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Synthesis of Cyclopentenones by an Asymmetric Nickel-Catalyzed [3+2] Reductive Cycloaddition of Enoates with Alkynes

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[1]EPFL Lausanne

Amongst the members of the family of five membered carbocyclic rings, cyclopentenones are of utmost importance in chemistry. They are found in numerous natural and synthetic products and also are versatile building blocks in several routes towards the synthesis of complex molecules.[1] Thus, the generation of cyclopentenones in a straightforward manner from readily available substrates remains an important target.

Several transition metal-catalyzed reactions for accessing cyclopentenones have been reported over the past years,[1] including an intermolecular nickel-catalyzed [3+2]-cycloaddition of enoates with alkynes.[2,3] We report an asymmetric nickel-catalyzed [3+2] reductive cycloaddition of enoates with alkynes to provide an efficient highly yielding and enantioselective route to chiral cyclopentenones from simple, stable, and readily available acyclic π-systems.

Mono-, Bis- and Penta-adducts of $M_3N@C_{80}$ (M = Y, Gd): Regioselective Addition Controlled by Endhedral Metal Clusters

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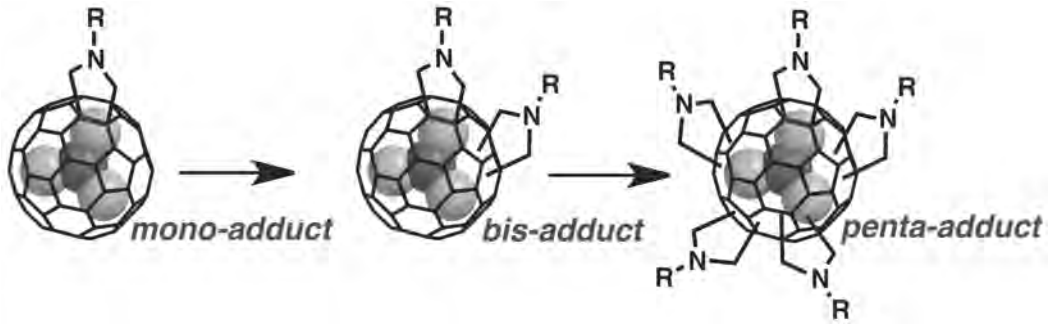
The trimetallic nitride template-endohedral metallofullerenes (TNT-EMF, $M_3N@C_{80}$) can be considered as a core of highly efficient MRI contrast agent as recently demonstrated by Dorn and co-workers [1]. Addressing the water-soluble fullerene materials, we have previously reported the mono-functionalization of $M_3N@C_{80}$ by the Prato reaction to further provide water-soluble materials with a combination of water-soluble polyethylene glycol moieties [2]. However, only weak relaxivity of water protons was observed in $Gd_3N@C_{80}$-PEG material presumably due to the carbon cages aggregation in aqueous media.



To avoid such aggregation of water-soluble $Gd_3N@C_{80}$ derivatives, we tried multiple addition of dipole to $M_3N@C_{80}$ core in this study. We prepared bis- and poly-adducts of $M_3N@C_{80}$ (M = Y, Gd) from mono-adduct as a starting material. Very interestingly, the bis-adduct (occurred at [6,6]-juction only) was obtained in a highly regioselective mannar presumably controlled the endohedral metallic cluster. As further addition, penta- adducts were obtained efficiently. Currently we are investigating the $Gd_3N@C_{80}$-based MRI contrast reagents based on this penta-adduct to obtain a material with higher relaxivity.

[1] H. C. Dorn and co-workers, *Bioconjugate Chem.* **2010**, *21*, 610.
[2] Y. Yamakoshi and co-workers, *J. Am. Chem. Soc.* **2012**, *134*, 20242.

Synthesis of functionalized pyridinium salts

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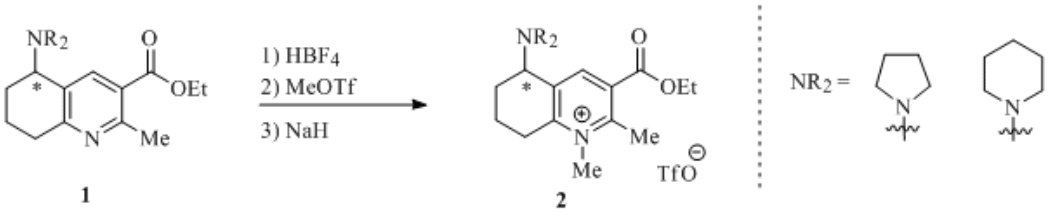
[1]University of Basel

In metabolism, NADH is involved in redox reactions, transferring a hydride from one molecule to another. The selective nature of NADH-based reductions has inspired the development of synthetic functional analogues.[1] This contribution describes our efforts in the synthesis of functionalized pyridinium salts, which could serve as mediators in hydride transfer reactions (*Scheme 1*).

Benzylic amines **1** could be easily prepared in a five step synthesis.[2] Hampering the nucleophilicity of the tertiary amine is necessary to achieve selective methylation of the nitrogen in the pyridine ring



1 2

Scheme 1. Preparation of functionalized pyridinium salts.

Upon protonation of **1** with tetrafluoroboric acid, the resulting ammonium salt was methylated with methyl trifluoromethanesulfonate resulting in the formation of a biscationic, highly reactive intermediate. Finally, deprotonation with sodium hydride afforded the desired pyridinium salts **2**

[1] V. A. Burgess, S. G. Davies, R. T. Skerlj, *Tetrahedron Asymmetry*, **1991**, *5*, 299.
[2] a) M. Litvic, M. Filipan, I.Pogorelic, I. Cepanec, *Green Chem*. **2005**, *7*, 771; b) A. Pyrko, *Chem. Heterocycl. Comp*. **1999**, *35*, 688; c) J. Uenishi, M. Hamada, S. Aburatani, K. Matsui, O. Yonemitsu, H. Tsukube, *J. Org. Chem.* **2004**, *69*, 6781

Synthesis of Porphyrins for Surface Chemistry and Materials Science

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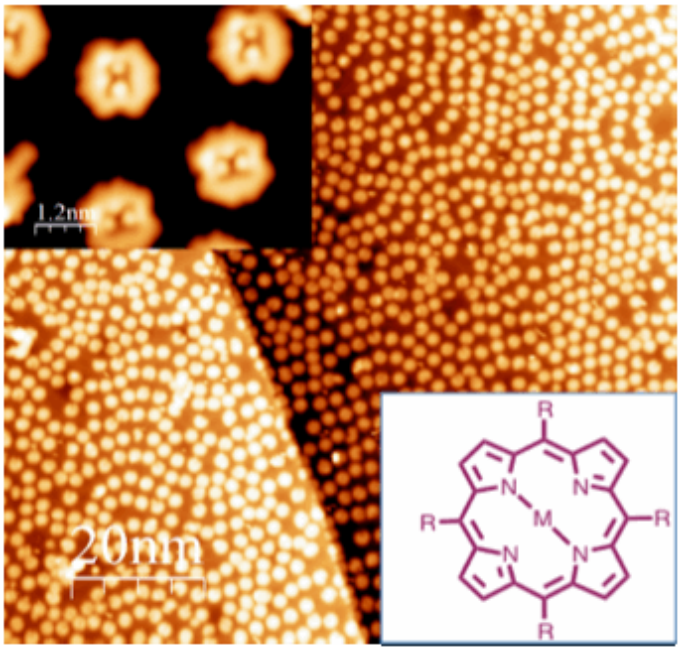
[1]University of Berne

Porphyrins are a class of macrocyclic molecules in the family of tetrapyrroles. By utilizing the tools of organic chemistry one can functionalize the meso positions to obtain a wide range of porphyrin derivatives. They have intense absorption in the visible region of the solar spectrum, with the strongest absorption at ~420nm. Herein, we present a series of porphyrins specifically engineered for applications towards surface/materials chemistry. One such porphyrin bears two moieties at trans meso positions, which can be sublimed onto a gold surface. At this point, temperature and voltage may be controlled to form carbon-carbon bonds between the porphyrins, which could yield insight into surface chemistry mechanisms. Other porphyrins that will be presented include a hetero-metallic triply fused porphyrin for magnetic spin studies on cobalt surfaces. This has an application as a magnetic “on/off” switch by controlling the high/low spins of the metal centers. Moreover, different coordinating ligands such as, CO, NH_3, NO and more, may be used to probe interesting binding and catalytic properties of the metal centers. Finally, porphyrins bearing phenylalkynyl moieties have been prepared for studies involving cycloaddition reactions on a surface. These reaction products will be characterized via STM measurements. Lastly, with a different focus, a functionalized zinc porphyrin dye used for dye-sensitized solar cells (DSSCs) will be presented. This porphyrin is covalently bonded to an electron rich π-extended aromatic system and an electron deficient anchoring group for adsorption onto semi-conducting metal oxides, such as TiO_2. The π system in combination with the porphyrin increases the absorption range of the solar spectrum.

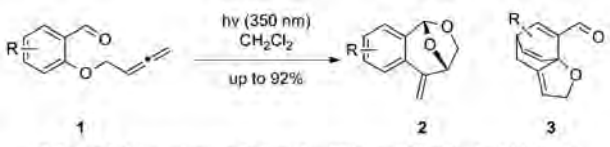


Towards the total synthesis of Augustamine

Lucile Bernet[1], Ursula Streit[1], Christian Bochet[1] *

[1]University of Fribourg

The new photocycloaddition of a relatily simple precursor affords two products bearing a high degree of complexity. Indeed, the intramolecular photocycloaddition between an allene and an aldehyde in **1** afforded two interesting structures: the benzoxepine moiety **2** and the bicyclo[2.2.2]octadiene core **3** (Scheme 1) [1].

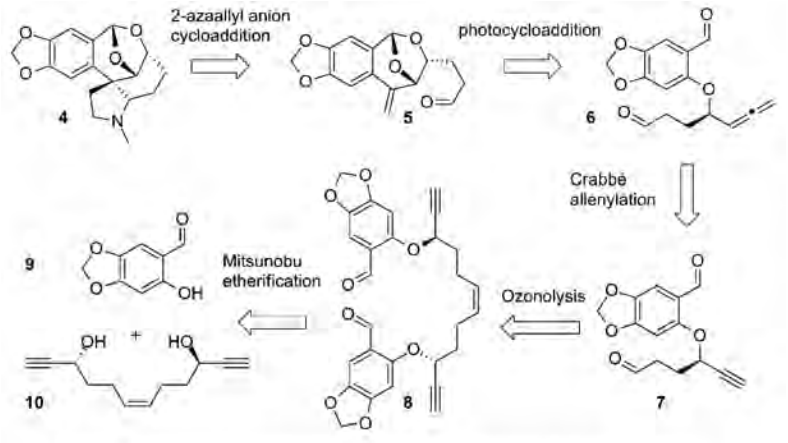


Scheme 1: Intramolecular photocycloadditions of allenyl salicylaldehydes.

To show the power and the applicability of this photocycloaddition, a natural product with a benzoxepine core was targetted: the Augustamine **4**. We envisioned the following retrosynthetic analysis for its total synthesis (Scheme 2):

The pyrrolidine ring of the Augustamine **4** will be assembled by an azaallyl anion cycloaddition. The benzoxepine structure **5** will be accessed by the new intramolecular photocycloaddition and the allene tether of **6** will come from the alkyne **7** using a Crabbé homologation. The aldehyde of the compound **7** will be obtained by the ozonolysis of the compound **8,** itself assembled by a Mitsunobu etherification between the phenol **9** and the diol **10**.

The challenges are threefold: a) to perform the photocycloaddition with a precursor substituted by a dioxolane, b) to introduce the chirality on the precursor and c) to control the diastereoselectivity in the product of the photocycloaddition.



Scheme 2: Retrosynthetic pathway towards the total synthesis of the Augustamine.

[1] Streit, U.; Birbaum, F.; Quattropani, A.; Bochet, C.G. *J. Org. Chem*. **2013**, *78*, 6890-6910 .

Stabilization of Disfavored Conformations inside an Adaptive Self-Assembled Fe_4L_4 Coordination Capsule

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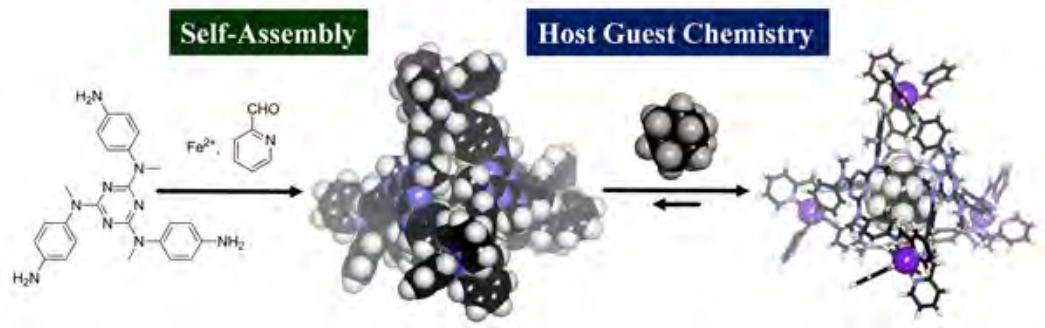
[1]University of Cambridge

Solvent-dependent host-guest chemistry and favoring of otherwise-disfavored conformations of large guests has been achieved with an adaptive self-assembled Fe_4L_4 coordination cage. Depending on the counter ion, this face-capped tetrahedral capsule is either soluble in water or in organic solvents and shows a solvent-dependent preference for encapsulation of certain classes of guest molecules: Aromatic guests were observed to bind only in water whereas the Fe_4L_4 cage has a high selectivity for non-polar aliphatic guests in acetonitrile. Due to the flexible subcomponents, this Fe_4L_4 cage is capable of adapting its shape to the encapsulated guest, thereby ensuring strong binding of both small and large guests. Binding constants have been calculated for a variety of guests and will be presented during the conference [1].



Upon encapsulation, large symmetric guest molecules show a significant lower symmetry and adopt conformations which are not thermodynamically favored in their free state due to confinement [2]. In addition, restricted motion about single bonds leads to diastereotopic protons on CH2 groups of encapsulated guests.

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[2] R. G. Chapman, J. C. Sherman, *J. Org. Chem.* **2000**, 65, 513-516.

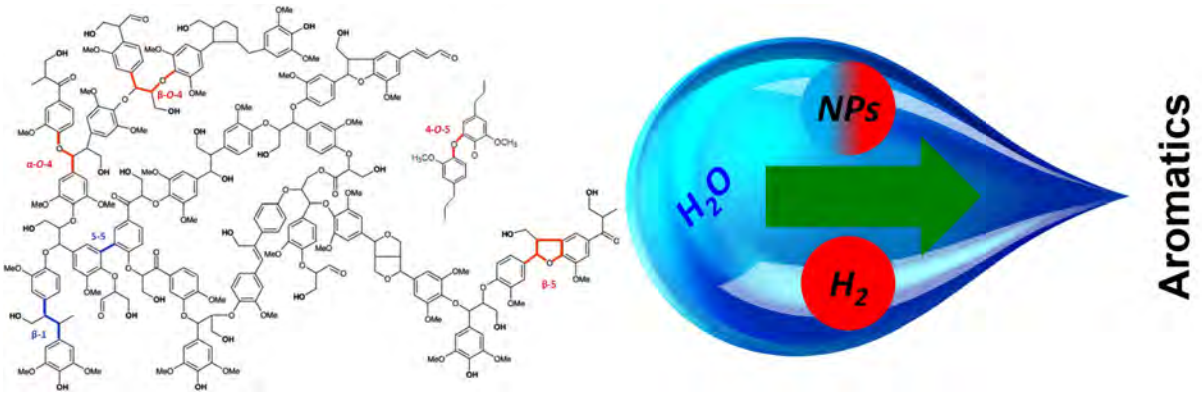
Cleavage of Aromatic C—O Bonds using Metal Nanoparticles in Aqueous Media

Safak Bulut[1], Paul Dyson[1] *

[1]EPFL Lausanne

Biomass conversion is an expanding research field that is motivated by the fact that biomass is a renewable raw material that could help to reduce the use of fossil-based feedstocks. In recent years, an interesting utilisation of biomass encompasses the developments of a biorefinery that produces both fuels and feedstock chemcials for industry.[1] In this contribution, we deal with lignin and its conversion into chemicals by using nanoparticle catalysts. Lignin accounts 25-40% of lignocellulose, the most abundant material produced in the world annually.[2]

Lignin is a three-dimensional amorphous biopolymer comprising methoxylated phenylpropane structures, which are connected to each other in different ways. However, the most frequent linkages in lignin involve oxygen atoms.[3] Thus, an effective depolymerisation of lignin requires the cleavage of strong aromatic C—O bonds. The focus of our research is to find effective and economically viable catalytic systems allowing the cleavage C—O bonds of aromatic ethers in green reaction media (e.g. aqueous systems).
For this purpose, we have developed metal nanoparticle catalysts and evaluated them in the hydrogenolysis of aromatic ethers as model compounds for the linkages in lignin. The results from these studies will be presented in detail.



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Enantioselective Michael Addition of Isocyanoactate to Vinyl Selenone:Access to α-Quaternary Amino Acids

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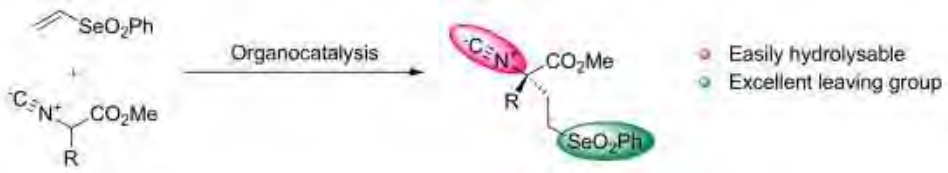
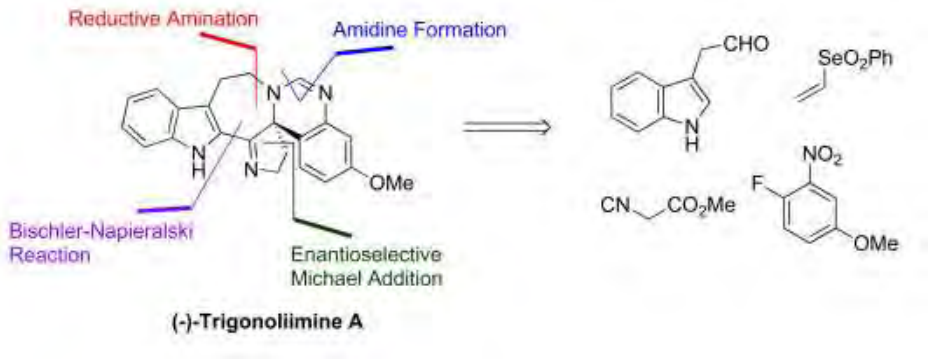
[1]EPFL Lausanne

Enantio enriched α-quaternary α-amino acids are presents in many natural products. Moreover, their resistance against enzymatic degradation and their rigid conformation makes them useful as peptidomimetics.[1]

We wish to present our approach towards this key structure through an organocatalyzed Michael addition of α-substituted α-isocyanoacetate to vinyl selenone. The use of isocyanoacetate as a glycine template is known but only few examples achieved an enantioselective transformation without a subsequent cyclization of the isonitrile part. The substitution of the selenoyl group makes this a versatile method to produce α-quaternary α-amino-acids.



The scalability of this transformation was then illustrated through an enantioselective synthesis of both (+)- and (-)-trigonoliimine A.[2]



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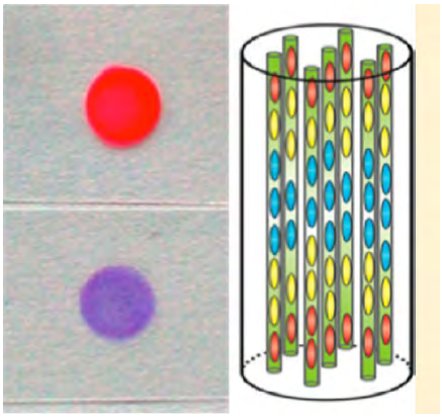
Broadband Dye-Zeolite L Composites for Luminescent Solar Concentrators

Pengpeng Cao[1], André Devaux[1], Dominik Brühwiler[2], Gion Calzaferri[3], Andreas Kunzmann [4], Peter Belser[1] *

[1]University of Fribourg, [2]University of Zurich, [3]University of Berne, [4]Optical Additives GmbH

The luminescent solar concentrator (LSC) is an architecture that collects and concentrates light using the luminescent properties of chromophores embedded in a waveguide. Combined with the low cost and flexible fabrication of organic materials, LSC has attracted many researchers' attention in the past decades.[1] However, there areseveral major challenges that kept LSCs from being widely used: e.g. limited stability of the luminescent organic species, high self-absorption, and poor understanding of the parameters governing device efficiency. The advent of advanced host-guest materials and sophisticated photon transport simulation models renewed interest in this technology.[2,3]

In our research, a new kind of dye-zeolite composite with photonic antenna function was prepared by embedding perylene dye as donor and Hostasol red as acceptor in the channels of zeolite L. In this chromophore system, self-absorption can be minimized through a Förster Resonance Energy Transfer cascade. The composite absorbs light over a large spectral range and transfers the energy to a final acceptor, which emits in the range of 600 nm to 620 nm. Though, in common LSC systems, where a high density of chromophores is a prerequisite for obtaining the desired photo physical properties, self-absorption and re-emission can often not be avoided. Thanks to the FRET-process in our system, we have proven that the self-absorption can be avoided or at least minimized. Our composite is constituted by the construction: dye1/dye2/zeolite L as a sandwich compound in which the donors/acceptor ratio is about 40:1.



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[3] (a) Patent EP 1873202 B1, granted 11.02.2009; Patent US 7,655,300 B2, granted 02.02.2010; Patents pending in China, Japan, South Korea, India.(b) Luminescence concentrators and luminescence dispersers on the basis of oriented dye-zeolite antennas. patent CH-698333, granted 15.07.2009; pending WO 2010/009560 A1.

Artificial Suzukiase Based on the Biotin-Streptavidin Technology

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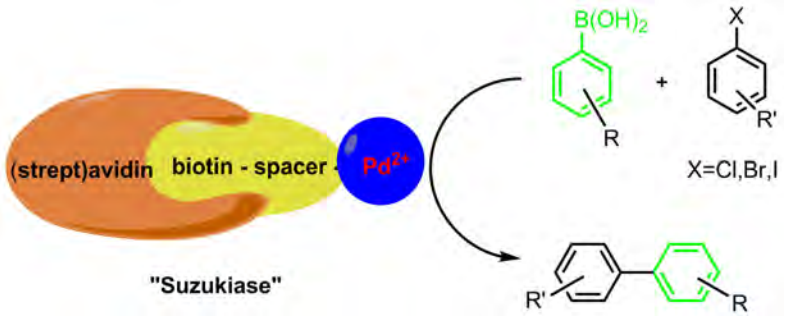
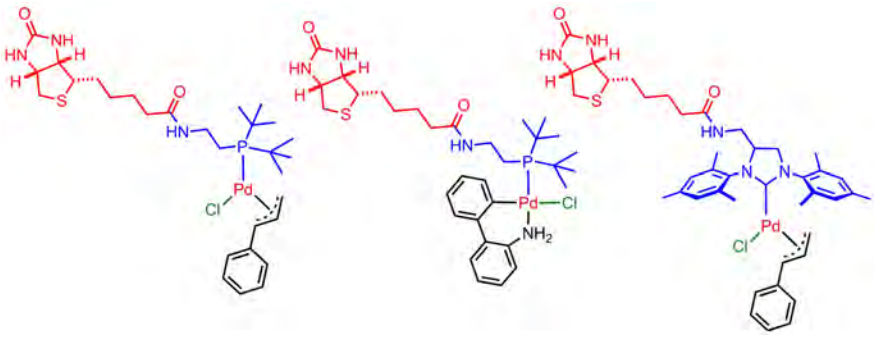
[1]University of Basel

In recent years, there has been growing interest in the creation of artificial metalloenzymes for enantioselective catalysis. The palladium-catalyzed Suzuki-Miyaura coupling is a C–C bond-forming reaction that has attracted much attention in this context. In stark contrast, this fascinating bond-forming reaction, Nature relies on very different mechanisms to create C–C bonds. We thus set out to investigate the potential of artificial metalloenzymes to create a Suzukiase and test its potential under physiological conditions.[1-5]

For this purpose, we synthesized a variety of biotinylated *N*-heterocyclic carbene- (NHC) and bulky phosphine ligands and tested these in the presence of a Pd-source combined with various streptavidin isoforms. Herein we present preliminary results on the chemogenetic optimization of an artificial Suzukiase (Figure. 1)





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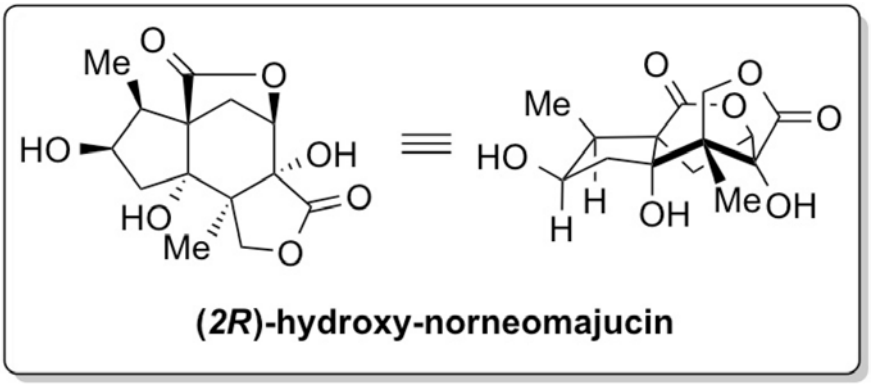
Studies Towards the Total Synthesis of (2R)-Hydroxy-Norneomajucin.

Erika Crane[1], Karl Gademann[1] *

[1]University of Basel

Over the past century, there has been a worldwide escalation in the prevalence of neurodegenerative diseases, such as Alzheimer's, Parkinson's and Huntington's disease.There are still no cures for these disorders and current therapeutics are only palliative.[1] More recently, emerging therapeutic approaches have focused on maintaining neuronal function in these disease models with small molecules that possess neurotrophic properties. A newly discovered norsesquiterpenoid, (*2R*)-hydroxy-norneomajucin, was reported to exhibit excellent neurite outgrowth-promoting activity in the primary cultures of fetal rat cortical neurons.[2] However, only 1.2 mg of the natural product was isolated from 3.5 kg of the fruits of *Illicium jiadifengpi*, an approximate 0.00003% yield (w/w), rendering extraction from natural sources for further biological investigations an impractical option. To better understand the neuritogenic activity of this natural product, we have begun studies toward its total synthesis. Our synthetic strategy represents a novel route toward the *seco*-prezizaane-type ring system, and a key characteristic of our approach is that it allows for flexible modification of fragment assembly. The overarching aim of this project is to utilize a multidisciplinary combination of organic synthesis and chemical biology to develop novel therapeutics for the advancement of neurodegenerative disease research.



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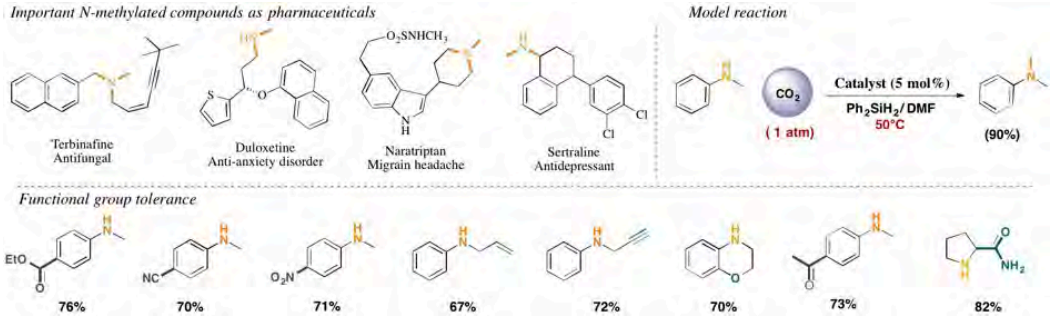
Metal Free Catalyst for Chemoselective Methylation of Amines Using CO_2 as a Methylating Agent

Shoubhik Das[1], Felix D. Bobbink[1], Gábor Laurenczy[1], Paul Dyson[1] *

[1]EPFL Lausanne

N-methylation of amines is an important step in the synthesis of many pharmaceuticals and has been widely applied in the synthesis of other key intermediates and chemicals.[1] Therefore, the development of efficient methylation methods has continuously attracted attention in recent years. Nevertheless, the most common methylation routes in industry employ toxic agents. Thus, the application of less toxic and more sustainable reagents is highly desired. In this respect, carbon dioxide is an attractive C1 building block because it is an abundant, renewable carbon source.[2] Our main aim was to develop a metal free catalytic system which is highly robust and stable, ready availability, inexpensive, and has a low toxicity.
Keeping this in mind, we developed a highly active, metal free catalytic system which operates under mild reaction conditions at atmospheric pressure and at 50°C. These reaction conditions are considerably milder than previous catalytic system known for this reaction and the organocatalyst also tolerates a wide variety of functional groups.[3-5] The chemoselective nature of the catalyst is highly attractive for the 'step-economy' in the synthesis of pharmaceuticals and fine chemicals.



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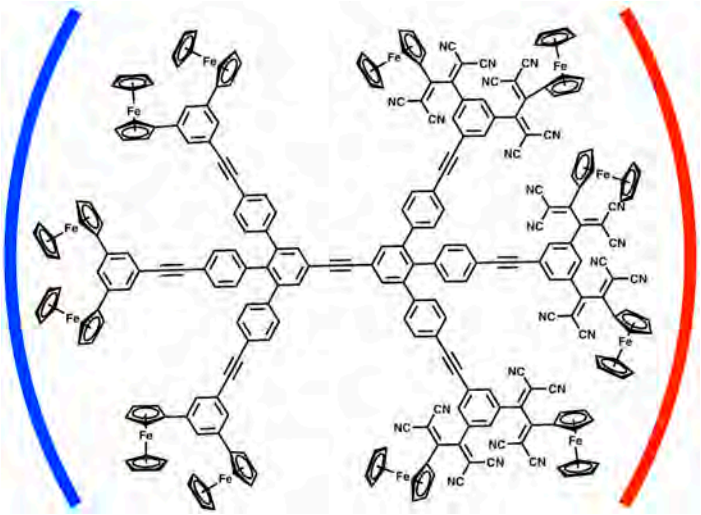
5 . K. Beydoun, T. vom Stein, J. Klankermayer, W. Leitner, *Angew. Chem. Int. Ed.* **2013**, 52, 9554.

Towards Zwitterionic Charge-Transfer Janus Dendrimers

Cagatay Dengiz[1], Benjamin Breiten[1], François Diederich[1] *

[1]ETH Zurich, Laboratory of Organic Chemistry, Department of Chemistry and Applied Biosciences, Vladimir-Prelog-Weg 3, CH-8093 Zurich, Switzerland

Dendrimers are described as repetitively branched, monodisperse, highly symmetric, spherical molecules (the terminology stems from the greek word “dendron” which means tree). *Janus* dendrimers bear the name of the mythological god of beginnings and transitions in ancient Roman religion. He is two-faced god since he looks to the future and past.Similarly, *Janus* dendrimers include two faces, named as dendrons. These dendrons have different functionalities or polarities, which makes them popular synthetic targets for chemists. By modifying this bifunctional groups, novel properties can be introduced into *Janus* dendrimers. The first *Janus*-type dendrimer synthesis was reported by Frechet and co-workers, in which the target dendrimer was obtained by the connection of two different dendrons. This gave access to an amphiphilic spherical dendrimer, in which one side is substituted with benzyl groups, while the other is substituted with carboxylate anions.[1] Until now, many dendrimers with multiple donor, multiple acceptor and push–pull donor–acceptor (D–A) systems were reported.[2] However, according to a literature survey, *Janus* D–A dendrimers constituting cationic and anionic hemispheres arising for intramolecular charge transfer, are still unknown. Our goal in this study is the first synthesis of *Janus* D–A dendrimers. If synthetically accessible, we are also hoping to investigate mono and multilayer formation due to Coulombic attraction between zwitterionic dendrimers and charged surfaces.[3]



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Towards a photochemically-promoted Native Chemical Ligation (PNCL)

Sebastian Dobarco[1], Christian Bochet[1] *

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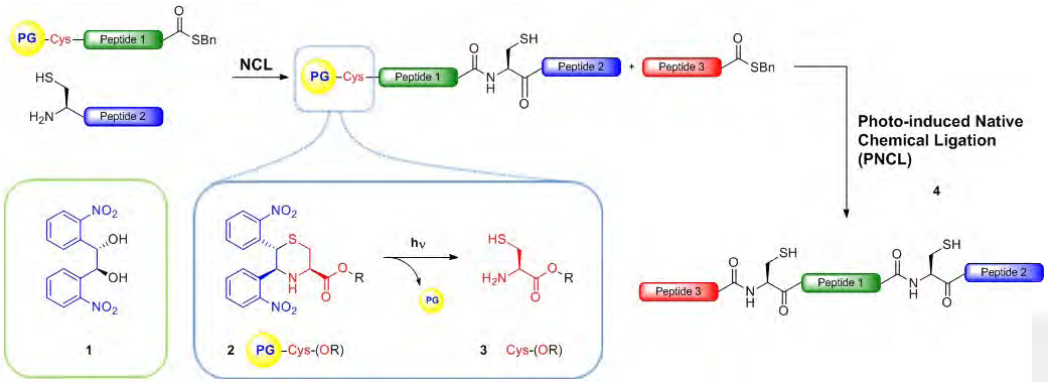
The chemical synthesis of large peptide constructs has seen tremendous growth over the past two decades, due to the development of efficient peptide ligation methods. Among them, the *Native Chemical Ligation* (NCL), first described by Kent and coworkers in 1994,[1a] became undoubtedly one of the most reliable processes for the formation of native peptide bonds. Based on the reaction between unprotected peptide segments containing an *N*-terminal Cysteine (Cys) residue and a *C*-terminal thioester, this chemoselective reaction showed quickly its power for accessing complex polypeptide chains. However, despite its high reliability and effectiveness for the formation of a native peptide bond at the ligation site, the ever-increasing need for large synthetic proteins highlighted the inherent limits of the method, especially for the assembly of multiple segments.
Common sequential peptide ligation strategies are based on the use of temporary Cys protecting groups, involving intermediate isolations steps or the need of reagent addition as well as pH adjustment in order to achieve their proper removal, leading to the next ligation step. Therefore, minimizing the interventions by carrying all the successive ligation steps in the same aqueous medium emerged as a valuable alternative. A step towards this “one-pot” approach could be the use of a photolabile removable protecting group for the Cys residue, potentially overcoming these limitations.[1b-c] Moreover, the photolytic deprotection could find possible applications in the assembly of large peptides within living organisms, allowing to some extent a localized and time-controlled ligation process.



A newly designed photolabile protecting group (**1**) was described in a previous communication and its effective use for the protection of ketones reported.[2] Efforts are thus being made in order to adjust this protecting group for the full protection of Cys residue (**2**), that would lead to a ligation of the peptide segments in a “one-pot” process, through the proper release of the Cys residue (**3**) upon appropriate irradiation (**4**).

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Outstanding Chiroptical Properties: A Signature of Enantiomerically Pure Alleno-Acetylenic Macrocycles and Monodisperse Acyclic Oligomers

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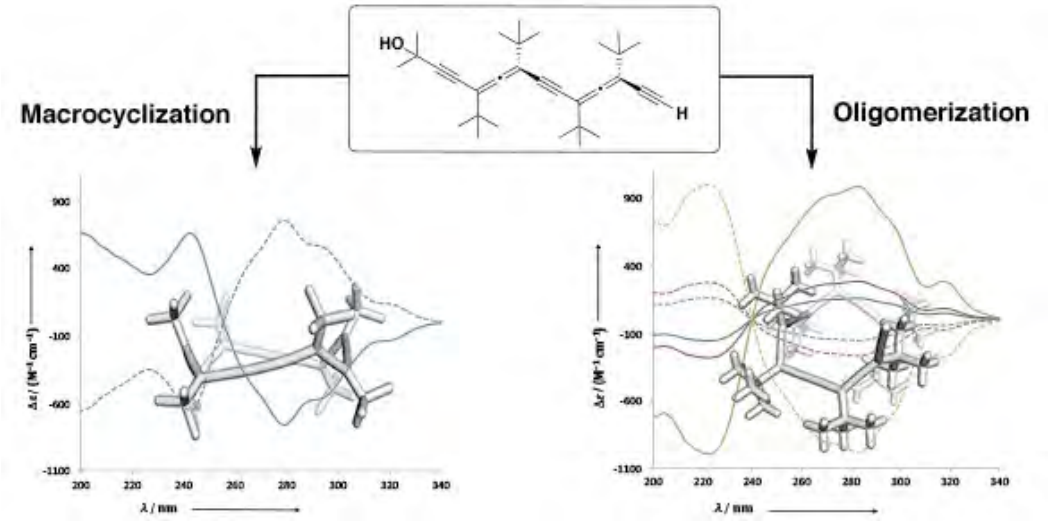
[1]ETH Zurich

A second series of shape-persistent alleno-acetylenic macrocycles and monodisperse acyclic oligomers with conformationally less flexible backbones were synthesized in enantiomerically pure form by short, high-yielding routes starting from optically active 1,3-diethynylallenes. The electronic circular dichroism (ECD) spectra of the D_2-symmetric, (*P,P,P,P*)- and (*M,M,M,M*)-configured macrocycles display remarkably intense chiroptical responses. A strong amplification of chirality is observed in the acyclic oligomeric series. Their preference for helical secondary structures of one handedness was supported by X-ray analysis and computational studies. This new set of data provides proof that outstanding ECD responses are a hallmark of alleno-acetylenic macrocyclic and acyclic oligomeric chromophores.



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Concentration controlled synthesis of Daisy Chains A [c2]daisy chain with the potential application as a molecular potentiometer

Sylvie Drayss[1], Yves Aeschi[1], Jürgen Rotzler[1], Marcel Mayor[1] *

[1]University of Basel

A wide variety of molecules were envisaged to mimic macroscopic electronic devices such as rectifiers, switches and wires.[1] Recent studies have shown that intermolecular π-π stacking interactions between two oligo-phenylene ethynylene (OPE)-rods are strong enough to form stable bimolecular junctions.[2-4] Inspired by these studies, an amphiphilic molecular rod comprising a terminal water soluble cyclophane was synthesized.[5] Driven by a strong hydrophobic effect, molecular daisy chains are formed in polar solvents depicting a stacked dimer with a mechanical adjustable π-overlapping surface.Functionalization with a thiol group renders the system accessible for potential applications as a molecular potentiometer.

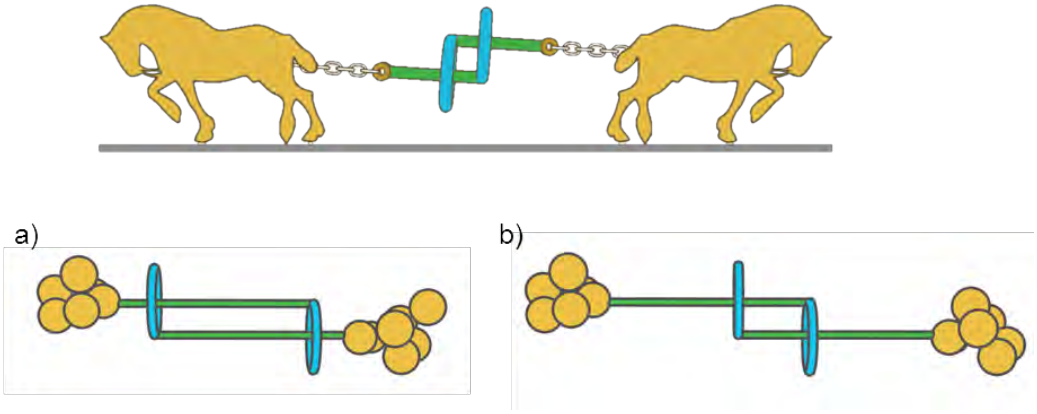

Figure1. Sketch of a stacked dimer in a molecular break junction acting as mechanically addressable potentiometer. a) high conductance state, b) low conductance state.

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Abietane diterpenoids from roots of Salvia leriifolia

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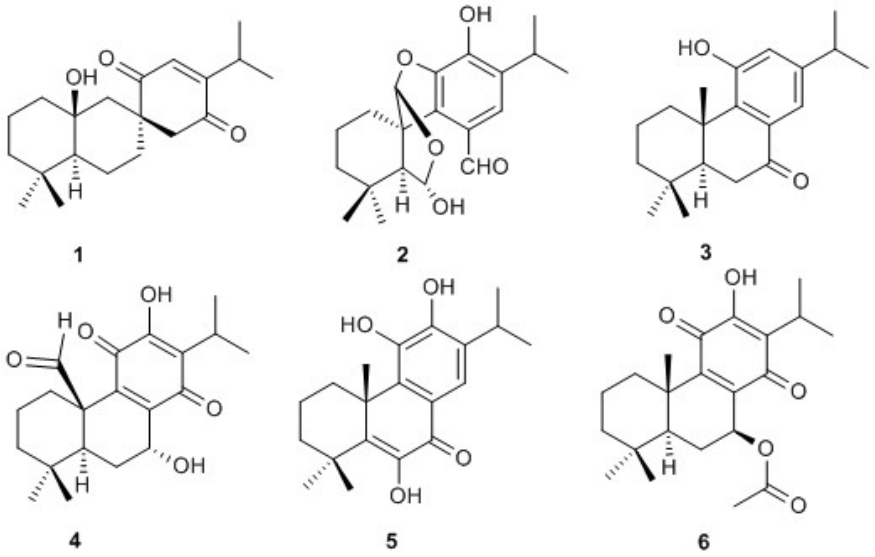
[1] Divisions of Pharmaceutical Biology, University of Basel, [2]Department of Phytochemistry, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, G. C., Evin, Tehran, Iran

As part of an ongoing project on the phytochemical profiling of endemic Iranian Lamiaceae, an *n*-hexane extract from roots of *Salvia leriifolia* was investigated. Six known abietane type diterpenoids were isolated and their relative configuration established by means of 1D and 2D NMR, and HRESITOFMS spectroscopy. Compounds **1** and **2** have been previously reported [1], but their absolute configuration was not determined at that time. We established the absolute configuration with the aid of electronic circular dichroism (ECD) spectroscopy [2]. Data were calculated using time dependent density function theory TDDFT/ B3LYP/6-31G** in MeOH as solvent, with the SCRF method in CPCM mode. A good match of experimental ECD spectra with calculated data led to the absolute configuration as depicted.



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Mono Thiomalonates in the Organocatalyzed Synthesis of 3,4-Dihydrocoumarins and 3,4-Dihydroquinolinones

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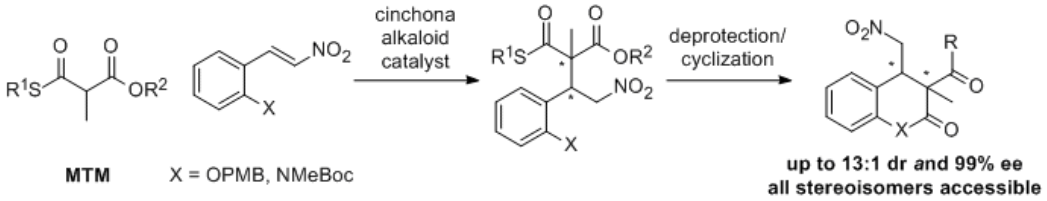
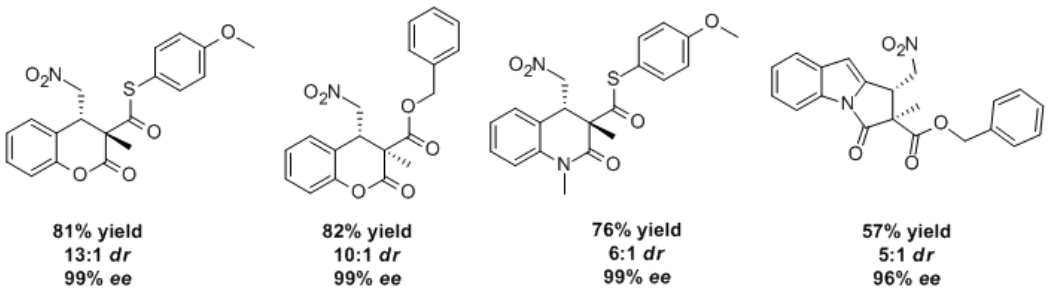
[1]ETH Zurich

Thioesters are versatile building blocks that allow for a wide range of subsequent transformation. In nature, malonic acid half-thioesters serve as thioester enolate equivalents and are used in the biosynthesis of fatty acids and polyketides. Herein, we report the organocatalyzed addition of mono thiomalonates (MTMs) to functionalized nitroolefines under mild conditions, followed by cyclization to heterocycles containing a quaternary stereogenic center.



This operationally simple method gives highly stereoselective access to a wide range of cyclic products with full stereocontrol, therefore enabling access to all stereoisomers with excellent enantio- and diastereoselectivity. The results show that MTMs are versatile synthons for stereoselective addition reactions of thioester enolates. In future work, we will expand these reactions of MTMs to other electrophiles and utilize their unique properties to access synthetically even more challenging structures.



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Photoionizable Porphyrin-Systems in Quantum Interference Experiments

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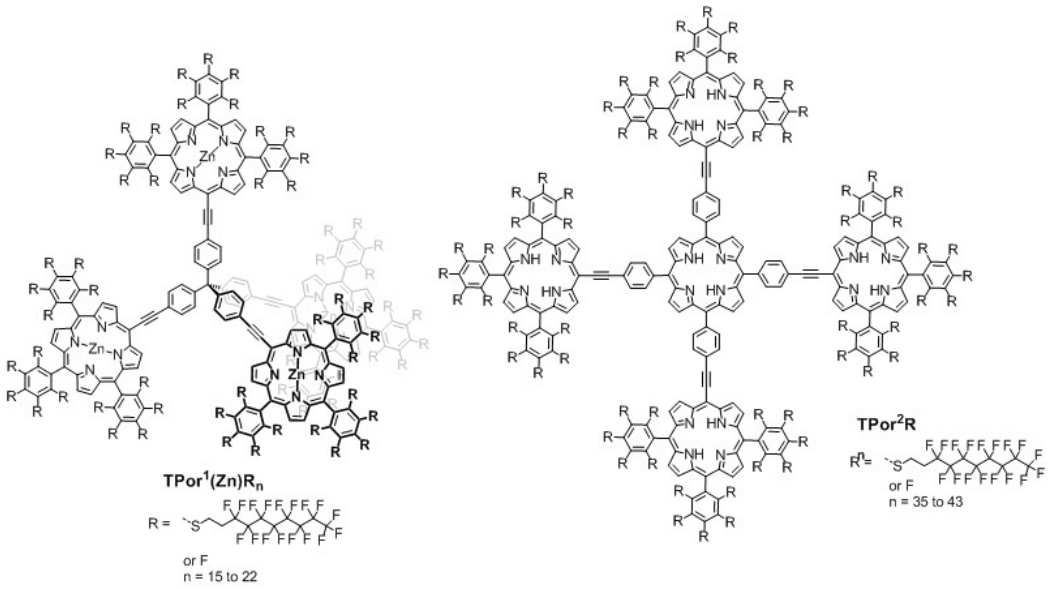
Matter-wave dualism is a fundamental concept in quantum physics. The observation of wave properties of heavy organic molecules can be used to approach the borderline between classical and quantum physics. Using a porphyrin library we were able to push the mass limit of interfering particles above 10’000 g/mol.[1,2] Motivated by the prospect to study quantum interference of even higher masses in a novel interferometer porphyrin-tetramer (**TPor(Zn)^{1}R$_n$**) and the fully conjugated pentamer (**TPor^{2}R$_n$**) were synthesized. Using a modular fourfold Sonogashira cross-coupling we were able to synthesize both multi-porphyrin systems. These libraries should push the mass limit of interfering particles above 20’000 g/mol. To perform the challenging quantum interference experiments using the novel interferometer photoionization and evaporation studies are performed. These studies show first promising ionization properties of the molecules.



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Electrophilic trifluoromethylation and the formation of quaternary stereogenic centers

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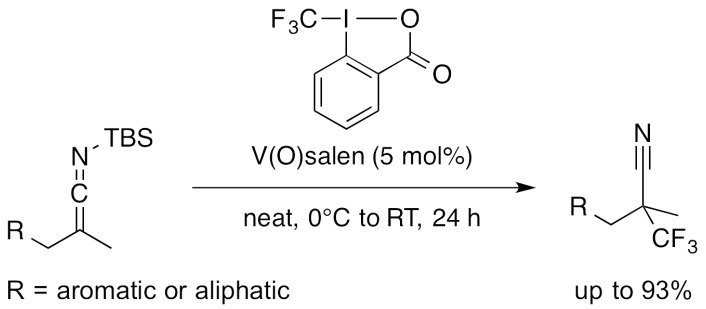
[1]ETH Zurich

Despite the wide application range of hypervalent iodine based reagents for electrophilic trifluoromethylation, the formation of quaternary carbons bearing a CF3-group still remains a challenge. This is even more true for their stereoselective synthesis. So far the only reported all-carbon substituted centers that undergo trifluoromethylation with the so-called Togni-reagents are beta-keto esters, alpha-nitro esters and silyl ketene acetals. The pool of quaternary carbon centers bearing a CF3-unit that have been synthesized via direct electrophilic trifluoromethylation in an enantioselective fashion is even smaller. The only direct electrophilic catalytic enantioselective trifluoromethylation of beta-keto esters was reported by Gade and coworkers using Togni-reagent, copper(II) triflate, and a chiral pincer ligand. [1]



To extend the scope of the reagents we have been working on the direct trifluoromethylation of secondary nitriles to form a quaternary carbon center, which can be used as an intermediate towards highly functionalized organic molecules.

The deprotonation of a secondary nitrile and subsequent addition of a direct electrophilic trifluoromethylating reagent only resulted in decomposition of the reagent.

To avoid harsh conditions with strong bases present in the reaction mixture silyl ketene imines have successfully been applied as nucleophiles in the alpha-trifluoromethylation of nitriles. After reaction optimization we were able to synthesize a variety of alpha-trifluoromethyl nitriles using 5 mol% of a vanadyl catalyst with a salen-type ligand in up to 93% yield. Furthermore, the reaction can be performed under solvent-free conditions, which is highly desirable. The products can be derivatized using standard protocols for the transformation of nitriles.

To the best of our knowledge, this is the first example for trifluoromethylation of silyl ketene imines, for vanadium-catalyzed activation of our reagents, and for neat reaction conditions. The development of an enantioselective version of this reaction is currently under investigation.

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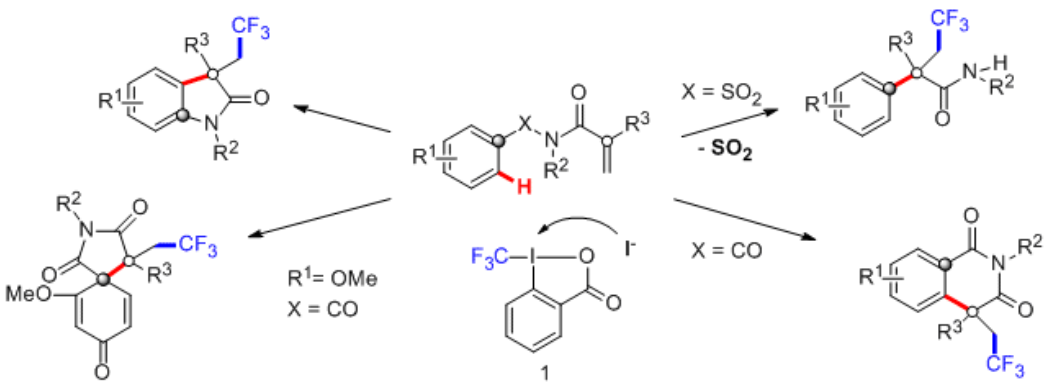
Metal-Free Aryltrifluoromethylation of Activated Alkenes

Noelia Fuentes [1], Wangqing Kong[1], Maria Casimiro[1], Estíbaliz Merino[1], Cristina Nevado[1] *

[1]Department of Chemistry, Winterthurerstrasse 190, CH-8057 Zurich, University of Zurich, Switzerland

The increasing presence of trifluoromethyl groups in agrochemicals, pharmaceuticals, and molecular materials stems from its unique ability to dramatically change the physical properties of these molecules, due to the high electronegativity and the metabolic stability of the C-F bonds.[1,2] Although transition-metal-catalyzed trifluoromethylation reactions have been developed,[3] metal-free processes have been much less explored.[3b,4] Our group has recently developed the first metal-free aryltrifluoromethylation of alkenes using mild reaction conditions.[5] In our strategy, nBu$_4$NI is able to activate Togni's reagent (**1**) by producing a highly reactive iodine(III) specie, which reacts with alkenes to form a new C-CF$_3$ bond. Trifluoromethylated isoquinolinediones and oxindoles can be synthesized in excellent yields and in a highly regioselective fashion. Trifluoromethylated spirobicycles and α-aryl-β-trifluoromethylamides containing an α-quaternary stereocenter can be also obtained with our methodology.



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Colorful Ion-Pair-π Interactions

Kaori Fujisawa[1], Cesar Beuchat[1], Marie Humbert-Droz[2], Tomasz Adam Wesolowski[2], Jiri Mareda[1], Naomi Sakai[1], Stefan Matile[1] *

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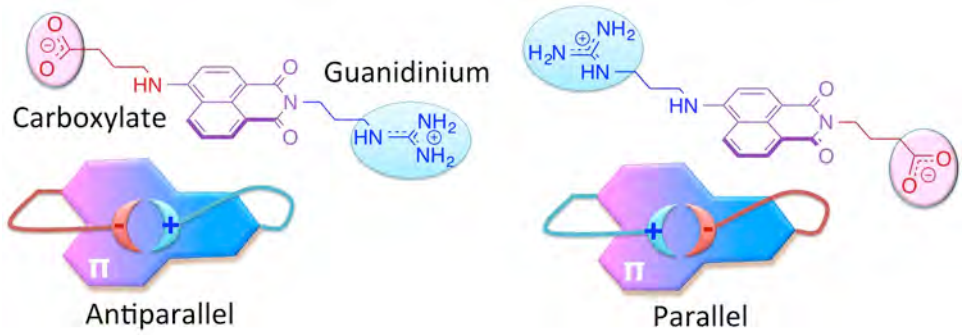
In nature, the ion-pair-π interactions are important for stabilizing protein folding. Many the cationic residues are in van der Waals contact with aromatic amino acids (cation-π interactions) [1]. The anion-π interactions occur between anions and π-acidic aromatic compounds and have been exploited for applications such as anion recognition, anion transport and artificial anion channels. We have used aromatic imides as platforms for investigating this unorthodox interaction. Computational simulations gave binding constants as high as E_{int} = -142 kJ mol^{-1} for naphthalenediimides with withdrawing cyano substituents in the core [2]. Artificial anion transporters showing high transport activity have been developed [3].
Here, we will present the construction of intramolecular ion-pair-π interactions and spectral modulation of these aromatic systems by ion-pair-π interactions using UV-vis absorbance spectroscopy: We will present colorful ion-pair-π interactions, and discuss their possible relevance in biology.



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Chemical synthesis towards a highly symmetric sulfur containing fullerene - shaped molecule

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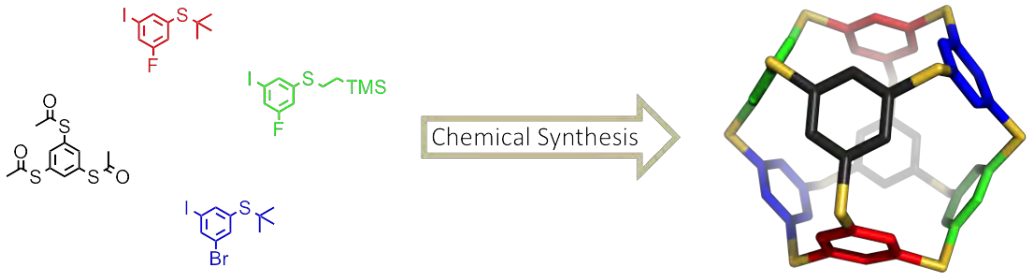
[1]University of Basel

Molecular structures with highly symmetric shapes like macrocycles, cubes or rods have since ever attracted the scientific field. In particular ball shaped structures consisting of identical subunits are expected to display promising optical and electronic properties. The most prominent representative within this family is the fullerene molecule.[1] It consist of sixty identical and indistinguishable carbon atoms forming a structure, which is very robust towards degradation. Nevertheless, due to the closed shell structure, supramolecular chemistry such as host - guest interaction are disabled. A higher porosity will be achieved by incorporating heteroatoms within a ball shaped molecule, called heterospherophanes. A theoretical study of the molecule **1** was reported by Ross *et al* in 1992,[2] and it's expected to act as a 3D organic metal with even more unusual behavior than C_{60}.



Herein we report a possible strategy towards the synthesis of this fully symmetric, sulfur containing fullerene like molecule **1**, which consists of eight identical subunits. The introduction of sulfur atoms may not only enables enhanced electronic and optical properties but also the porosity of this cuboctahedral structure is increased.

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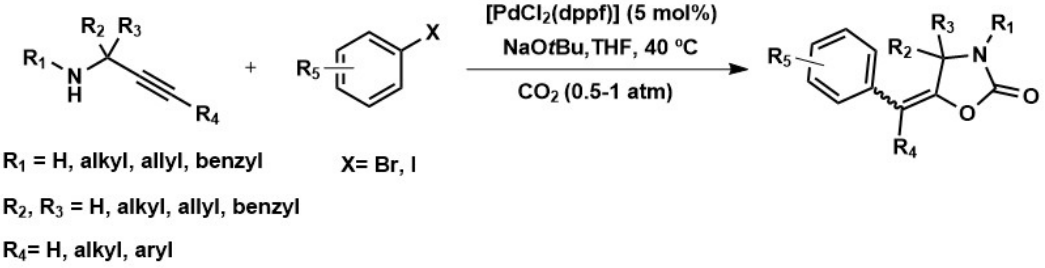
Palladium-catalyzed Sequential Carboxylative Cyclization-Cross-Coupling of Propargylic Amines with Aryl Halides

Patricia García Domínguez[1], Lorenz Fehr[1], Cristina Nevado[1] *

[1]University of Zurich

The large emissions of CO_2 to the atmosphere is an ever-increasing problem that encourages the chemical community to develop processes for capture and conversion of this inexpensive and non-toxic C1 source into valuable compounds such as carbamates.[1] In literature, several reports deal with CO_2 fixation by propargylamines to afford urethanes. Most of these methodologies involve harsh conditions and the use of metals or superbases.[2] On the other hand, sequential cyclization and cross-coupling of similar substrates with aryl halides has also been described to achieve useful building blocks.[3] Since the combination of the three processes (carboxylation-cyclization-coupling) in a single reaction is lacking, our group has developed a mild general protocol to achieve this goal. In presence of a base and a palladium catalyst a broad range of propargyl amine substrates were transformed into the corresponding 5-methylene-1,3-oxazolidin-2-ones under mild reaction conditions and low CO_2 pressures.



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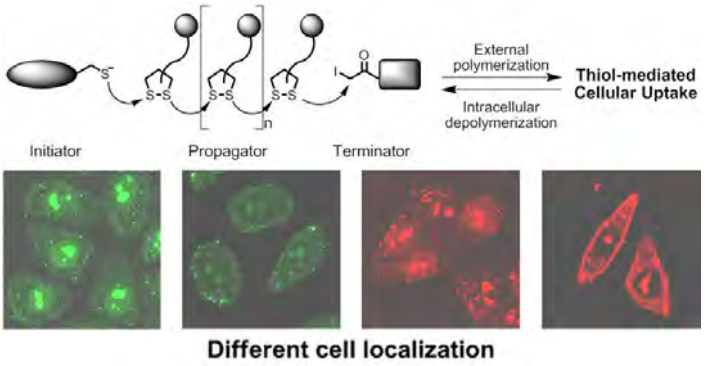
Cellular uptake of substrate-initiated cell-penetrating poli(disulfide)s

Giulio Gasparini[1], Eun-Young Bang[2], Guillaume Molinard[1], Sandra Ward[1], Aurélien Roux[1], Naomi Sakai[1], Stefan Matile[1] *

[1]University of Geneva, [2]Korea Istitute of Science and Technology

Cell-penetrating poly(disulfide)s (CPDs) are currently attracting increasing interest as promising molecular transporters [1]. These molecular vectors are held together by disulfide bonds that, after uptake, undergo reduction to thiol due to the presence of endogenous glutathione, drastically decreasing toxicity. Using a similar approach to surface-initiated ring-opening disulfide-exchange polymerization [2], we developed a new method to generate CPDs directly on a substrate of free choice [3]. This methodology allow us to covalently link the substrate to the CPDs and release it only when the cellular uptake occurs (Fig. 1).



Current efforts focus on the generation of various CPDs by substrate-initiated polymerization and on their use to deliver two different fluorescent probes into HeLa cells. Moreover, we investigate the effect of different functional groups present on the surface of the polymers on intracellular localization (cytosol, nucleoli, endosomes). Finally, special attention is dedicated to validate the hypothesis of thiol-mediated cellular uptake [4], both in vitro and in vivo, in order to explain the excellent performances of this new class of transporters.

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Synthesis of Cyano-Substituted Diaryltetracenes from Tetraaryl[3]cumulenes

Przemyslaw Gawel[1], Cagatay Dengiz[1], Aaron D. Finke[1], Nils Trapp[1], Corinne Boudon[2], Jean-Paul Gisselbrecht[2], François Diederich[1] *

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We developed a versatile, two-step synthesis of highly substituted 5,11-dicyano-6,12-diaryltetracenes, starting from easily available tetraaryl[3]cumulenes.[1] Reaction of tetraaryl[3]cumulenes with tetracyanoethylene in polar solvents gave 5,5-11,11-tetracyano-5,11-dihydrotetracenes in good yield. We propose that this unprecedented transformation is initiated by formal [2+2] cycloaddition of TCNE to the proacetylenic, central double bond of the cumulenes to give an intermediate zwitterion, which after an electrocyclization cascade and dehydrogenation yields the product dihydrotetracenes in a one-pot protocol. We also developed a subsequent copper-assisted, thermal decyanation/aromatization that provided the target 5,11-dicyano-6,12-diaryltetracene derivatives. These new chromophores were fully characterized by spectroscopic and X-ray crystallographic analysis. Interesting features of these new materials are their high thermal stability and promising fluorescence properties for potential use in optoelectronic devices. They represent selective chemosensors for Cu(I) ions, which coordinate to one of the CN substituents and form a 1:1 complex with an association constant of K_a = 1.5 x 10^5 L mol^{-1} at 298 K. Complexation is conveniently monitored by either UV/Vis or fluorescence spectroscopy.

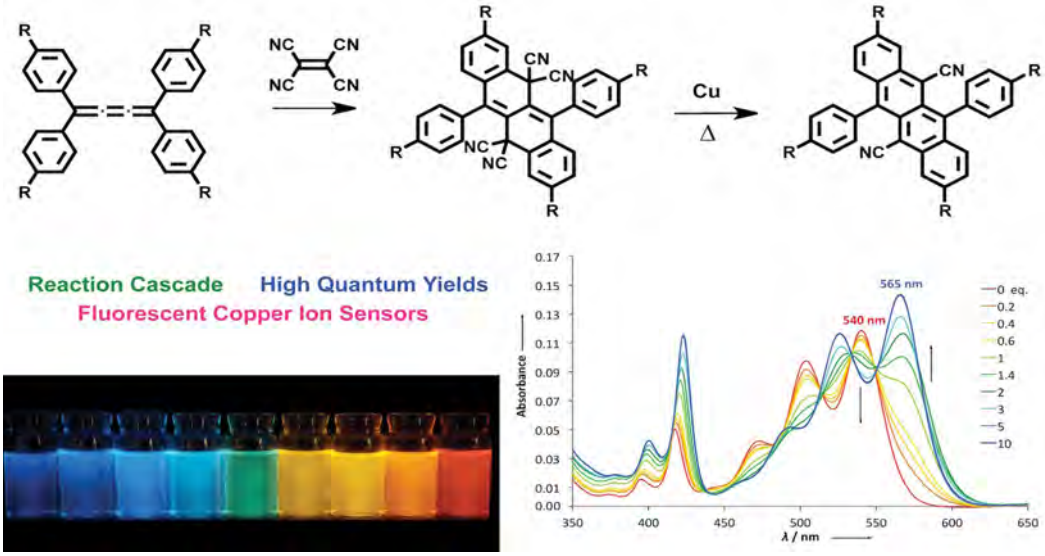

Figure 1. Up: Reaction scheme for the new transformation. Bottom Left: Photoluminescence of the tetracenes under UV light (366 nm). Bottom right: UV/Vis titrations of tetracenes with Cu^+.

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Supramolecular helicates with enantiopure alleno-acetylenes

Ori Gidron[1], Nils Trapp[1], François Diederich[1] *

[1]ETH Zurich

The formation of chiral supramolecular structures by coordination chemistry is extensively evolving, with applications such as chiral recognition and asymmetric catalysis.[1] While in most cases the moieties endowing chirality are peripherally attached, there are limited examples where the enantiopure moieties are directly embedded in the backbone.[2]

Recently, we introduced shape-persistent macrocycles and oligomers consisting of enantiopure alleno-acetylenes, which display significant nonlinear amplification of chiroptical properties with increasing number of chromophoric repeat units.. This nonlinear increase is explained by the formation of a secondary helical structure.[3] It was thus of great interest to explore the chiroptical properties of conformationally-stable supramolecular structures containing enantiopure allenes-acetylenes.

Herein we present the first supramolecular coordination structures containing enantiopure alleno-acetylenes in the backbone, which selectively form double-stranded or triple-stranded helices. The X-ray structure of the triple-stranded helicates reveals a potential cavity for encapsulation of small molecules. The chiroptical properties of the supramolecular structures along with TD-DFT calculations are discussed.

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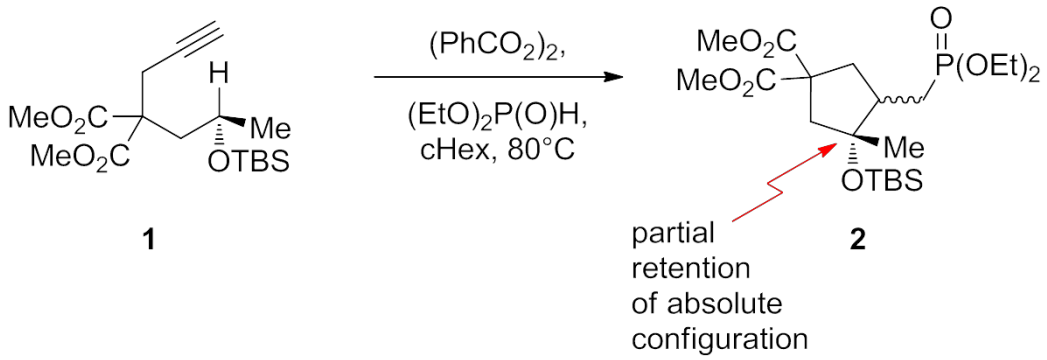
Retention of Absolute Configuration in Hydrogen Atom Transfer/Cyclisation Cascade

Christian Gloor[1], Valentin Soulard[1], Patrik Locher[1], Yvonne Kavanagh[1], Mark Pichowicz[1], Philippe Renaud[1] *

[1]University of Berne

Due to the nature of radicals, few stereoselective reactions are known in which a radical is generated at a chiral center with retention of the absolute configuration. In an early report by Heiba and Dessau, the formation of an optically active lactone was observed although the reaction proceeds through a radical at the chiral center *via* a 1,5-H shift.[1] The level of retention was however unknown. Recently, Curran and coworkers published a related cyclisation process of a-amide radicals involving retention of chirality.[2, 3]
Meanwhile, our group reported a radical cyclisation involving phosphonyl and thiyl radicals to access cyclopentane derivatives.[4] We decided to use this reaction as the starting point to study whether retention of chirality is possible and the factors influencing the stereochemical outcome.

The alkynyl malonate **1** was readily synthesized in a five-step procedure starting from (*S*)-(-)-ethyl lactate. Treatment of **1** with diethylphosphite afforded the cyclic product **2** with partial retention of configuration.



1 **2**

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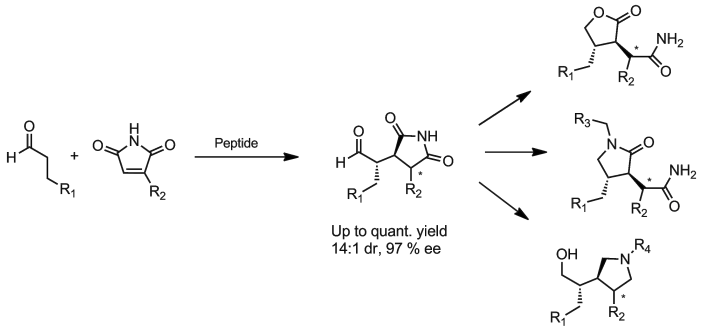
Peptide-Catalyzed Stereoselective Conjugate Addition Reactions of Aldehydes to Maleimides

Claudio Grünenfelder[1], Helma Wennemers[1] *

[1]ETH Zurich

Stereoselective conjugate addition reactions of aldehydes to maleimides offer an efficient entry into chiral succinimide derivatives which are present in numerous natural products and clinical drug candidates.[1] Tripeptides of the type Pro-Pro-Xaa (Xaa = acidic amino acid) have been introduced in our group as catalysts for aldol reactions and conjugate addition reactions of aldehydes to *β*-mono, *α*,*β*- and *β*,*β*-disubstituted nitroolefins.[2] We have now developed a peptidic catalyst, which is able to effectively activate aldehydes and maleimides and control the dia- and enantioselectivity in conjugate additions by hydrogen bonding.



Herein we present a highly selective tripeptide catalyzing the conjugate addition of aldehydes to maleimides and the subsequent transformation of the products into lactones, lactams and pyrrolidines. First mechanistic insights are presented that explain the observed stereoselectivity and the activation of the electrophile by the catalyst.[3]

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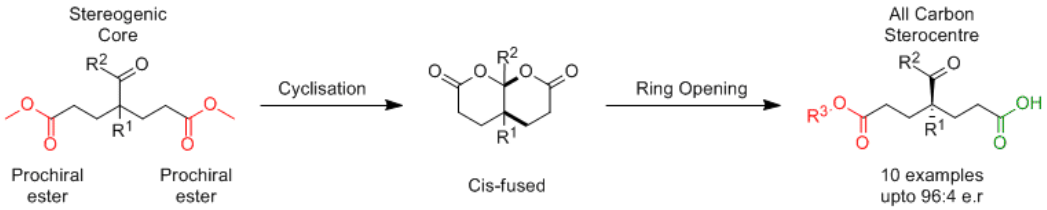
Phosphoric Acid-catalyzed Desymmetrization of Bicyclic Bislactones Bearing an All Carbon Quaternary Stereogenic Center: Catalytic Enantioselective Syntheses of (-)-Rhazinilam and (-)-Leucomidine B.

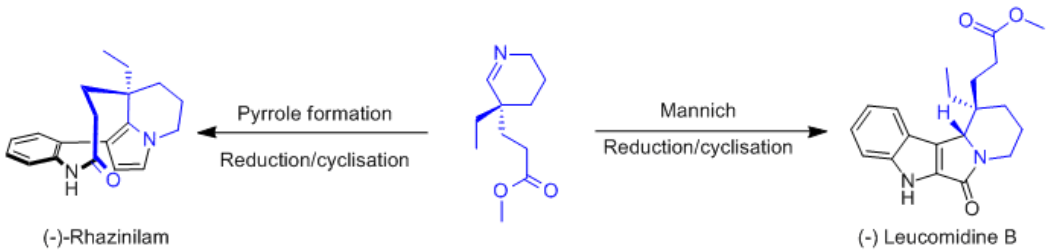
Jean-Baptiste Gualtierotti[1], Delphine Pasche[1], Qian Wang[1], Jieping Zhu[1] *

[1]EPFL Lausanne

Prochiral 10-carbon dimethyl 4-ethyl-4-formylpimelate, first introduced by Kuehne in 1964 [1], has often been used as a key starting material in the syntheses of diverse indol alkaloids such as vincamine or vincadifformine. However this monoterpene equivalent has never been used to its full potential as no straightforward access to an enantiopure derivate existed previously; herein we report a desymetrization protocol for the resolution of Kuehnes aldehyde [2]. The enantioselective cascade fragmentation of bicyclic bislactones derived from Kuehene's aldehyde in the presence of a chiral imidodiphosphoric acid gave enantiomerically enriched monoacids having an all carbon quaternary chiral center.



The concise enantioselective synthesis of (-)-Rhazinilam [3] and the first total synthesis of (-)-Leucomidine B [4] were subsequently developed from this common intermediate.



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Cyclic Carbo-Isosteric Depsipeptides and Peptides as a Novel Class of Peptidomimeticsand their Potential Biological Applications

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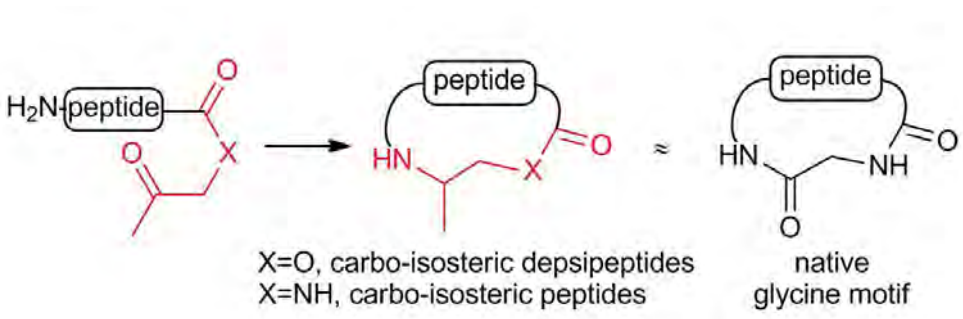
[1]Novartis Pharma AG, [2]Hans-Jörg Roth

Peptides with their important modularity and diversity are an attractive class of compounds to address difficult targets. They tend to have strong affinity for a broad range of biological targets. Despite promising applications, peptides have been underexploited, this could be rationalized by their poor bioavailability, lack of permeability and metabolic stability. Multiples factors are known to improve the pharmacological properties of peptidic drugs. A major strategy is the cyclization of peptides and as a state of the art option, cyclic peptidomimetics represent a powerful combination to access highly potent compounds with improved pharmacokinetic properties.

During our research to access diverse peptidic and pseudopeptidic macrocycles, we have developed a novel and highly efficient cyclization method to access a new class of cyclic carbo-isosteric depsipeptides and carbo-isosteric peptides. Our strategy requires easily accessible C-terminal methyl ketone ester or amide functionalized linear precursors as starting material. The well-known reductive amination has then been used to afford cyclic penta- to octa-pseudopeptides *via* selective intramolecular formation of a glycine peptidomimetic unit under moderate dilution.[1] Highly constrained cyclic carbo-isosteric tetra-depsipeptides were also successfully cyclized at high concentrations in respect to peptide standards. The flexibility of our novel method was confirmed by additional investigations which allowed to access various cyclic peptidomimetics containing a wide range of acid, nucleophilic, hydrophobic and aromatic backbone amino-acids.

From a structural aspect, X-ray structures of one carbo-isosteric depsipeptide and one carbo-isosteric peptide were successfully obtained. Complementary NMR conformational studies are currently under investigation to understand the impact of our motif on the 3D structure in comparison to the native peptide. Finally, promising results have been obtained regarding the potential biological applications of the developed glycine peptidomimetic unit.



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Study of Tris-(2-carboxyethyl)-phosphine oxide

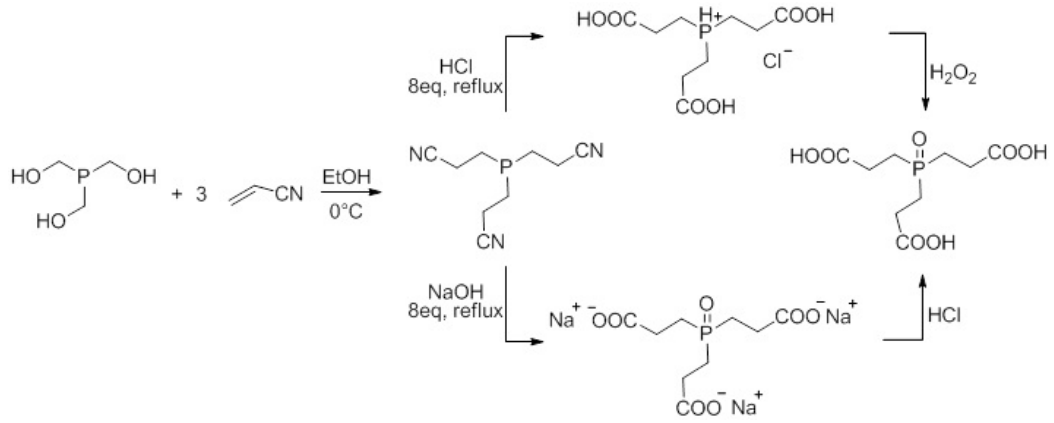
Jihane Haoues[1], Christelle Schenk[1], Reinhard Neier[1], Dr. Olivier Vallat[2]

[1]University of Neuchatel, [2]Febex SA, Bex, Switzerland

New class of nontoxic and environmental friendly fire retardants like phosphinate salts are used for the replacement of more toxic halogen containing flame retardants avoiding the liberation of hydrogen halides during combustion[1].

We will report the synthesis and studies of tris-(2-carboxyethyl)-phosphine oxide, in view of developing, characterizing new derivatives for the flameproof applications[2].

The properties and the synthesis of the ester tris-(2-carboxyethyl)-phosphine, the acid and the sodium salt of the acid starting from tris(hydroxymethyl)phosphine will be reported.



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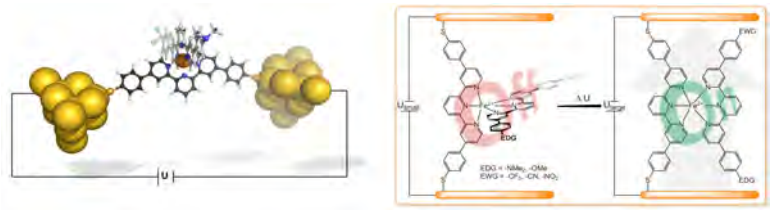
Design, Synthesis and Physical Investigation of Bias-Dependant and Mechanically Driven Single Molecular Spin Switches

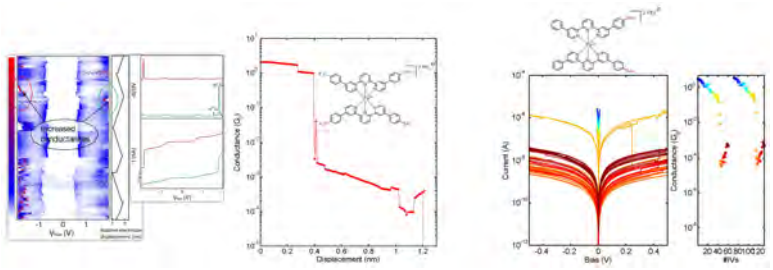
Gero Harzmann[1], Riccardo Frisenda[2], Herre van der Zant[2], Marcel Mayor[1] *

[1]University of Basel, [2]TU Delft

Several novel tailor-made homo- and heteroleptic Fe(II)-bisterpyridine complexes are reported. Their implementation into miniaturized electronic devices like circuits is of highest interest in the field of molecular electronics due to their potential capability of acting as bias-sensitive single molecular spin switches. Each investigated complex contains a core Fe(II)-ion exhibiting an externally addressable spin state, a symmetric thiol-terminated terpyridine (tpy) ligand allowing an immobilization between two Au-electrodes and a second tpy moiety consisting of adaptable dipolar push-/pull-systems providing the systems' desired sensitivity towards varying applied electric fields. Sufficient trans-molecular conductance is ensured by the rare 4,4''-disubstitution pattern at the tpy core accessible *via* an unprecedented *Suzuki-Miyaura* type assembly route.[1] The key synthons' versatility readily allows the alteration of the peripheral 4,4''-substituents at the tpy core.



Switching events found during mechanically controlled break junction (MCBJ) experiments underline the expected results and could be found for the bias-dependent structures as well as for the mechanically induced single molecular spin switches.



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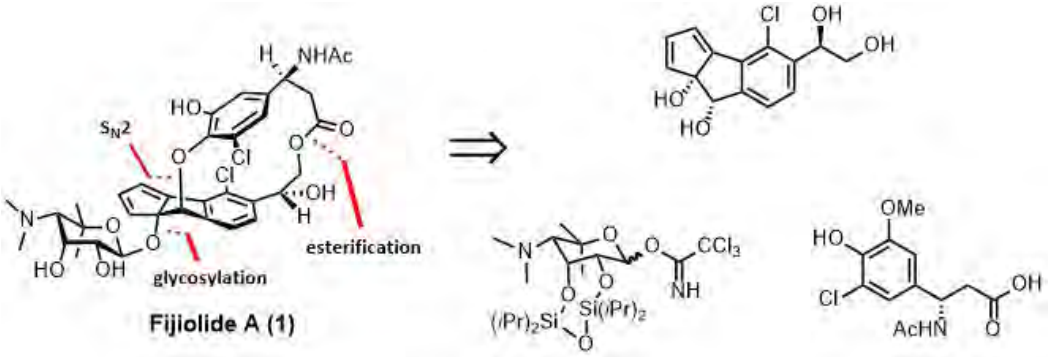
Synthetic Studies towards Fijiolide A

Christoph Heinz[1], Nicolai Cramer[1] *

[1]EPFL Lausanne

In 2010 *Fenical et al.* reported the isolation of Fijiolide A (**1**) from a marine-derived actinomycete of the genus *Nocardiosis*.[1] The chloroaromatic natural product was shown to exhibit remarkable biological activity by reducing the TNF-α-induced NFκB activation by 70% with an IC_{50} value of 0.57 μM. As an inducible transcription factor, NFκB regulates the expression of more than 400 different genes. Many of whom encode tumorgenesis relevant proteins, e.g. cyclooxygenase (COX)-2 or matrix metalloproteinase (MMP)-9.[1]
Apart from the pharmacological potential, Fijiolide A engages particular attention due to its highly complex molecular assembling. Thus, **1** consists of a chlorocyclopenta[α]indene carbon framework which forms a macrocycle with an attached β-tyrosine moiety. This 16-membered macrolactone acts as an aglykon of a ribopyranose unit. Ultimately, Fijiolide A exists as an atropisomer due to the hindered rotation of the β-tyrosine within the macrocycle.
1 possesses close structural resemblance with the aromatization products of numerous potent enediyne antitumor antibiotics, especially the C-1027 chromophore.[2] However, Fijiolide A is unique, since it is the sole Masamune-Bergman cyclization product displaying notable biological activity.[2,3]
We disclose our initial synthetic efforts towards Fijiolide A with the depicted disconnection strategy.



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Rotational restricted and functionalized CBP derivatives as host materials for phosphorescent organic light-emitting diodes

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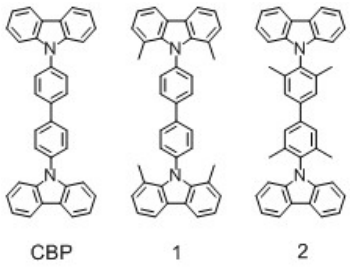
[1]Department of Organic Chemistry, University of Basel, St. Johanns-Ring 19, 4056 Basel, Switzerland

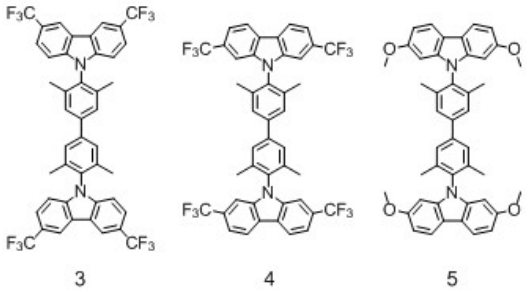
CBP (4,4'-dicarbazole-1,1'-biphenyl) has been successfully used as host material in green and red phosphorescent organic light emitting diodes (Ph-OLED).[1] Carbazole building blocks in CBP provide a high triplet energy state and thereby enable the use of CBP as matrix materials with an efficient energy transfer to a triplet emitter.[2] Unfortunately, the triplet energy of CBP (E_T: 2.56 eV) is lower than those of the classical blue triplet emitters (2.65 eV), resulting in poor device efficiency.

Research on structural modification of CBP to develop efficient energy transfer for blue emitters by increasing the host triplet state energy turns out to be of particular importance.

Two new derivatives were synthesized by introducing sterically demanding substituents to the biphenyl backbone of CBP. This modification leads to an angulated orientation of the carbazole subunit to the biphenyl backbone, which gives a less conjugated π-system. Thanks to this perpendicular alignment an increase of the triplet state energy was measured in molecules **1** and **2** compared to CBP.



Furthermore, the influence of either electron donating (-OMe) or electron withdrawing (-CF_3) groups at specific positions of the carbazole subunit in three new synthesized CBP derivatives was investigated and the results will be presented herein.



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Mechanistic insights into C-C coupling reactions mediated by Au(I)/Au(III) redox processes

Manuel Hofer[1], Cristina Nevado[1] *

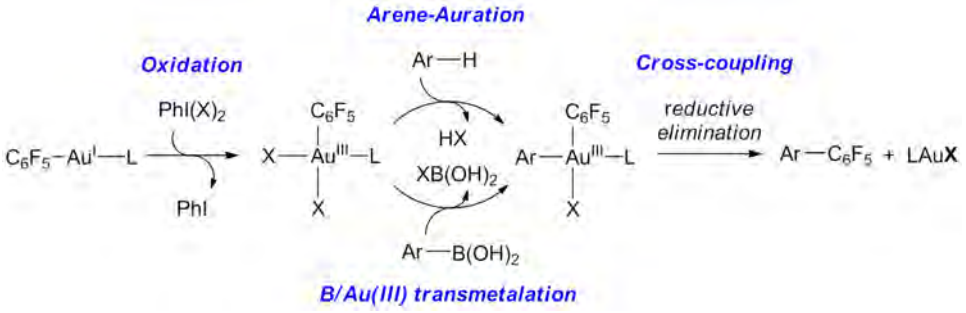
[1]University of Zurich

Gold-catalyzed cross-coupling reactions of arenes are rarely known in the literature [1-3]. Catalytic cycles in these transformations typically consist of a gold(I) to gold(III) oxidation step and an arene auration on gold(III) complexes. We set out to study the individual steps of gold(I)/gold(III) redox catalytic cycles yielding C-C cross-coupling products through stoichiometric experiments.

The oxidation of electron deficient arene-gold(I) complexes in the presence of strong oxidants such as hypervalent iodine(III) resulted in the formation of the corresponding aryl-gold(III) complexes, which could be isolated and characterized by X-ray diffraction analysis [4].

The reactivity of electron-deficient arene-gold(III) complexes towards nucleophilic aromatic and heteroaromatic counterparts was studied next. 1-Methylindole proved to be the most reactive reaction partner to form cross-coupling products whereas methoxybenzenes did not react. The ancillary ligand on gold also influenced the reactivity in the order PPh_3 P^tBu_3 IPr. The oxidative cross-coupling starting from the corresponding gold(I) complexes in presence of hypervalent iodine oxidants was also studied. In general, these reactions showed higher reactivity towards the corresponding cross-coupling products with $PhI(OAc)_2$ as oxidant [5].

Finally, we were interested to transfer electron deficient arenes to gold(III) complexes by B/Au(III) transmetalation in order to synthesize cross-coupling products by reductive elimination. Interestingly, electron-rich boronic acids remained unreactive, whereas electron-deficient ones underwent transmetalation in an efficient manner under neutral conditions [6].



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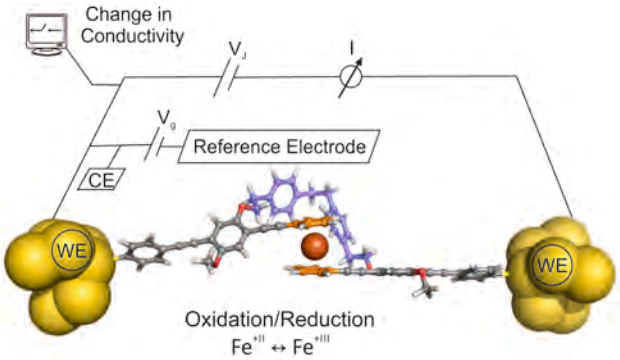
Ferrocene Comprising Macrocycle – Towards Rotational Restricted Molecular Wires

Viktor Hoffmann[1], Nicolas Jenny[2], Marcel Mayor[1] *

[1]University of Basel, [2]Sika Technology AG

Molecular wires containing redox active ferrocene structures are predicted to have an intrinsic transistor-like behavior when they are integrated into a three-terminal field-effect device [1]. The concept is based on the work of Sita et al. and is designed to enable electron transport by passing the electronically addressable ferrocene core [2]. It is assumed that by rotation around the central ferrocene unit a stacked conformation could lead to high conductance values. In our approach the two phenyl acetylene arms of the molecular wire are rotationally restricted by a styrene based bridging unit. To overcome the macrocyclic strain, a Ring Closing Metathesis (RCM) reaction is envisaged. By rigidifying the molecular wire, potential bypass events can be excluded. Incorporated into an electric current probing device, our approach is believed to generate current plateaus which can be altered by addressing the ferrocene with a gating bias.



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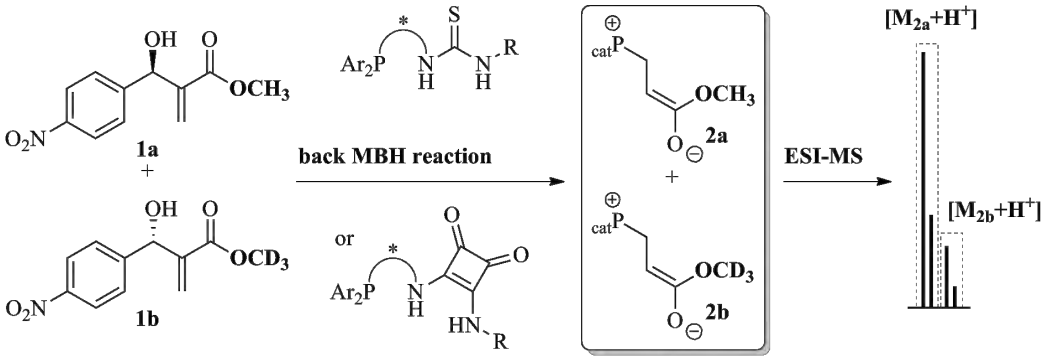
Screening of Chiral Phosphine-Based Organocatalysts for the Asymmetric Morita-Baylis-Hillman Reaction by Mass Spectrometric Monitoring of the Back Reaction

Patrick Isenegger[1], Florian Bächle[1], Andreas Pfaltz[1] *

[1]University of Basel

A catalyst screening method based on the ESI-MS analysis of charged reaction intermediates derived from mass-labeled quasi-enantiomeric substrates was developed in our group and was applied to several metal- and organocatalyzed processes. ESI-MS-based screening is fast, reliable, and operationally simple as it does not require work-up or purification steps [1]. Herein, the application of this method to the Morita-Baylis-Hillman (MBH) reaction is demonstrated.The charged intermediates **2a** and **2b** were formed by a phosphine catalyzed back MBH reaction with the mass-labeled quasi-enantiomeric MBH products **1a** and **1b**. According to the principle of microscopic reversibility, the ratio of **2a** to **2b** reflects the intrinsic selectivity of the catalyst for the corresponding forward reaction. The intrinsic enantioselectivity of several organocatalysts was successfully determined by ESI-MS screening and verified by HPLC analysis of the forward reaction, demonstrating the potential of this method for finding new selective organocatalysts for the MBH reaction.



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Stabilization of open-shell graphene fragment triangulene

Michal Juricek[1], Peter Ribar[1]

[1]University of Basel

Miniaturization of electronic devices can be achieved by use of small molecules possessing properties, which allow them to perform a desired function. Molecules that can be switched between two different states—“ON” and “OFF”—as a response to a stimuli are expected to serve one day as platforms for molecule-based memory devices. To increase the information storage capacity of a molecule, one can envisage using electrons as the information carriers or “quantum bits”. For example, molecule that would have three unpaired electrons, which can communicate with each other, could be in principle switched between eight—and not just two—energetically different spin states. Open-shell polycyclic aromatic hydrocarbons (OS-PAHs)[1] possess multiple unpaired electrons owing to their triangular topology and thus suit ideally for such purpose. The number of unpaired electrons in OS-PAHs increases as their size becomes larger, which consequently raises the number of spin states within one molecule. High reactivity of multi-spin systems—even those possessing just one unpaired electron—however, severely hampers their isolation and use. To this day, only persistent derivatives of the smallest OS-PAH—namely, phenalenyl—are known, while persistent OS-PAHs larger than phenalenyl remain to be made. Here we describe the design and synthesis of a derivative of triangulene (shown), which is expected to be stable enough to be isolated and characterized in the solid state for the first time. If successful, this strategy can be employed to access larger high-spin OS-PAHs.

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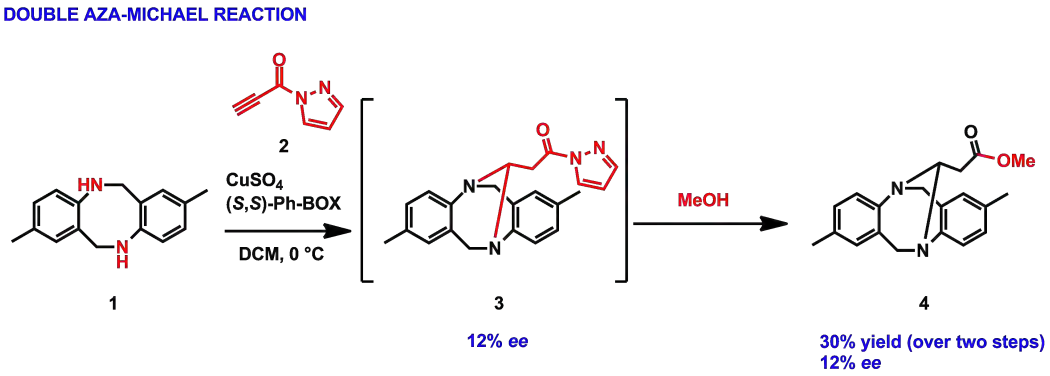
Enantioselective Synthesis of Tröger's Bases via Cu(II)-catalyzed Double Aza-Michael Addition

Takuya Kamiyama[1], Jan Cvengros[1] *

[1]ETH Zurich

Tröger's base is a rare example of a compound containing configurationally stable stereogenic nitrogens due to a high inversion barrier [1]. Its derivatives have been used for various applications including catalysis and molecular recognition [2]. So far, their preparation as single enantiomers has been a major challenge.



Our project focuses on performing asymmetric double aza-Michael reactions with tetrahydrodiazocine (**1**) and 1-propynoylpyrazole (**2**) in the presence of chiral catalysts to selectively form one enantiomer of the intermediate (**3**). A combination of copper(II) sulfate and (*S*,*S*)-Ph-BOX ligand gave the product (**4**) with a slight enantiomeric excess, isolated after methanolysis. Future work will be focused on the optimization of yield and enantioselectivity by varying the substrates, catalysts and reaction conditions.

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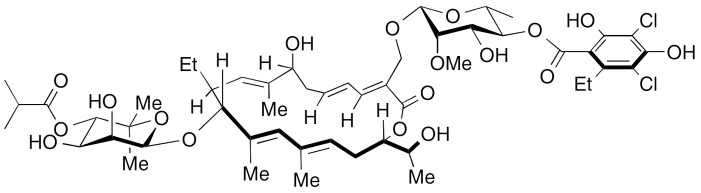
Towards the Total Synthesis of Fidaxomicin

Elias Kaufmann[1], Hideki Miyatake Ondozabal[1], Karl Gademann[1] *

[1]University of Basel

Fidaxomicin is a FDA-approved narrow spectrum antibiotic and currently used for the treatment of *Clostridium difficile* infections. This macrolide has also been found to exhibit potent biological activity against the multi-drug resistant *Mycobacterium tuberculosis* (0.1 mg/L), however its poor pharmakokinetics prohibit its use as a drug.[1] Surprisingly, in spite of its significant biological properties and unique molecular structure no efforts towards the synthesis of fidaxomicin have ever been reported since the first isolation in 1975.[2]



fidaxomicin

The total synthesis of this challenging 18-membered macrolide should pave the way to generate structurally diverse analogs and could provide new insights into the structure-activity relationship. In this context, we will present our investigations towards the total synthesis of fidaxomicin.

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Supramolecular Zippers Dispersing Single-Walled Carbon Nano-Tubes(SWCNTs)

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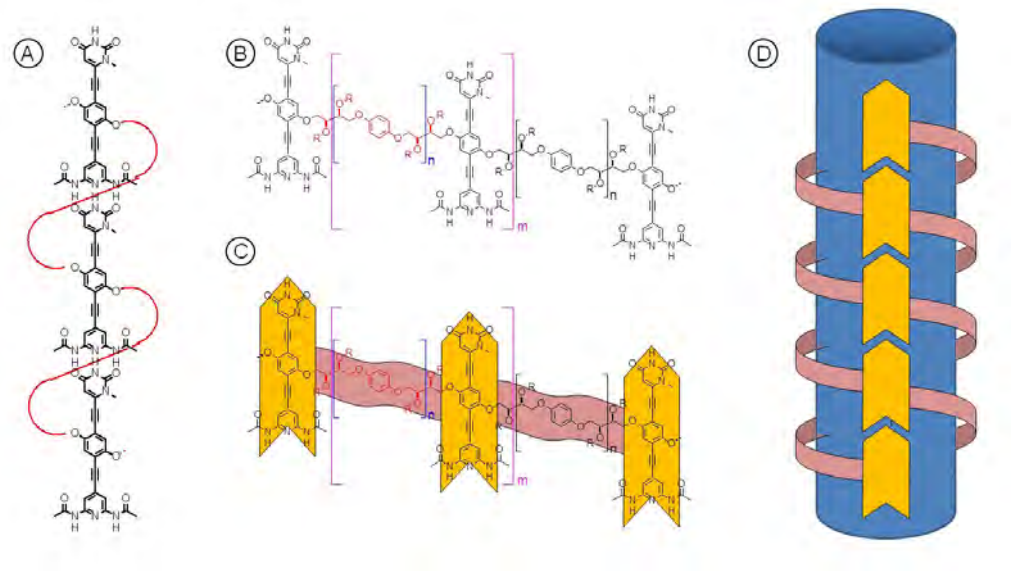
[1]University of Basel

Single walled carbon nanotubes (SWCNTs) have outstanding physical (mechanical and electronic) properties which depend on the arrangement of the carbon atoms when a graphene sheet is rolled into a tube. While chemistry does not provide tools to specifically access monodisperse tubes with given *n*,*m* indices, impressive steps were made in sorting tubes. In particular, some polymers and copolymers comprising rigid aromatic subunits display excellent selectivity towards specific nanotubes, as they form strong π-π stacking interaction with the nanotube surface, such as fluorene, and carbazole-based polymers.[1-4] In this research proposal we would like to develop a supra-molecular “zipper” to disperse reversibly SWCNTs with particular diameters, *n*,*m*-indices and hopefully even chirality. For this purpose we designed a self complementary structure. The triple hydrogen bonds formed between both terminal units enables the formation of supra-molecular polymers. In order to control the diameter of the tube we suggest to interlink the hydrogen bonding units via the central phenyl rings. The polymer structure comprises aryl units and flexible joints to favor its interaction with the CNT surface. Furthermore is comprises peripheral alkyl chains to provide the solubility of the polymer wrapped tube. In an aprotic solvent the formation of the supra-molecular polymer is only possible if the tube has a diameter enabling the surface alignment of the interlinking polymer backbone.



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Synthesis of chiral Ruthenium-cyclopentadienyl complexes and application to hydrative cyclisation of yne-enones

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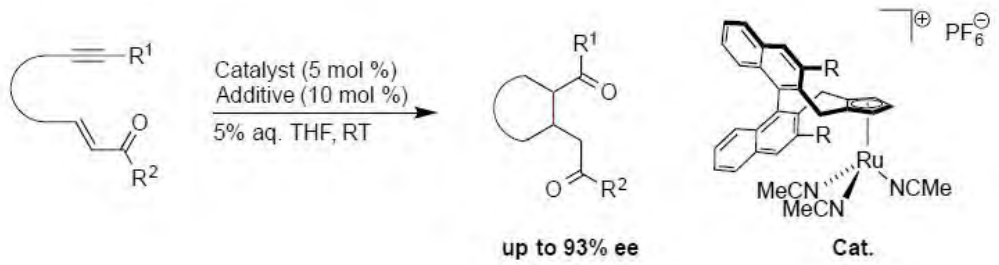
[1]EPFL Lausanne

Ruthenium catalyzed cycloisomerisations offer a rapid access to complex molecular frameworks in an atom economical fashion.[1] Therefore the cationic $[CpRu(MeCN)_3]PF_6$ complex found widespread application in organic synthesis. The endeavor to conduct these transformations in an enantio-selective manner led to several ligand design approaches, albeit resulting in mediocre selectivities. Recently our group pioneered in the development of highly efficient chiral Cp ligands for late transition metal catalysis[2] and we intend to explore their potential in combination with various metals.

Ruthenium (II) complexes derived from a 3,3 disubstituted *R*-Binol backbone proved to catalyze the hydrative cyclisation of yne-enones to the corresponding diketones in good diastereo- and enantioselectivity.[3] In this way the products containing two stereocenters are created providing valuable building blocks for follow up functionalizations.



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AFM tip functionalization by in situ click reaction

Rakesh Kumar[1], Ramakrishna Shivaprakash Narve[1], Nicholas D. Spencer[1], Yoko Yamakoshi[1] *

[1]ETH Zurich

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Chemical force spectroscopy (CFS) utilizes chemically functionalized AFM tips and provides a versatile tool for studying intermolecular interactions at a single molecular level.[1]For a single molecule force spectroscopy, immobilization of ligand on the AFM tip is critical[2] and we have developed a molecular tripod for a stable attachment of biomolecules to gold coated AFM tip through multiple covalent bonds.[3]

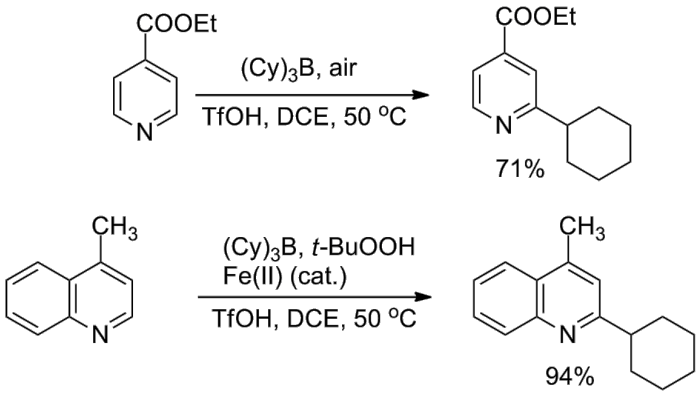
In this study, a facile and universal method for the functionalization of AFM tip was developed for the CFS study of the intermolecular interactions of biomolecules. A click chemistry of tripod-acetylene and azide–linker–biotin molecule was successfully carried out on the AFM tip surface and used for the CFS study of biotin–NeutrAvidin interaction.

A Simple Method for the Alkylation of N-Heterocycles with Trialkylboranes

Andrey Kuzovlev[1], Ioulia Gorokhovic[1], Philippe Renaud[1] *

[1]University of Berne

The addition of carbon-centered radicals on an electron-deficient heteroaromatic compounds (Minisci reaction)[1] has recently been the object of intense development.[2] Organoboranes, commercially available or easily prepared via hydroboration of olefins, represent a very attractive source of alkyl radicals.[3] We report here, that trialkylboranes[4] can be used in Minisci type reactions using either either air or iron(II)/tert-butylhydroperoxide as co-reagents.



This process compares well will the methods reported in the literature in term of yield and efficiency and, due to the versatility of the hydroboration reaction, allows the introduction of a broad variety of substituents.

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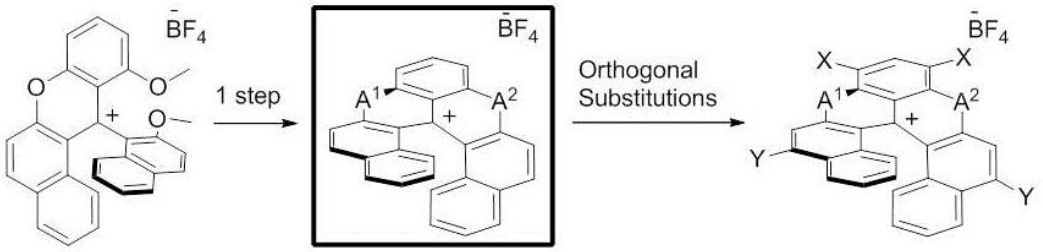
Modular Synthesis, Orthogonal Functionalization and Properties of Novel Cationic [6]Helicene

Maria Geraldine Labrador Beltran[1], Johann Bosson[1], Franck Torricelli[1], Eric Francotte[2], Jérôme Lacour[1] *

[1]University of Geneva, [2]Novartis Institutes for Biomedical Research

Helicenes are *ortho*-condensed polyaromatic compounds that are used in a variety of applications.[1] Their properties can be modulated by the selective introduction of substituents to the periphery of the helical cores or by changing the nature of the atoms within. In that context, our group has developed a new class of cationic diaza **2**, azaoxo **3** and dioxo **4** [6]helicenes.



1

2 A^1, A^2 = N-Alkyl
3 A^1 = N-Alkyl, A^2 = O
4 A^1, A^2 = O

These derivatives **2** to **4** are prepared in one step from a common advanced intermediate **1**. Straightforward, yet orthogonal, functionalization reactions afford a series of polysubstituted [6]helicenes.[2] Compounds **2** to **4** can be furthermore resolved into single enantiomers. Interesting, it is also possible to transform directly **2** into **3** and **3** into **4** despite the obvious helical strain. The importance of these transformations is evidenced in the strong modulation of the visible absorption and emission properties of these cationic dyes.[3]

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Organocatalyzed Direct Vinylogous Double Michael Addition of Unactivated α-Angelica Lactone to Enones

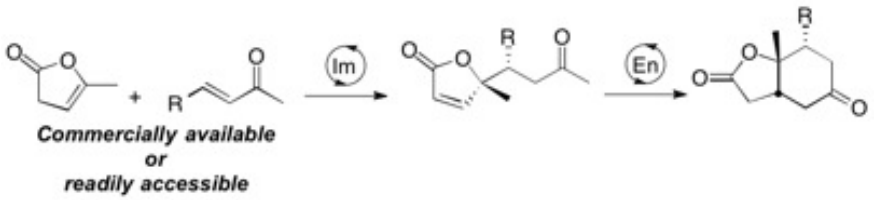
Roman Lagoutte[1], Alexandre Alexakis[1] *

[1]University of Geneva

Renewable α-Angelica lactone was found in a previous study to undergo vinylogous Michael addition directly, i.e. without prior activation, to enals under iminium activation with secondary amine catalysts, generating two new stereogenic centers in high yields, enantioselectivity and diastereoselectivity.[1] Upon conjugate addition, the resulting γ-butenolide possesses further functionality, which could potentially be used for a second intramolecular Michael addition.

To this end, we envisioned that the addition of α-Angelica lactone to alkyl enones under iminium catalysis followed by tautomerization and enamine activation could lead to functionalized tetrahydrobenzofuran-2(3*H*)-ones. This motif is present in or could be a valuable precursor to over 600 natural products.

The results of an extensive optimization study to obtain a versatile and user-friendly methodology converting readily available pronucleophile α-Angelica lactone, enones and catalytic system will be presented, as well as the conditions for the cyclization step.[2]



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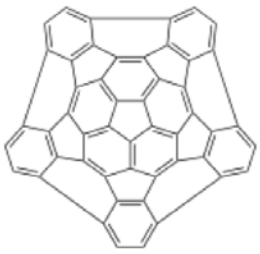
Pushing Corannulene to New Extremes: Synthesis of New, Curved Polycyclic Aromatic Hydrocarbons

Samuel Lampart[1], Jay Siegel[1] *

[1]University of Zurich

The interest of the chemical society in curved polycyclic aromatic hydrocarbons (PAHs) has been growing since the discovery of buckminsterfullerene[1] and carbon nanotubes.[2] A lot of effort has been made to synthesize bowl-shaped PAHs (also called buckybowls), as they constitute fragments of these two carbon allotropes.[3] Several buckybowls have been synthesized using flash vacuum pyrolysis.[3a] Due to the drawbacks of this technique, such as low yields and no functional group tolerance, the search for alternatives has been pursued.[3b,c] However, a general and robust method towards the solution-phase based synthesis of PAHs has not been provided so far.

We suggest another strategy thereto, by using a cross coupling reaction mediated by C–F activation.[4] The presented target molecules include a short carbon nanotube **1** and an icosahedrally symmetric polycyclic aromatic sphere **2**. Currently, only two organic molecules are known having such a high degree of symmetry: buckminsterfullerene and dodecahedrane. Therefore, the proposed sphere should have very interesting properties, especially in comparison with fullerene C60.



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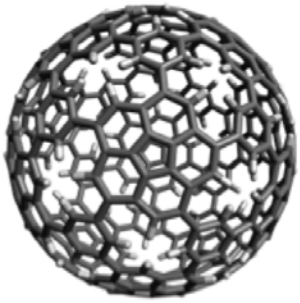

2

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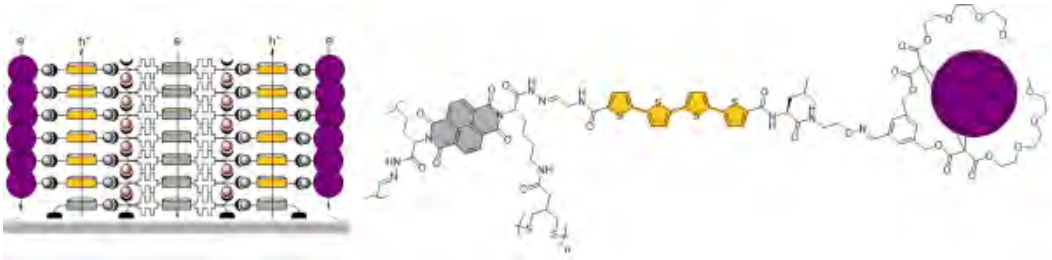
Triple-Channel Photosystems

Santiago Lascano[1], Altan Bolag[1], Adam Sobczuk[1], Hironobu Hayashi[1], Naomi Sakai[1], Stefan Matile[1] *

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

By looking at Nature, we can observe that, in the photosynthetic reaction center, the cofactors have two important characteristics: precise relative orientation and energy levels adapted for a redox gradient. This allows for an ultrafast charge separation after generation by light. To approach nature's precision and complexity, we have recently introduced Self-Organizing Surface-Initiated Polymerization (SOSIP) [1] as a new tool for the design of oriented multicomponent supramolecular n/p-heterojunction architectures. In SOSIP, the activation of an ITO-bound initiator followed by ring-opening disulfide-exchange polymerization of propagators allows for the creation of a central charge-conducting channel. To add supplementary channels next to this central channel, Templated Stack Exchange (TSE) has been included in the overall strategy [2]. After deprotection of hydrazine moieties on the first channel, the pores thus formed are filled by aldehydes, leading to the formation of hydrazones, chemoorthogonal to the preexisting disulfide bonds.
The next step towards complexity has been made with the creation of triple-channel photosystems using TSE of dyads after SOSIP [3]. These dyads are synthesized by condensing an aldehyde of choice with an alkoxyamine, thus forming a stable oxime bond. This approach increases the photocurrent generation up to 10 times in comparison to double-channel equivalents.

To further investigate the potential of this approach, we realized a collection of oligothiophene derivatives and fullerenes [4] for the synthesis of dyads with suitable electronic levels for the future creation of antiparallel hole- and electron-conducting redox gradients adducted to a central channel composed of colorless naphthalene diimides. The oligothiophene-fullerene dyads showed a photocurrent generation up to 5 times larger than the control dyad without fullerene, showing that both components of the dyad are active. We are now focusing on the synthesis and measurement of more oligothiophene-fullerene dyads to ultimately couple horizontal triads with vertical redox gradients.



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Novel 1,2,3-Triazolium Ionic Liquids For Dye-Sensitized Solar Cells

Genevieve Lau Pui Shan[1]

[1]EPFL Lausanne

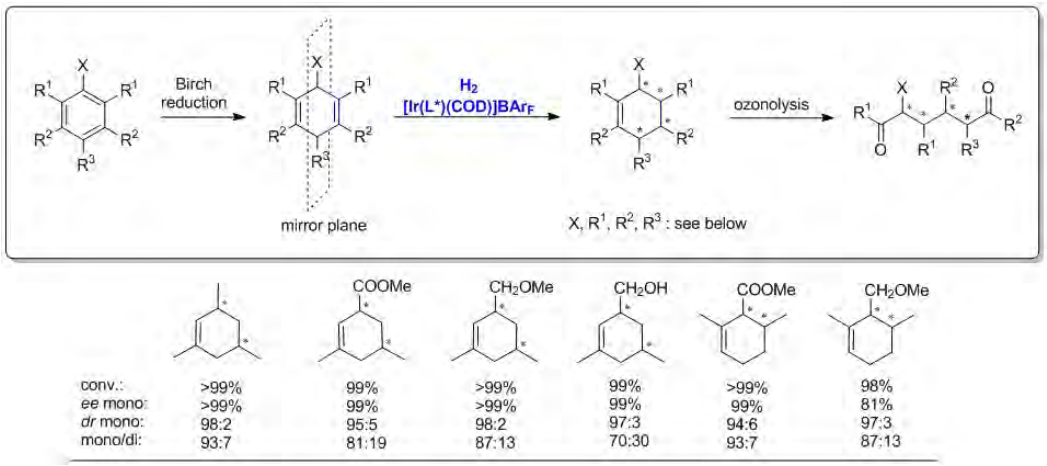
Ionic liquids are very attractive materials for use in various electrochemical applications as they typically possess high ionic conductivities, wide electrochemical windows, negligible vapour pressure, and are also non-flammable. Research in this area has focused largely on the imidazolium family of salts with far less attention placed on other cation families. Here, novel 1,2,3-triazolium ionic liquids were synthesized via the copper-catalyzed azide alkyne click reaction in good yields. These salts were applied as eutectic ionic liquid electrolytes in dye-sensitized solar cells (DSCs) and were found to afford good efficiencies. When these electrolytes were utilized together with a ruthenium-based photosensitizer, a device with 6% efficiency could be obtained. In addition, this system also gave highly stable devices that could retain ca. 90% of its initial value even after 1000 hour sun testing at 60°C. Furthermore, these new electrolytes were also found to be compatible with various organic and porphyrin-based dyes. In particular, the porphyrin-based device gave good efficiencies, exceeding the current record of 4.9% at full sun for porphyrin-ionic liquid-based devices. It is hoped that these encouraging results, which are of importance to the industrial application of DSCs, will generate greater interest in this relatively underexplored family of ionic liquids, leading to more practical applications in the future.

Keep It Simple! Using Asymmetric Monohydrogenation to Access Chiral Building Blocks

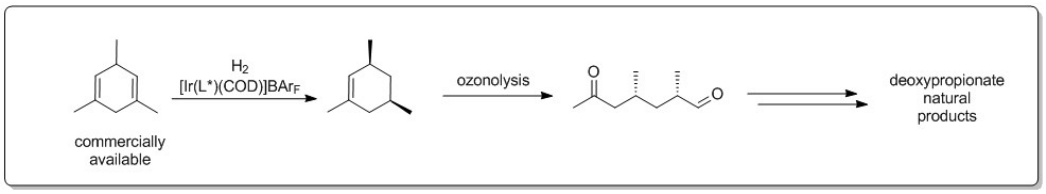
Charlotte Laupheimer[1], Andreas Pfaltz[1] *

[1]University of Basel

The desymmetrization of achiral compounds *via* enantioselective monohydrogenation is a powerful tool, as it enables installation of multiple stereogenic centers in a single symmetry breaking step. In this communication, we report a series of iridium-catalyzed enantioselective monohydrogenations of unfunctionalized olefins.[1] Different 1,4-dienes were prepared *via* Birch reduction and excellent enantioselectivities along with high diastereomeric excesses were accomplished in the monohydrogenation.



In addition, 1,3,5-trimethylcyclohex-1-ene was identified to be a key chiral building block for the synthesis of an enantiopure deoxypropionate unit, an essential motif found in numerous natural products.



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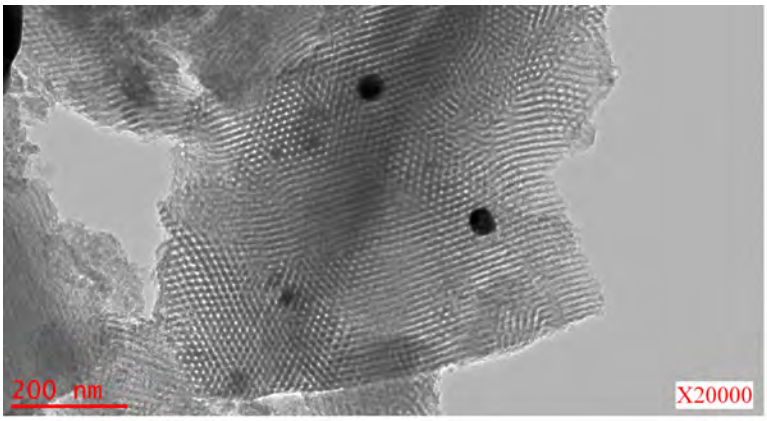
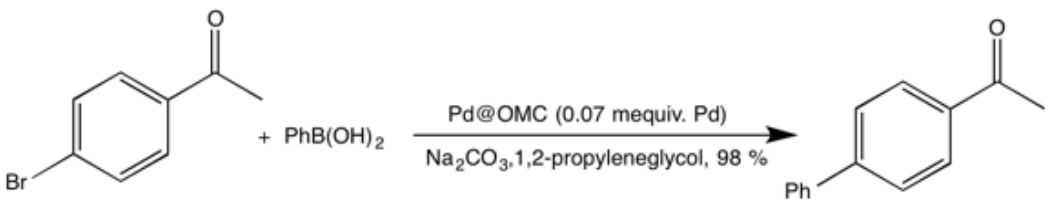
Direct synthesis of a magnetic Palladium-containing ordered mesoporous carbon from a biosourced precursor. Application to Suzuki couplings

Claude Le Drian[1], Clovis Peter[1], Antoine Derible[1], Julien Kiener[1], Julien Parmentier[1], Jean-Michel Becht[1] *

[1]Université de Haute-Alsace, Institut de Science des Matériaux de Mulhouse (UMR-CNRS 7361), 15 Rue Jean Starcky, 68057 Mulhouse cedex, France

The Suzuki coupling, the most powerful tool for the creation of aryl-aryl bonds, finds widespread applications for the synthesis of products possessing interesting pharmaceutical, biological or physical properties. It is generally performed in the presence of expensive homogeneous Pd catalysts that cannot be reused, and moreover often cause the annoying presence of Pd in products and waste. The development of efficient Pd catalysts that can be selectively recovered for reuse is therefore highly desirable.[1] For this purpose numerous magnetic Pd catalysts supported on magnetic cores covered by a polymeric, carbon or silica shell bearing ligands have been developed.[2] Starting from a biopolymer (tannin) as a carbon precursor and Pluronic® F127 surfactant as a pore structuring agent we present a simple, non-toxic and cheap one-pot synthesis of ordered mesoporous carbon (OMC) containing magnetic Fe and Pd nanoparticles (see TEM micrograph).[3] This material is particularly efficient to catalyze Suzuki reactions of aryl bromides and can be easily recovered after reaction by application of a magnetic field. It can be reused several times without significant loss of efficiency and the Pd leaching is low (less than 1% of the initial amount).





OMC : Ordered Mesoporous Carbon

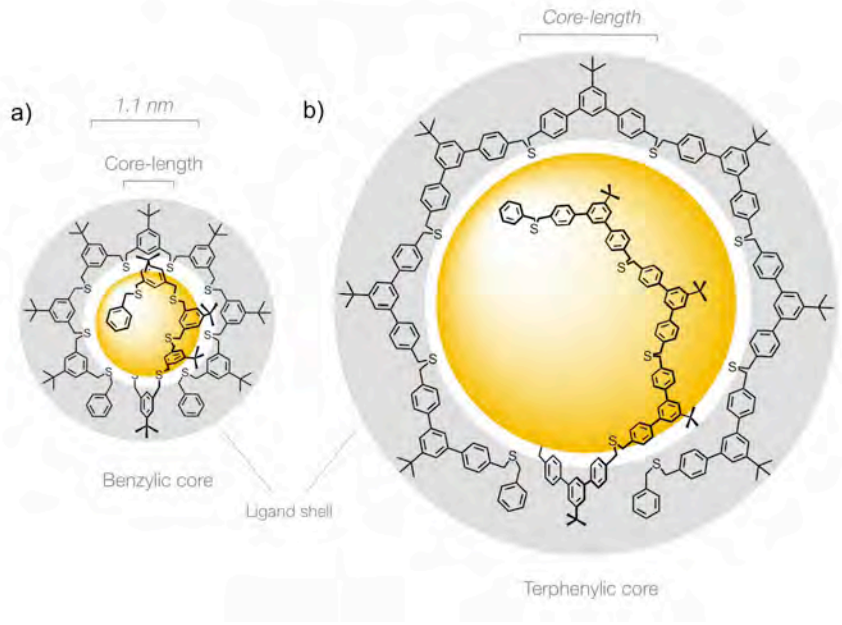
[1] Carine Diebold, Antoine Derible, Jean-Michel Becht, Claude Le Drian, *Tetrahedron* **2013**, *69*, 264-267.
[2] R. B. Nasir Baig, Rajender S. Varma, *Chem. Commun.* **2013,** *49***,** 752-770.
[3] Sébastien Schlienger, Anne-Laure Graff, Alain Celzard, Julien Parmentier, *Green Chem.* **2012,** *14***,** 313-316.

Linear Multidentate Thioether Ligands for the Synthesis of Stable Au NP's with Increased Sizes

Mario Lehmann[1], Marcel Mayor[1] *

[1]University of Basel

Over the last decade, synthesis of gold nanoparticles (Au NP's) has attracted increasing interest, and are promising materials for nanotechnology with applications in electronics, catalysis, and sensors[1]. While there is a plethora of reported nanoparticles stabilized by alkylthiols, the synthesis of ligand stabilized thioether-based NP's remains comparatively rare and unexplored. Depending on the length of such multidentate ligands, it is known that Au NP's can be stabilized with a diameter up to 1.1 nm.[3] Moreover, it was shown, that two of these heptameric ligands wind around one Au-NP (see figure 1, a)).



This presentation will discuss the synthesis of thioether-ligand stabilized Au NP's featuring larger particle-diameters than the recently reported Au NP's by Peterle et al (1.1 nm) described above. Figure 1 shows Au NP's with different sizes, whereas ligand of picture b) is a promising multidentate heptameric thioether-based ligand with a larger core-unit. While the benzylic core is enlarged by two phenyl-units in *meta*-position, each ligands still contains 8 thioether moieties, which sufficiently stabilize the Au NP.

[1] M.-C. Daniel, D. Astruc, *Chem. Rev.* **2004**, *104*, 293-346.
[2] T. Peterle, A. Leifert, J. Timper, A. Sologubenk, U. Simon, M. Mayor, *Chem. Comm.* **2008**, *29*, 3438-3440.

Oligoprolines as Scaffolds for Supramolecular Systems

Bartosz Lewandowski[1], Helma Wennemers[1] *

[1]ETH Zurich

Oligoprolines are a class of conformationally well-defined peptides that adopt, even at chain lengths as short as six residues, the highly symmetric polyproline II (PPII) helix secondary structure in which every third residue is stacked on top of each other in a distance of around 0.94 nm (Figure 1).[1] Additionally the length and functionalization pattern of these peptides can be easily fine-tuned by chemical synthesis.[2] For these reasons oligoprolines are ideal candidates to serve as scaffolds for supramolecular systems. We already demonstrated their efficacy by preparing functionalized oligoproline derivatives that were applied in the controlled growth of silver nanoparticles,[3] as ligands for targeting prostate cancer[4] and in hierarchical self-assembly of π–systems (Figure 1).[5]

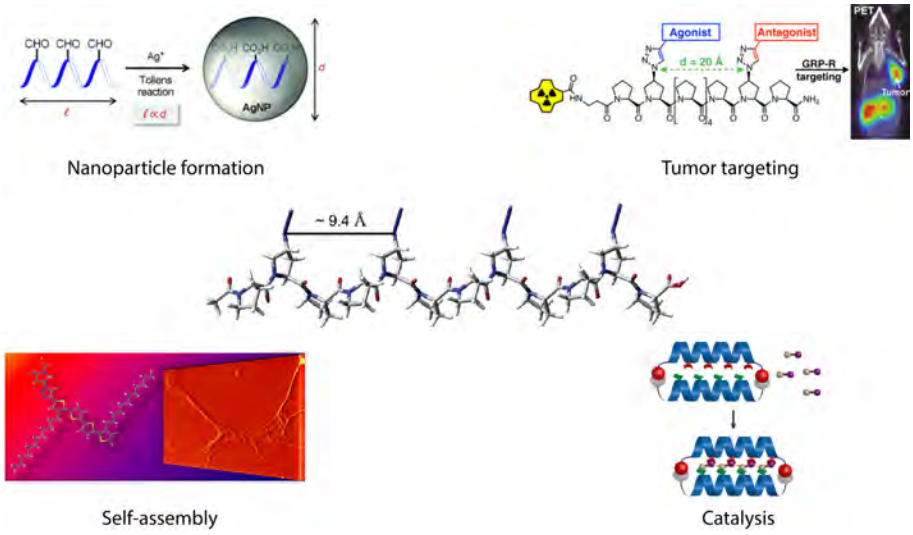


Figure 1. Model of an oligoproline adopting a PPII-helix and application scope of such functionalised peptides.

Recently we performed more detailed studies on the parameters defining the PPII helix in oligoprolines using X-ray crystallography[6] and EPR spectroscopy.[7] We managed to show that it is in fact a rigid scaffold of high persistence length in a variety of solvents. This prompted us to design new, oligoproline-based, supramolecular systems for regioselective catalysis and controlled oligomerisation, the properties of which are currently studied.

[1] Rabanal, F.; Ludevid, M. D.; Pons, M.; Giralt, E. *Biopolymers* **1993**, *33*, 1019 – 1028.
[2] Kümin, M.; Sonntag, L.-S.; Wennemers, H. *J. Am. Chem. Soc.* **2007**, *129*, 466–467.
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[6] Lewandowski, B.; Wilhelm, P.;Trapp, N.; Wennemers, H. *manuscript in preparation*
[7] Garbuio, L.; Yulikov, M.; Lewandowski, B.; Wilhelm, P.; Ziegler, L.; Jeschke, G.; Wennemers, H. *manuscript in preparation*

Synthesis of Alkynylated Heterocycles via Direct C-H Functionalization or Domino Reactions

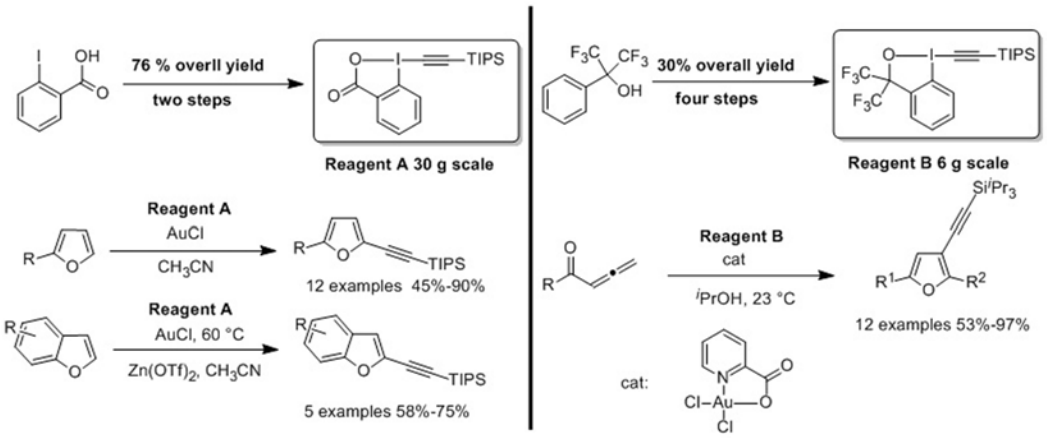
Yifan Li[1], Jérôme Waser[1] *

[1]EPFL Lausanne

(Benzo)furans and alkynes are important building blocks in medicinal chemistry and material science.[1] Currently, the method of choice to access alkynylated furans involves the Sonogashira reaction of pre-functionalized precursors. The synthesis of halogenated heteroarenes by deprotonation and halogenation is often challenging, due to a poor regioselectivity and a low tolerance to functional groups. Consequently, a mild method to achieve a more direct regioselective access to alkynylated heteroareneswould be highly desirable.

Based on our previous work on the Au-catalyzed direct alkynylation of (hetero)arenes,[2] we report herein two different protocols via direct alkynylation of (Benzo)furans and domino process to access C2-alkynylated (Benzo)furans and C3-alkynylated furans selectively with different Au catalysts and alkynyliodonium reagents.[3] The C2 direct alkynylation proceeds under mild conditions with good to excellent yields. In the case of benzofurans, a new method to activate the TIPS-EBX reagent (**A**) using $Zn(OTf)_2$ was discovered.[3b] In contrast, an unprecedented domino reaction led to C3 alkynylated furans using the combination of a Au (III) catalyst and bistrifluoromethyl benziodoxole reagent (**B**).[3a] The two alkynyliodonium reagents are easy to synthesize on gram scale.

Completing our previous research, the direct alkynylation of (benzo)furans has now been achieved with TIPS-EBX (**A**). The discovery that bistrifluoromethyl benziodoxole reagent (**B**) is exceptionally efficient during domino processes is expected to find broad application to access diverse alkynylated (hetero)arenes. Recent results for the synthesis of other alkynylated heterocycles by domino reactions will also be presented.



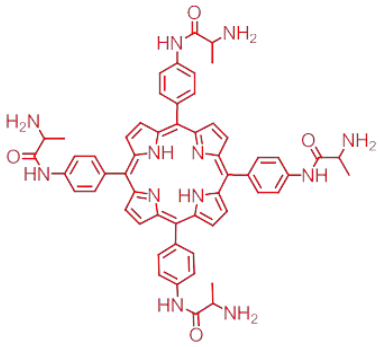
[1] a) J.M. Hopkins, B.A. Keay, P.W. Dibble in *Comprehensive Heterocyclic Chemistry II*, Chapter 3.08 (eds: A.R. *Katritzky, C.W, Rees, E.F, Scriven*), –Elsevier: Amsterdam 2008; b) F. Diederich, P.J. Stang, R.R. Tykwinski in *Acetylene chemistry*. Wiley-VCH: Weinheim 2005.
[2] a) J.P. Brand, J. Charpentier, J. Waser, *Angew. Chem., Int. Ed.* **2009**, *48*, 9346-9349. b) J.P. Brand, J. Waser, *Angew. Chem., Int. Ed.* **2010**, *49*, 7304-7307. c) J.P. Brand, J. Waser, *Org. Lett.* **2012**, *14*, 744-747.
[3] a)Y. LI, J.P. Brand, J. Waser , *Angew. Chem., Int. Ed*. **2013**, *52*, 6743-6747. b) Y. LI, J. Waser, *Beilstein J. Org. Chem*. **2013**, *9*, 1763-1767.

Supramolecular Control over Surface Deposition of Porphyrins

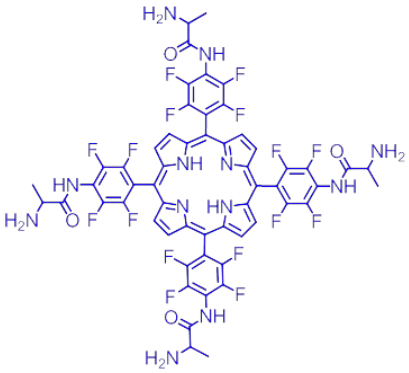
Kenan Li[1], Marcel Mayor[1] *

[1]University of Basel

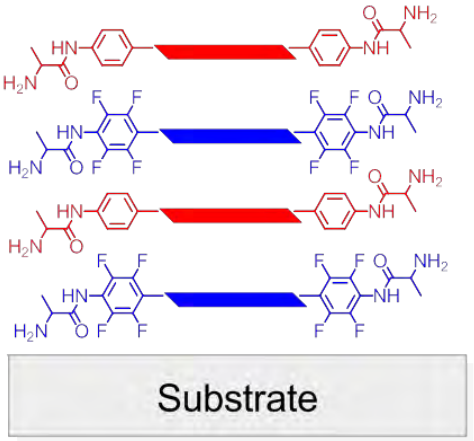
Flat and expanded aromatic systems tend to form stacks driven by π-π interactions. The stacks can be formed in solution and deposited on the surfaces of designed substrates. The devices are integrated in suited devices like “Field effect transistors” because the electronic transport in the stacks is along the axis [1]. However, to optimize the electronic transport, a perpendicular arrangement of the stack is required. Here, we choose porphyrins, which can convert sun light into chemical energy, as our target molecules aiming at controlling the porphyrin stacks by a stepwise growth strategy with π-π stacking interactions [2] and hydrogen bonds [3].



Unfluorinated-Porphyrin



Fluorinated-Porphyrin



[1] (a) X. Guo, S. Xiao, M. Myers, Q. Miao, M. L. Steigerwald, C. Nuckolls, Proc. Nat. Acad. Sci. USA, 2009, 106,691; (b) W. Pisula, A. Menon, M. Stepputat, I. Lieberwirth, U. Kolb, A. Tracz, H. Sirringhaus, T. Pakula, K. Müllen, *Adv. Mater.,* **2005**, 17, 684.
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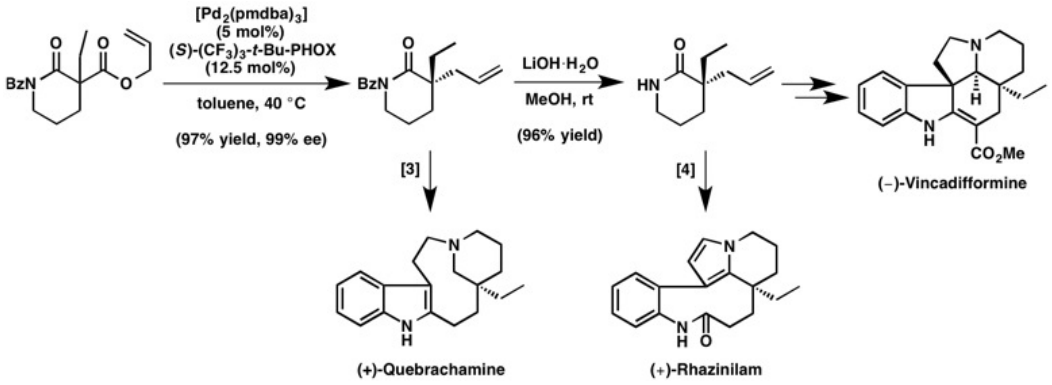
[3] P. Bhyrappa, S. R. Wilson, K. S. Suslick, *J. Am. Chem. Soc*., **1997**, 119, 8492.

Catalytic Enantioselective Synthesis and Utility of α-Quaternary Lactams

Marc Liniger[1], Douglas C. Behenna[1], Brian M. Stoltz[1] *

[1]California Institute of Technology, Division of Chemistry and Chemical Engineering, 1200 E California Blvd, Pasadena, CA 91125, USA

Catalytic enantioselective allylic alkylation has emerged as a powerful method for the construction of building blocks bearing quaternary carbon and fully substituted tertiary centers.[1] A recent addition is the the palladium-catalyzed decarboxylative allylic alkylation of lactams to form α-quaternary piperidone derivatives in good yields and excellent enantioselectivities.[2]



Herein, we wish to report our efforts to functionalize these lactams with the ultimate goal to achieve total syntheses of diverse quaternary, nitrogen-containing natural products such as (+)-quebrachamine,[3] (+)-rhazinilam[4] and (−)-vincadifformine.

[1] Mohr, J. T.; Stoltz, B. M. *Chem. Asian J.* **2007**, *2*, 1476.
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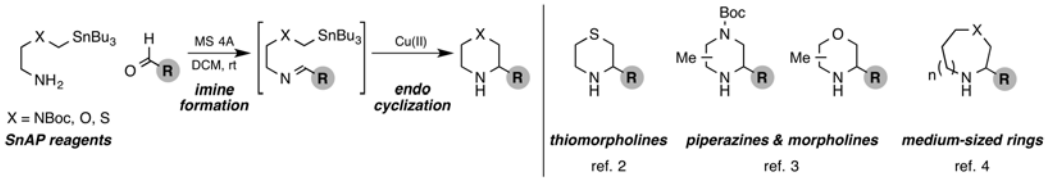
SnAP Reagents for the One-Step Synthesis of Unprotected, Substituted, and Saturated N-Heterocycles from Aldehydes

Michael Umberto Lüscher[1], Cam-Van T. Vo[1], Jeffrey W. Bode[1] *

[1]ETH Zurich

Saturated heterocycles are some of the most important scaffolds found in small biologically active molecules. Limitations in the solubility, pharmacokinetics, bioavailability, and IP positions of aromatics and heteroaromatics have led many scientists in the pharmaceutical industry to favor saturated heterocycles in recent years.[1] Despite the importance of these building blocks, their application in medicinal chemistry is restricted due to the lack of commercial availability and the fact that most current preparations of these scaffolds require long, impractical synthetic sequences and/or display limited functional group tolerance. To directly access these heterocycles, a variety of SnAP reagents were introduced.[2–4] The one-step sequence proceeds under mild conditions with broad functional group tolerance and gives access to a variety of substituted, saturated *N*-unprotected heterocycles.



This presentation will discuss the preparation of saturated N-heterocycles using SnAP reagents involving preliminary studies towards a catalytic enantioselective process.

[1] N. A. Meanwell, *Chem. Res. Toxicol.* **2011**, *24*, 1420–1456.
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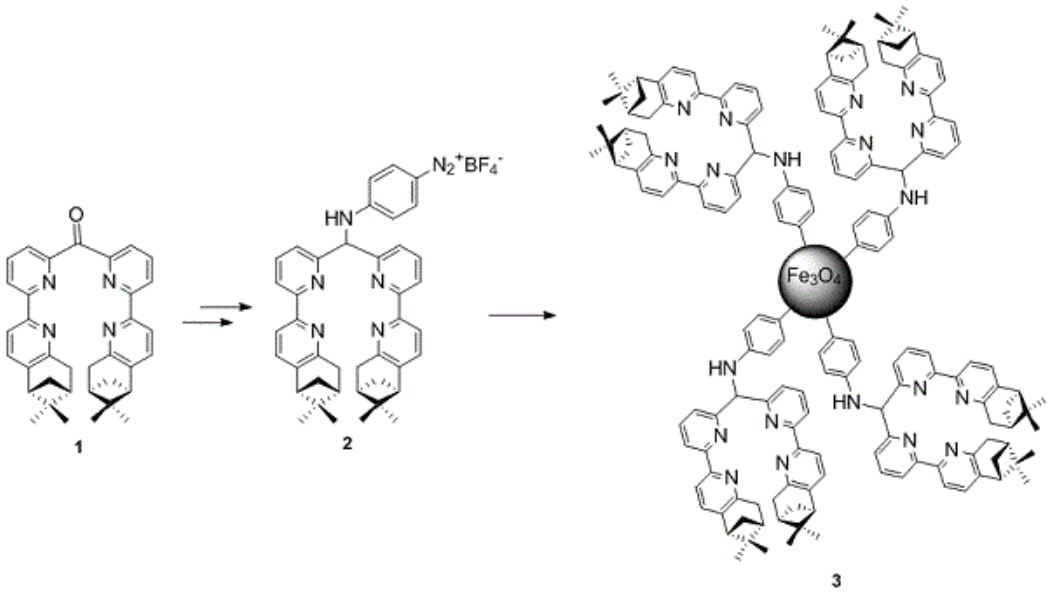
[3] M. U. Luescher, C.-V. T. Vo, J. W. Bode, *Org. Lett.* **2014**, *16*, 1236–1239.
[4] C.-V. T. Vo, M. U. Luescher, J. W. Bode, *Nat. Chem.* **2014**, *6*, 310–314.

Preparation of chiral functionalized magnetite nanoparticle for catalytic purposes

Olimpia Mamula Steiner[1] *, Radek Skupienski[1], Helen Stoeckli-Evans[2]

[1]School of Engineering and Architecture of Fribourg, [2]University of Neuchatel

Here we describe the synthesis of functionalized magnetite nanoparticles, Fe_3O_4 NPs (**3**), with a new enantiopure bis-bidentate ligand **1** derived from pinene bipyridine family.[1] These ligands have the ability to predetermine the chirality of the metal centers in coordination compounds[2] which are potential enantioselective catalysts in various reactions. The carbonyl spacer between the bipyridine units of **1** was used to prepare a diazonium salt derivative (**2**), the key intermediate for the NPs covalent functionalization used here.[3] The resulting superparamagnetic NPs have been characterized by TEM, DSC and TGA.



The nanosupported ligands are easily recoverable from solutions by applying a magnetic field. They have been used for catalytic tests in a model epoxidation reaction in presence of Fe(II), Fe(III) or Mn(II) cations. Homogenous catalysts containing similar ligands coordinated to the same ions have been also synthesized, characterized and tested in the same reaction for comparison purposes.

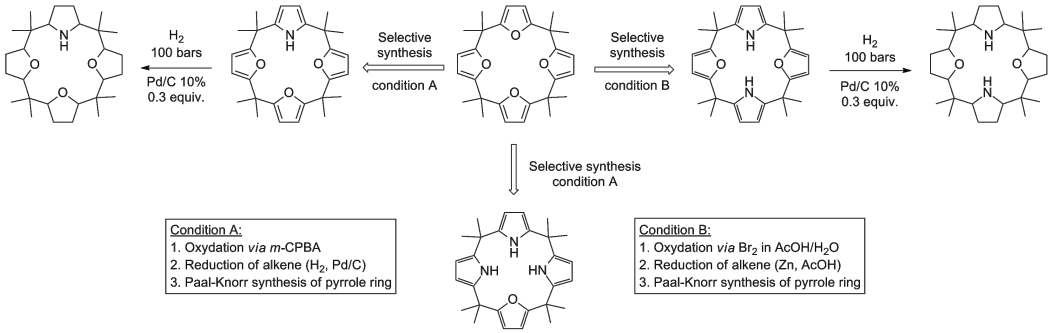
[1] A. Pöllnitz, R. Skupienski, O. Mamula* *et al.*, *Synlett*, **2013**, *24*, 2555
[2] O. Mamula,* M. Lama, H. Stoeckli-Evans, S. Shova, *Angew. Chem., Int. Ed*., **2006,** *45*, 4940.
[3] N. Griffete, F. Herbst, J. Pinson, S. Ammar, C. Mangeney, *J. Am. Chem. Soc.* **2011,** *133*, 1646.

Synthesis of Calix[n]pyrrole[m]furane: A potential new class of macrocyclic ligands

William Maupillier[1], Guillaume Journot[2], Reinhard Neier[1] *

[1]University of Neuchatel, [2]Neuchâtel

Selective syntheses of Calix[n]pyrrole[m]furane (n + m = 4) have been developed and optimized starting from Calix[4]furane, resulting of the simple Baeyer condensation reaction between furane and acetone in acidic condition. These compounds were used to understand the unexpected non-trivial total hydrogenation of Calix[4]pyrrole.[1]



These synthesized compounds offer interesting perspectives for the development of a new class of catalysts. Our Calix[n]pyrrole[m]furane analogues started to be studied for the synthesis of aliphatic polyesters[2] and synthesis of metal complexes of the totally reduced compounds is in progress.

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[2] Carine Robert *et al*. Tandem synthesis of alternating polyesters from renewable resources. *Nat. Commun*. **2011**, 2:586 doi: 10.1038 / ncomms1596

Anion-π Interactions in Organocatalysis

Jadwiga Gajewy[1], Zhao Yingjie[1], Naomi Sakai[1], Stefan Matile[1] *

[1]University of Geneva

Examples of anion-π interactions in catalysis remain elusive.[1-3] In our group, electron deficient naphthalenediimides (NDIs) have been shown to coordinate and stabilize anionic reaction intermediates through noncovalent interactions between anions and their π-acidic aromatic surfaces.[1,2] These NDIs have since then been applied in the stabilization of anionic transition states. Our initial studies provide strong evidence that anion-π interactions contribute to catalysis of Kemp elimination. Moreover, Michaelis-Menten analysis showed that by increasing the π-acidity of the catalysts, the stabilization of the anionic transition state and the rate also increases. Then the enolate chemistry was studied, in which we were able to prove that addition of anion-π stabilized reactive enolate intermediates to enones and nitroolefins occurs with transition state stabilizations of up to 11 kJ mol^{-1} (Figure 1).[3] Further modifications of catalysts were made by incorporation of different functional groups in the active site to demonstrate that anion-π interactions can accelerate other reactions which posess an anionic transition state.

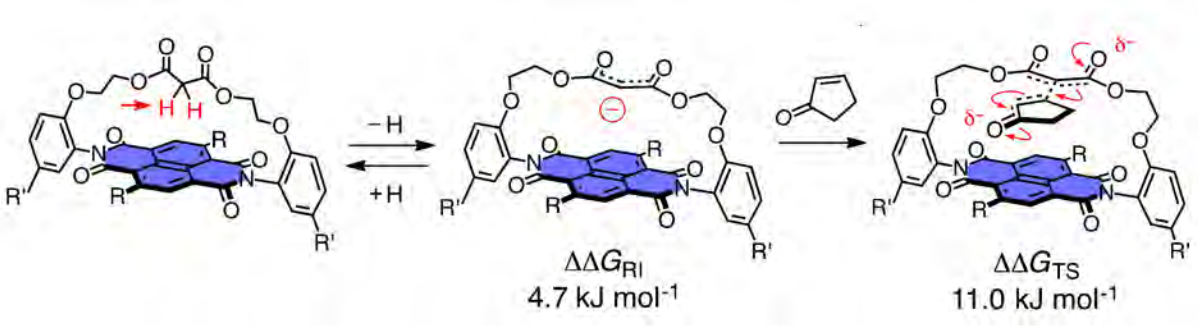


Figure 1: Accelerating enolate chemistry with anion-π interactions.

[1] Yingjie Zhao, Yuya Domoto, Edvinas Orentas, César Beuchat, Daniel Emery, Jiri Mareda, Naomi Sakai, Stefan Matile, *Angew. Chem. Int. Ed.*, **2013**, 52, 9940 –9943.
[2] Yingjie Zhao, César Beuchat, Yuya Domoto, Jadwiga Gajewy, Adam Wilson, Jiri Mareda, Naomi Sakai, Stefan Matile, *J. Am. Chem. Soc.*, **2014**, 136, 2101−2111.
[3] Yingjie Zhao, Naomi Sakai, Stefan Matile, *Nat. Commun.*, **2014**, DOI:10.1038/ncomms4911.

Photo/Redox-Switchable Resorcin[4]arene Cavitands

Jovana Milic[1], Igor Pochorovski[1], Marc-Olivier Ebert[1], Corinne Boudon[2], Jean-Paul Gisselbrecht[2], François Diederich[1] *

[1]ETH Zurich, [2]Université de Strasbourg

We have designed and optimized the first redox-switchable cavitand that is based on a redox-active quinone moiety and features switchable conformational and binding properties.[1] Conformational switching of this system relies on hydrogen bonding between the hydroxy groups of the hydroquinone unit and the neighboring hydrogen bond acceptor groups, which favors the vase conformation only in the reduced state of the cavitand. Various hydrogen bond acceptor groups were evaluated for their propensity to induce conformational switching between the kite and vase forms of diquinone-diquinoxaline resorcin[4]arene cavitands upon redox interconversion. Design guidelines for successful acceptors were derived, and the carboxamide acceptor was shown to be the best candidate. Based on this moiety, a redox-switchable triptycene-based basket that can completely encapsulate a guest in its closed vase conformation was prepared and studied, demonstrating association constants of up to 10^4 M^{-1}(in mesitylene-d_{12}) and exhibiting slow guest exchange kinetics with a half-life for guest release in the order of 10^4 s.[2] Further redesign of this quinone-based cavitand system is undertaken to allow switching in purely aprotic media that would set the stage for photoredox-switchable cavitand systems.[3]

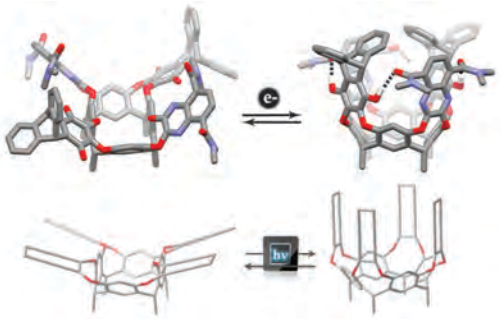


Figure 1. (Top) Redox interconversion of a redox-switchable resorcin[4]arene basket. (Bottom) Schematic of a photoswitchable resorcin[4]arene cavitand.

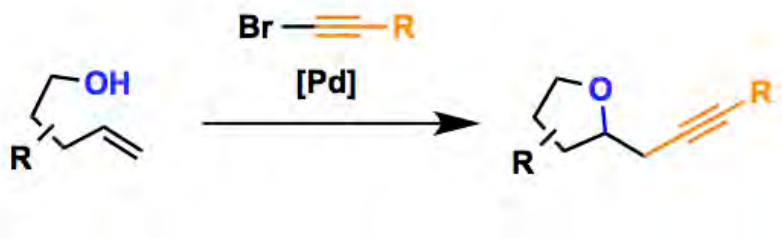
[1] I. Pochorovski, M-O. Ebert, J-P. Gisselbrecht, C. Boudon, W. B. Schweizer, F. Diederich, *J. Am. Chem. Soc*. **2012**, *134*, 14702–14705.
[2] I. Pochorovski, J. Milić, D. Kolarski, C. Gropp, W. B. Schweizer, F. Diederich, *J. Am. Chem. Soc.* **2014**, *136*, 3852–3858.
[3] I. Pochorovski, F. Diederich, *Acc. Chem. Res.* **2014**, doi: 10.1021/ar500104k.

Palladium-Catalyzed Oxy-Alkynylation of Olefins

Ugo Orcel[1], Jérôme Waser[1] *

[1]EPFL Lausanne

The difunctionalization of olefins constitutes a straightforward route to reach high molecular complexity from readily available substrates. Alkynes are extraordinary useful building blocks, therefore the development of new alkynylation methods is highly attractive to access key intermediates in synthesis. In 2013, our group reported the first palladium-catalyzed intramolecular oxy- and aminoalkynylation of non-activated olefins using bromoalkynes.1 Herein we report our recent attempts to extend this methodology to the intermolecular direct addition of oxygen-based nucleophiles and alkynes across electronically unbiased alkenes. Preliminary results showed a large functional group tolerance and high yields were achieved.



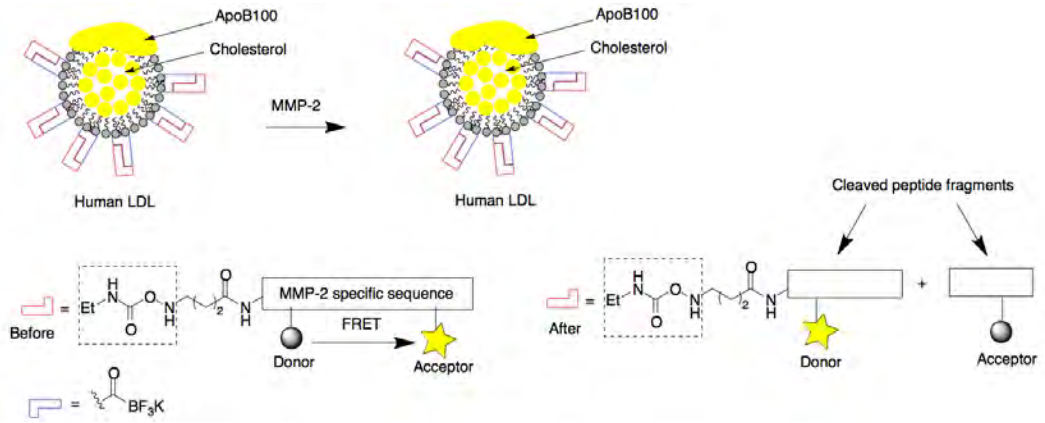
[1] (a) S. Nicolai, R. Sedigh-Zadeh, J. Waser, *J. Org. Chem.,* **2013,** 78, 3783-3801; (b) S. Nicolai, J. Waser, *Org. Lett.,* **2011,** 13, 6324-6327

Functionalized Low-Density Lipoprotein Nanoparticle as NIR Imaging Probe for Atherosclerosis with MMP2-specific Ligand Site

Sean Oriana[1], Yoko Yamakoshi[1] *

[1]ETH Zurich

Heart attack and stroke are still the leading causes of death in the world. Being able to quantify these vulnerable plaques caused by atherosclerosis early using a non-invasive method is really crucial. One way to approach this is by targeting the enzyme matrix metalloproteinase (MMP)2, which is overexpressed in atherosclerosis, and measure the metabolic activity of the plaques. Although several probes for MMP family have been previously reported, none of them are able of quantification of the plaques [1,2]. To address this limitation, our group is developing NIR-imaging agents targeting MMP2 using ligands with high binding and selectivity.



Incorporating an LDL-nanoparticle to the probe has been done previously in our group for atheroplaque imaging using MRI [3]. Based on this work, LDL-nanoparticle is again utilized as a carrier that can deliver our probe and be retained with a high level by the atheroplaque. Our molecular design also includes FRET pair that is attached on MMP2 selective ligand peptide that has been chosen from current literature due its high binding potency and selectivity at MMP2 [4].

[1] Weisleder, R., Tung, C. H., Mahmood, U., Bogdanov, A. Jr., *Nat. biotechnol.,* **1999**, 17, 375-378.
[2] Zhang, Y., So, M. K., Rao, *J. Nano Lett*. **2006**, 6, 1988-1992.
[3] Lowell, A. N., Qiao, H., Liu, T., Ishikawa, T., Zhang, H., Oriana, S., Wang, M., Ricciotti, E., FitzGerald, G. A., Zhou, R., Yamakoshi, Y., *Bioconjugate. Chem.* **2012**, 23, 2313-2319.
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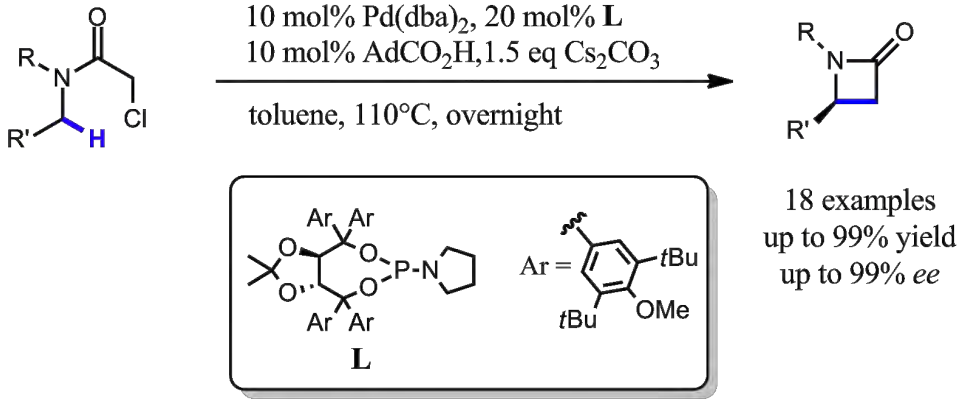
Access to β-Lactams by Enantioselective Palladium (0)-Catalyzed C(sp^3)-H Alkylation

Julia Pedroni[1], Michele Boghi[1], Tanguy Saget[1], Nicolai Cramer[1] *

[1]EPFL Lausanne

β-Lactams represent an indisputably relevant structural motif due to their broad biological activity and synthetic versatility. Although many syntheses are known, enantioselective approaches are rare and rather limited.[1] Asymmetric syntheses of chiral nitrogen-containing heterocycles via Pd (0)-catalyzed C-H activation have been continuously developed in our group.[2] Herein we report a novel approach to the β-lactam core via C(sp^3)-C(sp^3) bond formation employing the tailored TADDOL-based phosphoramidite ligand **L**.[3]



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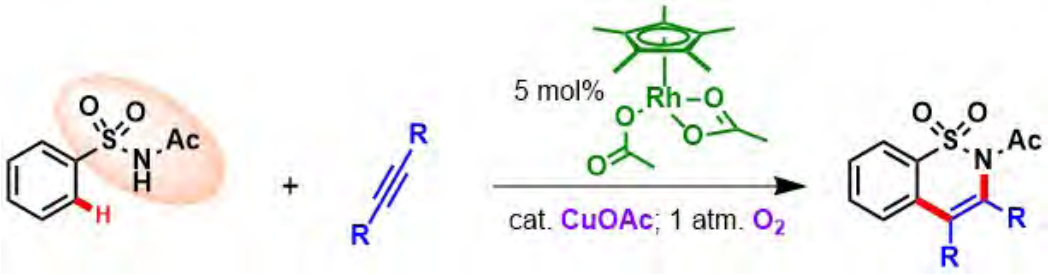
Rh^{III}-Catalyzed C-H Activation Rapid Access to Complex Organic Molecules

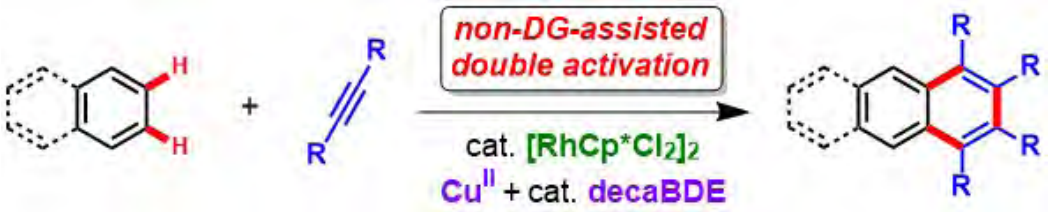
Van-Manh PHAM[1], Nicolai Cramer[1] *

[1]EPFL Lausanne

During the past decade, transition-metal-catalyzed C–H activation has emerged as an attractive strategy to prepare organic building blocks in a step and atom-economical fashion. An impressive number of transformations aimed at directly installing new C-C or C-X bonds have been developed based on this strategy.[1] Herein, we report our findings on Rh^{III}-catalyzed C-H activation of arylsulfonamide derivatives and subsequent cyclization with internal alkynes to provide an efficient route to arylsultams which play a pivotal role in medicinal chemistry.[2]



The use of directing groups (DG) on the substrate enhances efficiency and regio-selectivity of C-H functionalization. However, the DG has to be pre-installed into the starting material and removed after the C-H functionalization. Thus, C-H activation without the control of DGs remains challenging and would be a highly valuable synthetic tool. In this regard, we developed the Rh^{III}-catalyzed homologation of directing group-free arenes *via* double C-H functionalization to give access to larger condensed arenes which are of interest in material science due to their electro- and photochemical properties.[3]



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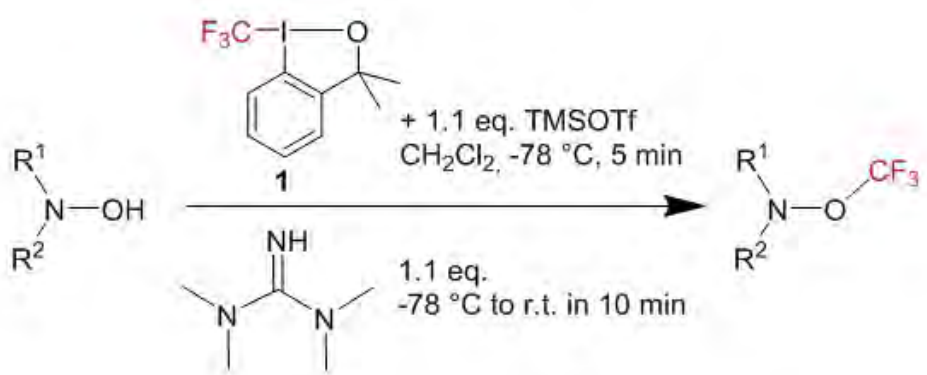
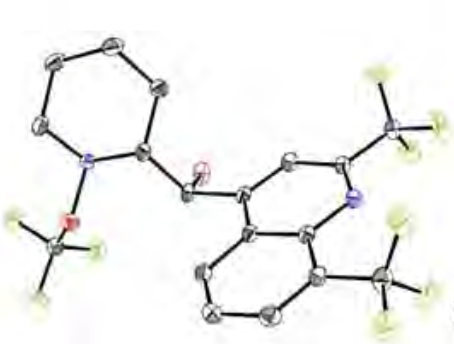
O-Trifluoromethylation of N,N-Disubstituted Hydroxylamines with Hypervalent Iodine CF_3 Reagents

Ewa Pietrasiak[1], Václav Matoušek[1], Antonio Togni[1] *

[1]ETH Zurich

Over the past few years, organofluorine chemistry has developed into a flourishing branch of organic chemistry. In this context, hypervalent iodine (III) compounds such as **1** developed several years ago in our group[1] are among the most versatile trifluoromethylating agents reported in the literature.[2]





$NOCF_3$ derivative of Mefloquine

Herein we describe the electrophilic trifluoromethylation of *N,N*-dialkyl hydroxylamines with aforementioned reagents.[3] In addition to experimental simplicity and excellent functional group tolerance the method allows to access a novel CF_3ON motif of currently unexplored properties. Trifluoromethylation of Mefloquine and Fluoxetine derived hydroxylamines yielded compounds of potential interest in medicinal chemistry. Preliminary mechanistic studies revealed the radical nature of the reaction. Furthermore, we demonstrated that electrophilic activation of reagent **1** together with deprotonation of the hydroxylamine with an external base has a beneficial effect on reactivity and selectivity. NMR analysis of products having a chiral scaffolds together with X-ray studies of two crystalline CF_3ON compounds unveiled the conformational behaviour of the CF_3ON group to act as a possible conformational lock in these structures.

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Synthesis and Applications of Ring-modified Vitamin B12 Derivatives

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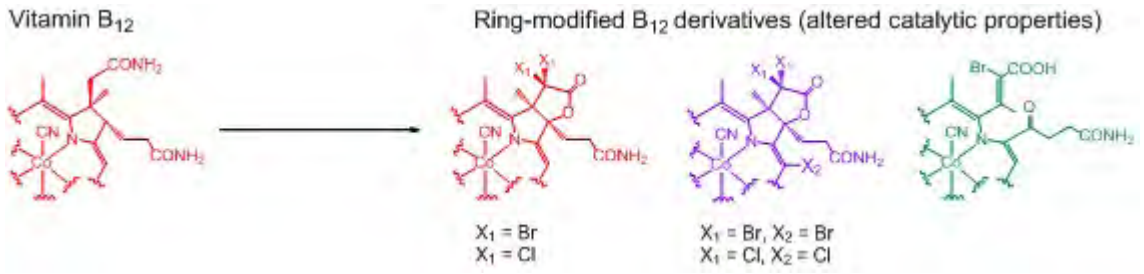
[1]University of Zurich

Vitamin B_{12} cofactors are essential for human metabolism and support cell-growth processes.[1] Therefore, fast proliferating cells in tumors or sites of bacterial infection consume increased amounts of this nutrient. The design of B_{12} surrogates which compete with the original cofactors and inhibit B_{12} dependent enzymes is a promising approach towards the development of anti-proliferative agents in cancer therapy and antibiotics.



We synthesized a series of ring-modified vitamin B_{12} derivatives with altered electronic properties.[2,3] The electronic properties of the corrin chromophore are responsible for the different colours and influence strongly the catalytic activity of the B_{12} cofactors. Studies on the physico-chemical properties and biological activity of these new derivatives are presented.

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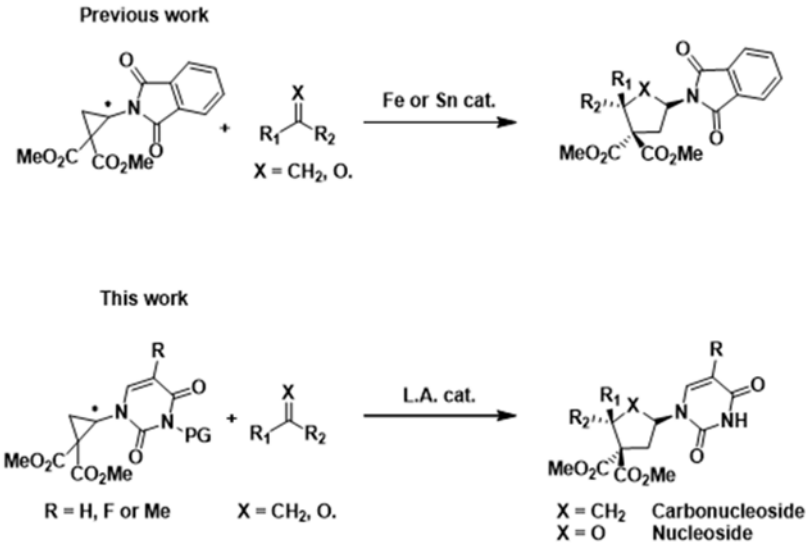
Synthesis of (Carbo)nucleosides Analogues via Formal [3+2] Annulation

Sophie Racine[1], Florian de Nanteuil[1], Eloisa Serrano[1], Jérôme Waser[1] *

[1]EPFL Lausanne

Nucleosides and carbonucleosides analogues are widely used as drugs against a large range of disorders such as HIV, malaria or tuberculosis. Due to the emergence of resistance against marketed drugs as reported by the World Health Organisation, there is a high interest in the discovery of new bioactive compounds against these diseases.

Our group has developed a new diastereoselective and enantiospecific formal [3+2] annulation reaction between phtalimide-cyclopropane and enol ethers or carbonyl compounds. This robust synthetic tool has demonstrated its utility for the synthesis of highly substituted cyclopentylamine and tetrahydrofurylamine derivatives.[1–3] Herein, we report the extension of this methodology to the synthesis of nucleoside and carbonucleoside analogues by using unprecedented purine based cyclopropanes.[4]



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The Synthesis and Properties of Porphyrin-based Molecular Dyads

Tristan Reekie[1], Lorenz Urner[1], Michael Sekita[2], Dirk Guldi[2], Jean-Paul Gisselbrecht[3], Corinne Boudon[3], François Diederich[1] *

[1]ETH Zurich, [2]Friedrich-Alexander-Universität Erlangen-Nürnberg, [3]Université de Strasbourg

The porphyrin moiety is an electron donor that can be linked via a bridging unit to an electron acceptor to produce a synthetic molecular dyad.[1] The majority of acceptors utilized to date include quinones, fullerenes, perylene diimides and derivatives.[2] To further investigate the utility of porphyrin based dyads new acceptor groups need to be developed and investigated.

The cycloaddition–retroelectrocyclization (CA–RE)[3] reaction between an electronically activated alkyne and electron poor alkene such as tetracyanoethylene (TCNE) gives rise to push–pull chromophores that when tethered to an electron donor act as strong electron acceptors.[4] These push–pull acceptors exhibit important physical properties, such as high thermal stability and non-planarity and can be easily accessed in high yields.[5]

The work to be presented involves the synthesis of electronically activated alkyne substituted porphyrin compounds and their subsequent reaction with electron poor alkenes to give a molecular dyad, an example of which is shown in Figure 1. The electrochemical and photophysical properties of the synthesized dyads will also be presented.

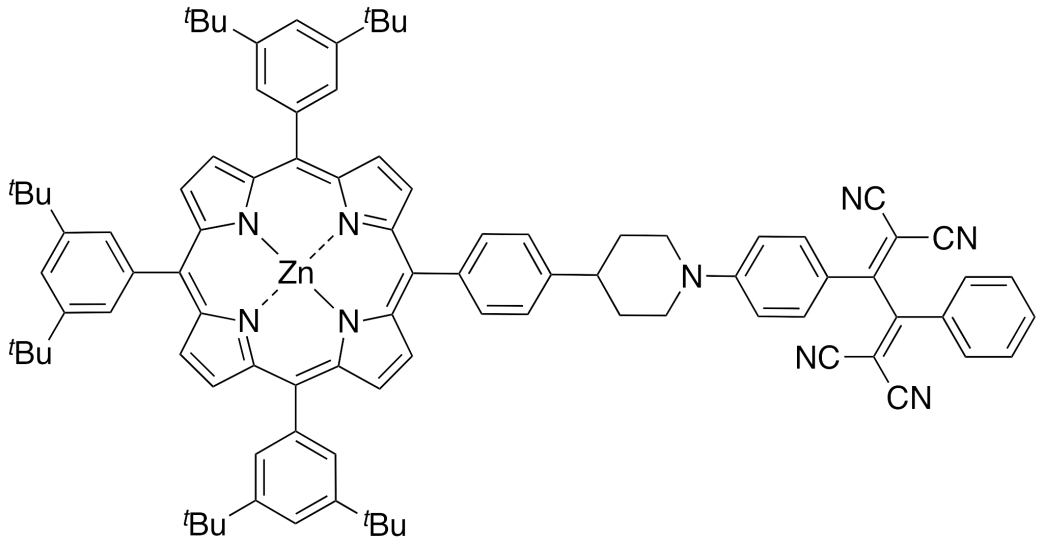

Figure 1. A representitive example of a porphyrin push–pull acceptor dyad.

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Stabilization of Genuine Non-Kekulé Diradical Triangulene in a Supramolecular Complex

Peter Ribar[1], Michal Juricek[1]

[1]University of Basel

Graphene can be viewed as an infinite 2D network of sp^2-hybridized carbon atoms (or fused benzene rings), in which each carbon atom participates in the network formally consisting of alternating single and double bonds. Of all possible ways to fuse the benzene rings to make graphene fragments (GFs) of a finite size, some combinations do not obey this alternating-double-bond rule and, as a result, they possess non-Kekulé structures that do not conform to the standard rules of chemical valence. For instance, it is not possible to connect all carbon atoms in the triangular three-ring system of triangulene (shown) with alternating single and double bonds. Two electrons always remain unpaired in all of its resonant structures and determine the open-shell diradicaloid character of triangulene derivatives. Only a handful of triangulene derivatives are known to this day. These rather rare examples, however, were only detected under strictly oxygen-free conditions in solution and at low temperatures. Here, we describe the synthesis of diradical triangulene and its stabilization in a supramolecular complex, with the ultimate goal to capture and isolate the unsubstituted, or “naked“, triangulene in the solid state for the first time. Experimental solid-state validation of triangulene’s triplet ground state is long-sought, as non-Kekulé GFs larger than trianguelene are promising candidates for future applications in molecular quantum electronic devices.

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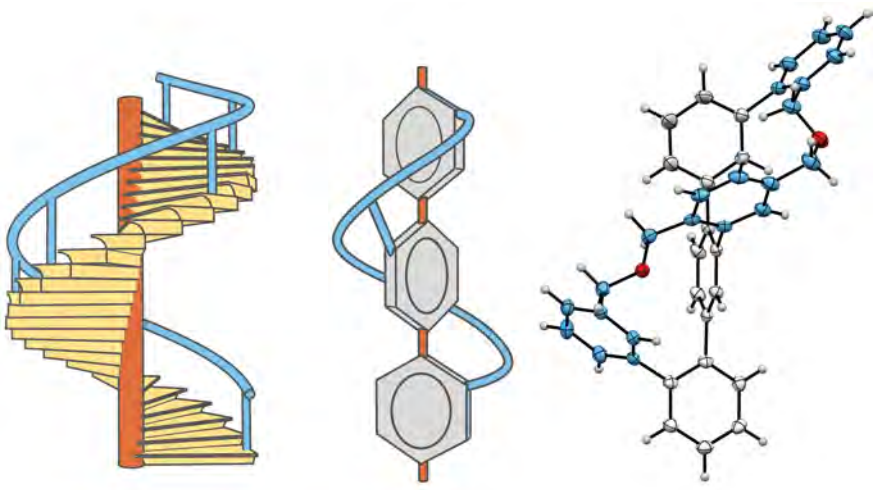
A Molecular Dance Ribbon

Michel Rickhaus[1], Marcel Mayor[1] *

[1]University of Basel

Polyaromatic hydrocarbons are a promising set of molecules to investigate how chirality relates with structure.
Here we like to report a novel concept[1] how to introduce helicity to an originally flat system: By assembling a ladder structure and extending one of the rails with respect to the other, a twist is introduced. The result is a structure that resembles a pirouetting dance ribbon.
Compared to the previously known bannister-oligomers as described by Vögtle and coworkers[1], our system interlinks three terphenyl rings by one bridge (instead of two) and thus lacks a point of inversion. As a result, our structure exists exclusively in the form of a pair of enantiomers. The envisaged racemization process can be best described as a twist, which a pirouetting dance ribbon would have to undergo to change its helicity.



The system was accessed over 12 steps and was fully characterized. X-Ray diffraction revealed indeed a helical structure as envisaged. The obtained high racemization barrier allowed us to separate and isolate both enantiomers by chiral HPLC, and subsequently study the racemization behavior in detail.

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Design of Novel Lipidic Cubic Phases for Membrane Protein Crystallization

Livia Salvati Manni[1], Alexandru Zabara[2], Andreas Plückthun[1], Jay Siegel[3], Raffaele Mezzenga[2], Ehud Landau[1] *

[1]University of Zurich, [2]ETH Zurich, [3]Tianjin University

Lipidic cubic phases (LCPs) are complex biomaterials of great potential in a variety of fundamental and applied areas such as membrane biology[i],[ii],[iii] , drug delivery[iv], food emulsifiers[v] and biodevices[vi]. They exhibit a unique combination of material properties- biocompatibility, biodegradability, optical transparency, adhesivity to hydrophilic and hydrophobic surfaces, deformability, and loadability with guest molecules of virtually all polarities and charge[vii].
Bicontinuous LCPs are three-dimensionally ordered molecular systems made up of a geometrically well-defined, curved lipid bilayer which is surrounded by two identical, yet non-connected aqueous channels. Lipid and water molecules diffuse freely within their respective molecular subsystem, and water can diffuse between the confined channels of LCPs and an excess reservoir. Variation of hydration, temperature and pressure affect phase transitions and formation of various phases with defined material properties .A new family of lipids with well-defined geometry and tail curvature was designed and synthesized in order to control the phase behavior and thus the material properties of the ensuing mesophases. The binary phase behavior of one such lipid was characterized by Small Angle X-ray Scattering (SAXS), and its phase diagram reveals a particularly stable Pn3m cubic phase at low temperature and absence of the high temperature, highly curved H_{II} reverse hexagonal phase. These novel properties open up various potential applications, most notably for low temperature membrane protein crystallization from LCPs. This application addresses one of the major stumbling blocks in membrane biology- the impossibility to crystallize thermally unstable membrane protein using LCPs, and its successful development will have important impact in the field.

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Understanding the role of ligands and additives in palladium mediated cross-coupling reactions using a combined computational and experimental approach

Italo Sanhueza[1], Franziska Schoenebeck[2] *

[1]ETH Zurich, [2]RWTH Aachen

Palladium-mediated cross-coupling reactions are a powerful class of transformations used to construct carbon-carbon bonds. [1] These transformations are generally multi-step processes that rely on additives or ligands to obtain high reactivity and selectivity. Although great development has been reported, the choice of additives and ligands is often not straightforward, particularly when their roles are not fully understood. [2] This presentation will give insight into recent cases where the ligand and additives have played a key role in determining the selectivity and/or reactivity of the palladium mediated reaction. Given the complexity of the reactions, a combination of experiments and computational tools where used to gain insight into the role of the additives and ligands. Such a case includes the double oxidative C-H functionalization reaction of arenes, in which the selectivity of C-H functionalization could be controlled by changing the anionic ligand (Fig. 1). [3, 4]

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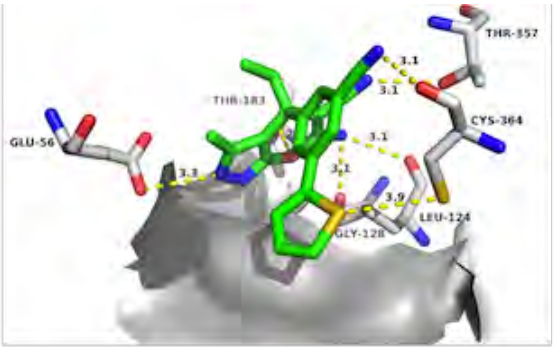
Inhibition of P. falciparum SHMT: Improvement of the pharmacokinetic properties to reach high in vitro activity

Geoffrey Schwertz[1], Anatol Schwab[2], Matthias Witschel[3], Matthias Rottmann[4], Ubolsree Leartsakulpanich[5], Sandro Tonazzi[1], François Diederich[1] *

[1]Laboratory of Organic Chemistry, ETH Zürich, Vladimir Prelog Weg 3, [2]ETH Zurich, [3]BASF AG, [4] Swiss Tropical and Public Health Insitute, Basel, [5]National Center for Genetic Engineering and Biotechnology, Thailand

Due to the emergence of drug-resistant strains, there is an urgent need of novel antimalarials. The folate cycle containing several enzymes was identified as promising target; some of them are already adressed by antimalarials[1]. However, inhibition of serine hydroxymethyl transferase (SHMT), a key enzyme of the folate cycle, has not been investigated so far. *A. Thaliana* SHMT inhibitors, based on a pyrazolopyran scaffold, demonstrated promising antimalarial activity on *P. falciparum* and *P. vivax*[2]. Because of pharmacokinetic limitations no significant activity in the *P. berghei* mouse model could be achieved. The binding mode was resolved by several X-ray crystal structures of *Pv*SHMT-ligand complexes. In this work the development of novel inhibitors to improve *in vitro* activity is focused on the derivatization of the exit-vector. Based on the high similarity of *P. vivax* and *P. falciparum* SHMT, the X-ray co-crystal structures can be utilized for 3D modeling to design small drug-like molecules against *Pf*SHMT to improve the pharmacokinetic properties. *De novo* structure-based design enabled us to identify a tetrahydronaphthyridine-based scaffold with favorable interactions to the SHMT enzyme.



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Direct Electrophilic Trifluoromethylation of Quinolones and Pyridones

Remo Senn[1], Antonio Togni[1] *

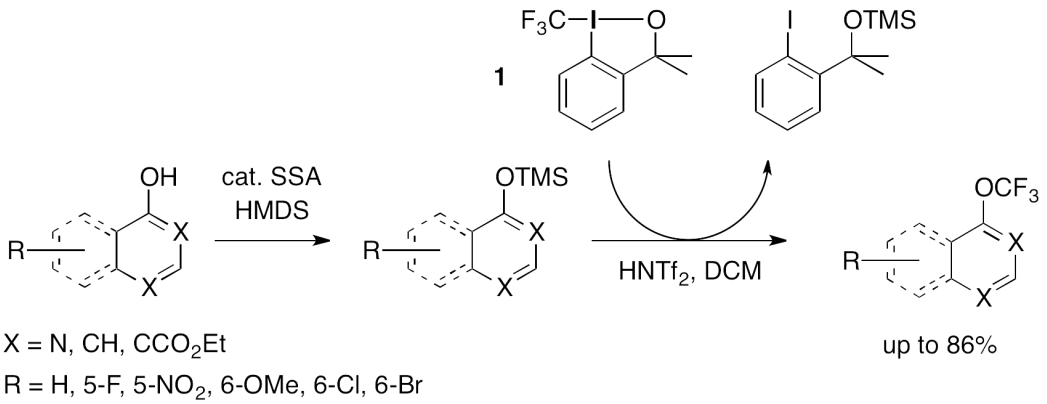
[1]ETH Zurich

Since their discovery in the late 70's quinolone based antibiotics belong to the most prescribed broad-spectrum antibacterial drugs. [1] Especially compounds based on the fluoroquinolone core structure like Norfloxacin, Ciprofloxacin, Ofloxacin have found extensive application in treating various infectious diseases. [2]

Although a myriad of compounds were evaluated to further optimise their antibacterial activity and pharmacokinetic properties, N-trifluoromethylated fluoroquinolones still represent a rarity. [3] This is mainly due to the fact that the only known procedure to access such compounds relies on oxidative desulfurisation-fluorination. [4]

Recently, we reported the direct electrophilic *N*-trifluoromethylaton of a variety of nitrogen containing heterocycles, such as tetrazoles, triazoles, indazoles and pyrazoles [5] using the hypervalent iodine reagent **1**, originallydeveloped in our group. [6]

After *in situ* trimethylsilylation, similar conditions were examined with a variety of quinolones and pyridones, which were thus converted to the corresponding *O*-trifluoromethylated species in good yield and functional group tolerance. Mechanistic investigations involving ^{19}F- and ^{29}Si-NMR 2D spectroscopy and competition experiments, revealed a reaction mechanism featuring complex pre-equilibria.



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Catechol Mediated Carbohydrogenation of Multiple Bonds

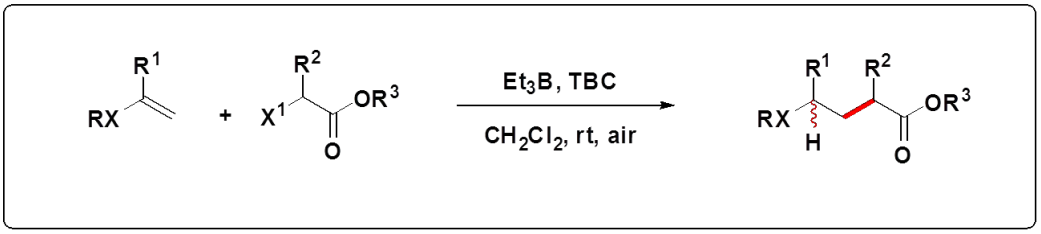
Sankar Rao Suravarapu[1], Guillaume Povie[1], Samuel Rieder[1], Martin Bircher[1], Philippe Renaud[1] *

[1]University of Berne

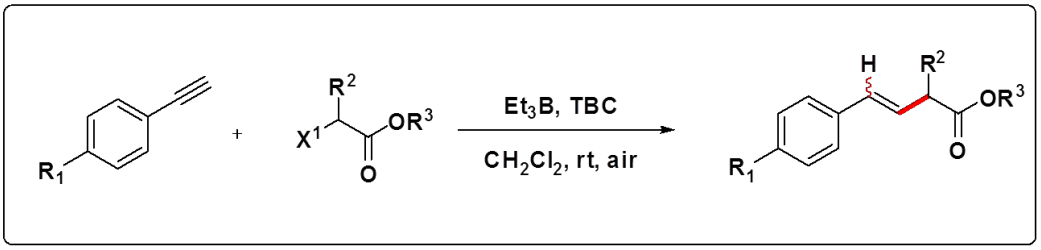
Very recently Renaud et.al [1] has developed radical chain reduction of organoboranes with catechols. To exploit the reactivity of 4-*tert*-butylcatechol (TBC) towards electron rich radicals, we envisioned, intermolecular reductive coupling between electron rich terminal alkenes and an electron poor radical precursors.

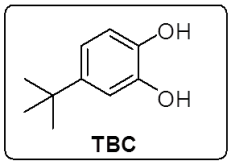
Herein we report a generalized method for the carbohydrogenation of electron rich terminal alkenes and terminal alkynes mediated by TBC by taking a-iodoester/a-xanthogenoesters as radical precursors shown in **Scheme 1** and **Scheme 2.**

Scheme 1



Scheme 2





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Synthesis of Novel, Molecularly-Defined Pyridine-Based Hybrid Materials

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Combining inorganic and organic components to produce functional hybrid materials is a very powerful approach to integrate a property defined at the molecular level into a material. Such rational design can result in synergetic effects that will take advantage of the stability of the inorganic function and the modularity of the organic scaffold embedded in the hybrid material. Hybrid organosilicas and periodic mesoporous organosilicas (PMOs) have been the focus of recent research due to their high surface area, high thermal stability as well as high density of uniformly distributed organic functionalities within the pores and the walls of the inorganic matrix.[1]This approach allows further elaboration into molecularly-defined heterogeneous catalysts.[2]

Here, we will describe our progress towards the preparation of high surface area hybrid organosilica materials containing tailored pyridine moieties as platform matrixes and catalysts.

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Synthesis and Fluorescence Properties of 5-Amino-4-Carboxamidthiazoles and Their Borate Complexes

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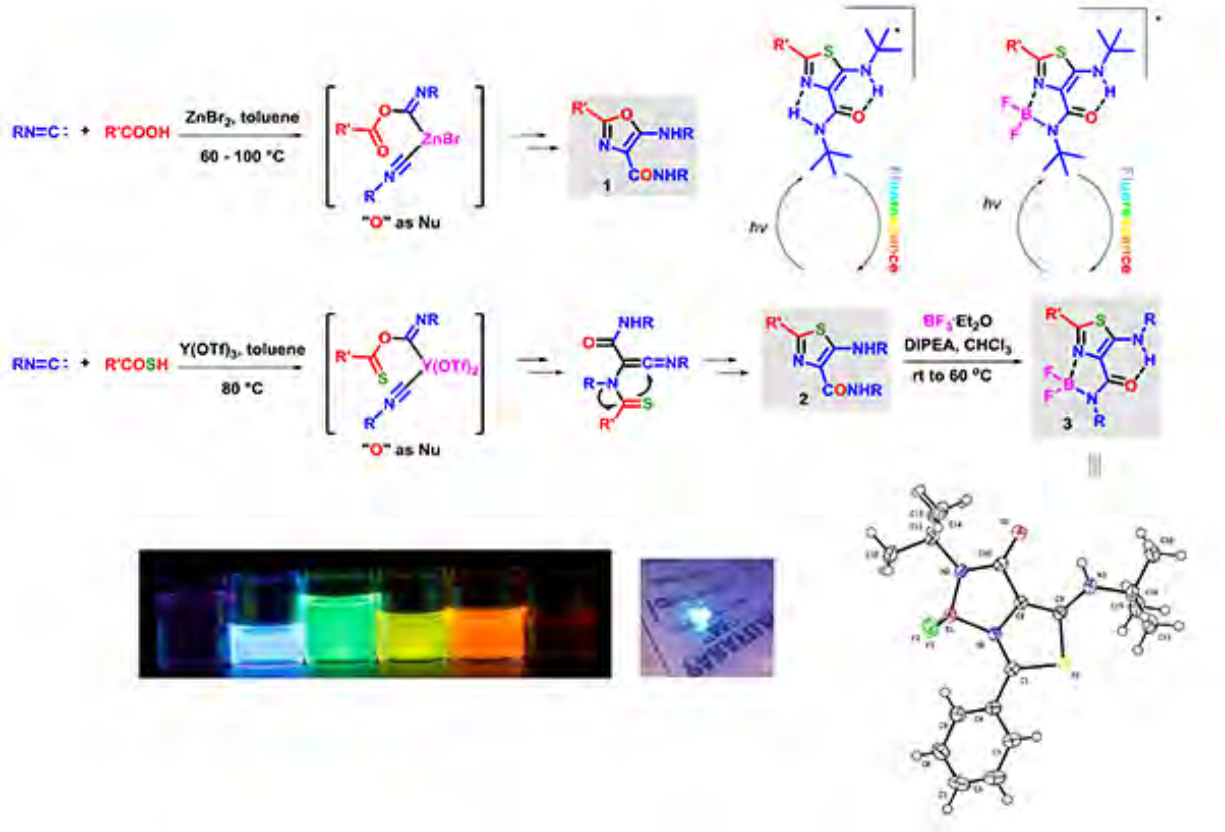
[1]EPFL Lausanne

Enabled by the discovery of new reactivity profile of isonitriles,[1] we have developed a novel Lewis acid-catalyzed co-trimerization of isonitriles with thiocarboxylic acids. The reaction afforded, from simple starting materials, 2-substituted 5-amino-4-carboxamidthiazoles in good to excellent yields with broad substrate scope.[3] Besides their known anticancer and anti-inflammatory activities,[2] we observed that 5-amino-4-carboxamidthiazoles displayed strong fluorescence emission upon UV irradiation.[3]



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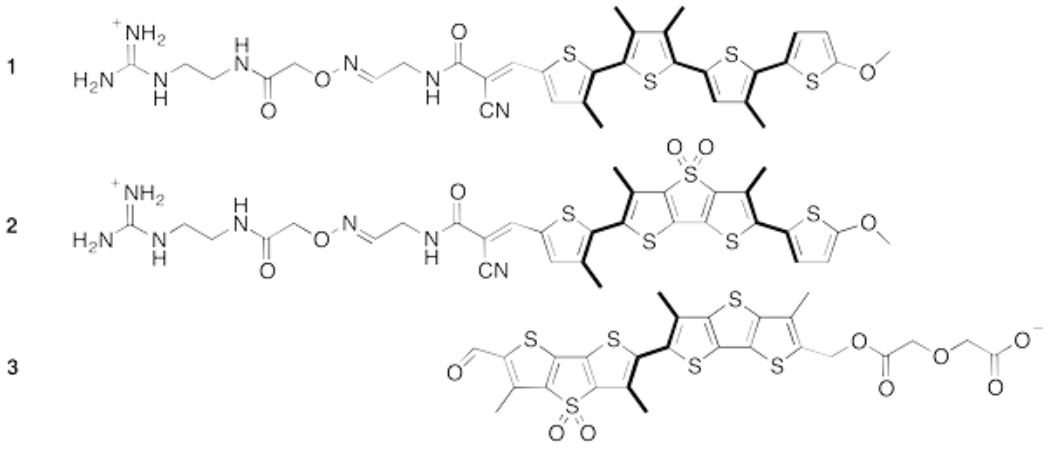
[2] WO2012161879A1.
[3] unpublished results.

Fluorescent Amphiphilic Push-Pull Oligothiophenes as Planarizable and Polarizable Membrane Probes

Quentin Verolet[1], Marta Dal Molin[1], Saeideh Soleimanpour[1], David Alonso[1], Naomi Sakai[1], Stefan Matile[1] *

[1]University of Geneva

Membrane characteristics such as fluidity, lateral tension and polarity are crucial parameters in many biological processes. Nowadays, fluorescent probes are one of the most promising candidates to study these parameters. Our group proposed the use of a new class of fluorescent probes that exploits the combination of chromophore planarization and polarization as an environment reporter [1]. We developed an oligothiophene push-pull chromophore **1** with a charged head to control the internalization and the position of the probe inside the membrane. The sensitivity of this probe towards fluidity changes arises from the planarization of the thiophene scaffold in the ground state induced by the passage to a more rigid environment. This planarization red shifts the absorbance spectra enough to discriminate the phase transition from L_d to S_o with the naked eye. For maximizing the mechanosensitivity of the probe **1**, a screening of the length of π-system and the deplanarization induced by the methylation of the oligothiophene scaffold was accomplished [2].



To improve the performance of the dye, a new generation of probes is being developed, using highly fluorescent units such as a rigid dimethyl-dithienothiophene-S,S-dioxide core **2** and **3**. It is expected that the increase of the contact areas of the monomer will improve the mechanosensitivity of the probe. In the same time the use of an inherently fluorescent unit should increase the quantum yield.

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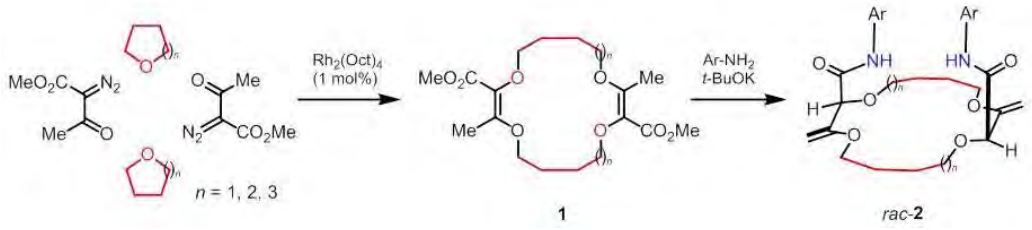
Synthesis of functionalized polyether macrocycles

Mahesh Vishe[1], Radim Hrdina[1], Laure Guénée[1], Jérôme Lacour[1] *

[1]University of Geneva

Polyether macrocycles are generally synthesized from linear molecules using intramolecular reactions. Recently, our group has developed several one-step syntheses of medium sized rings and polyether macrocycles by multicondensation reactions of simple cyclic ethers and diazo reactants under high concentration and non-templated conditions (see below).[1] Herein, we present a series of Rh(II)-catalyzed[2] reactions of diazocarbonyls and substituted tetrahydrofuranes and tetrahydropyranes that afford densely-functionalized 16- to 18-membered macrocycles in a single step and yields up to 60 %.[3] A rather high functional group tolerance is exhibited.Mechanistic rationals for these macrocyclization reactions and a comprehensive analysis of the influence of the introduced functional groups on the macrocyclic geometries will be detailed.

Of particular importance, an unprecedented amidation-isomerization sequence is now presented that allows the formation of deconjugated crown ethers as single diastereomer (*dr* 99 : 1). These compounds of type **2** display unique cylindrical conformations resulting hence in interesting properties.



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Pd(0)-Catalyzed Enantioselective Synthesis of 1,5-Enynes.

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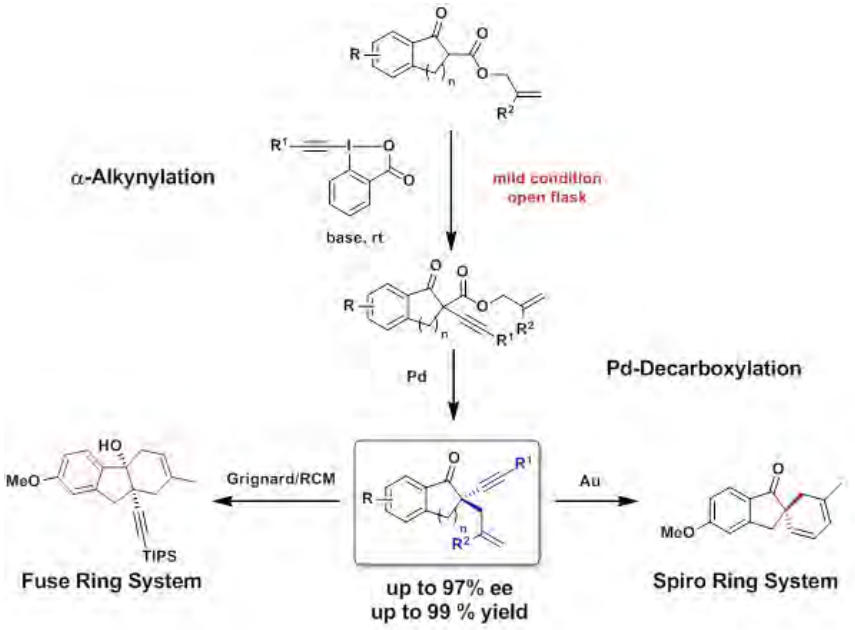
[1]EPFL Lausanne

1,5-Enynes are useful building blocks to increase molecular complexity in organic synthesis.[1] However, their asymmetric construction with a propargylic quaternary center still represents a synthetic challenge and no catalytic enantioselective method is yet available.Herein we present a general approach to access them by an electrophilic alkynylation/enantioselective palladium-catalyzed allylic decarboxylation sequence.[2] Our catalytic system is based on a palladium catalyst bearing chiral biphosphine ligands developed by Trost and co-workers[3] and affords chiral 1,5-enynes bearing a propargylic quaternary stereocenter in high yields and enantioselectivities via a DYnamic Kinetic Asymmetric Transformation (DYKAT). The required racemic alkynes were easily synthetized by the α-alkynylation of allyl β-keto esters using ethynyl benziodoxolone hypervalent iodine reagents. The products obtained were demonstrated to be versatile building blocks for the synthesis of fused or spiro polycyclic ring systems based on Au-catalyzed cycloisomerization reactions and ring-closing metathesis.



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Hierarchical self-assembly of nucleotide-appended oligopyrenotides into defined supramolecular objects.

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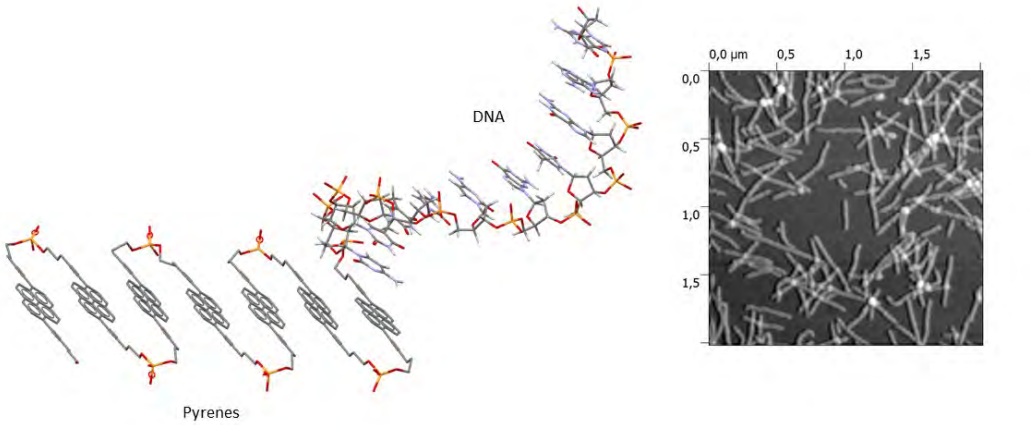
[1]University of Berne

Supramolecular DNA assembly blends DNA building blocks with synthetic organic and inorganic molecules giving structural and functional advantages both to the initial self-assembly process and to the final construct.[1]
Synthetic molecules can bring a number of additional interactions into DNA nanotechnology. Incorporating extended aromatic molecules as connectors of DNA strands allows folding of these strands through p-p stacking (DNA “foldamers”).[2]
In previous work it was shown that short oligopyrenotides (phosphodiester-linked pyrene oligomers) behave as staircase-like foldamers, which cooperatively self-assemble into two-dimensional supramolecular polymers in aqueous medium.[3]
Herein, we demonstrate that a 10-mer DNA-sequence modified with 7 pyrene units (see illustration) forms dimensionally-defined supramolecular polymers under thermodynamic conditions in water. We present the self-assembly behavior, morphological studies, and the spectroscopic properties of the investigated DNA-sequences (illustrative AFM picture shown below).



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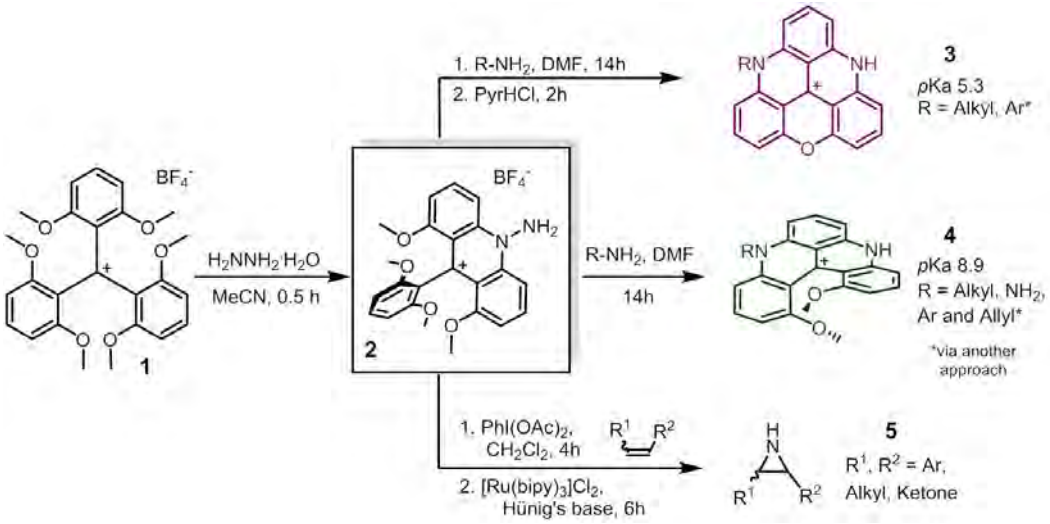
N-aminoacridinium cations: central building blocks for the synthesis of unprotected aziridines and pH-sensitive dyes synthesis

Antoine Wallabregue[1], Dimitri Moreau[1], Petr Sherin[1], Jean Grüenberg[1], Eric Vauthey[1], Jérôme Lacour[1] *

[1]University of Geneva

Cationic helicenes and triangulenes are unusual dyes and fluorophores with a broad spectrum of applications.[1]They are readily prepared from tris(2,6-dimethoxybenzene)methyl carbenium **1** by sequences of nucleophilic aromatic substitutions with nitrogen nucleophiles.



Herein, in a new development, the synthesis of novel *N*-aminoacridinium salt **2** is reported. It can be used for the preparation of p*H*-sensitive triangulene **3** and diaza [4]helicenes **4** thanks to particularly facile N-N bond cleavage reactions. Dyes and fluorophores of type **3** (*p*Ka 5.3) can be applied as specific probes for late endosomes. Moreover, compound **2** can be used as nitrogen source for the stereospecific aziridination of unfunctionalized olefins under metal-free oxidative conditions.[2] The corresponding NH aziridines **5** [3] are then obtained using mild reductive or photoreductive conditions.[4]

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Towards a Perylene-Based Cyclophane with Charge-Transfer Capability

Kevin Weiland[1], Marcel Mayor[1] *

[1]University of Basel

Donor-acceptor cyclophanes are desirable molecules for the use in molecular junctions, since they have tuneable electric conductivity upon UV-irradition.[1] A new perylene-based cyclophane will be synthesized containing a donor-active fumaric nitril moiety, starting from readily available perylene-3,4,9,10-tetracarboxylic dianhydride.

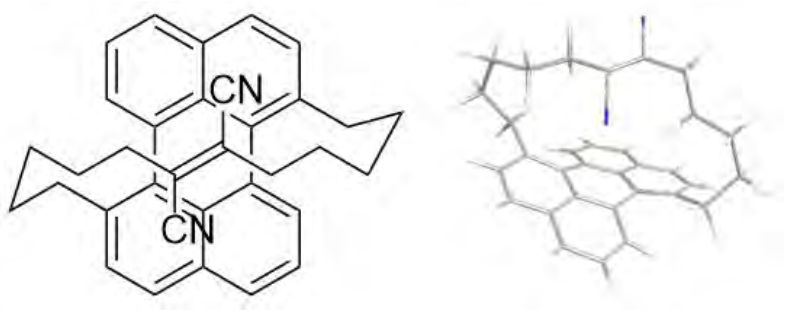

Figure 1: Molecular and three dimensional structure of the target compound.

The key step in the synthesis of the target compound will be the ring-closing-alkyne metathesis (RCAM) to give the triple-bond-containing macrocycle using *Schrock's* catalyst.[2] The resulting macrocycle will be further functionalized to give the target donor-acceptor-compound.

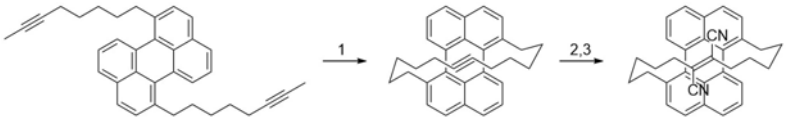

Figure 2: 1.) *Schrock's* RCAM catalyst, 2.) *trans*-bromination; 3.) *Rosenmund-von Braun* reaction.

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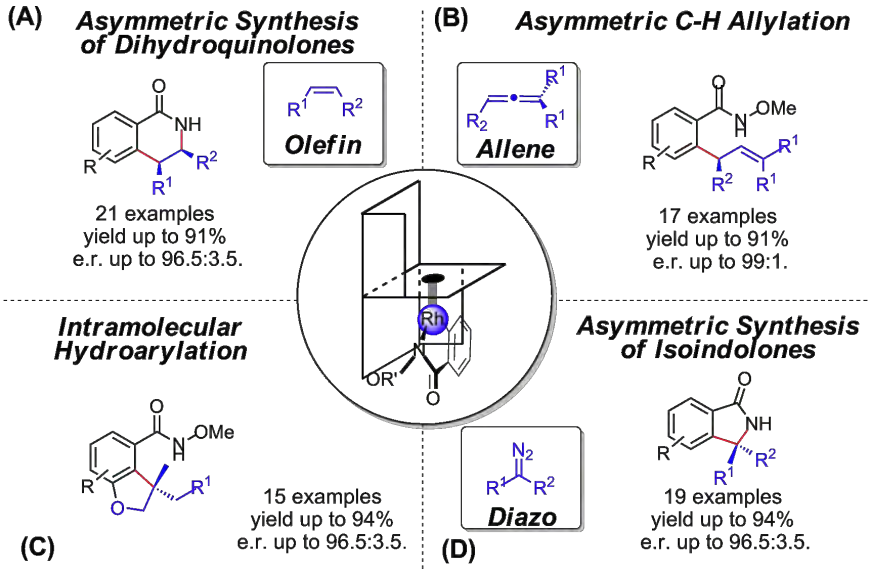
From the Blueprint of Chiral Cp-Ligands to the Landmark in Asymmetric Rh(III)-Catalyzed C-H Functionalization

Baihua Ye[1], Nicolai Cramer[1] *

[1]EPFL Lausanne

Cyclopentadienyl (Cp) based transition-metal-catalyzed C-H functionalization has become an important synthetic tool for the construction of molecular complexity from simple starting materials. Despite their high potential, the corresponding asymmetric transformations with late transition metal complexes, where the source of chirality solely stems from the Cp fragment, are completely elusive. We have elaborated facile and flexible syntheses of two tunable classes of enantiopure C_2-symmetric Cp ligands as the stereo-controlling elements. The viability of our novel concept to achieve high level of stereoselectivity was proved by four applications on asymmetric Rh(III)-catalyzed C-H functionalizations such as enantioselective synthesis of dihydroquinolones [1], asymmetric C-H allylations of benzamides [2], enantioselective hydroarylation to dihydrobenzofurans [3] and asymmetric synthesis of isoindolones [4]. Both classes of chiral Cp^{X*}-Rh complexes demonstrate high reactivity, delivering the products with excellent regio- and enantio-control.



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