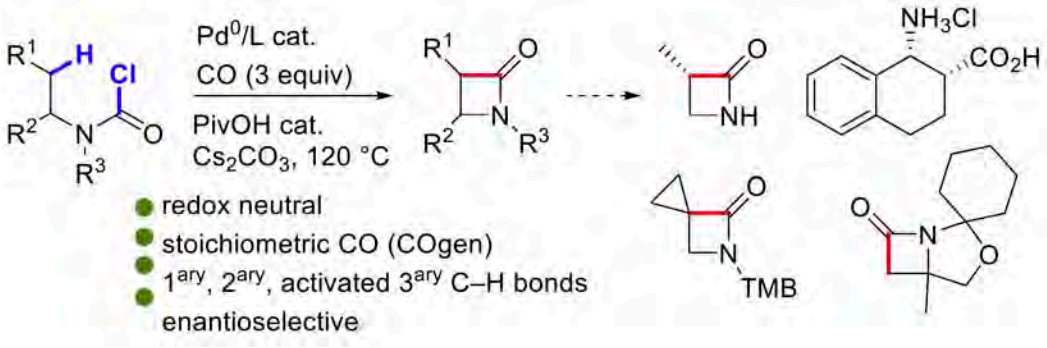
[1]Department of Chemistry, University of Basel, St. Johanns-Ring 19, 4056 Basel

β-Lactams are very important scaffolds for drug discovery and are also important synthetic intermediates for the synthesis of beta amino-acids [1]. In the past few years, C(sp^3)–H activation-based methods have been introduced to access this motif in a straightforward manner[2]-[5]. Inspired from the work of Takemoto [6], we developed a user-friendly and general method of synthesis of β-lactams, using intramolecular C(sp^3)–H activation, from carbamoyl chloride [7]. This method, employing Pd(0)/phosphine catalysis, in the presence of pivalic acid, cesium carbonate and CO gas allows the formation of a broad scope of functionalized beta-lactams. In addition, the feasibility of an enantioselective version using a chiral phosphonite ligand is demonstrated [5]. Finally, this method can be employed to synthesize valuable enantiopure free β-lactams and β-amino acids.



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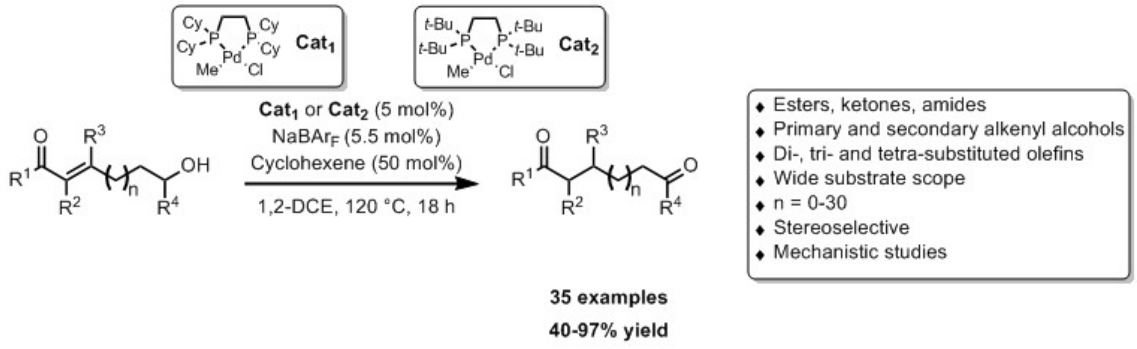
Palladium-Catalyzed Long-Range Deconjugative Isomerization of Highly Substituted α,β-Unsaturated Carbonyl Compounds

C. Romano[1], L. Lin[2], C. Mazet[2]*

[1]University of Geneva, [2]Universiy of Geneva

The long range isomerization/refunctionalization of olefins has emerged as an effective method for the construction of functionalized molecules. This redox neutral methodology relies on the use of transition metal complexes, with the economic and environmental advantage to avoid the formation of stoichiometric waste.[1] The main challenges for the successful development of such processes are (i) the difficult coordination of highly substituted (prochiral) olefins with metal catalysts,[2] severely narrowing the scope of these methodologies, and (ii) the control of the regioselectivity of metal hydride insertion across the C=C bond.[3]

Building on previous studies in our group,[4] we report herein the application of two Pd catalysts to the deconjugation, isomerization and refunctionalization of α,β-unsaturated carbonyls in good to high yields.[5] Our system isomerizes di-, tri- and tetra-substituted olefins to highly valuable aldehydes and ketones regardless the chain length (>35 examples). Preliminary mechanistic will also be presented.



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Enantioselective α-Arylation of O-Carbamates via Sparteine-Mediated Lithiation and Negishi Cross-coupling

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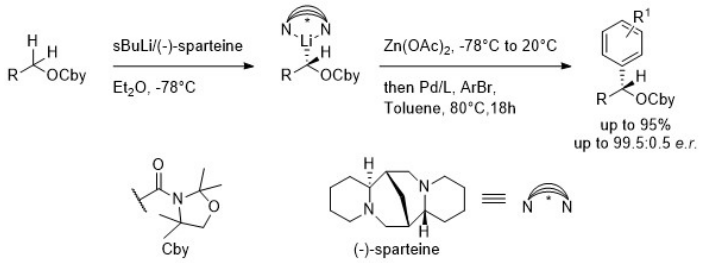
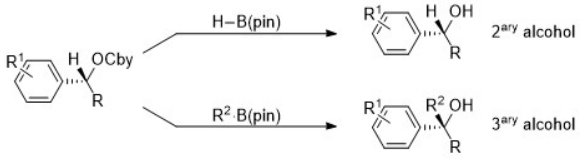
[1]University of Basel, Department of Chemistry, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

The enantioselective α-arylation of protected aliphatic alcohols is described. Hoppe's technology allows to perform the enantioselective α-lithiation in presence of sparteine. [1] After Li-Zn transmetalation and Negishi cross-coupling, highly enantioenriched benzylic alcohols are accessed. The method is compatible with a wide range of (hetero)aryl bromides and aliphatic alcohols.



Application of Aggarwal's lithiation-borylation sequence [2] provides a short and divergent access to a variety of enantioenriched secondary and tertiary benzylic alcohols. [3]



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Thermal Activation of Togni's Reagent Generates $F_3C^{\bullet}$!

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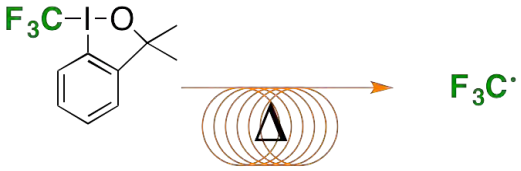
Since the original conception of Togni's reagents, they have become central to a plethora of trifluoromethylation strategies.[1] However, in stark contrast to the number of manuscripts published on their applications, dedicated mechanistic studies have been realized to a lesser extent. Nevertheless, a common feature found in most recent mechanistic schemes is the generation of an intermittent electrophilic trifluoromethyl radical ($F_3C^{\bullet}$) by action of a specific chemical activator. In this regard, especially metals (e.g. Cu salts, photoredox catalysts) as well as electron-rich organic materials (e.g. arenes, organic anions) are popular choices since these can potentially accomplish a single-electron reduction of the reagents. Most recently, we corroborated this elementary reduction step by means of pulse radiolysis and by relying on the solvated electron.[2] The present contribution showcases that simple thermal activation of Togni's reagent also furnishes $F_3C^{\bullet}$!



The thermal activation of Togni's reagent was explored in standard GC-MS equipment by means of gas phase trapping of the generated radicals with TEMPO.[3] To this end, a 1:5 mixture of Togni's reagent and TEMPO was studied by varying the temperature of the injection port - the latter serving as the reaction vessel. In these experiments, the abundance of TEMPO-CF_3 was shown to grow non-linearly with increasing temperature and a maximum efficiency of radical production was observed around 220 °C. Concomitantly, the release of methyl radicals ($H_3C^{\bullet}$) from the backbone occurred. Both events could also be identified by thermogravimetric analysis in conjunction with mass spectrometry (TGA-MS) of native reagent samples. In this contribution we will detail the experimental setup, acquired data and their mechanistic interpretation. Additionally, we will outline our attempts towards replication of these conditions in a laboratory scale setup to achieve additive-free radical trifluoromethylations with Togni's reagent.[4]

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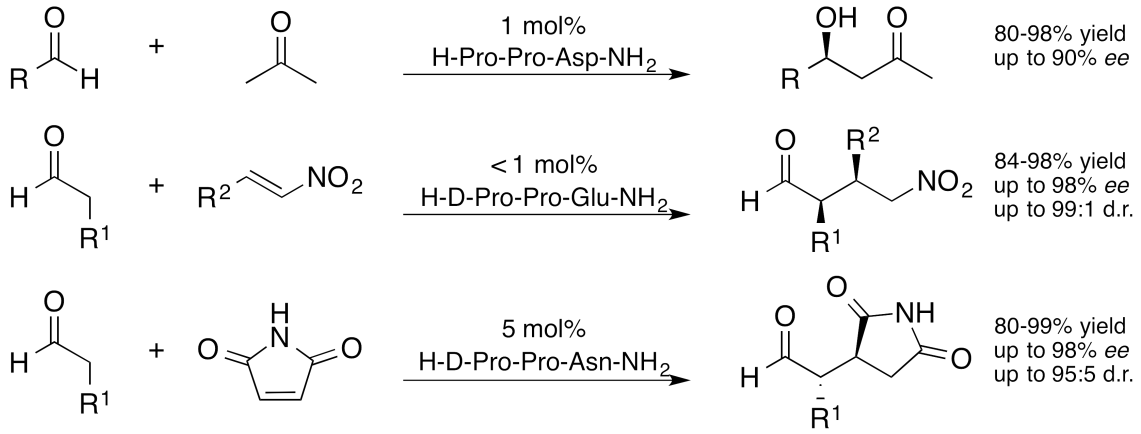
Conformational Investigation of Catalytically Active Peptides of the H-Pro-Pro-Xaa Type

T. Schnitzer[1], H. Wennemers[1]*

[1]ETH Zurich, Laboratory of Organic Chemistry, Zurich

Peptides of the type H-Pro-Pro-Xaa (Xaa = any amino acid) are highly reactive and stereoselective catalysts for organocatalytic C-C bond formations, such as aldol reactions (H-Pro-Pro-Asp-NH_2)[1] as well as conjugate addition reactions of aldehydes to nitroolefins (H-D-Pro-Pro-Glu-NH_2)[2] and unprotected maleimide (H-D-Pro-Pro-Asn-NH_2).[3] The peptide catalysts are so reactive that loadings of less then 1 mol% suffice to obtain the products in high yields, enantio- and diastereoselectivities and the peptides can be immobilized and used in flow chemistry.[4] Mechanistic studies using ESI-MS, React-IR and NMR spectroscopy allowed to elucidate crucial intermediates and potential resting states as well as the role of the intramolecular carboxylic acid.[5]



Recently, our interests focused on the structural features of H-Pro-Pro-Xaa type peptides and their consequences for reactivity and stereoselectivity of the catalyst.[6] Towards this goal, we have investigated the conformational features of these peptides using NMR experiments. The obtained data allowed for an even deeper understanding of the reaction mechanism and guided us also to new peptide structures with superior reactivity and stereoselectivity.

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Versatile Remote Functionalizations via C-H/C-C Bond Cleavage Under Mild Conditions

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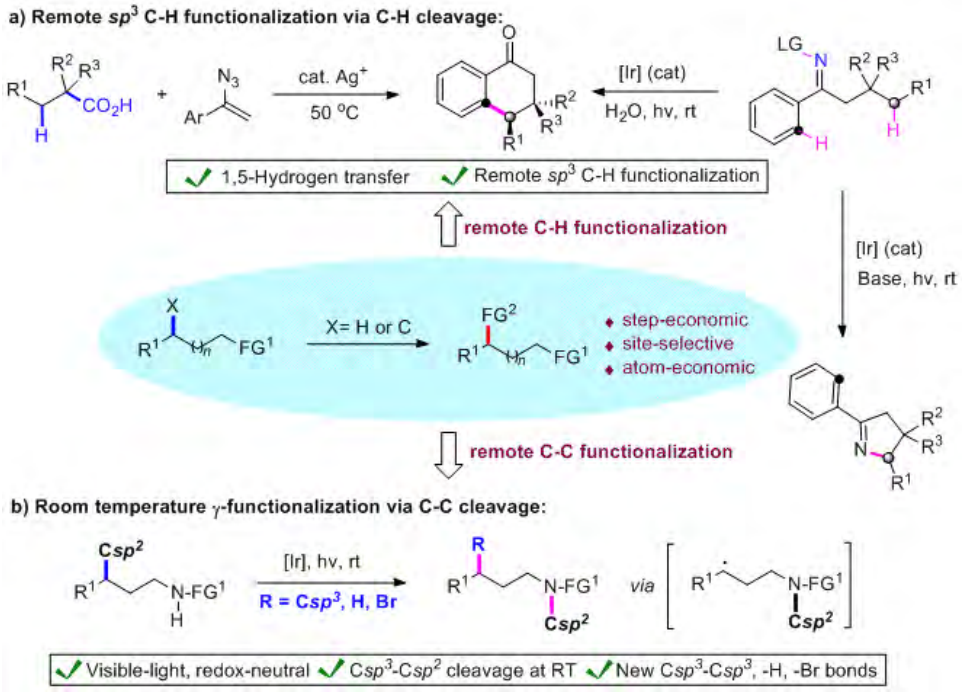
[1]University of Zurich

Exploiting inert bonds at non-reactive positions of organic molecules represents both an attractive and equally challenging endeavor. Unique opportunities to streamline the access to structural diversity and complexity can arise from the remote functionalization of C-H and C-C bonds present in distant positions to a functional group, which has fostered major efforts in this area.[1] Here, we describe a radical-mediated, directing-group-free regioselective 1,5-hydrogen transfer of unactivated Csp^3-H bonds followed by a Csp^2-H functionalization to produce, with exquisite stereoselectivity, a variety of elaborated fused ketones, which demonstrates that aliphatic acids can be strategically harnessed as 1,2-diradical synthons and that secondary aliphatic C-H bonds can be engaged in stereoselective C-C bond forming reactions.[2] We also present a redox-neutral, light-mediated functionalization of unactivated Csp^3-H bonds via iminyl radicals, to access divergent scaffolds via Csp^3-N or Csp^3-Csp^2 bond formation upon judicious choice of the reaction conditions.[3] On the other hand, we demonstrate the cleavage of unstrained C-C bonds under mild, visible-light mediated, redox neutral conditions. In situ generated C-centered radicals can be harvested in the presence of Michael acceptors, thiols and alkyl halides to realize diverse γ-functionalizations by forming new Csp^3-Csp^3, -H and –Br bonds, respectively.[4]



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High-resolution in 2D spectra using chemical shift encoding and spectral reconstruction

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[1]Department of Organic Chemistry, University of Geneva, 30 Quai Ernest-Ansermet, 1211, Geneva

High-resolution in the carbon dimension of 2D heteronuclear experiments, such as ^{1}H-^{13}C HSQC, has always been a problem because they are indirectly detected. Spectral aliasing [1] can be exploited by reducing the F1 spectral window, thus increasing resolution. The resolution enhancement factor is proportional to the reduction of the spectral window, within the same experimental time as a normal low-resolution spectrum. However, due to spectral aliasing, ambiguities in the chemical shift in the indirect dimension are introduced, making it difficult to determine their true chemical shift. Different methods have been reported to overcome these ambiguities [2,3].

We present here a generalisation of the chemical-shift encoding approach to resolve chemical shift ambiguities. The inclusion of an additional t_1' evolution time block, without quadrature discrimination, results in a signal splitting proportional to its ^{13}C chemical shift. Further processing allows a computer program to identify the partners for each peak splitting and calculate its true chemical shift based on the distance to the partner. Reconstructed full-width spectra are obtained by placing each peak at the position of its true chemical shift. The full and unambiguous reconstructed spectrum has the same resolution as the aliased spectrum, that is typically 10-100x higher than standard heteronuclear spectra.

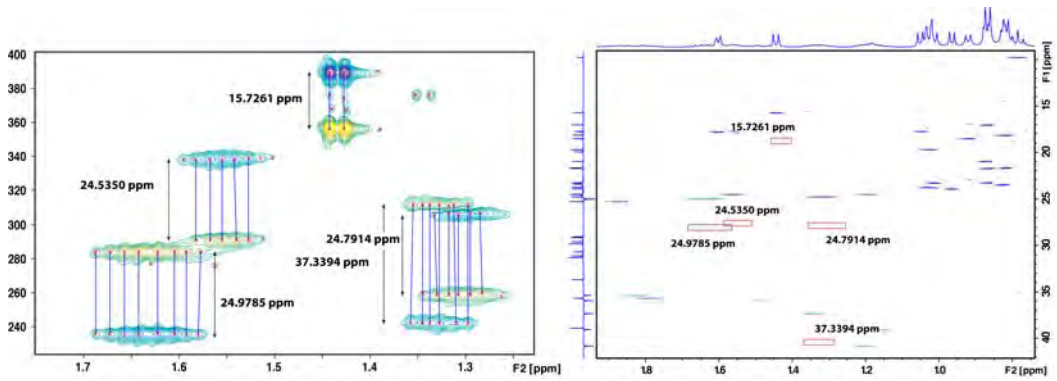

Figure 1. *(left) Example of an antiphase-splitted aliased edited HSQC spectrum with indirect dimension true chemical shift calculation. (Right) Expanded area of a reconstructed full-width edited HSQC spectrum. Highlighted signals correspond of the peaks shown on the left.*

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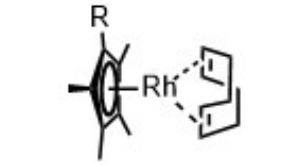
Synthesis of Highly Substituted Rh(I) and Ir(I) Cyclopentadienyl Half Sandwich Complexes via β-carbon Elimination

G. Smith[1], B. Audic[1], N. Cramer[1]*

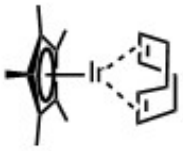
[1]EPF Lausanne

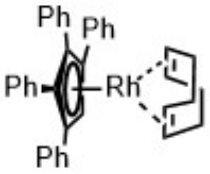
The cyclopentadienyl (Cp) ligand and its pentamethylsubstituted derivatives are of fundamental importance in organometallic chemistry. Cp complexes are known for most transition metals, and have been widely applied in numerous catalytic processes.[1] Experience in our research group has shown that the preparation of some highly substituted Cp derivatives can be extremely difficult with existing methods.

We present here a novel method for the synthesis of highly substituted Rh(I) and Ir(I) Cp complexes, employing a *β*-carbon elimination reaction as the key step. The newly formed complexes are obtained in high yields, and can be directly subjected to further catalytic transformations without any purification. This approach has enabled the synthesis of previously inaccessible ligand frameworks.



R = H, Me, *i*Pr, *t*Bu, Ph





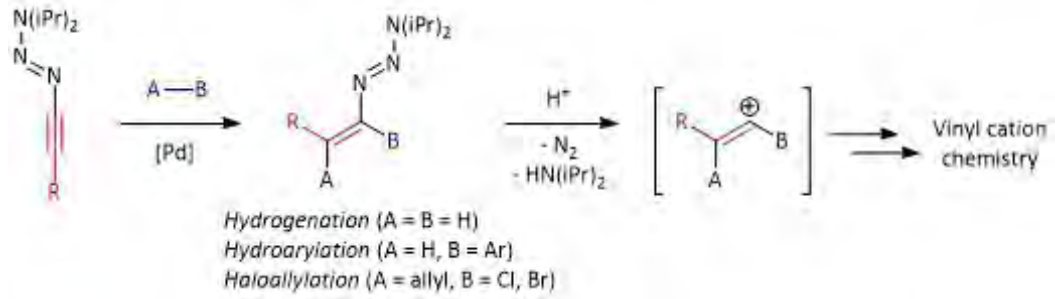
R = H, Me

Synthesis of Vinyl Triazenes by Pd-Catalyzed Addition Reactions to 1-Alkynyltriazenes

A. A. Suleymanov[1], K. Severin[1]*

[1]École Polytechnique Fédérale de Lausanne

In 2015, our group reported a synthetic method for the preparation of 1-alkynyltriazenes using nitrous oxide (N_2O), lithium N,N-dialkylamides and 1-alkynylmagnesiumbromides. [1] Subsequently, we have shown that 1-alkynyltriazenes have a similar reactivity profile as ynamides. [2] In this work, we have studied three Pd-catalyzed addition reactions to 1-alkynyltriazenes: semi-hydrogenation, hydroarylation with arylboronic acids, and haloallylation with allylhalides. Reactions have a broad scope and proceed with good to excellent yields and high regio- and stereoselectivity giving multisubstituted variety of vinyl triazenes. Treatment of vinyl triazenes with a strong acid leads to rapid formation of the corresponding vinyl cations, which can be captured by nucleophiles.



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Rh(III)-Catalyzed Asymmetric Synthesis of P-Stereogenic Phosphinamides

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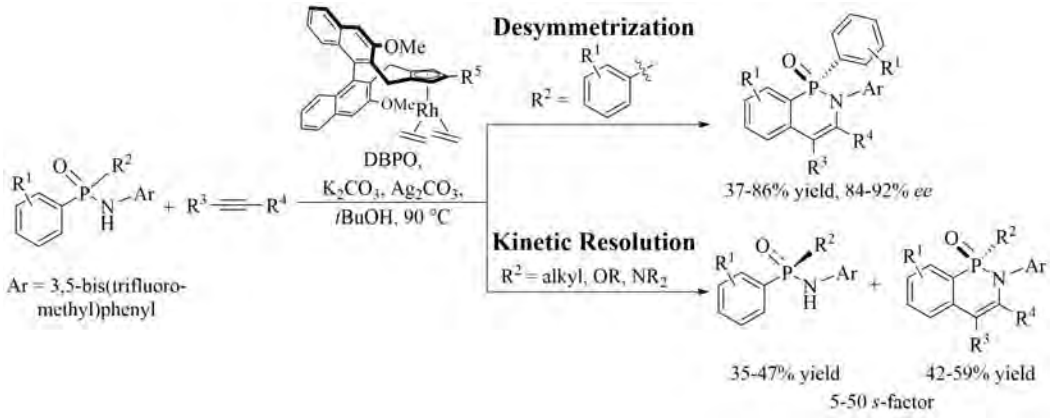
[1]LCSA EPF Lausanne

Chiral phosphorus compounds are widely employed as organocatalysts or ligands for enantioselective transition-metal catalyzed transformations.[1] Most commonly, the chirality comes from a stereogenic carbon, an axis of chirality, or a chiral plane. One might expect a better relay of chirality during catalysis with *P*-stereogenic phosphorus ligands due to a closer proximity to the transition metal. However, this area of research remains under explored due to challenges associated with *P*-stereogenic ligand synthesis.

Herein we report the first example of a chiral cyclopentadienyl[2] Rh(III)-catalyzed asymmetric synthesis of *P*-stereogenic phosphinamides. For prochiral phosphinamide substrates, enantioriched heterocycles were accessed *via* annulation with internal alkynes.[3] In contrast, with chiral phosphinamide substrates, kinetic resolution yielded both the cyclic phosphamides and unreacted starting materials, with selectivity-factors up to 50. Kinetic studies reveal that a concerted-metalation-deprotonation is the stereo-determining step when an inorganic base is employed, in contrast to previous reports from our group.[4]



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Radical Triggered Three-Component Coupling of Alkenylboronates, Halides, and Organolithiums

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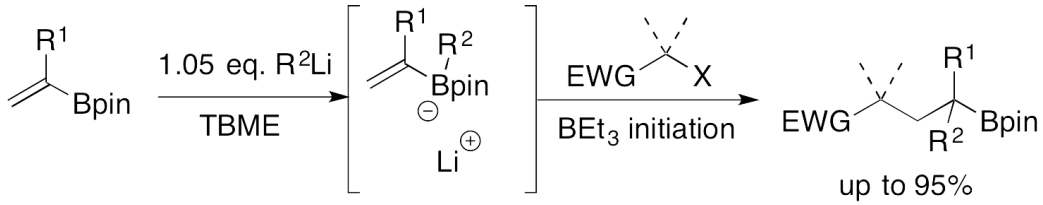
[1]University of Bern

The Atom Transfer Radical Addition (ATRA) reaction over alkenylboronates was employed by Matteson to showcase his now eponymous [1,2]-metalate shift.[1] However, the ATRA reaction suffers from poor efficiency arising from the stabilization that the vacant p-orbital of the boron gives to the radical product. Modifying the hybridization of boron from sp^2 to sp^3 can resolve this problem as has been seen with MIDA-alkenylboronates.[2] Better still is the combination of this logic to a [1,2]-metalate shift in order to exploit the synthetic utility of the vacant orbital.

Here, we report that the reaction takes place with good to excellent yields, initiated simply with triethylborane. In the late stages of our study other groups reported similar reactions,[3-4] but our mechanistic insight has allowed us to design a versatile reaction with simple conditions and operation. For example, we may couple tertiary organolithiums with relatively acidic alkenylboronates or radical precursors. Our system tolerates a wide range of radical precursors and primary-, secondary-, tertiary-, and aryl-organolithiums. We also present evidence to distinguish between alternative mechanisms; one involving a true ATRA or one involving a SET-oxidation and boron-ylid.



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Biomolecule functionalization using hypervalent iodine reagents

R. G. Tessier[1], D. P. Hari[1], R. Simonet-Davin[1], B. Fierz[1], J. Waser[1]*

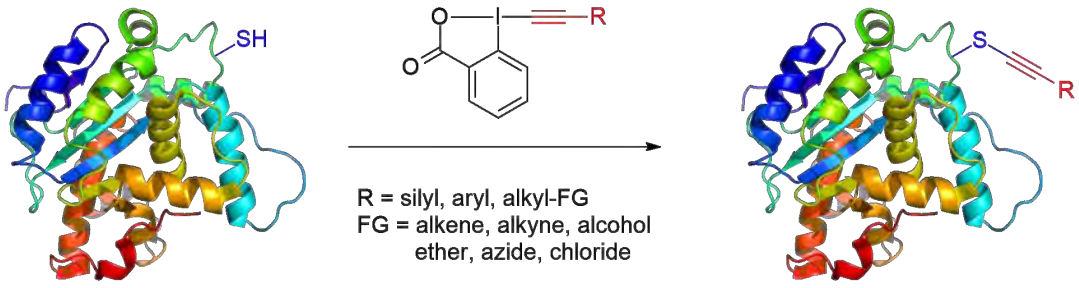
[1]EPF Lausanne

Organosulfur compounds are an important class of molecules, which is highlighted by the importance of cysteine residues for the structural stability and catalytic activity of proteins. Labelling methods selective for sulfurs into highly functionalized proteins are furthermore important tools in chemical biology.

Recently, our group developed a fast and practical thio-alkynylation reaction using the exceptional properties of hypervalent iodine reagents.[1] This reaction proceeds in less than 5 minutes, under air, with high tolerance towards a broad array of functional groups. The high chemoselectivity of these reagents led us to study their application in living cells in collaboration with the group of Prof. Adibekian. [2],[3]

This study demonstrated high chemoselectivity and intact reactivity in aqueous buffers, as well as a cell-membrane penetrating property for some of the hypervalent iodine reagents. Comparative studies showed that the new reagents are complementary in their protein targets when compared to iodoacetamide probes, the golden standard for cysteine functionalization in chemical biology.

Herein, we will present new advances concerning thio-functionalization on biomolecules using hypervalent iodine reagents.



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[3] Prof. Alexander Adibekian, School of Chemistry and Biochemistry, NCCR Chemical Biology, University of Geneva, 30 quai Ernest-Ansermet, Geneva (Switzerland).

Synthesis and modification of the structure of the ionic liquids to optimize their thermoelectric properties

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Ionic Liquids (IL) are organic salts with melting temperature typically below 100 °C. The unique properties of ionic liquids such as their excellent chemical and thermal stabilities (e.g. tetraethylammonium tetrafluoroborate can be heated up to 745°C [1].), their low vapor pressure, their important ionic conductivity makes them interesting compounds in material science and especially in thermoelectric generators (TEGs) for medical, pharma or electronic applications [2].

In our work, we describe the synthesis, physical, and thermo-electrochemical characterization of novel IL for application in thermoelectric generators (TEGs). We discuss the optimization of the chemical structure of IL regarding their thermoelectric properties via a structure-activity relationship approach [3]. The thermal stability of ionic liquids was investigated using thermogravimetric analysis in order to do a scale up of the synthesis of these ionic liquids.

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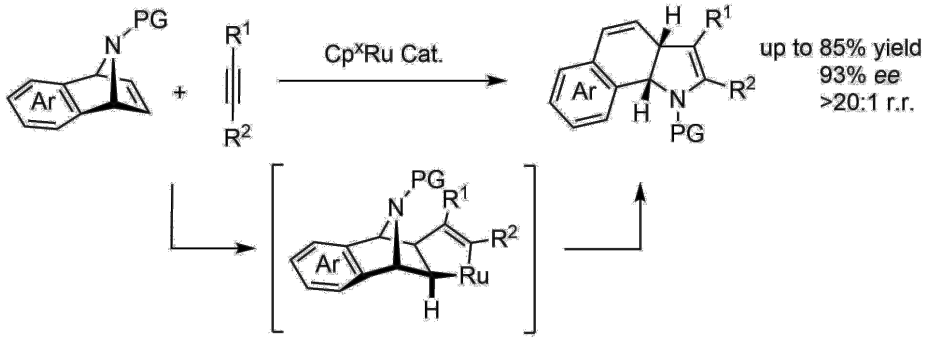
Novel Chiral CpxRu(II) Complexes for Asymmetric Catalysis: Enantio- and Regioseclective Synthesis of Dihydrobenzoindoles

S. Wang[1], N. Cramer[1]*

[1]LCSA EPF Lausanne

Cyclopentadienyl (Cp) group and its derivatives has emerged as powerful and versatile ligands for the construction of robust and catalytically competent transition-metal complexes. However, studies on chiral cyclopentadienyl (Cp^x) ligands in asymmetric catalysis have long remained underdeveloped. Recently, the synthesis and application of efficient Cp^x ligands has become an emerging field, which exhibited intriguing potentials particularly in Rh-catalyzed enantioselcetive C-H functionalizations.[1] Despite these elegant contributions, the design and synthesis of novel cyclopentadienyl ligands is still in its infancy, and the application of such ligands for alternative transformations are highly desirable. Herein, we report a concise and efficient synthesis of novel chiral Cp^xRu(II) complexes and demonstrate their potential in a highly enantio- and regioseclective synthesis of dihydrobenzoindoles *via* cyclization of azabenzonorbornadienes with alkynes.[2]



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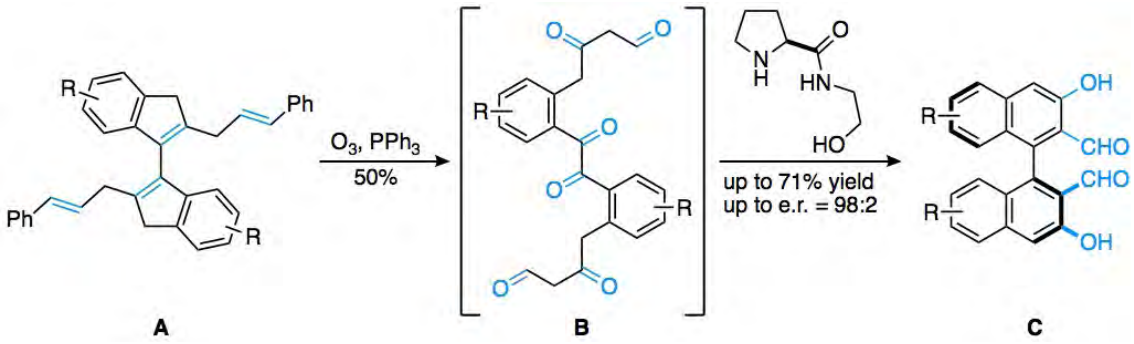
Atroposelective Double Arene-Forming Aldol Condensation: Synthesis of Tetra-ortho-substituted Binaphthalenes

R. M. Witzig[1], V. C. Fäseke[1], C. Sparr[1]*

[1]University of Basel

Due to their excellent suitability as ligands or organocatalysts for stereoselective catalysis, axially chiral molecules, such as biaryls, have received a great level of interest. However, despite their importance, the stereoselective synthesis of biaryl atropisomers remains challenging and resolution of racemic mixtures is still a frequently applied strategy for the preparation of enantiopure biaryls. Novel stereoselective methods to prepare axially chiral biaryls are therefore highly desirable. Of particular interest are strategies to make enantioenriched 2,2',3,3'-substituted binaphthalenes, privileged scaffolds in ligand design, as they would allow to replace cumbersome multi-step procedures which typically involve protecting group manipulations.

The presentation outlines our approach to stereoselectively prepare 2,2',3,3'-substituted binaphthalenes by a four-fold ozonolysis of cinnamyl indene dimers (**A**) to hexa-carbonyl substrates (**B**) followed by a secondary amine catalyzed double arene-forming aldol condensation. The reaction cascade proceeds with good overall yields and high enantioselectivities giving access to tetra-*ortho*-substituted binaphthalenes (**C**) which can be readily converted into established scaffolds for catalysis.



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Terminal-selective arylation of alkyl chains by regioconvergent Negishi coupling

K. ZHANG[1], S. DUPUY[1], A. GOUTIERRE[1], O. BAUDOIN[1]*

[1]University of Basel

Palladium-catalyzed C(sp^2)-C(sp^3) cross-couplings are particularly valuable tools in synthetic chemistry and hence a great deal of interest has emerged in this area.[1] Recently, our group has developed a new cross-coupling strategy based on the migration of an organopalladium species along an alkyl chain.[2] Through experimental and theoretical mechanistic studies, we have shown that this migration occurs through a beta-H elimination/rotation/insertion sequence.[3]

In this work, we have extended this migrative-coupling to simple and commercially available alkyl bromides. Under practical Barbier-type conditions involving magnesium insertion and transmetallation with $ZnCl_2$, a series of linear arylated products could be obtained in a regioconvergent manner with good to excellent linear/branched selectivities, thanks to the use of a suitable phosphine ligand. Moreover, this strategy could be coupled to a non-selective radical bromination process, which allowed the terminal-selective functionalization of simple alkanes in just two steps.[4]

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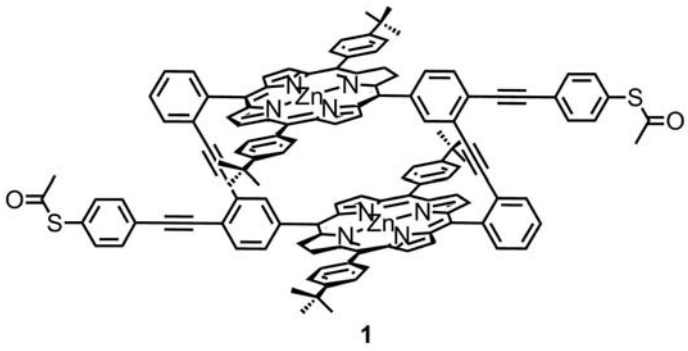
A Stretching Induced Molecular Switch

P. Zwick[1], M. Mayor[2]*

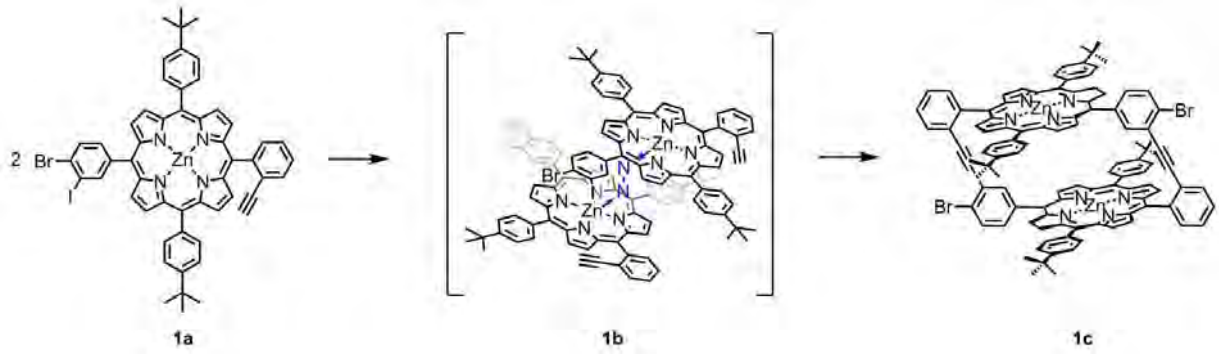
[1]Universität Basel, [2]University of Basel

The miniaturization of electronic devices by bottom-up approaches is of great interest. A novel molecular electronic component was reported, where conductance switching was achieved through mechanical manipulation in a mechanically controllable break junction (MCBJ)[1]. The poster shows the conceptual design of a proposed stretching induced d-orbital overlap dependent molecular switch **1.**



1

The switch is structurally based on a phenyl ethynylene cyclophane containing two porphyrin cores in face to face orientation. A thioacetate on each side of the macrocyclic structure allows gold electrode contacting in a MCBJ. The synthetic progress is summarized and shown on the poster. A dipyrromethane and two benzaldehyde derivatives are condensated to an assymetric porphyrin **1a**. It is proposed, that after complexation, a hydrazine templated pre-organised complex **1b** can be formed and closed to the macrocyclic structure **1c** by twofold *Sonogashira* cross coupling conditions. Metalation, *Sonogashira* cross coupling reaction and trans-protection of the thiols is proposed to affort the target compound **1**.



1a **1b** **1c**

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Coupling Pyridine and Triazoles in a Single Molecular Framework using Cycloaddition Reactions

R. Kaushik[1,2], S. C. Jain[1]

[1]Department of Chemistry, University of Delhi, Delhi-110007, India, [2]E-mail: kaushikreena1988@gmail.com

Cycloaddition reactions are among the most important tools for the synthesis of heterocycles. 1,2,3-Triazoles and 1,2,4-triazoles resulting from cycloadditions reactions are very interesting targets for the medicinal and pharmaceutical applications. These triazoles exhibit diverse biological activities such as antitumor, anti-inflammatory, antimalarial, anti-HIV and antimicrobial. These heterocycles have excellent pharmacokinetic characteristics, favourable safety profile, as well as the latent ability for the formation of hydrogen bonds with various other active molecules.

Pyridines, also display wide range of biological activities and hence have high medicinal value. We hypothesized that combining 1,2,3-triazole, 1,2,4-triazole and pyridine or their derivatives in a single molecular framework will result in more potent pharmacophores. Hence, we present here a novel approach undertaken by us to couple theses moieties in a single molecular frame using different cycloaddition reactions.

For this purpose, 5-methyl-1-(pyridin-3-yl)-1H-1,2,3-triazole-4-carbohydrazide was synthesized and reacted with phenyl isothiocyanate to obtain the carbothioamide which on cyclisation provided 5-(5-methyl-1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)-4-phenyl-4H-1,2,4-triazole- 3-thiol. Further alkylation of this with propargyl bromide gave the required alkyne intermediate. The cycloaddition of the alkyne with various synthesized azides using click chemistry gave 3-(4-(5-(((1-(aryl/heterocyclyl)-1H-1,2,3-triazol-4-yl)methyl)thio)-4-phenyl-4H-1,2,4-triazol-3-yl)-5-methyl-1H-1,2,3-triazol-1-yl)pyridines. Collaborative efforts are underway to screen these synthesized compounds for anticancer activities.

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Access to heterocycles bearing emergent fluorinated substituents — as FAR as possible

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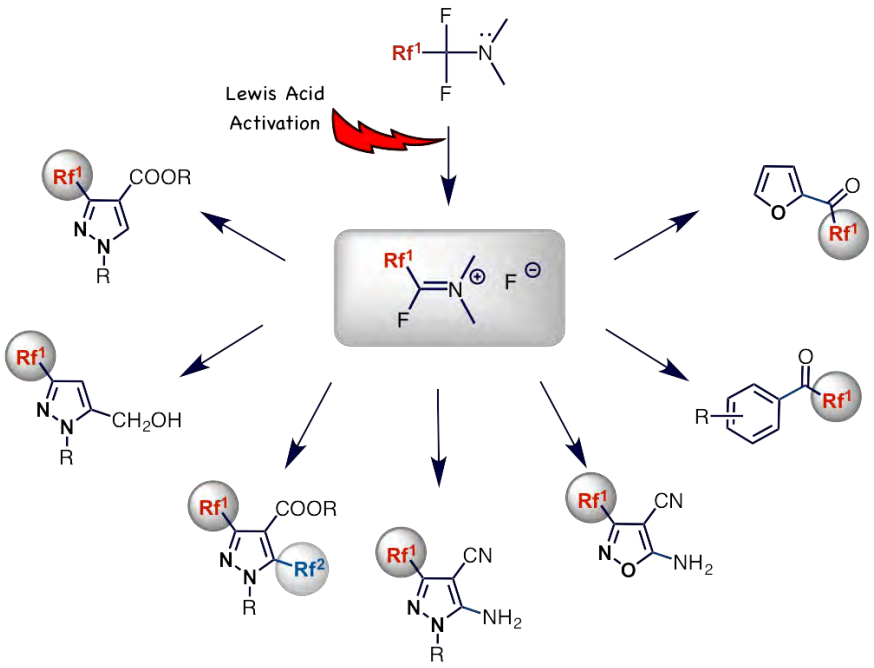
Organofluorine compounds play a key role in modern drugs and crop protection. Fluoroalkyl groups are popular functional groups and their introduction can significantly improve biological activity of active ingredients. α,α-Difluoroalkylamines like TFEDMA (HCF_2CF_2-NMe_2), Yarovenko ($HCFClCF_2$-NEt_2) or Ishikawa (CF_3CFHCF_2-NEt_2) reagents belong to the so-called **F**luoroalkyl **A**mino **R**eagents (**FAR**) and can be readily prepared from commercially available fluoro-olefins (monomers used for polymers production) and secondary amines. While these reagents have previously been used for the replacement of OH with fluorine in alcohols and carboxylic acids, we recently became interested in their use to prepare fluoroalkyl-pyrazoles. It has been demonstrated that FARs, after activation with Lewis acids such as BF_3 and $AlCl_3$, afford iminium salts with Vilsmeier-type activity. We have exploited this reactivity to prepare different fluorinated heterocycles, which are important building blocks for Life Science oriented research.[1-5]



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Irreversible cysteine-selective labelling of a protein using modular electrophilic fluoroalkylation reagents

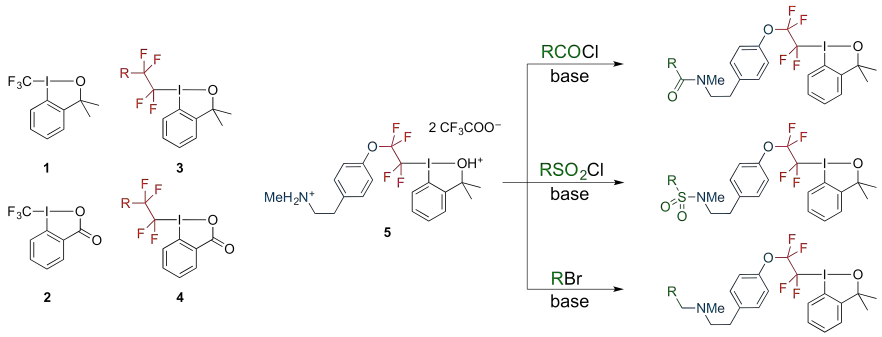
J. Václavík[1,2], R. Zschoche[2], I. Klimánková[1], V. Matoušek[3], P. Beier[1], D. Hilvert[2]*, A. Togni[2]*

[1]IOCB CAS Prague, [2]ETH Zürich, [3]CF Plus Chemicals

Hypervalent iodine-based compounds **1** and **2** have become popular reagents for formally electrophilic trifluoromethylation owing to their ease of use and reactivity with a broad variety of nucleophilic substrates [1]. In 2016, we extended the reagents bearing the terminal trifluoromethyl group by synthesizing a series of λ^3-iodanes **3** and **4** containing a CF_2CF_2R motif (where R = SAr, OAr, *N*-heterocycle) [2]. As the reactivity of the resulting reagents was comparable with that of the original ones (**1**, **2**) and the tetrafluoroethylene moiety can serve as a linker, giving the possibility of functional applications, we explored the potential of this concept further.

Reagents **3** and **4** were limited to rather basic structures as most functional groups would not tolerate the synthetic pathway. Hence, a reagent containing a secondary amine was prepared (**5**) and investigated in late-stage derivatization *via* mild formation of amides, sulfonamides and tertiary amines. Eventually, we arrived at 22 modular reagents containing manifold functional units (*e.g.*, tetraethylene glycol, biotin, and several fluorophores) [3].

All the reagents (**1**–**5**) display high reactivity toward thiols. Therefore, we envisaged that the modular λ^3-iodanes derived from **5** could be useful as reagents for cysteine-selective tagging of biomolecules. Indeed, when tested with artificial retro-aldolase RA95.5–8 S25C K210M, the exposed cysteine site was labelled selectively [3]. In contrast, the enzyme's active site containing a reactive lysine was left intact, which was not the case with conventional reagents based on maleimide and iodoacetamide. Therefore, the reagents' applicability goes beyond pure organic synthesis – they have the potential to constitute the basis of a new approach to protein labelling.



This work was supported by the Czech Science Foundation (grant no. 17-00598S).

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Enantioselective Total Synthesis of (+)-Peganumine A

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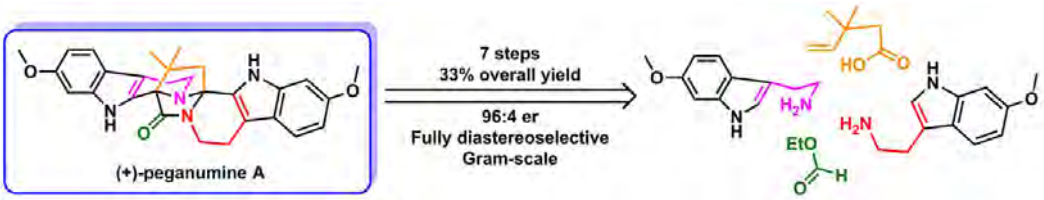
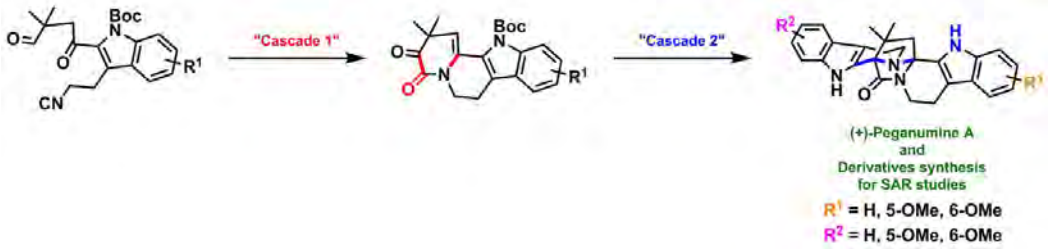
(+)-Peganumine A, a dimeric tetrahydro-β-carboline alkaloid, was isolated in 2014 from *Peganum harmala* L. by Li, Hua and coworkers.[1] This unprecedented octacyclic compound contains two quaternary stereocenters embedded in a unique 3,9-diazatetracyclo[6.5.2.0.0]pentadec-2-one scaffold. This molecule shows low μM cytotoxicity against various cancer cell lines.



The intriguing molecular architecture in conjunction with its significant bioactivity and extremely low isolation yield prompted us to undertake the total synthesis of peganumine A. Starting from simple commercially available materials, we used two key cascade reactions to reach the final target:

- "Cascade 1": A one-pot construction of an indolo[2,3-a]quinolizine tetracyclic skeleton from an ω-isocyano-γ-oxo-aldehyde *via* a sequence of an unprecedented C-C bond forming lactamization and a transannular condensation.
- "Cascade 2": A one-pot process merging two achiral building blocks into the final enantioenriched octacyclic structure *via* a sequence of asymmetric Pictet-Spengler reaction followed by an acid-catalyzed transannular cyclization. This domino process created two quaternary stereocenters with concurrent formation of two spirocycles and the 2,7-diazabicyclo[2.2.1]heptan-3-one unit with control of both the absolute and the relative stereochemistry.

In a single pass, we have synthesized gram-quantity of (+)-peganumine A in 7 steps and 33% overall yield.[2] This convergent route allowed us to synthesize the derivatives of peganumine A for future structure-activity relationship studies.



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Exploration of Pd(0)-Catalysed C(sp^3)–H Functionalisation Beyond Aryl Halides

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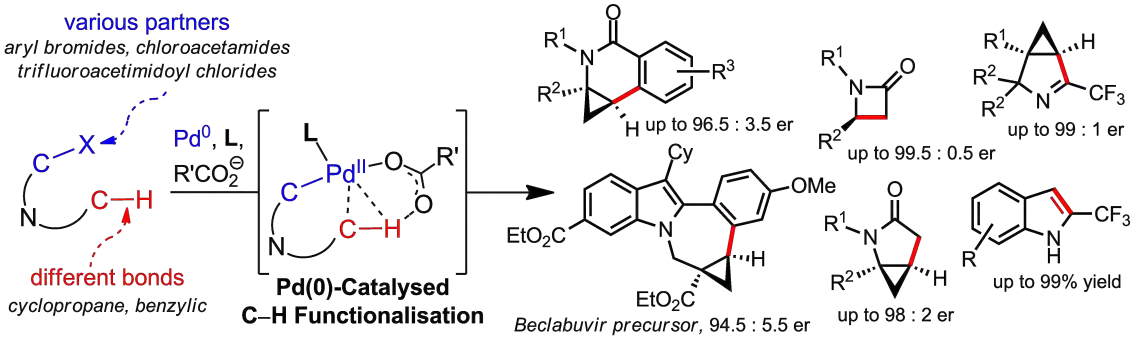
Nitrogen-containing heterocycles are prevalent motifs in biologically active compounds.[1] Transition metal catalysed enantioselective C–H functionalisations have become attractive alternatives for the selective synthesis of such scaffolds.[2] In the past years, the enantioselective synthesis of benzannulated *N*-heterocyclic building blocks *via* intramolecular Pd(0)-catalysed C(sp^3)–H bond arylation has been extensively investigated.[3] In this context, we have developed intramolecular aminocyclopropane arylations towards dihydroisoquinolinones and the Beclabuvir ring system.[4]

Our recent studies broaden the scope of Pd(0)-catalysed C–H functionalisations by using electrophilic partners other than aryl halides. Readily accessible chloroacetamides are efficiently functionalised, yielding valuable chiral b- and g-lactams in high yields and enantioselectivities with formation of a C(sp^3)-C(sp^3) bond.[5,6] Furthermore, indoles and versatile chiral imines bearing a CF_3-group are obtained by C–H functionalisation of trifluoroacetimidoyl chlorides.[7]



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Stereoselective Organocatalyzed Synthesis of α-Fluoro β-Amino and α-Fluoro γ-Nitro Thioesters

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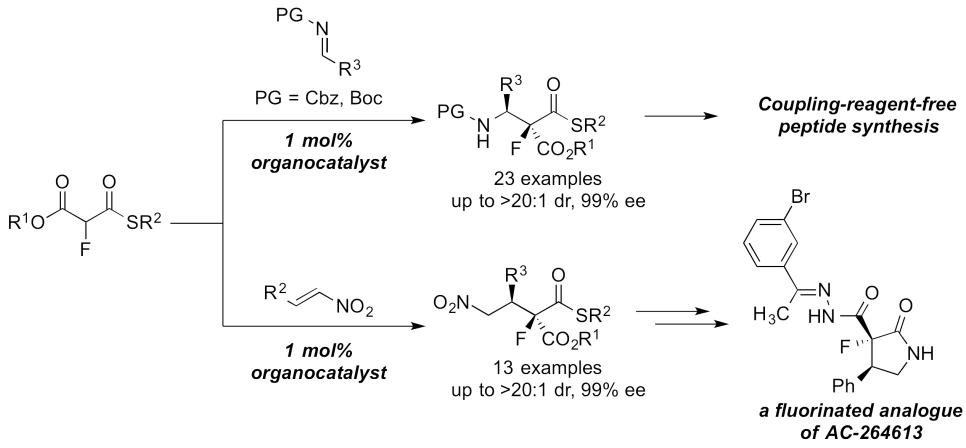
Fluorination and the incorporation of β-amino acids into peptides represent powerful strategies to enhance their proteolytic stability and to control their conformation.[1] These features are combined in α-fluoro-β-amino acids, which influence the conformation of β-peptides.[2] Recently, our group developed a stereoselective method to access fluorinated aldol products using fluorinated malonic acid half thioesters (F-MAHTs) as building blocks.[3] Herein we present highly stereoselective organocatalyzed Mannich reactions between fluorinated monothiomalonates (F-MTMs) and N-Cbz and N-Boc protected imines as well as Michael reactions between F-MTMs and nitroolefins.[4] These reactions require only 1 mol% of organocatalyst and provide access to the corresponding α-fluoro β-amino thioesters and α-fluoro γ-nitro thioesters, respectively. α-fluoro β-amino thioesters can be directly used for peptide synthesis in solution and on solid phase, whereas α-fluoro γ-nitro thioesters can be transformed into the corresponding fluorinated lactams, as showcased in the synthesis of a fluorinated analogue of AC-264613.[5]



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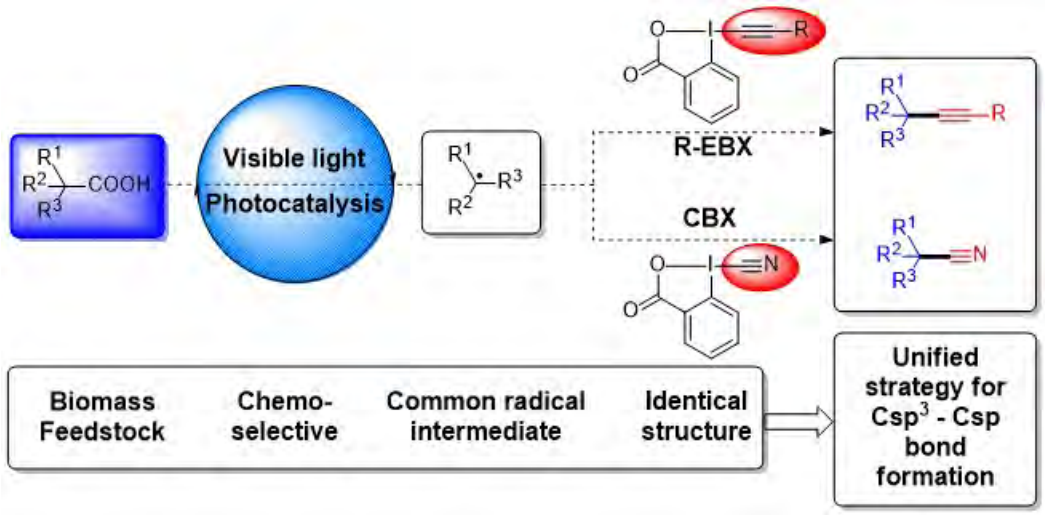
Decarboxylative Alkynylation and Cyanation using Photoredox Catalysis and Hypervalent Iodine Reagents

F. Le Vaillant[1], M. Wodrich[1], T. Courant[2], J. Waser[3]*

[1]EPF Lausanne , [2]Université Paris Descartes, [3]EPF Lausanne

Aliphatic alkynes and nitriles are functional groups of great significance, naturally occurring and broadly used as versatile building blocks in organic synthesis. They find applications from material to medicinal and pharmaceutical sciences. A unified strategy to access both classes of compounds under eco-friendly conditions is, therefore, highly desirable. Herein, we describe the straightforward decarboxylative alkynylation[1] and cyanation[2] of broadly available carboxylic acids using photoredox catalysis and cyclic hypervalent iodine reagents. In both reactions, the simplest benziodoxolone reagent was the most successful. Functional groups tolerance is high and reactions can be scaled up to generate useful intermediates in drug synthesis. According to computational and experimental studies, two different mechanisms can be proposed, based on the oxidation potential of the reagents: via radical intermediates for alkynylation, and carbocation intermediates for cyanation.



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New entries into amino-benzonorbornene chemistry

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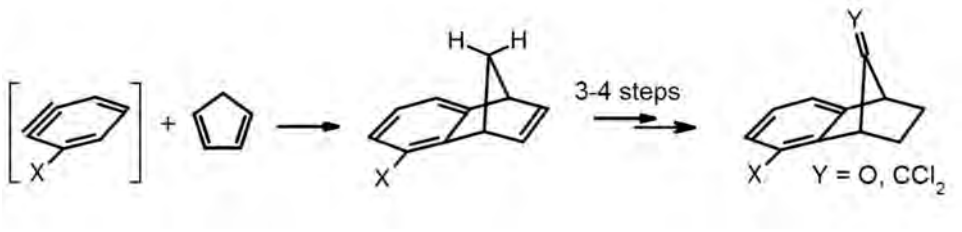
Raphael.dumeunier@syngenta.com

Cationic rearrangements based routes, from early Process Research towards two key intermediates of fungicidal active ingredients, will be disclosed. The synthesis of functionalized benzonorbonenes from cycloaddition between cyclopentadiene and benzynes, followed by rearrangements to adjust the substitution pattern and the functional groups, will be presented from the point of view of route scouting and novel reactions assessments.



The chemistry developed for targeting specific amino-benzonorbornene derivatives[1,2] will be broadened to, and exemplified by, other substrates. Rare or unprecedented electrophilic acylations and alkylations of double bonds by cations, triggering *in situ* further cationic 1,2-Wagner-Meerwein shifts will be disclosed; in both cyclic and acyclic series, [1,2]-shifts of aromatic rings led by β-cation stabilisation by silicon groups will also be exemplified.

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Enantioselective α-Arylation of O-Carbamates via Sparteine-Mediated Lithiation and Negishi Cross-coupling

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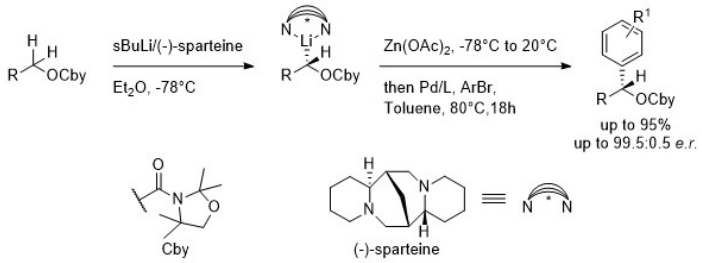
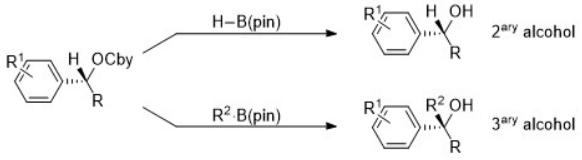
[1]University of Basel, Department of Chemistry, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

The enantioselective α-arylation of protected aliphatic alcohols is described. Hoppe's technology allows to perform the enantioselective α-lithiation in presence of sparteine. [1] After Li-Zn transmetalation and Negishi cross-coupling, highly enantioenriched benzylic alcohols are accessed. The method is compatible with a wide range of (hetero)aryl bromides and aliphatic alcohols.



Application of Aggarwal's lithiation-borylation sequence [2] provides a short and divergent access to a variety of enantioenriched secondary and tertiary benzylic alcohols. [3]



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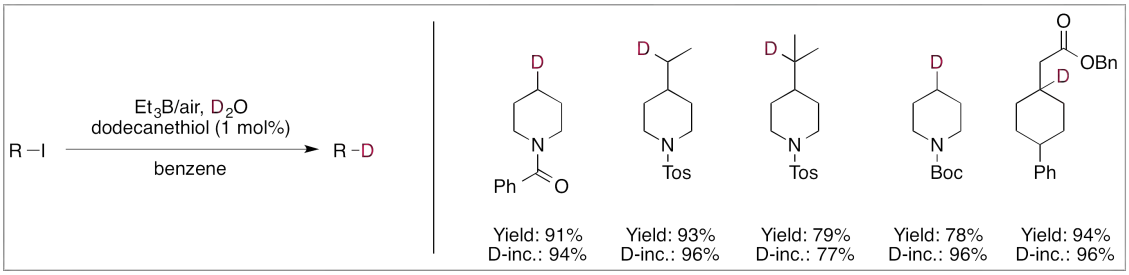
Radical Deuteration of Alkyl Iodides Catalyzed by Thiol and Mechanistic Studies on Deoxygenation Reactions of Xanthates

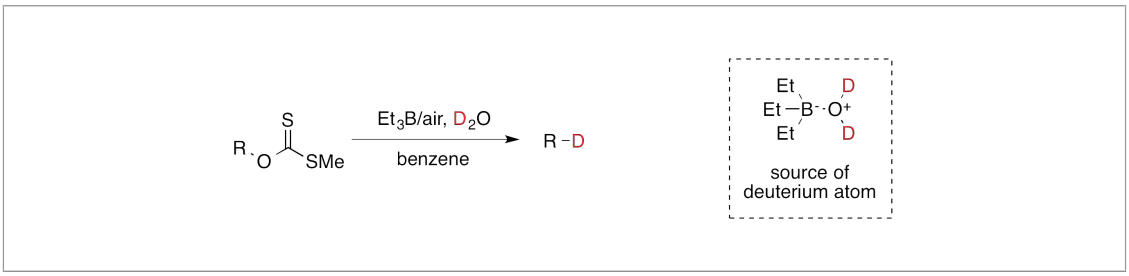
V. Soulard[1], G. Villa[1], D. Vollmar[1], P. Renaud[1]*

[1]University of Bern

Recently, there has been a growing interest in the pharmaceutical industries to incorporate deuterium in drugs candidates to improve their metabolism and pharmacokinetic properties[1]. A significant number of deuterated drug candidates (heavy drugs) have been synthesized and forwarded to clinical trials, such as Deutetrabenazine (Austedo®, TEVA pharmaceuticals) which is the first deuterated drug on the market. However, preparation of organic compounds selectively labelled with deuterium atom, remains a challenging synthetic problem. Radical deuteration of alkyl halides is one of the most efficient approach to perform this task. It is usually run using organotin deuterides[2] but this method has three major drawbacks: organotin deuterides are expensive, toxic[3] and led to product contamination.
We report here a method to deuterate alkyl iodides via a radical pathway with deuterated water as source of deuterium atom. Triethylborane is used to initiate and propagate the chain and dodecanethiol is used as a catalyst[4]. High deuterations and yields are obtained using this method which is compatible with a large range of functional groups.



The development of the deuteration method led us to discoveries that incite us to reinvestigate the mechanism of xanthates deoxygenation described by Wood *et al.*[5] (see below) who used heavy water activated by trialkylboranes as a source of deuterium atom.



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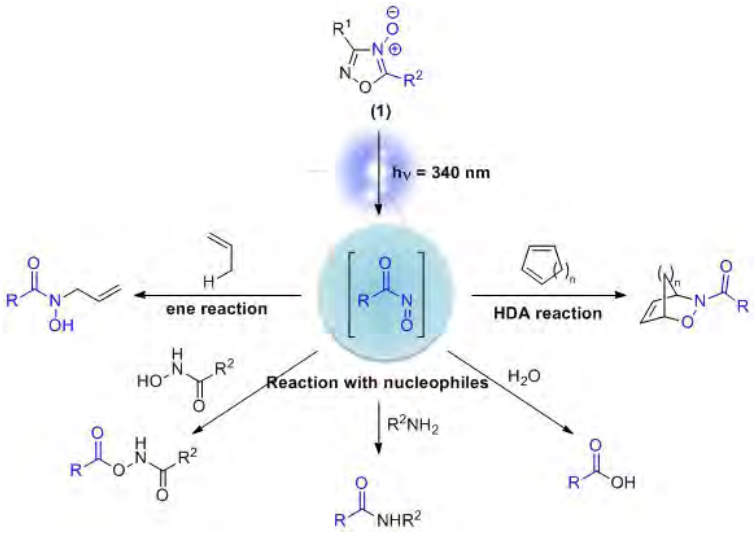
Photocleavage of 1,2,4-oxadiazole-4-oxide: A powerful tool for organic synthesis.

J. Loup[1], C. G. Bochet[1]*

[1]University of Fribourg

Nitrosocarbonyl species are very reactive compounds that have found many applications in organic synthesis[1]. These intermediates are involved in several useful reactions whose products serve as a versatile platform for further transformations.



The most common method to access to these molecules is by oxidation of the corresponding hydroxamic acid which prevents their use for sensitive substrates. In 1997, Caramella *et al.* showed that photolysis of 1,2,4-oxadiazole-4-oxide **1** allowed the smooth formation of these reactive intermediates[2]. This new method allows an easy access to the useful nitrosocarbonyl species without using any harsh conditions and could find many unique applications in organic synthesis. The first part of the project focuses on the development of a more robust and scalable synthetic road to access to 1,2,4-oxadiazole-4-oxide **1**. Once a reliable method will have been established, synthetic applications of photolysis of **1** will be addressed.

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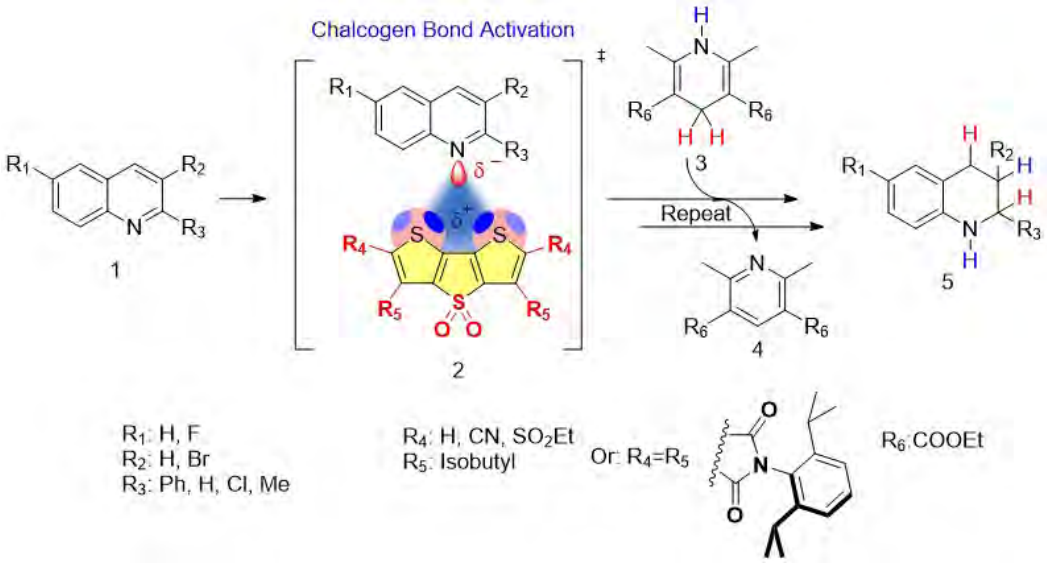
Chalcogen Bonding in Catalysis

S. Benz[1], J. López-Andarias[1], N. Sakai[1]*, S. Matile[1]*

[1]University of Geneva

Weak noncovalent interactions are the key to tailor make complex chemical systems to realize a specific function. Our most recent efforts geared towards expanding the toolbox of noncovalent interactions resulted in the application of chalcogen bonds to transmembrane transport and catalysis.[1,2] Chalcogen bonds arise when the electron deficient σ* orbitals, on sulfur, selenium or tellurium interact with a lewis-basic partner. Ideal spatial orientation of the sigma holes led us to select the scaffold of Dithieno[3,2-b;2',3'-d]thiophenes (DTTs) for bidentate chalcogen binding



Through interaction with the nitrogen lone pair DTTs are a privileged motive to activate imines and quinolines for Hantzsch ester mediated transfer hydrogenation. Over a 1000-fold rate enhancement, stronger activities with deeper σ holes and wider bite angles, chloride inhibition and correlation with computed binding strengths yield strong evidence for operational chalcogen bonds. Lessons learned are being currently applied to asymmetric catalysis with selenium based chalcogen binders.

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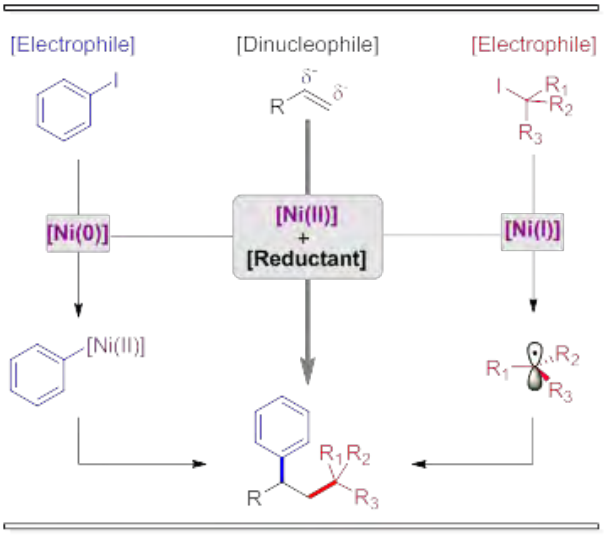
Transforming Olefins into Dinucleophiles

A. García-Domínguez[1], Z. Li[1], C. Nevado[1]*

[1]University of Zurich

Addition of two hydrocarbon derivatives across π-systems has been traditionally carried out using formally a nucleophile and an electrophile as reaction partners[1]. The multiple bond is thus conceptually considered as a (+/-)-dipole, which justifies the extensive use of electronic biased substrates.[2] Alkylative procedures that can be applied to a wide range of substrates independently of their intrinsic nature are still in high demand. Here, we present the first example of an intermolecular, three-component reductive dicarbofunctionalization of olefins with aryl iodides and alkyl iodides as reaction partners.[3] In contrast to previous methods[4], the reaction tolerates a wide range of olefins and the carbon sources do not require any additional functionalization. Interestingly, this process is characterized by the present of two different nickel cycles interconnected by the action of both, the unsaturated partner and the reductant.



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