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## 248

### Highly enantioselective epoxidation of alkenes and allylic alcohols using axially chiral iminium salts as catalysts.

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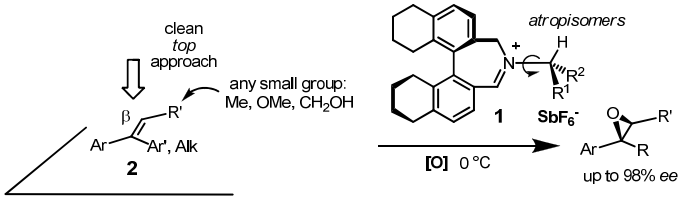
Biaryl (axially chiral) iminium salts of type **1** were prepared and used as catalysts in enantioselective epoxidation of unfunctionalized olefins [1]. These derivatives have shown excellent asymmetric efficiency (up to 98% *ee*) for a range of trisubstituted alkenes and allylic alcohols of type **2** [2]. Herein, we detail that the so far unexplained "lack" of stereochemical control from the chiral exocyclic appendage in this type of catalysts is due to the existence of atropisomers around the $N(sp^2)$-$C(sp^3)$ bond that links the azepinium core to the exocyclic stereocenter. Finally, we develop a general model to predict with certainty high selectivity in the formation of non-racemic epoxides of defined absolute configuration.




[1] E. N. Jacobsen, A. Pfaltz, H. Yamamoto, Editors, *Comprehensive Asymmetric Catalysis I-III, Volume 2*, **1999,** 503 pp.
[2] R. Novikov, G. Bernardinelli, J. Lacour, *Adv. Synth. Catal*., **2008**, *350*, 1113.; R. Novikov, G. Bernardinelli, J. Lacour, *Adv. Synth. Catal*., **2009**, *351*, 596.

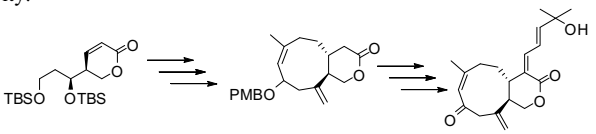
## 249

### Studies towards Total Synthesis and Biological Activity of *Xenicanes*.

Cotinica Hamel, Evgeny V. Prusov, Jürg Gertsch, Bernd Schweizer, Karl-Heinz Altmann*

ETH Zürich, Wolfgang-Pauli-Str. 10, CH-8093 Zürich, Switzerland

Secondary metabolites isolated from numerous marine species have become increasingly important lead structures for drug discovery.[1] Diterpenoids derived from soft corals of the genus *Xenia* exhibit a wide range of activities, including antiproliferative, antiangiogenic, or antibacterial effects. Of particular interest here is blumiolide C (**1**), which was isolated in 2005 by El-Gamal *et al*. and reported to exhibit potent *in vitro* antiproliferative activity.[2]




We achieved the first enantioselective total synthesis of the *Xenia* diterpenoid blumiolide C (**1**) in 27 steps (24 steps for the longest linear sequence) and 1% overall yield.[3] The synthesis is featured by unprecedented construction of the [7.4.0] oxabicylic ring system through the RCM-based formation of a nine-membered ring as the key step. Other crucial elements of our approach to **1** include an Evans aldol reaction, a highly diastereoselective mixed cuprate addition to an α,β-unsaturated δ-lactone, and a stereospecific dehydration reaction with $DCC/CuCl_2$ to introduce the side chain at α-position of the lactone ring. Our current efforts are devoted to the total synthesis of other members of *Xenicanes* family.

[1] *Anticancer Agents from Natural Products*, CRC Press LLC, **2005**.
[2] El-Gamal *et al*., *J. Nat. Prod.* **2005**, *68*, 1336-1340.
[3] K.-H. Altmann *et al*., *Angew. Chem. Int. Ed.* **2008**, *47*, 10081 –10085.

## 250

### Creation of quaternary aryl substituted asymmetric centers through conjugate addition

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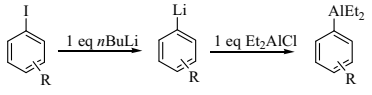
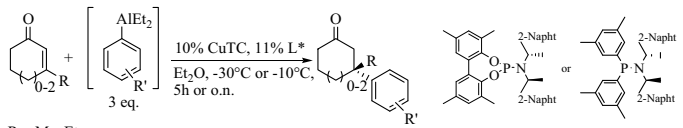
Enantioenriched all-carbon quaternary stereocenters are ubiquitous motifs in natural and pharmaceutical products. Cu-catalyzed conjugate addition can give access to these centers, but the introduction of bulky aryl groups is a challenge and requires special, Lewis acidic aryl alanes that can be generated from aryl iodides:




R = H, Me, OMe, $CF_3$, Br

These aryl alanes can be used in the Cu-catalyzed addition to a variety of cyclic enones allowing the creation of chiral aryl substituted quaternary centers.




R = Me, Et, *i*Bu; R' = H, Me, OMe, $CF_3$, Br; up to 98.6% ee, 87% yield




Both, electron-donating and electron-withdrawing groups give full conversion and very good ee.

[1] Christine Hawner, Kangying Li, Virginie Cirriez, Alexandre Alexakis, *Angew. Chem. Int. Ed.* **2008**, *47*, 8211.

## 251

### Total Syntheses and SAR studies of (-)-Zampanolide and (-)-Dactylolide

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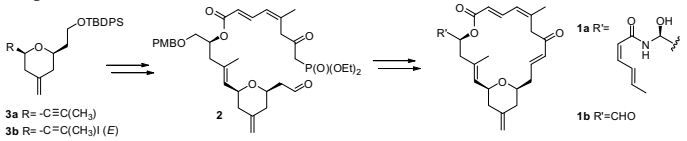
Institute of Pharmaceutical Sciences/ETH Zürich, Wolfgang-Pauli-Str. 10, CH-8093 Zürich, Switzerland

(-)-Zampanolide (**1a**) [1] and (-)-dactylolide (**1b**) [2] are structurally related polyketide-based macrolides, with a highly unsaturated 20-membered macrolactone core structure, which also includes a *cis*-2,6 disubstituted tetrahydropyran ring. While **1a** is a marine natural product, **1b** is the antipode of the natural product (+)-dactylolide. **1a** has been reported to exhibit low nM antiproliferative activity against different human cancer cell lines *in vitro* ($IC_{50}$s between 2-10 nM); in contrast, the related natural product (+)-dactylolide was found to be only moderate active, with $IC_{50}$s in the low μM range.




**3a** R= -C≡C($CH_3$)
**3b** R= -C=C($CH_3$)I (*E*)

In this contribution we present a new total synthesis of **1a** and **1b** together with the result of their biological evaluation. (For previous syntheses of **1a/b** see [3]). Some of the key features of our approach to **1a/b** are the stereoselective construction of tetrahydropyran **3a**, its conversion to the (*E*)-vinyl iodide **3b**, and the epoxide opening of PMB-protected (*R*)-glycidol with lithiated **3b**. Ring-closure was achieved by intramolecular HWE reaction with phosphono aldehyde **2**, which was followed by further elabortion into **1b** and **1a**. The chemistry developed in the course of the total syntheses provides the basis for analog syntheses and future SAR studies.

[1] Tanaka, J.; Higa, T. *Tetrahedron Lett.* **1996**, *37*, 5535.
[2] Cutignano, A. *et al. Eur. J. Org. Chem.* **2001**, 775.
[3] Ding, F.; Jennings, M. P. *J. Org. Chem.* **2008**, *73*, 5965 (and citations).

## 252

### Iron-Catalyzed Mizoroki-Heck Cross-Coupling reaction with Styrenes and Oxidative Coupling of Tertiary Amines with Terminal Alkynes

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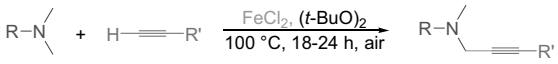
Iron-catalyzed carbon-carbon bond forming reactions have been a very hot topic in the recent years as they are non-toxic, cheap and environmentally benign.[1] Earlier, we have reported the iron-catalyzed selective coupling of aliphaticsulfonyl chlorides with Grignard reagents. We continued our efforts to apply iron-catalysis to other interesting reaction like Sonogashira-Hagihara coupling. Now, we have found that Mizoroki-Heck cross-coupling reactions of styrenes can be catalyzed with inexpensive and non-toxic $FeCl_2$ in DMSO and in the presence of *t*-BuOK and a ligand such as picolinic acid or proline below 60 °C.[2]


We have also developed a new iron-catalyzed oxidative C-C cross-coupling reaction between tertiary amines and terminal alkynes to generate propargyl amines.[3]




R = aromatic, aliphatic, benzyl

[1] (a) Bolm, C; Legros, J; Le Paih, J; Zani, L, *Chem. Rev*. **2004,** *104,* 6217 (b) Fürstner, A; Martin, R, *Chem. Lett.* **2005**, *34*, 624.
[2] Volla, C. M. Rao; Loska, R.; Vogel, P. *Adv. Synth. Catal.* **2008**, *350*, 2859.
[3] Volla, C. M. Rao; Vogel, P. *Org. Lett.* **2009**, *11*, 1701-1705.

## 253

### One-Pot Double Chain Elongation and Desymmetrization for Synthesis of Polyketide or Polypropionate Fragments

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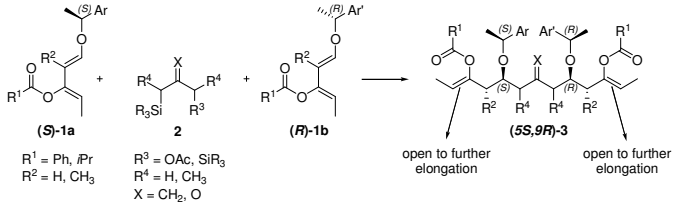
Laboratoire de glycochimie et de synthèse asymétrique, Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland

Polyketide and polypropionate natural products resemble an interesting class of compounds showing a wide range of biological activity. The most commonly used methods for their synthesis are aldol reactions or allylation of aldehydes. We have developed another efficient route to this family of compounds (**3**) involving a *hetero*-Diels-Alder reaction of sulphur dioxide to a 1,3-dioxy-1,3-diene (**1**) in the presence of a Lewis acid promoter, quenching of the obtained intermediate with a carbon nucleophile (e.g. enoxy- or allylsilanes (**2**)) and release of $SO_2$.[1]
With our methodology we are now able to carry out a bidirectional chain elongation using two different dienes (**1a**, **b**) with stereoselective control either as a one- or a two-pot process. The so-obtained *pseudo*-$C_2$- or -σ-symmetrical adducts are easily desymmetrized by selective deprotection for separate elaboration of the two sides leading to advanced polyketide or polypropionate fragments. The latest results will be presented.




[1] a) M. Turks, F. Fonquerne, P. Vogel, *Org. Lett.* **2004**, *6* (6), 1053; b) M. Turks, X. Huang, P. Vogel, *Chem. Eur. J.* **2005**, *11*, 465; and references therein.

## 254

### The Nonclassical Carbocation Problem in Gold-Catalyzed homo-Rautenstrauch Cyclizations

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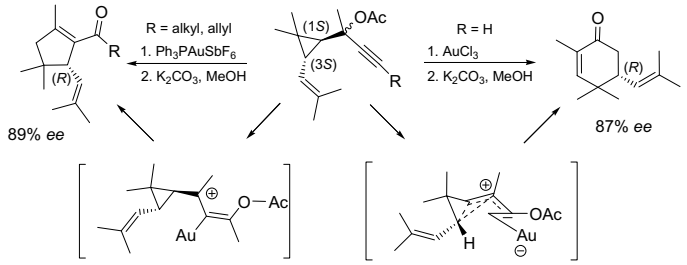
[1]Department of Chemistry, Fudan University, 220 Handan Road, 200433, Shanghai, P. R. China
[2]Givaudan Fragrances (Shanghai) Ltd., 298 Li Shi Zhen Road, 201203, Shanghai, P. R. China
E-mail: andreas.goeke@givaudan.com

The **Rautenstrauch cyclization** is an important reaction to synthesize cyclopentenones[1][2]. Homologous systems can be constructed to access Rautenstrauch cyclization products of larger ring sizes [3]. The high degree of chirality transfer in these reactions suggests that gold-stabilized **non-classical carbocations** with configurational stability are involved. With our study we will present new evidence for the recently discussed **nonclassical carbocation** character of intermediates in gold catalysis.




[1] V. Rautenstrauch, *J. Org. Chem*. **1984**, *49*, 950.
[2] X. Shi, D. J. Gorin, F. D. Toste, *J. Am. Chem. Soc*. **2005**, *127*, 5802.
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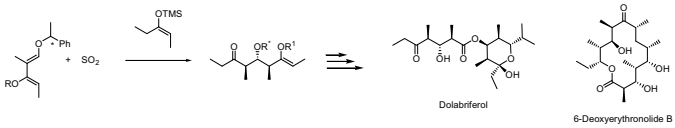
## 255

### Expeditious synthesis of *anti*,*anti*-Dipropionate Stereotriads Applications towards total synthesis of polypropionates

Sylvain Laclef, and Pierre Vogel*

Laboratory of glycochemistry and asymmetric synthesis (LGSA), Swiss Federal Institute of Technology (EPFL) CH-1015 Lausanne, Switzerland

Polypropionates constitute an important class of products with a wide range of interesting biological activities. Our group has shown previously that alkyl-substituted 1,3-dioxy dienes can undergo hetero-Diels-Alder reactions with $SO_2$, to give the corresponding sultines, which at low temperature in the presence of Lewis acids can be opened to zwitterionic intermediates.[1] The latter can be trapped by nucleophiles. This methods allows us, using (*E*)-enoxysilanes as nucleophiles to obtain *anti*,*anti*-dipropionate stereotriad in high diastereoselectivity. This common subunit found in polyketide-derived natural products has generally been recognized to be difficult to synthesize. Combination of our methodology and aldol chemistry allows one to achieve polypropionate fragments in a short sequence.




[1] Vogel, P.; Turks, M.; Bouchez, L.; Craita, C.; Huang, X.; Murcia, M. C.; Fonquerne, F.; Didier, C.; Flowers, C. *Pure Appl. Chem.* **2008**, *80*, 791-805..

## 256

### CpRu-catalyzed regio- and enantioselective decarboxylative allylic rearrangements

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Department of Organic Chemistry, University of Geneva
30 Quai Ernest Ansermet, CH1211 Geneva Switzerland
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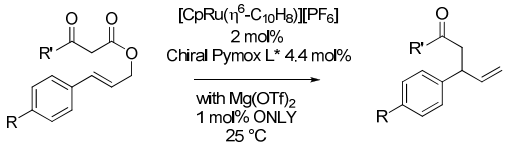
The stereoselective generation of tertiary or quaternary stereogenic centers by nucleophilic substitution still represents a challenge in natural product and medicinal chemistry. In this context, and in the field of enantioselective allylation in particular, $\eta^5$–arene Ru complexes can be of use.[1] Recently, we have shown that the CpRu(II) moiety can efficiently catalyze the decarboxylative allylic rearrangement of $\beta$-ketoesters or cinnamyl carbonates affording, in the presence of selected enantiopure ligands, the desired products with high regio- and enantioselectivity.[2] Now, we show that the reactivity of this catalytic system can be enhanced by using novel enantiopure pyridine-oxazoline carboxylates as ligands or by the addition of a *Lewis* acid as co-catalyst. In the latter case, the new set of catalytic conditions allows to obtain the rearranged products with higher branched to linear ratio and *ee* values and this at quite lower temperature.




[1] Mbaye, M. D. *et al*. *Chem*. *Commun*. **2004,** *1870*. Onitsuka, K. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2008**, *47*, 1454;
[2] Constant, S. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2007**, *46*, 2082. Austeri, M. *et al*. *Chem*. *Eur*. *J*. **2008**, *14*, 5737. Linder, D. *et al*. *Eur*. *J*. *Org*. *Chem*. **2008**, 5778.

## 257

### Copper catalysed C-H arylation of electron rich aromatics

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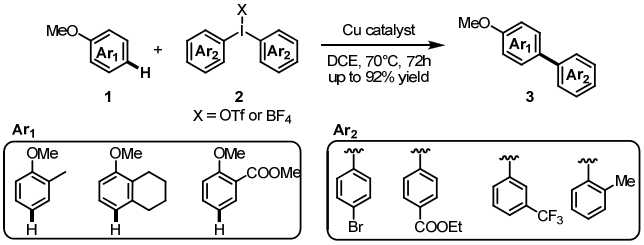
University of Cambridge, Department of Chemistry,
Lensfield Road, Cambridge, CB2 1EW, UK, mjg32@cam.ac.uk

Transition metal catalyzed C-H functionalization of C-H bonds is emerging as a powerful tool in organic synthesis.[1] Access to biaryl motifs from electron-rich arenes usually requires a two-step electrophilic halogenation/metal catalyzed cross-coupling sequence. Based on recent results from our group,[2] we have developed a *para*-selective copper catalyzed C-H arylation of electron rich aromatics utilizing iodonium salts as arylating agents.[3] Anisole derivatives of type **1** have been successfully arylated with yields up to 92%. Functionalities on the transferred aryl group **$Ar_2$** include halogens, esters, and nitro groups. Finally, applying this methodology to late stage functionalization of drug candidates offers a powerful tool to introduce diversity for biological activity studies.




[1] For review, see: (a) Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006,** *62,* 2439. (b) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417.
[2] (a) Phipps, R. J.;Grimster, N.P.; Gaunt, M.J. *J.Am.Chem.Soc.* **2008**, *130*, 8172. (b) Phipps, R. J.;Grimster, N.P.; Gaunt, M.J. *Science* **2009**, *323*, 1593.
[3] Liu, T.Y.; Ciana, C.L.; Brandt, J.R.; Gaunt, M.J.; *manuscript in preparation*

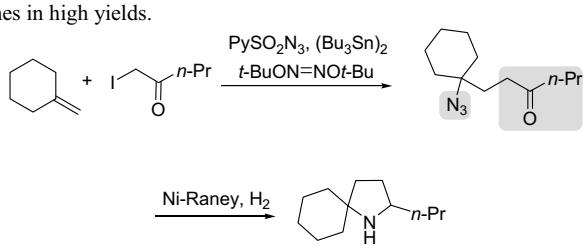
## 258

### Broadening the Scope of the Radical Carboazidation: Application to the Synthesis of Alkaloids

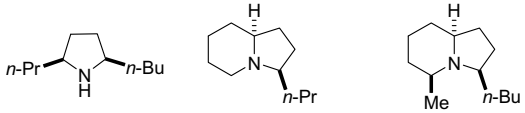
Guillaume Lapointe and Philippe Renaud*

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

Hereby is described an extension to the radical carboazidation[1]. By the use of α-iodoketones, a carboazidation/reductive amination sequence afforded amines in high yields.




This sequence was efficiently applied to the total synthesis of three different *Myrmicaria Melanogaster* alkaloids, including (±)-Monomorine I.




*Myrmicaria melanogaster* alkaloids **Monomorine I**

[1] Panchaud, P.; Chabaud, L.; Landais, Y.; Ollivier, C.; Renaud, P.; Zigmantas, S. ; *Chem. Eur. J.* **2004**, *10*, 3616.

## 259

### Peptides as Catalysts for Asymmetric 1,4-Addition Reactions of Aldehydes to Nitroalkenes

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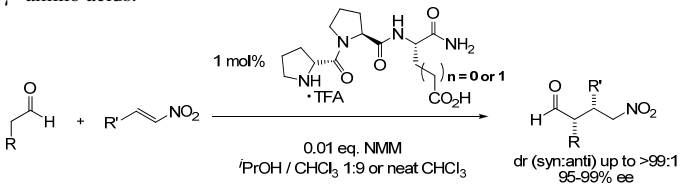
St. Johanns-Ring 19, CH-4056 Basel, Switzerland

Recently we introduced the peptide H-D-Pro-Pro-Asp-$NH_2$ and H-D-Pro-Pro-Glu-$NH_2$ as excellent catalysts for conjugate addition reactions of aldehydes to nitroalkenes. In the presence of only 1 mol% of the peptidic catalysts, a broad range of different aldehydes and nitroolefins, including nitroethylene, react readily with each other to afford the γ-nitroaldehydes in up to quantitative yields and excellent stereoselectivities.[1,2] In addition, we established a new catalytic route for the synthesis of chiral monosubstituted $\gamma^2$-amino acids.




Studies on related peptides and extensive kinetic studies using *in situ* FT-IR techniques led to an improved catalytic system requiring even lower catalyst loadings of far below 1 mol%.

1. M. Wiesner, J. D. Revell, H. Wennemers, *Angew. Chem., Int. Ed.* **2008**, *47*, 1871.
2. M. Wiesner, J. D. Revell, S. Tonazzi, H. Wennemers, *J. Am. Chem. Soc.* **2008**, *130*, 5610.

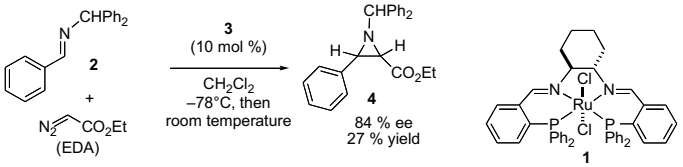
## 260

### Asymmetric Aziridination Catalyzed by Ruthenium / PNNP Complexes

Marco Ranocchiari and Antonio Mezzetti*

Dept. of Chemistry and Applied Biosciences, ETH Zürich, CH–8093 Zürich

Although aziridine-2-carboxylates are valuable precursors for α- and β-amino acids, asymmetric catalytic methods for their synthesis from imines are rare. Therefore, after the successful application in the *cis*-selective cyclopropanation of cationic catalysts derived from $[RuCl_2(PNNP)]$ (**1**) [2], we report the Ru/PNNP-catalyzed reaction between ethyl diazoacetate (EDA) and aromatic imines to give chiral aziridines. In the best reaction, benzhydryl imine **2** reacts with EDA in the presence of the elusive species $[RuCl(OEt_2)(PNNP)]^+$ (**3**), prepared by activation of **1** with $(Et_3O)PF_6$ (1 equiv), to give **4** with high enantioselectivity (84 % ee):




The yield is modest, though, owing to the concurrent formation of maleate. To optimize both the enantioselectivity and the aziridine yield, we are investigating the reaction mechanism. Preliminary studies disfavor both the coordination of the imine to ruthenium and the reaction of the imine with the previously reported carbene complex $[RuCl(CHCOOEt)(PNNP)]^+$ [1]. Monitoring the reaction between complex **3**, imine **2**, and $^{13}C$- or $^{15}N$-labeled EDA at low temperature we discovered a transient diazoester complex that apparently reacts with **2** to give aziridine **4**. It should benoted that a mechanism involving the activation of the diazoester is unprecedented is unorecedented in aziridination of imines.

[1] C. Bonaccorsi, A. Mezzetti, *Organometallics*, **2005**, *24*, 4953.

## 261

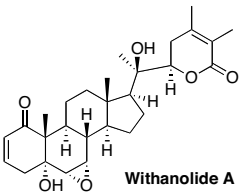
### Synthesis and Biological Evaluation of the Neuritogenic Steroidal Lactone Withanolide A and its Derivatives

Tom M. Woods, Henning Jessen, Karl Gademann

Chemical Synthesis Laboratory, EPFL, 1015 Lausanne, Switzerland

Neurodegenerative diseases, e. g. Alzheimer's, are becoming more prevalent due to an ageing population and the need for drugs capable of treating these diseases is becoming more urgent. Neuritic atrophy is considered one of the major causes for the loss of cognitive function in sufferers of neurodegenerative diseases.[1] The methanol extracts of the dried roots of *Withania somnifera* have been shown to induce neurite outgrowth and withanolide A was found to be one of the compounds responsible for this activity.[2]

Our efforts towards the total synthesis of withanolide A and its biological evaluation in neurite outgrowth assays will be presented. The investigation of SAR through the synthesis and biological evaluation of derivatives of the natural compound, with the aim of identifying simplified and more potent analogues that are better suited as therapeutic agents, will also be discussed.




Withanolide A

[1] a) De Kosky, S.; Scheff, S. W. *Ann. Neurol.* **1990**, *27*, 457. b) Terry, R. D.; Masliah, E.; Salmon, D. P.; Butters, N.; De Teresa, R.; Hill, R.; Hansen, L. A.; Katzman, R. *Ann. Neurol.* **1991**, *30,* 572.

[2] a) Kuboyama, T.; Tohda, C.; Komatsu, K. *NeuroReport.* **2000**, *11*, 1981. b) Kuboyama, T.; Tohda, C.; Komatsu, K. *Br. J. Pharmacol.* **2005**, *144*, 961.

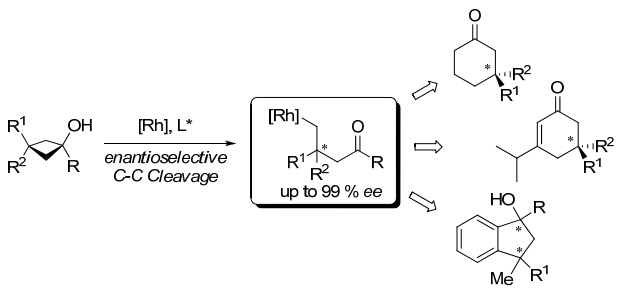
## 262

### Enantioselective Rhodium Catalyzed C-C Bond Activations

Tobias Seiser, Olivia A. Roth, Nicolai Cramer*

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

Reactions involving the activation of C-H bonds and C-C bonds by transition metal complexes have considerable synthetic potential because of their economic and ecological advantages. Small rings occupy a privileged position in C-C bond activations, as their cleavage releases ring strain. The potential of cyclobutane derivatives in such reactions has been recognized [1] and we started to investigate the reactivity of such compounds to enable the access to products with increased molecular complexity. We show that rhodium-catalyzed enantioselective β-carbon elimination from *tert*-cyclobutanols provide access to primary alkyl-metal species, highly reactive intermediates that lead to diverse products [2].

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## 263

### Application of N,N'-Naphtyl Substituted Saturated NHCs in Ru-Catalyzed Olefin Metathesis Reactions

M. Gatti, L. Vieille-Petit, X. Luan, A. Linden and R. Dorta.*

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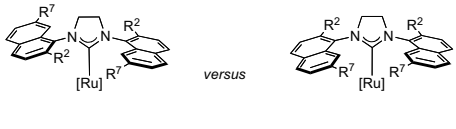
Olefin metathesis has attracted widespread attention as a versatile carbon-carbon bond-forming method. Many new applications have become possible because of major advances in catalyst design. State-of-the-art ruthenium catalysts are not only highly active but also compatible with most functional groups 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.

We report herein on the preparation of N,N'-naphtyl substituted *N*-heterocyclic carbenes as a new class of ligands for the Ru-catalyzed olefin metathesis reaction. This type of ligand molecules is normally obtained as a mixture of *syn* and *anti* isomers and the ratio between them depends on the substituents on the naphthyl rings (Fig.1).[1] Particular attention will be reserved to the synthesis of ruthenium catalysts where only the *syn* or the *anti* isomer is present. Analysis of activity and stability differences of these atropisomeric structures will be presented.




*anti* *syn*

[1] Luan X.; Mariz R.; Gatti M.; Costabile C.; Poater A.; Cavallo L.; Linden A.; Dorta R. *J. Am. Chem. Soc.* **2008**, *130*, 6848-6858.

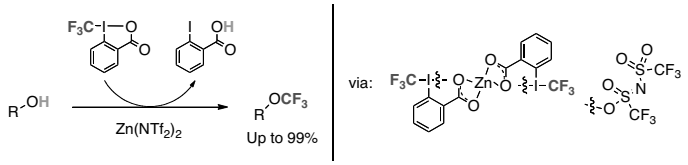
## 264

### Zn-Mediated Formation of Trifluoromethyl Ethers From Alcohols Using Hypervalent Iodine Trifluoromethylation Reagents

R. Koller, K. Stanek, D. Stolz, R. Aardoom, K. Niedermann, A. Togni

*Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology, ETH Zürich, CH-8093 Zürich, Switzerland*

The incorporation of fluorine atoms into biologically active organic molecules has become an increasingly important tool in the life science industry. The mild and selective synthesis of trifluoromethyl ethers is still a challenge to the synthetic community. None of the trifluorohalomethanes reacts with alcohols or their deprotonated form directly affording the corresponding trifluoromethyl ethers. The syntheses of these compounds require harsh reaction conditions and special equipment. We have overcome this problem by a direct transfer of an intact trifluoromethyl group from the hypervalent iodine reagent to alcohols, which occurs smoothly at rt upon activation by zinc bis(triflimide).[1] The corresponding trifluoromethyl alkyl ethers may be isolated in up to 81% yield. This constitutes a straightforward method for the preparation of trifluoromethoxy alkyl derivatives, compounds otherwise difficult to access. ESI-MS and PGSE-diffusion studies in solution, as well as the X-ray crystal structure of an intermediate show that the activation of the hypervalent iodine reagent by Zn(II) occurs via the formation of a 1 to 2 adduct.




[1] R. Koller, K. Stanek, D. Stolz, R. Aardoom, K. Niedermann, A. Togni, *Angew. Chem.* **2009**, *121*, in press.

## 265

### Nonnatural Phospholipids

Ilya Fedotenko, Pierre L. Zaffalon, Andreas Zumbuehl*

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

Lipids are at the heart and beginning of life. Surprisingly though, they were long being ignored and seen as a rather uninteresting class of molecules necessary only for building membranes. In recent years, this picture has started to change and the field of Lipidomics has already identified thousands of lipids that are involved in any conceivable part of a cell's functioning.[1] This new field is also providing ample opportunities for organic chemists.

Nature is building the class of phospholipids from a set of interchangeable building blocks: two hydrophobic acyl chains connected via an interface region to a hydrophilic headgroup.[2] Whereas a great variety of chains (saturation, length) and headgroups (zwitterionic, monoionic, acidic, basic, sugar substituted) exist, only few interfaces have been described in the literature, mainly glycerol in glycerophospholipids and the serine-derived interface of sphingolipids. We reasoned that it would be interesting and chemically challenging to introduce new, nonnatural interfaces and thus enhance the available building blocks for phospholipid synthesis.

In this presentation we will summarize our synthetic approach as well as the first biophysical studies with these new nonnatural phospholipids.

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[2] Zumbuehl, A. *Chimia*. **2009**, *63*, 63-65.

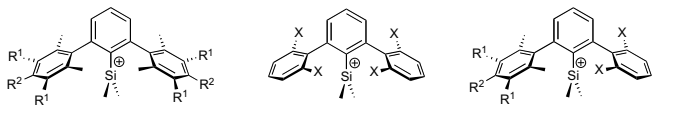
## 266

### Intramolecular Stabilized Silylium Ions: Mechanism of Interaction with Different Electron Demanding Substituents

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

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

The quest for stable silylium ions $R_3Si^+$ led to the development of two strategies in the synthesis of this class of incredibly reactive compounds. The positive silicon center can be protected by bulky substituents that block the trajectories for incoming nucleophiles, or it can be pacified by intramolecular interactions with an electron donating proximal environment. Our project deals with the synthesis of silylium ions where silicon carries 1',3'-terphenyl residue. The cation character at silicon is modulated by the terphenyl mojety, that offers at the same time steric protection and thermodynamic stabilization by donation of $\pi_{aryl}$ electron density to the positive center. Varying the π electron availability of the flanking rings allows the tuning of the acidity at silicon. Moving from methylated[1] (**1**) to halogenated (**2**) lateral rings, the silicon cation character is enhanced, as demonstrated by the more downfield shifted resonances in the $^{29}$Si NMR of **2** respect to **1**. The mechanism of interaction of the positive center with the lateral rings is better understood studying mixed systems (**3**), where silicon can choose to approach the π electron density of the methylated ring or the fluorine lone pairs of the halogenated one.



**1** $R^1$, $R^2$ = H, Me **2** X = F, Cl **3** X = F, Cl $R^1$, $R^2$ = H, Me

[1] S.Duttwyler, Q. Do, A. Linden, K. K. Baldridge, J. S. Siegel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1719.

## 267

### www.mylims.org : My database of chemical information

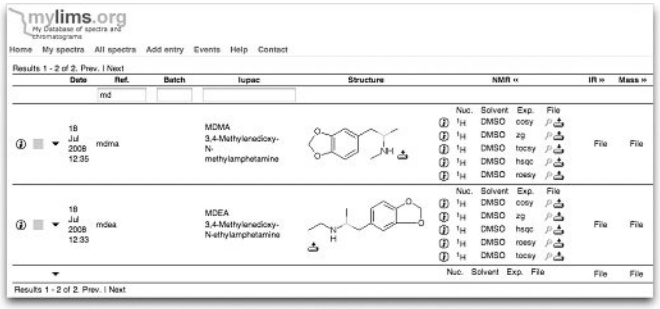
Luc Patiny

Institute of Chemical Sciences and Engineering (ISIC)
Ecole Polytechnique Fédérale de Lausanne (EPFL),
BCH 5121, 1015 Lausanne, Switzerland

The managment of chemical information like spectra and chromatograms is time consuming and requires many different softwares. Moreover journals ask that original spectra are part of supplementary materials.

In order to streamline the procedure, we have developped an on-line database that allows to virtually store and process any information related to a molecule without the needs to install any extra software. The possibility to share the information in read only or read/write mode with a selected group of collaborators have been implemented and the data can be made publicly available in one click.

This new service if accessible for free at http://www.mylims.org and during this talk we will present the whole workflow and the hidden features behind this tool.



## 268

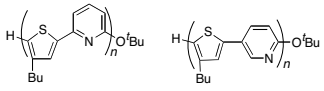
### Synthesis and Photophysical Characterization of Alternating Thiophene-Pyridine Olygomers

Silvia V. Rocha, Nathaniel S. Finney*

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

The study of thiophene polymers is very widespread, since they are π-conjugated conducting polymers that are very stable.[1] Despite the fact that polythiophenes are widely applied in Organic Light Emitting Devices, their physical properties cannot be directly correlated to their structure, due to the polydispersive character of polymers. In that respect, oligothiophenes are used as model compounds, since they are monodisperse and have well-defined structure.[2] Related materials are conjugated copolymers consisting of alternating donor-acceptor units, which leads to lower energy band gaps than those of the corresponding homopolymers.[3]

Having in mind the concepts highlighted above, a system consisting of alternating electron-rich thiophene and electron-poor pyridine units was designed. Two series of compounds were synthesized, differing on the substitution positions on the pyridine ring (Scheme). The optical properties of the oligomers as free bases and as protonated species were evaluated. The protonation was used as a model for an even more electron-deficient pyridine unit, and led to a significant red shift in emission.

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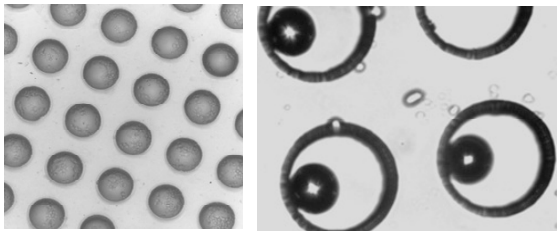
## 269

### Nanoliter Plates: New Screening Method in Solution of "One Bead One compound" Libraries

Grégory Upert,[1] Christoph Merten,[2] Helma Wennemers[1]

1) University of Basel, Department of Chemistry, St Johanns-Ring 19, 4056 Basel, Switzerland
2) Laboratoire de Biologie Chimique, ISIS/ULP, 8, allée Gaspard Monge, 67083 Strasbourg, France

"One bead one compound" (OBOC) libraries are potent tools to quickly access active members from a large number of different compounds. Numerous screening methods using on-bead assays were developed for discovering active compounds but only few screening in solution phase which could enlarge significantly the assay scope for OBOC libraries. With this aim, we have developed a new method using plates made of PDMS containing nanoliter wells. These nanoliter plates, manufactured using photolithography, were designed for holding one single bead with a diameter of 90 m. Each well can be considered as a nanoreactor where each bead is in solution and isolated from the others. Filling and cross-contamination experiments were carried out to validate this technique. The discovery of catalysts as well as enzyme inhibitors were evaluated in proof of concept experiments.



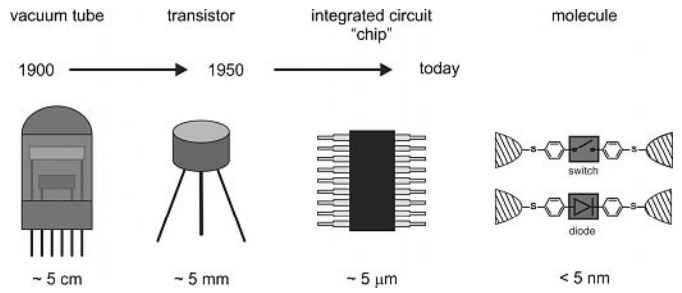
## 270

### New Functional Molecules For Molecular Electronics

Sergio Grunder, Roman Huber, Songmei Wu, Christian Schönenberger, Michel Calame & Marcel Mayor*

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

The ongoing miniaturization trend in the semiconducting industry will reach its physical barriers in the close future. A bottom up approach of integrating functional molecules in electronic devices could be a promising alternative. [1]




A new concept exploiting the different bonding strengths of certain anchor groups to gold electrodes in an electrochemical environment was proposed. [2] Herewith the synthesis and immobilization of other functional molecules with predicted switching or rectifying properties will be presented. Investigations on the electronic properties of integrated molecules are currently in progress.

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## 271

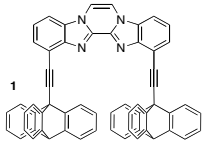
### Molecular Gears in Parallel

Derik K. Frantz, Kim K. Baldridge, Jay S. Siegel

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. 130º. 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 with the syntheses and computational data.




[1] Kottas, G. S.; Clarke, L. I.; Horinek, D.; Michl, J. *Chem. Rev.* **2005**, *105*, 1281.
[2] Iwamura, H.; Mislow, K.; *Acc. Chem. Res.* **1988**, *21*, 175.
[3] Frantz, D. K.; Baldridge, K. K.; Siegel, J. S. *Chimia*, in press.

## 272

### Molecular Rod Rotors and Their Solid State Internal Dynamics

Fitore Kasumaj[1], James R. Noyes[1], Jacco van Beck[2], Anthony Linden[1], Kim K. Baldridge[1], Beat H. Meier[2], Jay S. Siegel[1,*]

[1]Institute of Organic Chemistry, University of Zurich, Winterthurerstr. 190, CH-8057 Zürich,
[2]Laboratory of Physical Chemistry, ETH Zurich, Wolfgang-Pauli-Str. 10, CH-8093 Zürich

Molecular rod rotors consist of three distinct parts[1-3]: The stator, the axle and the rotator. We designed a class of molecular rod rotors based on a new class of stators, trioxatricornan[4,5], and the principle that high symmetry barriers tend to be lower in energy. The tricorans are rigid, tripod-shaped molecule with a large relative smooth surface area. As such they present a good approximation for an isosteric surface throughout 360 ° rotation for substituents attached to the central $sp^3$ hybridized atom.
Synthesis of our molecular-rod rotor requires assembly of an end cap stator, a spacer, and a rotator. The tricornan end caps derive from the combination of Martin's salt (R= H or t-butyl) with various carbanions. The simple phenyl spacer construct was studied in detail. X-Ray crystallographic, SSNMR- and computational studies support rapid rotational dynamics about the tricoran-phenyl-tricornan axis. Further studies on analogous molecular rod rotors are underway.

1. Kottas, G.S.; Clarke, L.I.; Horinek, D.; Michl, J. *Chem. Rev*., **2005**, *105*, 1281.
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4. Martin J.C.; Smith, R.G. *J. Am. Chem. Soc.* **1964**, *86*, 2252.
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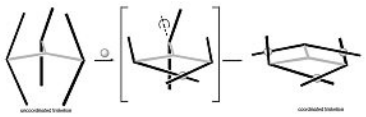
## 273

### Synthesis of the Trefoil Knot

Karla Arias, Eli Zysman-Colman, Anthony Linden, Jay Siegel

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

Chemists are interested in molecular knots and other topologically interesting structures, as these forms should correlate with new function while providing challenges for chemical synthesis. Among such targets, chemists have focused on the trefoil knot as one of the most fundamental. [1] [2]



Topological control using triskelion intermediate.

We synthesized a trefoil knot with the highest possible symmetry, $D_3$, with a metal-directed approach *via* a $D_3$-symmetrical template (Fig. 1) to obtain the desired alternating arrangement, followed by cyclization. [3][4]

[1] Mueller, J. E.; Du, S. M.; Seeman, N. C. *J. Am. Chem. Soc*., **1991**, *113*, 6306.
[2] Dietrich-Buchecker, C. O.; Sauvage, J. P. *Angew. Chem. Int. Ed. Engl*., **1989**, *28*, 189.
[3] Woods, C. R.; Benaglia, M.; Toyota, S.; Hardcastle, K.; Siegel, J. S. *Angew. Chem. Int. Ed. Engl*., **2001**, *40*, 749.
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## 274

### Discovery of new antimicrobial cyclic peptides in a self-encoded 15'625 member combinatorial library

Viviana S. Fluxà, Jean-Louis Reymond

Dept. of Chemistry and Biochemistry, University of Berne, Freiestrasse 3 3012 Berne, Switzerland

We report the synthesis of a self-encoded[1] one-bead one-compound photocleavable library of 15625 analogues of *Gramicidin S* and *Tyrocidine A*. Natural and non-natural amino acids were positioned following TagsFree[2] combinatorial approach. In order to screen the library, a high-troughput susceptibility test for bacterial growth was developed (**Fig. 1**). Several peptides inhibit gram-positive bacteria, with MIC values down to 3 μg $mL^{-1}$. The synthesis, screening protocols and biological evaluation will be discussed.

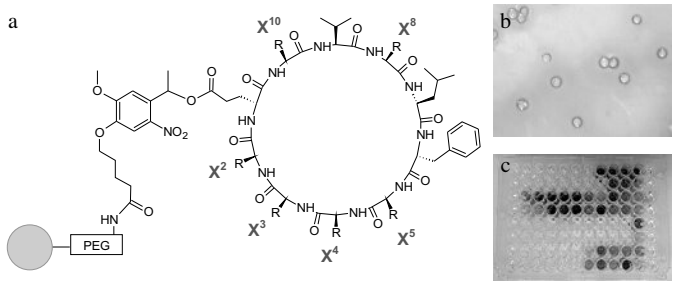



**Fig. 1**: a) Library . b,c) Antimicrobial tests

[1] Fluxà, V. S.; Reymond, J.-L., *Bioorg. Med. Chem*. **2009**, *17*, 1018.
[2] Kofoed, J.; Reymond, J.-L. *J. Comb. Chem*. **2007**, *9*, 1046.

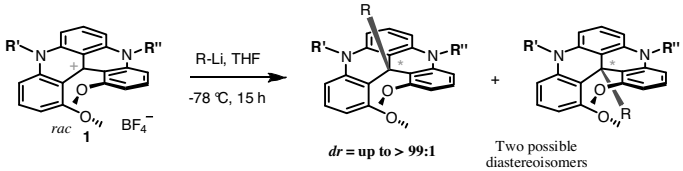
## 275

### Cationic Helicenes in Asymmetric Synthesis and Catalysis

Joyram Guin, Jerome Lacour*

Department of Organic Chemistry, University of Geneva, 30, quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland.
E-mail: joyram.guin@unige.ch, Jerome.Lacour@unige.ch

Helicenes are intensively studied for their excellent physical, chemical and optical properties [1]. Previously, it has been reported in our group that readily accessible super stable dimethoxyquinacridinium salts of type **1** (R' = R'') are highly configurationally stable more than [6]helicene [2]. To the best of our knowledge, for this and other helicenes, a facial discrimination of the enantiotropic faces has never been achieved. Herein, working with unsymmetrically substituted derivative of type **1** (R' ≠ R''), we show that the addition of a nucleophile to the helical electrophile can be highly diastereoselective (d.r. > 99:1). It clearly demonstrates that the two faces of an helicene can be highly heterotopic. Details on the origin of this selectivity will be described during the presentation.

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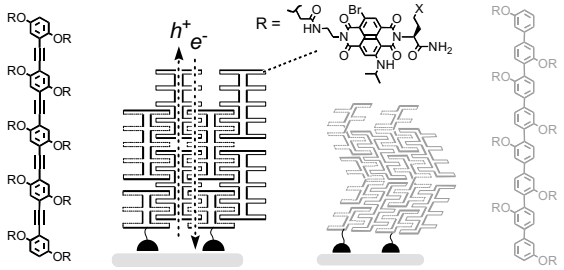
## 276

### Ordered and Oriented Supramolecular Surface Architectures for Soft Photovoltaics

Rajesh Bhosale, Alejandro Perez-Velasco, Velayutham Ravikumar, Ravuri S. K. Kishore, Oksana Kel, Eric Vauthey, Naomi Sakai and Stefan Matile

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

In organic optoeletronics, it is a key challenge to design supramolecular n/p-heterojunctions (SHJs) that transport electrons and holes efficiently. To create the required ordered and oriented surface architectures, we have recently introduced zipper assembly, where n-semiconducting naphthalenediimide (NDI) π-stacks are assembled along interdigitating strings of p-semiconducting *p*-oligophenyl (POP) rods [1, 2]. To evaluate the importance of topological matching in SHJ zipper architectures, we here introduce oligophenylethynyl (OPE) scaffolds with repeat distances that match the repeat of π-stacks.

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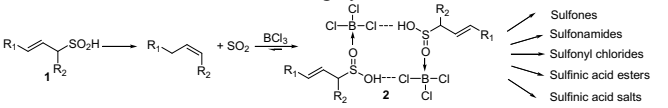
## 277

### The Endergonic Ene-Reaction of Alkenes and $SO_2$ Can Now Be Used to Prepare β,γ-Unsaturated Sulfones and Sulfonamides

Dean Marković,[‡] Adrián Varela-Álvarez,[†] José Ángel Sordo[†] and Pierre Vogel*[‡]

[‡]LGSA, EPFL, CH 1015 Lausanne, Switzerland and [†]LQC, Universidad de Oviedo, Principado de Asturias, Spain

In our group we develop $SO_2$ chemistry for synthesis of polyketides and polypropionates, coupling reactions of sulfonyl chlorides and new neutral silylation agents.[1] We have found polysulfones as organic catalysts for alkene isomerization.[2a] Based on our mechanistic work we have developed green, metal free chemoselective deprotection of allylic ethers.[2b]
Here we report studies on the potential energy surfaces of the desulfinylation of allylsulfinic acid by quantum calculations and together with kinetic data obtained for the reaction in absence or presence of additives.[2c] For the first time we manage to carry out the ene reaction of unactivated alkenes and $SO_2$. Although it's elemental character and high importance for chemical community, the ene reaction could not be applied because of its endergonicity. We found a way to stabilize the product of the reaction allylsulfinic acids by building tetrameric complex **2** of the acid with $BCl_3$. These stabilized complexes can be transformed to sulfones, sulfonyl chlorides, sulfonamides, sulfinic esters and salts in high yields.

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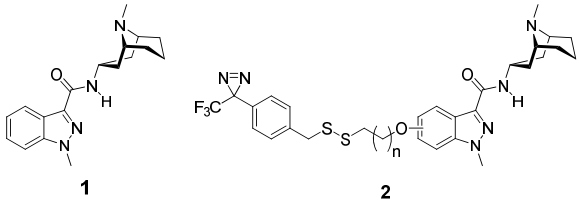
## 278

### Synthetic Neuroscience - Towards the Chemical Modification of a Ligand-gated Ion Channel Receptor

Martin Lochner,[‡,*] Hasan Y. Hallaq,[‡] Jenny Menary,[‡] James D. Stephenson,[‡] Sanjeev K. Vernekar[‡], Andrew J. Thompson,[§] and Sarah C. R. Lummis[§]

[‡]Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK
[§]Department of Biochemistry, University of Cambridge, Cambridge CB2 1QW, UK

Our efforts focus on the synthesis of smart modification reagents (**2**) which will facilitate the chemical and site-specific modification of the serotonin type-3 receptor (5-$HT_3$R). The 5-$HT_3$R is a ligand-gated ion channel which is responsible for rapid transmission of nerve impulses at the synapse [1].




1 2

The design of the synthetic modification reagents is based on the antagonist granisetron (**1**) which binds to the 5-$HT_3$R with high affinity [2]. We undertook a structure-activity relationship (SAR) study in order to identify ideal tethering positions for bulky biophysical tags on the granisetron core. Here we report the synthesis of several substituted granisetron derivatives and their affinities towards the 5-$HT_3$R.

[1] D. C. Reeves, S. C. R. Lummis, *Mol. Membr. Biol.* **2002**, *19*, 11.
[2] A. G. Hope, J. A. Peters, A. M. Brown, J. J. Lambert, T. P. Blackburn, *Br. J. Pharmacol.* **1996**, *118*, 1237.

## 279

### Diastereoselective synthesis of *nor* α-tocopherol

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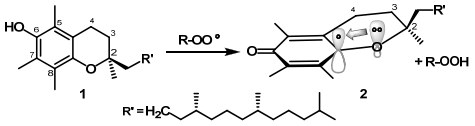
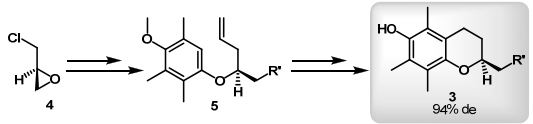
Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland
[$]Present address: Novartis Institute for Biomedical Research, Novartis Campus – Forum 1, CH-4056 Basel, Switzerland

α-Tocopherol **1** is the biologically most active member of the vitamin E compounds. **1** is a radical-chain-breaking antioxidant preventing membrane damage by trapping peroxy radicals R-OO·. This reactivity is associated with the stabilization of the tocopheryl radical **2** through the lone pair of the chromane oxygen. The stabilization of **2** depends on the substitution pattern at the aromatic ring, the configuration at C2 and the conformation of the heterocycle.




1 2

Calculations of the HOMO orbitals of **2** and the corresponding radical generated from *nor* α-tocopherol **3** revealed no difference regarding radical stabilization. In order to investigate the biological activity of **3** a straightforward synthesis was carried out starting from (+)-epichlorhydrin **4**, leading via the key intermediate **5** to **3** displaying an excellent diastereomeric excess (94% de).




4 5 3

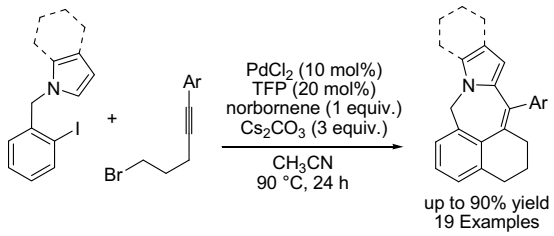
## 280

### A Convinient Synthesis of Indolo- and Pyrrolobenzazepines via a Threefold Norbornene-Mediated Domino Reaction

Valentina Aureggi, Marion Davoust, Kersten M. Gericke, Mark Lautens

Department of Chemistry, Davenport Chemical Laboratories, University of Toronto, 80 St. George Street, Toronto, ON, M5S 3H6, Canada

The development of tandem cross-coupling reactions is an attractive challenge in organic chemistry to allow rapid access to complex compounds by reducing the steps and the practical endeavor.
The strained norbornene occupies a special position within the field of C–H functionalization. Among the extensive work in the field, we have developed a practical synthesis of a novel class of fused heterocycles from 1-(2-iodobenzyl)-1*H*-pyrrole and -indoles with various bromoalkyl aryl alkynes (Scheme 1) [1]. This Pd(0)-catalyzed norbornene-mediated domino reaction allows the efficient formation of three challenging carbon-carbon bonds in a one-pot [1][2], and new seven-membered-ring fused heterocycles are obtained in moderate to excellent yields.




Scheme 1. Synthesis of tetra- and pentacyclic fused heterocycles

[1] V. Aureggi, M. Davoust, K. M. Gericke, M. Lautens, *Synlett.* **2009**, *6*, 1004.
[2] K. M. Gericke, D. I. Chai, M. Lautens, *Tetrahedron* **2008**, *64*, 6002.

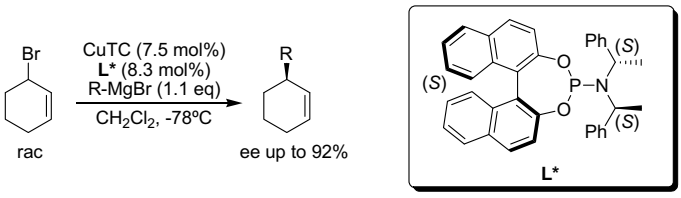
## 281

### Dynamic kinetic asymmetric transformation in copper catalyzed allylic alkylation

Alexandre Alexakis, Jean-Baptiste Langlois

Université de Genève, 30 quai Ernest Ansermet, CH-1211 Genève, Switzerland

Copper catalyzed asymmetric allylic substitution is extensively reported with achiral substrates [1]. However, with chiral substrates, it is well established that a clean $S_N$' occurs with either *syn* or *anti* stereochemistry, depending on the leaving group. Under these conditions, a racemic substrate affords a racemic product. We report here that, by increasing the leaving group ability of the substrate, it is possible to reverse the rate determining step, from the oxidative addition to the reductive elimination. Thus, the $Cu^{III}$ intermediates can interconvert through a *meso* pi-allyl intermediate [2]. This is unprecedented in copper catalyzed allylic substitution, and results in a dynamic kinetic asymmetric transformation, as it is well known in Pd chemistry [3].




[1] A. Alexakis, J. E. Bäckvall, N. Krause, O. Pàmies, M. Diéguez, *Chem. Rev.* **2008**, *108*, 2796-2823.
[2] A. Alexakis, J. –B. Langlois, *Submitted*.
[3] B. M. Trost, R. C. Bunt, *J. Am. Chem. Soc.* **1994**, *116*, 4089-4090

## 282

### Various thioether ligands for stabilizing nanoparticles

Jens Peter Hermes, Torsten Peterle, Marcel Mayor*

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

The full control over both, size and surface functionalization of metal nanoparticles would allow their integration in devices as stable building blocks. Size control enables to tune the particles' physical properties while the control over the functionalization allows to adjust its chemical behavior.
It was shown that oligomeric ligands based on benzylic thioethers are able to enwrap and stabilize gold nanoparticles with low integer numbers of ligands [1].
The ligands have been monofunctionalized to enable wet chemistry reactions of the stabilized nanoparticles to make them 'artificial molecules' with defined surface functionalities (Fig. 1a) for the formation of nanoparticle superstructures.
The oligimeric ligands have been modified to different dentritic structures (Fig. 1b, c) to gain more control over the size, the monodispersity and the desired monofunctionalization (Fig. 1d) of the formed particles.

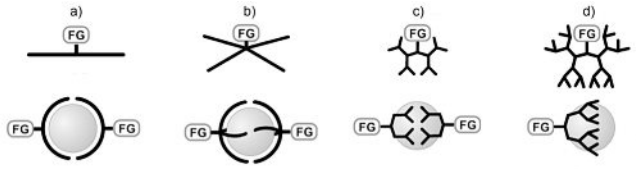



**Fig. 1.** Basic concept for the stabilization and functionalization of metal nanoparticles by a) linear oligomeric, b) dentritic oligomeric and c), d) dentritic thioether ligands; FG: functional group.

[1] T. Peterle, A. Leifert, J. Timper, A. Sologubenko, U. Simon, M. Mayor, *Chem. Commun*. **2008**, *29*, 3438.

## 283

### ENANTIOSELECTIVE OPENING OF OXYGENE BRIDGE BY $S_N2$' REACTION WITH ORGANOMETALLIC REAGENTS CATALYZED BY COPPER SALTS

Ludovic Gremaud, Renaud Millet, Alexandre Alexakis*

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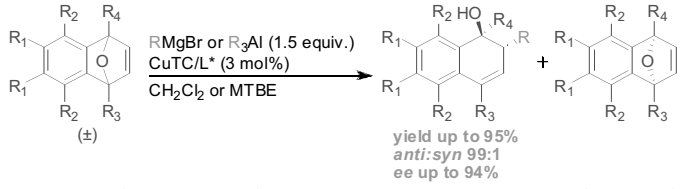
e-mail: Alexandre.Alexakis@chiorg.unige.ch

Enantioselective copper catalyzed allylic substitution is a useful method for carbon-carbon formation.[1] Vinylic oxygene bridge can be regarded as a subclass of allylic substrates affording useful allylic alcohols. The kinetic resolution of racemic substrate can easily lead to chiral allylic alcohols. Some organometallic reagents have already been sucessfully used for these reactions.[2] Recently, we reported the use of Grignard or organometallics reagents for such a reaction on 1,3-cyclohexadiene monoepoxide[3] or on substituted oxabenzonorbornadiene,[4] thus broadly widening the scope of reaction.




[1] (a) A. Alexakis, C. Malan, L. Lea, K. Tissot-Croset, D. Polet, C. Falciola, *Chimia*, **2004**, 60, 124 and references cited therein; (b) C. Falciola, A. Alexakis, *Eur. J. Org. Chem*., **2008**, 22, 3765.
[2] (a) M. Pineschi, *New. J. Chem*., **2004**, 28, 657; (b) O. Equey, A. Alexakis, *Tetrahedron: Asymmetry*, **2004**, 15, 1531.
[3] R. Millet, A. Alexakis, *Synlett*, **2007**, 435.
[4] Thesis of Dr. Renaud Millet, University of Geneva, **2009**.

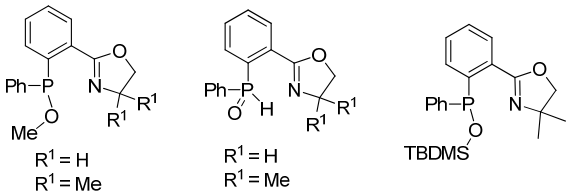
## 284

### Evaluation of SPO,N-Ligands in the Pd-Catalyzed Allylic Substitution by ESI-MS Studies

Christian Ebner, Constanze A. Müller, Andreas Pfaltz*

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

The palladium catalyzed allylic substitution is a very efficient reaction for the enantioselective formation of C-C or C-hetero atom bonds [1]. Therefore ligands for this reaction type, which are readily accessible and easy to handle are of very high interest.




Different SPO,N ligands were synthesized and their activity in the palladium catalyzed allylic substitution was tested. The results from preparative catalysis correlate with the ESI-MS screening, which was previously developed in our group [2]. We could determine their complexation motives by ESI-MS and X-ray analysis and therefrom explain their reactivities.

[1] B. M. Trost, D. L. Van Vranken, *Chem. Rev.* **1996**, *96*, 395.
[2] C. A. Mueller, C. Markert, A. M. Teichert, A. Pfaltz, *Chem. Commun.* **2009**, 1607.

## 285

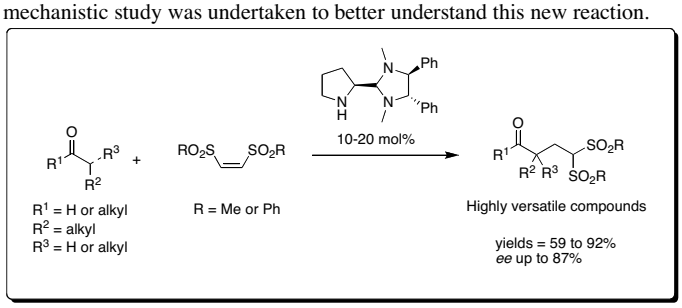
### Unprecedented 1,2 sulfone rearrangement in organocatalytic reactions

Alexandre Alexakis, Adrien Quintard

Department of Organic Chemistry, University of Geneva, Switzerland

Direct α-alkylation of carbonyl compounds remains a challenging task in enamine catalysis. An alternative method to these alkylated compounds has recently been developed in our group by using 1,1'-bis vinyl sulfones and 1,1'-bis vinyl phosphonates as Michael acceptors.[1] To broaden the scope of these reactions, we disclose here the use of 1,2-bis vinyl sulfones in enamine catalysis.

Using our recently developed aminal-pyrrolidine organocatalysts,[2] an unexpected rearrangement was observed leading to gem-disulfones. This unprecedented 1,2 sulfone shift was generalised to other nucleophiles. It leads in good yields and moderate to good enantioselectivities to useful gem disulfones using either ketones or aldehydes. This methodology represents a valuable alternative to the α-alkylation of carbonyl compounds. A short mechanistic study was undertaken to better understand this new reaction.




**1.a** S. Mossé, A. Alexakis, *Org. lett.* **2002**, *7*, 4361; **1.b.** S. Sulzer-Mossé, M. Tissot, A. Alexakis, *Org. lett.* **2007**, *9*, 3749.
**2** A. Quintard, C. Bournaud, A. Alexakis, *Chem. Eur. J.* **2008**, *14*, 7504.

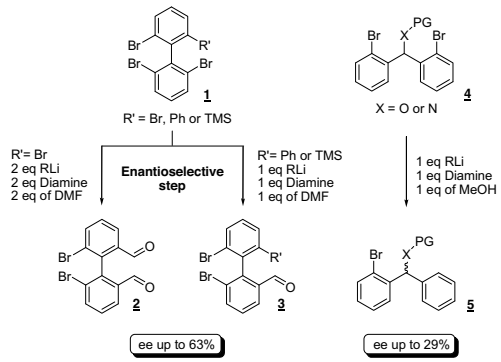
## 286

### Chiral bromine-lithium exchange catalysed by diamine

Quentin Perron, Alexandre Alexakis*

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

We reported here one of the first chiral halogen-lithium exchange.[1] Different class of prochiral polyhalides compounds have been tested in a chiral bromine-lithium exchange in presence of different diamines with enantiomeric excess up to 63%.[2]




[1] Fan, C.-A.; Ferber, B.; Kagan , H., B.; Lafon, O.; Lesot, P. *Tetrahedron: Asymmetry* **2008**, *19*, 2666–2677.
[2] Perron, Q.; Praz, J.; Alexakis, A. *Tetrahedron: Asymmetry* **2009,** *20*, 0000.

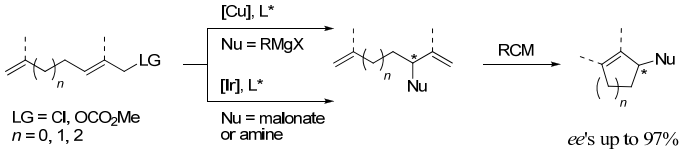
## 287

### ω-Ethylenic allylic substrates as alternative to cyclic substrates in copper and iridium-catalyzed asymmetric alkylation

Alexandre Alexakis, Francesca Giacomina

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

Asymmetric allylic alkylation is a fundamental C-C bond forming transformation in organic synthesis.[1]
In this field, cyclic allylic systems have been extensively studied as class of substrates although they show some limitations. Here, we report the use of ω-ethylenic allylic substrates as alternative. In particular, copper and iridium-catalyzed asymmetric allylic alkylation with hard and soft nucleophiles will be presented.




[1] Falciola, C. A., Alexakis, A., *Eur. J. Org. Chem.* **2008**, 3765-3780 and references therein.

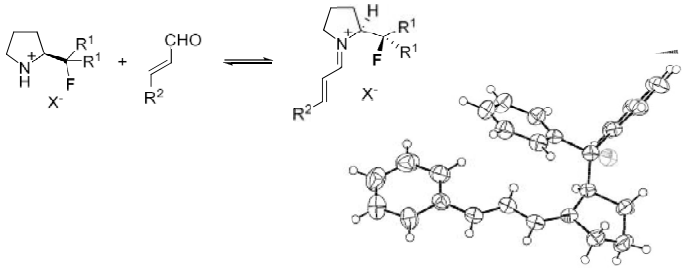
## 288

### The Fluorine-Iminium Ion *gauche* Effect

Christof Sparr[1], W. Bernd Schweizer[1], Hans Martin Senn[2] and Ryan Gilmour[1*]

[1] ETH Zürich, Wolfgang-Pauli-Strasse 10, 8093 Zürich, Switzerland
[2] University of Glasgow, Glasgow G12 8QQ, Scotland United Kingdom

Herein we describe the fluorine-iminium ion *gauche* effect and illustrate its potential as a valuable conformational tool. This phenomenon has been exploited in the design of a novel organocatalyst and showcased in the operationally simple, stereoselective epoxidation of α,β-unsaturated aldehydes.[1] The *gauche* effect, that is induced upon reversible formation of an iminium ion, is necessarily dynamic in nature and provides a powerful method for the preorganisation of transient intermediates that are central to secondary amine catalysed processes.



[1] C. Sparr, W. B. Schweizer, H. M. Senn and R. Gilmour, *Angew. Chem.* **2009**, *121*, 3111-3114; *Angew. Chem. Int. Ed.* **2009**, *48*, 3065-3068.

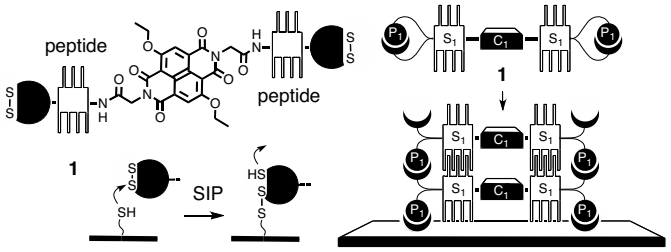
## 289

### Artificial Photosystems from Surface-Initiated Polymerization

Marco Lista, Andrea Fin, Jirí Mísek, Santanu Maity, Naomi Sakai and Stefan Matile

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

To build artificial photosystems on surfaces, chromophores ($C_1$) or chromophore arrays such naphthalenediimides (NDIs) and perylenediimides (PDIs), e.g. **1**, are equipped with structurizing ($S_1$), solubilizing, segregating as well as polymerizing units ($P_1$). For their heterogeneous, surface-initiated polymerization (SIP) into ordered polymer brush architectures, bioinsipred ring-opening polymerizations such as thioester or disulfide exchange are combined with chemoorthogonal routine approaches such as ATRP [1, 2]. Structurizers (beta-sheets) and segregators (fluorous phases) are added to position various π-stacks of different color and conductivity next to and on top of each other.




[1] Edmondson, S.; Osborne, V. L.; Huck, W. T. S. *Chem. Soc. Rev.* **2004**, *33*, 14.
[2] Sanders, J. K. M., *et al. Chem. Rev.* **2006**, *106*, 3652.

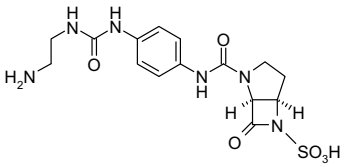
## 290

### Short Enantiospecific Synthesis of Bridged Monobactams

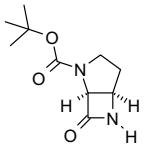
Xiaoping Wu, Lin Xu , Marc Muller*

Basilea Pharmaceutica International Ltd, Grenzacherstr. 487, CH-4005 Basel, Switzerland

The bridged β-lactam BAL0029735 [1] is a convenient synthon for the synthesis of a whole class of highly potent class C β-lactamase inhibitors such as BAL29880.



BAL29880



BAL0029735

The previously known laboratory synthesis of the synthon BAL0029735 is long (14 steps) and laborious [1] [2]. Therefore, we developed a new shorter and more economical synthetic route. The key step of our novel synthesis is a stereoselective intramolecular [2+2] cyclization of an imine with an *in situ* formed ketene/enolate moiety that establishes simultaneously the bicyclic system as well as the two chiral centers. This approach provides efficient access to bridged monobactam intermediates with a significant reduced number of steps [3].

[1] Heinze-Krauss I. et al, *J. Med. Chem.* **1998**, *41*, 3961.
[2] Hubschwerlen C:, Schmid G., *Helv. Chem. Acta* **1983**, *66*, 2206
[3] X.Wu, L. Xu , M. Muller, *Patent Application* WO2009/037229A1

## 291

### Challenging processes for a single-site Lewis acid catalyst

Andrei Bădoiu, E. Peter Kündig*

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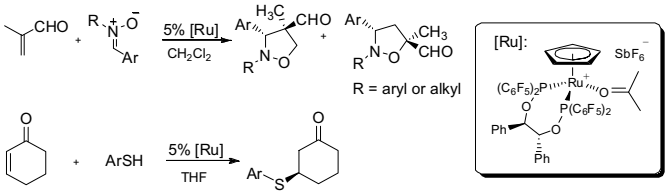
*peter.kundig@unige.ch

Mild Lewis acids, well-defined and stable iron and ruthenium complexes selectively bind and activate *α,β*-unsaturated carbonyl compounds for catalytic asymmetric Diels-Alder and 1,3-dipolar cycloaddition reactions.[1][2]

The importance of electronic effects in 1,3-dipolar cycloadditions with diarylnitrones[3] is confirmed by our latest results with synthetically more useful *N*-alkyl nitrones. In both cases the efficient catalysts lead to high yields and selectivities.




We have now extended the scope of reactions to catalytic asymmetric Michael additions of thiols to enones. The observed selectivity and activity for the substrates tested will be discussed in view of stereocontrol at the metal and reaction mechanism.

[1] a) Rickerby, J.; Vallet, M.; Bernardinelli, G.; Viton, F.; Kündig, E. P. *Chem. Eur. J.* **2007**, *13*, 3354 and ref. cit. [2] Brinkmann, Y.; Reniguntala, J. M.; Jazzar, R.; Bernardinelli, G.; Kündig, E. P. *Tetrahedron* **2007**, *63*, 8413. [3] Badoiu, A.; Bernardinelli, G.; Mareda, J.; Kündig, E. P.; Viton, F. *Chem. Asian J.* **2008**, *3*, 1298 and ref. cit.

## 292

### Synthesis of Triphenylene Dimer: Tailoring of Liquid Crystalline and Optical Properties

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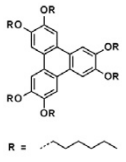
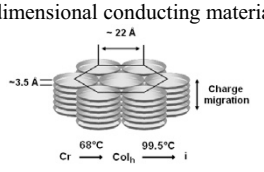
Av de Bellevaux 51, case postale 158, 2009 Neuchâtel, Switzerland

2,3,6,7,10,11-hexakis(alkoxy)triphenylene (**HAT)** are the most widely studied compounds in the field of discotic liquid crystals[1]. Such discotic compounds are of high interest due to their potential application in thin-film organic-electronic technology as one dimensional conducting materials[2].

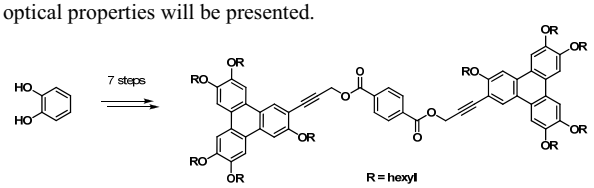



2,3,6,7,10,11-hexakis(hexyloxy)triphenylene (H6T)




Representation of the Hexagonal Columnar Mesophases (Col$_h$) formed by H6T

In such materials, the charge transport depend strongly on the molecular alignment in the liquid crystalline phase. Enhanced control over the self-organization of discotic compounds is expected by linking two discotic units with a rigid linker. The synthetic methodology, the liquid crystalline and optical properties will be presented.




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

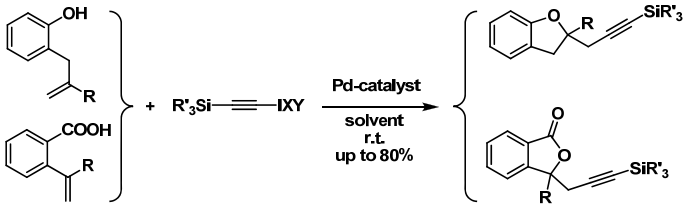
## 293

### Domino Wacker Cyclization-Periodinane Alkynylation

Stefano Nicolai[1],
Stéphane Erard[1], Davinia Fernández González[1] and Jérôme Waser* [1]

[1]Ecole polytechnique fédérale de Lausanne
Institut des sciences et ingénierie chimiques
CH-1015 Lausanne

A novel domino Wacker cyclization-periodinane alkynylation reaction is reported. Pd-catalyzed hetero cyclization of 3-alkenyl phenols and 2-alkenyl benzoic acids was followed by carbon-carbon coupling with an alkynyl hypervalent iodine reagent. Heterocyclic compounds containing an alkyne group were obtained in yields up to 80%. These products are easily further functionalized for the synthesis of bioactive compounds.

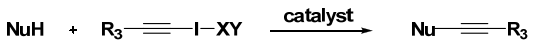



## 294

### Catalytic Alkynylation of Enolates

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

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




One of the most challenging problems in biochemistry and the pharmaceutical industry is the synthesis of new chemical structures of increasing complexity. Consequently, the development of new synthetic methods is an important task.[1] In particular, the stereoselective construction of the carbon backbone of organic molecules constitutes a formidable challenge.

Acetylenes are versatile intermediates in chemistry, biochemistry and material sciences. Usually, they are synthesized by addition of an acetylide anion to an electrophile. The reverse approach, via an electrophilic acetylene synthon, has been achieved for alkynylation reactions with alkynyliodonium salts.[2]

We report the first general catalytic method for alkynylation of nucleophiles using hypervalent iodine reagents under phase-transfer conditions. Furthermore, asymmetric induction was observed using cinchona derived catalysts under mild conditions.

[1] Kündig, P. *Science* **2006,** *314*, 430.
[2] Ochia, M.; Ito, T.; Takaoka, Y.; Masaki, Y.; Kunishima, M.; Tani, S.; Nagao, Y. *J. Chem. Soc. Chem. Comm*. **1990**, 118.

## 295

### Shape Switchable Azo-Macrocycles

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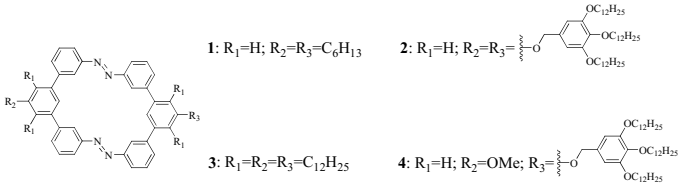
The development of photosensitive functional systems, which change their chemical and physical properties in response to optical stimuli, is a topic of current interest [1]. The photoinduced reversible *E/Z* isomerisation of azobenzene derivatives provides structural change to a considerable extent. The azo functionalized macrocycles **1-4** were envisaged to obtain optically addressable switches. Two rigid semicircles are interconnected by two azo groups. All four macrocycles **1-4** displayed *E*→*Z* photoisomerization upon irradiation at 313 nm. An *E/Z* ratio of 15:85 of the isomers was determined in their photo stationary states. The full back reaction required several weeks which indicates considerable stabilization of the *Z* isomer.




The rigid *m*-terphenyl semicircle was built up successfully through a *Suzuki* cross-coupling reaction, while the key cyclization was performed through a reductive dimerisation of two nitro functionalized semicircles.

[1] G. Pace, V. Ferri, Ch. Grave, M. Elbing, C. von Hänisch, M. Zharnikov, M. Mayor, M. Anita Rampi, P. Samorì, *Proc. Nat. Acad. Sci. USA*, **2007**, *104*, 9937-9942.

## 296

### New efficient strategy toward the synthesis of an advanced precursor of the CD spiroketal fragment of spongistatin 1

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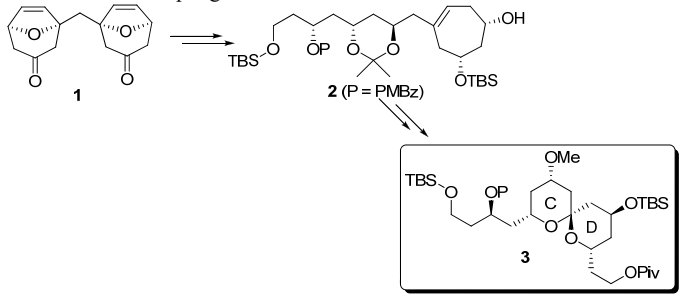
*Laboratory of Glycochemistry and Asymmetric Synthesis, BCH, EPFL CH-1015 Lausanne, Switzerland*

Following the isolation from marine sponges, in 1993, of a family of related highly oxygenated macrolactones named spongistatins, altohyrtins and cinachyrolides, impressive synthetic efforts have been devoted to the synthesis of these macrolides. Their highly potent activity as cancer cells growth inhibitors combined with a fascinating and complex architecture has prompted synthetic organic chemists to develop efficient routes to these molecules.[1] Following our previous report on the asymmetric synthesis of a precursor of the AB spiroketal subunit of spongistatin 1,[2] a similar strategy was developed for the preparation of the CD spiroketal fragment. The sequential and stereoselective functionalization of diketone **1** gave access to the highly oxygenated spiroketal **3** with all the functionalities of the CD subunit of spongistatin 1.




[1] a) Yeung, K.- S.; Paterson, I. *Chem. Rev.* **2005**, *105*, 4237. b) Gerber-Lemaire, S.; Vogel, P. *C. R. Chimie* **2008**, *11*, 1382.
[2] a) Favre, S.; Gerber-Lemaire, S.; Vogel, P. *Org. Lett*. **2007**, *9*, 5107.

## 297

### A Stable Neutral Semiquinone Radical

Chenyi Yi, Shi-Xia Liu, Antonia Neels, Silvio Decurtins

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Stable radicals have aroused much interest in recent years[1], because of their importance in organic synthesis and their potential use in single component organic conductors[2]. Among them, semiquinone radicals play an important role in biological systems, especially in the energy transfer and proton transfer processes. However, reports on stable semiquinone radicals are still rare. Herein, we show a simple way to synthesize neutral semiquinone radicals[3]. Their electrochemical and photophysical properties are described. The reaction mechanism is also discussed.

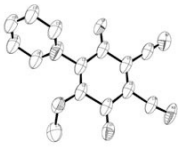

Figure 1. Crystal structure of 2,3-dicyano-1-hydroxy-5-methoxy-4-oxo-6-pyridiniocyclohexa-2,5-dien-1-yl ion radical. Hydrogen atoms are omitted for clarity.

[1] Hicks, R. G. *Org. Biomol. Chem.* **2007**, *5*, 1321.
[2] Pal, S. K.; Itkis, M. E. *et al. J. Am. Chem. Soc.* **2007**, *129*, 7163.
[3] Yi, C.; Liu, S. X. *et al. Org. Lett.* **2009**, *In press.*

## 298

### Stereoselective synthesis of monocyclic peloruside A analog

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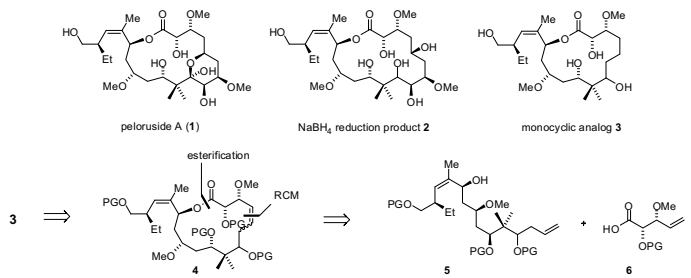
Peloruside A (**1**) is a marine natural product that was first isolated in 2000 [1]. It was shown to have potent taxol-like microtubule-stabilizing activity and to inhibit the growth of human cancer cells at nM concentrations [2]. The binding site of **1** on microtubules is as yet unknown and virtually no analogs of **1** have been described, with the notable exception of the $NaBH_4$ reduction product **2**. The latter was shown to retain significant biological activity, in spite of the loss of the pyranose ring [2].




In this contribution we will present the stereoselective synthesis of the simplified monocyclic peloruside A analog **3** together with data on its effects on the tubulin/microtubule system and its *in vitro* antiproliferative activity. Key steps of our strategy to **3** are the esterification of alcohol **5** with carboxylic acid **6** followed by the ring-closure through ring-closing metathesis (RCM).

[1] L. M. West *et al*., *J. Org. Chem.* **2000**, *65*, 445.
[2] K. A. Hood *et al.*, *Cancer Res.* **2002**, *62*, 3356.

## 299

### Gold Double Feature – Development of New Au-Catalyzed Domino Processes

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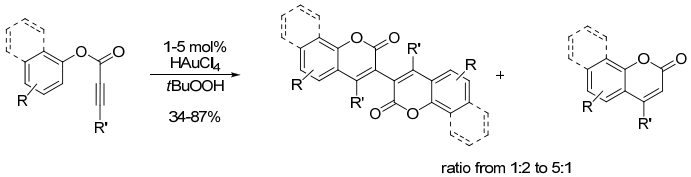
Transition metal catalyzed reactions are among the most powerful synthetic methods in organic synthesis. However, one catalyst usually promotes only one specific reaction. Therefore, consecutive transformations require work-up and change of the catalyst. With a careful control of the reaction conditions one metal would ideally perform multiple tasks in a "domino process".
The Au-catalyzed addition of acetylenes with arenes *via* C-H activation is well-known and leads to the formation of coumarins.[1] Recently, we could combine this reaction with a subsequent oxidative coupling performed by the same Au catalyst. This domino process represents a very quick and efficient tool for the construction of dicoumarins.[2] The concept will be transposed to other gold-catalyzed reactions to form interesting biaryl compounds, substructures of natural products and functional molecules.[3-4] Results will be discussed.




[1] Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669.
[2] Wegner, H. A.; Ahles, S.; Neuburger, M. *Chem. Eur. J.* **2008**, *14*, 1310.
[3] Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239.
[4] Hashmi, A. S. K. *Chem. Rev.* **2008**, *107*, 3180.

## 300

### Highly Efficient Catalytic Desymmetrization Reactions of Prochiral Complexes

Audrey Mercier, Xavier Urbaneja, Wee Chuan Yeo, E. Peter Kündig*

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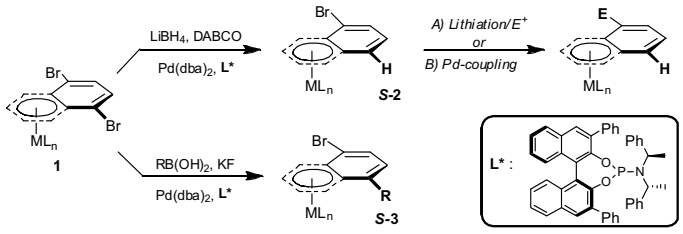
30 Quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland

The access to optically pure planar chiral complexes is of interest in both asymmetric synthesis and catalysis.[1] 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 dihalide compounds using a Pd/chiral bulky phosphoramidite catalyst. The very efficient enantioselective hydrogenolysis[2] has been further complemented by asymmetric Suzuki-Miyaura coupling.




[1] Kündig, E. P., Ed. *Transition Metal π-Complexes in Organic Synthesis and Catalysis*; Topics in Organometallic Chemistry, Vol 7, Springer Verlag: Heidelberg, **2004**.
[2] Cr-complexes: (a) Kündig, E. P.; Chaudhuri, P. D.; House, D.; Bernardinelli, G. *Angew. Chem. Int. Ed.* **2006**, *45*, 1092-1095. (b) Cumming, G. R.; Bernardinelli, G.; Kündig, E. P. *Chem. Asian. J.* **2006**, *1*, 459-468.

## 301

### Green chemistry using singlet oxygen

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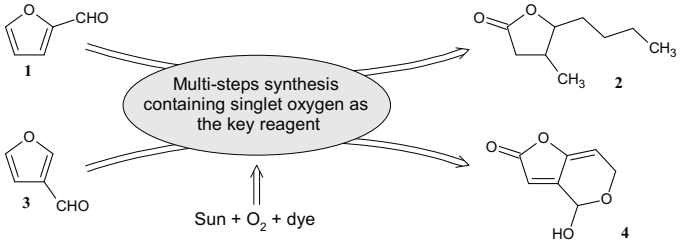
Green chemistry is an increasingly important topic. In this project we chose to exploit the chemistry of singlet oxygen, because this chemistry is particularly environment-friendly. Moreover its production is inexpensive, requiring only oxygen, visible light and a dye sensitizer. Two total syntheses will be presented. Synthetic routes were designed, using singlet oxygen as the key reagent. The additional chemical steps were planned in order to minimize the use of hazardous reagents and the quantity of waste.




The first synthesis starts from the inexpensive 2-furaldehyde **1** to afford the *cis*-whisky lactone **2** which is used is the cosmetic industry as a coconut, citrus or vanilla flavor.[1,2] The second synthesis starts from the 3-furaldehyde **3** and yields the antibiotic[3] patuline **4**.
These two syntheses will be scaled up to molar quantity using our solar photo-reactor composed of a 1 $m^2$ parabolic mirror.

[1] Masuda, M., Nishimura, K., *Chem. Lett.* **1981**, 1333.
[2] Maga, J. A. , *Food Rev, Int.* **1996**, *12*, 105.
[3] Boukouvalas, J., Maltais, F., *Tet. Lett.* **1995**, *36*, 7175.

## 302

### Chiral Ru Lewis Acid Catalyzed Intramolecular Diels-Alder Reactions

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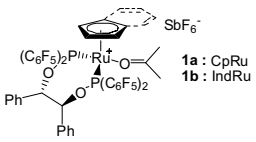
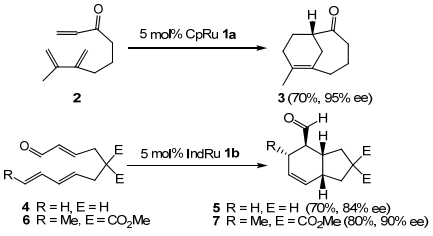
30 quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland.
*peter.kundig@unige.ch

Intramolecular Diels-Alder (IMDA) cycloadditions can be performed by using chiral Lewis acids with a single coordination site.[1,2] 1,6,8-Nona- and 1,7,9-decatrienes are classic precursors for the synthesis of a wide range of natural products.[3] We here report the extension of IMDA reactions catalysted by **1a** and **1b** from triene **2** [2] to trienes **4** and **6** giving cycloadducts **3**, **5** and **7**, respectively in good yields and excellent enantiomeric excesses.




The IMDA reaction of other trienes will also be discussed.

[1] Yamamoto, H.; Maruoka, K.; Imoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 12115. [2] Rickerby, J.; Vallet, M.; Bernardinelli, G.; Viton, F.; Kündig, E. P. *Chem. Eur. J.* **2007**, *13*, 3354. [3] Roush, W. R.; Dineen, T. A. *Org. Lett.* **2003**, *5*, 4725 and refs. cit.

## 303

### Iridium Complexes with P,O Ligands as New Catalysts for the Asymmetric Hydrogenation of Olefins

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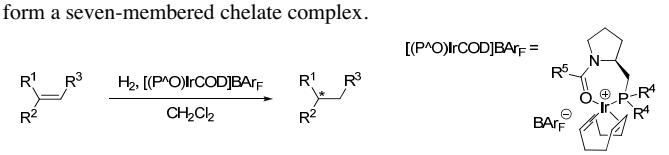
Iridium complexes with chiral P,N ligands are highly efficient catalysts in the asymmetric hydrogenation of a broad range of substrates, with generally excellent enantioselectivities.[1] Inspired by the coordination structure of those ligands to iridium(I) we have investigated simple chiral P,O ligands in order to evaluate both their binding affinity to iridium(I) and their efficiency as ligands in the iridium catalyzed hydrogenation of olefins. *L*-Proline proved to be a convenient modular scaffold allowing us to readily synthesize a library of chiral P,O ligands possessing a wide range of steric and electronic properties. X-ray crystallography of the resulting iridium complexes showed these P,O ligands to chelate in a bidentate fashion to iridium(I). These ligands contain a carbonyl oxygen atom as a donor site in addition to a phosphorus atom donor, both of these binding to iridium(I) to form a seven-membered chelate complex.




We found these complexes to be reactive in the iridium catalyzed hydrogenation of a range of unfunctionalized and functionalized trisubstituted olefins. Depending on the structure of the coordinating carbonyl substituent, moderate to high enantioselectivities could be achieved. The synthesis of these P,O ligands and their application in hydrogenation studies will be presented.

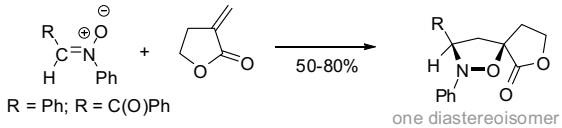
[1] S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res.* **2007**, *40*, 1402.

## 304

### Studies on the cycloaddition of nitrones with α-methylene-γ-butyrolactone and analogues

Anna Blyth,[1] Carole Desobry,[1] Sandrine Gerber-Lemaire[1] and Christophe Roussel[2]
[1]*ISIC - LGSA, BCH, EPFL, CH-1015 Lausanne, Switzerland*
[2] *ISIC, EPFL, CH B1 375, Station 6, CH-1015 Lausanne, Switzerland*

Heterocyclic spirocompounds represent an appealling class of molecules in synthetic organic chemistry. Indeed, their relative steric strain allows thermal, base or acid-promoted rearrangement to generate new and often unexpected heterocycles. The cycloaddition between dipolarophiles bearing an exocyclic double bond and appropriate 1,3-dipoles is one of the best methods to generate bicyclic spirocompounds.
Following previous studies by the groups of Goti [1] and Riche,[2] optimal conditions have been developed for the reaction of nitrones with α-methylene-γ-butyrolactone, resulting in complete regio- and stereoselectivities. Further investigations have also been performed to provide enantioselective conditions for these cycloadditions.




[1] Cacciarini, M. ; Cordero, F.M. ; Faggi, C. ; Goti, A. *Molecules* **2000**, *5*, 637.
[2] (a) Roussel, C. ; Fihi, R. ; Ciamala, K. ; Vebrel, J. ; Zair, T. ; Riche, C. *Org. Biomol. Chem.* **2003**, *1*, 2689. (b) Roussel, C. ; Ciamala, K. ; Vebrel, J. ; Riche, C., *Heterocycles* **2009**, in press.

## 305

### The synthesis of α-tocopherol and daurichromenic acid by means of Domino-Aldol-oxa-Michael reactions

Kegang Liu and Wolf-D. Woggon*

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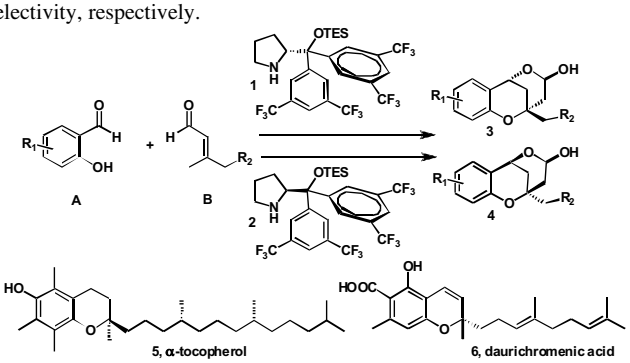
A general method has been developed for the synthesis of chiral chromanes and chromenes. The procedure employs the domino-Aldol-oxa-Michael reaction between various substituted salicylaldehydes **A** and allyl aldehydes **B** such as phytal, citral and farnesal. The proline derivatives **1** and **2** proved to be the best organocatalysts for these transformations leading to lactols **3** and **4** in good to excellent yields and high diastereoselectivity and enantioselectivity, respectively.




The key intermediates **3** and **4** were oxidized to the corresponding lactones that could be further elaborated to obtain for example α-tocopherol **5**[1] the biologically most significant member of the vitamin E family and daurichromenic acid **6** a chromene displaying high anti-HIV activity.

[1] Liu, K.; Chougnet, A.; Woggon, W.-D. *Angew. Chem. Int. Ed.* **2008**, *47,* 5827, *Angew. Chem.* **2008**, *120*, 5911.

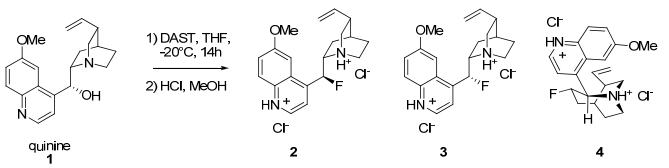
## 306

### Fluorinated Quinine Alkaloids: Synthesis, X-ray Structure Analysis and Anti-Malarial Parasite Chemotherapy

Christoph Bucher, Christof Sparr, W. Bernd Schweizer and Ryan Gilmour*

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

Herein we describe the synthesis of a structurally diverse library of quinine alkaloid surrogates by direct nucleophilic deoxyfluorination of the parent compound using DAST.[1]
Solid state conformational analysis by single crystal X-ray diffraction crystallography indicated a preference for the fluorine atom to orient itself *gauche* to the quinuclidine nitrogen in the cage conserved product series (**2** and **3**). Conversely, the first structural evidence of a vicinal fluorine atom at a stereogenic centre adopting an *anti* orientation relative to an electron deficient nitrogen centre was observed within the rigid molecular architecture of the ring expanded products (**4**).
Furthermore, the anti-malarial activity of the fluorinated alkaloids was assessed *in vitro* against the NF54 strain of Plasmodium falciparum identifying an inhibitor with activity in the nanomolar range.




[1] C. Bucher, C. Sparr, W. B. Schweizer, R. Gilmour, *Chem. Eur. J.* **2009**, *accepted for publication.*

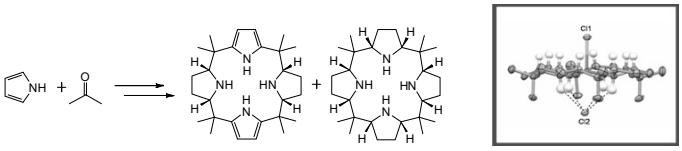
## 307

### Synthesis, Structure & complexation of reduced calix[4]pyrroles: toward new macrocyclic ligand

Guillaume Journot,[a] Andrea Gualandi,[b] Christophe Letondor,[a] Reinhard Neier*,[a]
[a] *Department of Chemistry, University of Neuchâte1, Neuchâtel, Switzerland;* [b]*Department of Chemistry, University of Bologna, Bologna, Italy*
e-mail address Reinhard.Neier@unine.ch

The *meso*-octaalkylporphyrinogens, known as calix[4]pyrroles, have been extensively studied since their discovery by Baeyer 120 years ago.[1] Formed by condensation of simple starting material, such as ketones and pyrroles, we present the method to partially and completely reduce calix[4]pyrroles.

Using this method we are able to isolate one pure fully reduced diastereoisomer from 64 possible stereoisomers.[2]



Structures and complexation properties of these new ligands will be also presented.[2]Reducing calixpyrroles might lead to a new generation of nitrogen-containing macrocycles with interesting properties.[2]

[1] A. Baeyer, *Ber. Dtsch. Chem. Ges.* **1886**, *19*, 2184.
[2] V. Blangy, C. Heiss, V. Khlebnikov, C. Letondor, J. Stoeckli-Evans, R. Neier, *Angew. Chem. Int. Ed.* **2008**, *48*, 1512.

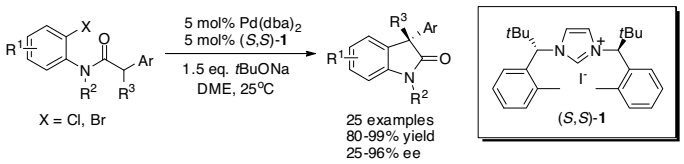
## 308

### Development of New Bulky *N*-Heterocyclic Carbene Ligands and their Application in Palladium-Catalyzed α-Arylation of Amides

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

University of Geneva, 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 (80-99%) and excellent asymmetric efficiency (up to 96% *ee*) [1]. It was found experimentally that the excellent enantioselectivity of this process resulted from introduction of both, a bulky *tert*-butyl group at the stereogenic centers and *ortho*-aryl subsituents. A crystal structure for a palladacycle complex containing the chiral NHC ligand and the substrate was obtained for the first time, which revealed the critical role of the *ortho*-aryl substituent of the ligand. Kinetic studies showed that the reaction is first order in substrate.




[1] (a) E. P. Kündig, T. M. Seidel, Y.-X. Jia, G. Bernardinelli, *Angew. Chem. Int. Ed.* **2007**, *46*, 8484; (b) Y.-X. Jia, J. M. Hillgren, E. L. Watson, S. P. Marsden, E. P. Kündig, *Chem. Commun.* **2008**, 4040.

## 309

### Identification of Catalytic Peptide Dendrimers by "Off-Bead" in Silica HTS of Combinatorial Libraries

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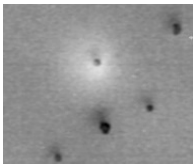
Peptide dendrimers investigated as enzyme mimics were identified as esterolytic catalysts by selection in a solid supported combinatorial library.[1] On-bead screening showed several false positive results. To avoid this we have developed an alternative assay that allows to screen catalytic reactions "off-bead".[2] A 65'536-member combinatorial library $(AcX^8X^7)_8(DapX^6X^5)_4(DapX^4X^3)_2DapX^2X^1$ was prepared on a photocleavable resin and assayed for hydrolysis of 1-butyryloxy-pyrene-2,7,8-trisulfonate and analogs by a simple procedure a) dry photocleavage from the support; b) bead spreading on a TLC impregnated with an aq. buffered substrate; c) hit identification as beads surrounded by a fluorescent halo indicative of catalysis.[3] The experiment provides active esterase dendrimers and reduces the false positive occurrence. "Off-bead" in silica assay is simple to implement and transferable to other libraries and reaction types.[4]



[1] (a) S. Javor, E. Delort, T. Darbre, J.-L. Reymond, *JACS* **2007**, *129*, 13238- 13246. (b) N. Maillard, A. Clouet, T. Darbre, J.-L. Reymond, *Nat.Protoc.* **2009**, *4*, 132-142.
[2] For "off-bead" assay see: L. J. Martin, B. R. Sculimbrene, M. Nitz, B. Imperiali, *QSAR Comb.Sci.* **2005**, *24*, 1149-1157.
[3] N. Maillard, T. Darbre, J.-L. Reymond, *J.Comb.Chem.* **2009** ASAP.
[4] J.-L. Reymond, V. S. Fluxà, N. Maillard, *Chem.Comm.* **2009**, 34-46.

## 310

### Synthesis of novel perfluoroalkyl-substituted polycondensed aromatic compounds for molecular electronics

Mauro K. Schindler, Titus A. Jenny*

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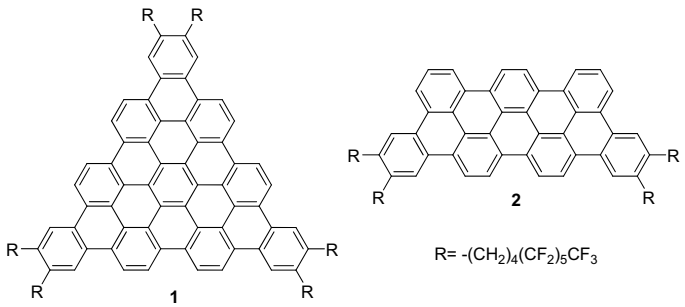
Organic semiconducting materials and molecular electronics are hot topics in material sciences. Optimized candidates for applications such as field effect transistors or field emission displays are benzo-ditriphenyleno-ovalenes **1** or dibenzo-phenanthro-heptaphenes **2**. The synthesis of these compounds is discussed.




DFT-D calculations on the dimers of the parent compounds (R=H) predicting the stacking geometries show that these molecules are promising candidates for replacing the hexabenzocoronenes (HBC), which have thoroughly been investigated [1].

[1] O. Aebischer, T. A. Jenny et al., *J. Mater. Chem.* **2007**, *17*, 1262

## 311

### Towards new functionalized HBC derivatives

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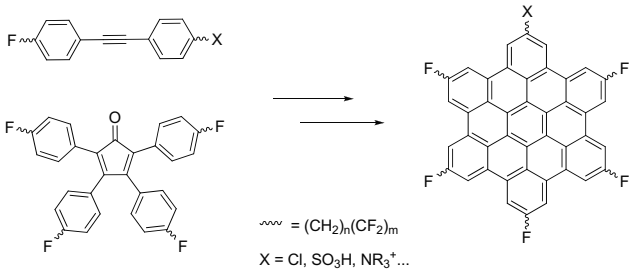
Université de Fribourg, Chemin du Musée 9, 1700 Fribourg, Switzerland

The functionalization of HBC (hexabenzocoronene) molecules allows to give special and interesting properties to the supramolecular systems formed by π-π stacking interactions, well-known for this kind of compounds. This prompted us to explore the influence of the introduction of a function such as sulfonic acid or an ammonium group at the end of one of the perfluorinated chains decorating the HBC core of molecules previously prepared by us[1].

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




The presence of the sulfonic group is expected to produce a supramolecular polyacid with possible applications in proton channel material comparable to Nafion®.

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## 312

### *Oligopyrenotides* – Abiotic Foldamers with Nucleic Acid-like Structural Properties

Florian Garo, Daniel Wenger, Vladimir L. Malinovskii and Robert Häner*

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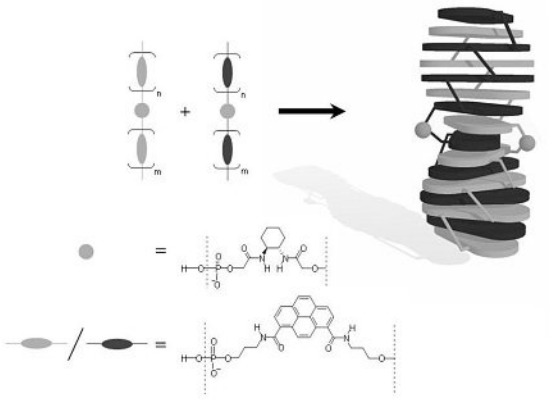
Freiestrasse 3, CH-3012 Bern

Abiotic phosphodiester oligomers consisting of achiral pyrene units and a chiral 1,2-diaminocyclohexane unit are described. Even if the structural analogy of *oligopyrenotides* and DNA were mainly based on aromatic stacking interactions, the similarities of the two systems regarding spectroscopic responses are remarkable. *Oligopyrenotides* adopt a well organized helical hybrid structure in aqueous solutions and show structural polymorphism by changing the ionic strength. Thermodynamic parameters of the hybrids were determined by thermal denaturation experiments.



## 313

### Iridium-Catalyzed Asymmetric Isomerization of Primary Allylic Alcohols

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30 quai Ernest Ansermet, 1211 Geneva, Switzerland
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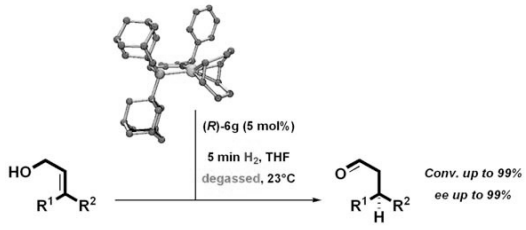
The catalytic asymmetric isomerization of allylic amines to enamines stands out as one of the most accomplished reaction in asymmetric catalysis. In contrast, the related asymmetric isomerization of primary allylic alcohols to the corresponding aldehydes still constitutes a significant challenge in organic synthesis. [1] Using appropriate reaction conditions, iridium-hydrides catalysts promote the isomerization of primary allylic alcohols under very mild reaction conditions. The best catalysts deliver the chiral aldehydes with unprecedented levels of enantioselectivity and good yields. Mechanistic hypotheses have been draw based on preliminary investigations. [2]

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## 314

### Enantioselective Hydrogenation of Enol Esters

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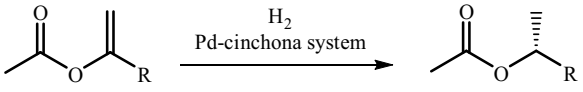
Among the various methods for preparing enantiopure compounds, catalysis is probably the most elegant and promising. Today only a few heterogeneous enantioselective catalysts are known to be sufficiently efficient for potential practical application[1]. Chirally modified nickel, platinum, and palladium have emerged as effective heterogeneous asymmetrical catalysts for the enantioselective hydrogenation of specific substrates. Nevertheless, the scope of reactants that can be hydrogenated with high optical yield is still rather narrow, and it remains a major challenge to extend the application range of these catalysts.

The preparation of chiral esters by the enantioselective hydrogenation of enol esters is of great interest. In general, these hydrogenations proceed with moderate enantioselectivity[2]. Here we report the asymmetric hydrogenations of enol esters, where enantiomeric excess up to 70% has been achieved in preliminary studies.

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## 315

### Synthetic approach to a *CH2*-glycosyl mimic of TF epitope

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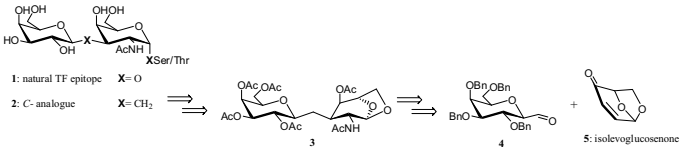
Swiss Federal Institute of Technology (EPFL), Batochime, 1015 Lausanne, Switzerland

The Thomsen-Friedenreich (TF) epitope **1** is a disaccharide which is found on the cell surface glycoproteins of various epithelial carcinomas.[1] Its *C*-analogues, such as **2**, are attractive synthetic targets due to their increased chemical and enzymatic stability and potential biological similarity to the native motif.

Our synthesis of *C*-linked disaccharides[2] starts with an Oshima-Nozaki coupling between a galactosyl carbaldehyde **4** and an enone **5**. After 1,4-addition of an amine to the derived enone, ketone reduction, Barton-McCombie deoxygenation of the CHOH linker and necessary protecting group manipulations, the intermediate **3** was obtained. Currently, studies of Lewis acid promoted α-*C*-allylation of **3** are under way. Cross-metathesis between the product of this allylation and suitable amino acid precursors[3] will lead to the target molecule **2**.




[1] G. F. Springer, *Science* **1984**, *224*, 1198.
[2] a) Y.-H. Zhu, P. Vogel, *Tetrahedron Lett.* **1998**, *39*, 31; b) R. Demange, L. Awad, P. Vogel, *Tetrahedron: Asymmetry* **2004**, *15*, 3573.
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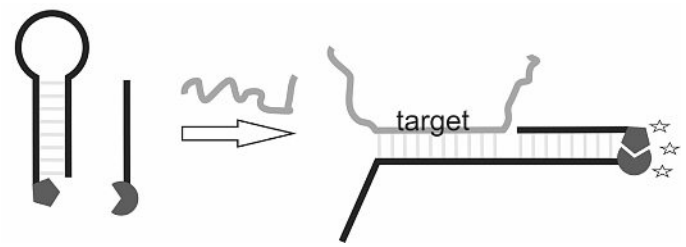
## 316

### Homo-DNA Molecular Beacons

Matthias Stoop, Caroline Crey-Desbiolles and Christian J. Leumann

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

Molecular beacons (MBs) are stem-loop DNA probes used for identifying and reporting the presence and localization of nucleic acid targets *in vitro* and *in vivo*. Recently, we showed that MBs with a homo-DNA stem exhibit increased DNA-target binding selectivity due to the orthogonality of the homo-DNA pairing system [1]. We now extended this project by introducing a novel approach for reporting the presence of a target which does not rely on fluorescence dequenching but on the *de novo* generation of fluorescence *via* homo-DNA templated chemical synthesis.

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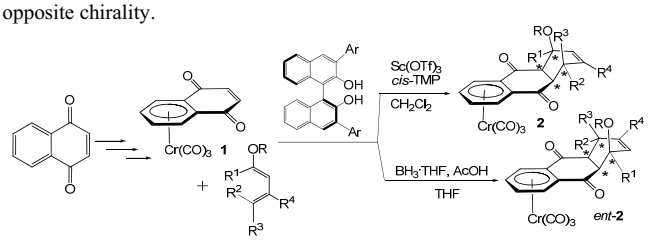
## 317

### Asymmetric Diels-Alder Cycloaddition for Efficient Desymmetrization of [Cr(CO)$_3$($\eta^6$-5,8-Naphthoquinone)]

Souad Ouizem, Patrick Romanens, Thierry Lomberget, Álvaro Enríquez García, Gérald Bernardinelli, E. Peter Kündig

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

Planar chiral [Cr($\eta^6$-arene)(CO)$_3$] complexes are powerful chirons in asymmetric synthesis.[1] Here we report an improved synthesis of [Cr(CO)$_3$($\eta^6$-5,8-naphthoquinone)] (**1**)[2] and its desymmetrization *via* asymmetric Diels-Alder reactions catalyzed by chiral Lewis acids to give highly enantioenriched cycloadducts **2**. Both scandium[3] and boron[4] Lewis acids with a chiral BINOL backbone efficiently catalyze this transformation. Depending on the Lewis acid, the same BINOL backbone yields cycloaddition products of opposite chirality.




[1] Kündig, E. P. (Ed), *Transition Metal Arene π-Complexes in Organic Synthesis and Catalysis: Topics in Organometallic Chemistry*, Vol. 7, Springer Verlag: Heidelberg **2004**.
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## 318

### Non-nucleosidic dialkynylfluorene modified oligonucleotides

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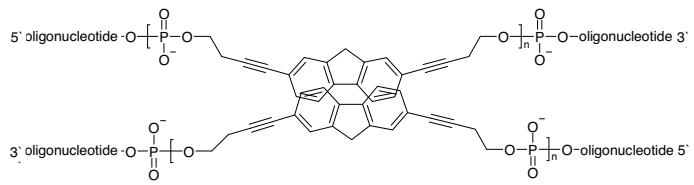
The use of fluorene as a base modification in DNA has been shown to be a valuable tool as a quencher-free molecular beacon [1]. In addition the expansion of the aromatic system by triple bonds is generally known to improve fluorescence properties of chromophores [2]. Based on this, we introduce a dialkynyl-substituted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

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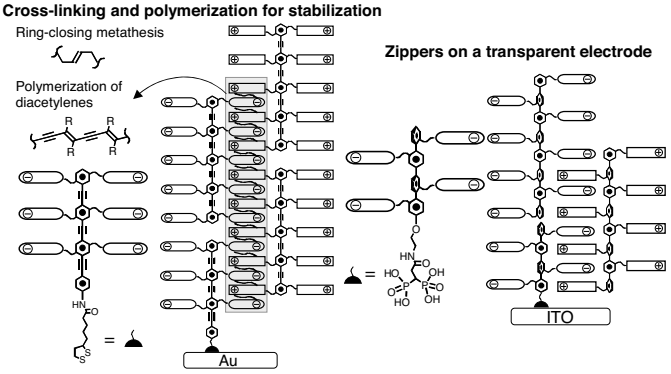
## 319

### Covalent Capture of Oriented SHJ Zipper Architectures on Transparent Surfaces

Shinichiro Sakurai, Jiří Míšek, Rajesh Bhosale, Naomi Sakai and Stefan Matile

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

Zipper assemblies of suitable building blocks can form highly organized nanoarchitectures that have been successfully used to create supramolecular n/p-heterojunctions (SHJs) [1]. Encouraged by very promising results with these artificial photosystems [2], we here explore covalent capture strategies to stabilize the long-range order of π–stacks of naphthalenediimides, and describe how to move on from gold and build on transparent surfaces.

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## 320

### Towards the Total Synthesis of Rhazinilam Analogue

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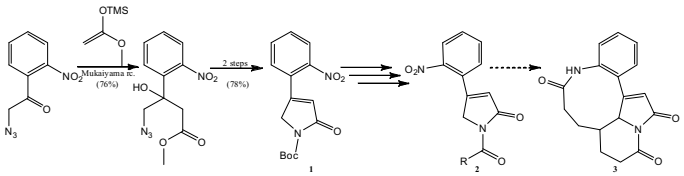
The alkaloid rhazinilam shows significant *in vitro* cytotoxicity, but no activity was found *in vivo* [1]. Our synthetic strategy is to replace, in the first time, the pyrrole ring by a corresponding pyrrole-2(5*H*)-one ring [2] using Mukaiyama crossed aldol reaction followed by Staudinger reaction. The planned synthesis of rhazinilam analogues of type **3** from *N*-acylated pyrrolone **2** should be available using the strategy developed by the group of Banwell [3].

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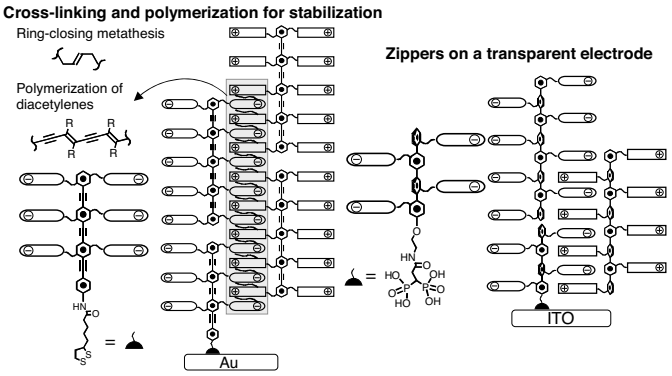
## 321

### Covalent Capture of Oriented SHJ Zipper Architectures on Transparent Surfaces

Shinichiro Sakurai, Jiří Míšek, Rajesh Bhosale, Naomi Sakai and Stefan Matile

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

Zipper assemblies of suitable building blocks can form highly organized nanoarchitectures that have been successfully used to create supramolecular n/p-heterojunctions (SHJs) [1]. Encouraged by very promising results with these artificial photosystems [2], we here explore covalent capture strategies to stabilize the long-range order of π–stacks of naphthalenediimides, and describe how to move on from gold and build on transparent surfaces.

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[2] Sisson, A. L.; Sakai, N.; Banerji, N.; Fürstenberg, A.; Vauthey, E.; Matile, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 3727.

## 322

### Synthesis of 1,3,5,7,9-penta-Substitueted Corannulene

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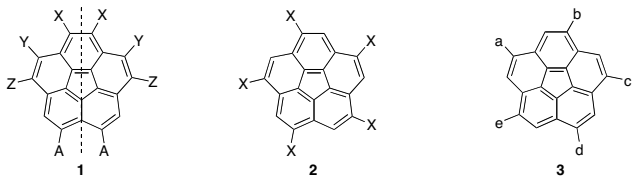
Institute of Organic Chemistry, University of Zurich, Winterthurerstr. 190, 8057 Zurich, Switzerland.

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]

Despite these efficient methods, a directed synthetic strategy for corannulene derivatives with five *different* groups at the 1,3,5,7,9-positions (**3**) remains a challenge. An additional challenge is to design unique functional groups for a, b, c, d and e, such that every site in **3** is selectively addressable. This platform is envisioned to be the basis for a library of corannulene derivatives.

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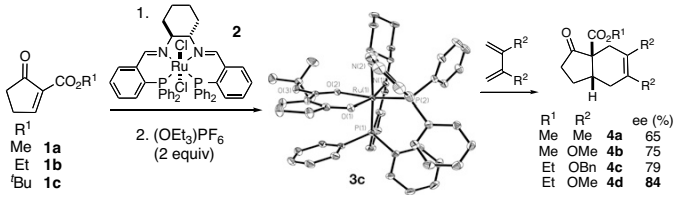
## 323

### Activation of Unsaturated β-Keto Esters by Ruthenium PNNP Complexes

C. Schotes, M. Althaus, and A. Mezzetti*

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

The formation of all-carbon quaternary stereocenters is a challenge in organic synthesis.[1] Following our studies on the catalytic functionalization of 1,3-dicarbonyl compounds,[2] we find that unsaturated β-ketoesters **1a–c** act as bidentate ligands in ruthenium(II) complexes with high diastereoselectivity depending on $R^1$. The X-ray structure of **3c** ($R^1$ = $^t$Bu) shows that one enantioface of **1c** is completely shielded. The ruthenium-bound β-ketoester undergoes Diels-Alder reactions with differently substituted dienes. The catalyst formed *in situ* from **2** and $(OEt_3)PF_6$ gives the bicyclic products **4a–d** in high yield (75–92%) and with up to 84% ee for **4d**. Water in traces increases the enantioselectivity up to 91% ee with **1c**.




As determined by derivatization and X-ray crystallography, (*S,S*)-**4a** is the main *S,S* enantiomer, in agreement with an ester-*endo* attack of the diene onto the open face of **1a**. This is the first enantioselective synthesis of **4a–d**, which are versatile synthons with separately addressable reaction sites.

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## 324

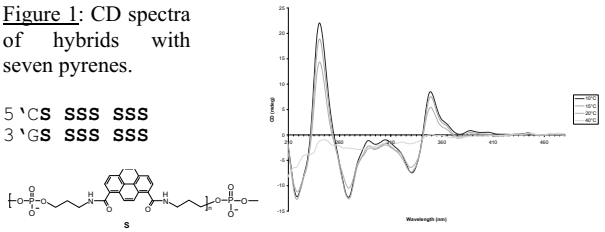
### Influence of the natural bases on the helical arrangement of oligopyrenes in DNA

Alina L. Nussbaumer, Vladimir L. Malinovskii, Florent Samain and Robert Häner

Department of Chemistry, University of Bern, CH-3012 Bern, Switzerland

DNA plays an eminent role in the design of well-defined nanostructures.
The combination of the natural oligonucleotide with synthetic building blocks like pyrene lead to a large increase in the number of possible constructs and applications.
Hybrids containing one to seven pyrene building blocks per strand have been investigated in our group in order to examine the influence of the replacement of base pairs on hybrid stability as well the organisation of the oligopyrene.[1]
Further it was observed that oligopyrene strands are highly sensitive to the chiral environment of either G or C or G C base pairs. These findings lead to new questions like for example: Is the helical arrangement of oligopyrenes dependent on the base? Is already one base enough for helical orientation? UV-Vis, Fluorescence and CD measurements are presented to answer these questions.

Figure 1: CD spectra of hybrids with seven pyrenes.

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## 325

### Investigation of intermolecular triple-helical formation by pyrene-modified oligonucleotides

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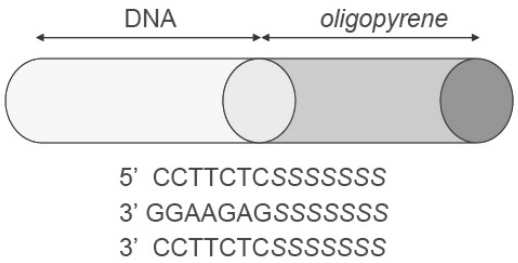
Freiestrasse 3, CH-3012 Bern

Previous studies about bi-segmental hybrids based on natural oligonucleotides and oligopyrenes have shown interesting structural properties in the modified part. [1] The stacking interactions and helical organization were analyzed in a double-stranded arrangement. In this study the behaviour by adding a third strand to form a triple-helical arrangement was investigated. The natural part of the oligonucleotide contains seven nucleic acid units (pyridine or purine base strands) and seven non-nucleosidic pyrene units (S, see illustration). Spectroscopic investigations (UV/Vis, CD and fluorescence spectra) will be presented.




[1] Malinovskii, V.; Samain, F.; Häner, R., *Angew. Chem. Int. Ed.* **2007**, 46, 4464-4467.

## 326

### Extending Self-Assembled Monolayers into the Third Dimension

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

Nicholas Reynolds, Thomas Jung

Department of Physics, University of Basel, 4056 Basel, Switzerland

Jennifer Wytko, Jean Weiss

Institut de Chimie, Université Louis Pasteur, 67070 Strasbourg, France

Complex molecular layers on surfaces with engineered architectures and properties are expected to play an important role in the development of future devices at the nanoscale. In contrast to the three-dimensional (3D) crystal packing of molecules or tectons, which has been a focus of research since years, surface and interface self-assemblies allow for the addressing of individual units. A detailed understanding of molecule-surface and intermolecular interactions is a crucial step towards controlling self-assembly processes on surfaces. Over the last years, several self-assembled porous networks have been created and imaged by STM (Scanning Tunneling Microscopy) under UHV conditions. The extension into the third dimension by means of a vertical vector allows for a deepening of pores in these systems, a possibility for optimizing host-guest chemistry or a functionalization out of the plane of the monolayer.

## 327

### An Enantiomerically Pure Alleno-acetylenic Macrocycle: Synthesis and Rationalization of its Outstanding Chiroptical Response[1]

José Lorenzo Alonso-Gómez,[1] Pablo Rivera-Fuentes,[1] Nobuyuki Harada,[2] Nina Berova,[2] François Diederich*.[1]

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2. Columbia University, 3000 Broadway, 10027, New York, USA

We have recently reported the preparation of enantiomerically pure 1,3-diethynylallenes (DEAs) by asymmetric synthesis and HPLC separation on a chiral stationary phase.[2] Herein, we present a short synthesis of shape-persistent alleno-acetylenic macrocycles, starting from these enantiomerically pure DEAs.

The proposed structure of the new enantiomeric macrocycles was fully confirmed by the spectral data. The stability of these compounds is remarkable. The macrocycles showed no decomposition or isomerization/racemization upon heating in solution to 110 °C. They are also stable under air atmosphere and in the presence of moisture for weeks. Unlike other allenic π chromophores previously reported,[2,3] these macrocycles underwent no photoisomerization under daylight. The CD curves for both enantiomers show extremely intense Cotton effects, with an intensity of the peaks around 253 nm of $\Delta\varepsilon = \pm 790\ M^{-1}\ cm^{-1}$. This outstanding chiroptical response was discussed on the basis of the experimental *g*-factor plot and semi-empirical calculations.

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## 328

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

Caroline Roost, Jay S. Siegel*

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What came before A? This is a fundamental question in origin of life science.
A pre-biotic DNA alphabet consisting of only pyrimidine bases has been proposed (Figure 1) [1]. A C-nucleotide (D), an analog of A, was synthesized to investigate this hypothesis (Figure 2). Furthermore, the synthesized C-nucleotide was incorporated into oligonucleotides to investigate its base pairing abilities [2].
Physical studies of nucleosides and oligonucleotides incorporating D help to test the fundamental 3-letter hypothesis. In addition, further efforts to optimize the synthesis of the new C-nucleotide (D) are undertaken.

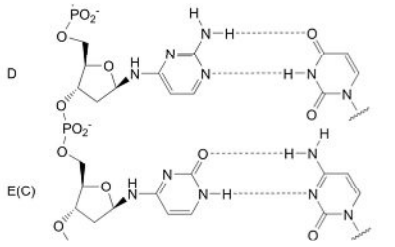


*Figure 1*: DNA, based on pyrimidine only.

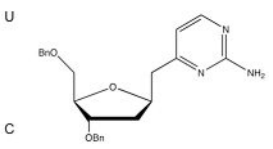


*Figure 2*: C-nucleotide **D**.

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## 329

### Novel compactly fused donor-acceptor systems incorporating tetrathiafulvalene and perylene-tetracarboxydiimide units

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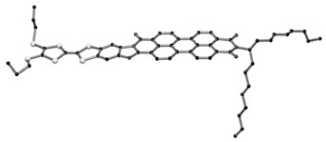
Organic, electrochemically amphoteric compounds and charge-transfer (CT) systems have been attracting much attention due to their potential applications in organic electronic devices. Research efforts have been directed towards the design of molecular electron donor (D) and acceptor (A) systems. The work at hand focuses on compactly fused, conjugated D-π-A assemblies comprising tetrathiafulvalene (TTF) and perylene-tetracarboxydiimide (PDI) moieties. TTF was chosen for its ability to donate one or two π-electrons under formation of relatively stable radical or dicationic species [1], PDI for its stability and photophysical properties [2]. Our type of TTF-PDI systems is a novelty as so far, these two units have only been combined via linkers and spacers rather than in a sterically controlled way.
The photophysical properties and redox-behaviour of TTF-π-PDI systems (See Figure for single crystal structure of one example) shall be presented.



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[2] F. Würthner *Chem. Commun.* **2004**, 1564-1579.

## 330

### Diastereoselective and Enantioselective Formations of Octahydrobenzoquinolines and Octahydrobenzoindoles

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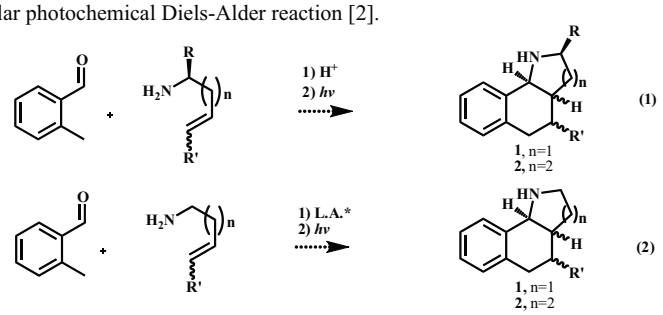
Dopaminergic system dysfunction in the central nervous system has been related to brain diseases. Pharmacological and biomedical evidence suggests the existence of the dopamine receptor subtypes. Different synthesis and studies have been developed, for biological activity of different categories of dopamine agonist drugs like phenethylamines, aminotetralins, or isochromans as well as octahydrobenzoquinolines, which incorporate the basic dopamine skeleton in their structure [1].
Two major ways, with a very limited number of steps, are explored to lead to the synthesis of the octahydrobenzoindoles **1** and the octahydrobenzoquinolines **2**, which are potent dopaminergics. A diastereoselective synthetic route **(1)** is developed first, followed by an enantioselective methodology **(2)** catalyzed by a chiral Lewis acid. The key step involves an intramolecular photochemical Diels-Alder reaction [2].

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## 331

### The First Total Synthesis of the Lythracea Alkaloid Vertine

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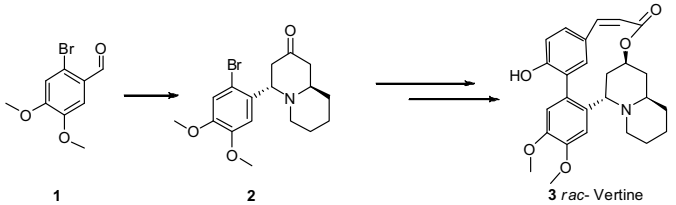
Department of Organic Chemistry, University of Geneva, 30 quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland

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; it is a sedative and has antiinflammatory properties.[2] The synthesis of the 12-membered lactone incorporating a Z-alkene, a diaryl unit and a hydropyridine is synthetically challenging. We here report the first total racemic synthesis of this alkaloid. The synthetic route towards *rac*-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 by methathesis.

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## 332

### Antiplasmodial lanostane triterpenoids from the mushroom *Ganoderma lucidum*

[1]Michael Adams, [1]Marco Christen, [1]Stefanie Zimmermann, [1]Inken Plitzko, [2]Reto Brun, [1]Matthias Hamburger

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*Ganoderma lucidum* mushroom, called lingzhi in Chinese and reishi or mannentake in Japanese has been used medicinally for thousands of years and is appraised as one of the most powerful remedies in traditional Chinese medicine. In a preliminary screen for antiplasmodial activity an ethyl acetate extract of *G. lucidum* was active with 79% inhibition at 4.9 µg/ml. We identified the active substances with HPLC based activity profiling. 350 µg of extract were separated by analytical HPLC and 35 one minute micro fractions were collected and tested for antiplasmodial activity. The most active time windows were identified, and compounds in these time windows were subsequently isolated using normal phase medium pressure column chromatography and semi-preparative HPLC. Structure elucidation was achieved by LC-TOFMS and 1- and 2-D NMR analysis with a 1mm TXI microprobe. The chemistry of *G. lucidum* is well studied, and over 200 substances, mostly polysaccharides and lanostane triterpenes, have been identified [1]. We report here several new lanostane triterpenoids and describe for the first time antiplasmodial activity for this compound class.

[1] R.M., Paterson Russel, *Phytochemistry.* **2006**, *67*, 1985-2001.

## 333

### Cell Penetrating Properties and Conformational Analysis of Functionalised Oligoprolines

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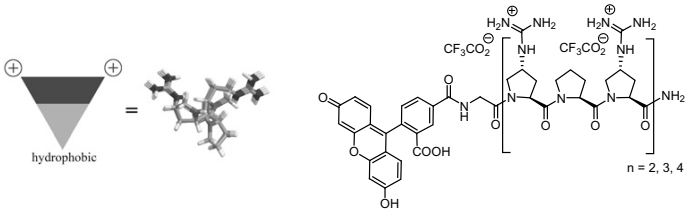
Department of Chemistry, University of Basel, St. Johanns-Ring 19, 4056 Basel, Switzerland

Our interest in oligoprolines as well-defined molecular scaffolds[1] led us to explore the ability of appropriately functionalised oligoprolines to translocate through cell membranes. Towards this goal fluorescein labelled amphiphilic oligoprolines were prepared that bear guanidinium and amino groups in every first and third position.[2] Compounds with different chain length as well as different charge densities were prepared and compared to reference oligopeptides without defined helical structure as well as to the established penetrating Tat peptide. Cellular uptake on live non-fixed HeLa cells was visualised by confocal microscopy and a counter staining was carried out with Hoechst 33342. To quantify the cell penetrating properties FACS experiments were performed and the toxicity of the oligoproline derivatives was evaluated by MTT assays.

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## 334

### Replacing Olefins by Alkanes in Aromatic Alkylation

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Alkanes are much more difficult to activate than olefins. However, direct reaction of alkanes instead of olefins highly simplifies reactor design, decreases cost of the feed, and may enhance catalytic stability. The use of alkanes and aromatics as raw materials can lead to valuable products and intermediates in chemical synthesis. The synthesis of alkylaromatics from alkanes and aromatics in superacidic media was reported [1]. This process suffered from many environmental and corrosion drawbacks. These drawbacks were overcome by using solid acids, such as zeolites, modified with Pt or Ga [2,3]. However, these showed low activity and selectivity towards alkylaromatic products at moderate reaction temperatures. We designed a reaction process and optimized conditions to react hexane in a one-pot reaction with benzene to hexylbenzenes with high selectivity (86%) over an environmentally friendly catalyst. As a catalyst, we used HY zeolite that was loaded with platinum particles of 1 to 2 nm in size. Coke formation was suppressed compared to the reaction with hexene and almost no cracking was observed. These results open up the possibility to use alkanes and aromatics for selective production of alkylaromatics.

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## 335

### New Antiplasmodial Natural Products from Cyanobacteria: Linking their Ecological Role to their Therapeutic Potential

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Cyanobacteria (formerly called blue-green algae) are prokaryotic photoautotrophs and can be found in freshwater or marine environments. They are known to produce algicidal compounds that can offer new approaches for the selective inhibition of the malaria parasite, *Plasmodium falciparum*, as this organism contains an organelle (apicoplast) of algal origin. Nostocarboline is a chlorinated N-methylated carbolinium alkaloid from *Nostoc* 78-12A [1]. Aerucyclamides A-D [2] are heterocyclic peptides that are ribosomally produced [3] by *Microcystis aeruginosa* PCC7806. Both compounds display submicromolar $IC_{50}$ values against *Plasmodium falciparum*, with a pronounced selectivity towards rat myoblasts. Their respective potential ecological role and therapeutic potential will be discussed.

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## 336

### NMR enantiodifferentiation and use in catalysis of a chiral 14-electron rhodium(III) complex

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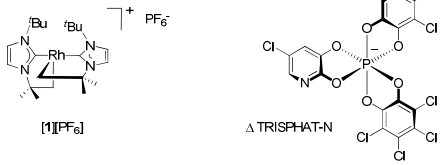
Coordinatively unsaturated metal complexes play a central role as intermediates in many catalytic processes. In this context, 14-electron derivatives are of special importance; these compounds being usually transient species generated *in situ*.[1] Previously, a stable $d^6$-$ML_4$ 14-electrons rhodium(III) complex has been synthesized and fully characterized.[2] This cationic complex **1** is chiral due to the orthogonal arrangement of the two bridged metallacycles. NMR studies with the novel coordinating TRISPHAT-N anion[3] reveal (i) an effective enantiodifferentiation of the enantiomers but also (ii) a strong binding of the pyridine moiety of the anion to the metal center and (iii) a rapid ligand exchange on the NMR time scale. This interesting combination of strong *Lewis* acid-base interaction and fast kinetics of coordination/decoordination is currently studied in the context of catalysis.

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## 337

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

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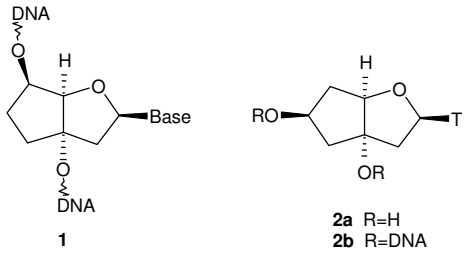
In the last two decades, a variety of modified nucleosides have been developed to improve antisense or siRNA oligonucleotide properties such as target affinity, nuclease resistance, and pharmacokinetics. It is well established that conformational restriction leads to an enhancement in binding affinity 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 novel thymidyl nucleoside **2a**, its incorporation into DNA and first pairing properties.




**1** **2a** R=H **2b** R=DNA

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## 338

### Silyl- and Carbon-Based Cations Derived from Sterically Enshrouded Silanes

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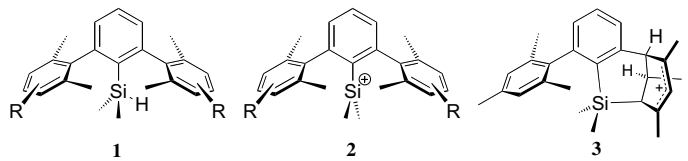
The extraordinary reactivity of silyl cations has made the search for free $R_3Si^+$ systems an inspiring challenge.[1] Recent studies in our group have focused on the synthesis and investigation of cations derived from sterically enshrouded silanes of the general strucure **1**. Hydride abstraction from the silyl core leads to a class of thermodynamically pacified, yet still highly reactive cations **2**.[2] The structure, dynamics, and tunability of these systems have been investigated.

Interestingly, treatment of **1** with a strong Brønsted acid affords allyl cations such as **3** in quantitative yield.[3] X-ray structures of the type **2** and **3** as well as a mechanistic study on the formation of **3** will be presented.

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## 339

### Silver-Nanoparticle Formation of Different Sizes Induced by Peptides Identified Within Split-and-Mix Libraries

Conelious Pfumbidzai, Grégory Upert, Kirsten Belser, Tünde V. Slenters, Laurent Mirolo, Katharina M. Fromm*, Helma Wennmers*

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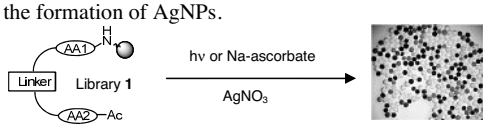
Silver-nanoparticles (AgNPs) are becoming increasingly important for manifold applications in e.g. imaging, catalysis, electronics and the development of antimicrobial coatings, and typically generated by chemical or light reduction of $Ag^+$-ions.[1] In recent years, peptides bearing functional groups that coordinate to $Ag^+$-ions are becoming attractive for the controlled formation of AgNPs with defined sizes, which presents to date still a challenge.[1] In our group, we employed colorimetric on-bead screening of split-and-mix library **1** as a tool to identify peptides that can selectively induce the formation of AgNPs.




**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)

Different colored beads, indicative of different sizes of AgNPs, were formed after treatment of **1** with light or Na-ascorbate as reducing agent. Interestingly, the identified peptides also generate AgNPs of different sizes both on the solid support and in solution phase thereby confirming the combinatorial assay results.[2]

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## 340

### Oligoazobenzenes – Switching in a New Dimension

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Light offers many advantages as a means for manipulating systems of either microscopic or macroscopic size: photons can be applied with extreme spatial and temporal resolution using modern laser techniques. Photons are perfectly clean, leaving no remaining contamination and, in contrast to matter, the photons do not interact with each other (at moderate intensities) allowing for multiplexing. For these reasons molecular assemblies with optical triggers are ideal systems for studying molecular processes as well as for the construction of molecular machines. The assembly of multiple azobenzene units connected in *ortho* position in a cycle leads to interesting compounds – the oligocyclo-*ortho*-azobenzenes.[1] Different substituted members of this class were prepared and their properties studied.[2] These investigations might ultimately lead to the development of molecular grabbers.

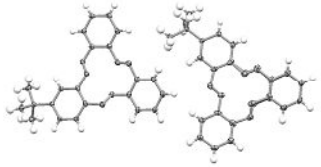

Figure 1. Solid state structure of *tert*-butyl-triscyco-*ortho*-azobenzene.

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## 341

### Acid-Catalyzed Formal Homo-Nazarov Cyclization

Filippo De Simone, Julien Andrès, Riccardo Torosantucci, Jérôme Waser*

Laboratory of Catalysis and Organic Synthesis, EPFL, 1015 Lausanne, Switzerland


Natural and synthetic compounds that contain heterocycles and/or carbocycles display a broad pharmacological activity. Consequently, the discovery of new methodologies to form cyclic structures is an important goal in organic chemistry. The Nazarov cyclization affords cyclopentenone products from divinyl ketones *via* a pentadienyl cation intermediate.[1] Using a cyclopropane ring in place of the double bond affords a complementary strategy to obtain the related cyclohexenone products *via* a "homo-Nazarov" process. However, forcing reaction conditions have limited this reaction to electron-rich aryl cyclopropyl ketones only.[2] We have developed the first catalytic homo-Nazarov like cyclization in the presence of 20 mol% toluenesulfonic acid at room temperature.[3] These mild conditions allow for the first time the efficient cyclization of both vinyl ether and allylsilanes, leading to the synthesis of fused hetero- and carbo-cycles. Application of this methodology in the synthesis of natural compounds is in progress.

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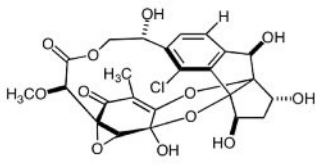
## 342

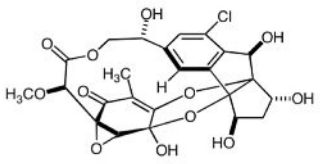
### Towards the Total Synthesis of Sporolides A and B

J.-Y. Wach and K. Gademann

Chemical Synthesis Laboratoty, EPFL, 1015 Lausanne, Switzerland

Sporolides A and B are secondary metabolites isolated by Fenical and coworkers [1] from the marine actinomycete *Salinispora tropica*. These heptacyclic molecules display a complex architecture, including a chlorinated cyclopentindane system, 10 stereogenic centers and 22 out of 24 carbons that are either oxygenated or $sp^2$ hybridized.


Sporolide A


Sporolide B

A first total synthesis of sporolide B has recently been published by Nicolaou and coworkers [2] and its biosynthetic origins has also been investigated [3]. We are reporting our progress towards the total synthesis of these architectonically complex marine natural products.

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## 343

### Multidentate Aryl Sulfoxides As Fluorescent Chemosensors For Metal Ions.

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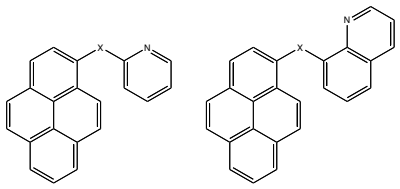
It is well establlished that aryl sulfoxides exhibit anomalously low fluorescence relative to the corresponding sulfides and sulfones.(1) It is known that sulfoxides can serve as ligands for various metal ions.(2) We have previously observed that tritation of simple aromatic sulfoxides with oxophilic metal ions such as $Li^+$ or $Zn^{2+}$ leads to significant fluorescence enhancement.(3) In order to further study this phenomenon, we have prepared multidentate ligands such as **1** and **2**, which are expected to bind metal ions with higher affinity than isolated aryl sulfoxides. Details of the synthesis and photophysical characterization of these and related melecules will be presented.



**1** **2**

**1a** X = S
**1b** X = SO

**2a** X = S
**2b** X = SO

[1] Vos, B. W.; Jencks, W. S. *J. Am. Chem. Soc.* **2002**, *124*, 2544-2547.
[2] Callan, J. F.; de Silva, A. P.; Magri, D. C. *Tetrahedron* **2005**, *61*, 8551-8588.
[3] Malashikhin, S.; Finney, N. S. *J. Am. Chem. Soc.* **2008**, *130 (39)*, 12846-47.

**344**

### New conformationally constrained bicyclo-DNA analogs

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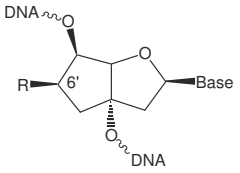
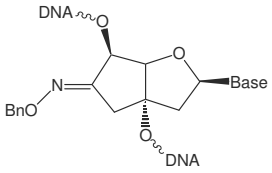
Within the past one and a half decade, the approach of conformational preorganization of double-stranded oligonucleotides has led to the production of a large number of nucleoside analogs with a backbone locked in a specific conformation. Our first contribution in this field of research was bicyclo-DNA (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 as well as on properties of correspondingly modified oligodeoxynucleotides.




**1** R = H, bc-DNA




**2** $bc^{ox}$-DNA

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

**345**

### A Biomimetic Approach Towards the Synthesis of Daphmanidins B and C

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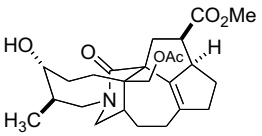
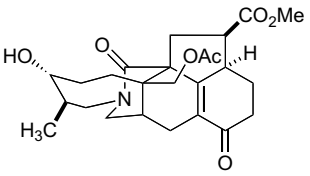
The use of small molecule neurotrophin mimics based on natural products is to date considered a promising strategy for the design of new therapeutic drugs against neurodegenerative diseases.[1] Daphaminidin C (**2**), a *Daphniphyllum* alkaloid, was isolated from the leaves of the Asian tree *D. teijsmanii* (Daphniphyllaceae) by Kobayashi *et al.* in 2004. This natural product possesses an unprecedented fused-pentacyclic skeleton and was found to increase the activity of NGF biosynthesis, revealing a novel mode of action and potential lead for therapeutic studies.[2] Our goal is to access daphmanidin B (**1**) [3], a postulated precursor to daphmanidin C (**2**), in order to evaluate the postulated biogenesis of the daphmanidin family.




daphmanidin B
(**1**)




daphmanidin C
(**2**)

[1] R. M. Wilson, S. J. Danishefsky, *Acc. Chem. Res.* **2006**, *39*, 539-549.
[2] H. Morita, N. Ishioka, H. Takatsu, T. Shinzato, Y. Obara, N. Nakahata, J. Kobayashi, *Org. Lett.* **2005**, *7*, 459-462.
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**346**

### Assessing Ring Strain and Stabilizing Effects – The Appropriate Choice of Chemical Equations

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Isogyric, isodesmic, homodesmotic, and hyperhomodesmotic equations are frequently used to assess energies associated with chemical concepts such as ring strain and aromaticity and often provide strikingly divergent quantitative values. While hyperhomodesmotic and homodesmotic equations more closely balance bonding and hybridization environments in the reactants and products than isodesmic or isogyric equations, they are not always appropriate for quantifying these concepts, since the large reference compounds they necessitate frequently contain perturbing energetic effects not present in the molecule being targeted. These factors make choosing proper reference equations for evaluating strain and stabilization energies non-trivial. Here the recently proposed generalized bond separation reaction (GBSR) scheme is utilized to examine the strain energies of small cycloalkanes and cycloalkenes in a uniform and non-arbitrary manner. Furthermore, the GBSR scheme is amended by introduction of radical counterparts, which allow examination of the open shell cycloalkyl and cycloalkenyl radicals. These equations illustrate the broad range of quantitative values possible for when balanced and unbiased chemical equations are not chosen to treat ring strain. For three- and four-member hydrocarbon rings, isodesmic equations generally provide the best assessment of the ring strain, while hyperhomodesmotic equations are more balanced and less biased for larger rings.

**347**

### Vesicles Formed by Non-Covalently Linked Amphiphiles: Highly Selective Self-Assembly of Host-Guest Molecules

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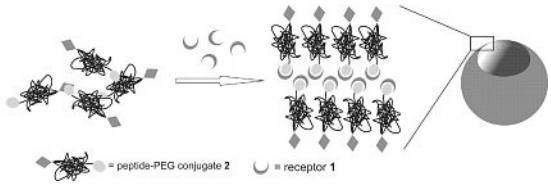
Like in Nature, molecular recognition offers the possibility of forming supramolecular structures by higher ordered self-assembly. We demonstrate here the use of a host-guest system,[1] consisting of a synthetic receptor and its tripeptidic guest, to induce the formation of vesicles. In an aqueous environment the pegylated and water-soluble tripeptidic guest undergoes a highly selective, non-covalent bonding to its hydrophobic receptor forming an amphiphilic building block that immediately self-assembles into a vesicular structure. This self-assembly process only occurs when exactly this host-guest system between a diketopiperazine receptor together with the selected tripeptide is used. We also demonstrate that the formation of vesicles is still possible when the peptide-PEG conjugate is functionalised with a fluorescent dye.




The combination of such modular systems, being tolerant of various moieties on the guest molecule, opens up interesting prospectives for the formation of selectively decorated vesicles.

[1] a) H. Wennemers, M. Conza, M. Nold, P. Krattiger, *Chem. Eur. J.* **2001**, 7, 3342-3347; b) M. Conza, H. Wennemers, *J. Org. Chem.* **2002**, 67, 2696.

**348**

### Tröger base: a new reactivity towards novel configurationally stable derivatives

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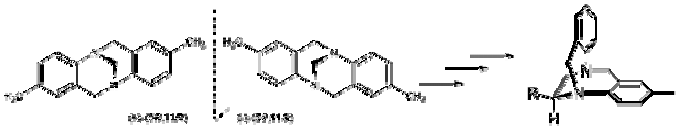
Tröger bases were discovered ca. 130 years ago, and since their resolution into single enantiomers, these compounds have been strongly studied for a variety of purposes[1]. Tröger bases, that is to say methano-bridged Tröger moieties, can unfortunately undergo facile racemization under acidic conditions[2]. This drawback can for instance be overcome by the synthesis of ethano-bridged derivatives[3]. However, only one route was so far reported for these compounds. Herein, we report a new, completely diastereoselective, chemical transformation that allows in few steps the efficient synthesis of several substituted ethano-bridged Tröger derivatives. Examples of reactivity and resolution of these new compounds will be discussed.



[1] Reviews: M. Demeunynck, A. Tatibouët, *Prog. Heterocyclic Chem.* **1999,** 1. B. Dolensky, J. Elguero, V. Král, C. Pardo, M. Valik, *Adv. Heterocyclic. Chem.* **2007**, *93*, 1.
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[3] Y. Hamada, S. Mukai *Tetrahedron: Asymmetry* **1996**, *7*, 2671. D.A. Lenev, D.G. Golovanov, K.A. Lyssenko, R.G. Kostyanovsky, *Tetrahedron: Asymmetry* **2006**, *17*, 2191.

**349**

### Counterion-Activated Translocation of Polyanions in Lipid Bilayers

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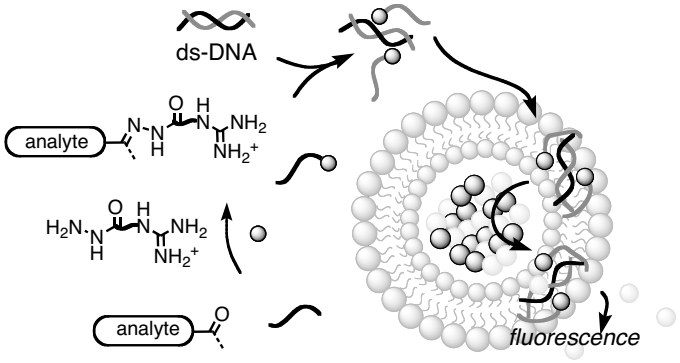
Dramatically expanding the concept of the dynamic biphilicity of multifunctional polyion-counterion complexes [1], total charge inversion is shown to lead from cell-penetrating peptides (CPPs) to countercation activation of polyanions as transmembrane transporters [2]. This is of interest to use aptamers and pattern recognition for signal generation, to combine DNA activation with signal amplification [3], and to ultimately apply lessons from sensing to dynamic gene delivery.




[1] Sakai, N.; Futaki, S.; Matile, S. *Soft Matter* **2006**, *2*, 636.
[2] Takeuchi, T.; Sakai, N.; Matile, S. *Faraday Trans.*, in press.
[3] Butterfield, S. M.; Miyatake, T.; Matile, S. *Angew. Chem. Int. Ed.* **2009**, *48*, 325.

**350**

### Sequential One-pot Additions to Thioiminium Ions

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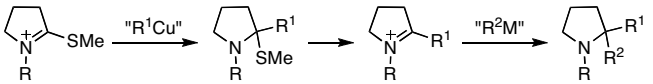
*Gem*-dialkylation of amides is a powerful method for alkaloid synthesis [1][2] and we therefore previously reported a practical method for the synthesis of symmetrical *gem*-2,2-disubstituted tertiary amines from the corresponding lactams [3].

Bosch and co-workers reported two cases of monoalkylation with copper derivatives [4]. This prompted us to further investigate their approach and we are now currently focusing on the sequential one-pot addition of two different nucleophiles on thiominium ions derivatives.

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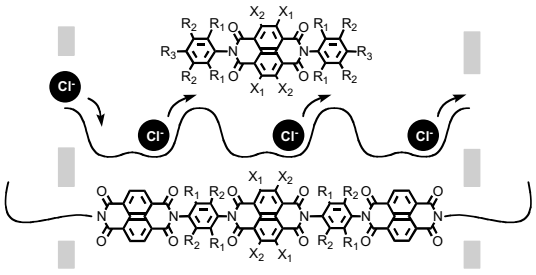
**351**

### Anion-π Interactions at Work

Ryan Dawson, Andreas Hennig and Stefan Matile

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

Anion-π interactions on the π–acidic surfaces of monomeric as well as cyclic and rigid-rod oligomers of naphthalenediimides (NDIs) are used to transport anions across lipid bilayer membranes. Emphasis is on the selectivity and the cooperativity of transport.




[1] Mareda, J.; Matile, S. *Chem. Eur. J.* **2009**, *15*, 28.
[2] Gorteau, V.; Bollot, G.; Mareda, J.; Perez-Velasco, A.; Matile, S. *J. Am. Chem. Soc.* **2006**, *128*, 14788.

## 352

### Mechanistic Investigations in the Reduction of *B*-Alkylcatecholboranes

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Departement für Chemie und Biochemie, Universität Bern, Freiestresse 3, 3012 Bern, Switzerland

In 2005, we reported that *B*-alkylcatecholboranes were reduced in the presence of methoxycatecholborane and methanol. The postulated mechanism involved a complexation of methanol to the boron, which resulted in a reduced BDE for the hydroxylic proton.
Exhaustive $^{1}H$, $^{13}C$, and $^{11}B$-NMR studies coupled with kinetic experiments proved the active reducing agent to be catechol rather than the postulated complex.
This study represents the first use of catechol antioxidants as powerful reducing agent in radical reactions. In the search for a successor to tributyltin-hydride, natural antioxidants could become cheap, easy-removable, and very versatile reagents in organic synthesis, exhibiting no or low toxicities.

[1] D. Pozzi, E. Scanlan, P. Renaud, *J. Am. Chem. Soc.* **2005**, *127*, 14204-14205.

## 353

### Large-Scale Production of Corannulene: Synthetic Approach and Application

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[a]Institute of Organic Chemistry, University of Zurich Winterthurerstrasse 190, 8057 Zürich, Switzerland
[b]Labor für Prozessforschung Winterthurerstrasse 190, 8057 Zürich, Switzerland
jss@oci.uzh.ch

Corannulene was first synthesized in 1966 by Barth and Lawton and is known to be the simplest curved surface of $C_{60}$.[1] Although improvements in the synthesis of corannulene has opened the door for a variety of mono, di, tetra, penta and deca substituted derivatives on gram-scale, the seven steps required to obtain corannulene take weeks to accomplish and yield only a few grams of the advanced intermediate.[2,3,4] This costly synthesis has become the Achilles' heal to corannulene based research. For this reason, we found it beneficial to optimize this synthesis for production on kilo-scale.

This work focuses on an academic approach to the large-scale production of corannulene starting from commercially available α-chloro-m-xylene. In order to accomplish such a synthesis effectively on large-scale, an extensive knowledge of physical organic chemistry was required. The kinetic following of intermediates, solubility studies, and understanding the specific reactivity of derivatives were just some of the key concepts that were addressed. An access to kilos of corannulene means a more liberal and adventurous approach to derivative chemistry, reactivity and mechanism.

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[3] Wu, Y.-Ti.; Siegel, J. S., *Chem. Rev.* **2006**, *106*, 4843.
[4] Sygula, A; Rabideau, P. W., *J. Am. Chem. Soc.* **2000**, *122*, 6323.

## 354

### New insight into mechanism of enantioselective hydrogenation of C=N double bond on Noyori's catalyst

Jan Přech[a], Marek Kuzma[b], Petr Kačer[a], Libor Červený[a]

[a]Department of Organic Technology, Institute of Chemical Technology, Technická 5, 166 28 Prague 6, Czech Republic
[b]Laboratory of Molecular Structure Characterization, Institute of Microbiology, Academy of Sciences of the Czech Republic, Vídeňská 1083, 142 20, Prague 4, Czech Republic

Enantiomerically pure compounds are of vital importance for a broad range of life sciences and fine chemical products, particularly for pharmaceuticals and agrochemicals. Enantioselective catalysis has developed to a valuable and versatile synthetic route for the manufacture of chiral compounds starting from achiral precursors.
*N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine)-*p*-cymene Ru(II)Cl complex (Noyori's catalyst) is very prominent catalyst for enantioselective hydrogenation of C=O and C=N double bonds under phase transfer conditions using HCOOH/TEA. The enantioselective hydrogenation using Noyori's catalyst with HCOOH requires presence a base (TEA, *t*-BuOK). It is expected that it is an acceptor of HCl [1] but NMR and FT-MS measurements showed that under these conditions is formed hydrid species, which contains coordinated TEA. The relative concentration of formate and hydride formed under reaction conditions is strongly influenced by HCOOH/TEA ratio. Also application of different amines as bases leads to changes of reaction rate and also diastereoselectivity in hydrogenation of methoxyl substituted 1-methyl-3,4-dihydroisoquinoline.

[1] Yamakawa M., Ito H., Noyori R., *J. Am. Chem. Soc.*, **2000**, 122 (7), 1466-1478

## 355

### Trifluoromethylation of Sulfonic Acids by 1-Trifluormethyl-1,2-benziodoxol-3-(1H)-one: Mechanistic Insight from Rate Studies

Antonio Togni, Jan M. Welch

ETH Zürich, Laboratory of Inorganic Chemistry, Wolfgang Pauli-Strasse 10, 8093 Zurich, Switzerland

The mechanism of trifluoromethylation of sulfonic acids by 1-trifluormethyl-1,2-benziodoxol-3-(1H)-one ("CF3") was probed using rate studies and linear free energy relationships. On the basis of $^{19}F$-NMR rate studies, an idealized second-order rate-law ($v = k_2$["$CF_3$"][$RSO_3H$]) is proposed and a value for $k_2$ at 298 K ($2.8 \pm 0.2 \cdot 10^{-3}$ $L \cdot mol^{-1} \cdot s^{-1}$) has been determined. In addition, the influence of a polar co-solvent (t-butanol) and substrate hydration on reaction rate have also been examined. Competition studies were utilized to compare the rate of trifluoromethylation of various para-substituted benzenesulfonic acids. From these experiments linear free energy relationships were established at 298 and 323 K showing a strong correlation to the Hammett parameter, $\sigma$, with only slightly negative slopes ($\rho$). The linear correlation to $\sigma$ suggests that the mechanism of reaction remains constant across the range of substituents tested and the very small value for ρ indicates that substituent effects on reaction rate are minimal. The lack of a significant substituent effect on the reaction rate may be indicative of a single electron transfer (SET) mechanism for the trifluoromethylation of sulfonic acids by 1-trifluormethyl-1,2-benziodoxol-3-(1H)-one.

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### Synthesis and reactivity of a novel chiral electrophilic trifluoromethylating reagent

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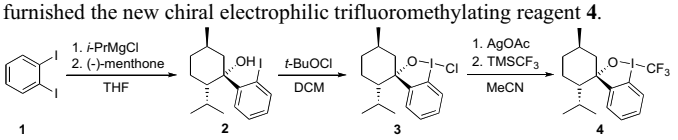
Electrophilic trifluoromethylation emerged as a powerful complementary tool for the synthesis of a variety of compounds bearing the $CF_3$ group at nucleophilic centers. An analysis of the literature revealed a surprising paucity of examples of electrophilic asymmetric trifluoromethylation.[1]
We previously reported the synthesis of hypervalent iodine compounds bearing a $CF_3$ group and their application in the trifluoromethylation of thiols, phosphanes, alcohols and enolates. We felt intrigued by the possibility of a chiral analogue of the parent compound.[2]
We have chosen cheap and commercially available (-)-menthone as chiral starting material. Applying our methodology for the preparation of tertiary *ortho*-iodobenzyl alcohols, we synthesized **2** which was subjected to *t*-BuOCl affording the 1-chlorobenziodoxole **3**.[3] Finally, ligand exchange furnished the new chiral electrophilic trifluoromethylating reagent **4**.




The application of **4** in asymmetric trifluoromethylation of $\beta$-nitroesters and phosphanes will be reported.

[1] N. Shibata, S. Mizuta, H. Kawai, *Tetrahedron: Asymmetry* **2008**, *19*, 2633.
[2] a) P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, 12, 2579; b) I. Kieltsch, P. Eisenberger, A. Togni, *Angew. Chem. Int. Ed.* **2007**, 46, 754.
[3] J. Cvengroš, D. Stolz, A. Togni, submitted for publication.

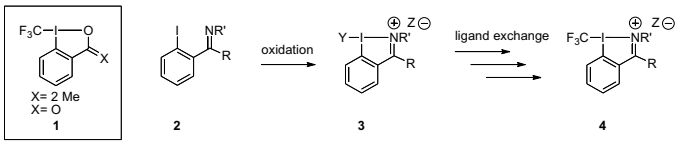
## 357

### Towards a new class of cationic hypervalent iodine reagents for electrophilic trifluoromethylation

Katrin Niedermann, Jan M. Welch, Ján Cvengroš, Nico Santschi, Antonio Togni*

Department of Chemistry and Applied Biosciences, ETH Zürich, Wolfgang-Pauli-Str. 10, 8093 Zürich, Switzerland

Recently we developed a new class of electrophilic hypervalent iodine trifluoromethylation reagents **1**, which exhibit good to excellent reactivity towards a variety of nucleophiles. These reagents are synthesized via oxidation, followed by a ligand exchange and the introduction of the $CF_3$ group from $TMSCF_3$.
To improve the reactivity of the $CF_3$ moiety towards nucleophiles, we outlined the synthesis to a new class of hypervalent iodine reagents. According to the established procedure, new cationic $\lambda^3$-I-compounds **3** were synthesized, in which the oxygen of the former reagent is now replaced by a nitrogen-donor.




If Y=Cl in compound **3**, X-ray structures show, that the I-N-bond is elongated as compared to the I-O bond in the analogous compounds. These results suggest an enhanced reactivity for the corresponding hypervalent iodine $CF_3$ reagent.

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### Towards the Synthesis of Benzo[*d*]xanthene Natural Products

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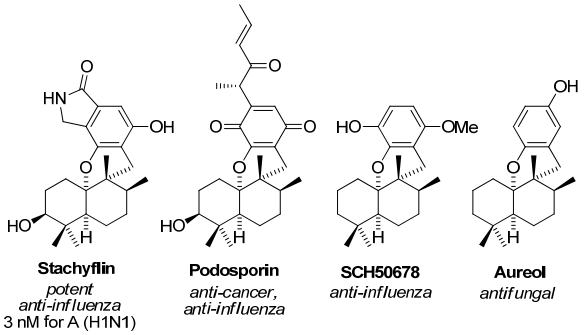
Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland

Benzo[*d*]xanthene natural products are a class of sesquiterpenes that display a host of different biological activities, including anti-viral activity. The most potent member is Stachyflin, which is a potent anti-influenza agent with an $IC_{50}$ for Influenza A H1N1 of 3 nM [1].




In order to further understand the mechanism of this inhibition, but also as a platform to generate synthetic analogues, we are interested in an efficient and modular access of the benzo[*d*]xanthene scaffold. We will report initial results of our approach.

[1] T. Kamigauchi, T. Fujiwara, H. Tani, Y. Kawamura, I. Horibe: PCT WO9711947 A1, 1997; J. Yoshimoto, M. Kakui, H. Iwasaki, T. Fujiwara, H. Sugimoto, N. Hattori *Arch. Virol.* **1999**, *144*, 865.

## 359

### Fluorescent Chemosensors for Metal Ions based on Photoinduced Electron Transfer from Sulfer

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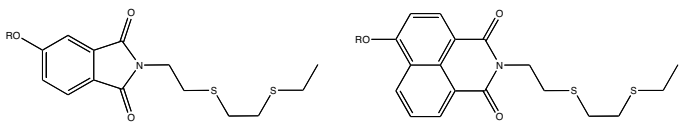
The emission of most standard organic fluorophores can be efficiently quenched by photoinduced electron transfer (PET) from a covalently linked $sp^3$-hybridized nitrogen atom. The presence of metal ions or protons capable of binding with the lone pair electrons of the nitrogen atom leads to the recovery of the fluorophore emission. This propriety is the basis for the majority of the known fluorescent chemosensors [1].
Fluorescence can also be quenched by sulfer atoms. Griesbeck and his collaborators showed for the first time that N-activated 4,5-dimethoxyphthalimides by sulfides give an efficiant intramolecular PET quenching of the fluorescence of the phthalimide moiety [2].
Inspired by this observation, we have synthesized a serie of phthalimides and naphthalimides fluorophores quenched by sulfide containing alkyl chain such as **1** and **2** and we have investigated their photochemical proprieties upon addition of different metal ions. This represent the first metal ion responsive fluorescent chemosensor based on PET from sulfur.




[1] J. F. Callan, A. P. de Silva, D. C. Magri, *Tetrahedron*, **2005**, 61, 8551.
[2] A. G. Griesbeck, S. Schieffer, *Photochem. Photobiol. Sci.* **2003**, *2*, 113.

## 360

### Efficient Total Synthesis of (–) Indolizidine 167B

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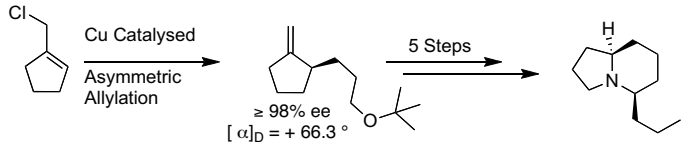
Indolizidine167B was isolated from skin of poison frogs belonging to the dendrobatidae family.[1] The total synthesis of (–) Indolizidine 167B has been achieved in 6 steps (> 20% overall yield) from allylchloride.




First optically pure material was prepared by copper catalysed asymmetric allylation developed by Prof. Alexakis group.[2] Carboazidation reaction and intramolecular Schmidt rearrangement sequence was successfully employed for the construction of azabicyclic moiety.[3, 4] Second stereocenter has been assigned by highly diastereoselective reduction of iminium ion.

[1] M. Edwards, J. Daly, C. Myers, *J. Nat. Prod.* **1988**, *51*, 1188.
[2] C. Falciola, K. Tissot-Croset, A. Alexakis, *Angew. Chem., Int. Ed.* **2006**, *45*, 5995.
[3] P. Renaud, C. Ollivier, P. Panchaud, *Angew. Chem.* **2002**, *114*.
[4] E. Nyfeler, *Ph.D Thesis, University of Bern* **2005**.

## 361

### The jungle of NMR spectra prediction

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Ecole Polytechnique Fédérale de Lausanne (EPFL),
BCH 5121, 1015 Lausanne, Switzerland

NMR spectroscopy is certainly the analytical methodology that provides the most information to organic chemists. In order to assign the spectra, NMR prediction programs are often used. But in the jungle of tools at the chemist's disposal, which one is the one to choose? Can we obtain reliable predictions with any method of prediction, in particular for exotic molecules developed at universities or in the pharmaceutical industry?

In order to answer those questions, we have collected a set of 1000 original molecules as well as their corresponding $^1$H NMR spectra. We have assigned non-ambiguous protons in those spectra (*i.e.* multiplicity and chemical shifts are enough to break ambiguity)

This set of molecules has been submitted for prediction to ChemDraw™ 11, NMRPredict™ , spinus (available for free on www.nmrdb.org) as well as to *ab initio* calculations using TURBOMOLE.

We will present the statistical analysis of the results that shows the accuracy of these different predictions compared to experimental values.

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### Intramolecular photocycloadditions of allenes to benzaldehydes

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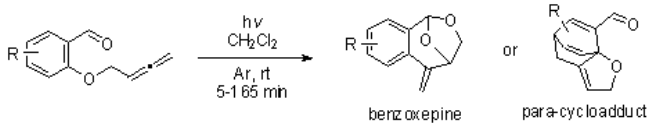
Photoexcitation is transmitting a substantial amount of energy to a substrate without thermal damage; this process can trigger normally impossible reactions. Excited aromatic compounds are for example capable of undergoing cycloadditions. We can distinguish three types of arene-alkene cycloadditions: *ortho*[1], *meta*[2] and *para*[3].
There have been few examples of *para*-photocycloadditions, as other competing photoinduced processes usually occur. However, we recently found that allenes are capable of additions to arenes in the intramolecular [4+2] mode[4]. Thus, photolysis of *o*-allenyl salicylaldehydes gave a mixture of benzoxepines and *para*-cycloadducts, in variable ratios. Interestingly, steric bulk on the aromatic ring favors the *para*-mode, and up to 96% of products containing a [2.2.2]bicyclooctadiene core were isolated. This new reaction opens new synthetic prospects in such photocycloadditons, because of the simplicity of the reactant and the high complexity of the cycloadduct.

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## 363

### Multi-cyanobutadienes as Strong Electron Acceptors for Photovoltaic Applications.

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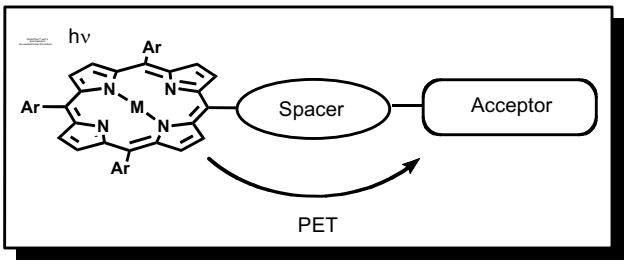
The idea of harnessing the Sun's energy to provide an ecological power source is not new. Fundamentally, this involves the use of a "light antenna" (*i.e.* electron donor) and an appropriate electron acceptor. The aim is to achieve photoinduced electron transfer (PET).

Herein, we report the synthesis of porphyrin-core donor-acceptor systems, utilising multi-cyanobutadienes as strong electron acceptors [1, 2].

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## 364

### Structure and Binding Properties of Cobalamin-Peptide Dendrimer Complexes

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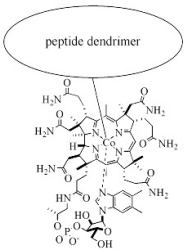
Many natural proteins incorporate cofactors to complement their functionality. While porphyrin-containing proteins have been studied in a number of synthetic model systems, only few synthetic macromolecules have been reported that mimic the direct cobalt coordination in $B_{12}$-dependent proteins. We recently showed the binding ability of various peptide dendrimer ligands to aquocobalamin.[1] To better characterize the binding interaction, we now report further studies by $^1$H NMR, ligand exchange, kinetics and UV/Vis titrations. The structural and functional properties of the cobalamin-peptide dendrimer complexes can be understood in terms of a structural model predicted by molecular dynamics simulations.

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## 365

### On the reactivity of stabilized carbene precursors with CpRu complexes

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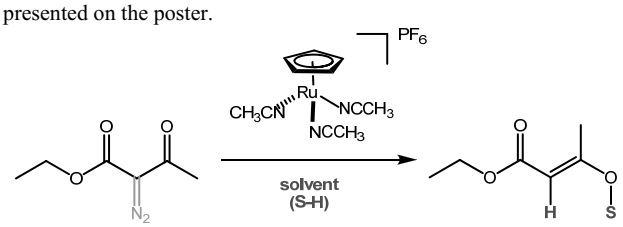
Diazo compounds have received increasing attention in recent years because of their large spectrum of applications in organic synthesis via transition metal catalysis. They are involved in many synthetic processes from cyclopropanation, metathesis, to C-H, O-H, N-H and S-H insertions using different metal sources such as Co, Cr, Fe, Rh, Ru, Cu and Ir complexes.[1] Our group has recently developed the use of CpRu (II) moieties as catalysts for enantioselective decarboxylative C-C and C-O bond forming reactions.[2] Herein, we report that these metallic complexes react with diazo derivatives considered usually as unreactive carbene precursors to yield, after involvement of the solvent, new chemical frameworks and reactivity. Details will be presented on the poster.

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## 366

### Synthesis of Nonnatural Phospholipids

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Phospholipids can be found all throughout nature, particularly in cell membranes. The balance between hydrophobic chains and hydrophilic headgroups causes lipids to self-assemble into various nanoparticulate systems. Such systems can also be created artificially and have been applied in diverse areas like DNA transfection, drug delivery, triggered release of fragrances, molecular recognition, or as protective environments for chemical reactions.[1,2]

Our group is particularly interested in the potential of phospholipids for applications in biology and medicine.[3] One of the major drawbacks of natural phospholipids is the low stability of the formed nanoparticles, which generally restricts their usefulness.

Inspired by the structure of phosphatidylcholines we designed a new platform of synthetic phospholipids. Here, we report the first synthesis yielding amine-bearing phospholipids as well as the first biophysical characterization of these nonnatural phospholipids.

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## 367

### Glycosidic constituents of *Guapira graciliflora*

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The Brazilian biodiversity represents a particularly rich source of new biologically active compounds. *Guapira graciliflora* (Mart. Ex J. A. Schmidt) Lundel (Nyctaginaceae) is an endemic small tree found in Atlantic forest and Cerrado which is used in folk medicine for cicatrisation [1]. Despite its medicinal use, there are no reports on its chemical composition. In the present work, we have investigated the constituents of the methanolic extract of *G. graciliflora* leaves collected at Itapetininga, São Paulo State, Brazil. The powdered dried leaves were percolated with methanol. A portion of MeOH extract was partitioned between *n*-BuOH and water. The *n*-BuOH portion was chromatographed on a Sephadex LH-20 gel column, eluted with MeOH. Fractions collected were checked by TLC for the presence of saponins and subsequently purified by HPLC-ELSD to afford several oleanane saponins including the new derivative 3-*O*-[β-D-xylopyranosy-(1→3)-β-D-galactopyranosyl-(1→3)-β-D-glucuronopyranosyl] oleanolic acid 28-*O*-β-D-glucopyranosyl ester. The compounds were identified by detailed spectroscopic analysis including 2D NMR and ESI-MS as well as acid hydrolysis. These results represent the first data on the chemistry of plants of the genus *Guapira*. The isolated compounds are being currently evaluated in various biological test systems including cytotoxic and antimicrobial assays.

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## 368

### Bio–Organic Protein Frameworks

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Over the last decades, tremendous efforts have been invested worldwide to gain more insight into self-assembly processes in order to produce new materials through the so-called bottom-up approach. By using streptavidin (as a linker) and a connector bearing three bis-biotinylated units, dendritic structures reaching a diameter of 200 nm have been obtained. Biotinylated SAMs in combination with QCM* measurements are used to monitor the self-assembly process step by step.

* QCM: Quartz Crystal Microbalance

## 369

### Addition Reactions of Trifluoromethanesulfonylazide to Alkenes

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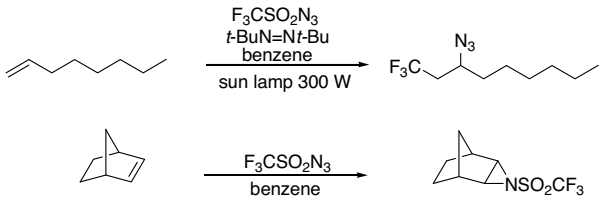
Trifluoromethanesulfonylazide is a versatile starting material for the synthesis of a variety of nitrogen-containing compounds.

Due to its electrophilic character, the azido group undergoes two different types of reactions depending on the selected alkene. Radical carboazidation reaction occurs with unactivated olefins like 1-octene whereas the 1,3-dipolar cycloaddition is observed with more electron-rich olefines and strained alkenes such as norbornene. The behaviour of trifluoromethanesulfonylazide has been studied in detail with a selection of alkenes.




## 370

### Free Radical Addition – Cyclization Strategy: Azidation of Dienes

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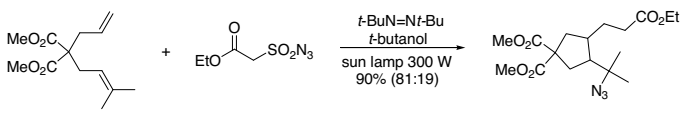
Intramolecular addition reactions of suitable alkyl radicals are particularly interesting since they readily afford a variety of ring systems commonly found in many natural products.[1]

A novel strategy is described in which an intermolecular carbon-centered radical addition to a terminal double bond followed by intramolecular cyclization and azidation leads to the formation of 3,4-substituted five membered carbocycles and heterocycles. Excellent levels of *cis*-selectivity are observed in accordance with the Beckwith-Houk model for selectivity in 5-*exo*-trig radical cyclizations. The reactions were conducted according to our previously reported procedure, involving ethyl 2-(azidosulfonyl)acetate, azo-*tert* butane as radical initiator and *t*-butanol as solvent.

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## 371

### HPLC-Based Metabolite Profiling of *Fredolia aretioides* Extracts

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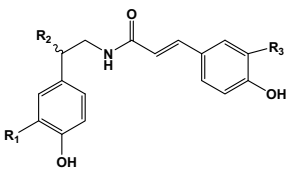
Plants of the family Chenopodiaceae are widely distributed in arid areas and on saline soils. Major chemical constituents known are alkaloids, steroids, terpenoids and flavonoids, which possess various biological activities and ecological functions. *Fredolia aretioides* grows in Saharan Africa and has been traditionally used for rheumatism, as a diuretic and antidote [1]. Phytochemical information about the species is scarce.

We analyzed the phytochemical profile of *F. aretioides* with a combination of analytical HPLC coupled to PDA, ELSD, APCI-, ESI-MS, and HRESI-MS detectors, and semi-preparative HPLC combined with off-line microprobe NMR. A series of phenolic amides and saponins were characterized in the methanolic leaf extract. This HPLC-based approach is a powerful method for metabolite profiling of complex extracts.

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## 372

### *p*-Dicyclobutabenzene Derivatives: Synthesis and Properties

Fabienne Furrer, Tetsu Arisawa, Toshiyuki Hamura, Keisuke Suzuki, Kim Baldridge and Jay Siegel

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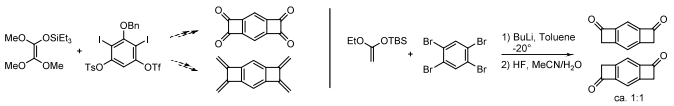
*p*-Dicyclobutabenzenes are strained aromatic compounds and – due to their comparatively high reactivity imposed by the strain – ideal precursors for more complex molecules such as natural products[1]. In addition they are of interest theoretically and as precursors for materials. An intriguing product starting from *p*-Dicyclobutabenzenes for instance would be the corresponding tricyclic 10π-systems.

In order to have a facile and quick access to *p*-Dicyclobutabenzenes, we have developed a synthetic route to the tricyclic framework, based on two successive [2+2] cycloadditions of ketene silyl acetals to a benzyne species. This pathway leads to di- or tetraketones of the *p*-Dicyclobutabenzene scaffold, which can be converted to various derivatives in a few simple steps.

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## 373

### Development of a Catalyst for the Inverse Electron Demanding Diels-Alder Reaction of 1,2-Diazines

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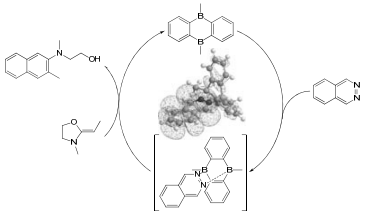
The inverse electron demanding Diels-Alder (IEDDA) reaction has gradually gained on interest over the past fifty years and nowadays offers a broad application spectrum.[1] Despite this work the reaction of 1,2-diazines as the diene is only scarcely disclosed. Herein, we present a novel strategy for the catalysis of an IEDDA reaction of 1,2-diazines by a bidentate Lewis acid. The concept is based on the following idea: A bidentate Lewis acid complexes the vicinal nitrogen atoms in order to withdraw electron density from the diazine, lowering the LUMO of the diene and facilitating the cycloaddition step according to the FMO-theory. The feasability of the general principle was supported by DFT calculations, NMR studies and finally proven on a model system. This novel catalytic IEDDA reaction of 1,2-diazines, allows an efficient entry into 1,2-substituted aromatic compounds, which are difficult to access by other means.

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