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Organic Chemistry **OC001**

INEOS Technologies: provider of sustainable polyolefin technology solutions

Bettonville, S., Ramjoie, Y., Van Eetvelde, G., Rondelez, D., McNally, J.

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Swiss based INEOS is one of the world's largest petrochemical companies. It comprises 15 businesses manufacturing a diverse mix of products including polyolefins, styrenics, PVC, phenol, acrylonitrile as well as biodiesel and bioethanol. INEOS Technologies licenses many of INEOS' proprietary technology platforms to third parties, and also develops and sells leading catalysts and additives. In the past 5 years INEOS Technologies has emerged as the most successful polyolefin licensor globally providing clients access to best in class PP and PE technology platforms.

This presentation focuses on INEOS Technologies' extensive developments of advanced polyolefin catalysts. These catalysts give access to polyolefin products with, for example, improved tensile strength, better stress-crack resistance, improved clarity, and higher impact resistance. They provide the polymer manufacturer low reactor fouling, reduced byproduct formation, and fast transitioning between grades. The polymer product fabricator enjoys lower energy costs in production, reduced polymer weight per article for targeted performance, and less reject / off-spec product.
With car fuel tanks as an example, opportunities are arising with these new catalysts to substitute energy intensive and expensive materials such as steel for cost effective and recyclable alternatives such as high density polyethylene. These advanced polyolefin catalysts improve overall efficiency and cost-effective production from manufacture of the polymer through to delivery of the final application to the consumer. Less energy consumed, less waste, better product performance, substitution of more expensive materials for recyclable alternatives – all increasing the sustainability and efficiency of the 130 million tonne per annum polyolefin industry**.**

Organic Chemistry **OC002**

The Concept and Use of Compact Modules at Roche

Mark Rogers-Evans

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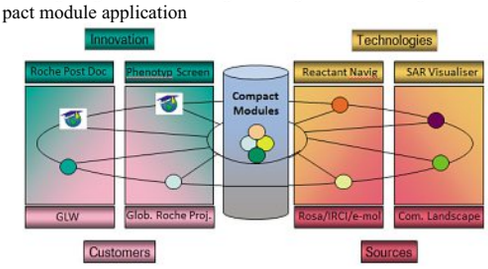
In recent years, there has been a resurgence of interest within the pharmaceutical community in "compact modules", that is, low-molecular-weight mono-, spiro or fused heteroalicyclic scaffolds that can be readily derivatized to provide surrogates for established medicinal-chemistry building blocks. Through a number of strategic collaborations initiated in 2005, Roche has seeked to be both pioneer and leader in the concatenated areas of module conceptualization, synthesis, scale up, availability, accessibility, distribution and application. The potential benefits to research projects are clear: to glean a competitive advantage by transforming and improving relevant molecular phys-chem, metabolic and safety properties, as well as securing ip position. This talk will briefly highlight some aspects of the current module value chain including:

i) How it has progressed via formal funding and informal networks from a largely local to globally driven activity
ii) Some contemporary activities of heuristic cheminformatics for module identification and retrieval
iii) Ensuring the optimum availability and utility of modules in order to leverage maximum value for current and future projects
iv) Investigating novel screening and target ID technologies to expand compact module application



Organic Chemistry **OC003**

Mono- and biheterocyclic tubulin polymerization promoters: design aspects, synthesis and fungicidal activity

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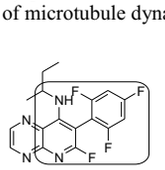
Pyrido[2,3-b]pyrazines [1], in which the pyridine moiety is fully substituted, as well as similar substituted monocyclic pyridazines [2], imidazoles [3] and pyrazoles [4] are highly active against a broad range of different phytopathogens, such as *Mycosphaerella graminicola* (wheat leaf blotch), *Alternaria solani* (potato and tomato early blight) and *Magnaporthe grisea* (rice blast) by promotion of the fungal tubulin polymerization, leading to a disruption of microtubule dynamics.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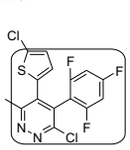
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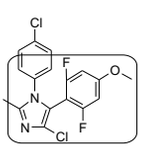
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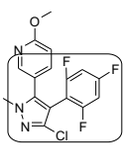
Ref. 4

Design aspects, synthesis and structure-activity relationship data of this class of experimental fungicides will be presented.

[1] P. C. Crowley, C. Lamberth, U. Müller, S. Wendeborn, K. Nebel, J. Williams, O.-A. Sageot, N. Carter, T. Mathie, H.-J. Kempf, J. Godwin, P. Schneiter, M. R. Dobler, *Pest Manag. Sci.* **2010**, *66*, 178.
[2] C. Lamberth, S. Trah, S. Wendeborn, R. Dumeunier, M. Courbot, J. Godwin, P. Schneiter, *Bioorg. Med. Chem.* **2012**, *20*, 2803.
[3] C. Lamberth, R. Dumeunier, S. Trah, S. Wendeborn, J. Godwin, P. Schneiter, A. Corran, *Bioorg. Med. Chem.* **2013**, *21*, 127.
[4] R. Dumeunier, C. Lamberth, S. Trah, *Synlett* **2013**, *24*, 1150.

Organic Chemistry **OC004**

A new approach to separate chemical shift and scalar coupling of 1D proton NMR spectra

Axelle Cotte, Damien Jeannerat

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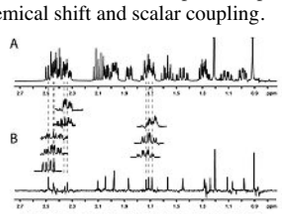
In ^{1}H spectra, the multiplet structure due to homonuclear scalar coupling makes it difficult to properly analyze 1D spectra in the case of complex samples with severe signal overlap. Obtaining 1D pure shift proton spectra is therefore a quite interesting decades-old challenge [1-4]. We propose here a new approach based on spacial encoding to quickly obtain high-resolution 2D spectra leading to homodecoupled 1D spectra after a simple processing. The experiment is based on the Zangger-Sterk element [5] and combined with spectral aliasing to increase the resolution in the indirect F1 dimension. The resulting 2D spectra show only diagonal signals with a multiplet structure only along the F2 dimension. A simple manipulation of the spectrum cleanly separates chemical shift and scalar coupling.



(A) Classical 1D and (B) homodecoupled 1D proton spectra of 4-Androstene-3,17-dione.

[1] M. Woodley and R. Freeman, *J. Magn. Reson. Ser. A* **1994**, *109*, 103
[2] J. A. Aguilar *et al*., *Angew. Chem. Int. Ed.* **2010**, *49*, 3901
[3] A. J. Pell *et al*., *Magn. Reson. Chem.* **2007**, *45*, 296
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[5] K. Zangger and H. Sterk, *J. Magn. Reson.* **1997**, *124*, 486

Organic Chemistry **OC005**

Phosphorus-doped π-conjugated organic architectures

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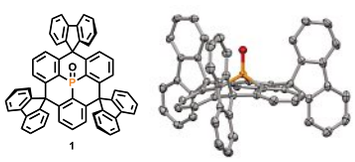
Department of Chemistry and Pharmacy, University of Erlangen-Nürnberg, Henkestrasse 42, D-91054 Erlangen, Germany

The most efficient strategy towards π-conjugated architectures with tailored properties is to incorporate heteroatoms directly into their sp^2-carbon skeletons [1]. While various nitrogen- and boron-containing polyaromatic architectures have recently been synthesized [2], π-systems with internal phosphorus atoms remain rather scarce. This is rather surprising as organophosphorus compounds often feature properties that are markedly different from those of their nitrogen analogues [3].



Here, we present a family of unprecedented phosphorus-centered π-systems, such as the trispirocyclic scaffold **1**. These compounds display not only appealing optoelectronic properties but also represent versatile platforms for the construction of various expanded phosphorus-doped organic architectures with desirable functions.

[1] P. O. Dral, M. Kivala, T. Clark, *J. Org. Chem.* **2013**, *78*, 1894.
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Organic Chemistry **OC006**

Synthesis and properties of novel indol-triarylcarbenium ions

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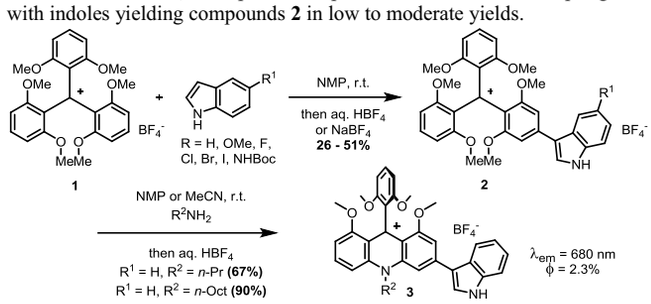
Triarylcarbenium **1**, a precursor for the triangulenium family of dyes[1,2], reacts traditionally with nucleophiles by *ipso*-substitution of the methoxy groups; functionalization of the aromatic subunits at other positions being so far limited.[3] In this context, we report the unprecedented direct C-C coupling of **1** with indoles yielding compounds **2** in low to moderate yields.



Compounds **2**, although formally more electron-rich, still react effectively with primary amines to form, with a somewhat surprising regioselectivity, the corresponding acridinium dyes **3**; these moieties presenting unusual fluorescence spectroscopy as well. Access to other indole-substituted carbenium ions, and especially triangulenium ones, as well as spectroscopic studies are in progress.

[1] B. Laleu, P. Mobian, c. Herse, B. W. Laursen, G. Hopgartner, G. Bernadinalli, J. Lacour *Angew. Chem. Int. Ed.* **2005**, *44*, 1879-1883.
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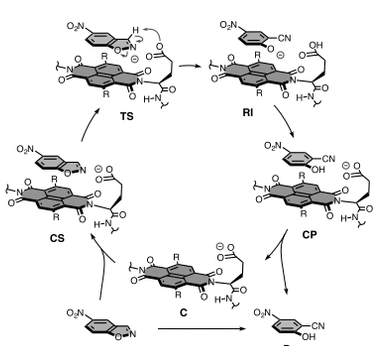
Organic Chemistry **OC007**

Catalysis with Anion-π Interactions

Yingjie Zhao, Yuya Domoto, Edvinas Orentas, Naomi Sakai, Stefan Matile*

University of Geneva, Geneva, Switzerland

We developed a conceptually innovative catalyst based on anion-π interactions. The Kemp elimination was chosen as a tool because the transition state of this reaction is anionic. Naphthalenediimides of varied π-acidity[1,2] with a covalently attached carboxylate as base were designed and synthesized as catalysts. According to Michaelis-Menten kinetics, the transition-state stabilization increased with increasing π-acidity of the catalysts. Thus the catalysis could be attributed to anion-π interactions.



[1] Dawson, R. E.; Hennig, A.; Weimann, D. P.; Emery, D.; Ravikumar, V.; Montenegro, J.; Takeuchi, T.; Gabutti, S.; Mayor, M.; Mareda, J.; Schalley, C. A.; Matile, S. *Nat. Chem.* **2010**, *2*, 533.
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Organic Chemistry **OC008**

Chiral Cp-ligands: stepping stone for asymmetric Rh(III)-catalyzed C-H functionalization

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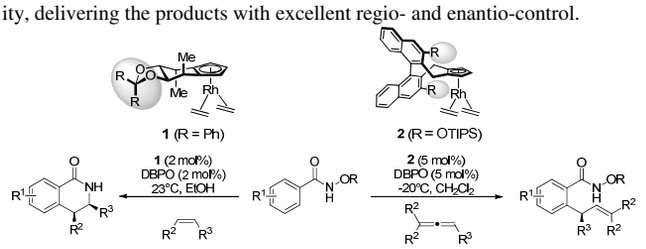
Laboratory of Asymmetric Catalysis and Synthesis, EPF Lausanne EPFL SB ISIC LCSA, CH-1015 Lausanne, Switzerland

Cyclopentadienyl (Cp) and pentamethylcyclopentadienyl (Cp*) ligands are of fundamental importance in organometallic chemistry and catalysis. Despite their high potential, asymmetric reactions with late transition metal complexes, where the sole source of chirality stems from the Cp fragment, are completely elusive. Recently, a particular interest in Cp*M (M = Rh, Ir, Co) complexes arose from their activity as C-H activation catalysts. We have elaborated facile and flexible syntheses of two tunable classes of enantiopure C_2-symmetric Cp ligands. To showcase their utility, the corresponding rhodium complexes **1** and **2** were applied in enantioselective synthesis of dihydroquinolones [1,2] and C-H allylations of benzamides [3] respectively. Both families of chiral Cp^{X*}-Rh complexes demonstrate high reactivity, delivering the products with excellent regio- and enantio-control.



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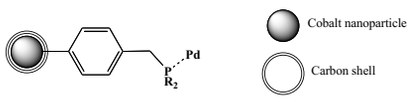
Organic Chemistry **OC009**

Magnetically recoverable, reusable, Pd catalysts for Suzuki couplings

Antoine Derible, Jean-Michel Becht and Claude Le Drian

Université de Haute Alsace, Institut de Science des Matériaux de Mulhouse (IS2M, UMR CNRS 7361), 15 rue Jean Starcky, F-68057 Mulhouse Cedex

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 presence of precious metal in products and waste. The development of efficient Pd catalysts that can be selectively recovered for reuse is therefore highly desirable.[1] We present here simple heterogeneous palladium catalysts supported on superparamagnetic cobalt nanoparticles[2] which can be easily and quantitatively recovered by magnetic separation. These catalysts are particularly efficient for Suzuki couplings from aryl bromides using ethanol as a solvent and were reused successfully several times without showing any loss of reactivity.



[1] C. Diebold, A. Derible, J.-M. Becht, C. Le Drian, *Tetrahedron* **2013**, *69*, 264.

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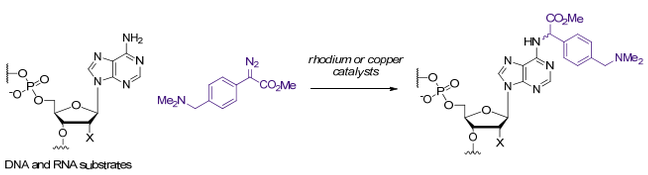
Organic Chemistry **OC010**

Catalytic Alkylation of Nucleic Acids

Kiril Tishinov, Na Fei, Stefanie Geigle, and Dennis Gillingham

Department of Chemistry, University of Basel, CH-4056, Basel, Switzerland

Nucleic acid polymers have diverse functions and yet their chemical structure is simple and repetitive. For synthetic chemists the functional group redundancy of nucleic acids presents a daunting challenge in chemo- and site-selectivity.[1] We have been developing organometallic catalysts for the site- and structure-specific targeting of DNA and RNA.2 In particular, rhodium and copper complexes3 in conjunction with α-diazocarbonyl compounds lead to N-H insertion reactions with the exocyclic amine groups in single-stranded regions of DNA and RNA. I will outline our efforts in identifying organometallic complexes that target nucleic acids and in developing ligand systems for these complexes that steer substrate selection.



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2. Kiril Tishinov, Kristina Schmidt, Daniel Häusinger, Dennis Gillingham "Structure-Selective Catalytic Alkylation of DNA and RNA" *Angew. Chem. Int. Ed.* **2012**, *51*, 12000-12004.
3. Kiril Tishinov, Na Fei, Dennis Gillingham "Simultaneous Cu(I)-catalysis of an azide-alkyne cycloaddition and an N-H insertion in water" *Submitted for Publication*

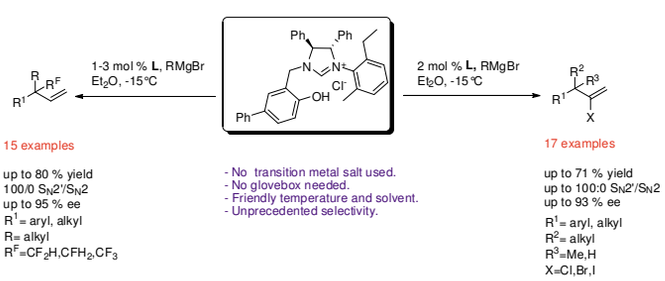
Organic Chemistry **OC011**

Transition metal-free Asymmetric Allylic Alkylation using Grignard reagents. What you cannot do using conventional metal catalyzed process.

David Grassi and Alexandre Alexakis

University of Geneva, Department of Organic Chemistry, 30 quai Ernest Ansermet, 1211 Geneva, Switzerland.

In all the outstanding contributions concerning the Asymmetric Allylic Alkylation dealing with transition metal catalyzed processes the challenge resulted in the right combination of a chiral ligand with the appropriate transition metal to reach high results. If the transition metal is removed and the ligand is solely used the formation of S_N2 adduct or an absence of reactivity have been always reported. We found out that using a bidendate NHC ligand we could trigger the S_N2' attack and access system that are reluctant to react with transition metal catalyzed processes.



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Organic Chemistry **OC012**

Iridium-catalyzed Double Diastereoselective Isomerization of Primary Allylic Alcohols

Houhua Li, Clément Mazet*

Department of Organic Chemistry - University of Geneva, 30 Quai Ernest Ansermet, 1211 Geneva 4, Switzerland

The transition metal-catalyzed asymmetric isomerization of primary and secondary allylic alcohols into the corresponding aldehydes and ketones has attracted renewed interest in recent years [1]. While the enantioselective isomerization of achiral allylic alcohols has already been disclosed by our group as well as others [2], the diastereoselective isomerization using chiral substrates in either racemic or scalemic form has never been studied.
Herein we describe the iridium-catalyzed double diastereoselective isomerization of 3,3-disubstituted primary allylic alcohols with a stereocenter at C4 [3]. With this protocol vicinal tertiary carbon centers could be installed in a stereocontrolled fashion. Both enantiomers of iridium catalyst catalyze the isomerization of (*Z*) and (*E*)-enantioenriched primary allylic alcohols and deliver the corresponding aldehydes in good yield, excellent diastereosemeric ratio and virtually perfect enantioselectivity. Moreover, stereodivergent reactions on racemic mixtures (RRM) were also achieved in the isomerizations of either (*Z*) or (*E*)-racemic substrates [4].

[1] For a recent review, see: L. Mantilli, C. Mazet, *Chem. Lett.* **2011**, *40*, 341-344.
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[3] H. Li, C. Mazet, Unpublished results.
[4] For a recent review, see: L. C. Miller, R. Sarpong, *Chem. Soc. Rev.*, **2011**, *40*, 4550-4562.

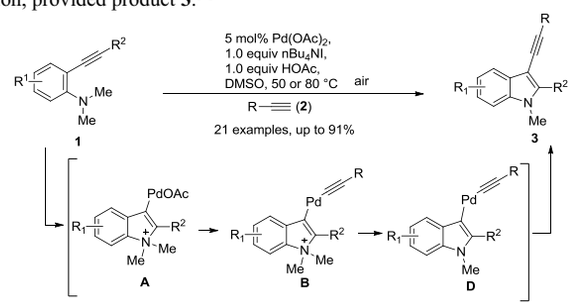
Organic Chemistry **OC013**

Palladium-Catalyzed Coupling of *ortho*-Alkynylanilines with Terminal Alkynes Under Aerobic Conditions: Efficient Synthesis of 2,3-Disubstituted 3-Alkynylindoles

Bo Yao, Qian Wang, Jieping Zhu*

Ecole Polytechnique Fédérale de Lausanne, EPFL-SB-ISIC-LSPN, BCH 5401, 1015 Lausanne (CH), Switzerland

The indole nucleus is an ubiquitous heterocycle found in many bioactive natural products, pharmaceuticals and agrochemicals. As part of our ongoing research,[1] we developed an efficient method through palladium-catalyzed coupling of *o*-alkynylanilines with terminal alkynes to afford 2,3-disubstituted 3-alkynylindoles in good to excellent yields. Intermediate **A** was characterized and a retro-aminopalladation of intermediate **B** was observed for the first time. Mechanistic study suggested that *N*-demethylation of **B** by iodide drove the reaction forward to **D** which, upon reductive elimination, provided product **3**.[2]



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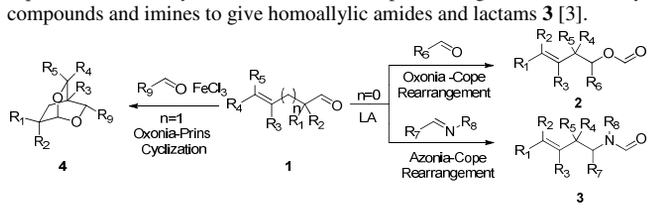
Organic Chemistry **OC014**

Iron(III) Chloride Catalyzed Oxonia-Prins Cyclization Reaction

Lijun Zhou,[a][b] Yue Zou,[b] Quanrui Wang,*[a] Andreas Goeke*[b]

[a]Department of Chemistry, Fudan University, 220 Handan Road, Shanghai 200433, PR. China
[b]Givaudan Fragrances (Shanghai) Ltd, 298 Li Shi Zhen Road, Shanghai 201203, PR. China

It is a major objective of synthetic chemistry to develop synthetic methods which proceed under mild conditions. Sigmatropic rearrangements have been particularly useful for this request. We have recently developed a tandem cross-dimerisation/oxonia-Cope reaction of β,γ-unsaturated carbonyl compounds and aldehydes to homoallylic esters and lactones **2** [1][2]. The concept was successfully extended to azonia-Cope rearrangements of carbonyl compounds and imines to give homoallylic amides and lactams **3** [3].



With further investigation on reaction of γ,δ-unsaturated carbonyl compounds and aldehydes, a novel $FeCl_3$-catalyzed oxonia-Prins cyclization reaction to give bridged acetal **4** was discovered. We will present our systematic study of this reaction and its application to natural product synthesis.

[1] Y. Zou, C. Ding, L. Zhou, Z. Li, Q. Wang, F. Franziska, A. Goeke. *Angew. Chem. Int. Ed.* **2012**, *51*, 5647.
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Organic Chemistry **OC015**

Peptide-catalyzed Stereoselective Conjugate Addition Reactions Generating All-Carbon Quaternary Stereogenic Centers

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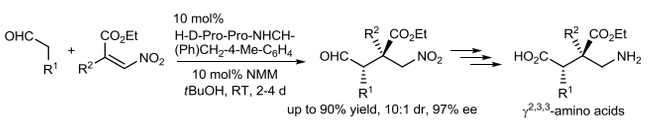
Laboratorium für Organische Chemie, ETH Zürich
Wolfgang Pauli-Strasse 10, 8093 Zürich, Switzerland

The stereoselective conjugate addition reaction of aldehydes to nitroolefins is an attractive reaction for the synthesis of valuable γ-nitroaldehydes.[1] Our group introduced tripeptides of the type Pro-Pro-Xaa (Xaa = acidic amino acid) as highly efficient catalysts for asymmetric conjugate additions of aldehydes to β-mono- and α,β-disubstituted nitroolefins.[2] We have now extended the substrate scope to reactions with β,β-disubstituted nitroolefins that are significantly more challenging substrates and provide γ-nitroaldehydes bearing an all-carbon quaternary stereogenic center.



We will present an effective peptidic catalyst for asymmetric conjugate additions of aldehydes to β,β-disubstituted nitroolefins, show initial mechanistic insights and that the resulting γ-nitroaldehydes can be readily converted into, for example, novel $\gamma^{2,3,3}$-amino acids with an all-carbon quaternary stereogenic center.[3]

[1] D. Roca-Lopez, D. Sadaba, I. Delso, R. P. Herrera, T. Tejero, P. Merino, *Tetrahedron: Asymmetry* **2010**, *21*, 2561.
[2] a) M. Wiesner, M. Neuburger, H. Wennemers, *Chem. Eur. J.* **2009**, *15*, 10103. b) M. Wiesner, G. Upert, G. Angelici, H. Wennemers, *J. Am. Chem. Soc.* **2010**, *132*, 6. c) J. Duschmalé, H. Wennemers, *Chem. Eur. J.* **2012**, *18*, 1111.
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Organic Chemistry **OC016**

Copper-Catalyzed Enantioselective Synthesis of Axially Chiral Allenes

Hailing Li and Alexandre Alexakis*

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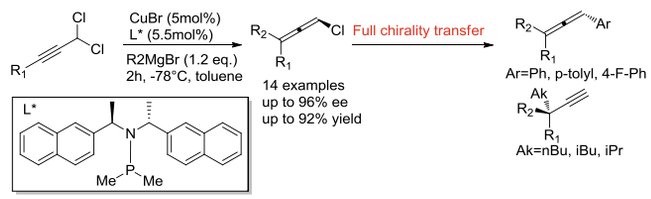
Quai Ernest Ansermet, 30, 1211, Geneva 4, Switzerland

Allene compounds have drawn more and more attention as a frequent building block and a versatile intermediate for organic synthesis.[1] A series of optically active chiral allenes could be obtained through chirality transfer, the main drawback was that these approaches required the stoichiometric amount of enantioenriched starting materials which were specific for each case and sometimes hard to prepare.

Herein, we reported a simple copper-catalyzed enantioselective synthesis of axially chiral chloroallenes from prochiral propargylic substrates, employing catalytic amount of easily prepared chiral SimplePhos ligand. Exclusive formation of desired allenes was observed with good enantioselectivities. Further transformations to trisubstituted allenes or terminal alkynes with propargylic quaternary carbon centre keep high level of enantiopurity.[2]



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Organic Chemistry **OC017**

Unexpected 3-Atoms Insertion of Ru-Metal Carbenes into Epoxides

Cecilia Tortoreto, Thierry Achard, Amalia Poblador-Bahamonde, Laure Guénée and Jérôme Lacour*

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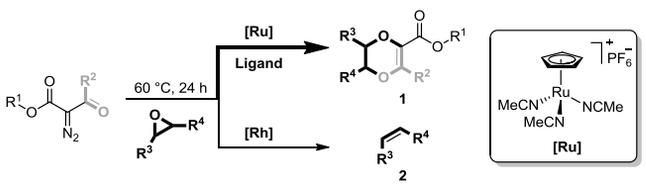
CpRu complexes are interesting alternatives to copper and dirhodium species for the catalyzed decomposition of diazo compounds.[1] Our group has recently shown that combinations of $[CpRu(CH_3CN)_3][PF_6]$ and diimine ligands catalyze the decomposition of α-diazo-β-ketoesters and allow further condensation, O-H and 1,3-C-H insertion reactions.[2]
In a new development, that uses epoxides as substrates, we describe the direct formation of unique dioxene species (**1**). The process is only possible through ruthenium cyclopentadienyle catalysis as, under Rh(II)-mediated reactions, olefines **2** are predominantly obtained.[3] Very high regio and stereoselectivity are observed and mechanistic insights will be given.



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Organic Chemistry **OC018**

Efficient in Vitro Encapsulation of Protein Cargo by an Engineered Protein Container

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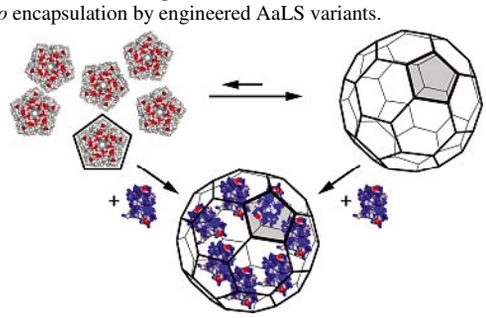
D-CHAB ETH Zurich,
Wolfgang-Pauli-Strasse 10, Zürich, Switzerland

Protein containers derived from viruses, mineral transporters, or enzymatic complexes find increasing number of applications in nanotechnology. They also serve for research on basic mechanisms of encapsulation processes, which is important to understand compartmentalization inside living organisms.
In our lab, we engineered a non-viral protein container (*Aquifex aeolicus* lumazine synthase - AaLS) to encapsulate charged molecules by introducing oppositely charged residues which drive selective electrostatic binding of the guests *in vivo*. Here we present our results on conditions and efficiency of *in vitro* encapsulation by engineered AaLS variants.



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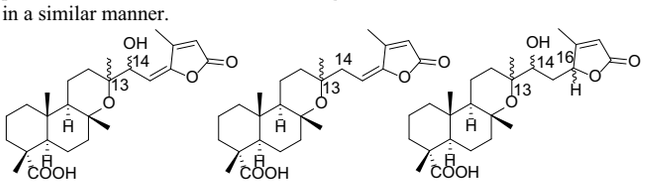
Organic Chemistry **OC019**

New sesterterpenoids from *Salvia mirzayanii* - stereochemical characterization by computational electronic circular dichroism

Ebrahimi SN,[1,2] Farimani MM,[2] Mirzania F,[2] Hamburger M [1]

[1]Division of Pharmaceutical Biology, University of Basel, 4056 Basel, Switzerland, [2]Department of Phytochemistry, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, G. C., Evin, Tehran, Iran,

Sesterterpenes are rare in nature and have been reported mostly from marine sponges and algae. Among terrestrial plants, Salvia species are a good source for these compounds. They exhibit diverse biological properties, such as anti-inflammatory, cytotoxic, anti-biofilm, antimicrobial, and anticancer activities. [1] In a project directed at novel bioactive metabolites from endemic Iranian Lamiaceae, we studied *Salvia mirzayanii*. We isolated five new manoyl oxide type sesterterpenoids, whose structures were secured by means of extensive NMR (1D and 2D) and MS spectroscopy. Structure elucidation revealed that compounds **1**-**3** only differ in their configurations at C-13 and C-14. Assignment of relative and absolute configurations was challenging due to free rotation around the C-13/C-14, but could be achieved by comparison of experimental and simulated ECD spectra of all possible stereoisomers. Absolute configuration of **4** and **5** were established in a similar manner.



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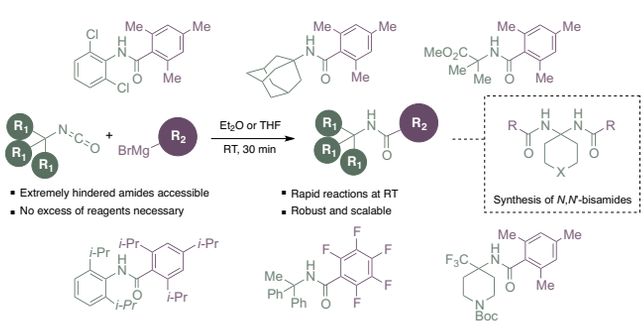
Organic Chemistry **OC020**

The Addition of Grignard Reagents to Isocyanates

Gabriel Schäfer, Coraline Matthey, Jeffrey W. Bode

ETH Zürich, Laboratorium für Organische Chemie,
Wolfgang-Pauli-Strasse 10, 8093 Zürich

Amide bond formation is widely regarded as the most used chemical reaction in drug discovery [1]. The most common way to prepare amides is the dehydrative coupling of amines with carboxylic acids by the action of a coupling agent. However, the preparation of sterically hindered and electron-deficient amides is known to be difficult by condensation chemistry. The direct coupling of Grignard reagents to isocyanates provides a facile and robust solution for the synthesis of these problematic amides. The coupling reaction proceeds in minutes, tolerates a number of functional groups, and needs no excess of reagents [2]. Furthermore, the Grignard addition to isocyanates can be applied to the synthesis of rare *N,N'*-bisamides.



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Organic Chemistry **OC021**

Oxidative Coupling Reactions of Grignard Reagents with Nitrous Oxide

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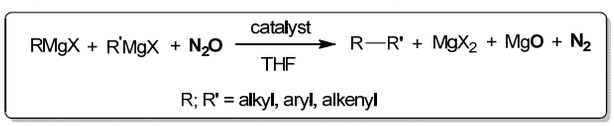
Ecole Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland

Nitrous oxide (N_2O, 'laughing gas') is a potent oxidation agent from a thermodynamic point of view[1]. In addition, it is an environmentally benign oxidant because the side product is dinitrogen. An obstacle in using N_2O in oxidation reactions is the inert nature of the gas. Heterogeneous catalysts can be used for the activation of nitrous oxide[2], but solution-based oxidation reactions with homogeneous catalysts have met only limited success. Many transition metal complexes are known to react with N_2O under mild conditions[3]. However, catalytic turnover is difficult to achieve. So far, only few examples are known and the catalytic efficiency of these systems is typically poor (TON $\leq$ 100). Herein, we describe oxidative homo- and cross-coupling reactions of Grignard reagents with N_2O as oxidant[4]. The reactions can be performed under mild conditions with low amounts of simple Fe, Co or Cu salts. Unprecedented turnover numbers of up to 9.4 x 10^3 are observed. Furthermore, it is demonstrated that N_2O displays distinct advantages over alternative oxidants such as dioxygen.



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Organic Chemistry **OC022**

Regio-, Enantioselective Aminofluorination of Alkenes

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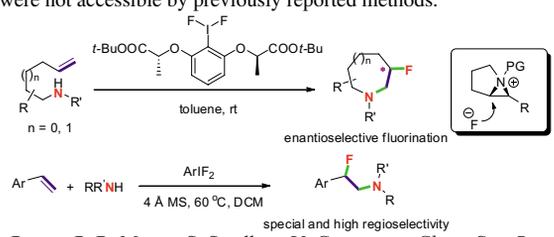
Institute of Organic Chemistry, Winterthurerstrasse 190, CH-8057 Zürich, University of Zürich, Switzerland

Carbon-fluorine bonds play an integral role in pharmaceuticals, agrochemicals, materials and tracers for positron emission tomography. Approximately 30% of all agrochemicals and 20% of all pharmaceuticals contain fluorine.[1] Given the utility of fluorine containing molecules, our group has recently developed an efficient methodology for the enantioselective formation of β-fluoropiperidines and β-azepanes from unactivated olefins which employed a novel chiral hypervalent iodine (III) difluoride as fluorine source.[2] Our mechanistic study revealed the likely involvement of an aziridinium intermediate in these transformations.

A highly regioselective intermolecular aminofluorination of styrenes has also been discovered. Interestingly, the 2-fluoro-2-phenylethanamine products were not accessible by previously reported methods.[3]



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Organic Chemistry **OC023**

Towards a DNA-Based Bacterial Sensor

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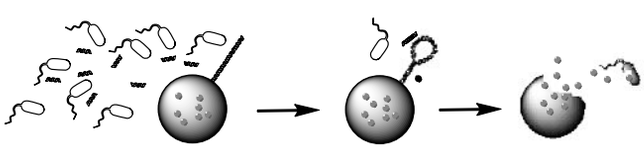
Bacteria release in their environment short strands of RNA with sequences specific to the species.
We are developing a sensor able to react with bacterial RNA and release a reactive compound to open up drug-containing nanocapsules.



The sensor is composed by two partially complementary DNA strands. One of them is fully complementary to a specific bacterial sequence and can therefore leave the sensor in the presence of bacteria. The second one has two complementary termini, so when the first strand is kept away by the bacterial strand, it folds forming a hairpin.
The new form put two chemical functions near enough to react and release an agent able to destroy the capsule.
DSC measurements showed that the hairpin is formed when the bacterial sequence is present.

Organic Chemistry **OC024**

Enantioselective Total Synthesis of Virosaine A and Related Natural Products

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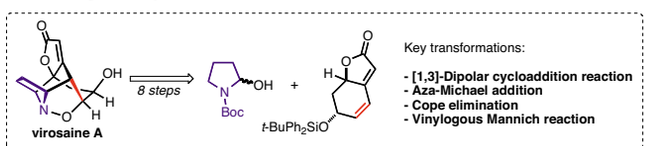
Department of Chemistry, University of Basel, St. Johanns-Ring 19,
CH-4056 Basel, Switzerland

The *Securinega* alkaloids are a family of bridged polycyclic natural products occurring in the plants of the *Securinega*, *Phyllanthus*, *Flueggea* and other genera in the Euphorbiaceae family.[1] In 2012, new pseudoenantiomeric alkaloids with unprecedented birdcage-shaped skeleton were isolated, namely virosaine A and virosaine B, from the twigs and leaves of *Flueggea virosa*.[2] Their densely functionalized, stereochemically complex architecture created an immense opportunity to pursue a challenging and stimulating total synthesis.



We will describe the first total synthesis of virosaine A along with two putatively related natural products bubbialidine and bubbialine, using the same advanced intermediate. The noteworthy chemical transformations include the formation of a tetracyclic precursor *via* an intramolecular aza-Michael addition, generation of a *N*-hydroxy-pyrrolidine through a Cope elimination process and the final intramolecular [1,3]-dipolar cycloaddition reaction to furnish a complex pentacyclic core.

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Organic Chemistry **OC025**

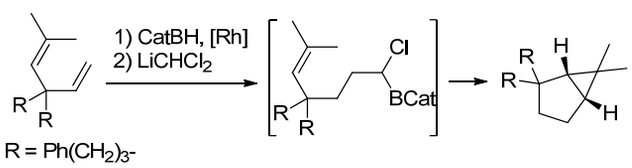
Generation of 1-Chloroalkyl Radicals from Organoboranes

Gong Xu, Monique Lüthy, Jacqueline Habegger and Philippe Renaud*

University of Bern, Department of Chemistry and Biochemistry, Freiestrasse 3, CH-3012 Bern, Switzerland

The generation of functionalized radicals from organoboranes remains challenging. We report here a versatile procedure involving 1-chloroalkyl radicals generated from *B*-alkylcatecholboranes via a Matteson type homologation procedure.[1,2] The homologation-radical reaction sequence is applicable to a wide range of substrates and it can be combined with an asymmetric hydroboration step.

When we tried to run radical cyclizations with the α-chloro *B*-alkylcatecholboranes derived from 1,4-dienes, we observed an unexpected intramolecular cyclopropanation. The scope and the mechanism of this surprising transformation will be discussed.



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Organic Chemistry **OC026**

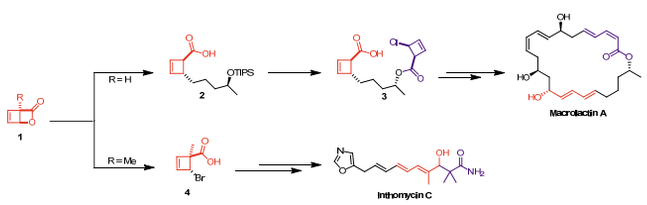
Stereodefined Synthesis of Functionalized Dienes: Streamlining Access to Polyene Natural Products

Caroline Souris, Fréderic Frébault, Davide Audisio and Nuno Maulide

Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470 Mülheim, Germany.

Dienylcarboxylate and -carbinol subunits are fundamental structural scaffolds present in various natural products. [1] Through simple modifications in the diene substitution pattern and olefin geometry, Nature is able to access remarkable structural diversity.

Herein, we will present the direct synthesis of stereodefined dienes from readily accessible lactone **1** and demonstrate their utility as key building blocks in polyene natural products synthesis. [2]



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Organic Chemistry **OC027**

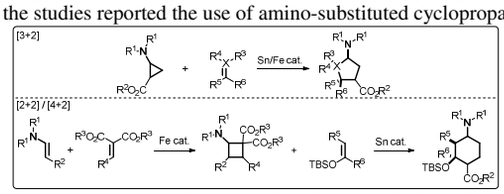
Synthesis and Reactivity of Nitrogen-Substituted Small Rings.

Florian de Nanteuil, Jerôme Waser

Laboratory of Catalysis and Organic Synthesis, EPFL BCH 4306, 1015 Lausanne, Switzerland.

Amino substituted carbo- and heterocycles are ubiquitous scaffolds in bioactive molecules and have been the focus of numerous studies during the last decades. In order to further diversify these important molecules, it is essential to have a fast and efficient access to their core structure.

At the pivotal point of our strategy lies the use of nitrogen-stabilized zwitterionic intermediates that offer the possibility to generate these cyclic structures via formal cycloaddition. In the past, donor-acceptor cyclopropanes have proven their synthetic utility as formal 1,3 dipole precursors but none of the studies reported the use of amino-substituted cyclopropanes.[1]



During the last two years, we have developed the annulation of aminocyclopropanes with enol ethers and carbonyl compounds as an efficient strategy to access highly substituted aminocyclopentanes and aminotetrahydrofurans.[2a,b,c] Herein, we report the details of this work as well as our more recent results on the synthesis of aminocyclobutanes using a cheap and non-toxic iron catalyst. These substrates were then successfully used as formal 1,4 dipoles for the synthesis of aminocyclohexanes.[2d]

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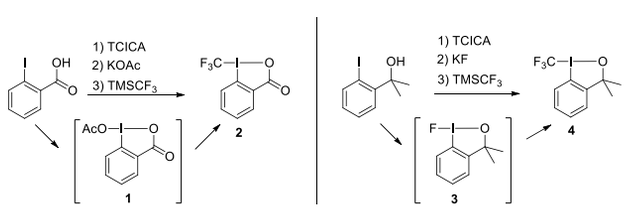
[2] a) F. de Nanteuil, J. Waser *Angew. Chem. Int. Ed.* **2011**, *50*, 12075 b) F. Benfatti, F. de Nanteuil, J. Waser *Org. Lett.* **2012**, *14*, 386 c) F. Benfatti, F. de Nanteuil, J. Waser *Chem. Eur. J.* **2012**, *18*, 4844 *d)* F. de Nanteuil, J. Waser, *Manuscript in preparation*

Organic Chemistry **OC028**

Optimized Synthesis of Hypervalent Iodine Reagents for Electrophilic Trifluoromethylation

Václav Matoušek, Ewa Pietrasiak, Julie Charpentier, Rino Schwenk and Antonio Togni

Department of Chemistry and Applied Bioscience, Swiss Federal Institute of Technology, ETH Zürich, CH-8093, Zürich



The current procedure[1] for the synthesis of the hypervalent iodine reagents for electrophilic trifluoromethylation **2** and **4** was subjected to optimization for large scale. In both cases the stoichiometric oxidants sodium metaperiodate and *t*-butyl hypochlorite, respectively, have been replaced by cheaper and less dangerous trichloroisocyanuric acid. The synthesis of reagent **2** has been accomplished in an one-pot procedure starting from 2-iodobenzoic acid. Reagent **4** was synthetized via fluoroiodane **3** as an intermediate within a short time without the need for a precisely defined temperature protocol. Furthermore, the reactivity of both this easily accessible fluoroiodane as well as of its fluorinated iodine(V) analogues was investigated leading to new possible applications in the area of electrophilic fluorination.

[1] Eisenberger, P.; Kieltsch, I.; Koller, R.; Stanek, K.; Togni, A. *Org. Synth*. **2011**, *88*, 68.

Organic Chemistry **OC029**

Towards the Total Synthesis of New Cembranolides

Raphael Schiess, Karl-Heinz Altmann

ETH Zürich, Institute of Pharmaceutical Sciences,
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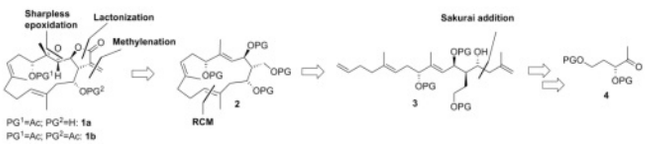
Cembranolides are diterpenoid natural products that are based on a 14-membered carbocyclic core structure. Numerous cembranolide variants have been described and they are associated with a wide range of biological activities. This includes the marine cembranolides **1a** and **1b** that were isolated in 2007 from the soft coral *Lobophytum michaelae* by Wang *et al*. [1] and found to be potent antiproliferative agents. In order to enable a more comprehensive biological profiling of these natural products we have embarked on the total synthesis of **1a** and **1b**. Our strategy entails macrocycle formation by RCM with diene **3** followed by the late stage establishment of the lactone ring.



So far, we have successfully implemented this concept up to the stage of macrocycle **2**, departing from methyl ketone **4** [2] (and ultimately from *L*-malic acid). This presentation will discuss the chemistry leading from **4** to **2**; the elaboration of **2** into target structures **1a** and **1b** is currently ongoing.

[1] L.-T. Wang *et al*. *Chem. Pharm. Bull.* **2007**, *5*, 766.

[2] R. Schiess *et al. Org. Lett*. **2011**, *13*, 1436.

Organic Chemistry **OC030**

Multi-Porphyrin Systems for Matter-Wave Interferometry

Lukas Felix[a], Markus Arndt[b], Marcel Mayor[a]

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[b]University of Vienna, Faculty of Physics, Boltzmanngasse 5, 1090 Vienna, Austria

Matter-wave dualism is a fundamental concept in quantum physics. The observation of wave properties of molecules can be used to approach the borderline between classical and quantum physics. Near-field optical time-domain ionization matter-wave interferometry (OTIMA) is a promising tool to investigate the wavelike behavior of large organic molecules such as porphyrin-trimer (**TriPorF$_n$**) and porphyrin-tetramer (**TPorF$_n$**).[1] Functionalization of the core structures with fluorous substituents leads to high mass compounds with relative high vapor pressures, which facilitates the generation of a steady molecule beam as needed for the interference experiments.[2]

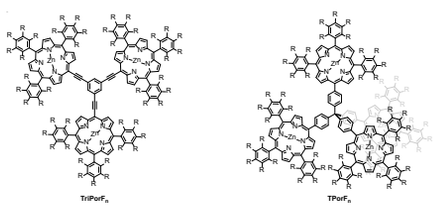

Figure 1: Porphyrin-trimer (**TriPorF$_n$**) and porphyrin-tetramer (**TPorF$_n$**) (R = (-S(CH$_2$)$_2$C$_8$F$_{17}$)$_n$ or -F).

[1] P. Haslinger, N. Dörre, P. Geyer, J. Rodewald, S. Nimmrichter, M. Arndt, *Nature Physics* **2013**, *9*, 144.
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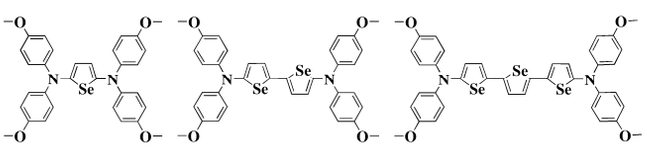
Organic Chemistry **OC031**

Mixed-valence phenomena in amino-decorated selenophenes

Ann Christin Jahnke, Oliver S. Wenger*

University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

While polythiophenes were the most studied polymers in the last decade [1] the amount of papers published on their selenium analogues increased in the last few years.[2] Promising properties like a smaller band-gap and lower oxidation- and reduction potentials have drawn the interest of using those compounds for various (opto)electronic applications.
Oligothiophenes in their one-electron oxidized forms can efficiently act as hole transfer materials [3] hence analogous or even more favorable behavior might be expected from oligoselenophene monocations.
We present here a set of three homologous molecules comprised of selenophene bridges of varying length between two tertiary amino groups. Our recent studies are working out the analogies and differences between thiophene and selenophene mixed valence species.



[1] *Handbook of Conducting Polymers,* 3rd ed. (Eds.: T.A. Skotheim, J.R. Reynolds), CRC, Boca Raton, FL, **2007**.
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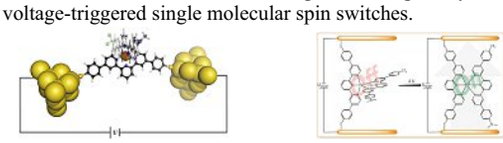
Organic Chemistry **OC032**

Design, Synthesis and Physical Investigation of a Voltage-Triggered Single Molecular Spin Switch

Gero D. Harzmann,[1] Riccardo Frisenda,[2] Enrique B. Linares,[2] Herre van der Zant,[2] Marcel Mayor[1]

[1]University of Basel, St. Johanns-Ring 19, 4056 Basel, Switzerland
[2]Kavli Institute of Nanoscience Delft University of Technology, Lorentzweg 1, 2628 CJ Delft, Netherlands

Herein several homo- and heteroleptic Fe(II)-bisterpyridine complexes are reported. The implementation of the heteroleptic complexes into miniaturized electronic devices like circuits is of high interest in the upcoming field of molecular electronics due to their potential capability of acting as applied voltage-triggered single molecular spin switches.



The designed complexes each contain a core Fe(II)-ion exhibiting an externally addressable spin state, a symmetric thiol-terminated terpyridine ligand allowing an immobilization between two Au-electrodes and another terpyridine 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 a very rare 4,4''-disubstitution pattern at the terpyridine 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 terpyridine core. Switching events found during mechanically controlled break junction (MCBJ) measurements underline the expected findings.

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Organic Chemistry **OC033**

DNA - multiporhyrinic systems: promising objects for materials science

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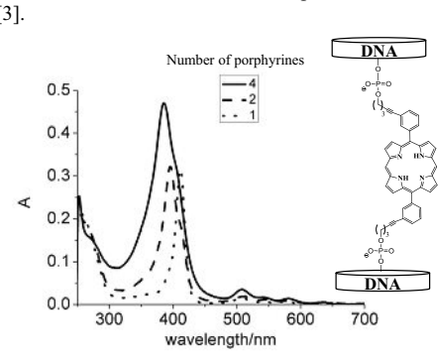
Porphyrin-containing materials are attractive objects for advanced light-harvesting systems [1]. Despite existence of numerous approaches to arrange porphyrines in a controlled and programmed way and therefore mimic natural photosynthetic systems, the problem of porphyrin`s arraying remains challenging [2]. Herein, we present an approach based on using DNA as a scaffold to hold porphyrines together. The whole spectroscopic investigation of the compounds containing several porphyrines and a possibility of their usage as molecular blocks for functional supramolecular architectures is discussed [3].



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Organic Chemistry **OC035**

Molecular TNT Sensors

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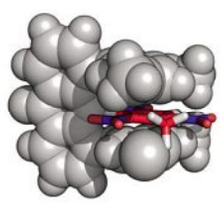
Fast and reliable detection of explosives or energetic materials has gained much attention due to security reasons but also its industrial applications.[1] TNT is not only one of the most abundantly used explosives but also detrimental to the environment and the human health.[2] Several systems for TNT detection are known, but most methods lack selectivity or are impractical.[3] The underlying concept of our sensor is to explore the influence of the electron deficient TNT on the fluorescence of an electron rich fluorophore, principally an Anthracene or a Xanthone with attached phenyl- or substituted phenyl substituents to increase the electron density of the system. The synthesis, characterization and sensing performances of a series of anthracene- and xanthone-based molecules are presented. Formation of a charge-transfer complex should alter the fluorescence of the chromophore.



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[3]] P. C. Ray, *J. Am. Chem. Soc.*, **2009**, *131 (38)*, 13806.

Organic Chemistry **OC036**

2D supramolecular polymers: nanosized, water-soluble «sheets»

M. Vybornyi, A. V.Rudnev, S.M. Langenegger, T. Wandlowski, R. Häner*

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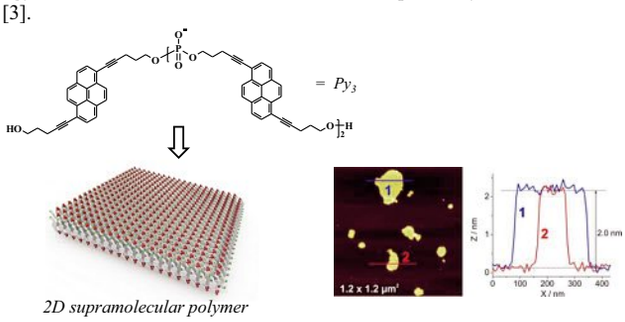
Self – assembly is a powerful tool for the construction of highly organized nanostructures [1]. Therefore, the possibility to control and predict pathways of molecular ordering on the nanoscale level is a critical issue for the production of materials with tunable and adaptive macroscopic properties. Herein, we demonstrate that designed molecule Py_3 forms dimensionally - defined supramolecular assemblies under thermodynamic conditions in water [2]. To study Py_3 self-assembly, we carried out whole set of spectroscopic and microscopic experiments. The factors influencing stability, morphology and behavior of «nanosheets» in multicomponent systems are discussed [3].



2D supramolecular polymer

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Organic Chemistry **OC037**

Modular Synthesis and Post-Functionalization of Cationic [6]Helicenes Controlling the Optical Properties of a New Family of NIR Dyes

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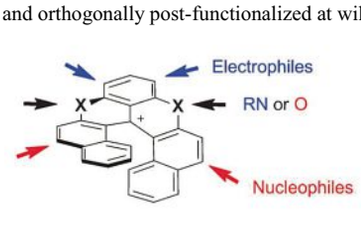
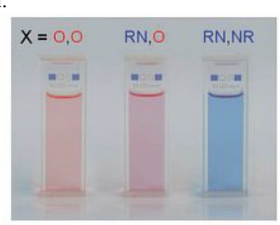
Helicenes are *ortho*-condensed polyaromatic compounds that are used in a variety of applications. Their properties are tailored *via* carefully selected functionalizations often installed prior to the formation of the helical cores.[1] Our group has recently developed a new family of cationic helicenes, namely dioxo-, azaoxo- and diaza[6]helicenes.[2] Those stable carbocations are accessible from a common precursor and can be selectively and orthogonally post-functionalized at will.





Interestingly, these salts are colorful dyes that absorb up to the NIR window and the functionalization pattern has a dramatic influence on those optical properties. Advantageously, they can be resolved as single enantiomers.

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Organic Chemistry **OC038**

Novel [1,2]-Stevens Rearrangement of Tröger Base Derived N^+-N^- Ylides

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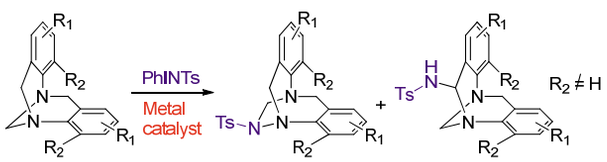
With the intrinsic goal of investigating the stereoselective [1,2]-Stevens rearrangement of chiral tertiary amines, in particular with Tröger bases, our group has reported a one-pot transition metal mediated diazo decomposition protocol for direct ylide formation for the enantiospecific synthesis of configurationally stable *ethano*-Tröger derivatives with high enantiomeric purity.[1,2]

Herein, we describe an efficient [1,2]-Stevens rearrangement of N^+-N^- ylides generated by treatment of *methano*-Tröger bases with the metal nitrene to afford a novel class of hydrazine Tröger bases. While regular Tröger bases exclusively afford unprecedented [1,2]-Stevens rearrangement of N^+-N^- ylides, the *bis-ortho* substituted Tröger bases undergo rearrangement as well as C-H insertion reactions. The details of this novel transformation including regioselectivity and stereospecificity will be presented.



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Organic Chemistry **OC039**

Highly Diastereo- and Enantioselective Organocatalytic Domino Michael/Aldol Reaction of Acyclic 3-Halogeno-1,2-Diones to α,β-Unsaturated Aldehydes

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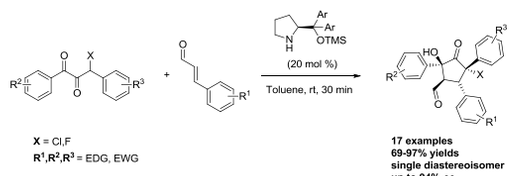
University of Geneva, quai Ernest Ansermet 30, CH-1211 Geneva 4, Switzerland.

Due to their diverse number of reactive centers, 1,2-dicarbonyl compounds represent very attractive scaffolds for organocatalytic cascade- or domino reactions. Recently, this type of compound has shown a wide utilization in asymmetric organocatalytic transformations.[1] Development of different activation modes increasing their nucleophilicity instead of competitive useless self-condensation has become a very attractive challenge. In contrast, 1,2-diones have rarely been described as pronucleophiles in organocatalytic reactions.[2] In this context, we disclosed the first organocatalytic domino Michael/aldol reaction of acyclic 3-halogeno-1,2-diones with α,β-unsaturated aldehydes to form challenging cyclopentanones with four contiguous stereogenic centers in excellent diastereoselectivities (>20: 1 dr), good yields (69-97%) and enantioselectivities (up to 94% *ee*).[3]



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Organic Chemistry **OC040**

Phosphorus Inversion of P-stereogenic C_1-symmetric Ligands

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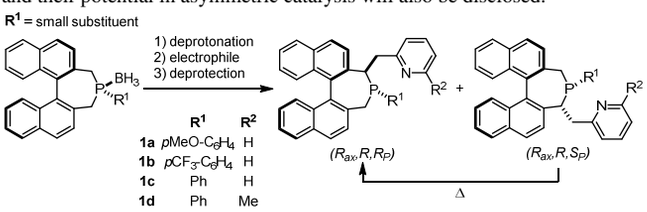
Quai Ernest Ansermet 30 CH-1211 Geneva 4 - Switzerland

Our group has recently designed a novel class of C_1-symmetric chiral (P,N) ligands that were found to provide high yield and enantiomeric excess in the intramolecular α-arylation of α-branched aldehydes.[1,2] These ligands feature three dinstinct elements of chirality: (i) the axial chirality of the binaphthyl backbone; (ii) the central chirality at the benzylic position; (iii) a stereogenic phosphorus center. Ligands with a large R^1 substituent are usualy prepared as single diastereoisomers. For ligands **1a-d** having a smaller P-substituent, 2 isomers were obtained in a typical 1.4:1.0 ratio. In the case of **1c**, the 2 isomers **1c**-(R_{ax},*R*,S_P) and **1c**-(R_{ax},*R*,R_P) were chromatographically separated and characterized by X-ray analyses. Upon heating the minor isomer **1c**-(R_{ax},*R*,S_P) quantitatively delivered **1c**-(R_{ax},*R*,R_P), thus indicating a formal P-interconversion is taking place. The thermodynamic and kinetic parameters associated with this phenomenon have been obtained. Complexation studies of both diastereomeric ligands and their potential in asymmetric catalysis will also be disclosed.[3]



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Organic Chemistry **OC041**

Access to congested quaternary centers by Pd-catalyzed intermolecular γ-arylation of unactivated α,β-unsaturated aldehydes

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In the last two decades, the α−arylation of enolizable carbonyl compounds has advanced with significant strides [1]. In this context, aldehydes have revealed particularly challenging substrates [2]. Our group has recently reported an enantioselective intramolecular α−arylation of α−branched aldehydes using novel chiral (P,N) ligands [3].

In a direct continuation of this work, and based on the vinylogous analogy [4], we set out to develop a related γ−arylation of γ−branched α,β−unsaturated aldehydes. In addition to the γ quaternary center, the products of such a remote coupling would bear substantial synthetic potential as derivatizations would be possible both at the olefinic position and the aldehyde functionality. We present herein our preliminary results in this direction.

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Organic Chemistry **OC042**

NHC-Copper Catalysts as Potent Tools to Address Asymmetric Conjugate Additions Challenges

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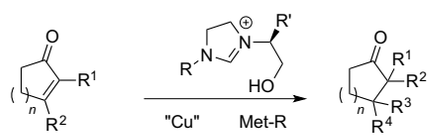
Université de Genève, Département de Chimie Organique, Quai Ernest Ansermet, 31, 1211 Genève 4, Switzerland

Synthesis of all-carbon quaternary centers remains a current challenge in the field of organic chemistry. Over the past decade, development of new catalysts for Asymmetric Conjugate Additions (A.C.A.) turned out to be a straightforward synthetic method to target high enantiomeric excesses in C-C bond formation.[1,2]
After developing NHC ligands to form quaternary centers starting to 3-substituted cyclopent- and cyclohexenones in high ee's,[3] we focused to expand the scope of this reation to long-date unreached challenges in copper catalyzed A.C.A. By simply tuning functionalities of non-activated Micheal Acceptors, Mauduit-type NHC-copper catalyts promoted the addition of organometallic reagents up to 93:7 e.r.[4] Our adducts were demonstrated to be valuable chiral synthons for various application.



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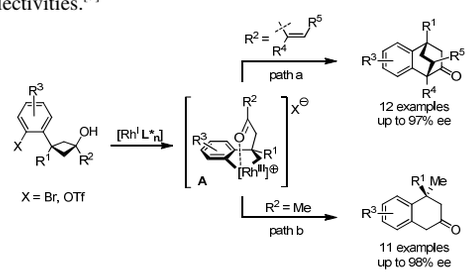
Organic Chemistry **OC043**

Exploiting Rh(I)-Rh(III) Cycles in Enantioselective Strain-promoted C–C Bond Cleavages

Laetitia Souillart, Nicolai Cramer*

Laboratory of Asymmetric Catalysis and Synthesis, EPFL SB ISIC LCSA BCH 4305, CH-1015 Lausanne, Switzerland

Our group reported rhodium-catalyzed enantioselective β-carbon eliminations from *tert*-cyclobutanols giving rise to alkyl rhodium species.[1] This key intermediate enables access to a diverse set of products via different downstream reaction pathways. So far, all these transformations were restricted to non-redox processes with rhodium(I) complexes.[2] We show herein that incorporating an additional redox process is opening the way to formal [4+2] cycloaddition (path a) or to C-H activation (path b), depending on the substitution on *tert*-cyclobutanols. Common intermediate rhoda(III)cycle **A** is leading to new product branches in high enantioselectivities.[3]



[1] a) T. Seiser, N. Cramer, *Angew. Chem. Int. Ed.* **2008**, *48*, 9294; b) T. Seiser, N. Cramer, *Angew. Chem. Int. Ed.* **2009**, *34*, 6320; c) T. Seiser, N. Cramer, *J. Am. Chem. Soc.* **2010**, *15*, 5340; d) T. Seiser, N. Cramer, *Angew. Chem. Int. Ed.* **2010**, *52*, 10163.
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[3] Manuscript in preparation.

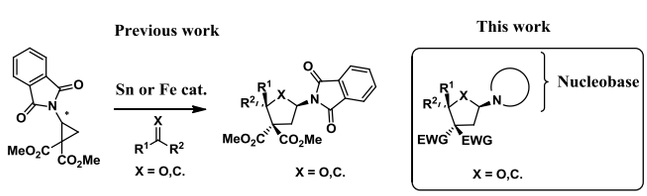
Organic Chemistry **OC044**

Synthesis of Nucleosides and Carbonucleosides Analogues via Formal [3+2] Annulation

Sophie Lucie Racine and Jérôme Waser

EPFL, SB ISIC LCSO 1007 Lausanne, Switzerland

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.



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Organic Chemistry **OC045**

Twisted Hydrocarbons – Novel Prototypes for Chiroptical Studies

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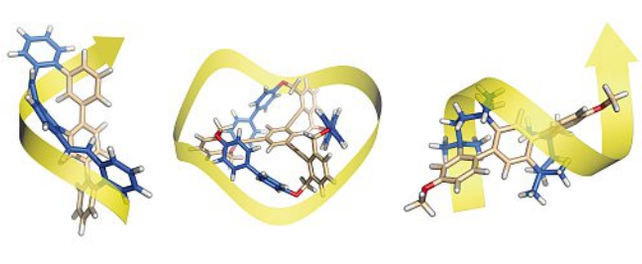
Polyaromatic hydrocarbons are a promising set of molecules investigating how chirality relates with structure. Three distinct polyaromatic structures with possibly interesting chiroptical properties are presented herein. Project **A** (see Figure) is a rotation restricted Geländer-Type Oligomer that is best described in terms of a bannister of a helical staircase. Project **B** is related to **A** but the chromophore is now the bannister itself, forcing the backbone to twist. Project **C** is best thought of in terms of a Mercedes Star where the chromophors around the rim cause chirality of the entire star.
Such structures should in principle be capable of not only absorb left or right handed circular polarized light differently (circular dichronism) as it is in the case with all chiral chromophors but also be capable of emitting circular polarized light (circular polarized luminescence). Especially this proposed capability of emitting circular polarized light is an essential feature towards pOLEDs and stereoscopic displays.



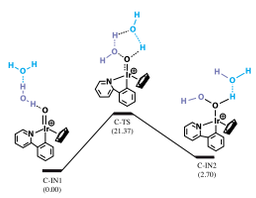
Organic Chemistry **OC046**

Adiabatic Reactive Molecular Dynamics for Homogeneous Water-Oxidation Catalysis

Franziska Hofmann, Andreas Pfaltz* and Markus Meuwly*

University of Basel, Department of Chemistry, Klingelbergstr. 80, CH-4056

The homogeneous oxidation of water to dioxygen is one of the most fundamental processes in nature. Iridium-half sandwich complexes, used as catalyst precursors, in combination with the primary oxidant cerium(IV) ammonium nitrate, have been proven to be efficient catalysts for long-lasting and rapid oxygen evolution[1]. To study the role of various Ir(III)-catalysts, a powerful tool is provided, which couples the Valbond Trans[2] force field (VBT) with the surface crossing algorithm, adiabatic reactive molecular dynamics (ARMD)[3]. To screen various Ir-catalysts in terms of their reactivity, molecular dynamics (MD) simulations of tetrahedral metal complexes are carried out in water, where ARMD enables bond breakage and bond formation to visualize reaction path ways. Therefore, the characterization of reactant, product and intermediate states is essential and requires accurate fitting of bonded and non-bonded parameters. The MD simulations pursue two aims, the evaluation of activation barrier heights and the clarification of the role of explicit solvents which is stabilizing the transition state in a beneficial way.



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[3] Lutz S. et al, *Chem. Phys. Chem.* **2011**, *13*, 305.

Organic Chemistry **OC047**

A [c2]daisy chain as a microscopic potentiometer

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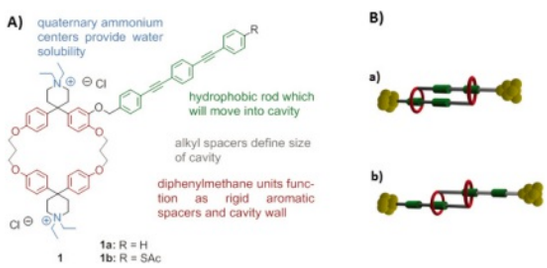
Recent studies have shown that intermolecular π-π stacking interactions between two oligo-phenylene ethynylene (OPE)-rods are strong enough to form stable bimolecular junctions.[1] Inspired by these results a stacked dimer **1** (**fig. A**) with a mechanically adjustable stacking surface was synthesized which can potentially mimic a microscopic potentiometer (**fig. B**). The [c2]daisy chain type dimer consists of two OPE-rods comprising a terminal water soluble loop which stabilizes the bimolecular assembly. The concentration-dependent aggregation behavior in polar solvents of an unfunctionalized,[2] as well as an S-acetyl functionalized derivative was investigated. Formation of higher oligomers was observed above a critical concentration opening the door towards novel mechanically interlocked materials.



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Organic Chemistry **OC048**

Cirsium spinosissimum Scop., a forgotten edible wild plant from Valais.

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[2] Ilis Institute & Laboratory, Impasse de la Passerelle 17, 2503 Bienne, Switzerland

In the course of an ethnobotanical survey on forgotten traditional food plants of the alpine region, we came to know about the ancient use of the spiniest thistle (*Cirsium spinosissimum* Scop., Asteraceae). The plant was traditionally eaten by shepherds similarly to an artichoke by cutting the surrounding leaves to reach the heart of the flower. Despite the fact that it grows abundantly in mountain regions, no information was available on its chemical constituents.

In a first step, we investigated the constituents of the aerial parts of *C. spinisossimum*. Extracts of different polarities were subjected to a comprehensive metabolite profiling using a dereplication platform combining HPLC-PDA-MS, and offline NMR analyses. A wide range of compounds including flavonoid glycosides, phenylpropanoids, sesquiterpene lactones, fatty acids, and a spermine derivative were identified online or after targeted isolation.

We further quantified substances relevant for nutrition such as β-carotene, fatty acids, ascorbic acid, and minerals in receptacles (edible part of the flower). Total phenolic compounds were determined as gallic acid equivalents and the major flavonoid glycosides, linarin and pectolinarin, were quantified by HPLC-UV. No compounds with reported toxicity or substance classes with known toxicological risks were detected. The crude ethanolic extract showed no sign of cytotoxicity on the intestinal Caco-2 cell line when tested at concentrations up to 500 µg/ml.

Organic Chemistry **OC049**

Screening of chiral organocatalysts for the Morita-Baylis-Hillman reaction by mass spectrometric monitoring of the back reaction

Patrick Isenegger, Florian Bächle, Andreas Pfaltz*

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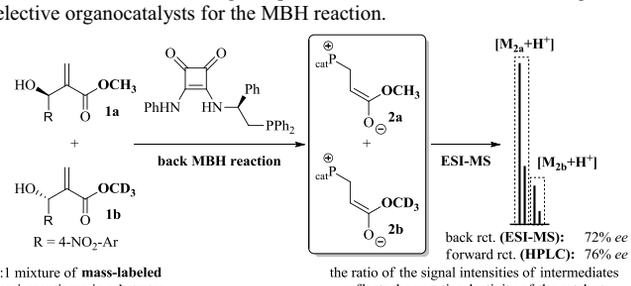
A catalyst screening method based on the ESI-MS analysis of charged reaction intermediates deriving from mass-labeled quasi-enantiomeric substrates was developed in our group and was applied to several metal- and organocatalyzed processes [1,2]. Herein, the application of this method to the Morita-Baylis-Hillman (MBH) reaction is demonstrated. The charged intermediates **2a** and **2b** were formed by a phosphine catalyzed back MBH reaction with the mass-labeled 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.



1:1 mixture of **mass-labeled** quasi-enantiomeric substrates

the ratio of the signal intensities of intermediates reflects the enantioselectivity of the catalyst

[1] For a review see: C. A. Müller, C. Markert, A. M. Teichert, A. Pfaltz, *Chem. Commun.* **2009**, 1607.
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Organic Chemistry **OC050**

Size Matters: Towards Linear Thioether Ligand Stabilized Au NP's with Increased Size and Long Term Stability

Mario Lehmann, U. Fluch, Marcel Mayor

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Over the last decade, ligand-stabilized gold nanoparticles (Au NP's) have attracted much interest and are promising materials for nanotechnology with applications in electronics, catalysis, and sensors.[1] Depending on the length of such heptameric linear thioether ligands, it is known that Au NP's can be stabilized with a diameter of around 1 nm. Moreover, it was shown, that two of these heptameric ligands wind around one Au NP.[2] Increasing the size of such nanoparticles to more than 2 nm would lead to an observable plasmonic band in the UV-Vis absorption spectra and thus would enable alternative, dedicated electronic measurements as well as more control in Au NP's coupling.[3] Therefore, two different linear heptameric thioether ligands with longer distance between the thioether moieties including bulkier ligand-shells are envisaged, which fulfill these requirements, to synthesize gold nanoparticles with increased, monodisperse sizes and long-term stability.

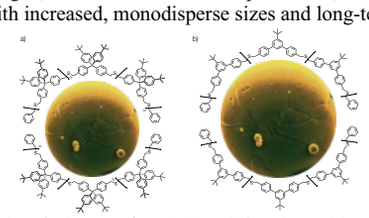

Figure: Conceptional picture of Au NP stabilization with two in length varying heptameric thioether ligands with: a) the tetraphenylic core and b) the terphenylic core.

[1] M.-C. Daniel, D. Astruc, *Chem. Rev.* **2004**, *104*, 293-346.
[2] T. Peterle, M. Mayor et al, *Adv. Funct. Mater.* **2009**, *19*, 3497-3506.
[3] J. P. Hermes, M. Mayor et. al, Chem. Eur. J. 2011, 17, 13473-13481.

Organic Chemistry **OC051**

Thermodynamic rigid backbones towards chiral electron delocalization in molecular wires

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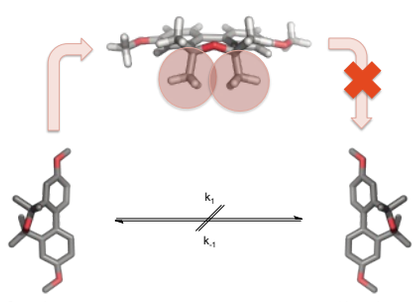
Biphenyl and bipyridine structural elements have been used in an astonishing amount of compounds in material science like non-linear optics, molecular electronics and catalysis to name just a few. Introducing axial chirality in such structural elements opens up a variety of new potential applications like POLED[1], or new powerful ligands for enantioselective catalytic processes. One of the major problems towards applications using axial chiral di-*ortho*-substituted biaryls are their relatively low atropisomerization energies[2].



[1] B. Kiupel *et. al.*, *Angew. Chem.*, **1998**, 110, 3206.
[2] J. Rotzler *et. al.*, *OBC*, **2013**, 11, 110

Organic Chemistry **OC052**

Rotational Restricted Molecular Wires

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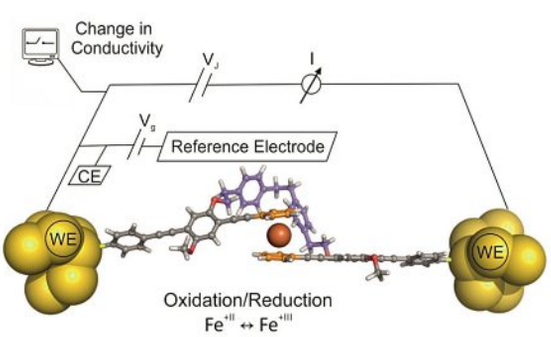
Molecular wires containing redox active ferrocene structures are predicted to have an intrinsic transistor-like behavior when they are integrated into a three-terminal field-effect device [1]. The construct is based on the work of Sita et al. and is designed to enable electron transport by passing the electronically addressable ferrocene core [2]. It is assumed that by rotating around the central ferrocene unit a stacked conformation could lead to high conductance values. In our approach the two arms of the molecular wire are rotationally restricted by a styrene based bridging unit. We believe that by rigidifying the molecular wire, a bypass event could be excluded.



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[2] L. Sita et al., *Phys. Rev. B*, **2005**, 71, 241401.

Organic Chemistry **OC053**

Iridium-Catalyzed Hydrogenation of Substituted Furans and Benzofurans

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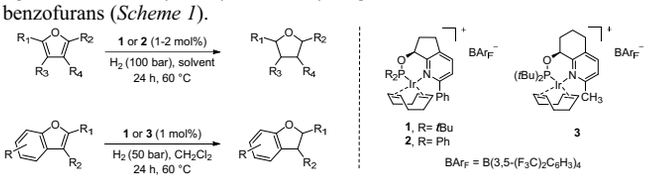
The stereoselective hydrogenation of heteroaromatics displays a promising method for the synthesis of chiral fully saturated heterocycles, representing important scaffolds in biologically active compounds. Although enantiomerically pure tetrahydrofuran and benzotetrahydrofuran units are present in many natural products, the asymmetric hydrogenation of the corresponding furans or benzofurans is scarcely studied. So far, the reduction of mono- and disubstituted furans has been realized using catalysts based on ruthenium and rhodium complexes leading to enantiomeric excess of 50% and 77%, respectively and our group has recently communicated the highly enantioselective reduction of 2-substituted furans using iridium based catalysts.[1] This contribution, describes the use of iridium complexes with chiral N,P ligand for the catalytic asymmetric hydrogenation of substituted furans and benzofurans (*Scheme 1*).



Scheme 1. Iridium catalyzed hydrogenation of substituted furans and benzofurans.

[1] a) T. Ohta, T. Miyake, N. Seido, H. Kumobayashi, H. Takaya, *J. Org. Chem.* **1995**, *60*, 357. b) M. He, D.-Q. Zhou, H.-L. Ge, M.-Y. Huang, Y.-Y. Jiang, *Polym. Adv. Technol.* **2003**, *14*, 273. c) S. Kaiser, S. P. Smidt, A. Pfaltz, *Angew. Chem. Int. Ed.* **2006**, *45*, 5194.

Organic Chemistry **OC054**

Irigermanone, a new iridal with unprecedented ketone function from Iris germanica.

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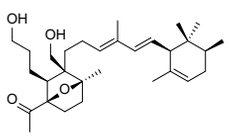
Pharmaceutical Biology, University of Basel,
Klingelbergstrasse 50, 4056 Basel, Switzerland

As part of our studies on indigenous traditional medicinal plants we have reinvestigated the lipophilic constituents of the rhizome of the German iris (*Iris germanica* L., Iridaceae). *I. germanica* is a widely distributed ornamental plant. Traditionally, its rhizomes have been used for different topical and oral applications, such as treatment of sores and freckles, as pain relief for teething children, in cosmetic preparations and in perfumery. Fractionation of the dichloromethane extract by a combination of Sephadex LH20 CC, and semi-preparative and preparative HPLC afforded a new iridal derivative, irigermanone (**1**), together with nine known congeners. The structure of **1** was established by HR-ESIMS and 1D and 2D NMR analysis.

Iridals are a group of more than 40 triterpenes derived from squalene through an uncommon biosynthetic pathway. These compounds have a restricted distribution in plants and have been so far only found in *Iris* spp. and *Belamcanda chinensis* (Iridaceae). They possess in common a seco-ring-A moiety and a typical α,β-unsaturated aldehyde moiety. To our knowledge, compound **1** is the first iridal derivative where the aldehyde function is replaced by a ketone.



1

Organic Chemistry **OC055**

Preparation of Antimalarial Endoperoxides by a Formal [2+2+2] Cycloaddition

Christophe Daeppen,[1] Elangovan Elamparuthi,[1] Marcel Kaiser,[2] Reto Brun,[2] Markus Neuburger,[1] Karl Gademann[1]

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

[2]Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute (STPH), Socinstrasse 57, CH-4002 Basel, Switzerland

Increased drug resistance of malaria parasites requires the development of novel therapeutic agents [1]. Endoperoxides constitute a prime source for the development of a second generation of antimalarial compounds.

In the course of the total synthesis of the natural product cyrneine A [2], the advanced intermediate **1** underwent an unexpected formal [2+2+2] reaction to give novel endoperoxides **2** and **3**, mediated solely by sunlight and air. Based on this surprising transformation, we prepared a series of endoperoxide hemiacetals and identified potent, micro- to nanomolar antimalarial agents based on this structural motif.

[1] World Health Organization. *World Malaria Report 2011*; World Health Organization: Geneva, Switzerland, 2011.
[2] Elangovan, E.; Fellay, C.; Neuburger, M.; Gademann, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 4071.

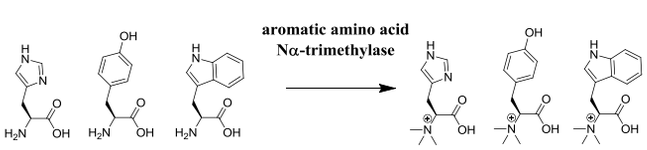
Organic Chemistry **OC056**

Identification of microbial aromatic amino acid Nα-trimethylases

Laëtitia Misson and Florian P. Seebeck

Department of Chemistry, University of Basel, St. Johanns-Ring 19, 4056, Basel, Switzerland

Abstract
Nα-trimethylated aromatic amino acids are ubiquitous secondary metabolites. Their specific physiological roles and their biosynthetic origin are largely unknown. We recently discovered a bacterial histidine trimethylase which is part of the ergothioneine biosynthetic pathway. In depth biochemical and structural characterization of this enzyme provided a key to discover fungal tryptophan and tyrosine trimethylases. Our investigation of the specificity determinants of this novel methyltransferase family, and their involvement in specific biosynthetic pathways will be discussed.



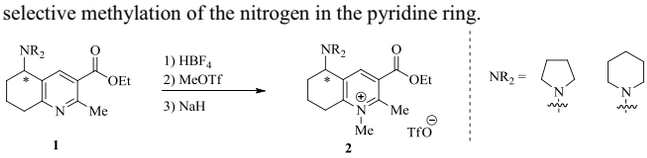
Organic Chemistry **OC057**

Synthesis of functionalized pyridinium salts

J. Auth, A. Pfaltz

University of Basel/ Department of Chemistry, St. Johanns-Ring 19, 4056 Basel, Switzerland

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.



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.

Organic Chemistry **OC058**

Influence of the Molecular Structure of the Core-Substituent in 2,6-Sulfanyl-Core-Substituted NDI

Pascal Hess, Marcel Mayor

University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

Core-substituted naphthalene diimides (NDIs) have tunable photoluminescent properties: by varying the core substitution of a particular NDI very low or high fluorescence quantum yields (FQY) can be obtained.[1] According to literature those FQYs are not only depending on the core substitution, but also on conformational changes which perturb the involved electron transfer processes. In 2010, Pugliesi et al. published the first time-resolved study on the charge transfer rate from a core substituent to the NDI unit. They compared different model compounds with three different moieties, which were directly attached to a 2,6-sulfanyl-core-substituted NDI, by investigation of their fluorescence quenching behavior (figure 1). Only when a phenylsulfanyl unit was linked to the core an ultrafast and efficient fluorescence quenching was detected.[2]

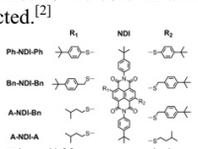


Figure 1: The different model compounds

Inspired by these results a tailor-made model compounds was designed and synthesized. It consists of a 2,6-sulfanyl-core substitution, with the substituents linked in a way that the fluorescence quenching should be reduced. The synthetic strategy of the target compound will be presented as well as the absorption and fluorescence studies.

[1] S. Gabutti, S. Schaffner, M. Neuburger, M. Fischer, G. Schäfer, M. Mayor, *Org. Biomol. Chem.* **2009**, *7*, 3222.
[2] I. Pugliesi, P. Krok, S. Lochbrunner, A. Blaszczyk, C. von Hänisch, M. Mayor, E. Riedle, *J. Phys. Chem. A* **2010**, *48*, 12556.

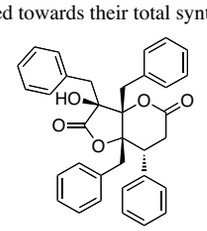
Organic Chemistry **OC059**

Studies Towards the Synthesis of Ophiodilactones A and B

Samuel Bader, Michael Lüscher, Karl Gademann*

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

In 2009, Matsunaga *et al*. reported the isolation of the tetrameric phenylpropanoids ophiodilactones A (**1**) and B (**2**) from the brittle star *Ophiocoma scolopendrina*. Both compounds show cytotoxic activity against P388 murine leukemia cell lines [1]. The γ,δ-dilactonic core structure is uncommon in nature and synthetic examples of similar skeletons are rare in literature [2]. The intriguing architecture combined with the biological activity of ophiodilactone A and B triggered our interest and motivated us to start a program directed towards their total synthesis.



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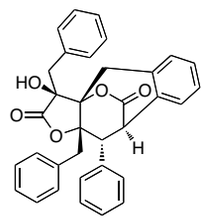


2

Key challenges of the synthesis are the four contiguous stereogenic centers, the dilactone moiety, and the unusual α-arylated lactone in compound **2**. We will present our recent efforts towards the total synthesis of the ophiodilactones A and B.

[1] R. Ueoka, T. Fujita, S. Matsunaga, *J. Org. Chem.* **2009**, *74*, 4396.
[2] W. Borsche, *Chem. Ber.* **1916**, *49/II*, 2538; T. Kapferer, R. Brückner, *Eur. J. Org. Chem.* **2006**, *9*, 2119; S. Hatakeyama, T. Matsubara, K. Takahashi, J. Ishihara, *Heterocyles* **2012**, *86*, 155.

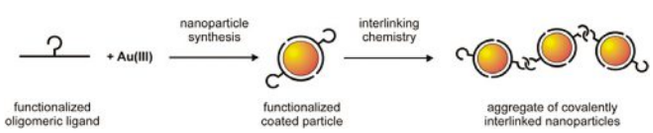
Organic Chemistry **OC060**

Synthesis of Highly Stabilized Noble Metal Nano Particles

Ulrike Fluch, Fabian Sander, Carla Cioffi and Marcel Mayor

Uni Basel, St. Johanns-Ring 19, 4056 Basel, Switzerland

Nano particles (NPs) have been of great interest in the last years because of their size dependent physical properties for example room temperature Coulomb blockade for small metallic NPs[1]. Gold is the most commonly used metal for NPs due to the efficient synthesis, potential as model system for colloids and surfaces[2] and for the high advanced surface chemistry. Future application for Au NPs is huge ranging from electronic devices and chemical sensors to biological labeling and catalysis and medical applications. One of the mayor challenges for the use of NPs in hybrid materials is the synthetic size control, the spatial arrangement and the stability. It has been shown that particles of about 1.3 nm size can be stabilized by multidentate ligands bearing thioethers for the stabilization of gold and ethers for the stabilization of silver NPs.



[1] Y. Jin, P. Wang, D. Yin, J. Liu, L. Qin, N. Yu, G. Xie, B. Li, *Colloids Surf., A.* **2007**, *302*, 366–370.
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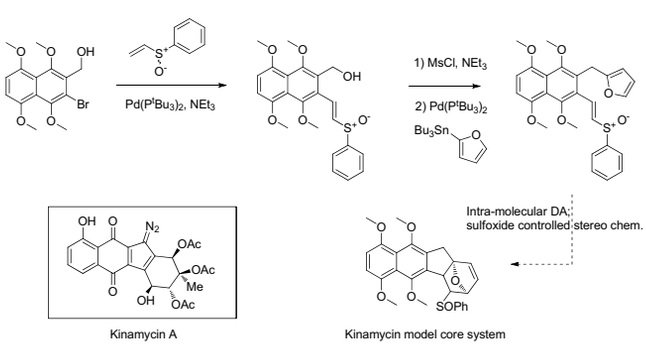
Organic Chemistry **OC061**

Studies towards the total synthesis of the diazo containing natural product kinamycin

Daniel G. Bachmann, Dennis G. Gillingham

University of Basel, St. Johannsring 19, 4056 Basel, Switzerland

A new route towards the total synthesis of kinamycin [1,2] is presented. During the studies a catalytic system for Heck arylation of vinyl sulfoxides was developed [3], which allows the efficient introduction of chirality in form of sulfoxides.



[1] Ito, S.; Matsuya, T.; Omura, S.; Otani, M.; Nakagawa, A., *J. Antibiot.* **1970**, *23*, 315.
[2] Lei, X.; Porco, J. A., Jr. *J. Am. Chem. Soc.* **2006**, *128*, 14790.
[3] Daniel G. Bachmann, Christopeher Wittwer, Dennis G. Gillingham *Manuscript in preparation*

Organic Chemistry **OC062**

Piperidine alkaloids from *Carica papaya* L. as potent antiplasmodial agents

Tasqiah Julianti[1], Samad Ebrahimi[1], Maria De Mieri[1], Markus Neuburger[2], Stefanie Zimmermann[1], Marcel Kaiser[3], Matthias Hamburger[1]

[1]Institute of Pharmaceutical Biology, University of Basel, 4056, Switzerland
[2]Department of Chemistry, University of Basel, 4056, Switzerland
[3]Swiss Tropical and Public Health Institute, University of Basel, 4051, Switzerland

Decoctions of *Carica papaya* leaves have been used in Indonesia traditionally to prevent and treat malaria [1]. To confirm this traditional use we investigated the presence of antiplasmodial agents in the leaves. Preliminary *in vitro* bioassay of methanolic extract at concentration of 4.8 µg/ml showed inhibition growth of *Plasmodium falciparum* (K1 strain) by 51%. HPLC-based activity profiling indicated alkaloids as the active compounds in the extract. We enriched these minor alkaloids in the extract and separated the alkaloidal fraction to obtained five piperidine alkaloids. By means of spectroscopic and computational methods, corroborated by X-ray analysis for the final confirmation, the structures of (-)-carpamic acid (**1**), (+)-methyl carpamate (**2**), (+)-carpaine (**3**) [2], along with a (+)-stereoisomer of carpaine (**4**) and a (+)-derivative of carpaine produced by monomethanolysis (**5**) were identified. Amongst the five isolated alkaloids, carpaine was the most active and selective antiplasmodial agent *in vitro*, with an IC_{50} of 0.21 µM against *Plasmodium falciparum* (K1-strain), and a selectivity index of 98 as determined in a cytotoxicity assay with rat myoblast L-6 cells. However, carpaine failed to reduce parasitaemia in an acute malaria mouse model (daily dose of 10 mg/kg BW intraperitoneally) with *Plasmodium berghei*.

[1] J.F. Rehena, *Master Thesis, Malang State University, Malang* **2009**.
[2] J.L. Coke, W.Y. Rice Jr., *J. Org. Chem.* **1965**, 30, 3420-2.

Organic Chemistry **OC063**

Investigation of Selectivity of Aromatic Stacking Interactions

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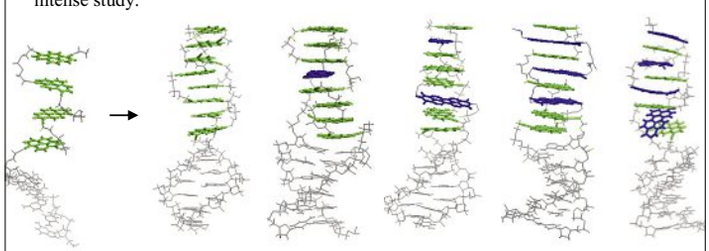
Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3 CH-3012 Bern, Switzerland

Aromatic π-π interactions are ubiquitous in nature. The interaction of aromatic compounds within biopolymers like peptides and oligonucleotides has a long standing history in respect of the understanding of folding and stability properties of these biomaterials or the development of drugs[1-2]. Thereby the specific interaction and recognition of elucidated aromatic compounds is a key element and under intense study.



The present project focuses on bioconjugates composed of a short DNA stem and multiple aromatic dyes. The main goal is to drive both, stability and selectivity of the double stranded DNA-like supramolecular structures by noncovalent interaction of the aromatic dyes. Thereby a selective interaction and stabilization of different elected aromats (pyrene in green and perylene in blue) is under investigation. The current research may lead to the design of DNA-like aromatic systems with tuned cooperative interactions to give rise to well defined nanostructured material.

(1) Salonen, L. M.; Ellermann, M.; Diederich, F. *Angew. Chem.-Int. Edit.* **2011**, *50*, 4808.
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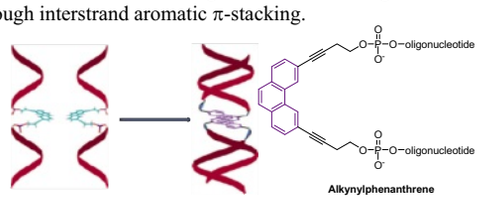
Organic Chemistry **OC064**

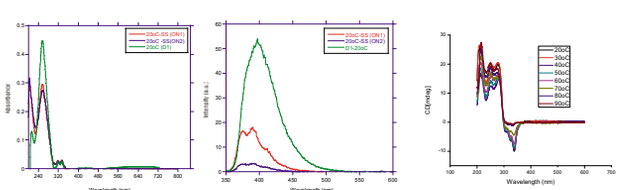
Alkynylphenanthrene Modified DNA

Rajendran Ganesh Kumar, Simon Langenegger and Robert Häner

Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, Bern, CH-3012, Switzerland

Oligonucleotides containing an alkynylpehenantrene as non-nucleosidic building block were synthesized. The effect of phenanthrene moiety on deuplex stability was investigated. Furthermore, properties of duplexes were studied with UV-Vis, Fluorescence, CD measurements. The alkynylphenanthrene modified oligonucleotide shows good stability in duplexes through interstrand aromatic π-stacking.





UV-Vis Fluorescence CD

[1] Langenegger, S. M.; Häner, R. *Helv. Chim. Acta.* **2002**, *85*, 3414.
[2] Bittermann, H.; Siegemund, D.; Malinovskii, V. L.; Häner, R. *J. Am. Chem. Soc.* **2008**, *130*, 15285.

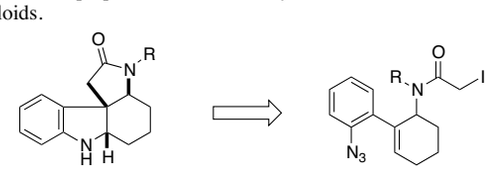
Organic Chemistry **OC065**

Studies Toward the Synthesis of the Core Structure of *Aspidosperma* Alkaloids

François Brucelle, Benjamin Wyler, Philippe Renaud*

Universität Bern, Departement für Chemie und Biochemie, Freiestrasse 3, CH-3012 Bern, Switzerland

Radical chemistry has become a powerful tool to create carbon–heteroatom bonds [1]. In particular, the formation of carbon–nitrogen bonds using organic azides as radical traps has attracted the attention of many different research groups [2]. We recently described a simple approach to prepare indolines and benzopyrrolizidinones *via* a radical cascade involving aryl azides [3]. After the successful application of this strategy to the synthesis of a mitomycin derivative, we decided to investigate a radical cyclisation sequence for the preparation of the tetracyclic core structure of *Aspidosperma* alkaloids.



[1] *Radicals in Organic Synthesis;* Renaud, P.; Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001
[2] (a) Kim, S.; Joe, G. H.; Do, J. Y. *J. Am. Chem. Soc.* **1994**, *116*, 5521. b) Patro, B.; Murphy, J. A. *Org. Lett.* **2000**, *2*, 3599. c) Panchaud, P.; Chabaud, L.; Landais, Y.; Ollivier, C.; Renaud, P.; Zigmantas, S. *Chem. Eur. J.* **2004**, *10*, 3606.
[3] Brucelle, F.; Renaud, P. *Org. Lett.* **2012**, *14*, 3048.

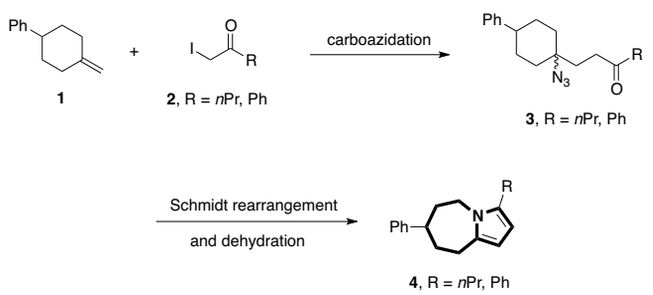
Organic Chemistry **OC066**

Radical Carboazidation and Schmidt Rearrangement/Dehydration Process to Pyrrolo[1,2-α]azepine Core Structure

N. Millius, A. Kapat, S. Fux, P. Renaud*

Universität Bern, Freiestrasse 3, 3012 Bern, Switzerland

Renaud et al.[1] developed a radical carboazidation reaction that formed a carbon-carbon bond and a carbon-nitrogen bond at once. This method was performed with α-iodo ketones **2** to get access to tertiary azides **3** bearing a carbonyl group in γ position. The followed Schmidt rearrangement under acidic conditions lead to the dehydrated pyrrolo[1,2-α]azepine core structure (bold) that is a common substructure in natural products.



1 **2**, R = *n*Pr, Ph **3**, R = *n*Pr, Ph **4**, R = *n*Pr, Ph

[1] P. Panchaud, L. Chabaud, Y. Landais, C. Ollivier, P. Renaud, S. Zigmantas, *Chem. Eur. J.* **2004**, *10*, 3606.

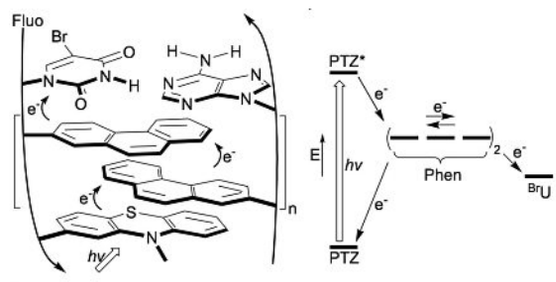
Organic Chemistry **OC067**

Excess Electron Transfer in DNA Containing a Phenothiazine Donor and Multiple Stable Phenanthrenyl Base-Pairs

Pascal Roethlisberger, Prof. Christian J. Leumann

University of Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

A system based on a oligonucleotide duplex containing a π-stacked phenothiazine as an electron donor, phenanthrenes as electron carriers and 5-bromouracil as an electron trap was used to study the excess electron transfer (EET) within the modified DNA. Increasing the number of phenanthrenyl base-pairs enhanced EET efficiency.



[1] N.A. Grigorenko, C.J. Leumann, *Chem. Eur. J.* **2009**, *15*, 639.
[2] N.A. Grigorenko, C.J. Leumann, *Chem. Commun.* **2008**, *14*, 5417.

Organic Chemistry **OC068**

Improving the Sensitivity of Nucleic Acid Detection with New Homo-DNA Reporters

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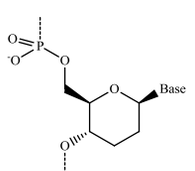
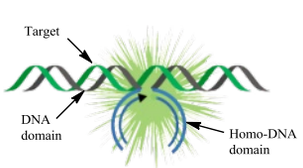
For accurate nucleic acid detection, both the sensing of a target and the generation of a signal are necessary. In order to enhance sensitivity, we successfully employed templated Staudinger reduction of a rhodamine azide by triphenylphosphine using bioorthogonal chimeric reporter strands composed of DNA and homo-DNA. [1] Homo-DNA is a DNA analogue with a six-membered ring sugar moiety, which can form duplexes in an anti-parallel fashion with itself but not with natural nucleic acids. [2] In addition, to improve the sensitivity of our design, we looked at an alternative signal generating chemistry that would not lead to the transient formation of a covalent intermediate between the two homo-DNA reporters.



Homo-DNA building block



Nucleic acid detection by chimeric oligonucleotides

[1] Stoop, M., Désiron, C., Leumann C.J., *Art. DNA: PNA & XNA* **2013**, *4*,28-33
[2] Hunziker, J., Roth, H. J., Bohringer, M., Giger, A., Diederichsen, U. Gobel, M. Krishnan, R., Jaun, B. Leumann, C., Eschenmoser, A. *Helv. Chim. Acta.*, **1993**, *76*, 259-352.

Organic Chemistry **OC069**

Modification of Cu(111) with buckybowls

Quirin S. Stöckl[1], Tobias Bauert[1], Davide Bandera[2], Manfred Parschau[1], Jay S. Siegel[2], Karl-Heinz Ernst[1,2]

1 Empa, Nanoscale Material Science, Dübendorf, Switzerland
2 Organisch-chemisches Institut, Universität Zürich, Switzerland

Interesting candidates for surface modifications for organic photovoltaics or controlled carbon nanotube growth are buckybowls, geodesic polyarenes and quasi-fragments of C_{60}. Corannulene (COR, $C_{20}H_{10}$) is the simplest curved fragment with a central pentagonal ring, surrounded by five aromatic C_6 rings. Fivefold symmetry is incompatible with the translational order in all 17 plane groups, and this system is therefore of fundamental interest for 2D self-assembly. We have studied therefore the self-assembly of the star-like pentaphenyl-corannulene (Ph_5Cor) with STM. The packing motifs basically consist of anti-parallel rows with interdigitated substituents. Results will be compared to structures found for other (penta-)substituted COR derivatives.

Organic Chemistry **OC070**

Optimizing the amide synthesis from lithium anilides and phenyl benzoates

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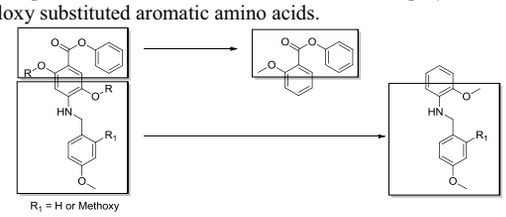
So-called Yokozawa[1] conditions have been used for the preparation of aromatic amide polymers (aramides) in the past. These conditions rely on the reaction of lithium anilides and benzoic acid esters. 2,5-dialkyloxy substituted 4-aminobenzoic acid esters (Figure, left) are important monomers for the synthesis of shape persistent linear and helical polymers. These monomers are sterically demanding and capable of chelating the lithium cation thereby hindering the polymerization process.
Here we describe model reactions (Figure, right) in order to optimize reaction conditions for this type of amide. The reaction between o-methoxy phenylbenzoate and lithium o-methoxy *N*-benzyl anilides was investigated under different reaction conditions (solvents, temperature, counter ion) using HPLC and NMR analysis. The results are discussed and a reactivity model is proposed.
The best conditions for such condensation of simple aromatic amide fragments can provide suitable reaction conditions for the polycondensation of di-alkyloxy substituted aromatic amino acids.



[1] Ryuji Sugi, Akihiro Yokoyama, Taniyuki Furuyama, Masanobu Uchiyama, and Tsutomu Yokozawa *J. Am. Chem. Soc.*, **2005**, *127*, 10172

Organic Chemistry **OC071**

Efforts to an asymmetric photochemical synthesis by kinetic resolution using chiral quenchers

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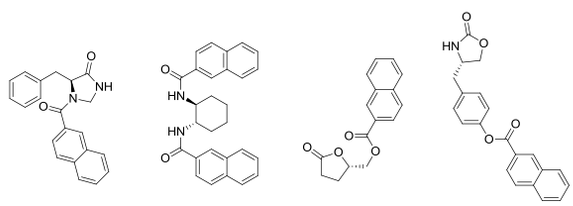
Department of Chemistry of Fribourg,
Chemin du Musée 9, CH-1700 Fribourg, Switzerland

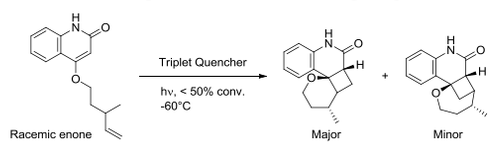
The excited states of photochemical reactions can be obtained by two ways: the substrate is excited by direct irradiation or indirectly by a sensitizer. On the contrary, the excited states can be deactivated by a quencher.

The aim of our project is the kinetic resolution in a photochemical reaction using a triplet quencher. The kinetic scenario is the following: the chiral triplet quencher is expected to deactivate only one enantiomer of a racemic triplet excited state. The other enantiomer could then react, leading to an enantiomeric enrichment in the product.

Synthesized Triplet Quenchers



The scenario of the kinetic resolution was tested with the intramolecular photocycloaddition in the presence of our chiral triplet quenchers.



Organic Chemistry **OC072**

Conditional Triggered Drug Release

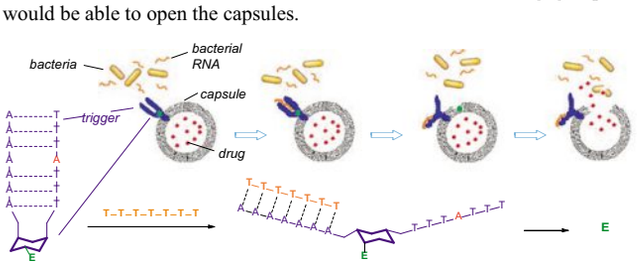
Tatiana Cotting, Elia Janett, Christian G. Bochet*

Department of Chemistry, University of Fribourg, Ch. du Musée 9,
CH-1700 Fribourg, Switzerland

The need of internal fixation devices or joint replacements as well as the percentage of infection is dramatically increasing. Treatment of the infection is most of the time difficult and means painful and expensive procedures. Until now the key to this situation was a coating with antimicrobial agents unfortunately the continuous release of antibiotics leads often to bacterial resistance and the quick aging of the coating involve a replacement.

The solution we propose is to encapsulate antibiotics in nano-reservoirs and to attach to the surface a trigger system able to break these containers only in presence of bacteria.

We are building a trigger system that is maintained in an unfavorable conformation. The trigger is composed of a cyclohexane core with two almost complementary oligonucleotide strands. We introduced some degree of mismatch in the two DNA strands in order to allow a single-stranded bacterial RNA to bind preferentially with one of the oligonucleotide strand and allow a conformational change. This change of conformation should allow an intramolecular reaction with release of a reactive leaving group that would be able to open the capsules.



Organic Chemistry **OC073**

New asymmetric bromine-lithium exchange application towards syntheses of natural product chiral building blocks

Julien Graff, Thibaut Debande, Laure Guénée and Alexandre Alexakis[1]

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30, Quai Ernest-Ansermet, CH-1211 Geneva 4, Switzerland

Email: alexandre.alexakis@unige.ch

Axial chirality is present in a wide range of biologically active natural products [1]. One of the most famous examples of this is glycopeptide vancomycin, possessing important antibiotic activities and isolated for the first time in 1953 from a soil bacterium *Amycolatopsis orientalis*. Axial chirality is also present in several other natural product families like bicoumarins (desertoïn C, isokotanin A and kotanin). Furthermore, we decided to select the bicoumarin scaffold to apply our direct asymmetric bromine-lithium exchange strategy. The aim of this work was to synthesize (+)-isokotanin A and (-)-kotanin chiral building blocks in high yields and ee [2].

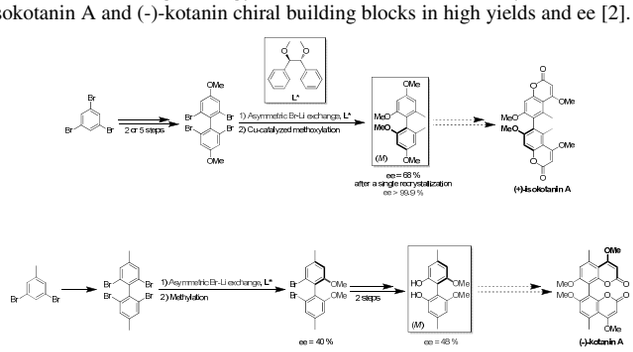


Fig. 1: (+)-Isokotanin A and (-)-kotanin chiral buiding blocks syntheses.

[1]G. Bringmann et al., *Chem. Rev.*, **2011**, 563 – 639.
[2]J. Graff, T. Debande, L. Guénée, A. Alexakis, *Org. Lett*, **2013**, submitted.

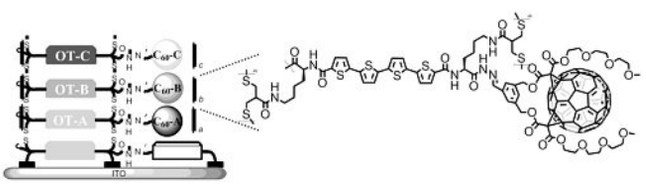
Organic Chemistry **OC074**

Supramolecular Heterojunction Photosystems with Oligothiophenes by Self-Organizing Surface-Initiated Polymerization (SOSIP)

Adam Sobczuk, Hironobu Hayashi, Altan Bolag, Naomi Sakai and Stefan Matile*

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

Nowadays the design and construction of well-organized p/n-heterojunction molecular architectures is still challenging [1]. Herein we would like to apply the SOSIP strategy to develop supramolecular p/n-heterojunctions (SHJs) assembled with oligothiophene (OTs) and fullerenes (C_{60}) derivatives [2]. In order to effectively separate and transport photogenerated charges, oriented SHJ architecture will be engineered to incorporate multicomponent redox gradients in each channel. SOSIP approach provides general access to multichromophoric assembly with charge transfer cascades and freely variable composition.



[1] M. Lista, E. Orentas, J. Areephong, P. Charbonnaz, A. Wilson, Y. Zhao, A. Bolag, G. Sforazzini, R. Turdean, H. Hayashi, Y. Domoto, A. Sobczuk, N. Sakai, S. Matile, *Org. Biomol. Chem.* **2013**, *11*, 1754
[2] A. Bolag, H. Hayashi, P. Charbonnaz, N. Sakai, S. Matile, *ChemistryOpen*, **2013**, doi: 10.1002/open.201300004.

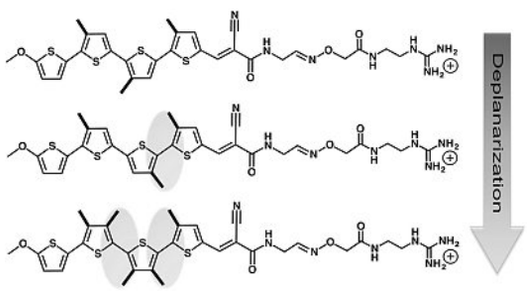
Organic Chemistry **OC075**

Gradually Twisted Push-Pull Oligothiophenes and Their Planarization in Confined Space

David Alonso Doval, Marta Dal Molin, SandraWard, Naomi Sakai, Stefan Matile*

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

In nature, the combination of chromophore planarization and polarization occurs in processes reaching from the chemistry of vision to the pigmentation of lobsters [1]. Increased conjugation and thus improved communication between the polarizing groups are responsible for a dramatic red shift upon flattening of these chromophores. These lessons from nature suggest that planarization and polarization could be combined to obtain conceptually innovative membrane probes. A series of systematically deplanarized push-pull oligothiophenes is designed and synthesized to determine the perfect twist for maximal spectroscopic response to their planarization within lipid bilayer membranes of different nature [2].



[1] A. Fin, A. Vargas Jentzsch, N. Sakai, S. Matile, *Angew. Chem. Int. Ed.* **2012**, *51*, 12736-12739.
[2] M. Dal Molin, S. Matile, *Org. Biomol. Chem.* **2013**, *11*, 1952-1957.

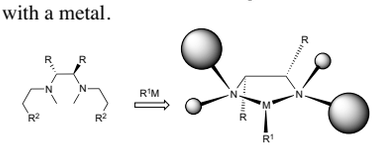
Organic Chemistry **OC076**

Synthesis of new chiral 1, 2 and 1, 4 -diamines for an application in asymmetric bromine-lithium exchange

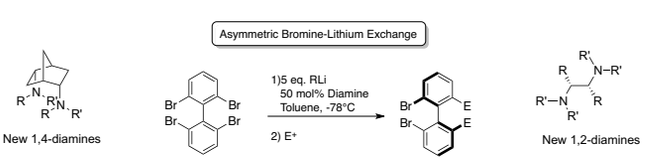
Jézabel Praz and Alexandre Alexakis*

University of Geneva, 30 Quai Ernest-Ansermet, CH-1211 Geneva

Chiral diamines are compunds of greatest interest in organic synthesis particularly as chiral ligand for organolithium reagents.
Previously our laboratory observed for 1,2-chiral tertiary diamines a transfer of stereochemical information to the nitrogen which become stereogenic open chelation with a metal.



A new type of 1,2 and 1,4-diamines were synthesized and applied in enantioselective bromine-lithium exchange. This reaction developped in our laboratory gave acces to axialy chiral molecules in good yield and excellent ee up to 97%.



Ligand design, scope, and limitation of the reaction will be presented.

[1] Jezabel Praz, Laure Guénée, Sarwar Aziz, Albrecht Berkessel* and Alexandre Alexakis*, *Adv. Synth. Catal.* **2012**, *354*, 1780-1790.
[2] Jezabel Praz and Alexandre Alexakis, *Unpublished results*, **2013**.

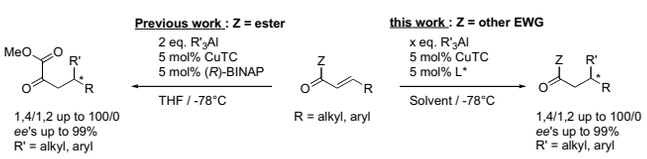
Organic Chemistry **OC077**

Enantioselective Copper Catalyzed 1,4-addition to challenging 1,2-Dicarbonyl like Michael acceptors

Sylvie Goncalves-Contal, Alexandre Alexakis*

Department of Organic Chemistry - University of Geneva
Quai Ernest-Ansermet 30, CH-1211 Geneva 4
Switzerland

The copper-catalyzed asymmetric conjugate addition (ACA) of organometallic reagents to Michael acceptors is among the most important methodologies to form a C-C bond in an enantioselective manner. In this field, a variety of α,β-unsaturated compounds have been successfully used.[1] More recently, β,γ-unsaturated α-ketoesters emerged to be a new class of challenging Michael acceptors for this key transformation.[2] Scope and limitations of the ACA to new 1,2-dicarbonyl substrates will be presented as well as their potential synthetic applications.



[1] a) Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, 3221. b) Alexakis, A.; Backväll, J. E.; Krause, N.; Pamies, O.; Diegues, M. *Chem. Rev.* **2008**, *108*, 2796. c) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824.
[2] Gremaud, L.; Alexakis, A. *Angew. Chem. Int. Ed.* **2012**, *51*, 794.

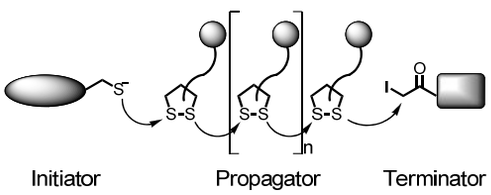
Organic Chemistry **OC078**

Cell-Penetrating Poly(disulfide)s Generated by Substrate-Initiated Polymerization

Giulio Gasparini, Eun-Kyoung Bang, Guillaume Molinard, Aurelien Roux, Naomi Sakai and Stefan Matile*

School of Chemistry and Biochemistry, University of Geneva, Geneva, Switzerland

Cell-penetrating poly(disulfide)s (CPDs) are currently emerging as cell-penetrating molecules thanks to their cytosolic degradation after uptake. Indeed, this liberates the substrate and suppresses toxicity, one of the key disadvantages associated with cell-penetrating peptides (CPPs) [1].



Using a similar approach to surface-initiated ring-opening disulfide-exchange polymerization, we developed a new method to generate CPDs directly on a substrate of free choice [2]. The polymerization process is characterized by gel-permeation chromatography and fluorescence resonance energy transfer, while the transmembrane activity is studied by fluorogenic vesicles and cellular uptake in HeLa cells.

[1] E.-K. Bang, M. Lista, G. Sforazzini, N. Sakai, S. Matile, *Chem. Sci.* **2012**, *3*, 1752-1763.
[2] E.-K. Bang, G. Gasparini, G. Molinard, A. Roux, N. Sakai, S. Matile, *J. Am. Chem. Soc.* **2013**, *135*, 2088-2091.

Organic Chemistry **OC079**

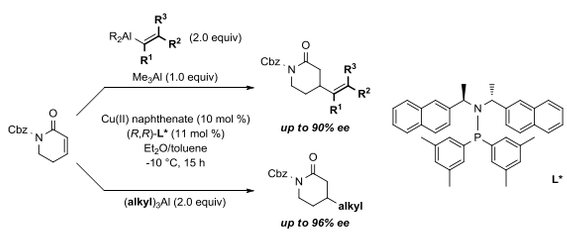
Copper-Catalyzed Asymmetric Conjugate Addition of Alkenyl- and Alkylalanes to α,β-Unsaturated Lactams

Pierre Cottet and Alexandre Alexakis*

Department of Organic Chemistry, University of Geneva, 30 Quai Ernest Ansermet, CH-1211 Geneva, Switzerland

Since nitrogen-containing heterocycles are ubiquitous in compounds of pharmaceutical interest, much effort has been dedicated to the development of new methodologies allowing for the formation of optically active derivatives of such compounds. Among the main reactions in organic synthesis, the asymmetric conjugate addition of organometallic species is one of the most powerful tools for enantioselective C-C bond formation.

In this context, alkenyl and alkyl groups have been successfully introduced to six-membered α,β-unsaturated lactams via a copper-catalyzed asymmetric 1,4-addition of the corresponding alanes [1]. Moderate to good yields and good to excellent enantioselectivities can be achieved by using a combination of the very cheap copper(II) naphthenate and a readily available phosphine amine ligand. The creation of an all-carbon quaternary stereogenic center, via Michael addition to a trisubstituted conjugated lactam, was also disclosed for the first time.



[1] P. Cottet, D. Müller, A. Alexakis, *Org. Lett.* **2013**, *15*, 828.

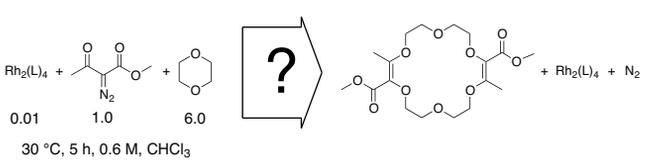
Organic Chemistry **OC080**

On the Mechanism of One-Step Multi-Component Macrocyclization Reactions

Daniele Poggiali [1], Diane Rix [1], Rafael Ballesteros-Garrido [1], Walid Zeghida [1], César Beuchat [2], Tomasz Adam Wesolowski [2], Jérôme Lacour [1]

[1] Department of Organic Chemistry, [2] Department of Physical Chemistry, University of Geneva, Quai Ernest Ansermet 30, CH-1211 Geneva.

Recently it has been shown that functionalized polyether macrocycles can be obtained in a single step by the condensation of 4 components, and this under high concentration and no-template effect. [1, 2, 3]
Herein we present a mechanistic study of such a Rh(II)-catalyzed reaction of diazodicarbonyls and 1,4-dioxane that affords 18-membered macrocycles. Kinetic information was gathered trough NMR, FT-IR and GC-FID monitoring. Further information was obtained via labelled substrate, trapping experiment, intermediate characterization study and in silico modelling.



[1] W. Zeghida, C. Besnard, J. Lacour, *Angew. Chem. Int. Ed.* **2010**, *49*, 7253.
[2] D. Rix, R. Ballesteros Garrido, W. Zeghida, C. Besnard, J. Lacour, *Angew. Chem. Int. Ed.* **2011** , *50*, 7308.
[3] R. Ballesteros Garrido, D. Rix, C. Besnard, J. Lacour, *Chem. Eur. J.* **2012**, *18*, 6626-6631.

Organic Chemistry **OC081**

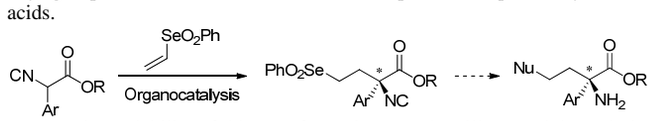
Enantioselective Michael Addition of isocyanoacetate with vinyl selenone: Access to α-Quaternary Amino-Acids

Thomas Buyck, Qian Wang, Jieping Zhu*

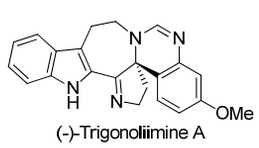
Laboratory of Synthesis and Natural Products, EPFL-SB-ISIC-LSPN, CH-1015 Lausanne, Switzerland

Enantio enriched α-quaternary 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 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 amino-acids.



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



[1] For a review on stereoselective synthesis of quaternary α-amino acids see: C. Cativiela, M. D. Díaz-de-Villegas, *Tet. Asym.* **2007**, *18*, 569-623
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Organic Chemistry **OC082**

Palladium-Catalyzed Enantioselective C–H Functionalization to Access Multiple Chiral Nitrogen-Containing Heterecycles

Nicolai Cramer, Tanguy Saget

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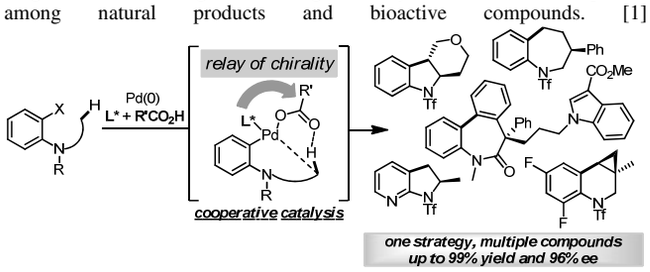
Transition metal catalyzed C–H activation has recently emerged as a powerful tool to access molecular complexity from cheap and widely available unfunctionalized starting materials. However, only few enantioselective methods are available because of the harsh conditions often required for such reactions. Herein, we present a general strategy to develop asymmetric processes in palladium-catalyzed C–H functionalization. Our approach is based on the cooperative effect between a chiral ligand and the carboxylate base required for the enantiodiscrimating concerted metalation-deprotonation step. This strategy allowed us to access efficiently a wide range of chiral nitrogen-containing heterocycles which are ubiquitous among natural products and bioactive compounds. [1]



[1] (a) T. Saget, S. J. Lemouzy, N. Cramer, *Angew. Chem. Int. Ed.* **2012**, *51*, 2238; (b) T. Saget, N. Cramer, *Angew. Chem. Int. Ed.* **2012**, *51*, 12842; T. Saget, N. Cramer, *unpublished results.*

Organic Chemistry **OC083**

Conversion of Lignin into useful Chemicals

Safak Bulut and Paul J. Dyson

Laboratoire de Chimie Organométallique et Médicinale, Institut des Sciences et Ingénierie Chimiques, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland (E-mail: *safak.bulut@epfl.ch*)

Biomass conversion is an expanding and one of the most popular research fields that appeared over the last years. This is certainly motivated by the fact that the biomass as a renewable raw material could considerably help to reduce the use of fossil feedstocks. In recent years, utilisation of biomass covers the developments of a biorefinery for producing feedstock for the chemical industry.[1-3] In this contribution, we deal with lignin and its possible conversion into chemicals by using suitable catalytic systems. Lignin accounts 25-40% of the ligno-cellulose, the largest material produced in the world yearly.[4]

Lignin is a three-dimensional amorphous biopolymer and consists of methoxylated phenylpropane structures, which are connected to each other on different ways. However, the most appeared linkage of the aromatics in lignin is that via an oxygen atom.[5] Thus, an effective depolymerisation of lignin can take place through cleavage of the strong aromatic C—O bonds. The focus of our research is to find an effective and economically catalytic system allowing the cleavage the C—O bonds of aromatic ethers.

For this issue, we synthesize various metal nanoparticles and test them by using aromatic compounds — as models for the linkages in lignin — and H_2 as the reactant (hydrogenolysis). Various catalysts, reaction conditions/media have been tested, and are presented in detail.

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Organic Chemistry **OC084**

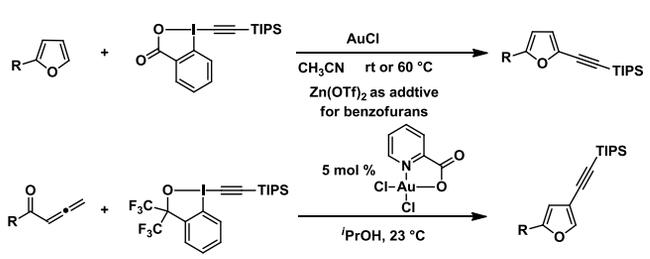
Regioselective Synthesis of 2- and 3-Alkynylated Furans via Au – Catalyzed C-H Functionalization and Domino Cyclization-Alkynylation

Yifan Li, Jonathan Brand, Jérôme Waser

EPFL, SB ISIC LCSO 1015 Lausanne, Switzerland

(Benzo)furans and alkynes are important building blocks in medicinal chemistry and material science. A mild method to achieve the regioselective synthesis of alkynylated furans and benzofurans would be consequently highly desirable.

Based on our previous work on the Au-catalyzed direct alkynylation of (hetero)aryls,[1] we report herein two different protocols for the synthesis of alkynylated furans and benzofurans. C2-alkynylated furans and benzofurans were obtained via direct C-H bond functionalization, whereas C3-alkynylated furans were obtained through a domino cyclization-alkynation from allenes. Fine-tuning of the properties of a hypervalent iodine alkynylation reagent and the gold catalyst was essential for success.[2]



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Organic Chemistry **OC085**

Direct Azidation of Carbonyl Compounds using a Bench-Stable Hypervalent Iodine Reagent

Maria Victoria Vita, Jérôme Waser

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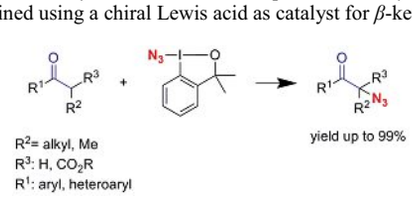
The introduction of azides into complex organic molecules is interesting as they are precursors of amines and can also be applied for bioconjugation via cycloaddition reactions.[1] Alpha azido carbonyl compounds in particular are versatile functional groups but are usually accessed by a multi-step synthesis due to the nucleophilic character of both enolates and azide salts. *Umpolung* of the azide is required for direct azidation of the enolate.

We present herein an efficient protocol to install an azide alpha to a carbonyl group using a well-defined, isolable hypervalent iodine reagent[2] as electrophilic azide transfer reagent. *β*-keto esters were first used to give the desired α-azido *β*-keto esters in excellent yields (up to 99%). Silyl enol ethers could be azidated in the presence of $Zn(OTf)_2$ as catalyst (15 mol %). The corresponding alpha ketones were obtained in good yields (up to 70%). In addition, preliminary results for the development of an asymmetric method were obtained using a chiral Lewis acid as catalyst for *β*-keto esters.



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Organic Chemistry **OC086**

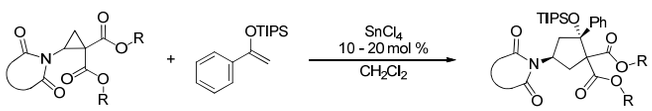
Catalytic [3+2] Annulation of Aminocyclopropanes and Enol Ethers

Eloísa Serrano, Florian de Nanteuil, Jérôme Waser

EPFL, SB ISIC LCSO 1007 Lausanne, Switzerland

Amino-substituted five-membered carbocycles are privileged scaffolds present in bioactive natural and synthetic compounds. In an effort towards their synthesis, our group has reported the first use of phthaloyl-protected aminocyclopropanes in the tin-catalyzed enantiospecific [3+2]-annulation with silyl enol ethers, to afford cyclopentylamines in high yields and diastereoselectivities.[1]

The present study aims to extend the scope of substituents on the nitrogen and diester to afford new aminocyclopropanes with a large range of electronic and steric properties. The synthesis of diverse new N-vinylimides was successfully achieved via a palladium-catalyzed transvinylation reaction.[2] The products were subjected to a rhodium-catalyzed cyclopropanation[3] in combination with different diazomalonates providing novel aminocyclopropanes. These new scaffolds were used in the tin-catalyzed [3+2]-annulation with silyl enol ethers to obtain cyclopentylamines in good yields. Recent results in the development of an enantioselective variation of the method will also be presented.



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Organic Chemistry **OC087**

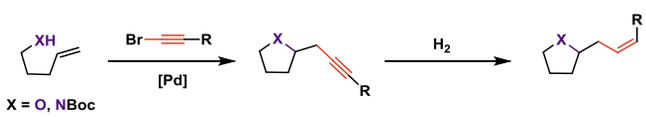
Palladium-catalyzed Nucleoalkynylation of Alkenes and Semi-hydrogenation of Alkynes

Ugo Orcel, Stefano Nicolai, Raha Sedigh-Zadeh, Jérôme Waser*

EPFL, LCSO, Lausanne CH-1015, Switzerland

Alkynes are an important class of building blocks due to their exceptional reactivity that enables numerous possible derivatizations. In 2013, our group reported the first palladium-catalyzed oxy- and aminoalkynylation using aliphatic bromoalkynes.[1] In this work, a simple one-pot hydrogenation protocol of the triple bond was developed using palladium on charcoal to access saturated alkyl chains.

Herein, we report a different in situ semi-hydrogenation reaction, which proceeds without added catalyst and high *Z* selectivity. The exceptional properties of palladium catalysts obtained from simple Pd(0) precursors and organic ligands for the mild and Z-selective semi-hydrogenation of alkynes were discovered and displayed complementary reactivity when compared to state-of-the-art Lindlar catalyst. A detailed investigation of the active catalyst in this hydrogenation and an extension of the scope to different types of alkynes will be further described herein.



[1] S. Nicolai, R. Sedigh-Zadeh, and J. Waser, *J. Org. Chem.* **2013**, DOI: *10.1021/jo400254q*.

Organic Chemistry **OC088**

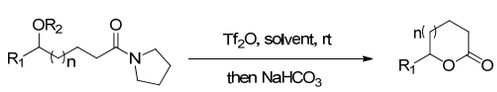
Direct Lactonisation through Amide Electrophilic Activation

Desislava Petkova,Viviana Valerio, Claire Madelaine and Nuno Maulide*

Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470 Mülheim, Germany.

Medium and large-sized lactones are a common feature of naturally occurring bioactive substances, and a variety of such compounds have been isolated to date [1]. Although a range of methods have been reported for the synthesis of the lactone functional group, activated tertiary amides have hardly been explored for this purpose.

Herein we report the direct lactonisation of protected alcohols onto otherwise inert, stable amides [2]. The reaction proceeds through in situ electrophilic amide activation under mild reaction conditions. The scope and the limitations of this transformation, as well as potential synthetic applications, shall be outlined and discussed in this presentation.



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Organic Chemistry **OC089**

Reusable Polymer-supported Pd Catalysts for the Suzuki Coupling in Water

Delphine Josien and Claude Le Drian

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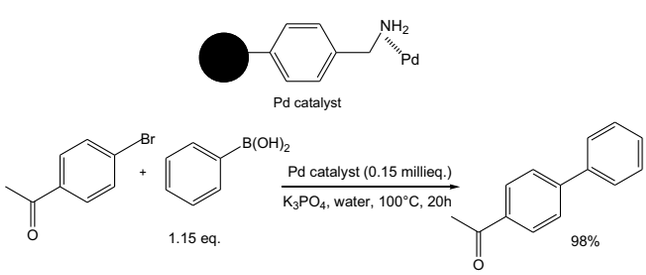
The Suzuki coupling, a very important reaction for aryl-aryl bond formation is usually performed in organic solvents and in the presence of a soluble (and therefore not recoverable) palladium catalyst. In accordance with Green Chemistry principles (conservation of a scare natural resource, palladium, and development of organic solvent-free processes), we present here a polymer-supported palladium catalyst allowing us to use water as solvent for the Suzuki coupling with almost quantitative yields. This catalyst is easily prepared in one step from commercially available aminomethylated Merrifield resin, is easily recovered after reaction, and can be reused at least 4 times without showing any significant decrease of reactivity.



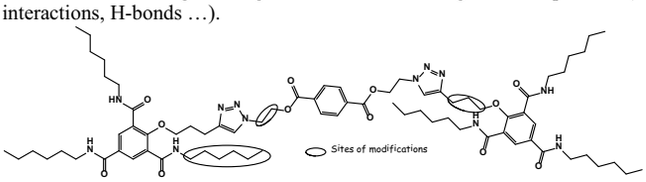
Organic Chemistry **OC090**

Study of the Self-Organization Process of 1,3,5-benzenetriamide Dimers: Modulation of H-bonds and π–π Interactions

Christian Invernizzi, Helen Stoeckli-Evans and Reinhard Neier*

University of Neuchâtel, Av. de Bellevaux 51, CH-2000 Neuchâtel

Self-organization of discotic liquid crystalline materials allow us to create that molecular columnar assembly that display unusually large charge migration, and which make such systems prime candidates for application in photovoltaic cells or light-emitting diodes[1,2]. In a previous study [3], we have observed that making discotic dimers leads to the formation of stable columnar mesophase at ambient temperature. Now, our objective is to rationalize the factor governing the columnar self-organization process (π interactions, H-bonds …).



We have prepared a series of dimers based on the benzenetriamides mesogen (BTA). We are trying to establish a structure-properties relationship by modifying different parameters such as the length and rigidity of the linker, the aliphatic side chains, or by expanding the aromatic core of the discotic unit. Here we present our progress in the synthesis of the dimers and a DOESY-NMR investigation of the H-bonds interactions in solution.

[1] Müllen, K., *Science*, **2001**, *293*, 1119.
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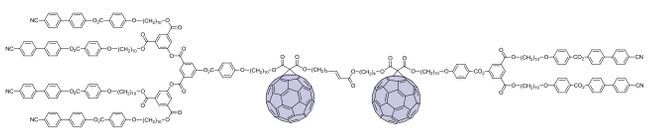
Organic Chemistry **OC091**

Liquid-crystalline fullerenes based on the cross-metathesis reaction

Virginie Russo, Robert Deschenaux

University of Neuchâtel, Av. de Bellevaux 51, 2000 Neuchâtel, Switzerland

Addition reaction of mesomorphic malonate-based dendrimers with C_{60} gave liquid-crystalline fullerene derivatives [1]. This approach represents an interesting way for the design of self-organizing structures based on fullerene, and opens the way to optoelectronic applications for this carbon allotrope, such as for the development of photovoltaic devices and molecular switches. The idea is now to design liquid-crystalline materials containing two fullerene units as model compounds for fullerene-based polymers (fullerene rich materials). The cross-metathesis reaction could be successfully applied to obtain such materials.



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Organic Chemistry **OC092**

Characterization of a Reduced *N*-Confused Calix[4]pyrrole

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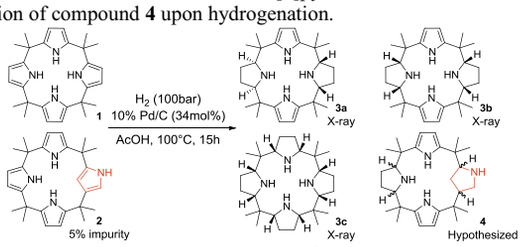
The *N*-confused calix[4]pyrrole is obtained in variable yields by the normal Baeyer condensation between pyrrole and acetone. These unusual *N*-confused macrocylces and their derivatives possess unusual properties and important reference compounds for our understanding of the tetrapyrrolic macrocycles. The controlled hydrogenation of calix[4]pyrrole previously developed in our group [1], gives access in one step to compounds **3a-c**, compounds which have been fully characterized.
During this study we noticed that some batches of calix[4]pyrrole were contaminated with 5% of *N*-confused calix[4]pyrrole **2** which could lead to the formation of compound **4** upon hydrogenation.



In contrast to the other products isolated so far, **4** is chiral and could be used in asymmetric transition metal catalyzed reactions or even as asymmetric organocatalyst. Herein we present the isolation and characterization of compound **4**, along with degradation studies of pure and contaminated **1**.

[1] a) G. Journot, C. Letondor, R. Neier, H. Stoeckli-Evans, D. Savoia, A. Gualandi *Chem. Eur. J.* **2010**, *16*, 4224-4230 ; b) G. Journot, C. R. Jones, V, Blangy, R. Neier, *Heterocycles.* **2012**, *85,* 749-797

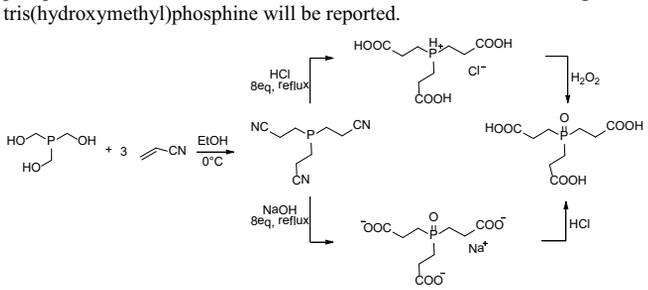
Organic Chemistry **OC093**

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

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

[1]Institute of Chemistry, University of Neuchâtel, Av. Bellevaux 51, 2000 Neuchâtel, Switzerland
[2]Febex SA, route des Placettes, 1880 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 flame-proof 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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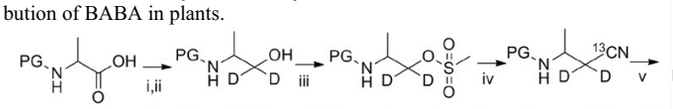
Organic Chemistry **OC094**

SYNTHESIS OF LABELED BETA AMINO BUTYRIC ACID FOR STUDY OF PRIMING PLANTS

Adrien Rizzi, Gaëtan Glauser(3), Armelle Vallat(3), Brigitte Mauch-Mani(2)*, Reinhard Neier (1) *

(1)Institute of Chemistry, University of Neuchâtel, Avenue Bellevaux 51 2000 Neuchâtel, Switzerland.
(2)Institute of Biologie moleculaire et cellulaire, Avenue de Bellevaux 51, 2000 Neuchâtel, Switzerland.
(3)Service analytique facultaire, University of Neuchâtel, Avenue de Bellevaux 51, 2000 Neuchâtel, Switzerland

Plants have a complex defense system able to recognize the presence of a pathogen put in place various responses adapted to the situation.
The protective effects of β amino butyric acid (or BABA) on plants have been well explored for over 20 years [1 2]. The molecular mechanisms responsible for these effects are poorly or not defined.
To trace the molecular mechanism of BABA induced resistance (BABA-IR) we propose to use labelled BABA for explore the fate of both enantiomers of BABA and to study their activity, metabolism and on second time distribution of BABA in plants.



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(2) Hamiduzzaman, MM; Jackab, G; Barnavon, L; Neuhaus, J.M; Mauch-Mani, B; *Mol Plant Microbe Interact*, **Aug 2005**, 18(8), *819-829*
(3) Jurriaan, T; Jackab, G; Toquin, V; Lavicoli, A; Maeder, M.N; Métraux, J.P, Mauch-Mani, B*; The plant Cell, **March 2005**, Vol.17,3, 987-999*

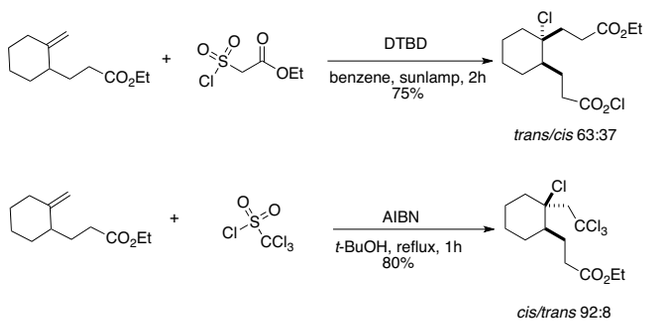
Organic Chemistry **OC095**

Trichloromethyl Group Transfer: Selectivity and Functionalization

Cédric Bürki, Lidong Cao, Karin Weidner and Philippe Renaud*

University of Berne, Freiestrasse 3, CH-3012 Berne, Switzerland

Recently, we reported a desulfitative atom transfer reaction [1] and we decided to investigate the scope of this reaction. We observed differences in the diastereoselectivity outcome influenced by the nature of the C-centered radical. Indeed, while the *trans* diastereoisomer was obtained with substituted radicals [2], the CCl_3-radical gave a high diastereoselectivity in favor of the *cis* diastereoisomer. A model to rationalize these results will be presented.



[1] K. Weidner, A. Giroult, P. Panchaud and P. Renaud, *J. Am. Chem. Soc.* **2010**, 132, 17511-17515
[2] S. Cren, P. Schär, P. Renaud and K. Schenk, *J. Org. Chem.* **2009**, 74, 2942-2946

Organic Chemistry **OC096**

Synthetical approaches to investigate proteins-nerve agents adducts

Julien Ducry[1,2], Christian G. Bochet[1], Christophe Curty[2]

[1]University of Fribourg, Chemin du Musée 9, CH-1700 Fribourg
[2]Spiez Laboratory, CH-3700 Spiez

Phosphonate nerve agents are among the most toxic compounds known. Unequivocal methods are required to confirm their use, which is prohibited by the Chemical Weapons Convention.[1] Adducts formed between proteins and phosphonates are good biomarkers and they will permit retrospective analysis thanks to their stability.[2]

Our goal is to investigate the coupling chemical reactions between the 20 natural amino acids and simi-nerve agents affording new potential biomarkers for the analytical investigation. The stable adducts could be incorporated in Solid Phase Peptide Synthesis giving peptidic reference standards for their unambiguous identification.[3] Furthermore, these adducts could give new information about the nerve agents' pharmacodynamic. In this contribution, the results concerning the adducts' synthesis will be shown.

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[2] Black, R. M. *J. Chromatogr. B*, **2010**, *878*, 1207.
[3] MacDonald, M.; Lanier, M.; Cashman, J. *Synlett*, **2010**, *13*, 1951.

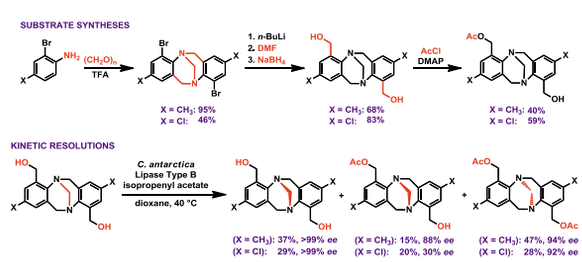
Organic Chemistry **OC097**

Enzymatic Resolution of Tröger's Base Derivatives

Takuya Kamiyama, Merve Sinem Özer*, Jan Deska* and Ján Cvengroš

Swiss Federal Institute of Technology, CH-8093 Zürich (Switzerland)
* University of Cologne, DE-50939 Cologne (Germany)

Tröger's base derivatives have been uses for various biological purposes [1] but their preparation as single enantiomers has been successful in limited cases. Our project focused on using enzymes to perform a kinetic resolution of analogues bearing hydroxyl groups.



Current work focuses on the building of ligands for asymmetric catalysis by performing functional group interconversions on the hydroxyl groups.

1. B. G. Bag, *Curr. Sci.* **1995**, *68 (3)*, 279

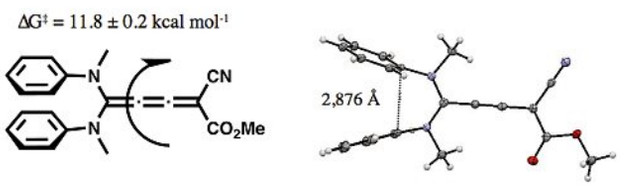
Organic Chemistry

OC098

Push-Pull Buta-1,2,3-Trienes: Exceptionally Low Rotational Barriers of Cumulenic C=C Bonds and Their Proacetylenic Reactivity

Przemyslaw Gawel, Yi-Lin Wu, Aaron D. Finke, W. Bernd Schweizer, François Diederich

Laboratory of Organic Chemistry, ETH Zürich, Hönggerberg, HCI, CH-8093 Zürich, Switzerland



A variety of asymmetric donor-acceptor-substituted 1,2,3-butatrienes were synthesized by developed procedures. The activation barriers to rotation were measured by variable temperature NMR spectroscopy, and found to be as low as 11.8 kcal mol^{-1}. The central bond of the cumulene moiety is shorted to 1.22 Å as measured by X-ray crystallography. The data show a high contribution of the charge-separated acetylene resonance structure in the ground state of this class of molecules. Recently, the [2+2] cycloaddition-retroelectrocyclization reaction of TCNE with push-pull [3]cumulenes was reported to give stable zwitterions.[1] By contrast, bis-anilino- and acceptor-substituted buta-1,2,3-triene derivatives gave stable radical structures upon reaction with TCNE and TCNQ, corroborating the pro-acetylenic character of push-pull [3]cumulenes.

[1] Y.-L. Wu, F. Tancini, W. B. Schweizer, D. Paunescu, C. Boudon, J.-P. Gisselbrecht, P. D. Jarowski, E. Dalcanale, F. Diederich, *Chem. Asian J.* **2012**, *7*, 1185.

Organic Chemistry

OC099

Expanding the Chemical Space for Push-Pull Chromophores: Homo-conjugated and Spiro Systems

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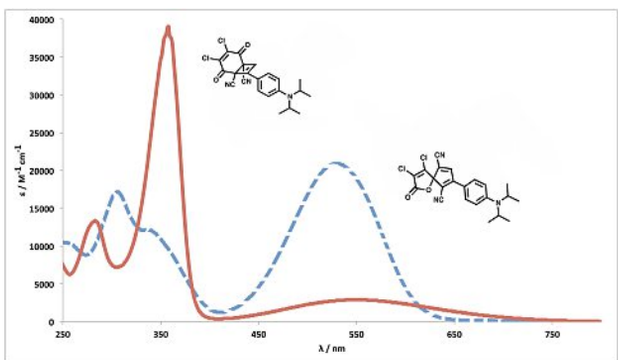

A one-step protocol was developed for the synthesis of push-pull spiro systems starting from homoconjugated push-pull chromophores. Recently, the [2+2] cycloaddition reaction of DDQ with various electron-rich alkynes was reported.[1] As a continuation of this study, we have prepared a series of spiro compounds to see the generality of the method and to investigate the structure-property relationships. Both homoconjugated adducts and spiro systems feature strong intramolecular charge-transfer interactions.

[1] S.-I. Kato, M. T. R. Beels, P. La Porta, W. B. Schweizer, C. Boudon, J.-P. Gisselbrecht, I. Biaggio, F. Diederich, *Angew. Chem. Int. Ed.* **2010**, *49*, 6207.

Organic Chemistry

OC100

Radical Chemistry of Amino Acids: Electrode Potentials

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Tyrosine and the associated tyrosyl radical are important one-electron transfer reactants in biology [1]. The reaction mechanism of ribonucleotide reductase involves electron transfers between Tyr, Trp, and Cys [2] over a distance of 35Å. Tyrosine is the ultimate electron donor in a pecking order consisting of Met, Trp, and Tyr≈Cys. As the range of published electrode potentials for Trp at pH 7 is +0.56 to +1.05 V, and +0.68 to +0.94 V for Tyr [3], we set out to determine a consistent set of electrode potentials.
By cyclic voltammetry, we measured $E^{\circ\prime}$ (TyrO$^{\bullet}$, H^{+}/TyrOH) = +0.98±0.02 V and $E^{\circ\prime}$ (Trp$^{\bullet}$, H^{+}/TrpH) = +1.00±0.01 V, thus $\Delta E^{\circ\prime}$= 0.02±0.02 V (K= 2) for electron transfer between Trp$^{\bullet}$ and Tyr; by pulse radiolysis, we found K = 9, corresponding to $\Delta E^{\circ\prime}$= 0.05 V. We recommend that the presently accepted values of $E^{\circ\prime}$ for Trp (+1.05V) and Tyr (+0.94 V), be replaced with +1.01 V and +0.97 V, respectively. For nitrotyrosine, we found +1.11±0.02 V by cyclic voltammetry. Pulse radiolysis experiments described in the literature suggest that the value of $E^{\circ\prime}$(Cys$^{\bullet}$,H^{+}/CysH) is similar to that of the Tyr couple; Schöneich and coworkers, and we have shown, however, that the S-centered radical is in rapid equilibrium with C-centered radicals in Cys and neighboring amino acids [4,5].

[1] J. J. Warren, J.R. Winkler, H.B. Gray, *FEBS Letters* **2012**, 586, 596-602.
[2] C. S. Yee, M. R. Seyedsayamdost, M. C. Y. Chang, D. G. Nocera, J. Stubbe, *Biochemistry* **2003**, 42, 14541-14552.
[3] M. R. Defelippis, C. P. Murthy, F. Broitman, D. Weinraub, M. Faraggi, *J. Phys. Chem.* **1991**, 95, 3416-3419.
[4] D. Hofstetter, B. Thalmann, T. Nauser, W.H. Koppenol, *Chem. Res. Toxicol.*, **2012**, 25, 1862-1867.
[5] O. Mozziconacci, T. D. Williams, C. Schöneich, *Chem. Res. Toxicol.*, **2012**, 25, 1842-1861.

Organic Chemistry

OC101

Development of a new method for site-specific etheno-DNA synthesis

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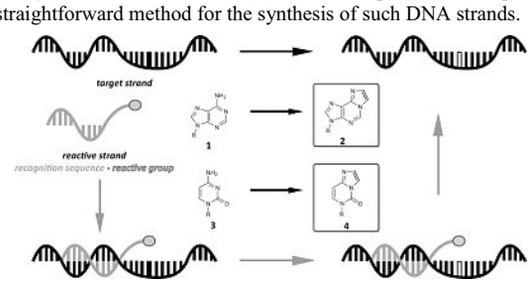
Etheno-bases (e.g. **2** and **4**) are nucleobase analogs that are well-known for their photophysical properties as well as their critical role in carcinogenesis [1]. The evaluation of mutational spectra and the investigation of essential repair pathways in different cell types have increased the demand for site-specifically modified etheno-DNA [2]. Here, we report the development of a new, straightforward method for the synthesis of such DNA strands.



An unmodified target strand is treated with a complementary reactive strand carrying a reactive group. Hybridization of the strands via base pairing will place the reactive group next to the target base (**1**, **3**) and induce the conversion to the corresponding etheno-base without affecting other bases. This new system represents a valuable alternative to existing methods and could contribute to a better understanding of diseases related to etheno-lesions.

[1] A. Barbin, *Mutat. Res.* **2000**, *462*, 55.
[2] N. Shrivastav, D. Li, J. M. Essigmann, *Carcinogenesis* **2010**, *31*, 59.

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Organic Chemistry **OC102**

Measurement of Residual Dipolar Couplings in ß-peptides using stretched polyvinyl acetate gels

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Restraints for NMR structure determination of small and medium-sized molecules are still mainly derived from NOEs and J-couplings alone. Both are sensitive only to the close structural neighborhood and thus the relative position of remote parts in the molecule is often not well defined. The incorporation of restraints derived from residual dipolar couplings (RDCs) in the structure calculation process helps to enhance global precision. Whereas for large biomolecules the use of RDCs in structure refinement is already a standard method, for smaller molecules it remains challenging. In the last 10 years a series of alignment media were introduced for the study of RDCs in small molecules in organic solvents.[1]

Here we present the determination of RDCs in ß-peptides using a stretched polyvinyl acetate (PVA) gel in methanol. For the synthesis of PVA a procedure from the literature was modified and the density of cross-links was optimized for medium-sized molecules.[2] The polymerization was carried out in a teflon tube and the resulting polymer stick was swollen in a NMR tube containing a solution of the peptide in CD_3OH.

[1] C. M. Thiele, *Eur. J. Org. Chem.* **2008**, 5673. G. Kummerlöwe, B. Luy, *Annu. Rep. NMR Spectrosc.* **2009**, *68*, 193.
[2] J. C. Freudenberger, S. Knör, K. Kobzar, D. Checkmann, T. Paululat, H. Kessler, B. Luy, *Angew. Chem. Int. Ed.* **2005**, *44*, 423.

Organic Chemistry **OC103**

From Collagen Model Peptides to Collagen Based Materials

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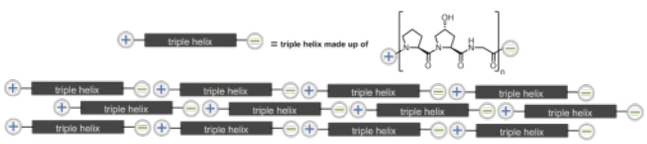
Collagen is the most abundant protein in mammals.[1] Due to its biocompatibility collagen based materials are interesting matrices in different medicinal applications, e. g. tissue engineering and delivery of proteins, drugs and genes. A promising approach to make collagen based materials more applicable uses short synthetically accessible collagen model peptides (CMPs).



We have shown that (4*R*)- and (4*S*)-azidoprolines can be incorporated in CMPs as conformation directing amino acids and sites for functionalization.[2] Currently, we further develop functionalizable collagen based materials. Our design involves the installation of ionic moieties bearing alkyl chains that are envisioned to trigger the formation of higher order structures and can be varied to gain deeper insights into the processes of fibril formation.

[1] J. Brinckmann, *Top. Curr. Chem.* **2005**, *247*, 1-6.
[2] a) R. S. Erdmann, M. Kümin, H. Wennemers, *Chimia* **2009**, *63*, 197-200. b) R. S. Erdmann, H. Wennemers, *J. Am. Chem. Soc.* **2010**, *132*, 13957-13959. c) R. S. Erdmann, H. Wennemers, *Angew. Chem. Int. Ed.* **2011**, *50*, 6835-6838. d) R. S. Erdmann , H. Wennemers,*Org. Biomol. Chem.* **2012**, *10,* 1982-1986. e) R. S. Erdmann, H. Wennmers, *J. Am. Chem. Soc.*, **2012**, *134,* 17117-17124.

Organic Chemistry **OC104**

Direct Electrophilic Trifluoromethylation of Quinolones and Pyridones

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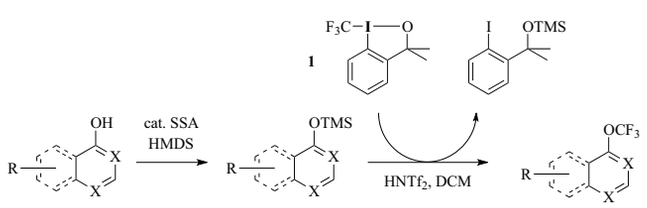
Since their discovery in the late 70's quinolone based antibiotics as Norfolxacin or Ciprofloxacin belong to the most prescribed broad-spectrum antibacterial drugs. [1] Although a myriad of compounds were evaluated to further optimise their antibacterial activity, trifluoromethylated fluoroquinolones still represent a rarity. [2]

Recently, we reported the direct electrophilic *N*-trifluoromethylaton of a variety of nitrogen containing heterocycles [3], using the hypervalent iodine reagent **1**, originally developed in our group. 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.



[1] V. T. Andriole (Ed.) *The quinolones*, Third Edition, Academic Press, 2000.
[2] Y. Asahina, I. *et al. Med. Chem.*, **2005**, *48*, 3443-3446.
[3] K. Niedermann, N. Früh, R. Senn, B. Czarniecki, R. Verel, A. Togni, *Angew. Chem. Int. Ed.,* **2012**, *11*, 6511-6515.