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Organic Chemistry, Lecture (Session A1) **273**

Aminal-pyrrolidine, highly efficient organocatalysts for α-functionalization of carbonyl compounds

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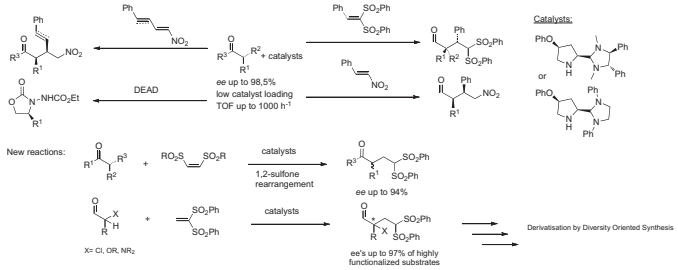
Department of organic chemistry, University of Geneva

Enamine organocatalysis has received tremendous attention in the last five years leading to considerable efforts in new catalysts developments. Unfortunately, most of them remain highly specific, as for the overstudied Michael addition to nitrostyrene. Thus, the development of new catalysts with broad applicability would be of high interest. We recently discovered that aminal-pyrrolidine were catalysts of choice for such purpose. Based on high steric hindrance and modularity of the catalysts, they afford high enantioselectivities on a broad range of different reactions. Furthermore, those catalysts were further applied to new highly challenging reactions.[2]



[1] a) A. Quintard, C. Bournaud, A. Alexakis, *Chem. Eur. J.* **2008**, *14*, 7504. b) A. Quintard, S. Belot, E. Marchal, A. Alexakis, *Eur. J. Org. Chem.* **2010**, 927. c) S. Belot, A. Quintard, N. Krause, A. Alexakis, *Adv. Synth. Catal.* DOI: 101002/adsc. 200900814.
[2] a) A. Quintard, A. Alexakis, *Chem. Eur. J.* **2009**, *15*, 11109. b) A. Quintard, A. Alexakis, *Chem. Commun.* accepted manuscript.

Organic Chemistry, Lecture (Session A1) **274**

Synthesis of Aspidospermidine and Goniomitine via the Selective Cyclization of Aminocyclopropanes

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[1]Laboratory of Catalysis and Organic Synthesis, EPFL, 1015 Lausanne, Switzerland
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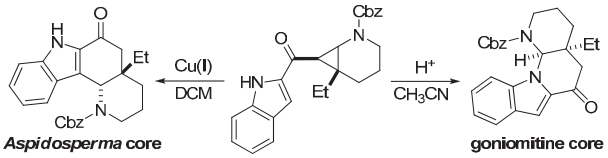

The importance of heterocyclic compounds in natural and synthetic drugs is well established. To facilitate access to complex scaffolds new cyclization reactions are needed. Our recent work on the first catalytic formal homo-Nazarov reaction allowed us to synthesize polycyclic cyclohexenones derivatives under mild conditions.[1]

Herein we report the first application of our method in the cyclization of aminocyclopropanes. Selective cyclization on the N1 or C3 position of indole heterocycles was simply achieved by changing catalyst and solvent. The power of our methodology is demonstrated in the formal total synthesis of aspidospermidine and the total synthesis of goniomitine, which allowed us to perform the first study of its bioactivity.[2]

[1] De Simone, F.; Andres, J.; Torosantucci, R.; Waser, J. *Org. Lett.* **2009**, *11*, 1023-1026.
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Organic Chemistry, Lecture (Session A1) **275**

Gold-Catalyzed Ethynylation of Arenes

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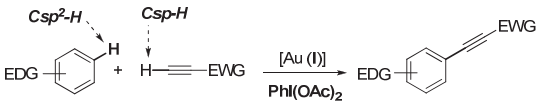
University of Zürich, Winterthurerstr. 190, CH-8057 Zürich Switzerland



The introduction of acetylenic groups into organic molecules is an important synthetic transformation. Of all the available methods, Sonogashira cross-coupling reaction is the most widely used [1]. This palladium catalyzed Csp-Csp^2 bond formation efficiently produces aryl-alkynes, which are precursors for bioactive natural molecules, pharmaceuticals and molecular organic materials.

Activation of aromatic C-H bonds, followed by C-C bond formation constitutes a conceptually attractive methodology since it avoids the otherwise necessary prefunctionalization of the aromatic counterpart [2].

Herein, we report a novel gold-catalyzed ethynylation of aromatic rings with electron-deficient alkynes via gold catalyzed C-H activation of both Csp-H and Csp^2-H bonds. This transformation provides aromatic propiolates difficult to prepare by other methods, highlighting the synthetic potential of gold chemistry [3].

[1] Sonogashira, K. In Metal-Catalyzed Reactions; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York 1998, p 203.
[2] Ru; Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; So noda, M; Chatani, N. *Nature*, **1993**, 366, 529.
[3] de Haro, T.; Nevado, C. *J. Am. Chem. Soc.*, **2010**, *132*, 1512.

Organic Chemistry, Lecture (Session A1) **276**

Efficient Catalytic Asymmetric Entry to Planar Chiral Complexes

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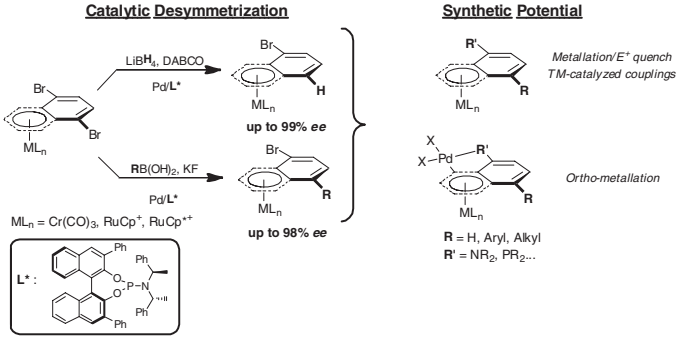
Department of Organic Chemistry, University of Geneva
30 Quai Ernest Ansermet, 1211 Geneva 4

Optically pure planar chiral complexes are of interest for both asymmetric synthesis and catalysis. We here report on an easy access to highly enantioenriched neutral Cr(CO)$_3$(naphthalene), RuCp(indenyl) and cationic RuCp*(naphthalene) complexes via desymmetrization of prochiral dibromoarene complexes using a Pd/bulky chiral phosphoramidite catalyst.[1,2] The potential utility of this reaction is illustrated with the synthesis of a wide range of highly enantioenriched planar chiral complexes.



[1] (a) Mercier, A. *et al. Chem. Eur. J.* **2010**, *in press*. (b) Kündig, E. P. *et al. Angew. Chem. Int. Ed.* **2006**, *45*, 1092-1095.
[2] (a) Mercier, A. *et al. Chimia*, **2010**, *64*, 177-179. (b) Mercier, A. *et al Chem. Comnun.* **2009**, 5227-5229.

Organic Chemistry, Lecture (Session A1) **277**

Stereoselective Syntheses of Monocyclic Peloruside A Analogs

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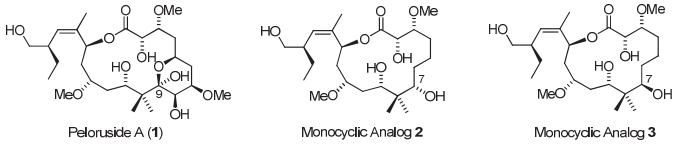
Institute of Pharmaceutical Sciences/ETH Zürich, Wolfgang-Pauli-Str. 10, CH-8093 Zürich, Switzerland

Peloruside A (**1**) is a marine natural product that was first isolated in 2000 [1]. It was shown to have potent taxol-like microtubule-stabilizing activity and to inhibit the growth of human cancer cells at nM concentrations [2]. The stereoselective synthesis of the simplified monocyclic peloruside A analog **2** has only recently been described in our group [3]. However it is not clear how the removal of the entire pyranose ring will affect the overall conformation of the macrocycle in **2** and, thus, the orientation of the 7-OH group, which is supposed to mimic the anomeric OH group attached to C9 in the natural peloruside A.



For that reason we will present the stereoselective synthesis of peloruside A analog **3** (having the opposite stereochemistry at C7) together with data on its effects on the tubulin/microtubule system and its *in vitro* antiproliferative activity. Key steps of our strategy to form **3** are a highly selective allyltitanation followed by a 1,3-*syn*-reduction, the assembly of building blocks *via* the addition of the side chain as a vinyl lithium species to the aldehyde and a ring closing metathesis to build up the macrocycle.

[1] L. M. West *et al.*, *J. Org. Chem.* **2000**, *65*, 445.
[2] K. A. Hood *et al.*, *Cancer Res.* **2002**, *62*, 3356.
[3] C. W. Wullschleger *et al.*, *Org. Lett.* **2010**, *12*, 1120.

Organic Chemistry, Lecture (Session A1) **278**

Synthesis of α-CF_3-substituted carbonyl compounds with relative and absolute stereocontrol using electrophilic CF_3-transfer reagents

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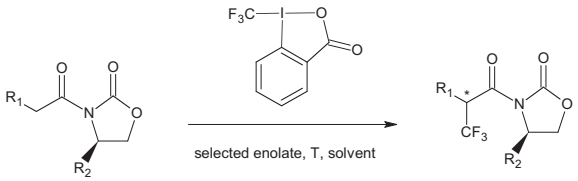
[1] Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology, ETH Zurich, CH-8093 Zürich, Switzerland

[2] Institut de Recherche en Chimie Organique Fine, Université de Rouen, Rue Tesnière, F-76821 Mont Saint Aignan Cedex, France

The quest for compounds bearing a trifluoromethyl group at stereogenic centres has become important recently.



The present work deals with the development of a practical synthetic method allowing efficient α-trifluoromethylation of chiral imides in a diastereoselective manner and the synthesis of related chiral derivatives. The introduction of a trifluoromethyl group at the enolizable position of Evans imides was performed using electrophilic hypervalent CF_3-iodine reagents[1]. Optimal reaction conditons in terms of temperature, solvent and enolate counterion were found, giving up to 10:1 dr and 93% isol. yield.

The trifluoromethylated products were subjected to a series of further synthetic transformations leading to related valuable CF_3-substituted building blocks.

[1] Eisenberger, P.; Gischig, S.; Togni,A., *Chem.-Eur.J.,* **2006**, *12*, 2579.

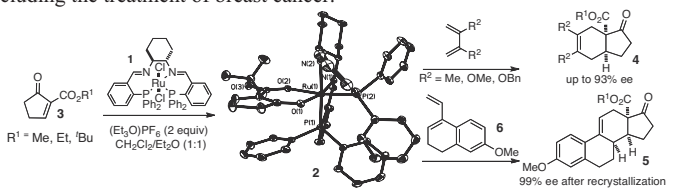
Organic Chemistry, Lecture (Session A1) **279**

Asymmetric Diels-Alder Reactions of Unsaturated β-Ketoesters Catalyzed by Chiral Ruthenium PNNP Complexes

Christoph Schotes and Antonio Mezzetti*

Department of Chemistry and Applied Biosciences, ETH Zürich, CH-8093 Zürich, Switzerland

The enantioselective formation of all-carbon quaternary centers is an area of intense research in which Diels-Alder reactions play a major role.[1] We report here dicationic ruthenium PNNP complexes that promote the enantioselective Diels-Alder reaction of α-methylene β-ketoesters with various dienes.[2] This methodology gives access to enantiomerically pure estrone derivatives, which are interesting in view of their potential applications, including the treatment of breast cancer.[3]



Complex $[Ru(OEt_2)_2(PNNP)](PF_6)_2$, formed in situ from $[RuCl_2(PNNP)]$ (**1**) and $(Et_3O)PF_6$ (2 equiv), catalyzes the Diels-Alder reaction of unsaturated β-ketoesters of type **3** to give the novel alkoxycarbonyltetrahydro-1-indanone derivatives **4** (9 examples) with up to 93% ee. A useful application of this method starts from Dane's diene **6** to yield estrone derivatives **5**, which were obtained with 99% ee after recrystallization with an ester-*exo*:*endo* ratio of up to 145:1. A rationale for the enantioselecivity can be derived from the crystal structure of **2**, which shows that the lower face of the substrate is shielded, resulting in an attack of the diene from the open *re* enantioface.

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[3] Review article: Biellmann, J. F. *Chem. Rev.* **2003**, *103*, 2019.

Organic Chemistry, Lecture (Session A1) **280**

Catalyst engineering for the enantioselective hydrogenation of ketones

Fatos Hoxha, Tamas Mallat, Alfons Baiker

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The development of heterogeneous catalysts for asymmetric hydrogenation of ketones over chiraly modified Pt-group metals is constrained due to various reasons, the most important being the difficulty to create well-defined catalytically active and stable chiral sites on a solid surface. In the last 20 years the major part of the research was aimed at finding the appropriate combination of catalyst, modifier, and the reaction conditions, without a profound analysis on the role of catalyst structure, metal particle size, surface morphology, and support. Here we report a systematic study of two crucial parameters: the role of metal particle size and support ionocity on the performance of cinchona-modified catalysts in enantiselective hydrogenation of ketones. The catalysts were prepared by single-step flame synthesis in order to minimize the role of impurities. A clear correlation was found between the metal particle size, the reaction rate and the ee in the hydrogenation of ethyl pyruvate over CD-modified Rh catalyst, where the ee increased by a factor of seven by varying the Rh mean size from 0.96 to 1.65 nm [1]. By changing the acid-base properties of the alumina in Pt/Al_2O_3 catalyst with SiO_2, or Cs_2O, we were able to vary systematically the electronic properties of Pt. A striking correlation was uncovered between the enantioselectivities (ee) and acid-base properties of the catalyst, indicating the support as a key factor in this reaction. The practical importance of our findings is demonstrated by the best ee of 94% achieved so far in the industrially relevant hydrogenation of ketopantolactone to *(R)*-pantolactone [2].

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Organic Chemistry, Lecture (Session A2) **281**

Highly Enantioselective Isomerization of Primary Allylic Alcohols Catalyzed by (P,N)-iridium Complexes

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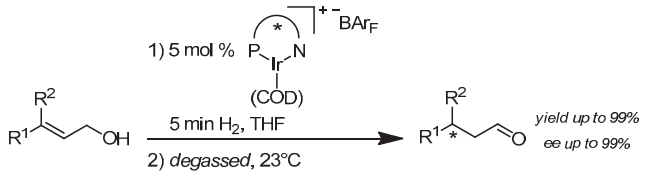
In contrast to the well established asymmetric isomerization of allylic amines into enamines, the asymmetric isomerization of allylic alcohols to aldehydes remains challenging. [1] We applied to this reaction a series of chiral (P,N)-iridium complexes that, under appropriate reaction conditions, isomerized primary allylic alcohols into aldehydes with high enantioselectivity. A mechanistic rational was proposed based on experimental evidences. [2]



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[2] a) L. Mantilli, C. Mazet, *Chimia* **2009**, *63*, 35; b) L. Mantilli, C. Mazet, *Tetrahedron Lett.* **2009**, *50*, 4141; c) L. Mantilli, D. Gérard, S. Torche, C. Besnard, C. Mazet, *Angew. Chem. Int. Ed.* **2009**, *48*, 5143; d) L. Mantilli, C. Mazet, *Chem. Commun.* **2010**, *46*, 445; e) L. Mantilli, D. Gérard, S. Torche, C. Besnard, C. Mazet, *Pure Appl. Chem.* **2010**, in press.; f) L. Mantilli, D. Gérard, S. Torche, C. Besnard, C. Mazet, *submitted.*

Organic Chemistry, Lecture (Session A2) **282**

Sequential Rhodium-Catalyzed Bond Activations

Tobias Seiser, Nicolai Cramer*

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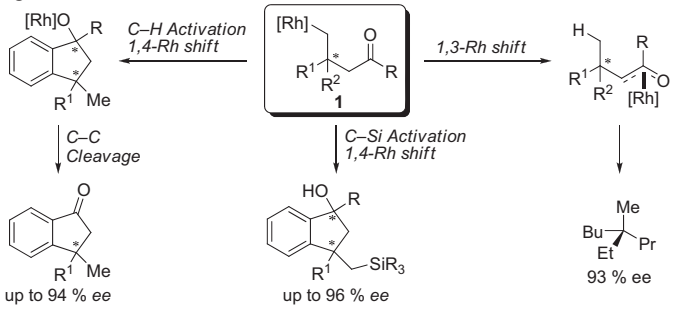
Activations of C–H and C–C bonds by transition-metal complexes has significant potential because of economic and ecological advantages. Enantioselective β-carbon eliminations from *tert*-cyclobutanols provide a convenient access to primary alkyl-Rhodium species **1** [1]. We show that these highly reactive intermediates are able to undergo a range of further bond activations. A large repertory of synthetically valuable products, all bearing quaternary stereogenic centers, can be accessed in excellent enantiomeric purity [2]. The different product forming manifolds are controlled by the ligand and the reaction conditions.



[1] T. Seiser, N. Cramer, *Org. Biomol. Chem.* **2009**, *7*, 2835; T. Seiser, N. Cramer, *Chimia* **2010**, *64,* 153.

[2] a) T. Seiser, N. Cramer, *J. Am. Chem. Soc.* **2010**, *132*, 5340; b) T. Seiser, G. Cathomen, N. Cramer, *Synlett* **2010**, *in press*; c) T. Seiser, N. Cramer, *submitted.*

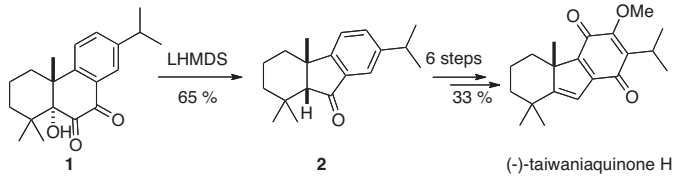
Organic Chemistry, Lecture (Session A2) **283**

Total Synthesis of (-)-Taiwaniaquinone H via a Proposed Biosynthetic Pathway

Chandan Kumar Jana[1], Rosario Scopelliti[2], Karl Gademann*[1]

[1]Department of Chemistry, University of Basel/St. Johanns-ring 19, CH-4056 Basel, Switzerland
[2]X-Ray Analysis, EPFL SB ISIC-GE, CH-1015 Lausanne, Switzerland

Taiwaniaquinoids are diterpene natural products featuring an unusual 6-5-6 tricyclic core isolated from *Taiwania cryptomeriodes*.[1] Valuable biological activity (such as aromatase inhibition) accompanied with their interesting structure renders them attractive targets for synthesis. Several synthetic approaches have relied mainly on ring forming reactions (e.g. Nazarov cyclization and Heck reaction) to build up the desired 6-5-6 skeleton of taiwaniaquinoids.[2] No biosynthetic proposal has been put forth so far for the formation of the C_{19} nor-diterpenoids. A biosynthetic hypothesis for the biogenesis of taiwaniaquinoids and its validation through a total synthesis of (–)-taiwaniaquinone H will be presented.



We propose that the ring contraction of suitably oxidized ferruginol or abietane derivative **1** to hydrofluorenone **2** is the key step for the biosynthesis of taiwaniaquinoids.[3] This biomimetic ring contraction allowed us to achieve a protecting group free total synthesis of (-)-taiwaniaquinone H.

[1] C. I. Chang, J. Y. Chang, C. C. Kuo, W. Y. Pan, Y. H. Kuo, *Planta Med*. **2005**, *71*, 72.
[2] Review: G. Majetich, J. M. Shimkus, *J. Nat. Prod*. **2010**, *73*, 284.
[3] C. K. Jana, R. Scopelliti, K. Gademann, *submitted*.

Organic Chemistry, Lecture (Session A2) **284**

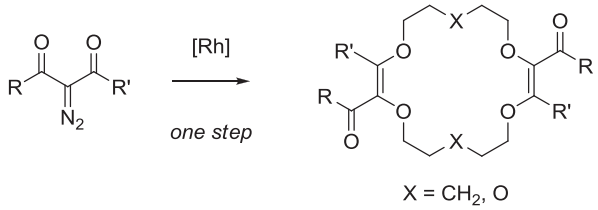
One-Step Synthesis of Functionalized Polyether Macrocycles

Diane Rix, Walid Zeghida, Céline Besnard and Jérôme Lacour*

Department of Organic Chemistry, University of Geneva, 30 quai Ernest Ansermet, CH1211 Geneva, Switzerland

Macrocycles are generally synthesized from smaller, usually linear, molecules using an intermolecular or, more favorably, an intramolecular reaction.[1] So far, to our knowledge, one-step synthesis of functionalized polyether macrocycles (cycle ≥ 14) from small readily-available building blocks have been rare under (i) high concentration (ii) non-templated conditions and (iii) using primarily intermolecular connections.

Vast arrays of synthetic transformations are possible using transition-metal-catalyzed decomposition of diazo compounds including cyclopropanation, insertion, dipolar addition, and ylide generation and rearrangement reactions but not macrocyclization reactions so far.[2] Here we present a Rh(II)-catalyzed reaction of two diazoketoesters and two cyclic ethers. That affords, in a single step and using high concentration conditions, 16- to 18-membered macrocycles in yields up to 75%.



[1] An, H.; Bradshaw, J. S., Izatt, R. M. *Chem. Rev.* **1992**, *92*, 543

[2] Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; Wiley: New York, 1998; p 652.

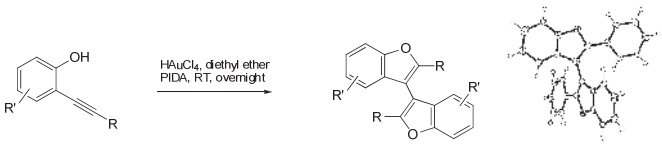
Organic Chemistry, Lecture (Session A2) **285**

Novel 3,3'-Bis(arylbenzofurans) via a Gold-Catalyzed Domino Process

Mathieu G. Auzias, Markus Neuburger, Hermann A. Wegner

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

Mild Lewis acidic gold catalysts are excellent activators for various π-systems opening novel routes for C–C bonds formation in complex molecules. Additionally, with their ability to insert into aromatic C–H bonds, Au-catalysts can also potentially promote oxidative coupling [1]. Ideally, gold would perform successively C–C bond formation and oxidative coupling: A transition metal catalyzed domino process [2].



Recently, we could combine the Au-catalyzed 5-*endo-dig* cyclization of 2-alkynyl phenols [3] with a subsequent oxidative coupling performed by the same Au catalyst, leading to the formation of novel 3,3'-bis(arylbenzofurans) [4]. This domino process represents a very efficient tool for the construction of such an interesting structural theme. First investigations show promising photochemical properties for this novel compounds.

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Organic Chemistry, Lecture (Session A2) **286**

Tin-Free Radical Carboazidation Reaction of Alkenes: Application to the Synthesis of Alkaloids

Karin Weidner, Philippe Renaud*

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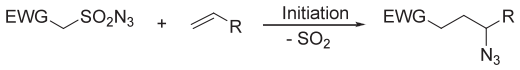
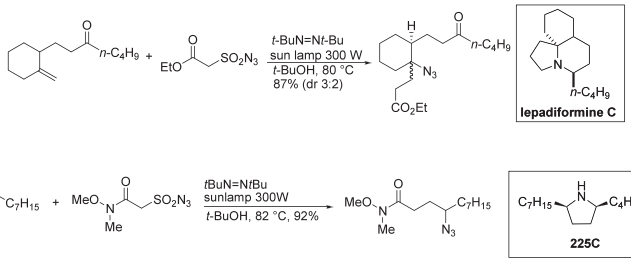
As part of our ongoing research program directed towards the synthesis of various biologically active alkaloids, we developed a new method for the radical carboazidation reaction of alkenes. This tin-free procedure allows for the formation of a carbon-carbon and a carbon-nitrogen bond in a single step by using a unique reagent. Sulfonyl azides giving an electrophilic radical after α-scission of SO_2 smoothly react with a large variety of alkenes according to the following equation.



The potential of this method was illustrated by the synthesis of the natural products lepadiformine C and pyrrolidine 225C.



Organic Chemistry, Lecture (Session A2) **287**

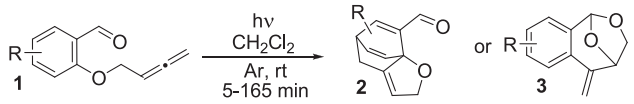
The intramolecular photocycloadditions of allenes to benzaldehydes and its application towards the total synthesis of natural products

Ursula Streit, Christian G. Bochet*

University of Fribourg, Chemin du Musée 9, 1700 Fribourg

Photoexcitation transmitts a substantial amount of energy to a substrate without thermal damage; this process can trigger normally impossible reactions. Excited aromatic compounds are for example capable of undergoing cycloadditions[1]. We can distinguish three types of arene-alkene cycloadditions: *ortho*[2], *meta*[3] and *para*[4].

As many other competing photoinduced processes usually occur, there have been few examples of *para*-photocycloadditions reported in literature. However, we recently discovered that allenes are capable to photocyclize with o-anisaldehydes in an [4+2] addition to afford the para-cycloaddition product **2** or a benzoxepine product **3**[5].



This unpresedented reaction opens new synthetic prospects in such photocycloadditions, because of the simplicity of the reactant and the high complexity of the cycloadduct. Effects of diverse substituents as well as implementation of the photocycloaddition as key step towards the total synthesis of natural compounds and their analogues will be discussed.

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Organic Chemistry, Lecture (Session B1) **288**

Selectivity Determination by ESI-MS Screening of Racemic Catalyst Mixtures

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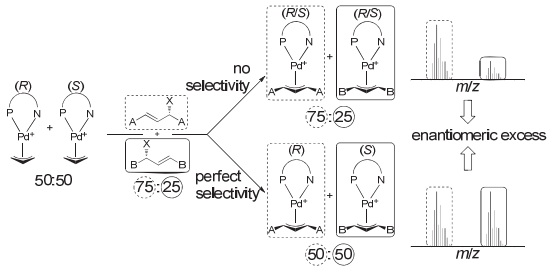
Ligand screening is an important but very time-demanding part in the development of enantioselective metal catalysts. Thus, the field of high-throughput screening continues to get more and more attention in research. Our group has recently developed a screening method, which allows for the selectivity determination of different catalysts in a very fast and easy fashion by ESI-MS analysis of reaction intermediates [1].



Herein we present an extension of this screening method based on a concept developed by Lloyd-Jones [2], which gives access to the selectivity of different catalysts upon use of racemic catalyst mixtures in the screening. The method has been successfully applied to the palladium catalyzed allylic substitution reaction and novel PHOX-derivatives have been examined in this fashion.

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Organic Chemistry, Lecture (Session B1) **289**

Controlled Release of Bioactive Volatiles from Dynamic Mixtures Obtained by Reversible Aminal Formation.

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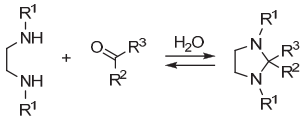
Dynamic combinatorial/covalent chemistry (DCC) was successfully applied to control the release of bioactive volatiles from dynamic mixtures which were obtained by reversible covalent bond formation with a suitable substrate in aqueous media. We now investigated the reversible aminal (imidazolidine) formation by reaction of secondary diamines with mixtures of fragrance aldehydes and ketones in aqueous media (Scheme) which turned out to be an efficient way to prolong fragrance evaporation in practical applications.[1]



The reversibility of the reaction and the composition of the equilibrium were investigated by ^{1}H-NMR spectroscopy in buffered aqueous solution using benzaldehyde as a typical volatile carbonyl compound. The solubility of the system in an aqueous environment and the nature of the substituents (R^1) at the *N*-atoms of the diamine were identified as the most important parameters contributing to the performance of the delivery system.[2] Dynamic headspace sampling and GC analysis demonstrated that the presence of a diamine in the mixture efficiently increased the long-lastingness of the fragrance evaporation with respect to a reference sample without diamine.[2]

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Organic Chemistry, Lecture (Session B1) **290**

Enantiopure Alleno-acetylenic Macrocycles and Helical Foldamers

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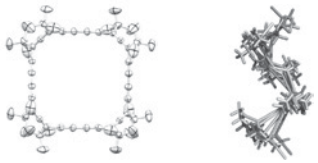
[2]Department of Chemistry, Columbia University, 10027 New York, USA.

We developed the asymmetric synthesis of a shape-persistent enantiopure alleno-acetylenic macrocycle by acetylenic homocoupling of optically pure 1,3-diethynylallenes.[1] In recent work, the solid-state structures of this compound (D_4-symmetric) was determined by single-crystal X-ray diffraction (see Figure). Optical and chiroptical properties were analyzed on the basis of time-dependent quantum chemical calculations. Recently, we also reported the synthesis, characterization, and chiroptical properties of the first length-defined, enantiopure alleno-acetylenic oligomers and demonstrated high chiral amplification upon changing from monodisperse dimer to hexadecamer.[2] We used a combination of electronic circular dichroism, optical rotatory dispersion, and theoretical calculations to show that these oligomers fold into single-handed helices (see Figure). These oligomers represent the first generation of a new class of helical foldamers, which exhibits impressive chiroptical properties.



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Organic Chemistry, Lecture (Session B1) **291**

Thermoresponsive nanomagnets: Towards magnetic soaps and recyclable detergents

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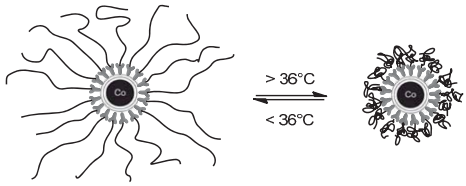
* Department of Chemistry and Applied Biosciences, Institute for Chemical and Bioengineering, ETH Zurich, CH-8093 Zurich, Switzerland



Magnetic nanoparticles are of increasing interest in various areas of contemporary technologies, emphasizing on drug delivery, catalysis, separation of biological species or wastewater purification mentioning just the most recent interests. Unfortunately, magnetic nanoparticles tend to agglomerate and grow to micronsized agglomerates due to the magnetic attraction. It would be strongly favorable to control the agglomeration by an external factor e.g. by using an amphiphilic polymer. Poly-N-Isopropylacrylamide (PNIPAM) is such an amphiphilic polymer with a switch temperature close to physiological conditions. Therefore, we covalently bound Poly-NIPAM to the surface of carbon coated metal nanoparticles, which were prepared by an industrial relevant flame spray synthesis process[1]. The polymer brushes counteract the magnetic attraction force by sterical hindrance. The resulting PNIPAM modified cobalt particles showed amphiphilic properties, depending on the temperature. Within this study, we showed that the amphiphilic particles translocated reversibly from hydrophilic to hydrophobic phases upon heating and cooling. We propose this effect for the use as magnetic soaps or as recyclable detergent.

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Organic Chemistry, Lecture (Session B1) **292**

Ag-Nanoparticle Formation in Different Sizes Controlled by Peptides

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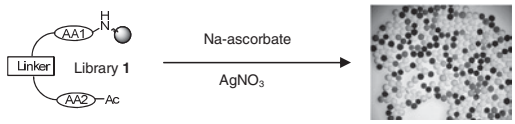
Silver-nanoparticles (AgNPs) are recently finding great and diverse applications in areas like imaging, catalysis and antimicrobial agents.[1] Previously, we introduced colorimetric on-bead screening of a split-and-mix library **1** for the identification of peptides that control the formation of AgNPs in different sizes.[2]



AAn: L-Ser, D-Ser, L-Asp, D-Asp, L-His, D-His, or L-Tyr
Linker: Gly, β-Ala, 6-aminohexanoic acid (Ahx), Pro-Aib, Pro-Gly, no linker, 2-aminocyclohexanoic acid (Achc)

The NPs generated by the peptides immobilized on a solid support are stable for months. The generation of stable AgNPs in solution phase proved to be a larger challenge. We will demonstrate how careful adjustments of the conditions allowed for increasing the stability of the AgNPs also in solution phase. In addition, initial experiments to evaluate the antibacterial activity of the AgNPs generated in the presence of different peptides will be presented.

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Organic Chemistry, Lecture (Session B1) **293**

Calix[4]pyrrolidine: synthesis and application in transition metal catalyzed oxidation.

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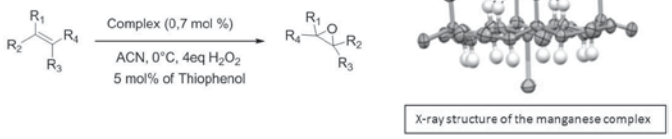
The *meso*-octaalkylporphyrinogens, known as calix[4]pyrroles, have been extensively studied since their discovery by Baeyer 120 years ago.[1] Hydrogenation of calix[4]pyrrole with a number of heterogeneous catalysts under different experimental conditions has been investigated.[2,3]
Using this method we are able to isolate one pure fully reduced diastereoisomer from 64 possible stereoisomers.[2,3] Structures of the manganese complexe will be also presented wich showed interesting oxidative properties.



X-ray structure of the manganese complex

Reducing calixpyrroles might lead to a new generation of nitrogen-containing macrocycles with interesting properties.[2,3]

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Organic Chemistry, Lecture (Session B1) **294**

Fragrance Sensing by Pattern Generation in Lipid Bilayers

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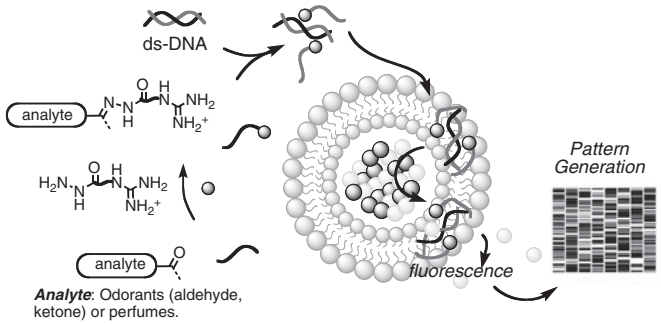
Department of Organic Chemistry, University of Geneva, Geneva, Switzerland

In mammals, odorants are detected in the olfactory epithelium, and about 350 olfactory receptors recognize more than 10'000 different odorants using a unique pattern recognition methodology [1]. The advantage of this sensing system is that little discriminatory power is needed for the signal generation [2]. We report herein a synthetic fragrant sensing system that operates, like olfactory receptors, by pattern recognition and in lipid membranes. This versatile approach allowed us to differentiate between pairs of enantiomers (muscone, citronellal, etc), cis-trans isomers, single-atom homologs (nonanal, octanal, heptanal, etc) as well as perfumes (Chanel Nº 5, Calvin Klein's Euphoria, etc).



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Organic Chemistry, Lecture (Session B2) **295**

Synthesis of Non-natural Amide-bearing Phospholipids

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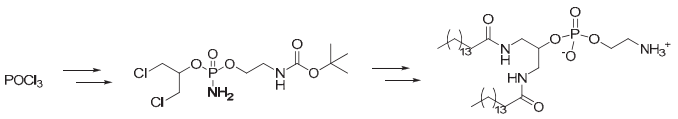
University of Geneva, Department of Organic Chemistry
CH-1211 Genéve 4

Artificial amide-bearing phospholipids are interesting compounds since they combine structural features of two different groups of natural compounds: glycerophospholids and phosphosphingolipids [1]. Today, only a few syntheses of amide-bearing phospholipids were reported [2].



We developed a methodology for the *de novo* synthesis of a library of 1,3-diamidophospholipids. Starting from cheap phosphorus oxochloride our approach features the use of a simple stable amidophosphate as a protected intermediate [3].

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Organic Chemistry, Lecture (Session B2) **296**

Stability and Dynamics of c-di-GMP

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Cyclic diguanylic acid (cyclic diguanosine monophosphate, c-di-GMP, CDG) is an important second messenger in bacteria that is primarily involved in signalling the switch between a motile (planctonic) and a sessile (biofilmrelated) lifestyle.[1][2] The molecule consists of two guanosine monophosphate (GMP) moieties linked by two phosphodiester bonds. Of particular importance for the in vivo situation and the in vitro characterization is the question whether CDG in solution occurs in monomeric or in its dimeric form. For better understanding the interaction of PleD, [3][4]WspR[5] and other proteins affected by CDG, the aggregation state of the messenger in solution is of fundamental interest. Computational methods - electronic structure calculations and molecular dynamics simulations – were used to characterize the structure, energetics and dynamics of solvated metal-free and metal-bound CDG. Estimations of binding free energies suggest that the CDG dimer is marginally stable with respect to its dissociated form (2 CDG) whereas the solvated Mg^{2+} − ion readily dissociates from $(CDG)_2$ and prefers water coordination. The simulations in solution suggest that metal-free CDG is thermodynamically stable by about 5 kcal/mol. This is in agreement with experimental studies which suggest that depending on the concentration of CDG present, dimers or higher oligomers form.[6]

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Organic Chemistry, Lecture (Session B2) **297**

Homo-DNA Probes for DNA and RNA Detection

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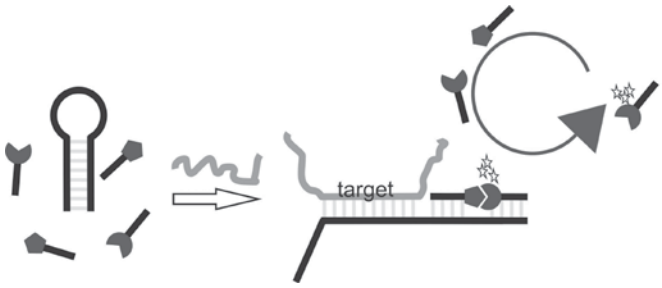
Homo DNA is known for its exclusive self pairing [1]. Recently, we showed that molecular beacons with a homo-DNA stem exhibit increased binding selectivity to a DNA target due to the orthogonality of the homo-DNA pairing system [2]. In extension of this work we developed novel nucleic acid detection systems in which homo-DNA in combination with Staudinger chemistry is used for selective fluorescence signal production and amplification.



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Organic Chemistry, Lecture (Session B2) **298**

Molecular control over the interparticle spacing in organic/inorganic hybrid dumbbells

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Gold nanoparticles are envisaged as single electron memory devices. For optimal performance the particles require a diameter below 2 nm to provide desirable coulomb blockade properties and a regular arrangement in a device [1]. Tailored functionalities on the particles' surface allow assembly of chemically addressable 'artificial molecules'.
We are able to form ligand stabilized Gold nanoparticles with a diameter of 1 nm [2]. These particles are stabilized by two monofunctionalized multidentate thioether ligands [3]. Using this functionality the nanoparticles can be interlinked covalently to form organic/inorganic hybrid dumbbells (Fig. 1).

Fig. 1. Gold nanoparticles formed in the presence of multidentate thioether ligands create covalent organic/inorganic hybrid aggregates via their peripheral functional groups (FG).

The interparticle spacing can be tuned by molecular control of the functional group. The presence of this functionality allows tuning of the ligand, opening up new applications for these hybrid aggregates. Dumbbells are also interesting candidates for molecular conductance measurements.

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Organic Chemistry, Lecture (Session B2) **299**

Fluorescent Chemosensors for Metal Ions based on Photoinduced Electron Transfer from Thiourea

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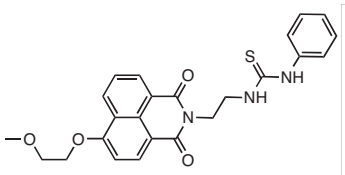
The goal of our project is the development of a new signaling process for fluorescent chemosensors. Until now nitrogen atoms are used for photoinduced electron transfer processes [1]. In our project thiourea will be used as a quencher moiety. Compound **1** was synthesized and shows a low quantum yield and a positive response by enhancement of the fluorescence upon addition of different metal ions. Electrochemical analysis were done to confirm that an electron transfer from the thiourea to a naphthalimide fluorophore is possible.

In order to have a better selectivity for the sensor, we will add other coordination position on the molecule. We will synthesize a series of naphthalimides fluorophores quenched by different thiourea and we will investigate their photochemical proprieties upon addition of different metal ions.



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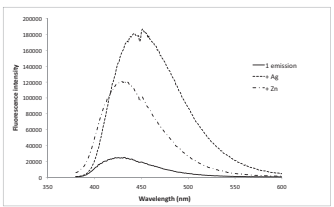

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Organic Chemistry, Lecture (Session B2) **300**

How to improve the chances of a successful crystallization of small molecules for a single crystal X-ray analysis?

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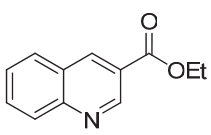
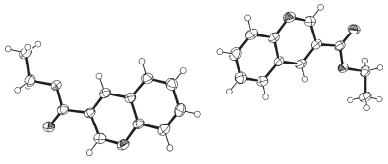
Generation of single crystals is one of the most decisive steps of a successful X-ray structure determination. This powerful technique depends upon the ability to grow single crystals of sufficient quality and size. Despite the fact that crystallization is an important purification technique which is thought in every Chemistry undergraduate curriculum, the techniques that yield single crystals can be quite different than the ones of "normal" crystallization.

Kroon and co-worker have summarized the different methods for growing crystals of organic molecules, though their list can be applied to most small molecules.[1] Hulliger has described in great detail crystallization techniques suitable for all kinds of type compounds.[2] While the crystallization behavior of molecules is dominated by its intrinsic properties[3], we would like to show that a careful screening of the solvents, including some "exotic" ones, allows to increase the chances of a successful crystallization. This is demonstrated for 3-carbethoxyquinoline (ORTEP representation of the asymmetric unit shown below) and other examples.





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Organic Chemistry, Lecture (Session B2) **301**

Electron transport through non-nucleosidic aromatic building blocks

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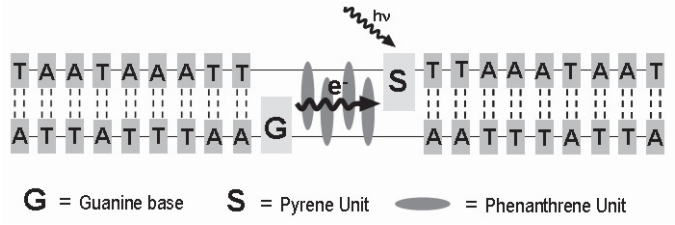
Department of Chemistry and Biochemistry, University of Bern
Freiestrasse 3, CH-3012 Bern

Electron transfer from a guanine base to an excited chromophore *via* an aromatic stack of several units is shown.

The electron transfer *via* a stack of two phenanthrene units incorporated into DNA, where the phenathrene acts as base surrogates, was published previously [1]. As the conductivity of DNA is limited by the electronic properties of the canonical bases [2], the tuning of the electronic behavior by incorporating designer units could possibly lead to an improvement of the charge transfer process.



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Organic Chemistry **302**

Synthesis of indole and indoline derivatives *via* radical cyclisation onto aryl azides

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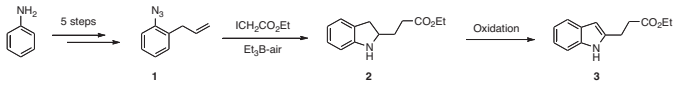
Indole and indoline-containing alkaloids have long been the subjects of intense interest because of their biological activities and because of the challenge posed by their complex structures. Intramolecular radical cyclisations onto azide groups to afford N-heterocycles have been pioneered by Kim et *al.*[1] using tributyltin or tris(trimethylsilyl)silyl radicals and iodoalkyl azides. This strategy was then applied by Murphy for the synthesis of the tetracyclic core of *Aspidosperma* alkaloids involving iodoaryl azides as key intermediates.[2]
Hereby we describe a novel approach to prepare indolines *via* a tandem radical addition/cyclisation using Et_3B-air as radical initiator. *Ortho*-azidoallylbenzene **1** is thus converted to the desired N-heterocycle **2** by addition of an ester substituted radical followed by cyclisation in an open to air process. The corresponding indole **3** can then be obtained by simple oxidation.



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Organic Chemistry **303**

Functionalization of Perfluoralkylated HBC

Nicolas Fragnière, Titus A. Jenny*

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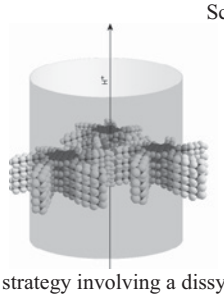
Previously formed HBCs (hexaperi-benzocoronene) substituted with perfluoralkylated side-chains[1] adopt a columnar supramolecular organization thanks to a pronounced π-π staking interaction[2]. Designed for electronic transport, new applications could be found for these kind of supramolecular structures by the introduction of functional groups such as a sulfonic acid or an ammonium salt at the end of one perfluoralkylated side-chain.
The HBC columns are expected to be oriented by the hydrophilic group ($-SO_3H$, $-NR_3^+$) and the hydrophobic perfluoralkylated side-chains to form proton channels (see scheme 1).

Scheme 1: Proton channel



A convergent strategy involving a dissymmetric tolane and a substituted tetraphenyl-cyclopentadienone is used to synthesize the desired products.

[1] O. F. Aebischer, P. Tondo, B. Alameddine, T. A. Jenny*, *Synthesis*, 2006, **17**, 2891–2896.
[2] Olivier F. Aebischer, Annina Aebischer, Bertrand Donnio, Bassam Alameddine, Massoud Dadras, Hans-Ulrich Güdel, Daniel Guillon and Titus A. Jenny*, *J. Mater. Chem.*, 2007, **17**, 1262 – 1267.

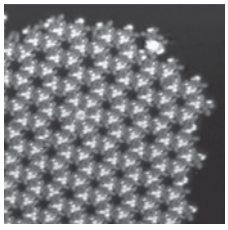
Organic Chemistry **304**

Learning a Lesson from Nature: Polarity Inversion in a Nanoporous Network

Petra Fesser[1], Leslie-Anne Fendt[1], Nikolai Wintjes[2], Thomas Jung[2], François Diederich[1]

[1]Laboratory of Organic Chemistry, ETH-Hönggerberg, CH-8093 Zürich
[2]Department of Physics, University of Basel, CH-4056 Basel

Two porphyrin derivatives and their self-assembling properties on a metal surface have been investigated by scanning tunneling microscopy (STM) under ultra-high-vacuum conditions (UHV). The two porphyrin derivatives are equipped at their opposing *meso*-positions with two voluminous imaging groups and two cyanophenyl groups, with and without an additional spacer unit respectively. Nanoporous networks that are held together by CN···H–$C(sp^2)$ hydrogen bonding and *van der Waals* interactions can be obtained in both cases. But the pore properties in the two systems are significantly different. Reverse polarities are found on the rim of the pores and also inside the network. It can be said that a possibility was found to invert a pre-existing nanoporous network [1]. This fact, which is unprecedented in the dry UHV environment, was inspired by a similar phenomenon found in the self-assembly of lipids in aqueous solutions.



[1] N. Wintjes, D. Bonifazi, F. Y. Cheng, A. Kiebele, M. Stöhr, T. Jung, H. Spillmann, F. Diederich, *Angew. Chem.* **2007**, *119*, 4167–4170; *Angew. Chem. Int. Ed.* **2007**, *46*, 4089–4092.

Organic Chemistry **305**

Gold Catalyzed Direct Alkynylation of Heterocycles

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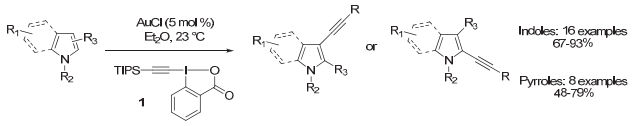
Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland



In the framework of sustainable chemistry, an important research field has emerged recently focusing on the direct functionalization of C-H bonds.[1] Despite the importance of alkynes in organic synthesis, material science and biological chemistry, studies toward the direct alkynylation of heterocycles were scarce compared to arylation and vinylation, with only two examples reported before 2009. The situation changed completely since then, and several new alkynylation methods have been reported.[2]

In 2009, we reported the unique properties of benziodoxolone alkynyl periodinane **1** in the presence of gold catalysts for the introduction of silylacetylenes on a large range of indoles and pyrroles with broad functional groups tolerance.[3] Recent investigations toward extension of the scope of the reaction and its application in more complex settings will be presented.

[1] a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007,** *107*, 174. b) Chen, X.; Engle, K. M.; Wang, D. H.; Yu, J. Q. *Angew. Chem. Int. Ed.* **2009,** *48*, 5094.
[2] A. S. Dibnuk, V. Gevorgyan *Angew. Chem., Int. Ed.* **2010**, *49,* 2096. And references therein.
[3] J. P. Brand, J. Charpentier, J. Waser, *Angew. Chem., Int. Ed.* **2009**, *48*, 9346.

Organic Chemistry **306**

Nanoliter Plates: Versatile Tools for On-bead and Off-bead Screenings of Split-and-mix Libraries

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[2] Genome Biology Unit - European Molecular Biology Laboratory (EMBL) Meyerhofstrasse 1, 69117 Heidelberg, Germany.

Split-and-mix libraries are versatile tools for the simultaneous generation and screening of a large number of different compounds provided that suitable screening methods are available.[1] Numerous screening methods using on-bead assays were developed for discovering active compounds but methods in solution phase allowing on-bead and off-bead screening are still limited. To answer this problem, we have developed a versatile method using plates made of PDMS containing a high density of nanoliter wells (Figure 1). These nanoliter plates, manufactured using photolithography, were designed to hold one single bead per well. Each well can be considered as a nanoreactor where each bead is in solution and isolated from the others, giving a single analysis by bead and allowing on-bead and off-bead screening. The discovery of catalysts as well as enzyme inhibitors was evaluated in proof of concept experiments.[1]

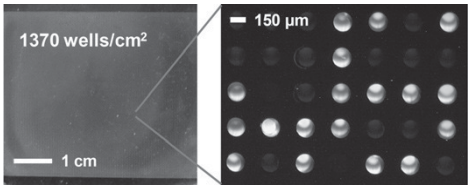

Figure 1: Nanoliter plate dimensions and example of a plate filled with fluorescent and non fluorescent beads.

[1] G. Upert, C. A. Merten, H. Wennemers, *Chem. Commun.* **2010**, *46*, 2209.

Organic Chemistry **307**

A new scalable solar synthesis of *trans*-Whiskey lactone

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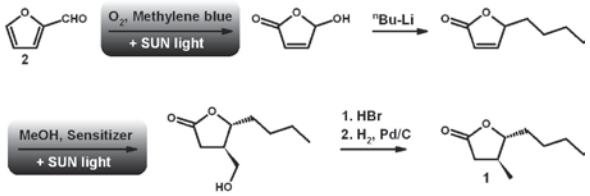
Green chemistry is an increasingly important topic. In this project, we selected as a synthetic target the commercially relevant *trans*-whiskey lactone **1,** a coconut, citrus, vanilla flavor used in perfume and cosmetic industry.[1,2] Since it appears that the sun is the only chemically usable renewable energy source, we endeavored to design a total synthesis, maximizing photochemical steps working in the spectral range of sun light.[3]



This total synthesis starts from the inexpensive renewable raw material 2-furfural **2**. The synthetic steps were optimized with a particular emphasis in the photochemical reactions. Finally, the whole synthesis was scaled up to multi-tens grams quantity. The photochemical steps were performed using our 1 m^2 parabolic mirror setup and Fribourg sun light.

[1] Masuda, M., Nishimura, K., *Chem. Lett.* **1981**, 1333.
[2] Maga, J. A., *Food Rev, Int.* **1996**, *12*, 105.
[3] Scharf, H.-D., Pohlmann B., Esser, P., *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2009.

Organic Chemistry **308**

Hyperforin: a Real Challenge for Total Synthesis

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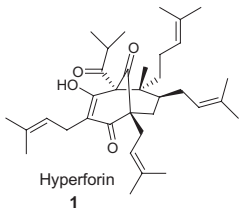
Hyperforin **1** is thought to be responsible of biological activity of St-John's wort extracts (*Hypericum perforatum*) against mild to moderate depression [1]. The challenging polyoxygenated bicyclo[3.3.1]nonane core common to the polyprenylated acylphloroglucinol (PPAPs) family has attracted the attention of several research groups [2]. Total synthesis of closely related Garsubellin A [3] and Clusianone [4] were published recently. In January 2010, Shibasaki published the first total synthesis of ent-Hyperforin **1** [5]. Here we described our recent progresses toward the total synthesis of Hyperforin.



[1] J. Barnes, L.A. Anderson, J.D. Phillipson, *J. Pharm. Pharmacol*. **2001**, *53*, 583
[2] R. Ciochina, R.B. Grossman, *Chem. Rev*. **2006**, *106*, 3963
[3] A. Kuramochi, H. Usuda, K. Yamatsugu, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2005**, *127*, 14200;
[4] P. Nuhant, M. David, T. Pouplin, B. Delpech, C. Marazano, *Org. Lett.* **2007**, *9(2)*, 287; V. Rodeschini, N.M. Ahmad, N.S. Simpkins, *Org. Lett.* **2006**, *8(23)*, 528
[5] Y. Shimzu, S. Shi, H. Usuda, M. Kanai, M. Shibsaki, *Angew. Chem. Int. Ed.*, **2010**, *49*, 1-5

Organic Chemistry **309**

The First Enantioselective Copper-Catalysed 1,4 Addition to α,β-Unsaturated Aldehydes with Various Organometallic Reagents

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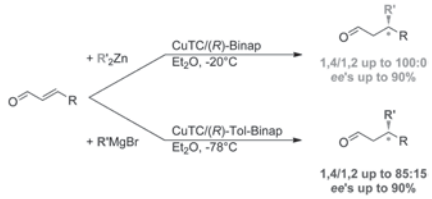
The asymmetric Cu-catalysed conjugate addition (A.C.A.) of organometallic reagents to Michael acceptors is amongst the most important methodologies to create a chiral C-C bond. In this field, a large variety of α,β-unsaturated compounds like α,β-unsaturated carbonyl derivatives, nitroalkenes, sulfones… have been successful used.[1] On the other hand, α,β-unsaturated aldehydes are more challenging substrates because of their high reactivity which undergo the undesired 1,2-addition. In literature, no example of enantioselective Cu-catalysed conjugate addition to enals is described. Herein, we reported the first enantioselective copper-catalysed conjugate addition to various α,β-unsaturated aldehydes, with diorganozinc and Grignard reagents.[2]



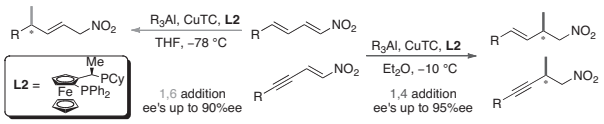
[1] a) A. Alexakis, C. Benhaim, *Eur. J. Org.* **2002**, 3221. b) A. Alexakis, J. E. Backvall, N. Krause, O. Pamies, M. Dieguez, *Chem. Rev.* **2008**, *108*, 2796. c) S.R. Harutyunyan, T. den Hartog , K. Geurts, A.J. Minnard, B.L. Feringa, *Chem Rev.* **2008**, 108, 2824.
[2] L. Palais, L. Babel, A. Quintard, S. Belot, A. Alexakis, *Org. Lett.* **2010**, in press.

Organic Chemistry **310**

Enantioselective and Regiodivergent Copper-Catalyzed Conjugate Addition of Trialkylaluminium Reagents to Extended Nitro-Michael Acceptors

Tissot Matthieu[1], Daniel Müller[1], Sébastien Belot[1], Alexandre Alexakis[1].

[1] Université de Genève, Département de chimie organique, 30 Quai Ernest Ansermet, 1211 Genève 4, Switzerland



The first highly enantioselective and regiodivergent conjugate addition of trialkylaluminium reagents to nitrodienes and nitroenynes is described. By a design of the substrate and a fine tuning of the reaction conditions it is possible to selectively form the 1,4 or 1,6 adduct. The same combination of catalyst, copper source and a ferrocene based phosphine ligand afforded enantioselectivities up to 95% and 91% respectively.

[1] Tissot Matthieu, Daniel Müller, Sébastien Belot, Alexandre Alexakis *Org. Lett.* **2010**, submitted.

Organic Chemistry **311**

Creation of quarternary stereogenic centers via copper-catalyzed asymmetric conjugate addition of alkenyl alanes to α, β-unsaturated cyclic ketones

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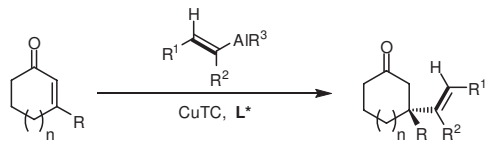
Department of Organic Chemistry, University of Geneva,

30 Quai Ernest Ansermet, 1211 Geneve 4, Switzerland

Despite the tremendous research efforts that have been made in the field of enantioselective creation of quarternary stereogenic centres via conjugated addition [1][2], the formation of all-carbon quaternary stereogenic centres bearing a vinyl-substituent still remains a challenge. From our experiences in this field of chemistry we envisaged the use of vinylaluminum reagents to overcome the well-known reluctance of these sterically hindered Michael acceptors to undergo intermolecular conjugated addition.



After extensive optimization of the reaction conditions we managed to add different aluminum alkenes to substituted Michael acceptors with good yields and high enantioselectivities.

[1] M. d'Augustin, L. Palais, A. Alexakis, *Angew. Chem. Int. Ed.* **2005**, *44*, 1376.
[2] C. Hawner, K. Li, V. Cirriez, A. Alexakis, *Angew. Chem. Int. Ed.* **2008**, *47*, 8211.

Organic Chemistry **312**

Asymmetric Bromine Lithium exchange

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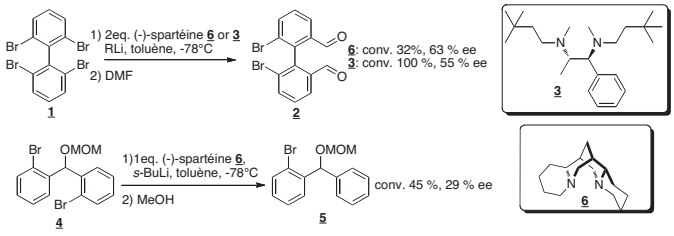
The first asymmetric bromine lithium exchange was described in 2009, with the publications of parallel works of the professors Alexakis[1], Kagan [2] and Brückner [3].

Previous work proved that it was necessary to use, at low temperature in toluene, some diamine to observe a Br-Li exchange. In our laboratory, we decided to use C_2 symetric chiral diamines **3**, **6** to realize this exchange enantioselectively.



Moderate ee for the asymmetric Br-Li exchange were obtain . Actually, our laborarory work on th elaboration of new C_2 symmetric diamine and optimization of the conditions to increase the ee and use different substarte to realize this exchange.

[1] A. Alexakis *et al.* , *Tetrahedron: Asymmetry* , **2009**, *20*, 1004–1007
[2] H.B. Kagan *et al.*, *Tetrahedron Asymmetry*, **2008**, *19*,2666-2677
[3] R.Brückner *et al.*, *Chem. Eur. J.*, **2009**, *15*, 6688-6703

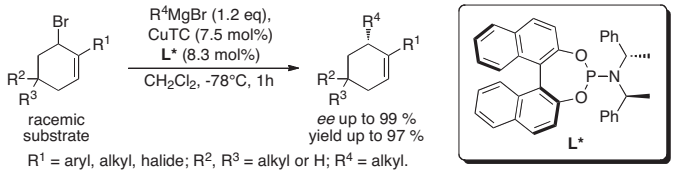
Organic Chemistry **313**

Dynamic Kinetic Asymmetric Transformation in Copper-Catalyzed Allylic Alkylation

Jean-Baptiste Langlois and Alexandre Alexakis

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

The copper-catalyzed asymmetric allylic alkylation (AAA) is one of the most studied reactions in organic chemistry.[1] Copper is particularly known to induce a high γ-selectivity stemming from a S_N2' process. This property has been mainly applied to the alkylation of prochiral substrates leading to the formation of stereogenic centers. However, the use of racemic substrates has been far less studied. In view of the fact that the reductive elimination is assumed to be fast, starting from a racemic substrate should lead to a racemic product. We will present here that an enantioenriched product (up to 99 % *ee*) can be quantitatively obtained using precise allylic substrates.[2] This result represents the application of a Dynamic Kinetic Asymmetric Transformation (DYKAT) as it is well known in Pd AAA.[3] The optimization, the scope and the mechanism of the reaction will be presented.



R^1 = aryl, alkyl, halide; R^2, R^3 = alkyl or H; R^4 = alkyl.

[1] a) A. Alexakis, J. E. Bäckvall, N. Krause, O. Pamies, M. Dieguez, *Chem. Rev.* **2008**, *108*, 2796; b) C. A. Falciola, A. Alexakis, *Eur. J. Org. Chem.* **2008**, 3765.

[2] a) J. B. Langlois, A. Alexakis, *Chem. Commun.* **2009**, 3868 ; b) J. B. Langlois, A. Alexakis, *Adv. Synth. Catal.* **2010**, *352*, 447.

[3] B. M. Trost, *Chem. Pharm. Bull.* **2002**, *50*, 1.

Organic Chemistry **314**

From Azidoproline to Functionalized Collagen Model Peptides

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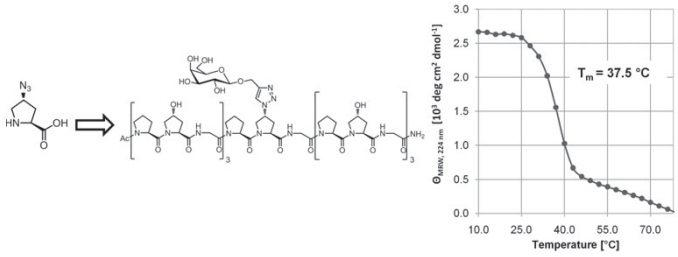
University of Basel, Department of Chemistry,
St. Johanns-Ring 19, 4056 Basel

The stability and many functions of collagen, which is the most abundant protein in mammals, depend to a large extent on functional groups attached to its backbone.[1] Aside from hydroxylations other modifications such as for example galactosylations are known to influence the stability of the collagen triple helix.[2] Thus, for a deeper understanding of the factors that govern the stability of collagen studies on functionalized collagens are important. The collagen single strands consist of repeating Xaa-Yaa-Gly units, among them, the Pro-Hyp-Gly triplet is the most stable and prevalent. Here we present the replacement of Xaa and Yaa residues by azidoprolines that allow for facile functionalization. Furthermore we present the impact of different functionalizations on the triple helix stability. The functionalizations are ranging from differently substituted triazolyl prolines over aminoprolines to differently substituted amidoprolines.



A galactose containing collagen model with a thermal transition at 37.5 °C.

[1] Shoulders, M. D.; Raines, R. T. *Annu Rev Biochem* **2009**, *78*, 929.
[2] Bann, J. G.; Peyton, D. H.; Bachinger, H. P. *Febs Lett* **2000**, *473*, 23

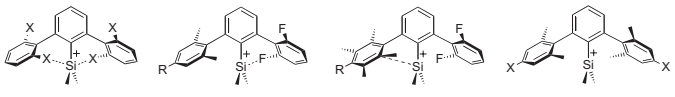
Organic Chemistry **315**

Synthesis of Intramolecularly Stabilized Organosilylium Ions

P. Romanato, A. Linden, K. K. Baldridge,* J. S. Siegel*

Organisch-chemisches Institut der Universität Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

After the evidence for the existence of a free silylium ion in 2002[1], efforts have been made to synthesize analog R_3Si^+ species where the silicon center, although sterically protected, is still available for reactions with small nucleophiles. This project deals with the synthesis of silylium ions bearing a 2,6-diarylphenyl scaffold with different electron demanding flanking rings Ar; varying the strength of Ar→Si^+ coordination would allow the tuning of the acidity at silicon. With this idea in mind we moved from a system with methylated flanking rings,[2] to systems with halogenated flanking rings (**1**): here the halogen lone-pairs pacify the positive charge, with slight enhancement of the Lewis acidity character at silicon. In case of mixed systems, with one methylated and one halogenated flanking ring (**2**, **3**), lone-pair stabilization is more effective than π (Ar) coordination in case of xylene and mesitylene substituents (**2**). Under investigation are now cations with an electron withdrawing element in the para position of the lateral rings (**4**). We are also testing the potential of these silylium ions as Lewis acid catalysts in Mukaiyama aldol additions with encouraging preliminary results.



1 X= F, Cl **2** R= H, CH_3 **3** R= H, CH_3 **4** X= F, Cl

[1] K.-C. Kim, C. A. Reed, D. W. Elliot, L. J. Mueller, F. Tham, L. Lin, J. B. Lambert, *Science* **2002**, *297*, 825.
[2] S.Duttwyler, Q. Do, A. Linden, K. K. Baldridge, J. S. Siegel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1719.

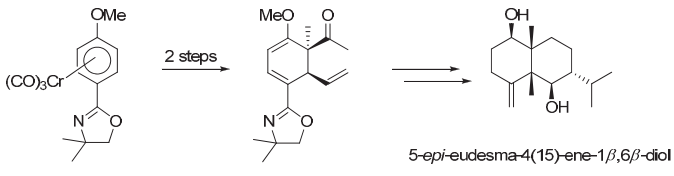
Organic Chemistry **316**

Towards the synthesis of a rare *cis*-eudesmane: the 5-*epi*-eudesma-4(15)-ene-1*β*,6*β*-diol

Zahia Mahiout, Séverine Lavy, Alejandro Pérez-Luna, E. Peter Kündig*

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

An efficient dearomatisation process of [Cr(arene)$(CO)_3$] complexes allows the sequential *trans* addition of a C-nucleophile and a C-electrophile across the arene double bond [1]. Followed by a ring closing metathesis, *cis*-fused ring system bearing a methyl group at one ring junction can be obtained [2]. This strategy will be used to synthesize the 5-*epi*-eudesma-4(15)-ene-1*β*,6*β*-diol [3].



5-*epi*-eudesma-4(15)-ene-1*β*,6*β*-diol

[1] *Transition Metal Arene π-Complexes in Organic Synthesis and Catalysis,* ed. Kündig, E. P, *Topics in Organomeallic. Chemistry*; vol. 7, Springer Verlag, Berlin, Heidelberg, New York, 2004.
[2] Kündig, E. P.; Bellido, A.; Kaliappan, K. P.; Pape, A. R.; Radix, S. *Org. Biomol. Chem.* **2006**, *4*, 342.
[3] Jiang, H. X.; Li, Y.; Pan, J.; Gao, K. *Helv. Chim. Acta* **2006**, *89*, 558.

Organic Chemistry **317**

Kinetic Isotope Effect in the Photolysis of *o*-Nitrobenzyl Derivatives

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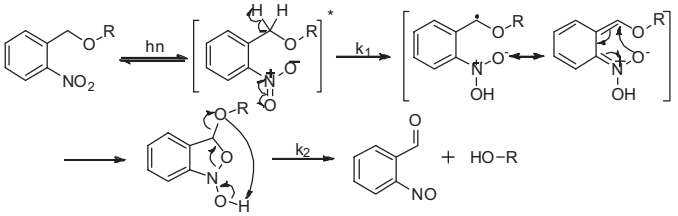
o-Nitrobenzyl derivatives can be used as photolabile protecting groups to protect many different functions, such as amines, acids, alcohols, phosphates and thiols, in very good yields.

It is therefore important to know the cleavage mechanism, which has not yet been completely elucidated, but which probably follows a Norrish type II mechanism involving 4 steps.[1]



The first and the last step involve the rupture of a C-H or an O-H bond. Isotope effects for the substitution of benzylic hydrogen atoms with deuterium atoms were observed.[2] Photolysis under different conditions allowed us to observe a dependence of the isotope effect on the nature of the protected molecule, on the wavelength of irradiation, on the temperature, on the presence of substituents on the aromatic ring and on the time needed to attain a certain conversion. The action of the by product, *o*-nitrosobenzaldehyde, as a photosensitizer for the triplet excited state, was postulated to explain these dependences.

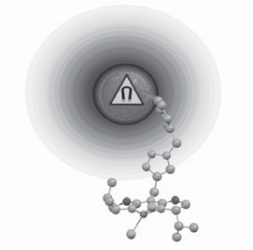
[1] Pelliccioli, A. P.; Wirz, J. *Photochem. Photobiol. Sci.* **2002**, 441-458; Zhang, K., Corrie, J. E. T. *J. Am. Chem. Soc.* **1999**, 121, 5625-5632
[2] Blanc, A.; Bochet, C. G. *J. Am. Chem. Soc.* **2004**, *126*, 7174-7175

Organic Chemistry **318**

Homogeneous Catalysts immobilized on C/Co-Nanoparticles

Alexander Schätz, Evagelos Athanassiou, Robert Grass, Wendelin J. Stark*

* Department of Chemistry and Applied Biosciences, Institute for Chemical and Bioengineering, ETH Zurich, CH-8093 Zurich, Switzerland



Catalysis is among the most important applications within the field of nanoscience. The large surface area of nanoparticles (NPs) qualifies them quite naturally to act either as heterogeneous promotors for catalytic reactions or as a support for homogeneous catalysts. Conventional heterogeneous supports (e.g. polystyrene) allow efficient catalyst recycling via filtration, albeit a substantial decrease in activity is frequently observed. On the other hand, soluble scaffolds usually require a second solvent for the selective precipitation of matrices out of the reaction mixture. NPs are considered a semi-heterogeneous support since they are readily dispersed in common solvents and exhibit an intrinsically high surface area, which is combined with almost homogeneous-like accessibility of the surface-bound catalytic sites. Moreover, particles amenable to magnetic separation do not call for catalyst filtration. We report examples of catalysts supported on highly magnetic C/Co-NPs that delivered superior results than their counterparts immobilized on various conventional supports [1].

[1] A. Schaetz, Robert N. Grass, Q. Kainz, W. J. Stark, O. Reiser, Chem. Mater. **2010**, *22*, 305.

Organic Chemistry **319**

Diazonium chemistry on graphene shows high reactivity towards single layer edges

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[1] Institute of Chemical an Bioengeneering, ETH Zurich, Zurich, Switzerland, [2] Solid State Physics Laboratory, ETH Zurich, Zurich, Switzerland, [3] JARA-FIT and II. Institute of Physics, RWTH Aachen, Aachen, Germany.

Chemical functionalization of graphene with carbon species extends the currently available derivatization methods, namely oxidation of graphene to graphite oxide and hydrogenation of graphene to graphane. Instead of oxygen or hydrogen a carbon atom is reliably attached to the graphene lattice. A previous study[1] has shown the potential for controlled modification of chemical and physical properties of graphene by reaction with a series of diazonium reagents. In the present study[2] we therefore use a combination of atomic force microscopy and confocal Raman spectroscopy to characterize the chemically introduced changes (sp^2 to sp^3) on graphene. These measurements clearly show that single and bi-layer have different reactivities toward the diazonium reagent. This opens the way to chemical distinction between single and bi-layer graphene. In addition the edge of single layer graphene reacts faster than the inner part of graphene flakes thus forming graphene-areas with defined boarders.

[1] F.M. Koehler, N.A. Luechinger, D. Ziegler, E.K. Athanassiou, R.N. Grass, A. Rossi, C. Hierold, A. Stemmer, W.J. Stark, *Angew. Chem. Int. Ed.*, **2009**, 48, 224
[2] F.M.Koehler, A. Jacobsen, K. Ensslin, C. Stampfer, W.J. Stark, in press, *Small*

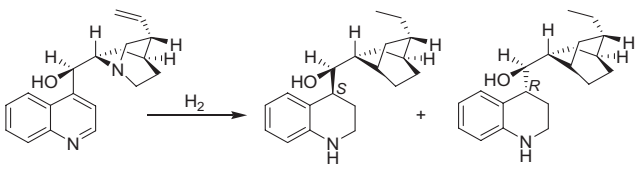
Organic Chemistry **320**

Diastereoselective hydrogenation of cinchonidine – a novel approach to improve the enantioselection on Pt

Erik Schmidt, Tamas Mallat and Alfons Baiker

ETH Zurich, Wolfgang-Pauli-Strasse 10, 8093 Zurich/Switzerland

Diastereoselective hydrogenation of the chiral modifier cinchonidine (Scheme 1) was found to limit the achievable *ee* in the asymmetric hydrogenation of ketones on supported Pt catalysts [1]. The use of model catalysts based on Pt colloids of defined crystallographic face proved the inherent structure sensitivity of this process, which can be used to improve the catalyst performance [1, 2]. Following this side reaction in detail revealed that interaction of substrate and modifier controls the adsorption behavior of the prochiral ketone *and* that of the alkaloid on the metal surface [3].



Scheme 1: Diastereoselective hydrogenation of cinchonidine

For certain substrates the interaction of the hydrogenated product with the modifier is preferred, which poisons the chiral sites and thus reduces the enantioselectivity. Based on the obtained mechanistic insight this limitation could be overcome by the use of achiral additives, which increased the *ee*.

[1] E. Schmidt, A. Vargas, T. Mallat, A. Baiker *J. Am. Chem. Soc.* **2009**, *131*, 12358-12367.
[2] E. Schmidt, W. Kleist, F. Krumeich, T. Mallat, A. Baiker *Chem.-Eur. J.* **2010**, *16*, 2181-2192.
[3] E. Schmidt, T. Mallat, A. Baiker *J. Catal.* **2010** doi: 10.1016/j.j.cat. 2010.03.003.

Organic Chemistry **321**

Asymmetric Catalysis and New Approach in 3,3-Disubstituted Oxindole Synthesis.

Dmitry Katayev, Yi-Xia Jia, and E. Peter Kündig*

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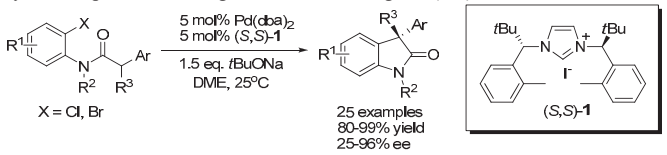
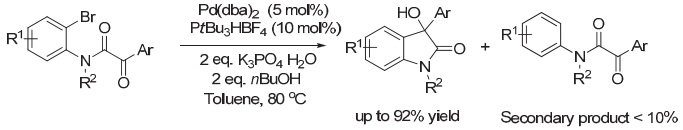
30 quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland

A new family of chiral Enders/Herrmann type *N*-heterocyclic carbene (NHCs) ligands was developed and successfully applied in the asymmetric palladium-catalyzed α-arylation of amides, delivering 3,3-disubstituted oxindoles in high yield and excellent asymmetric efficiency [1]. The critical role of the bulky alkyl group and the *ortho*-aryl substituent at the stereogenic center of the ligand was revealed in the crystal structure of a palladacycle complex containing the chiral *NHC* ligand (*S,S*)-**1** and the substrate.



Moreover, Pd/P*t*Bu$_3$-catalyzed intramolecular nucleophilic addition of aryl halides to α-ketoamides in the presence of *n*BuOH and base has been realized with high yields, providing a new, direct, and efficient synthetic strategy to obtain 3-hydroxyoxindoles [2].



[1] Y.-X. Jia, D. Katayev, G. Bernardinelli, T. Seidel, E. P. Kündig, *Chem. Eur. J.* **2010**, *in press.*
[2] Y.-X. Jia, D. Katayev, E. P. Kündig, *Chem. Commun.* **2010**, *46*, 130-132.

Organic Chemistry **322**

Oxindole Synthesis by Direct Coupling of Csp^2-H and Csp^3-H Centers

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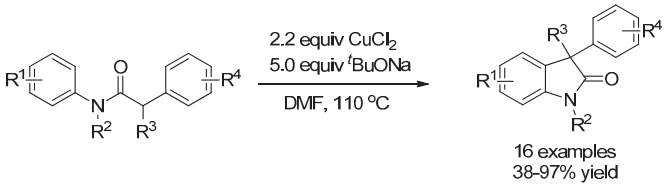
Oxindoles are common and important substructures in natural products and biologically active molecules. A robust, cheap and efficient copper mediated Csp^2-H, Csp^3-H coupling method for the conversion of anilides into disubstituted oxindoles in high yields has been developed in our group [1]. The key step of this transformation is an intramolecular radical addition reaction.



Applying the same protocol, we are currently interested to elaborate the substrate scope by employing heteroaromatic groups (pyridine, furan etc.) in the main skeleton.
An asymmetric variant of this protocol using chiral Lewis acids is under investigation.

[1] Y. X. Jia, E. P. Kündig, *Angew. Chem. Int. Ed.* **2009**, *48*, 1636-1639.

Organic Chemistry **323**

A highly sensitive, excimer-controlled molecular beacon

Sarah M. Biner, S. M. Langenegger, T. Meng, V. L. Malinovskii, R. Häner

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

Molecular beacons (MBs) are specifically designed DNA strands with a stem-and-loop structure used as fluorescence probes in the diagnostic field.[1] The previously investigated MB is selective and highly sensitive towards target sequences due to excimer controlled emission.[2] The excimer emission of the fluorophores (alkynylpyrene, Y) is hereby erased by the quencher molecules (perylenediimide, PDI, E) based on formation of a donor-acceptor (D-A) complex in the stem (see illustration). Spectroscopic investigations (UV/Vis, CD and fluorescence spectra) will be presented.

[1] Tyagi S., Marras S. A. E., Vet J. A. M. and Kramer F. R. Molecular Beacons: Hybridization Probes for Detection of Nucleic Acids in Homogeneous Solutions. www. molecular-beacons.org
[2] Häner R., Biner S. M., Langenegger S. M., Meng T., Malinovskii V. L., *Angew. Chem. Int. Ed.,* **2010**, *49*, 1227–1230.

Organic Chemistry **324**

A New Synthetic Approach to Side Chain-Modified Analogs of Cyclopropyl-Epothilone B

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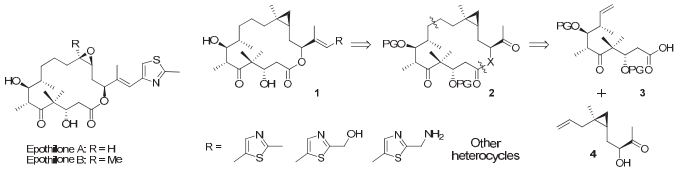
Wolfgang-Pauli-Strasse 10, HCI, CH-8093 Zürich, Switzerland

Epothilones (Epo's; Scheme 1) are microtubule-stabilizing agents with potent *in vitro* and *in vivo* antitumor activity.[1] Initially isolated from the myxobacterium *Sorangium cellulosum* with Epo A and B as the major variants, they quickly established themselves as important lead structures for anticancer drug discovery.[1] Among numerous other modifications,[1] the replacement of the epoxide ring by a metabolically more stable cyclopropane moiety has been shown to be well tolerated or even lead to enhanced cellular potency, and the same is true for a variety of side chain modifications. In a project that ultimately aims at the construction of antibody-drug conjugates we have now prepared a series of side chain-modified analogs of cyclopropyl-Epo B **1** and evaluated their antiproliferative and tubulin-polymerizing activity.

Scheme 1



The synthesis analogs **1** is based on a novel and highly flexible approach that relies on late stage introduction of the side chain through Horner-Wittig-Emmons chemistry and ring closure through RCM (Scheme 1). This contribution will discuss the details of the synthesis of macrolactone **2** from building blocks **3** and **4** and its elaboration into the desired target structures.

[1] K.-H. Altmann et al. *ChemMedChem* **2007**, *2*, 396.

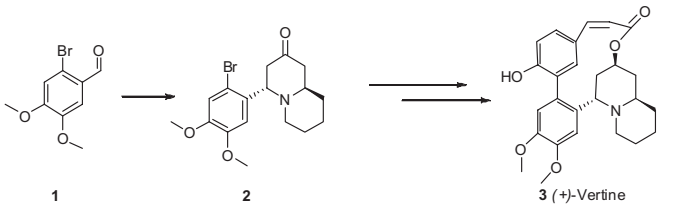
Organic Chemistry **325**

Asymmetric Synthesis of the Lythracea Alkaloid Vertine by RCM

Laetitia Boissarie-Chausset, Roman Àrvai, Graham Cumming and E. Peter Kündig

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

The biphenylquinolizidine alkaloid (+)-Vertine (also called cryogenine) was isolated in 1962 from *Decodon verticillatus (L.) Ell* (*Lythraceae*).[1] This natural product plays a role in glucose level regulation in blood and lowers blood pressure.[2] Its structure contains a 12 membered macrolactone with a Z-alkene, three stereogenic centers, two of which are part of the macrocycle, and an induced chiral aryl aryl axis. These features and the resulting synthetic challenges attracted our interest. We here report the first asymmetric total synthesis of this alkaloid. The synthetic route towards (+)-Vertine includes Pelletierine condensation,[3] Suzuki coupling and diastereoselective reduction. Metathesis then yields **3**. To our knowledge this is the first example of formation of a Z-alkene α to a carbonyl function by metathesis.



[1] J. P. Ferris, *J. Org. Chem*. **1962**, *27*, 2985.
[2] J.B. Harborne, Baxter H. *Phytochemical Dictionary. A Handbook of Bioactive Compounds from Plants*, Taylor & Frost, London. **1983**, 791.
[3] J. Quick, R. Oterson, *Synthesis*. **1976**, 745.

Organic Chemistry **326**

Evaluation of Synthetic Nucleoside Probes for O^6-alkyl-Guanosine DNA Damage

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[1]University of Minnesota, Minneapolis 55455 USA

[2]ETH Zurich, Schmelzbergstrasse 9, CH-8092 Zurich, Switzerland

Despite being formed at low levels and potentially eliminated by enzymatic repair, chemically induced DNA damage in the form of O^6-alkyl-guanosine adducts can lead to mutation and cancer. To test their formation and persistence in the context of genes involved in carcinogenesis, our goal is to develop specific DNA hybridization probes for this class of adducts. The present study focuses on factors influencing DNA duplex stability for DNA adducts paired against synthetic nucleoside probes. Synthetic nucleosides differing in steric properties and hydrogen bond forming capacities were prepared and paired against different DNA adducts. The resulting influences on DNA duplex stability were evaluated by measuring melting temperatures (T_m) of these modified duplexes and comparing them with control sequences. To test the influences of position of modification and/or neighboring base identity, adducts were paired against synthetic nucleosides in systematically designed sequences in which the position of the modified base pair varied. Data regarding the relationship of adduct and nucleoside probe structures, as well as sequence context, with DNA duplex stability will be presented.

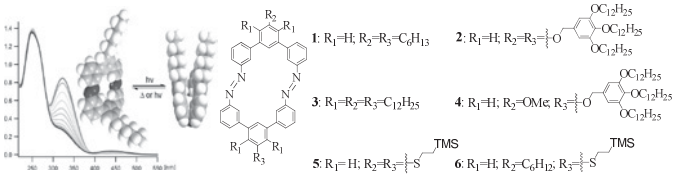
Organic Chemistry **327**

Shape Switchable Azo-Macrocycles

Marcel Müri[1], Marcel Mayor[1], Klaus C. Schuermann[2], Luisa De Cola[2]

[1]University of Basel, Department of Chemistry, St.Johanns-Ring 19, CH-4056 Basel, Switzerland
[2]Westfälische Wilhelmsuniversität Münster, Institut of Physics, Mendelstrasse 7, D-48149 Münster, Germany

The development of photosensitive functional systems which change their chemical and physical properties in response to optical stimuli is currently a topic of interest [1].



The photoinduced reversible *E/Z* isomerisation of azobenzene derivatives provides structural changes. The azo functionalized macrocycles **1-6** combine optically addressable switching units with different substitutions to make symmetric and asymmetric molecules designed for surface deposition. Two rigid semicycles are interconnected by azo groups. All six macrocycles **1-6** display *E*→*Z* photoisomerization upon irradiation at 313 nm. In their photo stationary state, an *E/Z* ratio of 15:85 was observed. The complete back reaction *Z*→*E* required several weeks, indicating the considerable stability of the *Z* isomer. The substituents were carefully chosen for surface functionalization either by absorption on graphite or by a covalent bond between sulphur and a gold surface.

[1] Marcel Müri, Klaus C. Schuermann, Luisa De Cola, Marcel Mayor, *Eur. J. Org. Chem.* **2009**, 2562-2575.

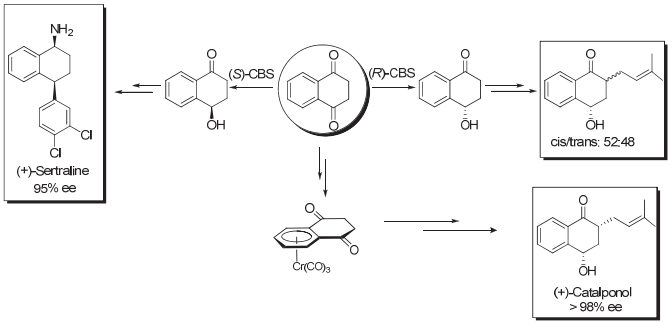
Organic Chemistry **328**

Efficient Asymmetric Syntheses of Sertraline and Catalponol from Tetralin-1,4-dione

Souad Ouizem, Alvaro Enriquez Garcia, Xin Cheng, Patrick Romanens, E. Peter Kündig*

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

CBS mono-reduction of tetralin-1,4-dione [1] leads to highly enantioenriched synthons suitable for short syntheses of biologically active molecules. The *R*-enantiomer provided a rapid access to Sertraline, an antidepressant [2], while the *S*-enantiomer was converted into Catalponol, an antitermitic agent [3]. A more selective route to reach Catalponol in good yield involves temporary complexation of tetralin-1,4-dione to the $Cr(CO)_3$ group [1].



[1] A. E. Garcia, S. Ouizem, X. Cheng, P. Romanens, E. P. Kündig, submitted.
[2] M. Lautens, T. Rovis, *Tetrahedron* **1999**, 55, 8967.
[3] C. A. McDaniel, *J. Chem. Ecol.* **1992**, 18, 359.

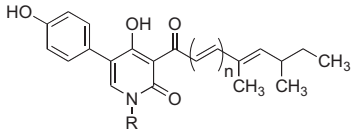
Organic Chemistry **329**

A Unified Approach Towards Pyridone Alkaloids

Henning Jacob Jessen and Karl Gademann

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

Neurodegenerative disorders, in particular Alzheimer's disease, increasingly affect our societies worldwide.[1] One strategy to combat these diseases comprises the regeneration of neuronal networks by stimulation of neurite outgrowth. [2] An attractive approach is based on the search for orally bioavailable small organic molecules that could mimic neurotrophin action.[3] Pyridone alkaloid metabolites – isolated from *Paecilomyces farinosus* – were recently found to be neuroactive. Farinosones A and C induced neurite outgrowth in the PC-12 cell line without displaying cytotoxicity.[4] Structurally related pyridone alkaloids comprise the biochromes pretenellin B, tenellin and bassianin. These have not been evaluated so far for their potential to induce neurite sprouting. We present an efficient unified stereoselective approach to the aforementioned natural products and their enantiomers. Further, a structure-activity relationship study of these compounds in the PC-12 assay will be discussed in detail.



R = H; n = 1: Pre-Tenellin B (**1**)
R = OH; n = 1: Tenellin (**2**)
R = OH; n = 2: Bassianin (**3**)
R = H; n = 3: Farinosone A (**4**)
R = OH; n = 3: Farinosone B (**5**)

[1] Scorer, C. A. *Drug Discovery Today* **2001**, *6*, 1207.
[2] Corcoran, J.; Maden, M. *Nat. Neurosci.* **1999**, *2*, 307.
[3] Pattarawarapan, M.; Burgess, K. *J. Med. Chem.* **2003**, *46*, 5277.
[4] Cheng. Y.; Schneider, B.; Riese, U.; Schibert, B.; Li, Z.; Hamburger, M. *J. Nat. Prod.* **2004**, *67*, 1854.
[5] Jessen, H. J.; Barbaras, D.; Hamburger, M.; Gademann, K. *Org. Lett.* **2009**, *11*, 3446.

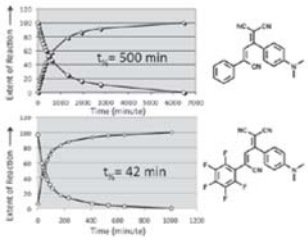
Organic Chemistry **330**

Towards Regioregular Polymers and Oligomers: The [2+2] Cycloaddition Approach

Fabio Silvestri, Markus Jordan, Kara Howes,Milan Kivala and François Diederich

Laboratorium für Organische Chemie, ETH, 8093, Zürich, Switzerland

Defect-free and regioselective formation of regular [AB]-type oligomers and polymers (oligomers and polymers consisting of alternate electron donor (D) and electron acceptor (A) units, featuring intermolecular charge transfer (CT), remains ambitious. In this contribution we present preliminary results about a [2 + 2] cycloaddition type polymerization, with particular attention to the reactivity of the electron-rich and electron poor moiety (i.e. Figure 1).



Activation of the electron-deficient part with electron-withdrawing groups is the key point of the presented method, as well as better understanding of how to improve the general reactivity (beside the polymerization ratio) and decrease the polydispersivity.

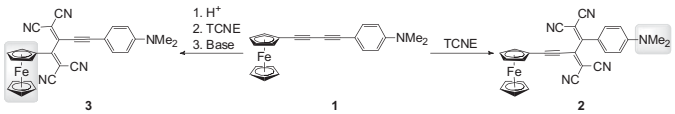
[1] A. Ajayaghosh, *Chem. Soc. Rev.* **2003**, *32*, 181–191.
[2] Z. Zhu et al., *Macromolecules* **2007,** *40,* 1981-1986.
[3] Diederich et al, *Acc. Chem. Res.* **2009**, 42, 235-248; *Angew. Chem. Int. Ed.* **2007**, 46, 6357–636.

Organic Chemistry **331**

Regioselective Addition of TCNE and TCNQ in Donor-substituted 4-Ferrocenylbuta-1,3-diynes

M. Jordan[1], M. Kivala[1], C. Boudon[2], J.-P. Gisselbrecht[2], P. Seiler[1], W. B. Schweizer[1], F. Diederich[1]

[1]Laboratory of Organic Chemistry, ETH Zürich, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich
[2]Laboratoire d'Electrochimie et de Chimie Physique du Corps Solide, UMR 7177, CNRS, Université de Strasbourg, 4, rue Blaise pascal, F-67000 Strasbourg



The electron acceptors 1,1,2,2-tetracyanoethylene (TCNE) and 7,7,8,8-tetracyanoquinodimethane (TCNQ) undergo a [2+2] cycloaddition and subsequent retro-electrocyclization with donor-substituted acetylenes to form new strong charge transfer chromophores in a "click"-type manner.[1] In the cycloaddition step, a difference was found for the two donors in unsymmetrically substituted buta-1,3-diynes (e.g. **1**) with respect to their activation of the neighboring C–C triple bond. Whereas the activation degree of the triple bonds by the donors is reflected by the Hammett constants of the latter,[2] $E_{ox,1}$ should not be used as a measure for the donating ability in this reaction. In the reaction of **1**, for example, TCNE selectively added to the acetylene moiety next to the more activating dimethylanilino donor to give solely **2**. After "switching off" the amino donor function by protonation, TCNE added to the triple bond next to the ferrocene which led to the exclusive isolation of **3** after neutralization. The effect of different donors was also checked in TCNQ additions to the same substrates, and the properties of the resulting donor-acceptor-functionalized systems were compared.

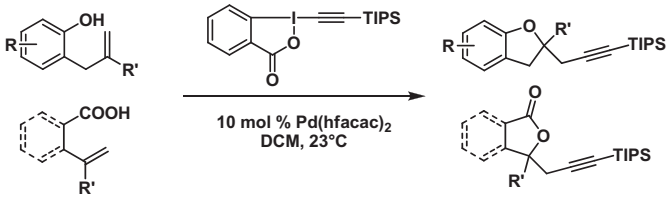
[1] T. Michinobu, C. Boudon, J.–P. Gisselbrecht, P. Seiler, B. Frank, N. N. P. Moonen, M. Gross, F. Diederich, *Chem. Eur. J.* **2006**, *12*, 1889.
[2] C. Hansch, A. Leo, R. W. Taft, *Chem Rev.* **1991**, *91*, 165.

Organic Chemistry **332**

Catalytic Oxyalkynylation of non-activated Olefins with Alkynyl Periodinane Reagents

Stefano Nicolai, Prof. Dr. Jérôme Waser*

Laboratory of Catalysis and Organic Synthesis, EPFL Lausanne, Switzerland



The Wacker cyclization is an effective method to access oxygen- and nitrogen-containing heterocycles.[1] Replacing the final β-hydride elimination through the reaction of the intermediate Pd σ-alkyl complex with an electrophile/oxidant has been extensively studied for the synthesis of new C-C, C-X, C-O and C-N bonds. However, C-C bond formation has been limited to SP^2 hybridized vinyl, carbonyl and aryl groups.

The first example of intramolecular Pd-catalyzed oxyalkynylation of non-activated alkenes using alkynyl periodinanes is reported herein.[2] Good yields were obtained with both phenols and aliphatic or aromatic carboxylic acids under operator-friendly conditions (room temperature, technical solvents, under air) to give functionalizable dihydro benzofurans and lactones. The use of a benziodoxolone-based reagent was essential for efficient acetylene transfer. Finally, recent investigations toward extension of the scope of the reaction and its application in more complex settings will be presented.

[1] Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285.
[2] Nicolai, S.; Erard, S.; Fernández González, D.; Waser. J. *Org. Lett.*, **2010**, *12*, 384.

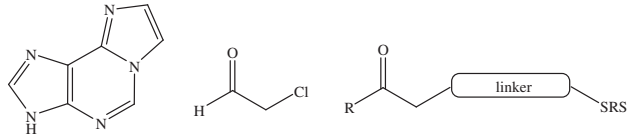
Organic Chemistry **333**

Site-specific incorporation of ε-adenine into DNA

David Egloff, Eva Freisinger*

University of Zurich, Institute of Inorganic Chemistry, Winterthurerstr. 190, 8057 Zürich, Switzerland

Etheno-bridged nucleobases such as ε-adenine (**1**), ε-cytosine and ε-guanine belong to a class of DNA lesions, which inhere miscoding properties and which are formed in different tissues upon exposure to carcinogens like vinyl chloride and urethane. Synthetically, etheno derivatives are usually obtained by the reaction of the nucleotide with chloroacetaldehyde (**2**), a metabolite of vinyl chloride. These modified bases, especially ε-adenine, attracted attention due to their fluorescence properties and the possible use as fluorescent probes [1]. Although some promising strategies have been developed [2, 3], the site-specific incorporation of ε-bases into DNA still suffers from low yields and extensive procedures.



1 **2** **3**

Our goal is to establish an efficient method for the site-specific incorporation of ε-adenine into single stranded DNA by the use of a short recognition sequence (SRS) that is linked to a chloroacetaldehyde analogue (**3**).

[1] K.V. Petrova, R.S. Jalluri, I.D. Kozekov, C.J. Rizzo, *Chem. Res. Toxicol.* **2007**, *20*, 1685.
[2] V.M. Carvalho, D. Gasparutto, P. Di Mascio, M.H.G. Medeiros, J. Cadet, *Bioorg. Med. Chem.* **2003**, *11*, 2445.
[3] A. Kobori, J. Morita, M. Ikeda, A. Yamayoshi, A. Murakami, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3657.

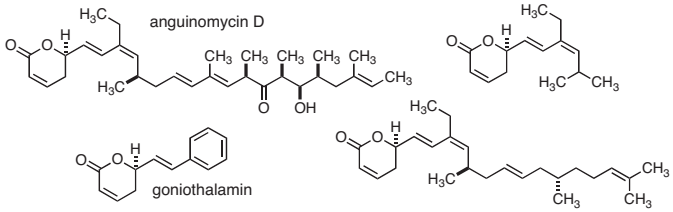
Organic Chemistry **334**

Controlling Protein Localization in Living Cells by Small Molecules

Jean-Yves Wach[1], Simone Bonazzi[2], Stephan Güttinger[3], Ulrike Kutay[3], Karl Gademann[1]

[1]University of Basel, Department of Chemistry, 4056 Basel, Switzerland
[2]Harvard University, Department of Chemistry & Chemical Biology, MA02318 Cambridge, USA
[3]ETH Zürich, Institut für Biochemie, 8092 Zürich, Switzerland

Natural products represent a major source of new drugs, in particular in the treatment of cancer. Derivatives obtained through synthesis can often display improved potency and selectivity[1] or serve as tool compounds for biological investigations[2].



We investigated the mode of action of the natural lactones anguinomycin C and D[3] and goniothalamin[4] by using total synthesis, design of analogs and biological evaluation of the inhibition of nucleocytoplasmic transport. Current studies are aimed towards the control of the localization of proteins in cells by small molecules.

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[2] Burke, M. D.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 46.
[3] Bonazzi, S.; Eidam, O.; Güttinger, S.; Wach, J.-Y.; Zemp, I.; Kutay, U.; Gademann, K. *J. Am. Chem. Soc.* **2010**, *132*, 1432.
[4] Wach, J.-Y.; Güttinger, S.; Kutay, U.; Gademann, K. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 2843.

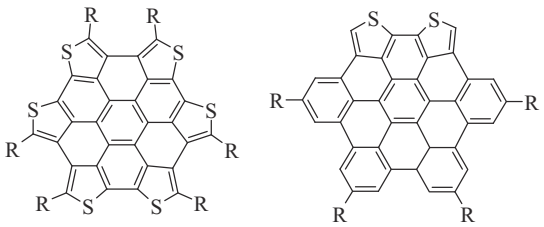
Organic Chemistry **335**

Synthesis of novel thienyl-functionalised polybenzenes

Deborah Gusmeroli, Titus A. Jenny*

Université de Fribourg, Chemin du Musée 9, 1700 Fribourg, Switzerland

Carbaceous fully-conjugated polybenzene compounds are well-known building blocks for materials due to their particular conductivity and self-aggregation behaviour. By inserting thienyl-fused moieties into the aromatic backbone it is possible to increase the charge carrier properties and hence the conductivity.[1] In addition these less symmetric discotic units should be able to aggregate with a well-defined orientation.[2] The peripheral functionalisation will complete the structure giving solubility or isolation as desired.[3]



The syntheses of both types of compounds rely on a modification of the classical chemistry exploited in the well-known synthesis of hxabenzocoronene structures. The polyaromatic core is built stepwise either via cyclotrimerisation or by Diels-Alder reaction of the corresponding tetraaryl cyclopentadienone and bisthienylacetylene. A final cyclodehydrogenation reaction gives the final fully-conjugate aromatic systems.

[1] J. L. Brusso et al, *Chemistry of Materials.* **2008**, *20*, 2084.
[2] X. Feng et al, *Nature Materials*, **2009**, *8*, 421
[3] O. Aebischer et al, *J. Material Chemistry*, **2007**, *17*, 1262

Organic Chemistry **336**

Synthesis of a *C*-Nucleotide modeled on 2,4-Diaminopyrimidine (D) as Nucleobase

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DNA with its four building blocks A, C, G, and T is the carrier of genetic information in all known living organisms no matter how different they are.

From which precusor did these nucleotides develop? This is a fundamental question in origin of live science.

A pre-biotic DNA alphabet consisting of only pyrimidine bases has been proposed (Figure 1) [1]. This alphabet contains a nucleotide (D) which easily can form C and U by hydrolysis (Figure 2).

To investigate this hypothesis, *C*-nucleotide D has been synthesised and incorporated into oligonucleotides. Among other results, this showed an influence of the nearest neighbours of **D** in the oligonucleotides on the base pairing abilities [2]. To quantify this influence, an abasic site phosphoramidite has been incorporated into the same sequence, replacing **D**.

Furthermore, additional efforts in optimising and scaling up the synthesis of **D** as well as in finding a way to synthesise *C*-nuclotide **E** are undertaken.

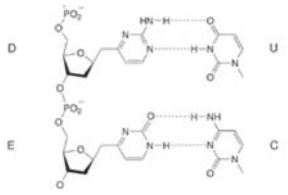

Figure 1: DNA, based on pyrimidine only.

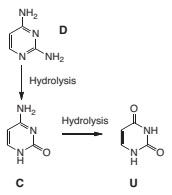

Figure 2: Hydrolysis of **D**.

[1] J. S. Siegel, Y. Tor *Org. Biomol. Chem.* **2005**, *3*, 1591.
[2] B. Bischof, Dissertation UZH **2009**, 73.

Organic Chemistry **337**

Asymmetric 1,3-Dipolar Cycloadditions of Nitrones to Acrylonitrile with new Ni(II) *Pigiphos*-Type Complexes

Laurence Bonnafoux, Jamal Moussa, Antonio Togni

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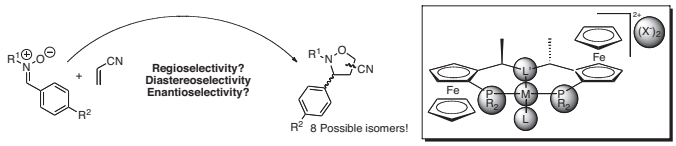
The addition of nitrones to alkenes is a highly challenging reaction in organic chemistry as regio-, diastereo- and enantioselectivity have to be controlled[1].

Our current work focuses on the 1,3-dipolar cycloaddition of nitrones to acrylonitrile. This reaction has been hardly studied[2].



All possible regio- and diastereoisomeric products (R^1= CH_3, Ph, Bn and R^2= OCH_3, CH_3, H, Cl, F, CF_3, NO_2) obtained under thermal conditions were completely characterized and their relative stereochemistry was elucidated by X-ray crystallographic analysis. Optimization of the reaction conditions (solvent, temperature, catalyst loading, metal, counteranion, ligand) was performed. When Ni(II) (*R*)-(*S*)-*Pigiphos* complexes were used, the 3,4-*trans* isomer was obtained as the major product (Selectivity 85:3:8:4) in up to 40%ee.

[1] Jones, R. C. F.; Martin, J. *The Chemistry of Heterocyclic Compounds: A Series of Monographs* **2003**.
[2] a) Shimizu, T.; Ishizaki, M.; Nitada, N. *Chem. Pharm. Bull.* **2002**, *50*, 908. b) Carmona, D.; Lamata, P. M.; Viguri, F.; Rodriguez, R.; Lahoz, F. J.; Fabra, J. M.; Oro, L., A. T*etrahedron: Asymmetry* **2009**, *20*, 1197.

Organic Chemistry **338**

Discovery of Esterolytic Histidine Oligomers Using Peptide Arrays

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Solid-phase synthesis of peptide constructs such as linear, cyclic or dendritic peptides represents one of the most practical entries into synthetic enzyme models. The structure-activity relationships in such peptide constructs are generally complex and their study requires combinatorial chemistry approaches involving the synthesis and screening of large libraries, typically using one-bead-one-compound libraries[1]. Herein we report a simple and practical catalysis screening protocol that allows one to assay peptide arrays prepared by the SPOT-technique on cellulose membranes[2]. The SPOT format delivers spatially encoded libraries which circumvents the problem of bead decoding. In addition assays in the SPOT format are known to be predictive of activities of the peptides in solution for the case of binding to biomolecules. To test the compatibility of SPOT-libraries for catalysis screening we prepared a 192-member library of dendritic and linear analogs of the catalytic peptide dendrimer **A3C** $(AcHT)_8(BHT)_4(BHT)_2BHTNH_2$ (*B*=L-2,3-diaminopropanoic acid) previously identified in a focused structure-activity relationship study of esterase peptide dendrimers and which catalyzes the hydrolysis of fluorogenic 8-acyloxypyrene 1,3,6-trisulfonates with high catalytic efficiency (k_{cat}/k_{uncat} = 90,000) [3] . Catalysis screening of the SPOT library confirmed the high activity of **A3C** over other analogs, providing the first evidence that SPOT library display is favourable for catalysis screening. The screening also pointed to the remarkable esterolytic properties of a simple linear histidine undecapeptide. A closer investigation of histidine oligomers from one to fourteen residues shows that these simple peptides indeed efficiently hydrolyze acyloxypyrene trisulfonates with rate accelerations up to k_{cat}/k_{uncat} = 5,000.

[1] N. Maillard et al., *J. Comb. Chem.* **2009**, *11*, 667-675
[2] R. Frank, *Tetrahedron* **1992**, *48,* 9217-9232
[3] E. Delort et al., *J. Org. Chem.* **2006**, *71*, 4468-4480

Organic Chemistry **339**

Approaches to Rhazinilam Analogue

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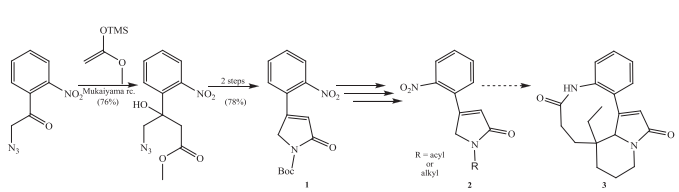
Institut de chimie, Université de Neuchâtel, Av. de Bellevaux 51, 2009 Neuchâtel, Switzerland

R-(-)-Rhazinilam is an unusual monopyrrolic product isolated from nature in 1973.[1] The synthesis and properties of rhazinilam has been studied for more than 35 years.[2] This alkaloid shows significant *in vitro* cytotoxicity, but no activity was found *in vivo*.[3] Our synthetic strategy is to replace, in the first time, the pyrrole ring by a corresponding pyrrole-2(5*H*)-one ring[4] using Mukaiyama crossed aldol reaction followed by Staudinger reaction. The planned synthesis of rhazinilam analogues of type **3** from *N*-acylated pyrrolone **2** should be available using the well-known strategy.[5]



[1] H. H. A. Linde, *Helv. Chim. Acta* **1965**, *48*, 1822.
[2] I. Kholod, R. Neier, *Targets in Heterocyclic Systems* **2009**, in press.
[3] O. Baudoin, D. Guénard, F. Guéritte, *Mini-Rewiews in Organic Chemistry* **2004**, *1*, 333.
[4] O. Vallat, A.-M. Buciumas, A. Neels, H. Stoeckli-Evans and R. Neier (2008. in preparation).
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Organic Chemistry **340**

Selective Rh-Catalyzed Domino C–H Activation/Annulation Sequence

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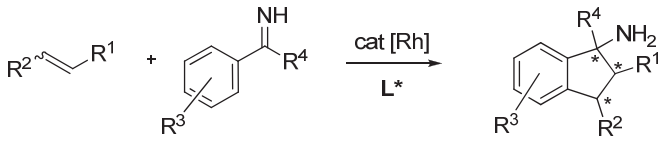
Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland

Transition-metal catalyzed cascade reaction sequences have emerged as powerful strategy for the rapid assembly of highly complex structures starting from widely available substrates [1]. C–H activation is particularly interesting to initiate such sequences because of its economic and ecological advantages [2]. We investigated reaction conditions that allow the enantioselective synthesis of tertiary carbiamines via Rh-catalyzed C–H activation annulation pathway. We report our initial results towards this goal.



[1] L. F. Tietze, G. Gericke, *Domino Reactions in Organic Synthesis*, Wiley, New York, **2006**.
[2] For a review on rhodium-promoted C–H activations see: D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624.

Organic Chemistry **341**

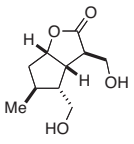
Enantioselective Total Synthesis of Gelsemiol and Biological Evaluation of its Neuritotrophic Properties

Massimo Binaghi, Patrick Burch and Karl Gademann*

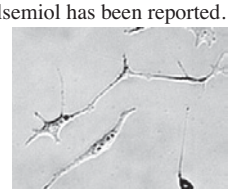
Department of Chemistry, University of Basel, St. Johanns-Ring 19 CH- 4056 Basel, Switzerland

Gelsemiol is a natural product belonging to the family of iridoids. It was isolated from *Gelsemium sempervirens*[1] and *Verbena littoralis* among others.[2] Gelsemiol markedly enhanced the activity of NGF, increasing the proportion of neurite-bearing cells and the extension of the neurite length.[2,3]

With 5 stereocenters within a 10 carbon framework, this bicyclic lactone possesses a significant structural complexity. So far, only few enantioselectives synthetic approaches to structurally related iridoids have been published, but no total synthesis of gelsemiol has been reported.



Gelsemiol



Potentiating Neurite Outgrowth

In this communication, we will report the first enantioselective total synthesis of gelsemiol, which is practical and efficient (10 steps, 15% overall yield). Biological evaluation of the target and close analogs in the PC-12 cellular assay will be presented.

[1] Jensen, S. N.; Kirk O.; Nielsen B.J.; Norrestam R. *Phytochemistry* **1987**, *26*, 1725.
[2] Yushan, L.; Yasushi, O. *J. Pharm. Soc. Jap.* **2004**, *124*, 417.
[3] Li, Y-S.; Matsunaga K.; Kato R.; Ohizumi Y. *J. Pharm. Pharmacol.* **2001**, *53*, 915.

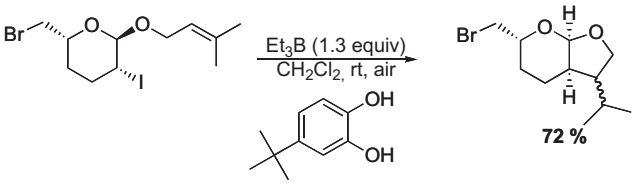
Organic Chemistry **342**

Catechols as Reducing Agents in Radical Chain Reactions: The Reduction of Alkyl Iodides

Guillaume Povie, Leigh Ford, Davide Pozzi, Giorgio Villa and Philippe Renaud*

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

Catechols are strong antioxidants: they rapidly transfer hydrogen atom to a wide range of radicals, and generally disrupt chain processes via recombination reactions of the stabilized aryloxy radical. We recently showed that their strong hydrogen atom donor ability could be used in combination with organoboranes in an efficient chain process.[1] The present study represents the application of this inexpensive method to the selective reduction of alkyliodides.



The mechanism is presented, and the scope and limitations of this mild, tin-free radical reduction are discussed.

[1] G. Povie, G. Villa, L. Ford, D. Pozzi, C.H. Schiesser, P. Renaud, *Chem. Commun*. **2010**, *46*, 803–805.

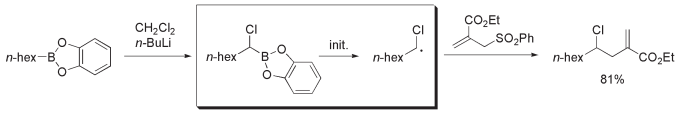
Organic Chemistry **343**

Functionalised *B*-Alkylcatecholboranes as Radical Precursors

Jacqueline Habegger, Monique Lüthy, Guillaume Povie, Philippe Renaud*

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

In previous studies we have shown that *B*-alkylcatecholboranes are efficient alkyl radical precursors.[1] The use of α-functionalised alkylcatecholboranes in radical reactions would enable the formation of more sophisticated products. Here we present a new methodology involving Matteson homologation [2] and a variety of radical transformations as one-pot processes.



[1] A. P. Schaffner, P. Renaud, *Eur. J. Org. Chem.* **2004**, 2291.
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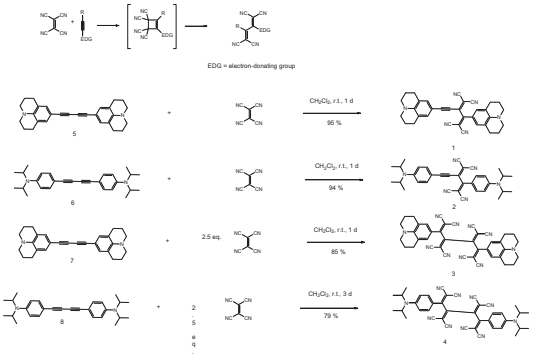
Organic Chemistry **344**

Octacyano-[4]dendralenes: a New Class of Cyano-Rich Organic Super-Acceptors

Benjamin Breiten, Yi-Lin Wu and François Diederich

Laboratorium für Organische Chemie, Department of Chemistry and Applied Biosciences, ETH-Zürich, CH-8093 Zürich, Switzerland

Among the large number of strong organic acceptors that have been described to date, cyano-based derivatives represent the most prominent class of compounds for optoelectronic device applications. In 2005 we showed that alkynes, substituted by a variety of organic donors, generally undergo facile, high-yielding [2+2] cycloaddition with TCNE, followed by cycloreversion of the initially formed cyclobutenes, to give nonplanar donor-substituted TCBDs, such as **1**–**2**. Recently, we could show that TCNE undergoes a second [2+2] cycloaddition to "electronically confused" alkynes bearing one electron-donating group and one electron-withdrawing group, yielding TCNE bis-adducts **3**–**4** (Scheme 1). Despite the two donor moieties, bisadducts **3**–**4** are potent electron acceptors that compete with TCNE and TCNQ in their ease of reversible electron uptake.

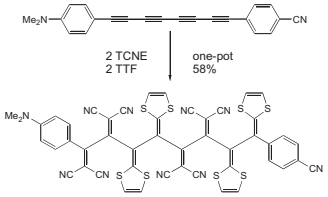


Organic Chemistry **345**

Synthesis and Studies of Chiral and Achiral AB–Type Oligomers with a Dendralene-Type Backbone

Jayamurugan, G.,[1] Frank, B. B.,[1] Kivala, M.,[1] Schweizer, W. B.,[1] Blanco, B. C.,[1] Breiten, B.,[1] Tykwinski, R. R.,[2] Jahnke, E.,[2] Boudon, C.,[3] Gisselbrecht, J. -P.,[3] Diederich, F.[1]

[1]Laboratory of Organic Chemistry, ETH-Zurich, CH-8093 Zürich
[2]Friedrich-Alexander-Universtät, 91054 Erlangen
[3]Université de Strasbourg, F-67000 Strasbourg (France)



A wide variety of AB-type oligomers containing donor-substituted 1,1,4,4-tetracyanobutadienes (TCBDs) and 1,2-bis(1,3-dithiol-2-ylidene)ethanes have been synthesized by [2+2] cycloadditions between tetracyanoethylene (TCNE) and donor-substituted alkynes, followed by electrocyclic ring opening of the initially formed cyclobutenes. TTF reacts in a similar way with electron-deficient alkynes. These sequential one-pot transformations are strictly electronically controlled and provide a new access to [AB]-type oligomers with dendralene-type backbones. The new multivalent systems showed complex conformational equilibria in solution as characterized by CD spectra of the chiral [AB]-type oligomers. Electrochemical studies by cyclic voltammetry and rotating-disk voltammetry showed large cathodic shifts of the first oxidation potentials for some of the chiral and achiral [AB]-type oligomers due to sterically enforced π-deconjugation of the acceptor and donor moieties. The intramolecular CT interactions and the third-order optical nonlinearity in these new push-pull type D–A chromophores were studied by UV-Vis spectra and degenerate four-wave mixing, respectively.

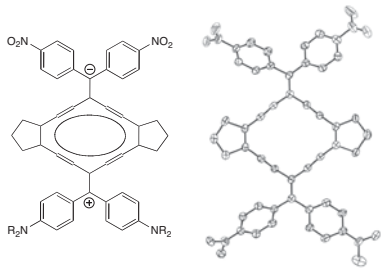
Organic Chemistry **346**

Proaromaticity: A Design Principle for Efficient Charge-transfer

Yi-Lin Wu[1], Filip Bureš[2], Peter D. Jarowski[1], W. Bernd Schweizer[1], François Diederich[1]

[1]Laboratory of Organic Chemistry, ETH Hönggerberg, CH-8093 Zürich
[2]Institute of Organic Chemistry and Technology, University of Pardubice, CZ-53210 Pardubice

We present a series of topologically related push-pull chromophores with non-conjugated, oligoenic, or radiaannulenic π-spacers. Analysis of IR and ^{1}H NMR spectra in conjunction with molecular structures determined by X-ray diffraction shows that these push-pull molecules have significant charge-separated ground states. This feature results in small optical gaps (near IR region) and diatropic magnetic environments inside the carbocycles, as suggested by nucleus-independent chemical shift (NICS) calculations. Utilizing such concept, the first proaromatic carbomacrocycle was synthesized.



Organic Chemistry **347**

Ureaphosphines: New P,O Ligands for the Iridium Catalyzed Asymmetric Hydrogenation of Various Olefins

Denise Rageot and Andreas Pfaltz

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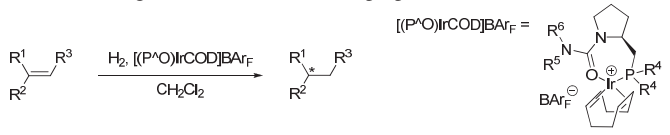
Iridium complexes with chiral P,N ligands derived from amino acids are highly efficient catalysts in the asymmetric hydrogenation of a broad range of substrates, with generally excellent enantioselectivities.[1] However, no catalysts based on P,O ligands have been described so far. Taking advantage of the naturally occurring "chiral pool", we have synthesized a library of simple P,O ligands derived from *L*-proline in order to evaluate their efficiency in the asymmetric iridium catalyzed hydrogenation of olefins.
X-ray crystallography of the resulting iridium complexes showed these ligands to chelate in a bidentate fashion to iridium(I). Thus, *L*-proline has proved to be a highly convenient modular scaffold to synthesize P,O ligands with a wide range of steric and electronic properties.



We found these complexes to be active and selective in the iridium catalyzed hydrogenation of a range of unfunctionalized and functionalized trisubstituted olefins. Depending on the substituents in the ligand and the structure of the tested substrate, enantioselectivities of up to 99% *ee* could be achieved. The synthesis of these P,O ligands and their application in hydrogenation studies will be presented.

[1] S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res.* **2007**, *40*, 1402.

Organic Chemistry **348**

Ionic Functional Protecting Groups for Peptide Synthesis

Benjamin W. Hankeln,[1] Thomas Vorherr,[2] Fritz Dick,[2] Helma Wennemers[1]

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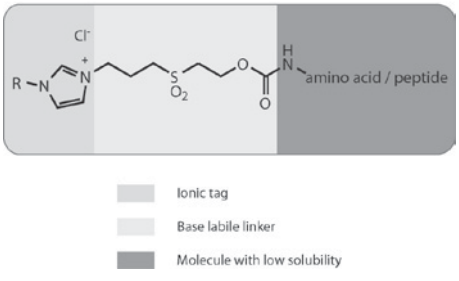
[2]BACHEM AG, Hauptstrasse 144, 4416 Bubendorf, Switzerland

We present newly designed ionic functional protecting groups (fpg) to facilitate the synthesis and purification of peptides. Their design is derived from ionic liquids and common protecting group schemes. In general they consist of an ionic tag and a linker.
The main goal is to increase the solubility of peptides to allow for the purification of peptides that are otherwise too insoluble for purification by HPLC. For example, a base labile linker is placed between the ionic tag and the N-terminus of the peptide. The observed increase in the solubility of a simple test peptide by attaching the ionic tag is strikingly high.
The presentation will provide details on the synthesis of the peptide-ionic tag conjugate, its purification and the removal of the fpg.



[1] a) J.W. Hojfeldt, K.V. Gothelf, *J. Org. Chem.* **2006**, *71*, 9556-9559
b) W. Miao, T.-H. Chan, *J. Org. Chem.* **2005**, *70*, 3251-3255
[2] For other ionic protecting groups see also: K. Wahlström, A. Undén, *Tetrahedron Lett.* **2009**, *50*, 2976-2978 and papers cited therein.

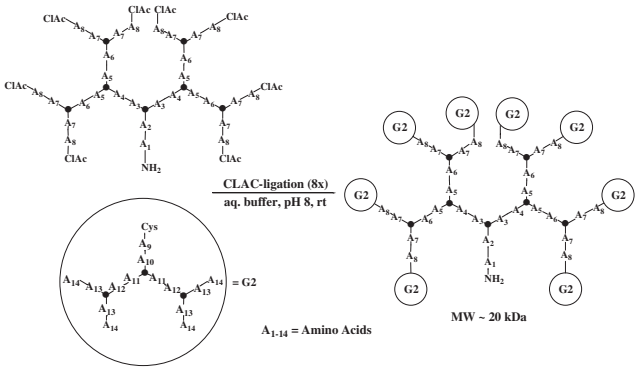
Organic Chemistry **349**

Convergent Synthesis of Peptide Dendrimers by the CLAC (Chloroacetyl) Ligation

Nicolas A. Uhlich, Tamis Darbre, Jean-Louis Reymond*

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

Herein we report the convergent synthesis of large, protein-sized 4th and 5th generation peptide dendrimers by the convergent multiple (up to 8x) CLAC (chloroacetyl) ligation of 2nd and 3rd generation peptide dendrimers. In the CLAC ligation, dendrimers with a C-terminal cysteine residue at their core couple in multiple copies by substitution of the chlorine atom at the multiple chloroacetylated N-termini of another peptide dendrimer. This ligation does not require special building blocks or catalysts and provides products in high yields and purities. The method opens the way to the investigation of large peptide dendrimers as protein and enzyme models [1,2].



[1] Review: T. Darbre, J.-L. Reymond, *Acc. Chem. Res.* **2006**, *39*, 925.
[2] N. A. Uhlich, A. Natalello, R. U. Kadam, S. M. Doglia, J.-L. Reymond and T. Darbre, *ChemBioChem* **2010**, *11*, 358.

Organic Chemistry **350**

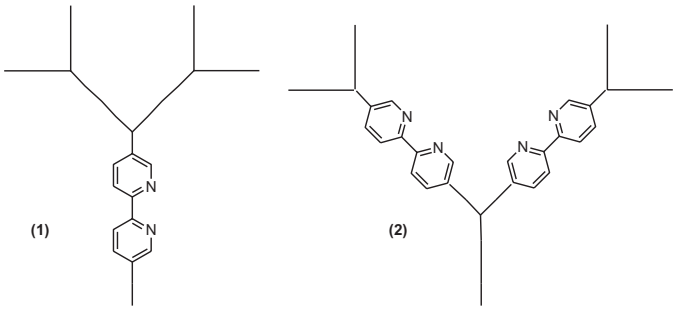
Bipyridyl-based dendrimeric assemblies for transition metal complexation

Piero Geotti-Bianchini, Nicolas A. Uhlich, Tamis Darbre, Jean-Louis Reymond

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

We have recently reported[1] the synthesis of a combinatorial library of peptide dendrimers carrying a bipyridyl-derived amino acid (Bpy) in the focal point (**1**). The ability of such Bpy-containing dendrimer to bind Fe(II) is strongly modulated by the properties of the amino acid residues in the sequence.

We have now prepared dendrimers carrying two Bpy residues, one in each of the two first generation branches (**2**). The presence of two bidentate ligands in the same molecule strengthens metal binding.



[1] N. A. Uhlich, P. Sommer, C. Bühr, S. Schürch, J.-L. Reymond, T. Darbre, *Chem. Commun.* **2009**, 6237.

Organic Chemistry **351**

Synthetic and Kinetic Understanding of Sulfide Oxidation for Fast Transfer from Batch to Micro Reactor

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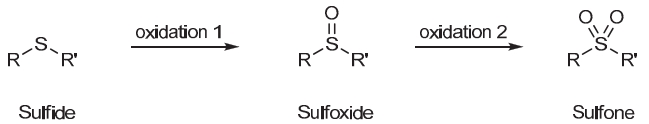
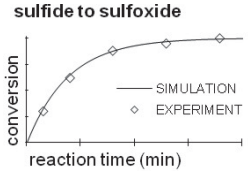
[1]Ecole d'ingénieurs et d'architectes de Fribourg, cp 32, 1705 Fribourg
[2]HE-SO Valais/Sion, 1950 Sion

The oxidation of sulfides to sulfoxides is critical regarding potential over-oxidation to the corresponding sulfone and thermal safety problems associated with the reagents typically used.



We screened several oxidation methods and for the *green* oxidant H_2O_2 in THF and in AcOH the kinetic parameters and thermal safety data were determined by RC-1 and DSC studies. These data were used for simulation of the continuous process and to allow a smooth and fast transfer into the micro reactor system.



The experimental results from the oxidation reaction in the micro reactor confirmed the kinetic simulation and for the fast reaction in AcOH a positive mixing effect could be observed.

[1] T. Noguchi, Y. Hirai, *Chem. Commun.,* **2008**, 3040-3042
[2] Golchoubian, H.; Hosseinpoor, *Molecules* **2007**, *12*, 304-311

Organic Chemistry **352**

C-C cross-coupling reactions catalyzed by an aminophosphine based pincer complex of palladium – Part 1

Christian M. Frech[1], Jeanne L. Bolliger[1]

[1]University of Zürich, Winterthurerstrasse 190, 8057 Zürich

Palladium-catalyzed cross-coupling reactions belong nowadays to the most important C-C bond forming reactions in organic chemistry. Although recent developments have led to a considerable increase in the activity of Heck, Sonogashira and Suzuki catalysts e.g. of which some allow the use of sterically hindered substrates and even aryl chlorides occasionally at room temperature, their syntheses are often time consuming, difficult, and/or require the use of expensive starting materials. Furthermore, many suffer from their poor thermal stability, low functional group tolerance and/or sensitivity towards both, air and moisture, and therefore require inconvenient inert-atmosphere techniques for their successful use, which strongly limits their applicability in industrial processes, for example.

We recently reported the short and simple synthesis of the aminophosphine-based pincer complex $[Pd(Cl)(C_6H_3(NHP(piperidinyl)_2)_2]$ (**1**), which was shown to exhibit excellent activity in various C-C cross-coupling reactions.[1-4]

The synthesis and catalytic performance of **1** in C-C cross-coupling reactions will be presented in consecutive two parts.

[1] Bolliger, J. L., Blacque, O., Frech, C. M.* *Angew. Chem., Int. Ed.* **2007**, *46*, 6514.
[2] Bolliger, J. L., Blacque, O., Frech, C. M.* *Chem. Eur. J.* **2008**, *14*, 7969.
[3] Bolliger, J. L., Frech, C. M.* *Adv. Synth. & Catal*. **2009**, *351*, 891.
[4] Bolliger, J. L., Frech, C. M.* *Adv. Synth. & Catal*. **2010**, *in press*.

Organic Chemistry **353**

C-C cross-coupling reactions catalyzed by an aminophosphine based pincer complex of palladium – Part 2

Jeanne L. Bolliger[1], Christian M. Frech[1]

[1]University of Zürich, Winterthurerstrasse 190, 8057 Zürich

Palladium-catalyzed cross-coupling reactions belong nowadays to the most important C-C bond forming reactions in organic chemistry. Although recent developments have led to a considerable increase in the activity of Heck, Sonogashira and Suzuki catalysts e.g. of which some allow the use of sterically hindered substrates and even aryl chlorides occasionally at room temperature, their syntheses are often time consuming, difficult, and/or require the use of expensive starting materials. Furthermore, many suffer from their poor thermal stability, low functional group tolerance and/or sensitivity towards both, air and moisture, and therefore require inconvenient inert-atmosphere techniques for their successful use, which strongly limits their applicability in industrial processes, for example.

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[1] Bolliger, J. L., Blacque, O., Frech, C. M.* *Angew. Chem., Int. Ed.* **2007**, *46*, 6514.
[2] Bolliger, J. L., Blacque, O., Frech, C. M.* *Chem. Eur. J.* **2008**, *14*, 7969.
[3] Bolliger, J. L., Frech, C. M.* *Adv. Synth. & Catal*. **2009**, *351*, 891.
[4] Bolliger, J. L., Frech, C. M.* *Adv. Synth. & Catal*. **2010**, *in press*.

Organic Chemistry **354**

An efficient photodeprotection of 2-naphthaldehyde acetals

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Modern light sources trigger photochemical deprotection reactions at fast rates and with high spatial precision. Photochemical reactions have mainly been used in functional group protection for organic synthesis[1] and have found various applications in the in vitro detection of biological dynamic processes in living cells[2] or in the controlled release of volatiles in perfumery[3].

Broadening the scope of a photochemical deprotection reaction widens the tool box of methods. The photochemical conversion of 2-naphthaldehyde acetals **1a-b, 3** into the corresponding 2-naphthyl carbonyl **2, 4** was achieved using photons as only reagent in wet acetonitrile[4]. We now report our preliminary studies to establish the scope and limitation of this photoinduced reaction and to characterize the process on a practical level.

[1] Pillai, V. N. R., *Synthesis*. **1980**, 1.; Pillai, V. N. R., *Org. Photochem.* **1987**, *9*, 225.; Givens, R. S.; Kueper, L. W., *Chem. Rev.,* **1993**, *93*, 55.; Bochet, C. G., *J. Chem. Soc., Perkin Trans. 1.* **2002**, 125.
[2] Goeldner, M.; Givens, R. S., *Dynamic Studies in Biology: Phototriggers, Photoswitches and Caged Biomolecules*, Eds.; Wiley-VCH: Weinheim, Germany, **2005**.;
[3] Herrmann, A., *Angew. Chem. Int. Ed.* **2007**, *46*, 5836.
[4] Thevenet, D.; Neier, R., *Org.Lett.* submitted.

Organic Chemistry **355**

Design and Syntheses of dimers using "Click" chemistry: Towards high organization in columnar mesophases

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Av. De Bellevaux 51, case postale 158, 2009, Neuchâtel, Switzerland

The discotic liquid crystals[1] are of great interest due to their one dimensional conducting properties[2] and potential applications in thin-film organic-electronic technology. In such materials the charge transport depends strongly on the molecular alignment in the mesophases.

Preliminary studies regarding the syntheses of several novel linkers are reported here. Enhanced control over self-organization of discotic compounds is expected by linking two discotic units with "semi-rigid" linker. Based on the X-Ray studies of our model compounds, the structural properties will be discussed.

[1] Laschat. S.,et al, *Angew. Chem. Int. Ed*., **2007**, *46*, 4832-4887.
[2] Mullen. K., *Science*, **2001**, *293,* 1119-1122

Organic Chemistry **356**

DNA-DNA Interstrand Cross-links

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[2]Eidg.Technische Hochschule Zürich, Schmelzbergstrasse 9, 8006 Zürich

Interstrand cross-links (ICLs) are cytotoxic lesions that involve covalent linkage of both strands of a DNA duplex and are formed by a variety of important anti-tumor agents.[1, 2] Despite the clinical importance of ICLs, little is known about the structure or repair of these lesions. To help overcome this obstacle, we are pursuing the total synthesis of site-specific ICL DNA. Our contribution focusses on the synthesis of a photocaged crosslink precursor which remains stable upon incorporation into oligonucleotides. After annealing to a complementary strand and selective activation of the precursor by irradiation, well-defined ICLs that are exactly the same as the lesions resulting from *Bis*-Chloroethylnitrosurea (BCNU) are generated. The resulting products can be used to study ICL influences on DNA structure and ICL repair mechanisms. The results of such studies should facilitate the rational design of new anti cancer drugs.

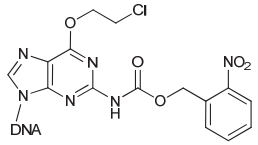

FIGURE 1 Synthetic precursor to mimic ICL caused by BCNU

[1] Schärer, O.D., *ChemBioChem*, **2005**, *6* ,27 - 32.
[2] Noll, D.M., T.M. Mason, and P.S. Miller, **2006**, *106*, 277 – 301.

Organic Chemistry **357**

A Versatile Reagent for Phospholipids Synthesis

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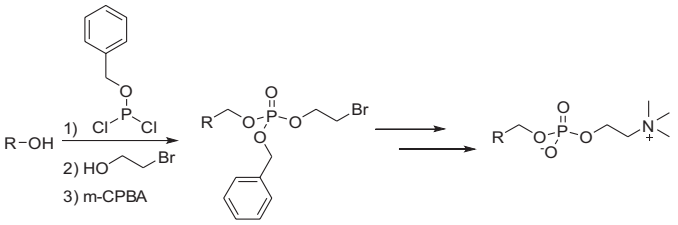
University of Geneva, Department of Organic Chemistry, 30, Quai E. Ansermet, CH-1211 Genève 4

We have recently started to work on the synthesis of non-natural phospholipids [1]. Meeting difficulties (oxidation, low reactivity, double addition) with common procedures using P(III) or P(V) chemistries, we developped a new synthesis to introduce phospholipid headgroups such as phosphocholine or phosphoethanolamine.



Benzyldichlorophosphite (BDCP) can be easily made by reacting benzyl alcohol with PCl_3 followed by removal of the solvents under vacuum [2]. BDCP is stable enough to be handled in air for a short period of time. It reacts readily with primary and secondary alcohols. The addition of a second alcohol yields asymmetric phosphites in a straigthforward fashion. Oxydation (*m*-CPBA) and deprotection (TFA) give the final product.

In this communication we present a series of phospholipids that have been synthesized following the BDCP-methodology, a versatile alternative for the traditional phospholipid syntheses.

[1] Zumbuehl, A.; *Chimia* **2009**, *63*, 63-65.
[2] Amigues, E. J.; Greenberg, M. L.; Ju, S.; Chen, Y.; Migaud, M. E.; *Tetrahedron* **2007**, *63*, 10047-10053.

Organic Chemistry **358**

Towards the Synthesis of Cycloparaphenylenes

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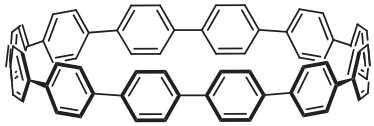
Department of Chemistry, University of Basel, St.Johanns-Ring 19, 4056 Basel, Switzerland

Cycloparaphenylenes have increasingly fascinated chemist due to their interesting properties over the last decades.[1] These molecules have very special characteristics due to their distorted aromatic system and their radially oriented π-orbitals. Moreover, they could act as models for segments of armchair-type carbon nanotubes.



[12]-Cycloparaphenylene

We are interested in the development of a general synthesis of paracyclophanes as templates for a rational chemical synthesis of Carbon Nanotubes. The preparation of carbon nanotubes (CNTs) with specific size and structure is still one of the holy grails of CNT research. We are currently investigating a new selective synthesis of cycloparaphenylenes via a highly modular approach to different ring sizes and various aromatic and heteroaromatic nanohoops structures. Latest results of our endeavor will be discussed.

[1] B.D. Steinberg, L.T. Scott, *Angew. Chem. Int. Ed.*, **2009**, *48*, 5400.

Organic Chemistry **359**

Comparative Study of Strained Oligophenylenes

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

Oligophenylenes attracted recently much attention due to their potential in molecular electronics. Introducing strain into those compounds should have an effect on these special properties.[1] Preparation of oligophenylenes with tethers of different length and comparing the strained and linear oligophenylenes will give more insights into the effect of strain on aromatics in general.

Besides the synthesis the influence of additional functional groups will be studied. The efforts towards the preparation of these interesting molecules and their properties will be discussed.

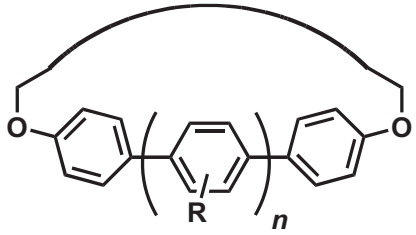


Figure 1. : Strained oligophenylenes.

[1] T. Kawase, H. Kurata, *Chem. Rev.* **2006**, *106*, 5250−5273.

Organic Chemistry **360**

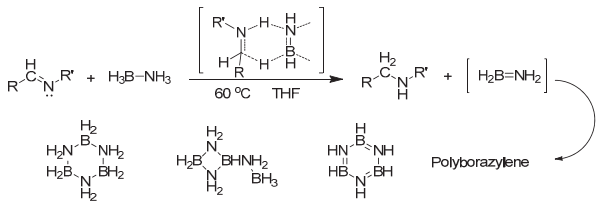
Metal-Free Transfer-Hydrogenation of Imines with Ammonia-Borane: A Mechanistic Study

Xianghua Yang, Lili Zhao, Thomas Fox, Zhi-Xiang Wang, and Heinz Berke*

Anorganisch-chemisches Institut, Universität Zürich, Winterthurerstr.190, 8057 Zürich, Switzerland

Ammonia-borane (H_3N-BH_3, AB) is considered a feasible material for chemical hydrogen storage due to its potentially very high storage capacity (19.6 weight % H) and has thus attracted much research attention [1]. The storage function is connected to the processes of dehydrogenation (fuelling) and hydrogenation (re-fuelling) of the storage compounds. Our approach to the dehydrogenation of AB was to use a transfer-hydrogenation process with imines.

Indeed, AB was successfully applied as a hydrogen donor in hydrogenations of imines under mild conditions in the absence of a catalyst [2]. The mechanism of this metal-free transfer-hydrogenation was studied both theoretically and experimentally. The kinetic data and isotope labelling studies were supportive of a concerted double H transfer mechanism.



[1] a) W. Grochala, P. P. Edwards, *Chem. Rev.* **2004**, *104*, 1283; b) T. B. Marder, *Angew. Chem., Int. Ed.* **2007**, *46*, 8116; c) C. W. Hamilton, R. T. Baker, A. Staubitz, I. Manners, *Chem. Soc. Rev.* **2009**, *38*, 279.
[2] X. Yang, L. Zhao, T. Fox, Z.-X. Wang, H. Berke. *Angew. Chem. Int. Ed.* **2010**, *49*, 2058.

Organic Chemistry **361**

Towards the Total Synthesis of Cyrneine A, a Cyathane Diterpene Promoting Neurite Outgrowth

Elangovan Elamparuthi[1], Cindy Fellay[2], Karl Gademann[1,*]

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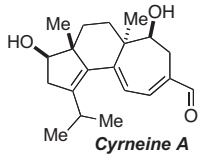
[2] EPFL, ISIC, 1015 Lausanne, Switzerland

Cyathane diterpenes possess an unusual angularly fused 5-6-7 tricyclic framework with 1,4-*anti* methyl groups at the angular quaternary centers. Ayer and coworkers isolated the first natural product of this class in 1971.[1] In 2006, the two cyathane diterpenes cyrneines A and B were isolated from the mushroom *Sarcodon cyrneus*.[2] In this isolation report, this class of natural products was reported to mimic or to induce the activity of neurotrophins.[2] In later studies, cyrneine was postulated to act via a Rac1-dependant mechanism.[3] We will report on our synthetic studies towards these targets.



Cyrneine A

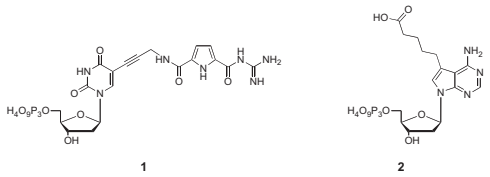
[1] A. D. Allbutt, W. A. Ayer, H. J. Brodie, B. N. Johri, H. Taube, *Can. J. Microbiol*. **1971**, 1401 – 1407.
[2] M. C. Marcotullio, R. Pagiott, F. Maltese, Y. Obara, T. Hoshino, N. Nakahata, M. Curini, *Planta Med*. **2006**, *72*, 819-823.
[3] Y. Obara, T. Hoshino, M. C. Marcotullio, R. Pagiotti, N. Nakahata, *Life Sciences* **2007**, *80*, 1669

Organic Chemistry **362**

Synthesis and enzymatic incorporation of $dU^{Gcp}TP$ and $dA^{Val}TP$

Marcel Hollenstein[1]

[1]Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern, Switzerland.



1 **2**

Besides its fundamental role as blueprint of life, DNA has become one of the quintessential tools of modern research. In particular, methods of *in vitro* selections have led to the discovery of a plethora of nucleic acid sequences with a broad range of applications [1]. An alluring and prepotent strategy for the generation of modified nucleic acid libraries is through the enzymatic polymerization of nucleoside triphosphates adorned with functional groups [2]. In this context, the modified analogues $dU^{Gcp}TP$ (**1**) and $dA^{Val}TP$ (**2**) were designed to be used for the generation of a peptide-cleaving DNA enzyme. Indeed, $dU^{Gcp}TP$ bears a guanidinocarbonyl pyrrole (Gcp) moiety which has been shown to confer acid-base catalysis of RNA linkages [3]. Moreover, $dA^{Val}TP$ bears a valeric acid type of side chain that could mimic aspartates found in the active site of various zinc proteases. Triphosphates **1** and **2** were synthesized and tested for their compatibility with *in vitro* selection methods, which requires the analogues to be substrates both for polymerases in primer extension reactions and PCR.

[1] G. F. Joyce, *Angew. Chem. Int. Ed*. **2007**, *30*, 6420.
[2] M. Hollenstein, C. J. Hipolito, C. H. Lam, D. M. Perrin, *Nucleic Acids Res*. **2009**, *37*, 1638.
[3] N. J. V. Lindgren, L. Geiger, J. Razkin, C. Schmuck, L. Baltzer, *Angew. Chem. Int. Ed*. **2009**, *48*, 6722.

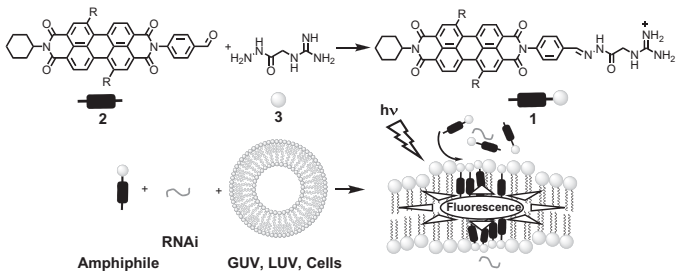
Organic Chemistry **363**

Dynamic Fluorescent Probes for Membrane Characterization

Andrea Fin, Javier Montenegro, Toshihide Takeuchi, David Alonso, Naomi Sakai and Stefan Matile*

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

New fluorescent probes that partition into membrane domains and act as amphiphiles (*e.g.* **1**) for the transport of polyions across the lipid bilayer are introduced as an innovative membrane labeling methodology. This system is based in the dynamic covalent linkage between a charged head and a fluorescent tail. For the fluorophore moiety we focus on core substituted naphthalendiimides (cNDIs) and perylenediimides (cPDIs, *e.g.* **2**) [1]. For the hydrophilic head we use amino acids, peptides or (oligo)hydrazides such as **3**. We hope to use these cholesterol mimics amphiphiles to visualize the membrane heterogeneity [2] and perhaps illuminate processes such as cellular uptake [3] using polyions (*e.g.* RNAi, CPPs).



[1] Perez-Velasco, A.; Gorteau, V.; Matile, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 921-923.
[2] Bagatolli, L. A. *Biochim. Biophys. Acta* **2006**, 1758, 1541-1556.
[3] Takeuchi, T.; Kosuge, M.; Tadokoro, A.; Sugiura, Y.; Nishi, M.; Kawata, M.; Sakai, N.; Matile, S.; Futaki, S. *ACS Chem. Biol.* **2006**, *1*, 299-303.

Organic Chemistry **364**

Asymmetric Intramolecular Diels-Alder Reactions Using Chiral Ruthenium Lewis Acids

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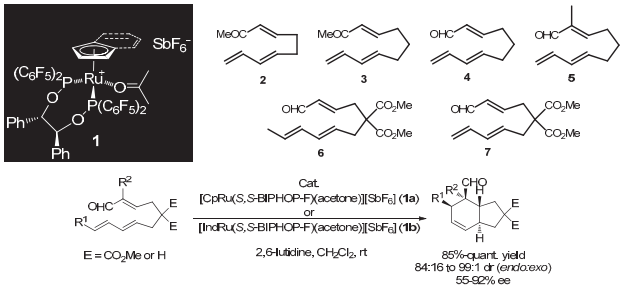
Cationic cyclopentadienyl (**1a**) and indenyl (**1b**) complexes of ruthenium incorporating chiral fluoroaryl phosphinite ligands are efficient Lewis acid catalysts for asymmetric Diels-Alder reactions with enals. [1] We have also reported that catalyst **1a** is capable to coordinate and activate enones in asymmetric inter- and intramolecular Diels-Alder reactions. [2] Now, the substrate scope for IMDA reactions has been extended to trienes **2-7**. Especially trienals **4-7** furnish the corresponding adducts in excellent yield with good enantio- and diastereoselectivity in the presence of **1a** or **1b** (recoverable) under mild conditions.



[1] Kündig, E. P.; Merbach, A. E.; Saudan, C. M.; Viton, F.; Weber, J.; Alezra, V.; Bernardinelli, G.; Corminboeuf.; Frey, U. *J. Am. Chem. Soc.* **2004**, *126*, 4843 and references therein.
[2] Kündig, E. P.; Rickerby, J.; Vallet, M.; Bernardinelli, G.; Viton, F. *Chem. Eur. J.* **2007**, *13*, 3354.

Organic Chemistry **365**

A Dialkynylfluorene - Derived DNA Hairpin Mimic

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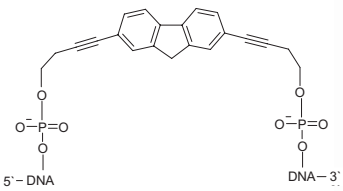
The use of fluorene as a base modification in DNA has been shown to be a valuable tool as a quencher-free molecular beacon [1]. In addition the expansion of the aromatic system by triple bonds is generally known to improve fluorescence properties of chromophores [2]. Based on this, we introduce a dialkynyl-substituted fluorene derivative (**1**) as a non-nucleosidic building block mimicking a hairpin (**2**). The remarkable stabilization of the hairpin as well as the induced CD spectrum is presented.



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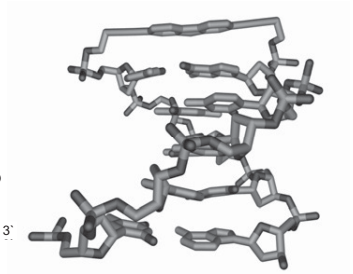


2

[1] Jin Ho Ryu, Young Jun Seo, Gil Tae Hwang, Jin Yong Lee and Byeang Hyean Kim, *Tetrahedron,* **2007**, *63*, 3538.
[2] Holger Bittermann, Doreen Siegemund, Vladimir Malinovskii, Robert Häner, *JACS,* **2009,** *130*, 15285.

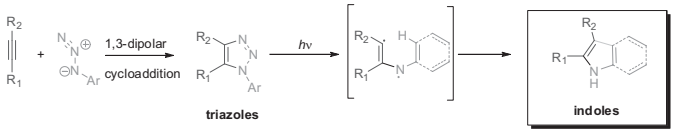
Organic Chemistry **366**

Photochemical transformation of 1*H*-1,2,3-triazoles

Isak Alimi, Christian G. Bochet*

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

The formation of triazole by 1,3-dipolar cycloaddition of azides with alkynes is very efficient and well-exploited process for more than four decades.[1] On the other hand, little has been done to use triazoles as building blocks for further transformations. We intend to explore their photochemical transformations, as their nitrogen-nitrogen multiple bonds set the stage for a potential extrusion of dinitrogen,[2,3] and their highly conjugated nature facilitate the absorption of light. In this work, we have generated a library of triazoles that were then photolysed into indoles (Scheme 1).



Scheme 1: Indoles formation *via* photolysis of triazoles

[1] Huisgen, R., *J. Org. Chem,* **1969**, *33,* 2291
[2] Märky, M., Hansen H. and Schmid H., *Helv. Chim. Acta,* **1979**, *62,* 2129-2153
[3] Mitchell, G., Rees, C. W., *J. Chem. Soc., Perkin Trans. I,* **1986,** 399

Organic Chemistry **367**

Efficient α-Chlorination of Aldehydes using Trichloromethanesulfony Chloride as a New Chlorinating Reagent

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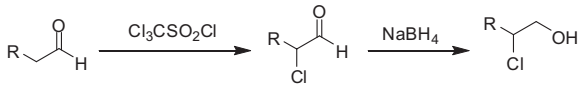
α-Chloroaldehydes and ketones are versatile building blocks in organic synthesis that can be transformed into a variety of useful structures. Thus, various methods have been developed for the preparation of these compounds. However, sulfonyl chloride as the source of chlorine for α-chlorination of aldehydes and ketones haven't been investigated extensively.[1] Here we reported an organocatalytic α-chlorination of aldehydes using commercial available trichloromethanesulfonyl chloride (Cl_3CSO_2Cl) as a new chlorinating reagent.



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Organic Chemistry **368**

Efficient Radical Addition Reactions via Desulfonylation Chlorine-Atom Transfer

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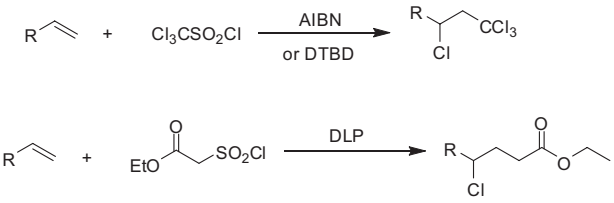
Among various types of radical process, halogen atom-transfer radical addition reactions have received considerable attention because of their atom-economic nature and high efficiency.[1] Due to the strong C-Cl bond dissociation energy, Cl-atom transfer reactions are mostly limited to polychlorinated substrates and often require the use of transition metal catalysts.[1] Recently we found that desulfonylation chlorine-atom transfer radical addition reactions of trichloromethanesulfonyl chloride and ethyl chlorosulfonyl acetate to various olefins can be efficiently initiated by AIBN, 1, 2-di-tert-butyldiazene (DTBD) and lauroyl peroxide (DLP). These reactions show good compatibility with a broad range of functional groups.



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Organic Chemistry **369**

Building 2D crystals from fivefold-symmetric molecules

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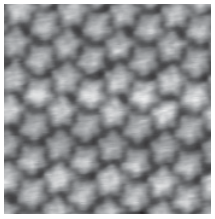
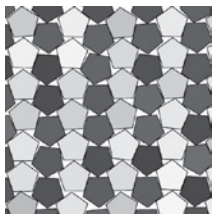
STM investigations of fivefold-symmetric buckybowl selfassembly with bulky side groups reveal packing strategies for the molecules as previously predicted for hard pentagons.
The local adsorbate geometry of corannulene on Cu(111) is such, that a hexagonal ring is oriented parallel to the surface plane and the C5 axis of molecule is tilted with respect to the surface normal [1]. Therefore, corannulene forms a quasi-hexagonal lattice at room temperature. The pentachloro and pentamethyl derivatives with their bulky substituents do not allow such tilt. The intramolecular STM contrast does not vary as observed for corannulene, indicating that there is no pronounced tilt of the bowl. The structures of the derivatives reveal new close-packing strategies. The pentachloro derivative forms a striped lattice with the pentagonal molecules arranged in antiparallel rows and the pentamethyl molecules form a more disordered rotator phase in which the azimutal orientation of the molecules is random [2]. Interestingly, these observed structures are compatible with results of mechanical modeling experiments and Monte-Carlo simulations of hard pentagons [3].





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Organic Chemistry **370**

8-(2-pyridyl)-2'-deoxyguanosine for the detection of G-quadruplex folding

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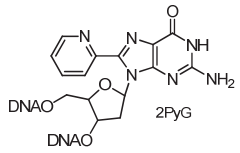
Certain guanine-rich DNA sequences are known to self-assemble into four-stranded structures called G-quadruplexes [1]. While it has been proposed that these conformations may have important biological functions, direct evidence for their existence *in vivo* has remained elusive [2]. The development of fluorescent nucleoside analogues that maintain their hydrogen bonding interactions with other bases may facilitate the monitoring of quadruplex formation both *in vitro* and *in vivo*. For this purpose, 8-(2-pyridyl)-2'-deoxyguanosine (2PyG) was identified as a particularly promising candidate, displaying encouraging environment sensitivity and showing no fluorescence quenching in the context of nucleic acids. Upon incorporation into DNA, this guanosine analog displays fluorescence enhancement in the context of G-quadruplex as compared to unstructured and duplex strands. This increased emission efficiency is a result of energy transfer between natural DNA bases and the probe. This represents the first such observation made in G-quadruplex structures. 2PyG is therefore an important new tool for studying energy transfer processes in G-quadruplexes.



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Organic Chemistry **371**

Unexpected supramolecular structures of functionalized Helicenes on Cu(111)

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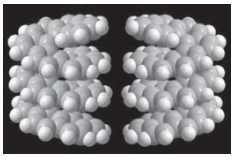
[1]ETH-Zürich/Laboratorium für Organische Chemie, 8093 Zürich, Switzerland

[2]Department of Physics, University of Basel, 4056 Basel, Switzerland

[3]Swiss Federal Laboratories for Materials Testing and Research (EMPA), Ueberlandstrasse 129, 8600 Dübendorf, Switzerland

Recent studies of cyano-functionalized [7]helicenes revealed fascinating self-assembly properties. STM measurements clearly showed that these [7]helicenes underwent spontaneous resolution into enantiomerically pure domains upon deposition on Cu(111) surfaces. Furthermore, their self-organization yielded distinctly defined long-range ordered molecular structures in the sub-monolayer range.

DFT calculations – for example on the racemization barriers – predict unexpected trends for the physicochemical properties of higher helicenes. A homology study of higher helicenes will show how racemization barriers and chiroptical properties evolve. Additionally, their self-assembly behavior on metal surfaces will be examined by STM. For the purpose of these studies, we develop novel, versatile synthetic strategies providing direct access to higher helicenes of various lengths.



Organic Chemistry **372**

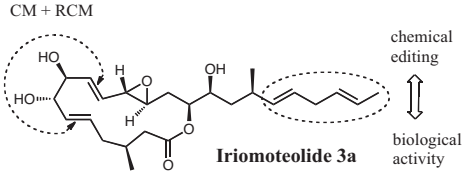
Synthetic Tools in Chemical Biology:

Total Synthesis and Biological Evaluation of Iriomoteolide-3a and Analogues

Riccardo Cribiù, Corinna Jäger, Cristina Nevado*

University of Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

Application of a combined Cross Metathesis-Ring Closing Metathesis approach (CM-RCM) led to the stereocontrolled synthesis of Iriomoteolide-3a, [1], confirming its absolute stereochemistry [2]. Chemical editing of the molecule in a *D*iverted *T*otal *S*ynthesis (*DTS*) campaign has provided non-natural "irio-like" compounds. The antiproliferative activity of this small collection of molecules against different cancer cell lines has been determined. Interestingly, some of the analogues have comparable activity to the natural product (nM).



These results have opened the possibility to use Iriomoteolides as probe molecules in chemical biology. Studies to elucidate both, its mode of action and cellular targets, are currently underway.

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Organic Chemistry **373**

Ring-Closing Metathesis of Challenging Substrates

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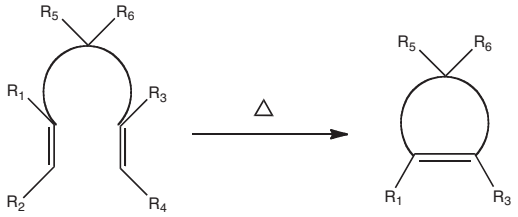
Olefin metathesis has attracted widespread attention as a versatile carbon-carbon bond-forming method.[1] Many new applications have become possible because of major advances in catalyst design. State-of-the-art ruthenium catalysts are not only highly active but also compatible with most functional groups and easy to use. In this line, the use of NHCs as ancillary ligands has been shown to be especially fruitful, presenting excellent functional group tolerance and selectivity.[2]

We report herein on the application of ruthenium-based metathesis catalysts in challenging ring-closing metathesis reactions (RCM). The goal of our research is to find short synthetic pathways to obtain highly functionalized 5-, 6- and 7-membered rings.



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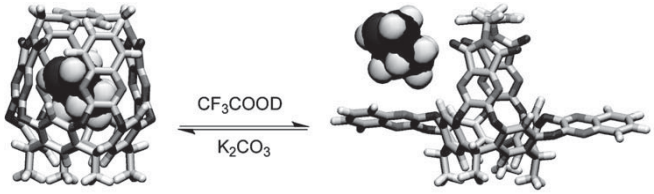
Organic Chemistry **374**

Complexation Studies Using NMR and ITC with Resorcin[4]arene-Based Container Molecules as Hosts and Small Molecular Guests

D. Fankhauser, J. Hornung, F. Diederich

ETH Zurich, Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland



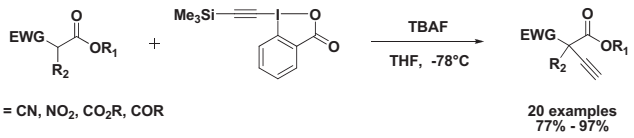
Complexation studies were performed with a variety of saturated cyclic molecules of different polarities as guests and resorcin[4]arene-based container molecules as hosts. Association constants were measured using two different methods: NMR spectroscopy and ITC (Isothermal Titration Calorimetry). Furthermore, NMR spectroscopy was used to investigate the reversible conformational switching of the host (*vase* ⇆ *kite*) as indicated in the Figure. The complexation of the guest is affected by addition of acid or base due to a conformational change of the host.

Organic Chemistry **375**

Metal Free Alkynylation of Soft Enolates

Davinia Fernández González [1] and Jérôme Waser* [1]

[1] Laboratory of Catalysis and Organic Synthesis, EPFL, 1015 Lausanne, Switzerland



EWG = CN, NO_2, CO_2R, COR

20 examples
77% - 97%

Acetylenes are versatile intermediates in chemistry, biochemistry and material sciences. The use of acetylenes in addition reactions to carbonyl compounds, cycloaddition or coupling reactions make them very interesting intermediates in organic synthesis. Usually, they are synthesized by addition of an acetylide anion to an electrophile. The reverse approach, via an electrophilic acetylene synthon, has been achieved in the case of soft nucleophiles like ketoesters by using alkynyliodonium salts.[1,2]

We report the first general method for the alkynylation of soft nucleophiles using a hypervalent iodine reagent, which displays higher reactivity than alkynyliodonium salts.[3] The developed reaction conditions led to high yields of unprotected acetylenes. The scope of the reaction was extended to substrates such as cyano and linear keto esters, as well as nitro esters which were transformed into the protected amines. Furthermore, asymmetric induction was observed using a cinchona derived phase-transfer catalyst.

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Organic Chemistry **376**

Switching in 3D - Cyclotrisazobenzenes

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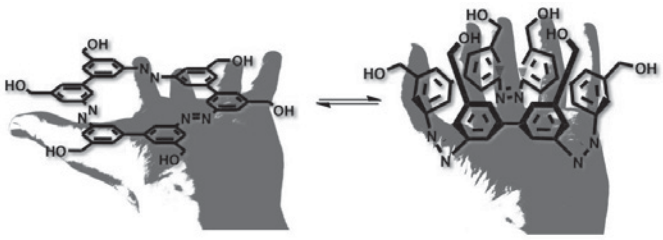
University of Basel, St. Johanns-Ring 19, CH-4056 Basel

Azobenzenes are a versatile class of compounds, which find applications in various areas. Not only does their family make up several of the most important organic dyes and pigments, they also exhibit photochromism. The structural change from *E* to *Z* geometry, which is induced when subjected to UV-light, widens their potential applications and makes them an exciting topic especially for functional materials. Furthermore, the isomerization is completely reversible in most cases. Our research interest focuses on fully conjugated macrocyclic azobenzenes[1]. Isomerization of these macrocycles from $E \rightarrow Z$ should switch the planar 2D arrangement to a 3D bowl shaped structure. Therefore, these switchable scaffolds are perfectly suited for the design of molecular grippers. Due to their structural change from 2D to 3D, they could bind guests, such as cations, in their *E*-isomeric form and release them again upon irradiation. The preparation of different derivatives of those functional π-systems as well as properties is described



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Organic Chemistry **377**

Design of New P,N Ligands for Iridium Catalyzed Asymmetric Hydrogenation

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Iridium catalyzed hydrogenation combines all of the requirements for modern asymmetric synthesis, such as, perfect atom economy, low catalyst loading, high conversion and ideally, high enantiomeric induction. Several research groups have focused on the development of chiral P,N-[1a-b] and C,N-ligands.[1c] However no ligand has a universal substrate scope. Our group recently published a report on a class of very efficient ligands based on a bicyclic phosphinite-pyridine system **1**.[2] Based on this work, we continue to develop new systems such as **2**, where the oxygen atom bound to phosphorous is replaced by nitrogen, which allows us to have an additional position (R^3) for fine tuning.
The synthesis of iridium complex containing these ligands and the results of our hydrogenation studies will be presented.

1 **2**

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Organic Chemistry **378**

Selective Pd-Promoted Cascade C-C Activation/Cyclization Sequence

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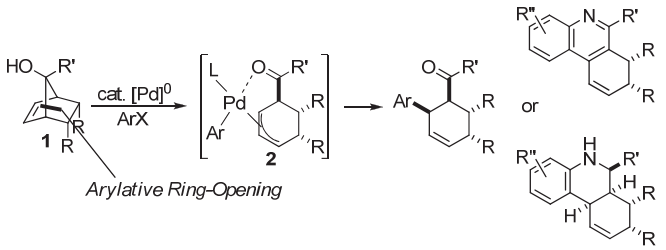
The development of efficient and sustainable procedures towards the synthesis of complex molecules is an important task for modern organic chemistry because of their economic and ecological advantages. Ways to improve efficiency include transition-metal catalyzed activations of C–C bonds and the use of cascade reactions that allow for a rapid increase in molecular complexity [1]. We investigate palladium-catalyzed ring opening reactions of norbornene derived tertiary alcohols **1**. The π-allyl intermediate arising from such retro-allylative fragmentation (**2**) can be trapped with aryl halides in excellent selectivities leading to tetrasubstituted cyclohexenes. This procedure can be extended to cascade reactions providing access to highly substituted quinolines and tetrahydroquinolines [2].



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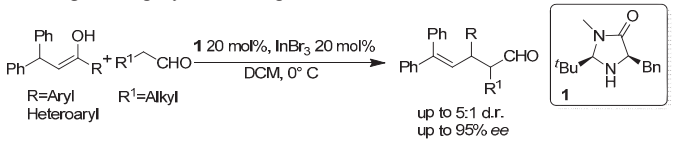
Organic Chemistry **379**

Indium(III) Promoted Organocatalytic Enantioselective Allylic Alkylations of Aldehydes with Alcohols

Fides Benfatti[1], Montse Guiteras Capdevila[2], Luca Zoli[2], Marco Stenta[1] and Pier Giorgio Cozzi[2]

[1]Laboratory of Catalysis and Organic Synthesis Ecole Polytechnique Fédérale de Lausanne, BCH 4418, 1015 Lausanne, Switzerland
[2]Dipartimento di Chimica "G.Ciamician", Alma Mater Studiorum Università di Bologna, via Selmi 2, Italy)

Organocatalysis has grown explosively in the last few years,[1] becoming an exciting area of research, and organocatalytic modes of activation are now considered in the synthetic approach of complex natural products.
Activation modes of organocatalysis allow new reactivity, increasing the creativity of organic chemists towards the invention of new reactions.
Recently, the combination of organocatalysis with metal catalytic processes produced exciting strategies for the development of innovative transformations and for challenging difficult synthetic problems.[2]
The present contribution deals with a conceptually new approach towards the organocatalytic allylation of aldehydes with allylic alcohols, by the use of organocatalysts developed by MacMillan, and $InBr_3$ as a co-catalyst, avoiding the employment of expensive Pd and Ir metal salts.



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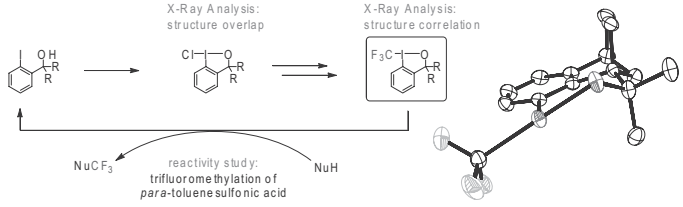
Organic Chemistry **380**

Structure and Reactivity of New Hypervalent Iodine Reagents for Electrophilic Trifluoromethylation

Katrin Niedermann, Jan M. Welch, Antonio Togni

Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology, ETH Zurich, 8093 Zürich, Switzerland

Since their first publication in 2006,[1] electrophilic trifluoromethylating agents based on hypervalent iodine are known to react with a variety of carbon- and heteroatom-centered nucleophiles.[2] In order to enhance the reactivity and selectivity of the trifluoromethylation based on hypervalent iodine we synthesized a variety of new I(III)-monochlorides, including six-membered heterocycles and cationic derivatives, as precursors for new electrophilic trifluoromethylating agents.



For a comparative structural study three of the monochlorides were transferd to the corresponding trifluoromethylating reagents. A reactivity study of the trifluoromethylation of *para*-toluenesulfonic acid was conducted using the method of initial rates.

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Organic Chemistry **381**

Accessing Funtionalized Allene Intermediates By C–C Fragmentation

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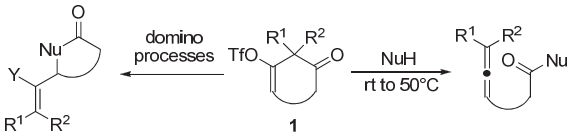
Laboratory of Organic Chemistry, ETH Zurich
Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland

The rich structural and reactivity profile of allenes render them uniquely versatile synthetic intermediates [1]. Williams and co-workers recently reported a synthesis of functionalized allenes *via* Grob-type fragmentation of vinyl triflate such as **1** [2]. However, this method requires the use of lithium and Grignard reagents or strong bases such as NaHMDS, thus limiting severely the range of nucleophiles. We will report mild conditions that largely broaden the scope of the reaction. For example simple alcohols and amines can be now used and the reaction is also suitable for the initiation of domino processes giving access to a range of synthetically useful compounds in a single step from simple precursors.



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Organic Chemistry **382**

On the Nature of Gold-Stabilized Non-Classical Carbocations

David Garayalde and Cristina Nevado*

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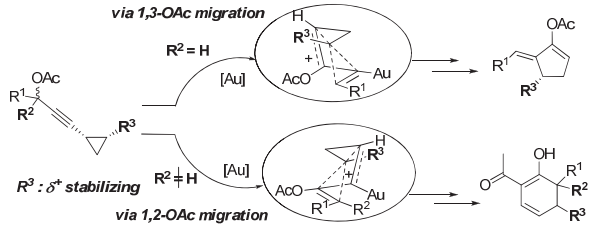
Gold complexes are powerful soft Lewis acids which efficiently activate propargyl carboxylates towards 1,2-acyloxy migration and/or [3,3]-sigmatropic rearrangement. Two different but mechanistically related intermediates characterize these competitive processes: 1,2-migration processes *via* metal "carbenoid" formation, whereas [3,3]-sigmatropic rearrangement form allenyl acetate as intermediate [1].

We have previously reported a gold-catalyzed acetoxy rearrangement/cyclopropyl ring expansion to acess 5- and 6-membered rings from 1-cyclopropyl propargyl acetates [2]. The intelligence gathered in this process aid us to present here a complete study on the reactivity of 3-cyclopropyl propargyl acetates and enol ethers with Au(I) and Au(III) catalysts via gold-stabilized "nonclassical carbocationic" intermediates revealing the intrinsic stereospecific nature of these transformations [3].



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Organic Chemistry **383**

Biological applications of cationic [4]Helicenes

Nathalie Mehanna,[1] Oksana Kel,[2] Petr Sherin,[2] Eric Vauthey[2] and Jérôme Lacour[1]

[1] Organic Chemistry Department, University of Geneva, Switzerland
[2] Physical Chemistry Department, University of Geneva, Switzerland

Cationic [4]helicenes of type **1** display applications in synthesis, photochemistry and photophysics – biological applications being so far essentially overlooked.[1] These molecules are interesting for their intrinsic chirality; the *P* or *M* enantiomers being usually readily available through resolution protocols.[2] Herein, we report on their selective interactions with DNA and Avidin.[3] Series of enantiopure derivatives were prepared with either short alkyl or tailored biotin-functionalized side chains. Monitoring of the interactions was performed by steady-state and ultrafast time-resolved fluorescence methods. The results will be discussed in details.

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Organic Chemistry **384**

Expanding the Set of Interactions Available to Generate Function

Andreas Vargas Jentzsch, Jiří Míšek, Shinichiro Sakurai, Javier Montenegro, Leonardo Bertone, Naomi Sakai and Stefan Matile*

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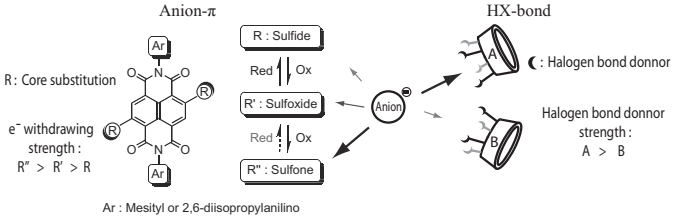
To create functional supramolecular systems, expansion of the set of non-covalent interactions available is fundamental. The anion-π interactions were studied, caught at work and successfully proven to matter for the function on artificial anion transporters through a bilayer membrane [1]. Halogen bond (HX bond) interactions were recently observed in solution and their capacity as binding interaction in weak halide receptors was shown [2].



The anion binding by the means of those interactions can be tuned accordingly to the core substitution (anion-π) or the halide used (HX bond). This offers the opportunity to use them for the design of anion transporters with promising properties. Moreover, the anion transport studies shall reveal more about these fundamental yet neglected interactions.

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Organic Chemistry **385**

Synthetic Analogs of Telomestatin

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DNA is a structurally dynamic molecule. For certain DNA sequences, the double-stranded duplex is in equilibrium with single-stranded DNA structures such as G-quadruplex or i-motif. The biological function of these structures is not clear but has recently been implicated in gene regulatory processes. Influencing the quadruplex-duplex equilibrium by stabilizing or destabilizing one or the other form can therefore probe the biological function of this equilibrium.

Large, planar molecules such as porphyrins [1], phthalocyanins [2] and Telomestatin [3] show selective stabilization of G-quadruplex structures and also exhibit promising anti-cancer activities *in vitro* [4] and *in vivo* [5]. Due to the presence of a single thiazoline unit and macrocyclic ring strain, Telomestatin is not a fully planar molecule. Our design efforts have been directed towards telomestatin analogs that are fully planar. These efforts have resulted in a series of macrocyclic polyzoles containing a thiazole unit at every second position and imidazole or oxazole units at the remaining positions. Here we describe the design and synthesis of these analogs.

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Organic Chemistry **386**

Tröger base: New organometallic approach towards novel configurationally stable derivatives

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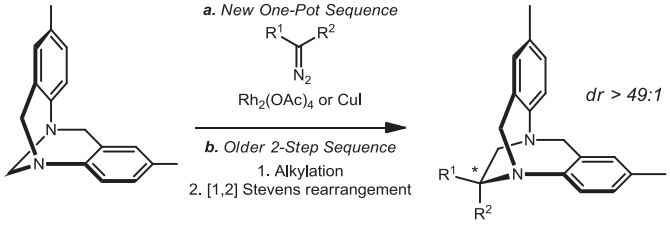
Tröger base was discovered about 130 years ago and, since its resolution into single enantiomers, this class of compounds has been extensively studied for variety of purposes.[1] Methano-bridged Tröger bases unfortunately undergo facile racemisation under acidic conditions.[2] This drawback can, for instance, be overcome by synthesizing ethano-bridged derivatives.[3] Recently, we have reported a novel two-step sequence for the synthesis of such compounds with full stereocontrol at the newly generated stereogenic centre (path b).[4] Herein, we report yet another approach based on reactions with electrophilic metal carbene intermediates allowing, this time, to add and control a quaternary stereogenic carbon atom at the newly formed bridge (path a).



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Organic Chemistry **387**

Supramolecular n/p-Heterojunction with Zipper Assembly Architecture of Cascade Triple Redox Gradients Photosystems

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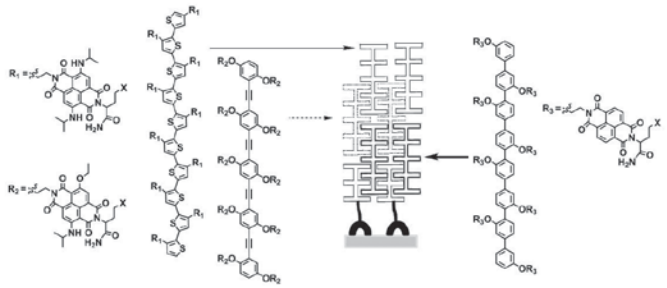
Department of Organic Chemistry, University of Geneva, Geneva, Switzerland

In organic optoelectronics, it is a key challenge to design supramolecular n/p-heterojunctions (SHJs) that transport hole and electron effiently. We here explore the zipper assemblies [1,2] of triple redox gradient, where n-semiconducting blue, red and yellow naphthalenediimide (NDI) π-stacks are assembled along interdigitate strings of p-semiconducting oligothiophene (OT), oligophenylethynyl (OPE) and *p*-oligophenyl (POP) rods, respectively. This study would establish the construction of the first oriented multicolored antipallel redox gradients (OMARG-SHJ) photosystems.



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Organic Chemistry **388**

New stereostructures of Biflavonoids from *Garcinia preussii* Engl.

Bernadette Biloa messi [1,2], Karine Ndjoko Ioset[2], Alain meli lannang[3], Augustin.Ephraïm Nkengfack[1], Barbara Hertlein[4], Gerhard Bringmann[4], Jean-Luc wolfender[2] , Kurt Hostettmann[2]

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The Genus *Garcinia* (clusiaceae) is known to be a rich source of phenolic compounds such as xanthones, benzophenones and biflavonoids. *G.preussii* Engl. (syn *G.epuntata* Stapf) is traditionally used in Congo (Brazzaville) to treat stomachache. The investigation of the methanolic extract of bark, fruits and leaves of *G. preussii* lead to the isolation of nine 3, 8”-linked biflavonoids. Among which, were identified new isomers of *Garcinia* Biflavonoids (GB) series together with one new chromone-flavanone. This type of secondary metabolites exhibits remarkable pharmacological activities such as antihepatotoxic and bactericidal properties. As the biological activity often depends on the absolute configuration, the configurational assignments of GB series were revised to prove the presence of selected atropisomers in different parts of the plant. The full stereostructures of several 3, 8” linked biflavonoids as well as of the new chromone-flavanone were established by means of 2D-NMR investigations and of circular dichroism (CD) experiments, in combination with quantum chemical CD calculations.

Organic Chemistry **389**

Fe(II)-catalysed asymmetric hydrosilylation of ketones

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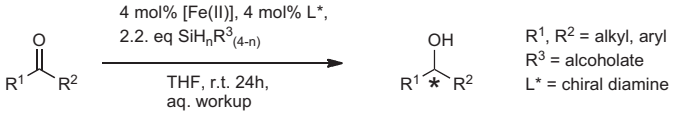
Fe(II) catalysts for asymmetric hydrosilylation of ketones (Scheme 1) have been generated *in-situ* using four new chiral ligands combining a cyclopentadienyl donor with a diamine unit (Figure 1). The influence of solvent, temperature, bulkiness of the ligand as well as the active oxidation state of the iron during catalysis have been investigated. In this system, only Fe(II) precursors lead to active catalysts, unlike in many well-known reactions requiring Fe(III)[1]. The new chiral ligands also stabilize the Fe(II) species significantly giving a much more robust system, as compared to catalysts just deriving from simple precursors.



Scheme 1. Asymmetric hydrosilylation of ketones.

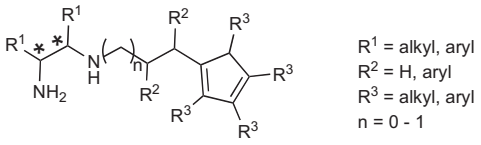


Figure 1. Basic core of the new chiral ligands.

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Organic Chemistry **390**

New Polyoxygenated 8- or 9-Membered Rings

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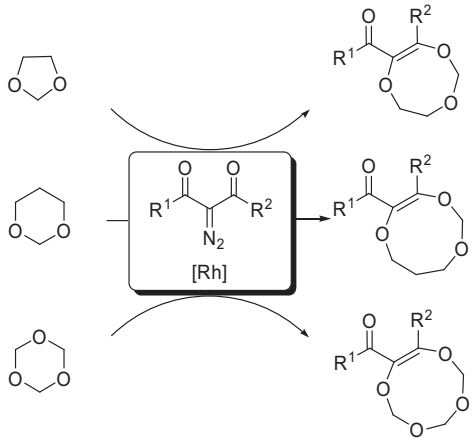
Whereas strategies for the making of functionalized 3-7 membered rings are numerous in synthetic chemistry, those applied to 8-9 membered rings are less common due to entropic reasons essentially. Herein, we report the use of dioxolane, 1,3-dioxane and trioxane, in ring expansion reactions leading to functionalized polyoxo 8- or 9-membered rings in moderate to good yields (40-85%). This novel process employs catalytic amounts of $Rh_2(OAc)_4$ and α-diazo-β-keto esters[1] as co-substrates.



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Organic Chemistry **391**

Switching on fluorescence selectively at cytosine bases

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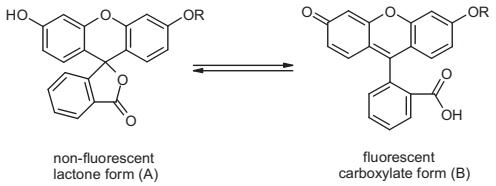
The hydrogen sulfite catalyzed transamination at the C4-amino group of cytosine is a well known reaction to attach various groups, including immunoreactive groups, fluorescent or spin labels [1,2]. Fluorogenic compounds have found extensive use as probes for a wide range of intracellular biomolecules and processes by becoming fluorescent only after activation by a specific chemical or enzymatic event [3].



While mono-O-substituted and unsubstituted fluorescein is in equilibrium with the highly fluorescent carboxylate form under neutral and basic conditions (B), di-O-substituted fluorescein compounds solely exist in the non-fluorescent lactone form (A). Our present efforts are focused on the synthesis of non-fluorescent compounds that can be coupled to cytosine in transamination reactions and that allow to specifically switch on fluorescence on demand.

Financial support from the Swiss National Science Foundation is gratefully acknowledged (SNF-Förderungsprofessur PP002-119106/1 to EF).

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Organic Chemistry **392**

Addition of Mono-organocopper Reagents to Thioiminium Ions

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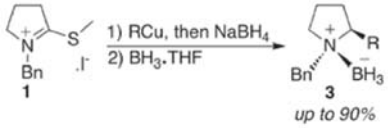
Gem-Dialkylation of thioiminium ions is a powerful method for alkaloid synthesis but the creation of a stereogenic quaternary center at the alpha position of the nitrogen atom still remains a challenging task.[1][2]

Bosch and co-workers reported two examples of monoalkylation[3] of thioiminium ions with organocuprate derivatives which prompted us to further investigate their approach. Herein we wish to report significant improvements in the mono-addition of various milder cuprous derivatives, as well as our advances in the sequential one-pot addition of two different nucleophiles onto thioiminium ions.



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Organic Chemistry **393**

Excess Electron Transfer through Phenanthrenyl Containing DNA

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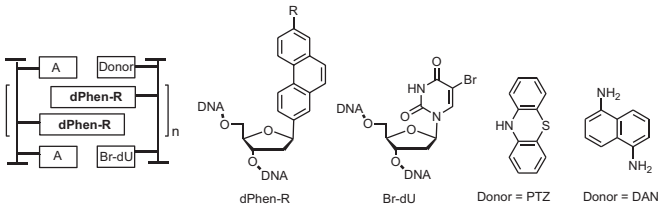
2′-Phenanthrenyl-C-nucleosides (dPhen-R, R= NO_2, NH_2, H) were recently synthesized and incorporated into oligodeoxyribonucleotides as non-hydrogen bonding nucleobase replacements [1]. It was shown that excess electron transfer (EET) occurs from an excited 5-(pyren-1-yl)uridine electron donor through an internal dPhen-R (R = H) pair to 5-bromodeoxyuridine (Br-dU) as the acceptor [2]. Since the reduction potential of phenanthrene is higher than that of pyrene, the EET from the excited 5-(pyren-1-yl)uridine likely occurs by a superexchange/tunneling mechanism. In order to observe EET by the more efficient electron hopping/molecular wire mechanism, the synthesis of oligodeoxyribonucleotides containing derivatives of phenothiazine (PTZ) and 1,5-diaminonapthalene (DAN) as electron donors with a higher reduction potential is pursued.



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Organic Chemistry **394**

Regioselectivity *vs*. Stereoselectivity: The Addition of a Cyclotriveratrylene-based Tris-malonate to C_{60} Revisited

Carlo Thilgen[1], Agnieszka Kraszewska[1], Pablo Rivera-Fuentes[1], Gwénaël Rapenne[2], Jeanne Crassous[3], Ana G. Petrovic[4], José Lorenzo Alonso-Gómez[4], Elisa Huerta[5], François Diederich[1]

[1]Laboratorium für Organische Chemie, ETH Zürich, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich, Switzerland, thilgen@org.chem.ethz.ch
[2]CNRS, CEMES, BP 94347, 29 rue J. Marvig, 31055 Toulouse, France
[3]Sciences Chimiques de Rennes, UMR CNRS 6226, Université Rennes 1, Campus de Beaulieu, 35042 Rennes, France
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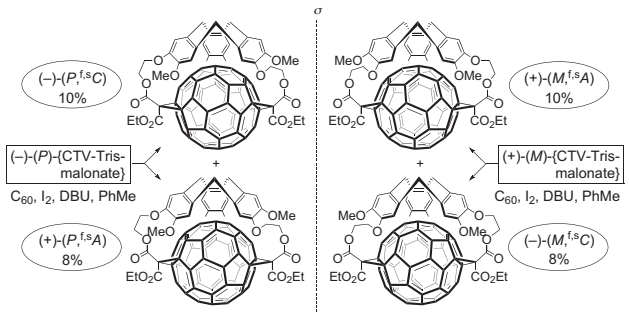
The triple *Bingel* addition of enantiomerically pure cyclotriveratrylene (CTV)-tethered tris-malonates to C_{60} was reinvestigated with focus on the question of regio- *vs*. diastereoselectivity. Experimental and theoretical electronic and vibrational circular dichroism studies allowed full characterization of the tris-adducts, showing that, contrary to earlier reports, the addition is regioselective, yielding only *trans*-3,*trans*-3,*trans*-3 tris-adducts.



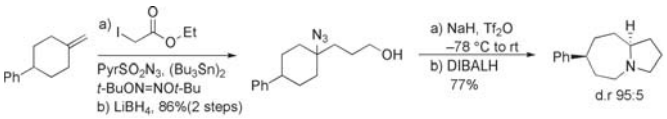
Organic Chemistry **395**

Formation of C-C bond *via* Intramolecular Schmidt Rearrangement Involving Primary Activated Azidoalcohol

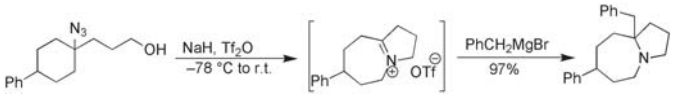
Ajoy Kapat and Philippe Renaud*

University of Berne, Freiestrasse 3, CH-3012 Bern (Switzerland)

Azaquaternary and azatertiary centre containing azabicyclic system is integral part of several biologically active alkaloids. [1] We have developed a powerful method to synthesize azabicyclic ring system from exocyclic olefin *via* radical carboazidation[2], reduction followed by intramolecular Schmidt rearrangement under nonacidic condition.[3]



Recently we have been successful to form azaquaternary center *via* intramolecular Schmidt rearrangement followed by reduction of iminium ion by carbon-centered nucleophiles in one pot.



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Organic Chemistry **396**

Probing DNA Adduct Structure-Activity Relationships: Synthesis and Characterization of Phenolic 2'-Deoxyguanosine Adducts

Heidi Dahlmann[1], Shana J. Sturla[1]

[1]ETH Zürich, Institute of Food, Nutrition, and Health, 8092 Zürich

Heteroatom-substituted aromatic xenobiotics, such as aromatic amines, heterocyclic amines, and phenols, from sources such as industrial emissions, environmental chemicals, and food preparations, are of concern as potential human carcinogens. Relevant biotransformations may include metabolic activation and DNA alkylation, leading to nitrogen- or oxygen-linked covalently bound DNA adducts at the 8-position of 2'-deoxyguanosine (dGuo). Depending on their chemical structure, these adducts may disrupt DNA replication and result in point or frameshift mutations. To further understand how the chemical structures of adducts impact their distinct mutagenic profiles, we have synthesized a series of oxygen-linked phenolic 8-dGuo adducts. These modified nucleobases will be incorporated into DNA oligonucleotides for structural and physical characterization, as well as for polymerase-mediated primer extension studies to explore their mutagenic potential. The results will be compared with the extensive data available for their *N*-linked counterparts.

Organic Chemistry **397**

Salvichlorodin, a Diterpene Possessing a New Skeleton

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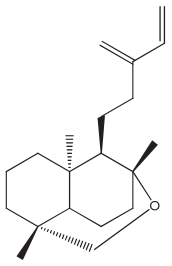
Division of Pharmaceutical Biology, University of Basel, 4056 Basel

The genus *Salvia* comprises some 900 species worldwide and is the largest genus of the family Lamiaceae. *Salvia* is represented in the flora of Iran by 58 species, 17 of which are endemic. Some of these species are used as medicinal, aromatic and ornamental plants. Diterpenoids are the most important class of compounds responsible for biological activities found in numerous *Salvia* species [1]. A new diterpene, salvichlorodin (**1**) was isolated from the aerial parts of endemic *Salvia chloroleuca* Rech. f. & Aell. A hexane extract of the aerial parts was fractionated by normal-phase column chromatography on silica gel. Final purification of compounds was achieved by preparative reversed-phase HPLC. The structure of **1** was established by extensive spectroscopic measurements including 1D- and 2D-NMR (COSY, HSQC, HMBC, HSQC-TOCSY) and HR-MS. The relative configuration was determined by NOESY experiments. Salvichlorodin (**1**) posseses a new diterpenoid skeleton biogenetically derived from the bicyclic labdane scaffold. The seven-membered heterocyclic ring confers high rigidity to the molecule.



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Organic Chemistry **398**

New flavone 8-C-glycosides from *Haberlea rhodopensis* Friv.

Samad N. Ebrahimi[1], Frank Gafner[2], Matthias Hamburger[1]

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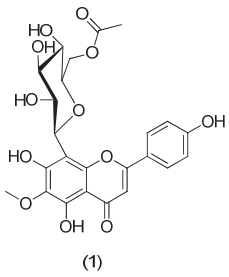
[2]Induchem AG, Industriestrasse 8a, CH-8604 Volketswil

Haberlea rhodopensis Friv. (Gesneriaceae) is a perennial resurrection plant native of the Balkans. As a poikilohydric organism, *H. rhodopensis* is dessication tolerant [1]. Its behavior under dehydration and rehydration has been the subject of several photosynthetic and metabolic studies. On the other hand, information on its secondary metabolites remains scarce.

Fractionation of a methanolic extract of the leaves of *H. rhodopensis* by a combination of liquid/liquid solvent extraction, preparative and semi-preparative HPLC on RP-18 yielded two new flavones C-glycosides, hispidulin-8-C-(6-O-acetyl)-*β*-D-galactopyranoside (**1**), and hispidulin-8-C-[6-O-acetyl-2-O-(4-hydroxy-3,5-dimethoxybenzoyl)]*β*-D-galactopyranoside (**2**), along with two known phenolic glycosides, myconoside and pauciflosides. The structures of **1** and **2** were established by extensive spectroscopic measurements including 1D- and 2D-NMR (COSY, HSQC, HMBC) and HR-ESIMS.



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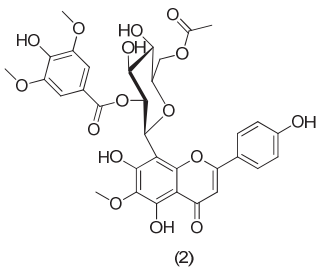

(2)

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Organic Chemistry **399**

Modular synthesis of cationic helical dyes

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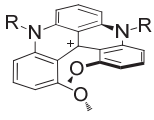
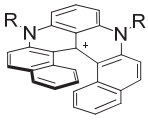
Department of Organic Chemistry, University of Geneva, 30 quai Ernest Ansermet, CH1211 Geneva, Switzerland

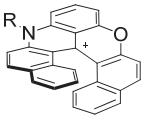
Helicenes are ortho-condensed polyaromatic compounds which are chiral due to the helical conformation of their backbone.[1] Whereas hundreds of neutral helicenes can be found in the literature, only few cationic derivatives have been reported.[2] Previously, we have shown that the enantiomers of cationic [4] diazahelicenes of type **1** can be separated.[3]



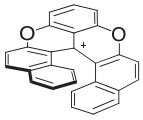
(*M*) - **1**



(*P*) - **2**



(*P*) - **3**



(*P*) - **4**

Herein, we report on novel cationic diaza, aza oxa and dioxa [6] helicenes (**2**, **3** and **4**) which are all readily prepared using a single modular 5-steps synthetic sequence. The diaza derivative **2** being furthermore readily resolved and selectively functionalized on the benzene or the naphthalene rings through orthogonal substitution process.

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Organic Chemistry **400**

Synthesis of Artificial Photosystems by Self-Organizing Surface-Initiated Polymerization

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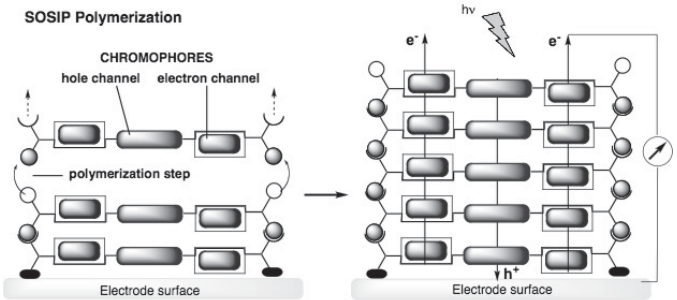
Department of Organic Chemistry, University of Geneva, Geneva, Switzeland

Bicontinuous donor-acceptor (D-A) arrays at the molecular level have attracted increasing scientific and technological interest because of their potential applications in organic photovoltaics [1]. In these bilayer organic solar cells, electrons and holes generated by exciton dissociation at the interface of n- and p-semiconductors travel through gradient-free bulk layers [2]. But it is still difficult to achieve the desirable vertical arrangement of bicontinuous D-A arrays on an electrode [3]. In this aim we use the self-organizing surface-initiated polymerisation (SOSIP) to form, by a bottom-up manner, a polymer brush surface [4].



[1] Thompson, B. C.; Fréchet, J. M. J. *Angew. Chem. Int. Ed.* **2008**, *47*, 58.
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Organic Chemistry **401**

Magnetically recoverable and reusable heterogeneous Pd catalysts for Suzuki reactions

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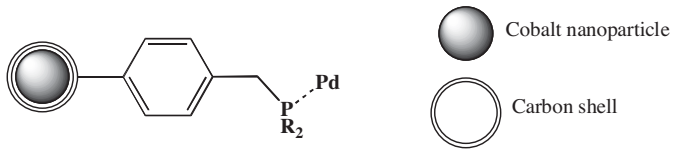
The Suzuki coupling, the most important reaction for aryl-aryl bond formation, is generally performed with expensive homogeneous Pd catalysts that cannot be recovered for reuse, and moreover often cause the presence of sizeable amounts of palladium in products and waste. The development of Pd catalysts that can be easily recovered for reuse is therefore highly desirable, particularly because of sustainable development-related concerns [1].

We will present here the preparation and reactivity of simple and efficient heterogeneous palladium catalysts supported on superparamagnetic cobalt nanoparticles which can therefore be easily and quantitatively recovered by magnetic separation. These catalysts are particularly efficient for Suzuki couplings from aryl bromides and have been reused several times.



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Organic Chemistry **402**

Synthesis of 1,3,5,7,9-penta-Substituted Corannulene

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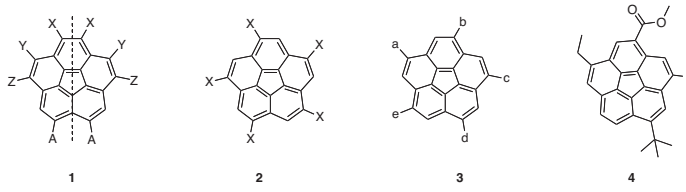
Institute of Organic Chemistry, University of Zurich, Winterthurerstr. 190, 8057 Zurich, Switzerland.

The most widely used method to access corannulene derivatives with mirror symmetry (**1**), follows the route from the corresponding naphthalene derivative to the substituted fluoranthene.[1] The general synthesis of *sym*pentasubstituted corannulenes with 5-fold symmetry (**2**) was achieved using the pentachloride, i.e., **2**, with X = Cl, which in turn comes from a five-fold symmetric chlorination of the parent hydrocarbon.[2]

A directed synthetic strategy for corannulene derivatives with five *different* groups at the 1,3,5,7,9-positions (**3**) was elaborated. An immediate precursor to **3**, corannulene derivative **4** was successfully synthesized.
An additional challenge is to introduce unique functional groups for a, b, c, d and e, such that every site in **3** is selectively addressable.



[1] Seiders, T. J.; Elliot, E. L.; Grube, G. H.; Siegel, J. S. *J. Am. Chem. Soc.* **1999,** *121*, 7804.; Sygula, A.; Rabideau, P. W. *J. Am. Chem. Soc.* **2000**, *122*, 6323.
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Organic Chemistry **403**

Amplification of chirality by supramolecular polymerization of pyrene oligomers

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The field of supramolecular polymers has emerged as a separate area of materials research. Their structural and functional properties largely depend on the nature of the non-covalent interactions between the individual units.[1] Spectroscopic measurements (absorbence, fluorescence and CD) showed that short oligomers of pyrenes connected via flexible phosphodiester linkers form organized structures and show chiral amplification. By adding of only 1% of pyrene oligomer modified with the base C, highest anisotropy was observed (Figure 1).
These observations are compatible with the formation of supramolecular polymers and represent the first example of supramolecular polymerization observed with oligomeric building blocks that are not pre-organized.

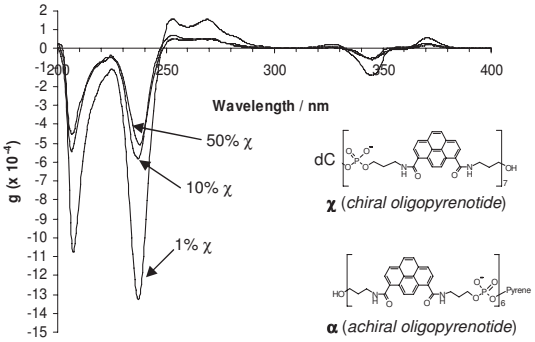

Figure 1: CD spectra (anisotropy factor g) of different mixtures of α and χ.

[1] T.F.A de Greef, E.W. Meijer, *Nature* **2008**, *453*, 171-173.

Organic Chemistry **404**

Loops vs. Stems: Benzylic Sulfide Oligomers Forming Carpet Type Monolayers

Fabian Sander[1], Torsten Peterle[1], Nirmalya Ballav[2], Florian von Wrochem[3] Michael Zharnikov[2], Marcel Mayor[1]*

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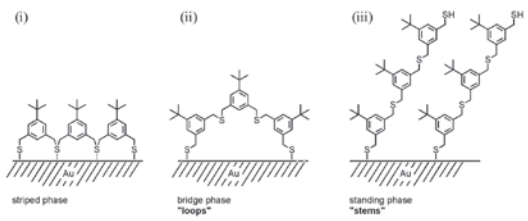
[2] Angewandte Physikalische Chemie, Universität Heidelberg, Im Neuenheimer Feld 253, 69120 Heidelberg, Germany; [3] Material Science Laboratory, Sony Deutschland GmbH, Materials Science Laboratory, Hedelfinger Strasse 61, 70327 Stuttgart, Germany;

Chain-like oligomers consisting of several in *meta* position interlinked benzylic sulfides and terminal benzylic thiols were synthesized and the nature of the molecular monolayers formed by their self-assembly on gold (111) substrates was investigated.[1] The fabricated films were characterized by high-resolution X-ray photoelectron spectroscopy and near-edge X-ray absorption fine structure spectroscopy. The target molecules were found to form dense and contamination-free SAM-like "carpet" films on gold (111). the predominant molecular conformation in these films were bridges ("loops") (ii) formed by the covalent attachment of both terminal thiols with a minor amount of molecules which were bound by only one thiol group as upright standing "stems" (iii) protruding the SAM.



[1] Fabian Sander, Torsten Peterle, Nirmalya Ballav, Florian von Wrochem,Michael Zharnikov, Marcel Mayor *J. Phys. Chem. C*, **2010**, 4118.

Organic Chemistry **405**

Molecular Gears in Parallel

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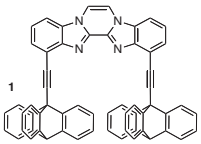
Organic Chemistry Institute, University of Zurich, Winterthurerstrasse 190, 8057 Zurich, Switzerland

Triptycene (Tp)-based molecular rotors[1] that rotate in a truly geared fashion were first described by Mislow and Iwamura in the 1980s.[2] These systems resemble molecular bevel gears and hold the interacting Tp groups at an angle of ca. 130°. In our laboratory, we are currently undertaking the design, synthesis, and computational studies of molecular gears of type **1**, which comprise Tp rotators with parallel rotational axes.

Analysis of the structure of Tp reveals that an axle-to-axle distance of ca. 8 Å,[3] which is found between the 4- and 4'-positions of 2,2'-bibenzimidazole (BBI), could allow for correlated rotation between interacting Tp groups that lie in parallel. Calculations on **1** in the M06-2X/cc-pVDZ basis set suggest the Tp groups in this molecule will exhibit efficient correlated rotation. Derivatives of **1** have been synthesized and desymmetrized derivatives thereof will be subjected to VT-NMR experiments to confirm the presence or absense of correlated rotation in these molecules. The outcomes of these studies will be presented along with the syntheses and computational data.



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Organic Chemistry **406**

New Synthetic Strategy for Amine-Terminated Oligothiophenes

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Building MXG, Station 12, 1015 Lausanne, Switzerland

Supramolecular self-assembly represents a convenient pathway to create optoelectronic materials from monodisperse π-conjugated oligomers.[1] Our work focuses on the synthesis and characterization of novel oligothiophenes bearing substituents capable of hydrogen-bonding to enhance crystalline order and optimize the π–π stacking interaction. Here we report a synthetic strategy for amine-terminated oligothiophenes. By utilizing a bulky imide protecting group to enhance the solubility of the higher oligothiophenes, these compounds can be readily synthesized and purified in a few steps on the multi-gram scale. Furthermore, the amine-terminated oligothiophenes could be converted to various amides.

[1] F. J. M. Hoeben, P. Jonkheijm, E. W. Meijer, A. P. H. J. Schenning, *Chem. Rev.* **2005**, *105*, 1491.

Organic Chemistry **407**

Quantum interference distinguishes between constitutional isomers

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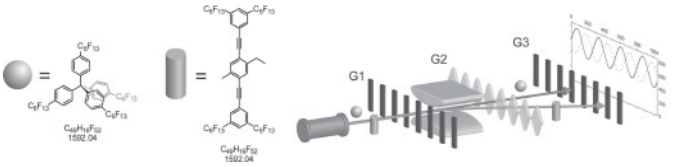
[1] Department of Chemistry, University of Basel, St. Johannsring 19, 4056 Basel, Switzerland
[2] Faculty of Physics, University of Vienna, Boltzmanngasse 5, 1090 Vienna, Austria

Matter wave interferometry has intrigued several generations of scientists because the delocalization of massive objects, as introduced by de Broglie in 1923,[1] is regarded both as a fundamentally non-classical, non-intuitive phenomenon and as an important ingredient in quantum-based measurement devices.

De Broglie quantum interference describes the center of mass motion of a massive body and yet it has been shown to be sensitive to the molecular structure and differences between constitutional isomers.[2]



Here, we present the synthesis and the matter-wave interference experiments of two tailor-made constitutional isomers having different total susceptibilities leading to different de Broglie interference shifts in the presence of external electric fields.

[1] L. de Broglie, *Nature* **1923**, *112*, 540.
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Organic Chemistry **408**

[2+2]- and [2+4]-Cycloadditions Using Benzynes and Corannulynes

Fabienne Furrer[1], Mihaiela Stuparu[1], Toshiyuki Hamura[2], Keisuke Suzuki[2], Jay S. Siegel[1]

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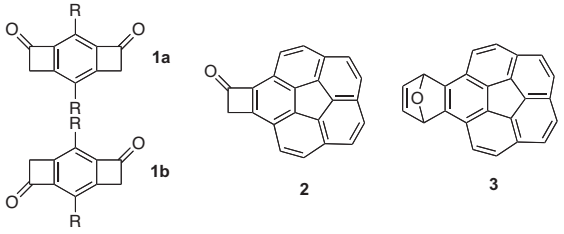
[2] Tokyo Institute of Technology, Department of Chemistry, O-okayama, Meguro-ku, Tokyo 152-8551, Japan

Cycloaddition reactions have been proven to be a very powerful, and therefore frequently used, tool in organic synthesis. They do not only provide a pathway to polycyclic systems, often in a stereoselective way, but can also deliver reactive precursors to even larger structures.

A [2+2]-cycloaddition using substituted benzynes and ketene silyl acetals (KSA's) has been developed recently [1]. This method was adjusted to afford the *p*-bisaddition products (**1a** and **1b**) of very simple benzene precursors. Our present efforts lie in the conversion of this method to the larger and bowl-shaped corannulynes to give structures like **2** and the extension of the method to [2+4]-cycloadditions using furane to give derivatives of **3**.



1a **1b** **2** **3**

[1] T. Hamura, T. Arisawa, T. Matsumoto, K. Suzuki, *Angw. Chem. Int. Ed.* **2006**, *45*, 6842.

Organic Chemistry **409**

Bidentate Lewis Acid Catalyzed Inverse Electron demanding Diels-Alder reaction – From Calculations to a New Principle in Catalysis

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[2]Department of Chemistry, University of Basel, Klingelbergstr. 80, Basel

In the shadow of the normal Diels-Alder reaction the inverse electron demanding Diels-Alder (IEDDA) reaction has gradually gained on interest over the past fifty years.[1] An interesting class of dienes are 1,2-diazenes as they give access to 1,2-substituted aromatic compounds in a single step. However, due to the high LUMO energies of 1,2-diazenes they are rather unreactive in the IEDDA reaction. Herein we report a bidentate Lewis acid as a catalyst for such an IEDDA reaction, which was identified by *ab initio* calculation and further complexation studies. The general principle relies on lowering the LUMO energy of the 1,2-diazene in order to facilitate the cycloaddition step. Detailed computational studies are employed to further elaborate mechanistic aspects. First simulations of NMR properties of 2-substituted furans revealed a strong solvent effect on the spectroscopic data. Although methods to calculate NMR parameters are commonly implemented in software packages such as Gaussian 03,[2] these methods are not cost effective for the description of solvated systems. Great efforts have been made towards the inclusion of discrete solvents, even in a dynamic fashion by molecular dynamics (MD) simulations.[3] In this contribution we describe the first catalyzed IEDDA reaction of 1,2-diazenes. Also, the calculations of the NMR properties of selected dienophiles using a combined MD/ab initio approach to correctly quantify solvent effects are reported.

[1] R. A. Carboni, R. V. Lindsey, *J. Am. Chem. Soc.* **1959**, *81*, 4342; D. L. Boger, *Chem. Rev.* **1986**, *86*, 781. [2] M. J. Frisch et al., *Gaussian 03, Revision D.02*, Gaussian, Inc., Wallingford, CT, **2004**. [3] M. Kaupp, M. Bühl, V. G. Malkin, 'Calculation of NMR and EPR parameters: theory and applications', Wiley-VCH Verlag, Weinheim, 2004; .M. Dračínský, P. Bouř, *J. Chem. Theory Comput.* **2010**, *6*, 288; R. E. Bulo, C. R. Jacob, L. Visscher, *J. Phys. Chem. A,* **2008**, *112*, 2640; A. Bagno, F. Rastrelli, G. Saielli, *J. Org. Chem.* **2007**, *72*, 7373; C. Benzi, O. Crescenzi, M. Pavone, V. Barone, *Magn. Reson. Chem.* **2004**, *42*, 57 C. Ramalho, C. A. Taft, *J. Chem. Phys.* **2005**, *123*, 054319.

Organic Chemistry **410**

Corannulene derivatives as surface polymer, supramolecular membrane aggregate and dyestuff

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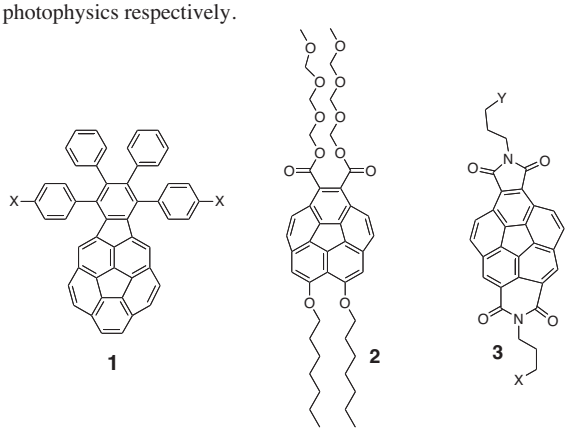
University of Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

The simplest member of the 'Buckybowls' family is corannulene, a $C_{20}H_{10}$ hydrocarbon representing the polar cap of C_{60} [1]. Like other corannulene derivatives, derivative 1,2 and 3 could have interesting properties on polymerization on solid surface, supramolecular aggregation chemistry and photophysics respectively.



Currently we are focused on the solution phase synthesis of potential precursors of these three target molecules [2].

[1] A. Sygula *et al*. *Tetrahedron* **2001**, *57*, 3637-3644.
[2] T. Jon Seiders, Eric L. Elliot, Gunther H Grube, and Jay S. Siegel *J. Am. Chem. Soc*. **1999**, *121*, 7804-7813.

Organic Chemistry **411**

Chemical Process for the Production of Corannulene: Application of Physical Organic Chemistry Methods to Synthesis on Kilo-Scale

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Organic Chemistry Institute and Labor für Prozessforschung, University of Zurich - Winterthurerstrasse 190, 8057 Zürich, Switzerland

Corannulene (**1**) was first synthesized in 1966 in 16 steps with less than a 1% yield.[1] This synthesis on milligram-scale, albeit pioneering, was not suitable for preparing enough material for further application. Improvements in the synthesis of **1** have opened the door for a variety of mono, di, tetra, penta, hexa and deca substituted derivatives on gram-scale.[2] These derivatives can be used as a template for a variety of higher order structures, such as graphite tubes/caps, liquid crystals, dendrimers, polymers, cruciforms, cyclophanes and molecular clefts. To exploit the materials chemistry of such derivatives, it would be advantageous to have a chemical process for production of **1** on kilo-scale.

Although the synthesis of corannulene on multi-gram scale has been well documented (**Fig 1**), successful scale-up of the synthesis of **1** required overcoming many obstacles. Following the kinetics of intermediates, understanding the specific reactivity of derivatives, performing multiple solubility studies, and dramatically improving purification techniques has led to an efficient chemical process for **1** on kilo-scale; this optimization decreases the cost of **1** from over $1000/gram to $20/gram.

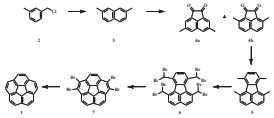

Figure 1. Synthesis of corannulene (**1**).

1. Barth, W.E.; Lawton, R. G. *J. Am. Chem. Soc.* **1966**, *88*, 380.
2. Wu, Y.-T.; Siegel, J. S. *Chem. Rev.* **2006**, *106*, 4843.

Organic Chemistry **412**

Towards continuous synthesis of radiopharmaceuticals:

A microfluidic module for solvent exchange

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Laboratory of Organic Chemistry, ETH Zurich, Wolfgang-Pauli-Str. 10, CH-8093 Zurich, Switzerland

Positron emission tomography (PET) is an important technique for medical diagnosis capable of imaging metabolic pathways in the living body [1]. Among suitable radiopharmaceuticals, [^{18}F]FDG is by far the most commonly used radiotracer. Due to the short half-life of the radionuclide ^{18}F ($t_{1/2}$ = 110 min), a fast, selective, on-demand production is required. Recently, improved yields and speed [^{18}F]FDG synthesis in a microfluidic based system was demonstrated [2]. Microfluidic systems offer controlled and reproducible reaction conditions as well as an easy shielding of the entire microchip [3]. However, a breakthrough would be the *continuous* operation of the microfluidic reactor for radiopharmaceutical synthesis. One key challenge of such a continuous-flow microreactor is the development of a module that facilitates the efficient exchange of solvents. In this contribution, we demonstrate the exchange of organic and aqueous solvents in a microfluidic droplet generating device made of the polymer polydimethoxysilane. The introduction of hot nitrogen into a stream of solvents with different boiling points results in formation of microsized gas bubbles with high surface-to-volume ratio and enables fast evaporation of the volatile solvent, and enrichment of the less volatile solvent. The gas phase is removed downstream in a branched microchannel design. We show the functioning of the microfluidic module for the mixture of water/acetonitrile, which is utilized in the synthesis of [^{18}F]FDG. The approach is generally applicable for the synthesis of other radioactive compounds, and can be employed in microfluidic reactors made of other materials such as glass.

[1] L. Cai, S. Lu, V. W. Pike, *Eur. J. Org. Chem*. **2008**, *17*, 2843
[2] C.-C. Lee, G. Sui, A. Elizarov et al., *Science* **2005,** *310*, 1793
[3] A. M. Elizarov, *Lab Chip* **2009**, *9*, 1326

Organic Chemistry **413**

Synthetic Strategies Towards a Carbazole Based Macrocycle

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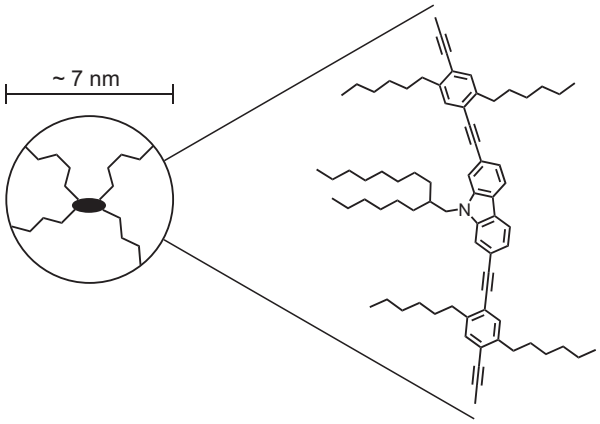
[1]University of Basel, Department of Chemistry, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

Template directed synthesis of macrocycles larger than 7 nm diameter consisting of a single molecular structure is a great synthetic challenge [1]. Clever use of protecting groups and relative functional group reactivates is required in order to achieve a monodispersed end product.



A range of polar acetylene protecting groups (PGs) were employed in a statistical reaction strategy. Orthogonality in the deprotection of these PGs was employed to selectively reveal acetylene moieties for palladium couplings. Carbazole moieties will allow insertion of a semi-rigid template facilitating an efficient cyclisation and aid in subsequent surface deposition experiments.

[1] Marcel Mayor, Claudia Didschies, *Angew. Chem., Int. Ed.* **2003**, *42*, 3176.

Organic Chemistry **414**

Synthesis of 6'-hydroxy bicyclo-[3.3.0] nucleosides

Anna-Barbara Gerber, Christian Leumann

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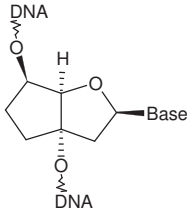
In the last two decades, a variety of modified nucleosides have been developed to improve antisense or siRNA oligonucleotide properties such as target affinity, nuclease resistance, and pharmacokinetics. It is well established that conformational restriction leads to an enhancement in binding affinity and biostability due to an entropic advantage. In the context of conformational restriction our laboratory synthesized and characterized the analogue bicyclo-DNA **1**[1]. In continuation of this work we now envisaged the synthesis of 6'-hydroxy bicyclo nucleosides to investigate its structure-affinity relationship in complementary binding to DNA and RNA.

We present the synthesis of the thymidyl and adenyl nucleosides **2a**, their incorporation into DNA and first pairing properties.



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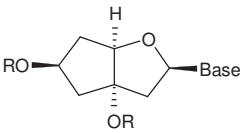

2a R=H
2b R=DNA

[1] M. Tarköy, M. Bolli, B. Schweizer, C.J. Leumann, *Helv. Chim. Acta*, **1993**, *76*, 481-510.

Organic Chemistry **415**

Fluorescence based Metal ions detection

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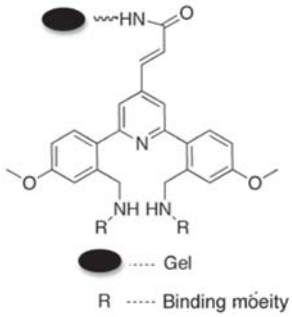
Presence of Metal ions can be both - good and bad, e.g., cellular Ca(II) is essential for life but, Hg(II) caused poisioning at Minamata Bay. This motivates us towards their detection. Literature is full of various methods for detection of metal ions. Fluorescence is one of the most sensitive analytical tools available, but most metallic analytes are non-fluorescent in nature. Our objective is to develop combinatorial libraries of fluorescent chemosensors – molecules which on binding to non-fluorescent substrates provide fluorescence response. To that purpose we would exploit conformational restriction as a signaling mechanism, which we expect will minimize structural restriction of the binding domains. [1,2]



[1] Jesse.V. Mello, Nathaniel.S. Finney, *J. Am. Chem. Soc.* **2005**, *127, 10124*.
[2] Sergey.A. Malashikhin, Kim.K. Baldridge, Nathaniel.S. Finney, *Org. Lett.* **2010**, 12, *940*.

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New conformationally constrained bicyclo-DNA analogs

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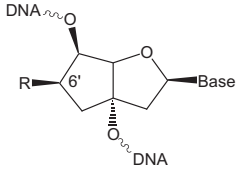
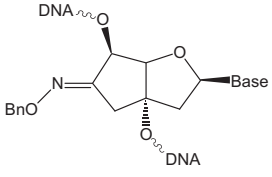
Within the past one and a half decade, the approach of conformational preorganization of double-stranded oligonucleotides has led to the production of a large number of nucleoside analogs with a backbone locked in a specific conformation. Our first contribution in this field of research was bicyclo-DNA (bc-DNA) which bears an ethylene bridge between carbons 3' and 5' of the deoxynucleoside unit. In the bicyclo-DNA scaffold, our focus of interest revolves around the improvement of RNA affinity and cell permeability. Using a structure/affinity approach on the bc-DNA skeleton **1**, we found the position 6' to be a site of choice for the introduction of various substituents, as e.g. an oximo functional group in the case of bc^{ox}-DNA **2** [1].

We now wanted to introduce a lysine substituent into position 6' in order to reduce the net charge of the oligonucleotide and thus improve its cell permeation properties. We report on the synthesis of the corresponding nucleoside carrying the base thymine and its incorporation into oligodeoxynucleotides. Properties of such oligomers as well as cell transfection experiments are presented.



1 R = H, bc-DNA



2 bc^{ox}-DNA

[1] S. Luisier and C. J. Leumann, *ChemBioChem* **2008**, *9*, 2244-2253.

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Influence of the Structure of Phosphoramidates on Flame Retardant Properties of Cellulose

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The effectiveness of phosphoramidates in providing flame retardancy to cellulose varies considerably and mostly depends on the chemical environment of the phosphorus atom. Investigations of the structure-property relationship is the key to understand the mechanism of action of phosphoramidates on cellulose. Phosphorus in various chemical states interact with cellulose through acidic intermediates to reduce its flammability. Although numerous investigations on the reaction mechanisms of phosphorus-containing compounds have been performed [1,2], the exact mechanism of action was not elucidated so far.

This research focuses on the investigation of the influence of phosphoramidate structure on thermal decomposition and burning behavior of cellulose. For this study, dimethyl- (DMP), diethyl- (DEP), di-n-butyl- (DBP), di-isopropyl- (DIP) and diphenyl-phosphoramidates (DPP) were taken.

Cellulose in form of cotton fabrics was impregnated with the phosphoramidates from ethanol solution. The burning behavior of phosphoramidates-treated samples was estimated using Limiting Oxygen Index (LOI) Test. Thermal behaviour was evaluated using thermogravimetric analysis (TGA) and microscale combustion calorimetry (MCC). The surface of the chars left after the LOI test was investigated using Scanning Electron Microscopy (SEM) and elemental analysis. Further attempts to get an insight into the mode of actions of phosphoramidates were contrived using evolved gas analysis techniques such as TGA-FTIR-MS.

[1] Gaan, S. and G. Sun, *Polym Degrad Stab*, **2007**, *92*, 968.
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Diastereoselective and Highly Enantioselective Henry Reactions Catalyzed by Copper(II) Complexes

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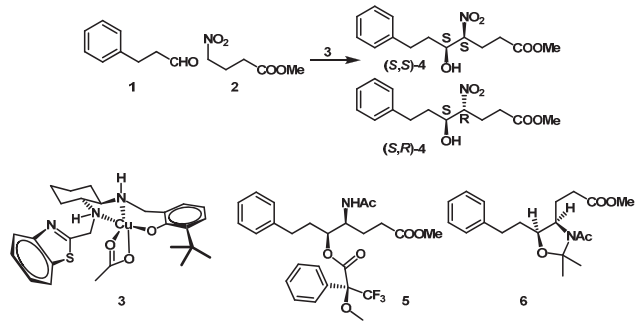
We have recently shown that Cu(II) complexes of C_1 symmetric ligands are versatile catalysts for the synthesis of chiral nitro alcohols from various aromatic aldehydes and nitromethane.[1] In order to optimize the catalytic system for diastereoselective transformations we have prepared various ligands and investigated the corresponding Cu(II) complexes for the reaction between **1** and **2**. Best results where obtained with complexes such as **3** (5 mol% in THF, -20^{0}C) which gave (*S*,*S*)-**4** as the major product (86%) and (*S*,*R*)-**4** as the minor component (13%). The corresponding enantiomers were produced below 1%. The absolute and relative configurations of the nitro alcohols were determined by ^{1}H-NMR of the Mosher ester **5** and the acetal **6**, respectively.



[1] G. Zhang, E. Yashima, W.-D. Woggon, *Adv. Synth. Catal.* **2009**, *351*,1255-1262.