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Inorganic and Coordination Chemistry **249**

## Ligand-Mediated Decarbonylation as an Efficient Synthetic Method to Re(I) and Re(II) Dicarbonyl Complexes

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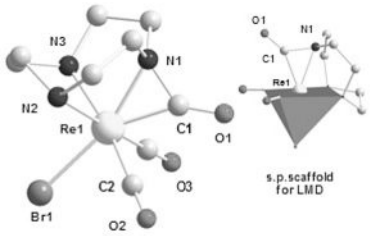
Chemistry of rhenium (II) is the least developed among the eight common oxidations states of this element. This is likely to be true due to a lack of versatile Re(II) precursors as starting material. Compounds of $d^5$ Re are attractive for medicinal inorganic chemistry and as precursors for single-molecule magnets.[1]-[2] A synthetic approach to Re(II) complexes would therefore be useful for a systematic exploration of the reactivity patterns of these molecules. We present an efficient high yield synthesis of Re(I) and Re(II) dicarbonyl complexes via an unprecedented ligand-mediated decarbonylation (LMD) reaction. We show that the LMD may be considered as generally applicable to *fac*-$[Re(CO)_3]^+$ complexes of tridentate aliphatic amine ligands. Structural authentication of key intermediates is presented.




[1] E. J. Schelter, F. Karadas, C. Avendano, A. V. Prosvirin, W. Wernsdorfer and K. R. Dunbar, *J. Am. Chem. Soc.*, 2007, **129**, 8139-8149.
[2] E. J. Schelter, A. V. Prosvirin, W. M. Reiff and K. R. Dunbar, *Angew. Chem. Int. Ed.*, 2004, **43**, 4912-4915.

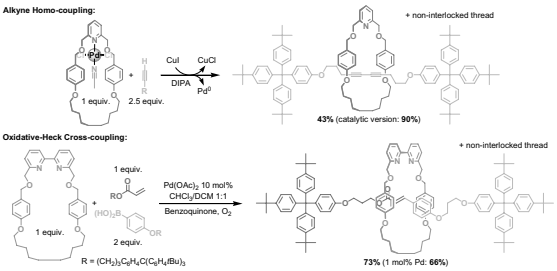
Organic Chemistry **250**

## Rotaxanes *via* Palladium Active-Metal Template Strategies

José Bernà, James D. Crowley, Stephen M. Goldup, Kevin D. Hänni, Ai-Lan Lee and David A. Leigh

University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, UK. (kevin.haenni@gmail.com)

In contrast to the classic 'passive template' approach,[1] an 'active-metal' template strategy[2] involves a metal center which acts as both a template *and* the catalyst for covalent bond formation in the construction of mechanically interlocked architectures.




Palladium-catalyzed reactions are often the method of choice for the formation of C-C bonds in chemical synthesis. The development of both homo[3] and heterocouplings[4] based on Pd active-metal templates opens the possibility to use these methodologies for the assembly of [2]rotaxanes. The reactions are mild, high-yielding, versatile and only a catalytic amount of the template is required.

[1] M. C. Thompson, D. H. Busch, *J. Am. Chem. Soc.* **1964**, *86*, 3651-3656; [2] V. Aucagne, K. D. Hänni, D. A. Leigh, P. J. Lusby, D. B. Walker, *J. Am. Chem. Soc.* **2006**, *128*, 2186-2187; [3] J. Bernà, J. D. Crowley, S. M. Goldup, K. D. Hänni, A.-L. Lee, D. A. Leigh, *Angew. Chem. Int. Ed.* **2007**, *46*, 5709-5713; [4] J. D. Crowley, K. D. Hänni, A.-L. Lee, D. A. Leigh, *J. Am. Chem. Soc.* **2007**, *129*, 12092-12093.

Organic Chemistry **251**

## Synthesis, properties and applications of Nickel(II) bisimidazol-2-ylidene complexes

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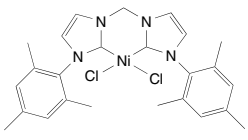
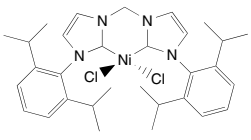
Since their discovery [1], *N*-heterocyclic carbenes (*N*HCs) especially derived from imidazolium salts have been used as ligands in different organometallic catalysis [2], but few have been used for olefin polymerisation. On the other side, the growing importance of nickel complexes as olefin polymerisation catalysts [3], led us to develop a new olefin polymerisation catalyst containing bisimidazolium ligands.




**1**




**2**

In this work, the synthesis of two new nickel(II) bisimidazolium-2-ylidene complexes is described. They are obtained by transmetalation from the corresponding silver carbene complexes. Surprisingly the two complexes differ very much both with respect to structure and catalytic behaviour. Most interestingly the violet pseudotetraedric complex **2** reversibly binds dioxygen, a feature totally absent in the square planar complex **1**.

[1] A. J. Arduengo, R. L. Harlow, M. Kline, *J. Am. Chem. Soc.*, **1991**, *113*, 361-363.
[2] W. A. Herrmann, *Angew. Chem. Int. Ed.*, **2002**, *41*, 1290-1309.
[3] S. Benson, B. Payne, R. M. Waymouth, *J. Polym. Sci., Part A: Polym. Chem.*, **2007**, *45*, 3637-3647.

Organic Chemistry **252**

## The Biomimetic Synthesis and Final Structure Determination of (–)-Centrolobine

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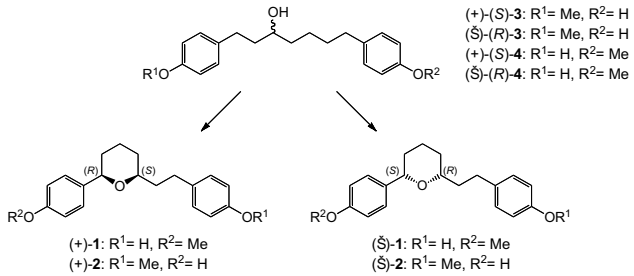
In previous work we have shown that 2,6-disubstituted tetrahydropyrans could be biomimetically synthesized by oxidative cyclization of their corresponding phenolic alcohols [1].




In order to correct structural inconsistencies of (–)-centrolobine ((–)**1**) [2], a physiologically active constituent of *Centrolobium robustum* [3], the congeners **1** and **2** were prepared from their precursors **3** and **4** (*ee* > 99%). The key step is the oxidative cyclization by DDQ, a biomimetic equivalent of phenoloxidase.

[1] P. Rüedi, M. Juch, *Curr. Org. Chem.* **1999**, *3*, 623.
[2] L. V. Alegrio, R. Braz-Filho, O. Gottlieb, *Phytochemistry* **1989**, *28*, 2359; A. F. de C. Alcântara, M. R. Souza, D. Piló-Veloso, *Fitoterapia* **2000**, *71*, 613; V. Böhrsch, S. Blechert, *J. Chem. Soc., Chem. Commun.* **2006**, 1968.
[3] I. L. De Albuquerque, C. Galeffi, C. B. Casinovi, G. B. Marini-Bettòlo, *Gazz. Chim. Ital.* **1964**, *94*, 287.

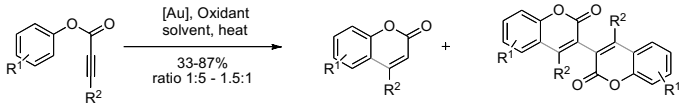
Organic Chemistry **253**

**A New Au-Catalyzed Cylization-Oxidative Coupling Reaction**

Sebastian Ahles, Hermann A. Wegner

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

Transition metal catalyzed reaction are among the most powerful synthetic methods in organic synthesis. However, one catalyst usually promotes only one specific reactions. This means, that for every transformation you have to work up the reactions and change the catalyst. Ideally, one metal would perform multiple different tasks. This demands a careful control of the reaction conditions.
The gold catalyzed cyclization of acetylenes with arenes via C-H activation is well known.[1] Recentely, we could combine this reaction with an oxidative coupling by the same Au catalyst.[2] Turn-over was achieved by re-oxidation of the gold catalyst. This method is a very efficient entry to dicoumarins, substructures of natural products and functional molecules.




[1] Z. Shi, C. He, *J. Org. Chem.* **2004**, *69*, 3669.
[2] S. Ahles, H. A. Wegner, *in preparation*.

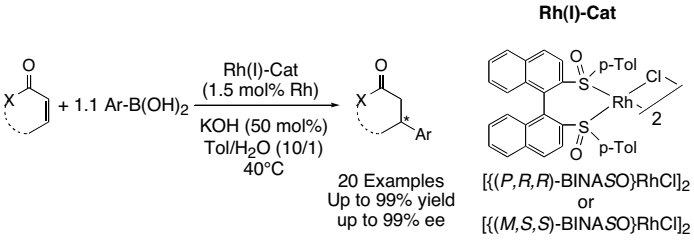
Organic Chemistry **254**

**Asymmetric 1,4-Addition of Arylboronic Acids to Electron-Deficient Olefins Catalyzed by Rhodium(Bis-Sulfoxide) Complex**

Ronaldo Mariz, Xinjun Luan, Michele Gatti, Anthony Linden, Reto Dorta*

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

A bis-sulfoxide with a binaphthyl backbone is introduced as a readily available, chiral ligand entity in late-transition metal catalysis. Ligand p-tol-BINASO [where p-tol-BINASO is 1,1'-binaphthalene-2,2'-diyl-bis-(p-tolylsulfoxide)] is obtained in pure form in one single synthetic step from relatively cheap, commercially available starting materials. Precatalyst [{(P,R,R)-p-tol-BINASO}RhCl]2 was synthesized in high yield and structurally characterized by X-ray diffraction.




The precatalyst shows both excellent reactivity and selectivity in the asymmetric 1,4-addition of arylboronic acids to cyclic, α,β-unsaturated ketones and esters[1].

[1] Ronaldo Mariz, Xinjun Luan, Michele Gatti, Anthony Linden, Reto Dorta, *J. Am. Chem. Soc*. **2008**, *130*, 2172.

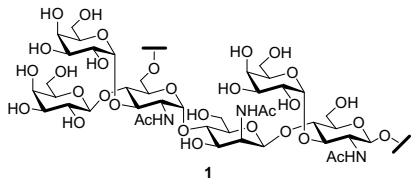
Organic Chemistry **255**

**Synthesis of Bacillus Anthracis major cell-wall polysaccharide repeating unit**

Matthias A. Oberli, Pascal Bindschädler, Tim Horlacher, Marie-Lyn Hecht, Daniel B. Werz, Peter H. Seeberger*

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

Infections caused by the Gram-positive, spore forming soil bacterium *Bacillus anthracis* results in very serious disease [1]. Inhalation of spores that are ground into fine particles that penetrate the lung of people will kill most victims within very short time. Hexasaccharide **1** was isolated and structurally characterized [2]. This polysaccharide is also species-specific and differs from that of closely related *B. cereus* strains.




**1**

We present the first synthesis of the hexasaccharide repeating unit of vegetative cells walls [3], as well as the first results targeting the development of a vaccine candidate and systems for pathogen detection.

[1] M. Mock, A. Fouet, *Annu. Rev. Microbiol.* **2001**, *55*, 647.
[2] B. Choudhury, C. Leoff, E. Saile, P. Wilkins, C. P. Quinn, E. L. Kannenberg, R. W. Carlson, *J. Biol. Chem.* **2006**, *281*, 27932.
[3] M. A. Oberli, P. Bindschädler, D. B. Werz, P. H. Seeberger, *Org. Lett.* **2008**, *10*, 905.

Organic Chemistry **256**

**The Total Synthesis of Valerenic Acid**

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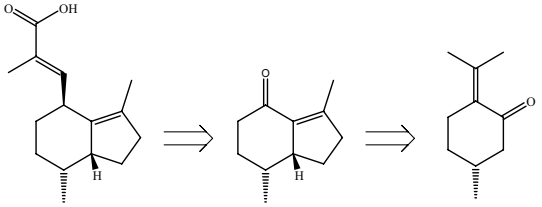
Swiss Federal Institute of Technology (ETH) Zürich, Institute of Pharmaceutical Sciences,
Wolfgang-Pauli-Strasse 10, CH-8092 Zürich, Switzerland

Valerenic acid (**1**) is a major constituent of the medicinal plant *Valeriana officinalis L.* (valerian) from which it was first isolated in 1957 [1]. Valerenic acid (**1**) is a sesquiterpenoic acid with a unique carbon skeleton [2] and shows biological activity as a positive allosteric modulator of the prominent ionotrope $GABA_A$ receptor complex [3].



Valerenic Acid **1** α,β-unsaturated Ketone **2** Pulegone **3**

Up to now no stereoselective total synthesis of valerenic acid (**1**) has been described in literature. Here we report the first enantioselective total synthesis of valerenic acid (**1**) based on the bicyclic ketone **2** as a key intermediate and the natural compound pulegone (**3**) as a readily available source for the stereo center at C7. This synthesis forms the basis for the establishment of an SAR for valerenic acid (**1**) with respective to its effects on the $GABA_A$ receptor.

[1] A. Stoll, E. Seebeck, *Ann. Chem.* **1957**, *603*, 158-168.
[2] Buchi, G., T. L. Popper, et al., *J. Am. Chem. Soc.* **1960**, *82*, 2962-2963.
[3] S. Khom, I. Baburin, et al., *Neuropharmacology* **2007**, *53*, 178-187.

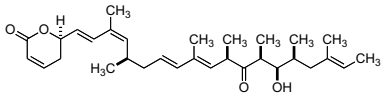
Organic Chemistry **257**

## Total Synthesis, Configuration and Biological Evaluation of Anguinomycin C

Simone Bonazzi,[1,2] Stephan Güttinger,[3] Ivo Zemp,[3] Ulrike Kutay,[3] and Karl Gademann*[,1]

[1] Chemical Synthesis Laboratory, EPFL, 1015 Lausanne, Switzerland
[2] Laboratorium für Organische Chemie, ETHZ, 8093 Zürich, Switzerland
[3]Institut für Biochemie, ETHZ, 8093 Zürich, Switzerland

Natural products provide interesting lead structures for cancer research and thus enable promising chemical approaches. Anguinomycin C, an antitumor antibiotic belonging to the leptomycin family and isolated from *Streptomyces*, selectively targets retinoblastoma tumor suppressor protein (pRB) inactivated cancer cells and exerts only growth arrest on normal cells.[1]



We present the first total synthesis of anguinomycin C characterized by Cr-catalyzed hetero-Diels-Alder reaction, tandem hydrozirconation-Negishi coupling, Negishi coupling with stereoinversion and enolate alkylation and aldol reaction with the DIOZ auxiliary.[2] This route allowed to establish the absolute configuration of the compound. In addition, anguinomycin C was evaluated as a potent inhibitor of nuclear-cytoplasmic transport. Current studies are directed at elucidating the mode of action, as well as the generation of more potent analogs.

[1] Y. Hayakawa, K.-Y. Sohda, K. Shin-Ya, T. Hidaka, H. Seto, *J. Antibiot.* **1995**, *48*, 954-961.
[2] S. Bonazzi, S. Güttinger, I. Zemp, U. Kutay, K. Gademann, *Angew. Chem. Int. Ed.* **2007**, *46*, 8707-8710.

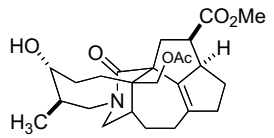
Organic Chemistry **258**

## Synthetic Studies on Daphmanidins B and C Based on Biosynthetic Considerations

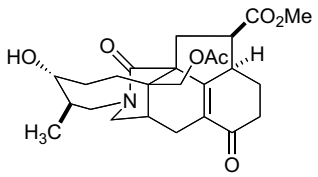
Adrien K. Lawrence and Karl Gademann*

Chemical Synthesis Laboratory, EPFL, 1015 Lausanne, Switzerland

To date, the use of small molecule neurotrophin mimics based on natural products is considered a promising strategy for the design of new therapeutic drugs against neurodegenerative diseases.[1] Our attention was drawn to daphaminidin C (**2**), due to its complex architecture and interesting biological activity. This *Daphniphyllum* alkaloid was isolated from the leaves of the Asian tree *D. teijsmanii* (Daphniphyllaceae) by Kobayashi *et al.* in 2004 and possesses an unprecedented fused-pentacyclic skeleton.[2]Furthermore,daphmanidin C (**2**) 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.
[3] J. Kobayashi, S. Ueno, H. Morita, *J. Org. Chem.* **2002**, *67*, 6546-6549.

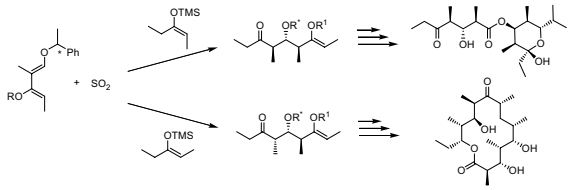
Organic Chemistry **259**

## New organic chemistry : Expeditious synthesis of polypropionates

Sylvain Laclef, Maris Turks, Pierre Vogel*

EPFL, SB ISIC LGSA, BCH-5401, CH-1015 Lausanne, Switzerland

Polypropionates and polyols are an interesting class of natural compounds with an exceptional profile of biological activity. Our group has shown that simple alkyl-substituted 1,3-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. The latter can be trapped by nucleophiles.
An asymmetric version of this oxyallylation has been developed, using 1,3-dioxy substituted dienes. In this way, complex polypropionate fragments can be achieved by a short sequence [1]. Combination of our methodology and aldol chemistry allows one to achieve polypropionate fragments. Efforts toward the synthesis of Erythronolide, Dolabriferol and analogues will be presented.



[1] Vogel, P.; Turks, M.; Bouchez, L.; Markovic, D.; Varela-Alvarez, A.; Sordo, J.A. *Acc. Chem. Res.* **2007**, *40*, 931.

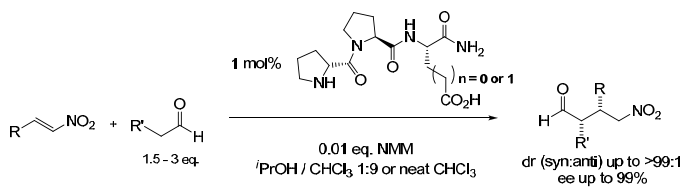
Organic Chemistry **260**

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

Markus Wiesner, Jefferson D. Revell and Helma Wennemers

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

Recently our group introduced the peptide H-Pro-Pro-Asp-$NH_2$ as an efficient catalyst for direct aldol reactions.[1] Guided by conformational analysis studies we have now extended the scope to conjugate addition reactions. We demonstrated that the peptide H-D-Pro-Pro-Asp-$NH_2$ is an excellent catalysts for addition reactions of aldehydes to nitroalkenes. Using only 1 mol% of the peptidic catalyst affords the γ-nitroaldehyde in up to quantitative yield and selectivities of up to 99% ee.[2] Even nitroethylene reacts readily with aldehydes in the presence of only 1 mol% of the peptide H-D-Pro-Pro-Glu-$NH_2$. The resulting mono-substituted addition products were obtained in up to 90% yield and up to 99% ee and were easily converted into monosubstituted $\gamma^2$-amino acids. [3]




1. P. Krattiger, R. Kovasy, J. D. Revell, S. Ivan, and H. Wennemers, *Org. Lett.* **2005**, *7*, 1101-1103.
2. M. Wiesner, J. D. Revell, H. Wennemers, *Angew. Chem., Int. Ed.* **2008**, *47*, 1871.
3. M. Wiesner, J. D. Revell, S. Tonazzi, H. Wennemers, *J. Am. Chem. Soc.* **2008**, *130*, 5610.

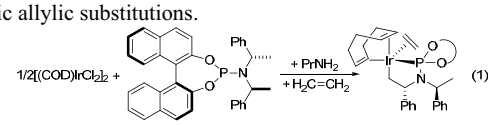
Organic Chemistry **261**

## Iridium Catalyzed Allylic Substitutions: Mechanism and Catalysts Improvements by Rational Design

Dean Markovic, John F. Hartwig

Yale University, P.O. Box 208107, 06520 New Haven, Connecticut, USA and University of Illinois at Urbana-Champaign, 600 S. Matthew, 61801Urbana, Illinois, USA

The key allyl intermediate and resting state of the iridium catalyst in the asymmetric allylation of amines will be presented.[1] Active allyl intermediate was isolated and characterized by X-ray diffraction. The intermediate is an octahedral complex where allyl is $\eta^3$-ligand. Stochiometric nucleophilic attack of aniline on the complex was studied. The complex was active as a catalyst for allylic ammination.
The resting state is a complex of the metallacyclic catalyst with the olefinic unit of the allylamine product. The species containing *N*-phenyl cinnamylamine complex have been isolated in pure form. Its mimic, a related ethylene complexes have been prepared on multigram scale (equation 1). The simple synthesis of these metallacyclic iridium complexes gives rise to a single-component, highly active and enantioselective catalysts for the asymmetric allylic substitutions.




Kinetic data on the overall catalytic cycle for the allylic ammination will be discussed. The rates of the catalytic reaction are first-order in allylic carbonate, amine, and catalyst, and inverse-first order in product. This combination of data, along with the observation that the resting state is stable toward 1.5 equiv of allylic carbonate, implies that the reaction of the iridium(I) species with the allylic carbonate is reversible and endoergic, and that this intermediate reacts with the nucleophile to form product.

[1] Markovic, D.; Harwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 11680.

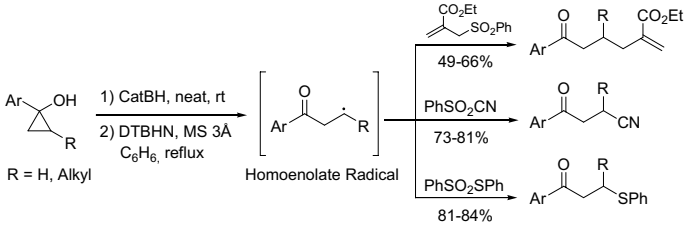
Organic Chemistry **262**

## Catecholborane Mediated Generation of Homoenolate and Enolate Radicals

Martin Pouliot,[a] Philippe Renaud,*[a] Armido Studer,*[b] Thomas Vogler[b]

[a] Department für Chemie und Biochemie, Universität Bern, Freiestrasse 3, 3008 Bern, Switzerland; [b] Organisch-Chemisches Institut, Westfälische Wilhelms-Universität, Corrensstrasse 40, 48149 Münster, Germany.

Homoenolate radicals are generated from catecholborate esters prepared by the reaction of readily available cyclopropanols with catecholborane. Treatment of the thus in situ formed cyclopropoxycatecholborane intermediates with a radical initiator lead to the homoenolate radicals which react efficiently with radical traps to afford allylated, cyanated and sulfanylated products in good yields.




Extension of this methodology to the generation of enolate radicals from catecholboron enolates will also be presented.

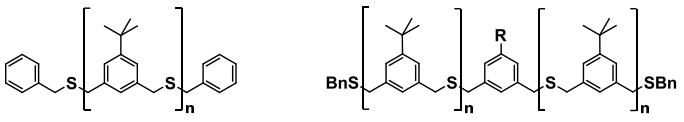
Organic Chemistry **263**

## Thioethers Control Nanoparticles

Torsten Peterle, Marcel Mayor*

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

The full control over the size and the spatial arrangement of nanoparticles is still a major challenge. However, this control is required *e.g.* for the use in single electron memory devices, where only particles with diameters below 2 nm provide the required coulomb blockade properties [1].
It was shown that multidentate thioether ligands of type **1** are able to stabilize small gold nanoparticles with diameters from 1 to 5 nm with low integer numbers of ligands [2].




These ligands have been monofunctionalized with different functional groups to structures of type **2** in order to be able to control the spatial arrangement of the gold nanoparticles by synthetic chemistry (*e.g.* 'Click-Chemistry' or alkyne homocoupling). Also, dendritic modifications of the thioether ligands are under investigation as stabilizers for gold nanoparticles to gain further control of the size and monodispersity of the formed particles.

[1] G. Schmid, U. Simon, *Chem. Commun.* **2005**, 697.
[2] T. Peterle, A. Leifert, J. Timper, A. Sologubenko, U. Simon, M. Mayor, *Chem. Commun.* **2008**, DOI: 10.1039/b802460j.

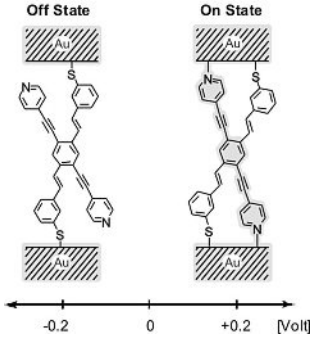
Organic Chemistry **264**

## New Cruciform Structures Toward Coordination Induced Single Molecule Switches

Sergio Grunder, Roman Huber, Maria Teresa González, Christian Schönenberger, Michel Calame & Marcel Mayor*

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

The trend of decreasing the size of current devices in the semiconductor industry increases the interest of new concepts which allow following this miniaturization trend beyond physical barriers.[1] Therefore single molecule switches have attracted considerable attention in the last few years.




A new concept has been proposed which exploits the different bonding strengths of certain anchor groups to gold electrodes in an electrochemical environment.[2] Herewith the synthesis of the second generation of these cruciform switches will be presented. Immobilization experiments and investigation of the switching mechanism of the second generation switches are currently in progress.

[1] N. Weibel, S. Grunder, M. Mayor, *Org. Biomol. Chem.* **2007**, *5*, 2343.
[2] S. Grunder, R. Huber, V. Horhoiu, M. T. González, C. Schönenberger, M. Calame, M. Mayor, *J. Org. Chem.* **2007**, *72*, 8337.

Organic Chemistry **265**

### A Novel Detection Method for the Explosive TATP.

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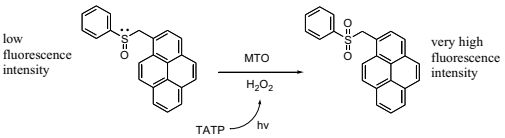
The importance of methods for the rapid, reliable detection of explosives is greater than ever. Triacetone triperoxide (TATP) has emerged as a weapon in the Middle East and been used by suicide bombers. TATP is distinguished by *Extraordinary Availability, Widespread Use, Difficulty of Detection* (does not contain nitro groups or fluorophores).

We suggest here a novel method for indirect detection of trace amounts of TATP based on the extremely low fluorescence of sulfoxides in comparison with sulfones.

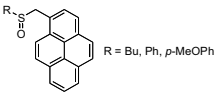
Our approach involves oxidation of sulfoxide, which leads to an increase in fluorescence emission (*Scheme 1*).

*Scheme 1*

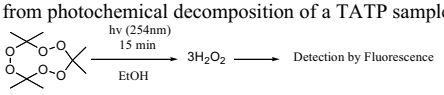



A series of sulfoxides bearing different substituents on the sulfur atom and with pyrene as the signaling subunit have been synthesized. All sulfoxides have been investigated in terms of TATP detection (*Scheme 2)*.

*Scheme 2.*




Significant fluorescence enhancement can be seen upon addition of $H_2O_2$ derived from photochemical decomposition of a TATP sample and MTO as a catalyst.




Organic Chemistry **266**

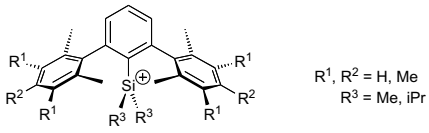
### Synthesis and Study of 2,6-Diarylphenylsilyl Cations

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

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

Silylium ions $R_3Si^+$ are tri-coordinate cations with a formal positive charge on the central silicon atom. The isolation and structural characterization of a planar $R_3Si^+$ system without coordination by solvent or counterion molecules was accomplished only six years ago.[1,2]

In this project, we examine the structure, dynamics and tunability of 2,6-diarylphenylsilyl cations **1**. In these cations, the lateral rings prevent the silicon center from interacting with solvent or anion molecules and also lead to an overall stabilization of the molecule by donating π electron density into the empty 3p(Si) orbital.[3] With an increasing number of methyl groups on the flanking rings, the π systems become more electron-rich, and a better shielding of the silicon nucleus is observed in the $^{29}Si$ NMR spectra. A general investigation of quantitative stubstituent effects on the stability of the cations will be presented.




**1**

[1] J. B. Lambert, Y. Zhao, S. M. Zhang, *J. Phys. Chem.* **2001**, *14*, 370.
[2] K.-C. Kim, C. A. Reed, D. W. Elliot, L. J. Mueller, F. Tham, L. Lin, J. B. Lambert, *Science* **2002**, *297*, 825.
[3] S. Duttwyler, Q. Do, A. Linden, K. K. Baldridge, J. S. Siegel, *Angew. Chem. Int. Ed.* **2008**, *47*, 1719.

Organic Chemistry **267**

### Model Reactions for the Synthesis of Heterocorannulene

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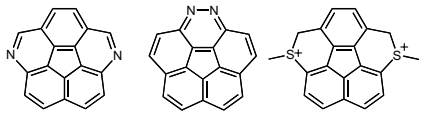
The discovery of buckminsterfullerene has stimulated much interest in the chemistry of bowl-shaped polycyclic aromatic hydrocarbons, such as corannulene.[1] Such bowl-shaped compounds can be expected to exhibit unique physicochemical properties related to the buckminsterfullerene surface. The heterofullerene $C_{59}N$ has been studied extensively, but smaller heterobuckybowls remain completely unknown, except to theoreticians.[2] The only known heterobuckybowl that has been successfully prepared contains sulfur atoms. No heteroatom replacement of corannulene ($C_{19}XH_9$) are known.[3]

Our primary targets are diaza and sulfur derivatives of corannulene. The synthetic approach takes advantage of methods we developed for the synthesis of 1,6,7,10-tetrasubstituted fluoranthenes and related azafluoranthenes. Recent results will be presented.



[1] Barth, W.; Lawton, R. J. Am. Chem. Soc., **1966**, 88, 380; **1971**, 93, 1730.
[2] Priyakumar, U.; Sastry, G. J. Org. Chem. **2001**, 66, 6523.
[3] Imamura, K.; Takimiya, K.; Otsubo, T.; Aso, Y. Chem. Commun., **1999**,1859.

Organic Chemistry **268**

### Synthesis of A C-Nucleotide and Investigation of Its Base Pairing Ability.

Benno Bischof, J.S. Siegel*

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What came before A? This is a fundamental question in origin of life science.

A pre-biotic DNA precursor based only on pyrimidine nucleobases as seen in *Figure 1* has been proposed [1]. In order to investigate this hypothesis in a model system we synthesized C-nucleotide **D** as an analogue of **A** and incorporated it into oligonucleotides to investigate its base pairing ability in details [2].

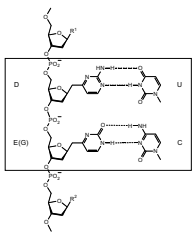
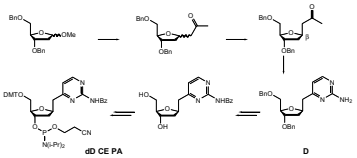



*Figure 1*: Pyrimidine based DNA.




*Scheme 1*: Synthesis of **D**.

5'- C G C A U G X G U A C G C -3' X=A, D
3'- G C G U A C Y C A U G C G -5' Y=A, D, G, U, C

*Figure 2*: Investigated Oligonucleotides.

[1] J.S. Siegel, Y. Tor *Org. Biomol. Chem.* **2005**, *3(9)*, 1591.
[2] G. Vesnaver, K.J. Breslauer *Proc. Natl. Acad. Sci.* **1991**, *88*, 3569.

Organic Chemistry **269**

**Structure-Selective Fluorescent Probes for G-Quadruplex DNA**

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Institute of Organic Chemistry, University of Zürich, Winthurerstrasse 190, CH8057, Switzerland

DNA is typically regarded as a uniform double helix that is acted upon by proteins to regulate its expression and replication. DNA structure, however, is highly dynamic and its functions are potentially diverse. Intramolecular, four-stranded DNA structures known as quadruplexes can form in the 3' single-stranded telomeric overhangs of chromosomes in vivo.[1] Some groups have proposed that quadruplex formation in the promoter regions can regulate transcription initiation, but little direct evidence supports this hypothesis.[2] Towards this goal, we have synthesized and characterized small-molecule fluorescent probes for G-quadruplex DNA derived from promoter region sequences that bind with $K_d$ values of approximately 1.0 nM. These compounds are highly selective, exhibiting over 1,000-fold lower affinities to double stranded DNA. Importantly, the fluorescence emission from these probes (ex 625, em 705) increases by over 200-fold upon G-quadruplex binding. When applied to living mammalian cells, these probes stain nuclei bright red, and exhibit relatively little short-term cytotoxicity. Here we describe the design, synthesis, and characterization of small molecule fluorescent probes for G-quadruplex DNA that may help prove to existence and location of G-quadruplex DNA in vivo.

[1]. C. Schaffitzel, I. Berger, J. Postberg, J. Hanes, H.J. Lipps, A. Pluckthun, *Proc. Natl. Acad. Sci*. USA, **2000**, *98*, 8572.

[2]. (**a**) A. Siddiqui-Jain, C.L. Grand, D.J. Bearss, L.H. Hurley, *Proc. Natl. Acad. Sci*. USA, **2002**, *99*, 11593. (**b**) T. Saha, K. Usdin, *FEBS Lett*., **2001**, *491*, 184. (**d**) P. Catasti, X. Chen, R.K. Moyzis, E.M. Bradbury, G. Gupta, *J. Mol. Biol*., **1996**, *264*, 534. (**e**) S. Cogoi, F. Quadrifoglio, L.E. Xodo, *Biochemistry*, **2004**, *43*, 2512. (**f**) A. Lew, W.J. Rutter, G.C. Kennedy, *Proc. Natl. Acad. Sci*. U S A., **2000**, *97*, 12508.

Organic Chemistry **270**

**Nonviral Gene Therapy Vectors**

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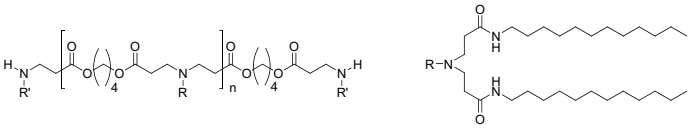
University of Geneva, quai E. Ansermet 30, 1211 Geneva, Switzerland; MIT, 77 Massachusetts Avenue, Cambridge MA, USA

Gene Therapy has the potential to revolutionize medicine. Efficient and safe nucleic acid delivery into mammalian cells in vivo remains a critical obstacle to the widespread use of DNA and RNAi-based therapeutics. Our approach is to synthesize libraries of nonviral Gene Therapy vectors and to test the molecules in a high-throughput assay.



Starting from an amine two routes have been followed:
1) Solvent-free mixing of amines with diacrylates at elevated temperatures resulted in poly(β-aminoester)s. Using an molar excess of diacrylate, acrylate terminated polymers were synthesized that were end-capped with different amines.[1] Plasmid-DNA transfections into HUVEC cells showed transfections at levels comparable to an adenovirus.[2]
2) Solvent-free mixing of amines with long-tailed acrylamides lead to the synthesis of lipid-like molecules, lipidoids. Members of the library showed unsurpassed transfection efficiencies of small interfering RNAs in non-human primates.[3]

[1] G.T. Zugates et al., *Bioconjugate Chemistry*, **2007**, *18*, 1887.
[2] G.T. Zugates et al., *Molecular Therapy*, **2007**, *15*, 1306.
[3] A. Akinc et al., *Nature Biotechnology*, **2008**, *26*, 56.

Organic Chemistry **271**

**Synthesis of 8-Substituted-2'-Deoxyguanosines for the Detection of DNA Folding**

Anaëlle Dumas, Nathan Luedtke*

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

Certain guanine-rich DNA sequences are known to self-assemble into four-stranded structures called G-quadruplexes [1]. While it has been proposed that these conformations may have important biological functions, direct evidence for their existence *in vivo* has remained elusive [2]. The development of internal probes for the detection of DNA folding may facilitate the monitoring of quadruplex formation both *in vitro* and *in vivo*. Fluorescent nucleoside analogues that maintain their hydrogen bonding interactions with other bases are potential candidates for this purpose. Towards this goal a number of fluorescent 8-aryl and 8-(2-(aryl-2-yl)vinyl-2'-deoxyguanosines were prepared using palladium-catalyzed cross-coupling chemistry. A new strategy involving the protection of the $O^6$-position of guanosine was developed to gain synthetic access to compounds which could not be prepared according to reported protocols. Photophysical characterisation of the resulting products revealed encouraging environment sensitivity and emission at relatively long wave lengths. One modified of the 8-aryl-2'-deoxyguanosine has been incorporated into G-quadruplex forming DNA sequences using standard phosphoramidite chemistry and its properties studied. The different environments experienced by the base in duplex and quadruplex DNA structures, notably in the presence of zinc, were reflected in the photophysical characteristics of the internal probe.

[1] Catasti, P.; Chen, X.; Mariappan, S. V. S.; Bradbury, E. M.; Gupta, G. *Genetica* **1999**, *106*, 15.
[2] Schaffitzel, C.; Berger, I.; Postberg, J.; Hanes, J.; Lipps, H. J.; Pluckthun*, A. Proc. Nat. Acad. Sci. U.S.A.* **2001**, *98*, 8572.

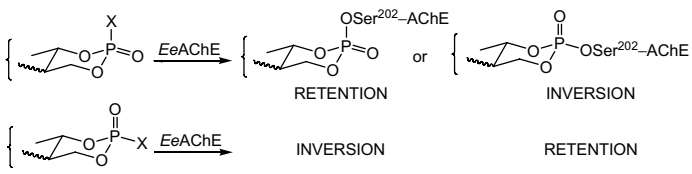
Organic Chemistry **272**

**The Stereochemical Course of the Irreversible Inhibition of Acetylcholinesterase by Optically Active Phosphadecalins**

Michael Wächter, Peter Rüedi*

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

Continuing our studies on the inhibition of acetylcholinesterase by organophosphates we have synthesized different enantiomerically pure phosphadecalins. Representing acetylcholine mimetics, they are useful probes for the investigation of the physiologically active conformation of acetylcholine [1] and the stereochemical pathway of the inhibition reaction [2].




*cis*- and *trans*-decalins
X = electron withdrawing group, *e.g.*, F, Cl, 2,4-dinitrophenoxy
*Ee*AChE = Acetylcholinesterase from *Electric Eel*

The inhibitors were characterized by enzyme kinetic experiments. $^{31}$P-NMR investigations with the totally inhibited *Ee*AChE were performed to elucidate the stereochemical course of the reaction. First results of these experiments are presented.

[1] S. Furegati, F. Gorla, A. Linden, P. Rüedi, *Chem. Biol. Interactions* **2005**, *157–158*, 415.
[2] S. Furegati, O. Zerbe, P. Rüedi, *Chem. Biol. Interactions* **2005**, *157–158*, 418.

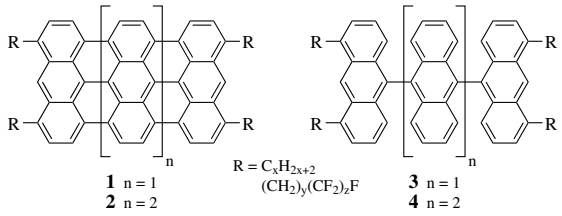
Organic Chemistry **273**

## On the Road to New Polycondensed Aromatic Hydrocarbons

Patrick Tondo and Titus A. Jenny*

Université de Fribourg, Département de Chimie, Chemin du Musée 9, CH-1700 Fribourg, Switzerland

Polycondensed aromatic hydrocarbons (PAHs) are known for their tendency to form conducting columnar assemblies, which could be used as molecular wires. Most of the work has been devoted so far to the study of hexa-*peri*-benzocoronene (HBC) derivatives. Decorating the HBC core with perfluorinated side chains permitted to minimize lateral interactions between columnar assemblies, thus maximizing the $\pi$-$\pi$ stacking in the columnar axis and simultaneously providing highest solubility of the supramolecular assemblies in appropriate solvents such as hexafluorobenzene [1]. An alternative to the disc-shaped HBC could be rectangular-shaped molecules of the type of **1**. Preliminary calculations allow us to expect for this structure a further improved $\pi$-$\pi$ stacking behavior as compared to the HBC's.




Strategies for the synthesis of the so far unknown tri- and tetraanthryl core structures **1** and **2** from the newly synthesized precursors **3** and **4** are discussed.

[1] Aebischer O. F., Aebischer A., Donnio B., Alameddine B., Dadras M., Güdel H.-U., Guillon D. and Jenny T. A. , *J. Mater. Chem.*, **2007**, *17*, 1262.

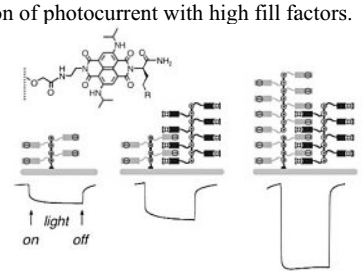
Organic Chemistry **274**

## Zipper Assembly of Rigid-Rod π-Stack Cascade Architectures for Photocurrent Generation

Kishore Ravuri, Velayutham Ravikumar, Aude Violette, Shin-ichiro Sakurai, Rajesh Bhosale, Santanu Maity, Marco Lista, Oksana Kel, Natalie Banerji, Eric Vauthey, Naomi Sakai, and Stefan Matile*

University of Geneva, Department of Organic Chemistry
Geneva, Switzerland

In organic photovoltaic devices, it is a challenge to design molecules that efficiently absorb sunlight and function as molecular n/p heterojunctions and at the same time possess structural features facilitating vectoral supramolecular organization compatible to multicomponent architectures. We introduce a highly modular, bottom-up design strategy of a zipper assembly based on rigid-rod π-stack architectures composed of *p*-oligophenyl or OPE rods and naphthalenediimide (NDI) stacks [1, 2]. The design creates a modular layer-by-layer assembly, whose 3-D propagation can be effectively controlled and fine tuned for efficient photoinduced stack/rod charge separation needed for the formation of n/p-heterojunctions and subsequently for the generation of photocurrent with high fill factors.




[1] Sakai, N.; Sisson, A. L.; Bürgi, T.; Matile, S. *J. Am. Chem. Soc.* **2007**, *129*, 15758-15759.
[2] Sisson, A. L.; Sakai, N.; Banerji, N.; Fürstenberg, A.; Vauthey, E.; Matile, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 3727-3729.

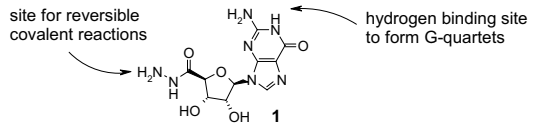
Organic Chemistry **275**

## Reversible Hydrazone Formation Within Supramolecular Hydrogels: New Perspectives to Control the Release of Bioactive Volatiles.

Andreas Herrmann,[a]* Barbara Levrand,[a] Florence Vigouroux-Elie,[a] Nampally Sreenivasachary[b] and Jean-Marie Lehn[b]*

[a]*Firmenich SA,* Division Recherche & Développement, B.P. 239, CH-1211 Geneva 8, Switzerland.
[b]*ISIS, Université Louis Pasteur,* B.P. 70028, F-67083 Strasbourg, France.

Reversible hydrazone formation was found to be very efficient to control the evaporation of volatile aldehydes and ketones in practical applications [1]. As a further step to develop novel delivery systems for bioactive volatiles, we now combined the possibility of reversible covalent bond formation with the generation of supramolecular assemblies, in which the active molecules can not only reversibly react with the hydrazide, but also get physically trapped inside the supramolecular structure. Guanosine-5'-hydrazide (**1**) forms stable supramolecular hydrogels in the presence of alkali metal cations by selective self-assembly to a G-quartet structure [2].




The stability of the hydrogels in the presence of bioactive volatile carbonyl compounds was analysed by rheology measurements, and the controlled release of the volatiles from the gel structure was followed by dynamic headspace analysis [3].

[1] B. Levrand, W. Fieber, J.-M. Lehn, A. Herrmann, *Helv. Chim. Acta* **2007**, *90*, 2281.
[2] N. Sreenivasachary, J.-M. Lehn, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 5938.
[3] J.-M. Lehn, N. Sreenivasachary, A. Herrmann, WO 2006/100647, 2006.

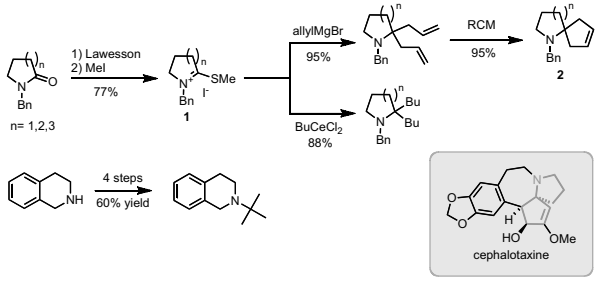
Organic Chemistry **276**

## Efficient Conversion Of Lactams And Amides Into 2,2-Dialkylated Amines

Alessandro Agosti, Britto Sebastian, Philippe Renaud*

Dept. Chemie und Biochemie, Universität Bern
Freiestrasse 3, 3012 Bern

2,2-dialkylated amines are important structural motifs in organic chemistry as useful building blocks for natural products synthesis. Specifically, *gem*-diallylated pyrrolidines were used as starting materials for the synthesis of azaspirocyclic natural compounds such as cephalotaxine and pinnaic acid. Presented here is a facile method for the construction of *gem*-dialkylated amines from their corresponding lactams and amides, featuring the alkylation of thioiminium ions **1** with Grignard and organocerium reagents.[1] Furthermore, treatment of the *gem*-diallylated heterocycles with Grubbs catalyst afford the corresponding aza-spirocycle **2** in nearly quantitative yield.




We are currently exploiting this methodology for the synthesis of natural alkaloids.

[1] Agosti, A.; Sebastian, B.; Renaud, P. Org. Lett., **2008**, *10*, 1417

Organic Chemistry **277**

## Synthesis of the Trefoil Knot

Karla I. Arias, Eli Zysman-Colman, Jon C. Loren, Anthony Linden, Jay, S. Siegel

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

Chemists are interested in molecular effigies of knots and other topologically interesting structures, because these new molecular forms should correlate with new function and provide challenges for chemical synthesis. Synthesis of such complex molecular architectures leads to the development of new synthetic methods and strategies. Among such target structures, chemists have focused on the trefoil knot as the most fundamental one. [1] [2]

The goal of this project was to synthesize a trefoil knot with the highest possible symmetry, $D_3$. In this strategy, we used a metal-directed approach via a $D_3$-symmetrical triskelion template (Figure 1) to obtain the desired over-under arrangement, followed by cyclization [3].

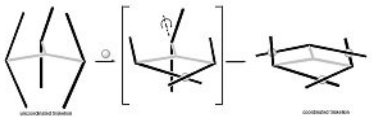
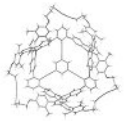


**Figure 1:** Topological control using triskelion intermediate.

Successful cyclization occurred in good yield (88%) using a modified Eglinton coupling protocol. The structure was initially inferred from ESIMS, IR, and $^1$H-NMR, and the crystal structure confirmed the desired topology and connectivity (Figure 2) [4].



Organic Chemistry **278**

## CpRu-catalyzed regio and enantioselective decarboxylative etherification of allyl aryl carbonates

Martina Austeri, David Linder and Jérôme Lacour

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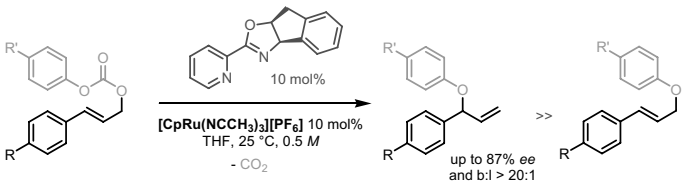
Regio and enantioselective nucleophilic substitution of asymmetrically substituted allylic carbonates still represents a challenge in organometallic catalysis[1]. In this context, only a few examples of this transformation mediated by ruthenium complexes are reported, and in the field of the Ruthenium catalyzed in particular. Recently, we have discovered that a combination of CpRu(II) moiety and enantiopure pyridine-oxazoline ligand, can efficiently catalyze the transformation of cinnamyl aryl carbonates into non racemic allyl aryl ethers. Complete conversions, good branched to linear ratios and good levels of enantioselectivity can be obtained[2].




[1] Bruneau, C.; Renaud, J. L.; Demerseman, B. *Chem. Eur. J.* **2006**, *12*, 5178. Mbaye, M. D.; Demerseman, B.; Renaud, J. L.; Toupet, L.; Bruneau, C. *Angew. Chem. Int. Ed.* **2003**, *42*, 5066. Zaitsev, A. B.; Gruber, S.; Pregosin, P. S. *Chem. Commun.* **2007**, 4692.

[2] Austeri, M.; Linder, D.; Lacour, J. *Chem. Eur. J.* **2008**, DOI:10.1002/chem.200800619.

Organic Chemistry **279**

## A versatile ruthenium catalyst: from cycloadditions to Michael additions

Andrei Bădoiu, Florian Viton, E. Peter Kündig*

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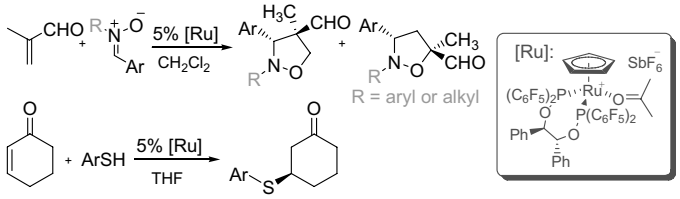
*peter.kundig@chiorg.unige.ch

Well-defined, stable one-point binding chiral iron and ruthenium complexes selectively coordinate and activate *α,β*-unsaturated carbonyl compounds. We have applied these mild Lewis acids as catalysts for asymmetric Diels-Alder reactions and 1,3-dipolar cycloaddition reactions.[1][2]

We now report new data on the latter with diarylnitrones. The *endo* isoxazolidines are obtained exclusively in high yields and ee's. The regioselectivity correlates directly with the electronic properties of the nitrone. This is shown by experimental and computational data.[3]

This poster also reports our preliminary results of asymmetric Michael addition reactions of thiophenols to enones.




[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] a) Badoiu, A.; Brinkmann, Y.; Viton, F.; Kündig, E. P. *Pure Appl. Chem.* **2008**, *80*, 1013; b) Badoiu, A.; Bernardinelli, G.; Mareda, J.; Kündig, E. P.; Viton, F. *Chem. Asian J.* **2008**, *in press*.

Organic Chemistry **280**

## Controlled Dimerization of AGT fusion proteins via Photoactivation

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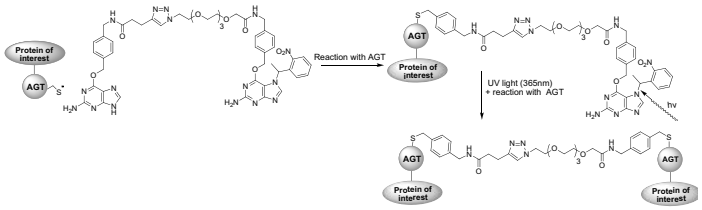
Dimerization of proteins plays an important role in many biological processes such as signal transduction, transcription, apoptosis and protein degradation [1]. Small organic molecules can be used as tools to control and study dimerization dependent processes. Here, we report a general method to induce the dimerization of $O^6$-alkylguanine-DNA alkyltransferase (AGT) fusion proteins via photoactivation. This approach is based on specific and covalent reaction of AGT with benzylguanine (BG) derivatives [2]. The reaction of AGT with BG was masked by introducing a photolabile group 1-(2-nitrophenyl) ethyl (NPE) on N7 of guanine [3]. We synthesized a BG-BG dimer with one of the BG moieties caged with NPE. The molecule was used to control dimerization of AGT fusion proteins by UV light in vitro.




[1] J. D. Klemm, S. L. Schreiber, G. R. Crabtree, *Annu. Rev. Immunol.* **1998**, *16*, 569. [2] A. Keppler, S. Gendreizig, T. Gronemeyer, H. Pick, H. Vogel, K. Johnsson, *Nat. Biotechnol.* **2003**, *21*, 86. [3] S. Banala, A. Arnold, K. Johnsson, *ChemBioChem* **2008**, *9*, 38.

Organic Chemistry **281**

**Total Synthesis and Configurational Assignment of Farinosone C and its Epimer**

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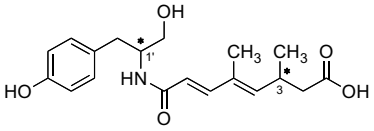
Neurodegenerative disorders, in particular Alzheimer's disease, increasingly affect our societies worldwide.[1] One successful therapeutic strategy for these health issues represents the regeneration of neuronal networks, *e.g.* the stimulation of neurite outgrowth.[2] An attractive alternative is based on the search for orally bioavailable small organic molecules that could mimic neurotrophin action.[3] New pyridone alkaloids metabolites - isolated from *Paecylomyces farinosus* - were recently found to be neuroactive.[4] Our interest was focused on farinosone C (**1**) - a biogenetically related amide - which has not been synthesized and which induced neurite outgrowth in the PC-12 cell line.




farinosone C (**1**)

The absolute configuration of two stereogenic centers, which were unassigned in the isolation and structure elucidation report,[4] was established by total synthesis. The synthetic approach and related studies of farinosone C (**1**) and its epimer will be discussed.

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

Organic Chemistry **282**

**Solid-Phase Oligosaccharide Synthesis: Preparation of a Novel Linker and its Evaluation with Different Glycosylating Agents**

Pascal Bindschädler, Lenz Kröck, Bastien Castagner, Davide Esposito, Peter H. Seeberger*

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

In recent years, efforts have been undertaken to create an automated solid-phase oligosaccharide synthesizer that will allow non-specialists to assemble oligosaccharides using a defined set of oligosaccharide building blocks [1]. The linker, the connection between the solid support and the first monosaccharide, can be viewed as support-bound protecting group. Consequently, the linker is of utmost importance for the entire synthetic process as its chemical nature determines the reaction conditions that can be used during the assembly, and the cleavage conditions required to liberate the final product from the resin [1]. So far, our linker of choice was an octendiol based linker that allows cleavage of the final oligosaccharide product from the resin by cross metathesis using Grubbs' catalyst in the presence of ethylene [2].
Here, we will disclose the preparation and the structure of a novel linker and its application to the synthesis of complex oligosaccharides. Beside *N*-phenyl trifluoroacetimidates, the novel linker enables us, for the first time, to use thioglycoside monosaccharide building blocks. Simple base-mediated cleavage of the linker from the resin followed by hydrogenation provides oligosaccharides suitably equipped for conjugation to carrier proteins or immobilization on glass-slide microarrays.

[1] P. H. Seeberger, *Chem. Soc. Rev.* **2008**, *37*, 19.
[2] R. B. Andrade, O. J. Plante, L. G. Melean, P. H. Seeberger, *Org. Lett.* **1999**, *1*, 1811.

Organic Chemistry **283**

**Toward the First Total Synthesis of the Lythracea Alkaloid (+)-Vertine**

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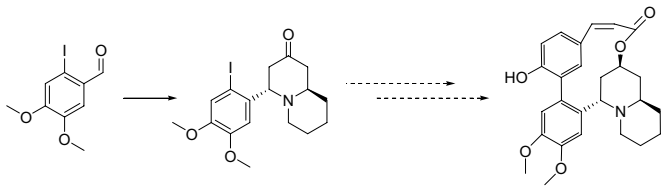
The biphenylquinolizidine alkaloid (+)-Vertine (also called cryogenine) was isolated in 1962 from *Decodon verticillatus (L.) Ell.,* a plant of the loosestrife family (*Lythraceae*) [1]. Clinically observed effects of Vertine include anticholinergic, antispasmodic, hyperglycaemic, hypotensive, and vasodilator activity [2]. We here report a first approach toward the synthesis of this alkaloid.




**1** **2** **3** (+/-) Vertine

The synthetic route towards (+/-) Vertine includes Pelletierine condensation [3], Suzuki coupling and diastereoselective reduction. Metathesis should then yield **3**.
The same strategy could be employed for our asymmetric synthesis from a planar chiral enantiomerically pure aldehyde complex [4]**.** Progress in this endeavour will be reported.

[1] Ferris J. P. *J. Org. Chem*. **1962**, *27*, 2985.
[2] Harborne J.B., Baxter H. *Phytochemical Dictionary. A Handbook of Bioactive Compounds from Plants*, Taylor & Frost, London **1983**, 791.
[3] Quick, J.; Oterson, R. *Synthesis* **1976**, 745.
[4] Ratni H., Kündig E. P. *Org. Lett*. **1999**, *1*, 1997.

Organic Chemistry **284**

**Bio–Organic Protein Frameworks**

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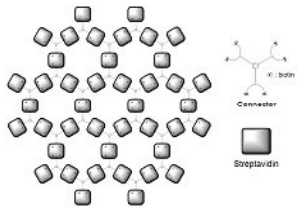
Institute of Chemistry, University of Neuchâtel, Av. Bellevaux 51, CP 158, CH-2009 Neuchâtel, Switzerland.




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. On the basis of the work which has been previously reported in our lab [1], we are now trying to reach higher orders of self-assembled protein nanostructures by using streptavidin (as a linker) and new connectors bearing three bis-biotinylated units. Anchoring on a biotinylated surface is used to monitor the self-assembly process of bio-organic protein frameworks step by step using QCM, PM-IRRAS and SPR*. This approach has the potential for building diverse nanostructures in a controlled fashion, such as linear threads, dendrimers and 2D networks.

* QCM: Quartz Crystal Microbalance
PM-IRRAS: Polarization modulation-infrared reflection-adsorption spectroscopy
SPR : Surface Plasmon Resonance

[1] Sabina Burazerovic, Julieta Gradinaru, Julien Pierron, Thomas R. Ward, *Angew. Chem. Int. Ed.* **2007**, 46, 5510 –5514.

Organic Chemistry **285**

## Large Scale Synthesis of Decachlorocorannulene

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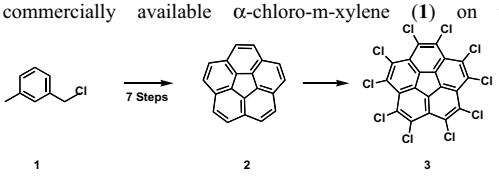
[b]Labor für Prozessforschung Winterthurerstrasse 190, 8057 Zürich, Switzerland

Over the past two decades there has been an increase in the interest of nanotubes both for their unique macroscopic properties as well as practical application.[i] The first of these fullerenes, $C_{60,}$ was accidentally discovered in 1985 by Kroto, Curl, and Smalley while using laser spectroscopy to reproduce the carbon chemistry that takes place in the atmosphere of a star.[ii] This method of exposing graphite to extreme temperatures to produce $C_{60}$ is efficient, but limited to only this molecule. For this reason, it is the interest of our group to synthesize carbon nanotubes using only solution-phase chemistry, starting from decachlorocorannulene (**3**).
Corannulene (**2**) was first synthesized in 1966 by Barth and Lawton and is known to be the simplest curved surface of $C_{60}$.[iii iv] Improvements in the synthesis of **2** have opened the door for a variety of mono, di, tetra, penta and deca substituted derivatives via cross-coupling reactions with their respective halocorannulene precursors.[v vi] This work focuses on the optimization of **3** starting from commercially available α-chloro-m-xylene (**1**) on the industrial scale.




1 2 3

[i] Colbert, D. T. Single-wall nanotubes: a new option for conducting plastics and engineering polymers. *Plastics Additives & Compounding* [online] **2003**.
[ii] Kroto, H. W.; Heath, J. R.; O'Brian S. C.; Curl, R. F.; Smalley R. E. *Nature* **1985**, 318, 162.
[iii] Jones, C. S.; Elliott, E.; Siegel, J. S. *Synlett*, **2004**, 1, 187.
[iv] Barth, W. E.; Lawton, R. G. *J. Am. Chem. Soc.* **1966**, *88*, 380.
[v] Wu, Y.-Ti.; Siegel, J. S. *Chem. Rev.* **2006**, 106, 4843.
[vi] Huang, R.; Huang, W.; Wang, Y.; Tang. Z.; Zheng, L. *J. Am. Chem. Soc.* **1997**, *119*, 5954.

Organic Chemistry **286**

## S-Trifluoromethylation of Cysteine Side Chains in α- and β-Peptides

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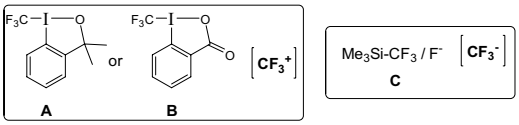
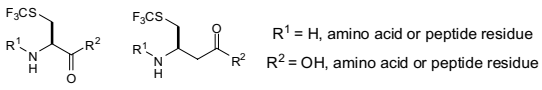
Laboratory of Organic Chemistry & Laboratory of Inorganic Chemistry[§]
ETH-Zürich, Hönggerberg, HCI, CH-8093, Zürich, Switzerland

Nervous System Research, Novartis Pharma AG, WSJ-386/745, CH-4002 Basel, Switzerland

The 10-I-3 hypervalent iodine compounds **A** and **B** have recently been introduced as selective electrophilic trifluoromethylating reagents [1] (*umpolung* of the *Ruppert-Prakash* reagent **C** [2]).




We have now tested whether the new reagents are capable of transferring the $CF_3$-group to α- and β-peptides carrying cysteine and various unprotected side-chain functional groups. Peptides consisting of 2, 8 and 13 amino acids were employed. The most complex substrate was the reduced form of octreotide (Sandostatin®). In all cases the desired $F_3C$-S-derivatives were isolated. The results of biological tests with trifluoromethylated octreotides will be reported.




[1] P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, *12*, 2579.
[2] I. Ruppert, K. Schlich, W. Volbach, *Tetrahedron Lett.* **1984**, *25*, 2195.

Organic Chemistry **287**

## Convenient method to substitute 3-furaldehydes in position 2

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A two steps synthetic sequence leading to the formal substitution of 3-furaldehydes on position 2 was studied. The first step corresponded to the attack of a Grignard reagent on the 3-furaldehyde **1** to afford the 3-(1-hydroxysubstituted)furans **2**. The second step, an oxidative rearrangement using singlet oxygen, yielded 2-substituted-3-furaldehydes **3**. Reaction of various furans with singlet oxygen is well described in the literature[1,2]; however, γ–hydroxybutenolide derivatives, described as the main product, were not formed in our case. On the other hand, this approach is a mild version of NBS-promoted related rearrangement.[3]


An extensive optimization of reaction conditions was carried out for the oxidative rearrangement, including solvent, reaction temperature, acid, reducing agent as well as post-reaction time. A small library of 3-(1-hydroxylsubstituted)furans **2** was prepared and then converted to 2-substituted-3-furaldehydes **3** using our optimized reaction conditions affording the desired aldehyde in moderate to high yields.

[1] Kernan, M. R., Faulkner, D. J., *J. Org. Chem*., **1988**, *53*, 2773.
[2] Aquina, M., Bruno, I., Riccio, R., Gomez-Paloma, L., *Org. Let.,* **2006**, *8*, 4831.
[3] Walsh, J. P., Kelly, A. R., Kerrigan, M. H., *J. Am. Chem. Soc.*, **2008**, 130, 4097.

Organic Chemistry **288**

## Desymmetrization Reactions *via* Enantioselective C-C-Bond Cleavage

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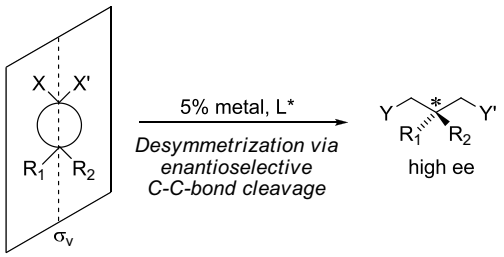
The desymmetrization of a preinstalled symmetrically substituted quaternary carbon center is a convenient access to chiral quaternary centers [1]. We envisioned that a transition metal catalyzed selective cleavage of one of the two prochiral carbon-carbon single bonds of a symmetrical cyclic skeleton would open an avenue for the asymmetric synthesis of all-carbon stereogenic centers *via* the pathway shown below.




We will report our initial results of this concept.

[1] T. Rovis in *New Frontiers in Asymmetric Catalysis*, pp 275-311, Eds.: K. Mikami, M. Lautens, John Wiley & Sons: Hoboken, 2007.

Organic Chemistry **289**

**Alkylation of benzene over mesoporous SAPO catalysts**

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ETH Zurich, Institute for Chemical and Bioengineering, Wolfgang-Pauli-Strasse 10, 8093 Zurich, Switzerland

The alkylation of aromatic and cyclic molecules is used for production of fine chemicals, dyestuffs, detergents, and scents. In many industrial processes, these alkylations are still performed in the presence of toxic and corrosive liquid acids. To make alkylations more effective, environmentally friendly, and cheaper much effort is being made to replace liquid acids by zeolites and zeolitic materials [1]. However, the use of microporous zeolites as catalyst is often hampered by diffusion limitation, which can cause loss of activity and selectivity and lead to catalyst deactivation. Using mesopore-containing materials as catalyst can solve this problem [2].
We performed alkylation of benzene with 1-hexene over conventional and mesoporous silicoaluminophosphates. The self-synthesized catalysts were extensively characterized with XRD, BET, NMR, TEM, and TPD-TGA to determine their structure and acidic properties.
The conversion of 1-hexene over mesoporous samples was much higher than over microporous SAPO and the selectivity to bulkier alkylated products increased. The results of XRD, BET, $^{27}Al/^{29}Si/^{31}P$ MAS NMR, and TPD-TGA of propylamine of the synthesized materials confirm that this improvement is because of decreased diffusion limitation in the catalyst pores.

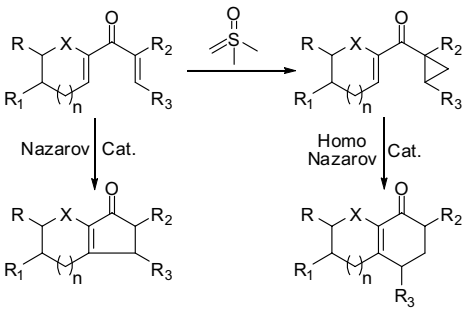
[1] C. Perego, P. Ingallina, *Catal.Today* **2002**, *73*, 3.
[2] M. Choi, H.S. Cho, R. Srivastava, C. Venkatesan, D.-H. Choi, R. Ryoo, *Nature Mater.* **2006**, *5*, 718.

Organic Chemistry **290**

**Catalytic method for a formal homo-Nazarov reaction**

Filippo De Simone, Julien Andres and Jerome Waser*

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




The broad pharmacological activity of heterocylic and carbocyclic compounds is well documented. Consequently, the discovery of new methodologies to form these key compounds is an important endeavor. The well known Nazarov cyclization affords five membered rings from divinyl ketones *via* a pentadienyl cation intermediate.[1]
Starting from the same substrates we have developed a complementary strategy to obtain the related 6 member rings. Thus, Corey-Chaykovsky cyclopropanation was followed by an unprecedented catalytic formal homo-Nazarov cyclisation. This successful reaction sequence further establishes the versatility of divinyl ketones in the context of diversity oriented synthesis of polycyclic heterocycles.

[1] Frontier, A. J. ; Collison, C. *Tetrahedron.* **2005**, *61*, 7577.

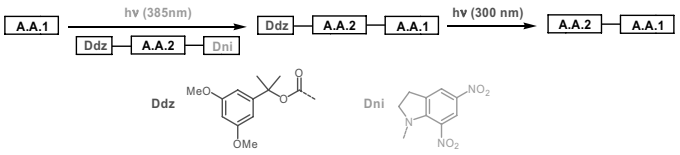
Organic Chemistry **291**

**Photochemical and Sequential Synthesis of a Precursor of Bioactive Pentapeptide OGP (10-14)**

Jean-Luc Débieux, Christian G. Bochet*

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

The osteogenic growth peptide (OGP) is a naturally occurring tetradecapeptide that has attracted considerable clinical interest as bone anabolic agent and hematopoietic stimulator [1]. In vivo studies on animals have demonstrated that the synthetic peptide OGP (10-14), reproducing the OGP C-terminal active portion [H-Tyr-Gly-Phe-Gly-Gly-OH] increases bone formation, trabecular bone density and fracture healing.
Full photochemical synthesis of a precursor of OGP (10-14), Ddz-Tyr($^t$Bu)-Gly-Phe-Gly-Gly-O$^t$Bu, was accomplished sequentially using both photochemical acylation and deprotection [2] [3] [4]. In this strategy, the peptide bond is created by irradiation under mild conditions, using a 5,7-dinitroindoline (Dni) moiety as photoacylating group (sensitive at 385 nm), and the amino group is released by photodeprotection, using α,α-dimethyl-3,5-dimethoxybenzyloxycarbonyl (Ddz) as photolabile protecting group (sensitive at 300 nm). The peptide is prepared in a totally neutral medium, avoiding the use of harsh deprotection reagents such as trifluoroacetic acid or piperidine, and coupling reagents such as DCC, DMAP or HOBt.



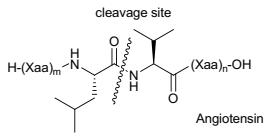

[1] A. Spreafico, *et al. J. Cell. Biochem*. **2006**, *98*, 1007-1020.
[2] C. Helgen, C.G. Bochet, *Synlett* **2001**, 1968-1970.
[3] C. G. Bochet, *et al. Eur. J. Org. Chem*. **2007**, 2073-2077.
[4] C. G. Bochet, *Perkin Trans. I* **2002**, 125-142.

Organic Chemistry **292**

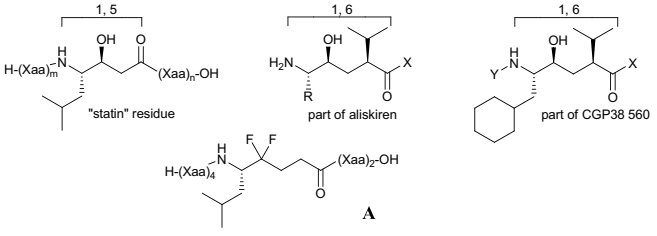
**Preparation of a Peptidase Renin Inhibitor**

Gildas Deniau[a], Michael Limbach[a], Holger Sellner[b], Dieter Seebach[a*]

[a] Laboratorium für Organische Chemie, Department für Chemie und Angewandte Biowissenschaften, ETH-Zürich, CH-8093 Zürich, Schweiz;
[b] Novartis Institute of Biomedical Research, Protease Platform, Novartis Pharma AG, CH-4002 Basel, Switzerland.




Renin is the aspartyl protease that cleaves the substrate Angiotensin (H-Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Asn-Glu-OH). Replacement of the two amino-acid residues Leu and Val at the cleavage site by amino-hydroxy-acid moieties is a strategy for the development of renin-inhibitors (see statin[1], Aliskiren[2] and CGP38 560[3]). We have now prepared a 5-amino-(4,4)-difluoro-carboxylic acid and incorporated it into a heptapeptide **A**. The synthesis of **A** and the results of renin-inhibition tests will be reported.




[1] C. A. Mark *et al.*, *J. Med. Chem*. **1989**, 32, 1652; [2] C. Jensen *et al.*, *Nature Reviews Drug discovery*, **2008**, 7(5), 399; [3] P. Bühlmayer *et al.*, **1988**, 31(9), 1839.

Organic Chemistry **293**

### Synthesis and Use of a Biaryl Template for Protein Epitope Mimetics

David Egloff, Khaled Abou Hadeed, John A. Robinson

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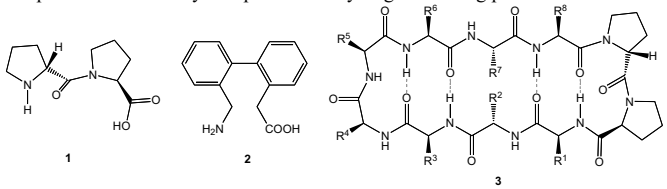
The inhibition of pathophysiological protein-protein interactions represents a promising strategy for treatment of different diseases. β-Hairpin motifs are often found on protein epitope surfaces, that mediate these interactions, and the use of mimetics, emulating their structural and electronical features, is well established in inhibitory peptidomimetic chemistry.

β-Hairpin mimetics consist of a loop sequence that is grafted on a semi-rigid template in order to constrain a stable hairpin structure. The template used in most cases so far is D-Pro-L-Pro **1** since it shows the most successful results in stabilizing hairpin structure [1]. One drawback, however, is the fact that the template should be incorporated at non-hydrogen-bonding **3** but not at hydrogen-bonding positions [2]. Computer models suggest that this problem could be overcome by incorporation of the biaryl template **2** at a hydrogen-bonding position.



The aim of the project was to find an effective synthetic route for the biaryl template **2** and to analyse the structure of β-hairpin mimetics containing this template at a hydrogen-bonding position by NMR.

[1] R. Fasan, R. L. A. Dias, K. Moehle, O. Zerbe, D. Obrecht, P. R. E. Mittl, M. G. Grutter, J. A. Robinson, *ChemBioChem* **2006**, *7*, 515.
[2] J. A. Robinson, *Synlett* **2000**, 429.

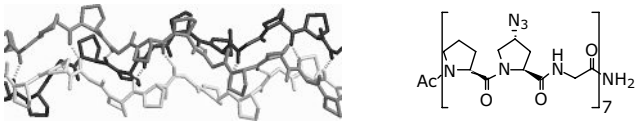
Organic Chemistry **294**

### Functionalizable Collagen Model Peptides

Roman S. Erdmann, Helma Wennemers

Departement Chemie, St. Johans-Ring 19, 4056 Basel, Switzerland.

Collagen is the most abundant protein in mammals. Understanding the tripelhelical collagen structure and factors that have an influence on this structure is important. The collagen triple helix consists of X-Y-Gly reapeating units, with Pro-(4*R*)Hyp-Gly as the most stable one in nature. Raines *et al*. showed by replacing (4*R*)Hyp with (4*R*)Fluoroproline that stereoelectronic effects contribute to the stability of the collagen helix.[1] The Wennemers group showed that the azido group exerts a similarly strong stereoelectronic effect[2], e.g. (4*R*)Azidoproline (Azp) can be used to stabilize the PPII conformation within polyprolines.[3] In this work we incorporated Azp into the collagen triple helix and demonstrate that the triple helix derived from H-(Pro-(4*R*)Azp-Gly)$_7$-OH has a comparable stability as that of H-(Pro-(4*R*)Hyp-Gly)$_7$-OH. The advantage of the azidoproline containing peptide is its functionalizability by 1,3-dipolar cycloadditions.



Triplehelical collagen structure (left) and model peptide (right).

[1] S. K. Holmgren, K. M. Taylor, L. E. Bretscher, R. T. Raines, *Nature* **1998**, *392*, 666-667.
[2] L.-S. Sonntag, S. Schweizer, C. Ochsenfeld, H. Wennemers, *J. Am. Chem. Soc.* **2006**, *128*, 14697-14703.
[3] M. Kümin, L.-S. Sonntag, H. Wennemers, *J. Am. Chem. Soc.* **2007**, *129*, 466-467.

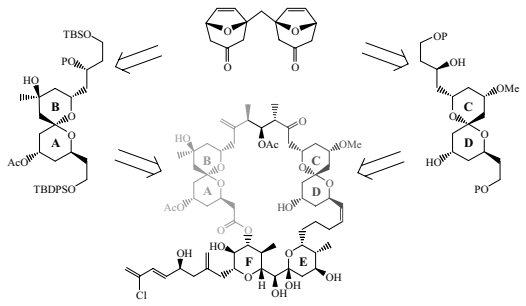
Organic Chemistry **295**

### New desymmetrisation strategies toward the non-iterative synthesis of AB and CD-spiroketals of spongistatin 1

Sylvain Favre, Sandrine Gerber-Lemaire* and Pierre Vogel*

Ecole Polytechnique Fédérale de Lausanne, Batochime, CH-1015 Lausanne

Discovered in 1993, spongistatin 1 is a complex marine macrolide that represents a formidable synthetic challenge and displays extraordinary potent antitumor activities against human cancer cell lines [1]. After the synthesis of the EF fragment [2], we report here an application of Vogel's methodology to the straightforward preparation of advanced precursors of the AB and CD spiroketals.



Spongistatin 1

In particular, taking advantage of an early desymmetrisation, new synthetic pathways have been developed culminating with the synthesis of an advanced precursor of the AB spiroketal [3]. Moreover, a new synthetic approach towards an expeditious access to the CD-spiroketal is now in progress in our research group.

[1] Yeung, K-S.; Paterson, I. *Chem. Rev*. **2005**, *105*, 4237.
[2] Lemaire-Audoire, S.; Vogel, P. *J. Org. Chem*. **2000**, 65, 3346.
[3] Favre, S; Gerber-Lemaire, S; Vogel, P. *Org. Lett.* **2007**, *9*, 5107.

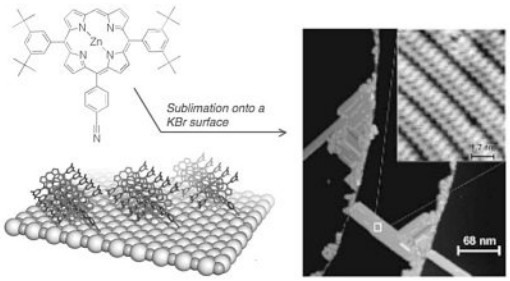
Organic Chemistry **296**

### Nano-Engineering of Molecular Porphyrin Wires on Insulating Surfaces

Leslie-Ann Fendt, Sabine Maier, Lars Zimmerli, Thilo Glatzel, Oliver Pfeiffer, Ernst Meyer, François Diederich*

ETH Zürich, Laboratorium für Organische Chemie, Hönggerberg HCI, Wolfgang-Pauli-Strasse 10, 8093 Zürich (Switzerland)

Well-ordered nanostructures of meso-(4-cyanophenyl)-substituted Zn(II) porphyrin molecules are formed along step edges and along specific directions of KBr(001). Short molecular wires, ring-like structures, long molecular wires (>250 nm), and oriented multiwires (see image) are observed by high-resolution non-contact force microscopy on these insulating surfaces. Small intermolecular distances of 0.5-0.6 nm indicate π−π stacking of the porphyrin rings, which is comparable to natural and biomimetic light harvesting structures.




S. Maier, L.-A. Fendt, Th. Glatzel, O. Pfeiffer, L. Zimmerli, F. Diederich, E. Meyer, *small*, in press.

Organic Chemistry **297**

## Double Chain Elongation and Desymmetrization for Synthesis of Polypropionate Fragments

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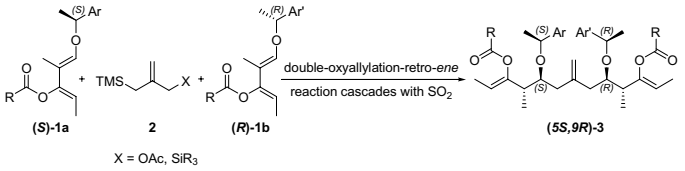
The most commonly used methods for polypropionate fragment synthesis are aldol reactions or allylation of aldehydes. Our group developed another route to this family of compounds involving a *hetero*-Diels-Alder reaction of sulphur dioxide to a 1,3-dioxy-1,3-diene (**1**) in the presence of a Lewis acid promoter, generating a zwitterionic species, which can react with carbon nucleophiles such as enoxy- or allylsilanes (**2**). After retro-*ene* reaction $SO_2$ is released and polypropionate fragments (**3**) are obtained.[1]
In this presentation we shall demonstrate that we are able to make a bi-directional chain elongation by two successive oxyallylation reactions. The so-obtained *pseudo*-$C_2$- or -σ-symmetrical adducts are easily desymmetrized by selective deprotection.



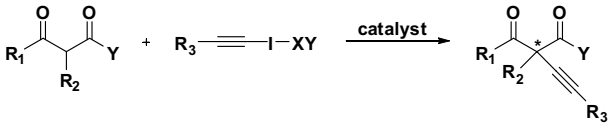

[1] a) M. Turks, F. Fonquerne, P. Vogel, *Org. Lett.* **2004**, *6* (6), 1053; b) M. Turks, X. Huang, P. Vogel, *Chem. Eur. J.* **2005**, *11*, 465; c) L. C. Bouchez, M. Turks, S. R. Dubakka, F. Fonquerne, C. Craita, S. Laclef, P. Vogel, Tetrahedron **2005**, *61* (48), 11473; and references therein.

Organic Chemistry **298**

## Catalytic Alkynylation of Enolates

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

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




Biochemistry and the pharmaceutical industry urgently require new chemical structures of increasing complexity which selectively interact with biomolecules. 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 the alkynylation of *β*- ketoester enolates with alkynyliodonium salts.[2] There is only one example of asymmetric alkylynation of enolates using propionate derivatives as electrophiles.[3]

We report the first direct catalytic alkylynation with hypervalent iodine reagents under phase-transfer conditions. Furthermore, asymmetric induction was observed using cinchona derived catalysts.

[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.
[3] Poulsen, T. B.; Bernardi, L.; Aleman. J.; Ovegaard, J.; Jørgensen, K. A. *J. Am. Chem. Soc*. **2007**, *129*, 441.

Organic Chemistry **299**

## Introducing Chirality and Vertical Vectors to Supramolecular Assemblies on Surfaces

Petra Fesser, Michael Schär, François Diederich

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

Serpil Boz, Mihaela Enache, Thomas Jung
Department of Physics, University of Basel, 4056 Basel, Switzerland

Since the “top-down” approach for the miniaturization of devices is about to reach certain limits, the “bottom-up” approach by molecular self-assembly on metal substrates is a promising alternative. Over the last years, several self-assembled porous networks have been created and imaged by STM (Scanning Tunneling Microscopy) under UHV conditions. However, no reports of enantioselective recognition of a chiral guest inside these pores exist - even though an increasing number of self-assembled porous networks featuring homochiral domains have been presented.

Chiral helical molecules are promising building blocks for introducing chiral elements into porous networks, which could lead to enantioselective recognition of chiral guests, or steering of the rotation sense of a trapped chiral molecule (rotary switch).

Organic Chemistry **300**

## Screening of Chiral Organocatalysts by ESI-MS

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

Electrospray ionisation mass spectrometry (ESI-MS) has become a powerful tool for investigating the mechanisms of many reactions and has also found use in high-throughput screening. In our group, ESI-MS was applied to monitor positively charged intermediates in a palladium-catalyzed allylic substitution and copper- and organocatalyzed Diels-Alder reaction. Using *quasienantiomeric* mass-labelled substrates, a rapid screening protocol for chiral catalysts was developed.

Here we report a successful application of this method to the organocatalytic Michael addition of malonates to unsaturated aldehydes. Based on the principle of microscopic reversibility, it is possible to determine the enantioselectivity of organocatalytic Michael addition by screening the intermediates of the *retro*-Michael addition. Several catalysts with excellent selectivity have been identified and applied in the preparative reaction. This procedure was extended to multi-catalyst screening. Up to 6 catalysts have been synthesised in one pot and the crude mixture was subjected to the mass spectrometric screening.

*Financial support by the Swiss National Science Foundation is gratefully acknowledged*.

[1] C. Markert, A. Pfaltz, *Angew. Chem. Int. Ed.* **2004**, *43*, 2497-2500; C. Müller, A. Pfaltz, *Angew. Chem. Int. Ed.* **2008**, *47*, 3363-3366; A. Teichert, A. Pfaltz, *Angew. Chem. Int. Ed.* **2008**, *47*, 3360-3362.
[2] S. Brandau, A. Landa, J. Franzèn, M. Marigo, K.A. Jørgensen, *Angew. Chem. Int. Ed.* **2006,** *45*, 4305-4309.

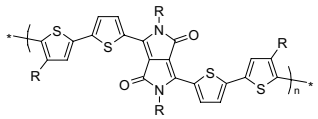
Organic Chemistry **301**

**DPP-based polymers**
**A new class of photoactive polymer material**

Mathieu Turbiez[1], Hans-Jörg Kirner[1], Frank Bienewald[1], Jean-Charles Flores[1], Lukas Bürgi[2], Reto Pfeiffer[2], Martijn Wienk[3], René Janssen[3], Harri Kopola[4], Henrik Sandberg[4]

[1)] Ciba Inc., Group Research, Basel, Switzerland
[2)] CSEM, Basel, Switzerland
[3)] Eindhoven University of Technology, Eindhoven, The Netherlands
[4)] VTT Electronics, Espoo, Finland

Diketopyrolopyrole (DPP) based polymers is a new class of compound exhibiting unique properties.



It shows clear ambipolar transport of charges with a very high electron and hole mobility in the range of $10^{-1}$ $cm^2$/Vs. Following from this, Organic Light Emitting Transistors has been made. For appropriate voltages, holes from one electrode and electrons from the other can be injected at the same time and recombine radiatively. It's also showing a high absorption in the visible range which makes it a good candidate for solar application. This absorption goes even to the Near IR and can be useful for Infrared Photodetectors.
In this poster, latest achievements and future plans on these different applications will be presented.

Organic Chemistry **302**

**On-bead cyclization in a combinatorial library of 15,625 octapeptides using TagsFree encoding method**

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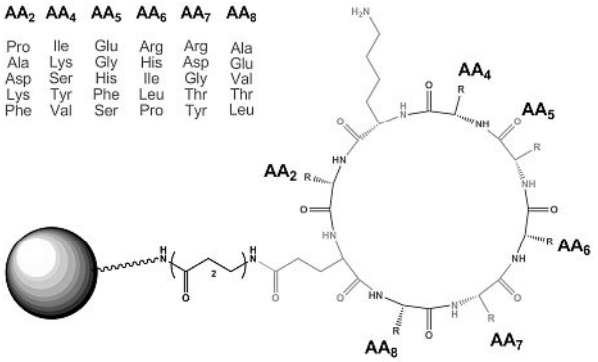
Dept. of Chemistry and Biochemistry, University of Berne, Freiestrasse 3 3012 Berne, Switzerland

Herein we report a self-encoding one-bead one-compound library of 15625 cyclic octapeptides[1] using a combinatorial split and mix approach. A new encoding method – TagsFree[2]– based on amino acid analysis and computational methods, was applied to identify the sequences. The library was used to study the sequence dependence of the on-bead cyclization propensity[3]. We are currently working in the application if this technology in the field of antibiotics.




[1] Dummy P., *Org. Biomol. Chem*., **2006**, *4*, 2628.
[2] Kofoed, J.; Reymond, J.-L. *J. Comb. Chem.* **2007**, *9*, 1046.
[3] Fluxa, V.; Reymond, J.-L., *Bioorg. Med. Chem*. **2008**, *Available online 30 January 2008*

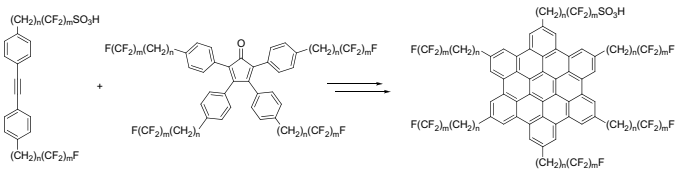
Organic Chemistry **303**

**Synthesis of new perfluoralkylated HBC derivatives functionalized with a sulfonic acid**

Nicolas Fragnière, Titus A. Jenny*

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

Polycondensed aromatic hydrocarbons (PHA) are well-known to self-organize by π-π stacking to form highly ordered monomolecular columns. The morphology of the resulting materials can be controlled by adjusting the parameters n, m and x (number of side chains) of the perfluoralkylated side chains [1]. This prompted us to explore, whether the introduction of a sulfonic acid functionality on one of the six side chains would be tolerated by the supramolecular system giving eventually access to a new type of supramolecular polyacids.




The synthesis of **3** involves a convergent strategy, which uses steps in analogy to reactions already developed in the group [2].

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

Organic Chemistry **304**

**Property Tuning of Charge-Transfer Chromophores: Modulation of the Spacer**

Brian Frank, Dr. Filip Bures and Prof. Dr. François Diederich

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

Highly conjugated, carbon-rich organic molecules featuring tunable structural and optoelectronic properties have been recognized as promising candidates for use in next-generation electronic and optoelectronic devices. Especially molecular and polymeric donor–acceptor (D–A) chromophores have attracted much attention due to their highly polarized π-conjugated structures, resulting in efficient second- and third-order nonlinear optical (NLO) effects.
Our laboratory reported strong intramolecular charge-transfer (CT) interactions and high third-order optical nonlinearities for small push-pull chromophores **1** - **6** (Figure 1). Useful structure-activity relationships with predictive power were established, highlighting the dependence of third-order optical nonlinearity from the energy of the longest-wavelength CT transition and the extension of the linear donor-acceptor conjugation pathways.

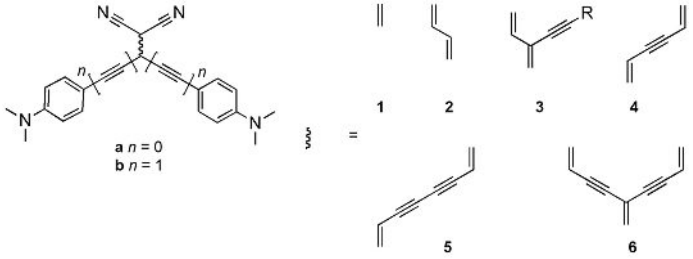



Figure 1. Expanded DMA-substituted cyanoethynylethenes **1** - **6** with different spacers between donor and acceptor moieties.

Based on these results new chromophores have been designed in order to further investigate the effects of different spacers between donor and acceptor functions.

Organic Chemistry **305**

## Molecular Gears in Parallel: Geared Triptycene Rotators on Bibenzimidazole-Based Stators

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

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

For decades, chemists have been fascinated by the concept and utility of molecular rotors.[1] Geared propeller systems have received particular attention, as the correlated motion of the rotators offers a nanoscale analog to bevel gears, which are ubiquitous in macroscale devices and machines. Triptycene-based rotators were the first to be implemented into truly geared molecular rotors[2] and have been commonly used rotators in molecular devices.[1]

We have recently synthesized and studied the structural properties of a series of 1,1'-bridged 4,4'-diaryl-2,2-bibenzimidazole.[3] The fused 6- and 5-membered rings of benzimidazole offer a perfect 90º angle between substituents at the 4- and 2-positions. Thus, 1,1'-bridged derivatives of 2,2'-bibenzimidazole contain two of these 90º angles, placing substituents at the 4,4'-positions ca. 8 Å apart and in parallel.

Synthesis of 1,1'-bridged 4,4'-bis(triptycen-9-ylethynyl)-BBI molecular gears has been accomplished *via* palladium-catalyzed cross-coupling of 9-ethynyltriptycene to 1,1'-bridged 4,4'-dibromo-BBI. Computational methods have also been applied to these geared systems. Detailed analysis of these results will be presented.

[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.; Sullivan, A. A.; Linden, A.; Yasui, Y.; Siegel, J. S.; *Manuscript in Preparation*.

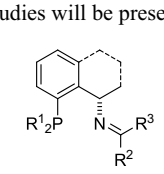
Organic Chemistry **306**

## Synthesis of new modular P,N-Ligands for iridium-catalyzed asymmetric hydrogenation

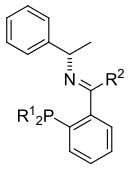
Adnan Ganic, Matthias Maywald, Andreas Pfaltz*

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

Iridium-catalyzed asymmetric hydrogenation is a simple and powerful method to convert unfunctionalized olefins into chiral compounds. Several research groups have focused on the development of chiral P,N-ligands,[1a-b] however no ligand has universal substrate scope. Therefore, we developed an easily accessible, highly modular ligand system **L1**. The structure of **L1** is similar to that of **L2**, which was already synthesized by *Brunner*,[3] but has never been applied in iridium-catalyzed hydrogenation. Ligand **L1** was successfully synthesized from commercially available chiral amines through a directed *ortho* lithiation and subsequent condensation. Only ligands with the imine moiety derived from aliphatic aldehydes could be converted to the corresponding iridium complex. Ligands containing aryl groups on the imine moiety undergo cyclometalation under complexation conditions.
The synthesis of iridium complexes with these ligands and the results of hydrogenation studies will be presented.




**L1**




**L2**

[1] a) S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res.* **2007**, *40*, 1402; b) K. Källlström, I. Munslow, P. G. Andersson, *Chem. Eur. J.* **2006**, *12*, 3194; c) X. H. Cui, K. Burgess, *Chem. Rev.* **2005**, *105*, 3272.
[2] H. Brunner, A. F. Rahman, *Chem. Ber.* **1984**, *117*, 710.

Organic Chemistry **307**

## Atroposelective Synthesis of Enantiomerically Pure Bissulfoxide Moieties and Their use as Ligands in Latetransition Metal Chemistry

Michele Gatti; Ronaldo Mariz; Xinjun Luan; Emma Drinkel; Tony Linden; Reto Dorta.

Organic Chemistry Department, University of Zurich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland.

New enantiomerically pure bissulfoxide moieties with atropisomeric backbones have been successfully synthesized by the addition of the corresponding aryllithium compounds to optically pure sulfinates.[1,2,3] Depending on the sulfinates and the organolithium precursors used, moderate to excellent degrees of atroposelection were observed during their synthesis.
The synthetic route allows for good tuning of the electronic properties on the sulfur, offering easy modifications on both the sulfinate and the backbone sides of the ligand framework.
Complexation studies of the chiral ligands with late transition metals will be presented and an in depth study on their electronic behavior compares and classifies this ligand family.
Finally, we will report first results on the use of these chiral pre-catalysts in asymmetric catalytic transformations.

1) Han, Z.; Krishnamurthy, D.; Grover, D.; Fang, Q. K.; Su, X.; Wilkinson, H. S.; Lu, Z.-H.; Magiera, D.; Senanayake, C. H. Tetrahedron 2005, 61, 6386.
2) Solladie, G.; Hutt, J.; Girardin, A., Synthesis 1987, 67, 173.
3) Fernandez, I.; Khiar, N.; Llera, J. M.; Alcudia, F., J. Org. Chem. 1992, 57, 6789-6796

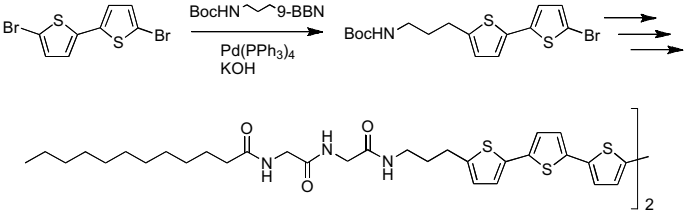
Organic Chemistry **308**

## Synthesis of a Peptide Substituted Sexithiophene and Study of an *B*-Alkyl Suzuki-Miyaura Cross-Coupling

Jan Gebers, Holger Frauenrath*

ETH Zürich, Department of Materials, Wolfgang-Pauli-Str. 10, HCI H520, 8093 Zürich, Switzerland

Oligothiophenes are promising organic materials for the use in electronic devices such as field effect transistors.[1] As the electric properties of oligothiophenes highly depend on their nanoscopic organization, we synthesized an oligopeptide substituted sexithiophene which is envisioned to attain highly ordered phases due to hydrogen bonding between the peptide moieties. A convergent synthesis for this novel type of peptide-substituted sexithiophenes has been developed. As a key intermediate 5-bromo-5'-(*N*-Boc-3-aminopropyl)-2,2'-bithiophene was synthesized via a *B*-alkyl *Suzuki-Miyaura* cross-coupling. The reaction suffered from sideproduct formation, therefore, different reaction parameters and the catalytic pathway were investigated.







[1] S. Allard, M. Forster, B. Souharce, H. Thiem, U. Scherf, *Angew. Chem.* **2008**, *120*, 2.

Organic Chemistry **309**

### Exploring the Substrate Specificity of OxyB, a P450 Enzyme Involved in Vancomycin Biosynthesis

Nina Geib, Katharina Woithe, Odile Meyer, Tanja Wörtz, Katja Zerbe, John A. Robinson

University of Zürich, Winterthurerstrasse 190, 8057 Zürich, Switzerland

OxyB is a cytochrome P450 enzyme that catalyzes the first oxidative phenol coupling reaction during vancomycin biosynthesis[2]. The preferred substrate is a linear peptide linked to a peptide carrier protein (PCP) domain of the glycopeptide antibiotic non-ribosomal peptide synthetase. Previous studies have shown that OxyB can efficiently oxidize a model hexapeptide-PCP conjugate[3,4] into a macrocyclic product by phenolic coupling of the aromatic rings in residues-4 and -6.

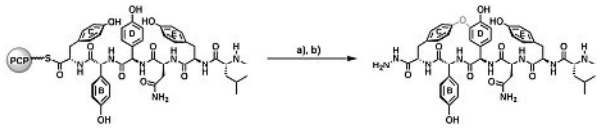



**Fig. 1.** OxyB catalyzed conversion of the model PCP-bound hexapeptide into monocyclic product. a) OxyB, spinach ferredoxin, *E. coli* flavodoxin reductase, NADPH, $O_2$ b) $NH_2NH_2$.

In this work, the substrate specificity of OxyB has been explored using a series of N-terminally truncated peptides. Deletion of one or three residues from the N-terminus afforded a penta- and a tripeptide that were also efficiently transformed into the corresponding macrocyclic cross-linked product by OxyB. The tripeptide, representing the core of the macrocycle in vancomycin created by OxyB, is thus sufficient, as a thioester with the PCP domain, for phenol coupling to occur.

[1] Zerbe, K. et al., *Angew. Chem. Int. Ed.* **2004**, *43*, 6709
[2] Woithe, K. et al., *J. Am. Chem. Soc.* **2007**, *129*, 6887
[3] Geib, N. et al., *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3081

Organic Chemistry **310**

### Towards Automated Reaction Screening and Synthesis Using Continuous-Flow Systems

Karolin Geyer and Peter H. Seeberger, Laboratory for Organic Chemistry
Swiss Federal Institute of Technology (ETH) Zurich
Wolfgang-Pauli-Strasse 10, 8093 Zurich (Switzerland)

Microreactors gain increasing interest in the scientific community due to their wide-ranging applications in many different areas of chemistry.[1] Miniaturizing reactions offers many advantages for synthetic chemists such as high-throughput scanning of reaction conditions, precise control of reaction variables, the use of small quantities of reagents, increased safety parameters, and ready scale-up of synthetic procedures. Microreactor technology is mostly investigated and applied in pharmaceutical and fine chemical industries for production processes,[2] and for proof-of-principle studies in analytical scale.[3]
Silicon-glass microreactors (Figure 1) were chosen to perform chemical transformations since oxidized silicon and borosilicate deliver properties similar to the ones of glass flasks, which render the reactors comfortable to handle for synthetic chemists.

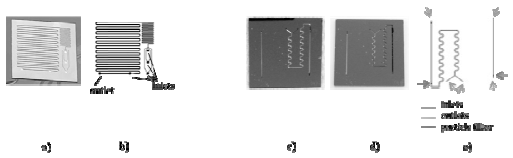


Figure 1: Silicon-glass microreactor. a) Photograph of a 78 µL device.[3c] b) Scheme of the 78 µL device. c) Photograph of a packed bed reactor, not filled. d) Photograph of a packed bed reactor, filled. e) Scheme of the packed bed reactor.

Additionally, an automated microreactor system to perform chemical reactions using both microreactor designs was developed. The system consists of independent pumps, pressure sensors, a temperature-controlled microreactor chipholder and a fraction collector (Figure 2). This setup allows for the performance of manifold optimization reactions while varying reaction time, reaction temperature, and the reagent proportions whereas scale-up of the established synthetic procedure can be achieved by scale-out.

Organic Chemistry **311**

### Towards the synthesis of pyrrolidino pseudouridine

Michael Gisler, Christian J. Leumann

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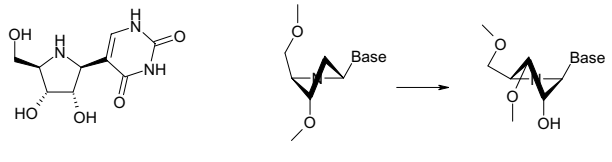
Pyrrolidino nucleotides as third strand constituents are expected to stabilize DNA triplexes because of salt-bridge formation between target DNA duplex phosphate residues and the pyrrolidino ring nitrogens of the third strand, in addition to the base-base contacts (dual recognition). Stability measurements of the pyrrolidino 2'-deoxy-pseudoisocytidine[1] and the pyrrolidino 2'-deoxy-pseudouridine[2] showed that the former modification lead to a stabilization, whereas the latter destabilized the triplex. One possible explanation is that the conformation of the pyrrolidino 2'-deoxy-pseudouridine (2'-endo) is generally unfavorable for dual recognition. We therefore decided to synthesize pyrrolidino pseudouridine for which the 3'-endo conformation can be expected to be energetically more favorable. We present the synthesis of pyrrolidino pseudouridine as well as its incorporation into triplex forming oligonucleotides.




pyrrolidino pseudouridine 2'-endo 3'-endo

[1] Mayer, A.; Häberli, A.; Leumann, Ch. J., *Org. Biomol. Chem.*, **2005**, *3*, 1653.
[2] Häberli, A.; Leumann, Ch. J., *Org. Lett.*, **2002**, *4*, 3275.

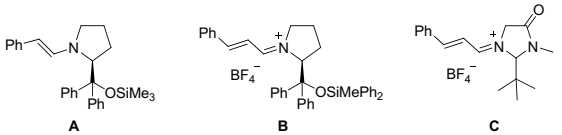
Organic Chemistry **312**

### Isolation and X-Ray Structures of Intermediates in Organocatalysis

Uroš Grošelj, D. Michael Badine, W. Bernd Schweizer, and Dieter Seebach*

Laboratorium für Organische Chemie, Department für Chemie und Angewandte Biowissenschaft, ETH-Zürich, HCI-Hönggerberg, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich, Schweiz

The X-ray crystal structures **A**-**C** have been determined. The enamine **A** is the type of reactive intermediate involved in nucleophilic additions of aldehydes (or ketones) to various electrophiles. Iminium ions such as those in structures **B** and **C** are the generally accepted reactive intermediates in *Michael* additions catalyzed by diarylprolinolethers or by BMI.[1-4] The new structures will be compared with those of other prolinol derivatives and with *N*-acyl-pyrrolidines and imidazolidinones. The significance of these structures for the stereoselectivities of organocatalytic reactions will be discussed.



**A** **B** **C**

[1] For general reviews see: (a) C. F. Barbas *III*, *Angew. Chem*. **2008**, *120*, 44; (b) A. Berkessel, H. Gröger, 'Asymmetric Organocatalysis: From Biomimetics Concepts to Applications in Asymmetric Synthesis', Wiley-VCH, Weinheim, 2005.
[2] Review on diarylprolinolethers: C. Palomo, A. Mielgo, *Angew. Chem*. **2006**, *118*, 8042.
[3] Preparation of (*R*)- and (*S*)-BMI: R. Fitzi, D. Seebach, *Angew. Chem*. **1986**, *98*, 363.
[4] Papers covering the use of BMI and other imidazolidinones as catalysts in *Michael* additions and in radical coupling reactions: (a) G. Lelais, D. W. C. MacMillan, 'History and Perspectives of Chiral Organic Catalysts' in 'New Frontiers in Asymmetric Catalysis', John Wiley & Sons, New Jersey, 2007, pp 313-358; (b) T. D. Beeson, A. Mastracchio, J.-B. Hong, K. Ashton, D. W. C. MacMillan, *Science* **2007**, *316*, 582; (c) H.-Y. Jang, J.-B. Hong, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2007**, *129*, 7004; (d) M. P. Sibi, M. Hasegawa, *J. Am. Chem. Soc*. **2007**, *129*, 4142.

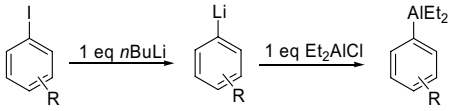
Organic Chemistry **313**

## Creation of Quaternary Aryl Substituted Asymmetric Centers through Conjugate Addition

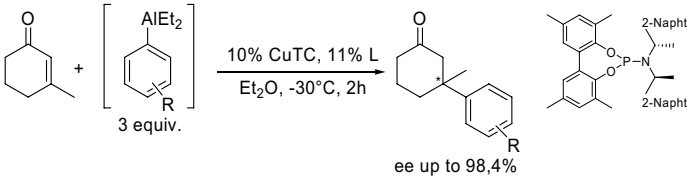
C. Hawner, A. Alexakis*

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

A new reaction sequence has been developed to generate aryl alanes from aryl iodides:




These aryl alanes were subsequently used in the copper catalyzed asymmetric conjugate addition reaction to 3-methyl-2-cyclohexen-1-one.




Both, electron-donating and electron-withdrawing groups were tested and full conversion and very good ee were obtained in all cases.

Organic Chemistry **314**

## Applications of CD Spectroscopy in the Nano-Biosciences: A Look Beyond Structural Studies

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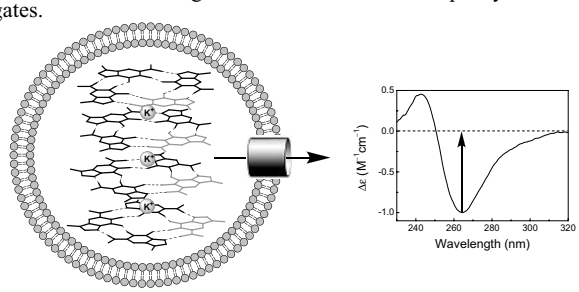
University of Geneva, Department of Organic Chemistry
Geneva, Switzerland

Circular dichroism (CD) spectroscopy is commonly used for structural studies, e.g. for the determination of stereoisomers or the secondary structure of peptides and proteins.[1] However, other applications of CD spectroscopy, such as functional studies and sensing applications are scarce. Herein, we describe our efforts to broaden the scope of CD spectroscopy: First, we introduce a method to determine the activity of ion channels, membrane pores and cell-penetrating peptides, which is based on the CD detection of self-assembled G quartets[2] and second, we demonstrate the use of exciton-coupled CD (ECCD) to selectively detect polyphenols in green tea by multivalent binding with achiral anthracene-phenylboronic acid conjugates.




[1] K. Nakanishi, N. Berova, R. W. Woody, *Circular dichroism – principles and applications*, Wiley VCH, Weinheim, 2nd Ed. **2000**.
[2] A. Hennig, S. Matile, *Chirality* **2008**, DOI: 10.1002/chir.20526.

Organic Chemistry **315**

## The Negishi Reaction in Carbon *sp-sp* Cross-Couplings

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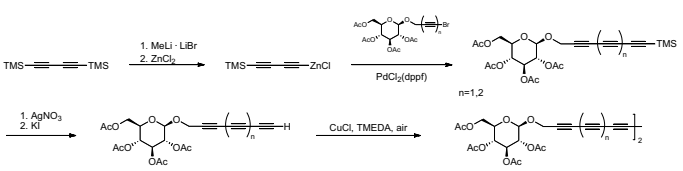
ETH Zürich, Department of Materials, Wolfgang-Pauli-Str. 10, HCI H 520, 8093 Zürich, Switzerland

Nanostructured carbon materials offer intriguing perspectives for emerging technologies such as hydrogen or lithium storage. Our approach towards the preparation of such materials relies on the synthesis, self-assembly, and subsequent carbonization of amphiphilic, carbohydrate-substituted oligo(ethynylene)s. The crucial step in our synthesis is a carbon *sp-sp* hetero-coupling which is a challenging task in organic synthesis. Commonly used protocols such as the Sonogashira reaction suffer from side product formation. Above all, the homo-coupling reaction is a major issue which we also observed in our attempted synthesis of glucose-substituted oligo(ethynylene)s. Subsequent investigations on the Negishi protocol as an alternative revealed its potential in these transformations. Particularly convenient was the fact that the required zinc alkynyl derivative was obtained *in situ* from the stable bis(trimethylsilyl)butadiyne [1]. This rendered the Negishi protocol a useful tool in the synthesis of conjugated acetylene chains up to the octayne.




[1] Holmes, A.; Jones, G. *Tetrahedron Lett.* **1980**, *21*, 3111.

Organic Chemistry **316**

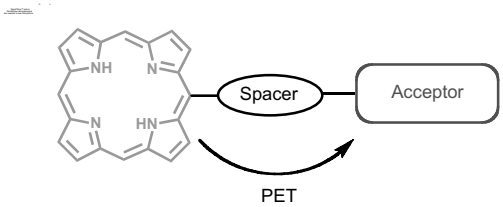
## Multi-cyanobutadienes as Strong Electron Acceptors for Photovoltaic Applications.

Kara Howes, Philippe Reutenauer, José Lorenzo Alonso Gómez and François Diederich.

Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Hönggerberg, CH-8093 Zürich, Switzerland.

The idea of harnessing the Sun's natural energy to provide an ecological power source is extremely attractive. Indeed, the replication of the photosynthetic process has been extensively studied, the aim being to achieve Photoinduced Electron Transfer (PET), to ensure the formation of charge-separated species.

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




[1] T. Michinobu, C. Boudon, J-P. Gisselbrecht, P. Seiler, B. Frank, N. N. P. Moonen, M. Gross, F. Diederich. *Chem. Eur. J.* **2006**, *12*, 1889.
[2] P. Reutenauer, M. Kivala, P. D. Jarowski, C. Boudon, J-P. Gisselbrecht, M. Gross, F. Diederich. *Chem. Commun.* **2007**,4898.

Organic Chemistry **317**

### Use of Aryl Zinc Reagents in Asymmetric Substitution of Allylic Carbonates Catalyzed by Iridium.

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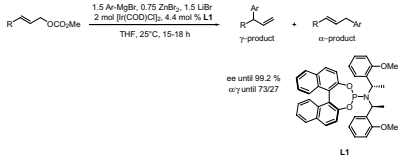
Université de Genève, Département de chimie organique, 30 quai Ernest Ansermet, 1211 Genève 4, Switzerland

Iridium catalyzed asymmetric allylic substitution is becoming a very usefull methodology to obtain different adduct with a γ-selectivity. Associated with phosphoramidite ligands, this process leads to very high enantioselectivity and yield[1]. The most important examples were performed with stabilized nucleophiles (malonates[2]) or heteronucleophiles (amines[3], alcohols[4], etc…). We describe herein the first use of hard nucleophiles (aryl zinc reagents) in this reaction[5]. We chose to add this nucleophile to cinnamylcarbonates and derivatives, which are classical substrates in allylic substitution to challenge a new process. The nucleophiles were formed in situ by transmetallation from arylmagnesiumbromide reagents to zinc bromide in order to form the diarylzinc species. Lithium bromide was added to this solution of nucleophile in order to break possible aggregates[3a]. Addition of these nucleophiles on cinnamylcarbonate, at room temperature in THF catalyzed by $[Ir(COD)Cl]_2$ and **L1**, gives a good enantioselectivity (up to 99.2 % ee) but a moderate regioselectivity (up to 73/27 in favour of the γ-product) after 18 h.




It is interesting to note that both aryl groups of the zinc reagent are reactive because we need only 0.75 eq of diarylzinc species to complete the reaction. This methodology could be applied to obtain a key intermediate in the synthesis of sertraline.

[1] First association: Bartels, B.; Helmchen, G. *Chem. Comm* **1999**, 741.
[2] (a) Bartels, B.; Garcia-Yebra, C.; Helmchen, G. *Eur. J. Chem. Soc* **2003**, 1097 (b) Alexakis, A.; Polet, D. *Org. Lett* **2004**, *6*, 3529.
[3] (a) Polet, D.; Alexakis, A.; Tissot-Croset, K.; Corminboeuf, C.; Ditrich, K. Chem. Eur. J 2006, 12, 3596 (b) Leitner, A.; Shekhar, S.; Pouy, M. J.; Hartwig, J. F. J. Am. Chem. Soc 2005, 127, 15506

Organic Chemistry **318**

### Effects of Terminal Functional Groups on the Stability of the Polyproline II Structure

Michael Kümin and Helma Wennemers*

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

The left-handed polyproline II helix (PPII) plays an important role in many biological processes, for example recognition events at protein-protein interfaces. Factors like solvation [1], steric interactions between the pyrrolidine rings [2] and dipole-dipole interactions within the backbone [2,3] are known to influence the stability of the PPII helix.
This poster presents investigations into the influence of functional groups at the C- and N-termini on the stability of the PPII helix. Proline 12-mers with free or capped end-groups were synthesized and their conformation was studied by circular dichroism spectroscopy. The different tendencies of these peptides to switch between the two possible helical conformations of oligoprolines were analysed and correlated to calculated dipole moments.

PPII (favoured in water) PPI (favoured in 1-PrOH)

As in α-helical structures the macrodipole was found to influence the stability of the helices.

1] A. Rath, A. R. Davidson, C. M. Deber, *Biopolymers (Pept. Sci.)* **2005**, *80*, 179-185.
2] J.-C. Horng, R. T. Raines, *Protein Sci*. **2006**, *15*, 74-83.
3] M. Kümin, L.-S. Sonntag, H. Wennemers, *J. Am. Chem. Soc.* **2007**, *129*, 566-467.

Organic Chemistry **319**

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

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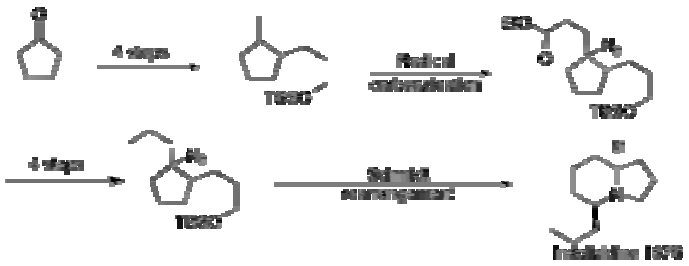
Department of Chemistry and Biochemistry, University of Berne, Freiestrasse 3, 3012 Berne (Switzerland)

Indolizidine167B wasisolatedfrom skin of poison frogsbelonging to the dendrobatidae family.[1] The total synthesis of Indolizidine 167B has been achieved in 10 steps (> 20% overall yield) from cyclopentanone.



The quaternary carbon center has been introduced by a radical carboazidation reaction.[2] The azabicyclic core has been constructed*via* a highly diastereoselective intramolecular Schmidt rearrangementinvolvingactivatedprimary alcohol.[3]

[1] Review: Daly, J.W. *J. Nat. Prod*. **1998**, 61, 162
[2] Renaud, P.; Olliver, C.; Panchaud, P. *Angew. Chem. Int. Ed*. **2002**, 41, 3460.
[3] Review: E. Nyfeler, P. Renaud, *Chimia***2006**, *60*, 276.

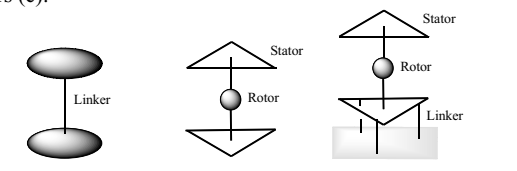
Organic Chemistry **320**

### Towards the Synthesis of Surface-Bound Azimuthal Rotors from Trioxatricornan-Based Free Rotors

Fitore Kasumaj; Jay S. Siegel

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

Trioxatricornan[1] is a rigid, tripod-shaped molecule with a large surface area and a height of *ca.* 1.5Å.[2-4] The vertex is an $sp^3$ tertiary carbon center that can be substituted via $S_N1$ reactions. Trioxatricornan-based sandwich compounds were achieved via subsequent coupling reactions between alkylated derivatives, and the syntheses and structural properties of select derivatives are reported (a). Of these, structures which contain aromatic groups within the linker unit (b) are free rotors whose rotational barriers can be monitored and extracted by $^1$H-NMR. Current studies involve modification of a trioxatricornan stator unit to the extent that it can be attached to gold or copper surfaces via sulfide or cyanide bridges, respectively, to achieve azimuthal rigid rotors (c).[5]




(a) Sandwich compound (b) free rotor (c) surface bound azimuthal rotor

[1] Martin J.C.; Smith, R.G. *J. Am. Chem. Soc.* **1964**, *86*, 2252.
[2] Lofthagen, M; Dissertation, **1990** Universtity of San Diego, USA
[3] *(a)* Lofthagen, M.; VernonClark, R.; Baldrige, K.K.; Siegel, J.S. *J. Org. Chem.* **1992**, *57*, 61. *(b)* Lofthagen, M.; Siegel, J.S.; Hackett, M. *Tetrahedron*, **1995**, *51*, 6195.
[5] Kottas, G.S.; Clarke, L.I.; Horinek, D.; Michl, J. *Chem. Rev*., **2005**, *105*, 1281.

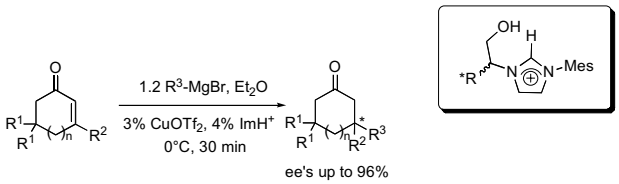
Organic Chemistry **321**

## Copper catalyzed asymmetric conjugate addition of Grignards to trisubstituted enones. Formation of all carbon quaternary chiral centers

S. Kehrli, A. Alexakis*

Université de Genève, Département de Chimie Organique, 30, quai Ernest Ansermet CH-1211 Genève 4, Switzerland.

The use of the asymmetric conjugate addition to create enantioenriched allcarbon quaternary centers have been recently disclosed.[1] After using $R_3Al$ reagents [2], our group tried Grignard reagents on the Cu-catalyzed asymetric conjugate addition to trisubstituted cyclic enones.
We obtain enantioenriched all carbon quaternary centers with up to 96% ee. The chiral ligand, a diaminocarbene (NHC), is directly generated in-situ. The combination of Grignard reagents and NHC is unprecedented in conjugate addition.




We will report here, our last result on this area and especially on different substrates.

[1] For reviews on asymmetric conjugate additions see : a) Alexakis A., Benhaim C. ; *Eur. J. Org. Chem.* **2002**, 3221-3236. b) Krause, N.; Hoffmann-Röder, A. ; *Synthesis* **2001**, 171. c) Hayashi T. ; *Acc. Chem. Res.* **2000**, *33*, 354-362.
[2] D'Augustin, M.; Palais, L.; Alexakis, A. ; *Angew. Chem. Int. Ed.* **2005**, *44*, 1376-1378.
[3] Martin, D. ; Kehrli, S. ; d'Augustin, M. ; Alexakis, A. ; Clavier, H. ; Mauduit, M. ; *J. Amer. Chem. Soc*. ; **2006**, *128*, 8416-8417.

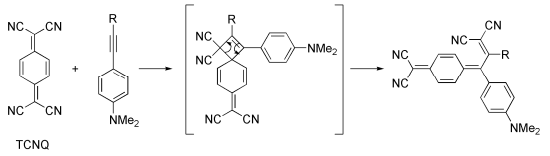
Organic Chemistry **322**

## New Transformations of 7,7,8,8-Tetracyanoquinodimethane (TCNQ): Charge-Transfer Chromophores by [2+2] Cycloaddition with Alkynes

Milan Kivala,[a] Corinne Boudon,[b] Jean-Paul Gisselbrecht,[b] Paul Seiler,[a] Maurice Gross,[b] François Diederich*[a]

[a] Laboratorium für Organische Chemie der ETH Zürich, ETH-Hönggerberg, CH-8093 Zürich, Switzerland
[b] Laboratoire d'Electrochimie et de Chimie Physique du Corps Solide, LC3–UMR 7177, CNRS, Université Louis Pasteur, F-67000, France

Strong electron acceptor 7,7,8,8-tetracyanoquinodimethane (TCNQ) has already been reported in the early 1960s. However, while the reactivity of TCNQ has been thoroughly explored, some of the structural features of this molecule have obviously been ignored.




Here, we describe a novel, completely regioselective thermal [2+2] cycloaddition of TCNQ with *N*,*N*-dialkylanilino-substituted alkynes, followed by ring opening of the initially formed cyclobutene derivative to yield a new type of non-planar chromophores featuring intense low-energy intramolecular charge-transfer bands and appealing redox properties [1][2]. First attempts to prepare charge-transfer complexes between these powerful acceptors and various electron donors, such as ferrocene derivatives, were successful.

[1] M. Kivala, C. Boudon, J.-P. Gisselbrecht, P. Seiler, M. Gross, F. Diederich, *Chem. Commun.* **2007**, 4731.
[2] P. Reutenauer, M. Kivala, P. D. Jarowski, C. Boudon, J.-P. Gisselbrecht, M. Gross, F. Diederich, *Chem. Commun.* **2007**, 4898.

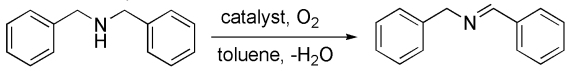
Organic Chemistry **323**

## Nature of the Active Species in the Gold Catalyzed Aerobic Oxidation of Dibenzylamine

Linda Kovacs, Tamas Mallat, Jan-Dierk Grunwaldt, Frank Krumeich, Alfons Baiker

ETH Zürich, Inst. f. Chemie-/ Bioingenieurwissenschaft, Wolfgang-Pauli-Strasse 10, ETH Hönggerberg, CH-8093 Zürich, Switzerland

Imines are important intermediates in organic chemistry[1] and their formation by the oxidation of amines has been well applied in natural product synthesis.[2] We have made the unprecedented observation that $Au(OAc)_3$ can be applied as highly active catalyst in the oxidation of dibenzylamine to dibenzylimine using molecular oxygen as the only oxidant (Scheme below).




The fate of the active gold component in this reaction was studied by *in situ* X-ray absorption spectroscopy (XANES and EXAFS) using a specially designed cell. These investigations combined with electron microscopy revealed that in the early stage of the reaction $Au(OAc)_3$ is dissolved and subsequently reduced by the amine and the *in situ* formed gold nanoparticles are the real active sites of the reaction.
Our findings lead to a simple synthetic procedure using a commercially available gold salt which upon interaction with the amine forms highly active gold nanoparticles. Formation of gold nanoparticles during dibenzylamine oxidation was proved independently also by transmission electron microscopy.

[1] J. S. M. Samec, A. H. Ell, J. E. Backvall, *Chem. Eur. J.* **2005**, *11*, 2327.
[2] Y. Jinbo, H. Kondo, M. Taguchi, F. Sakamoto, G. Tsukamoto, *J. Org. Chem.* **1994**, *59*, 6057.

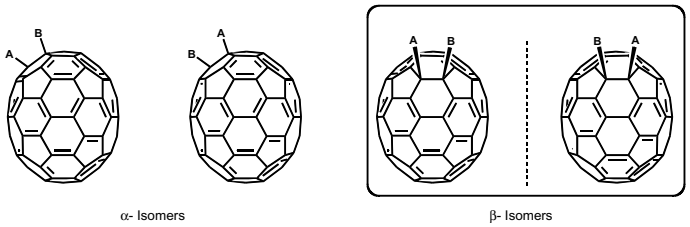
Organic Chemistry **324**

## Preparation of the First Enantiopure $C_{70}$-Adducts with a Non-Inherently Chiral Addition Pattern

Agnieszka Kraszewska, François Diederich

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

By addition of an enantiopure nitrile oxide to $C_{70}$, two constitutionally isomeric α- and two diastereomeric separable β-fullerene-fused isoxazolines are obtained.[1] Although fullerene-fused isoxazolines are known to be particularly inert,[2] a modification of the sidechain, associated with the removal of the external stereogenic center, can be carried out successfully in a carefully designed system. During this step the α-adducts become $C_2$-symmetric, while the β-adducts are separately transformed into enantiomeric fullerene derivatives. Until now, such β-adducts with a non-inherently chiral addition pattern were only obtained as a racemic mixture. In the present work they were isolated in enantiomerically pure form for the first time.




[1] M. S. Meier, M. Poplawska, A. L. Compton, J. P. Shaw, J. P. Selegue, T. F. Guarr, *J. Am. Chem. Soc*. **1994**, *116*, 7044.
[2] M. S. Meier, M. Poplawska, *Tetrahedron* **1996**, *52*, 5043.
[3] C. Thilgen, F. Diederich, *Top. Curr. Chem.* **1996**, *199*, 135.

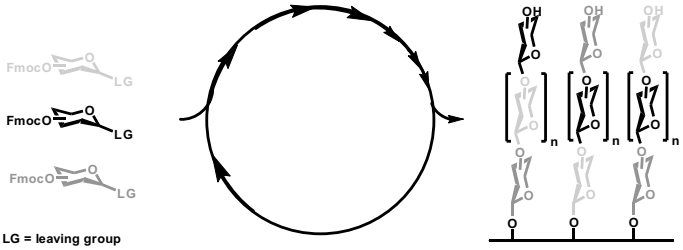
Organic Chemistry **325**

## Streamlining Automated Oligosaccharide Synthesis: Rapid Access to Immobilized Oligosaccharides for Biological Assays

Lenz Kröck, Pascal Bindschädler, Bastien Castagner, Davide Esposito, Tim Horlacher, Peter H. Seeberger

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

Cell-surface oligosaccharides play important roles in numerous biological processes e.g. the immune response, inflammation and cell-cell adhesion.[1] The understanding of these processes to date is incomplete. Oligosaccharide microarray assays are on the way to become an important tool towards the understanding of these processes on a molecular level.
The newest generation of our automated oligosaccharide synthesis platform[2] provides rapid access to such microarrays by streamlining the process from the monomeric building blocks to the immobilzed oligosaccharides. Here we present the most recent advances achieved by our group.




[1] A. Varki, et al. Eds. *Essentials of Glycobiology*; Cold Spring Harbor Laboratory Press: Cold Spring Harbor, **1999**.
[2] O. J. Plante, E. R. Palmacci, P. H. Seeberger, *Science* **2001**, *291*, 1523-1527.

Organic Chemistry **326**

## Tandem 1,5-Hydrogen Atom Transfer - Cyclization Mediated by Sulfur and Phosphorus Centered Radicals

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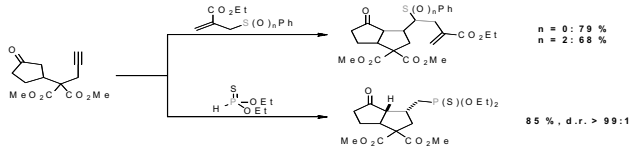
Our interest in developing tin-free process to run alkenyl radical mediated 1,5-hydrogen atom transfer - cyclization reactions led us to use thiophenol as the mediating agent.[1] This methodology was applied to the short and efficient synthesis of erythrodiene.[2] We report here an extension of this reaction to allylsulfides and allylsulfones. This tandem reaction now comprises a new allylation step at the end of the cascade and allows to create two C-C bonds and one C-S bond in a single operation.
We also previously developed a similar tandem reaction using phosphites as the mediating agent. This reaction has been used to elaborate a wide variety of simple bicyclic and spirocyclic systems, unfortunately with only low to good stereoselectivity.[3] We would like to report here an improved procedure involving thiophosphites. This cascade reaction can now be carried out under milder conditions and leads to enhanced diastereomeric ratios. Furthermore this type of thiophosphonates has been proven to be more efficiently transformed.[4]




[1]. F. Beaufils, F. Dénès, B. Becattini, P. Renaud, K. Schenk, *Adv. Synth. Catal.* **2005**, *347*, 1587
[2]. M. Lachia, F. Dénès, F. Beaufils, P. Renaud, *Org. Lett.* **2005**, *7*, 4103
[3]. F. Beaufils, F. Dénès, P. Renaud, *Angew. Chem. Int. Ed.* **2005**, *44*, 5273
[4]. M. P. Healy, A. F. Parsons, J. G. T. Rawlinson, *Org. Lett.* **2005**, *7*, 1597

Organic Chemistry **327**

## Enhancing the Scope of the Radical Carboazidation: Synthesis of *N*-Heterocycles via a Carboazidation/ Reduction Sequence

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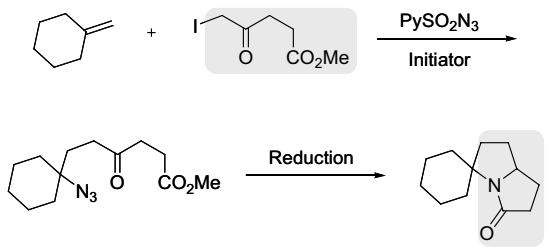
Mono-, bi-, tricyclic amines and amides were obtained in good yield through a radical carboazidation/reduction sequence using α-iodoketones as substrate.[1] This sequence offers a new, concise route to complex alkaloids which otherwise could be troublesome to synthesize.




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

Organic Chemistry **328**

## Rapid Access To Substituted Alicyclic Molecules *Via* Dearomatisation Of [Cr(Arene)(CO)$_3$] Complexes

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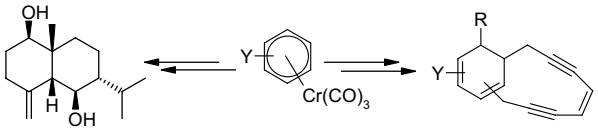
Temporary complexation and activation of an arene by the electrophilic chromium tricarbonyl group allows the sequential *trans* addition of a C-nucleophile and a C-electrophile across an arene double bond [1]. This Cr-mediated dearomatisation sequence can be combined with ring closing metathesis to access *cis*-fused ring systems bearing a methyl group at one ring junction [2]. We will use this strategy in our synthetic approach to the 5-*epi*-eudesma-4(15)-ene-1*β*,6*β*-diol, a rare *cis*-eudesmane[3]. Polysubstituted cyclohexenones could be obtained using this nucleophile/electrophile addition reaction with [Cr(anisole)(CO)$_3$] complexes [4]. These building blocks offer a route of access to novel bicycloenediynes and their study in the Bergman cyclisation.




[1] *Transition Metal Arene π-Complexes in Organic Synthesis and Catalysis,* ed. Kündig, E. P, *Topics in Organomeallic. Chemistry*; vol. 7, Springer Verlag, Berlin, Heidelberg, New York, 2004.
[2] Kündig, E. P.; Bellido, A.; Kaliappan, K. P.; Pape, A. R.; Radix, S. *Org. Biomol. Chem.* **2006**, *4*, 342.
[3] Jiang, H. X.; Li, Y.; Pan, J.; Gao, K. *Helv. Chim. Acta* **2006**, *89*, 558.
[4] Kündig, E. P.; Sau, M.; Perez-Luna, A. *Synlett* **2006**, 2114.

Organic Chemistry **329**

## Synthesis of Three Different Halogen-Containing Protein Epitope Mimetics and Measurement of Their Binding Affinity Against HDM2

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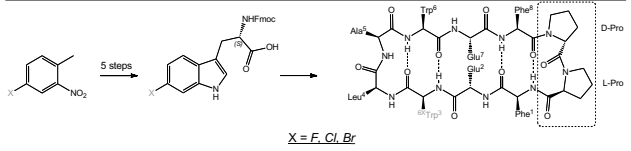
The possibility of forcing small, cyclic peptides into β-hairpin conformation, using a D-Pro-L-Pro template, leads to an interesting class of molecules in drug and vaccine discovery, due to their ability to reproduce the conformational and electronic properties of functional native protein epitopes. In recent work, several of these so-called protein epitope mimetics (PEMs) were synthesized and proved to show binding affinity in such protein-protein interactions as p53/HDM2 [1]. The PEMs are mimicking an amphiphilic α-helix containing a LXXWF motif, where X corresponds to any amino acid. In order to optimize the binding and learn more about its mechanism, three different halogen-containing PEMs were synthesized using the Fmoc solid phase peptide synthesis. Therefore the (L)-6-halogen-substituted-*N*-Fmoc-tryptophans were synthesized in five steps, using L-Acylase [2] to get stereo-selectivity.




The binding affinities were measured using a surface plasmon resonance assay. Thereby, it has been shown that introducing a chloride results in higher binding affinity, whereas introducing either a fluoride or a bromide does not change the affinity significantly.

[1] R. Fasan, R. L. Dias, K. Moehle, O. Zerbe, D. Obrecht, P. R. Mittl, M. G. Grutter, J. A. Robinson, *ChemBioChem* **2006**, *7*, 515.
[2] Y. Konda-Yamada, C. Okada, K. Yoshida, Y. Umeda, S. Arima, N. Sato, T. Kai, H. Takayanagi, Y. Harigaya, *Tetrahedron* **2002**, *58*, 7851.

Organic Chemistry **330**

## New Chiral N-Heterocyclic Carbene Ligands and Their Application in Asymmetric Metal-Catalyzed Transformations

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The last decade has unimpeachably witnessed the fruitful use of N-heterocyclic carbenes (NHCs) as spectator or active ligands for transition-metal catalysts and as organic catalysts on their own.[1] Owing to their strong σ-donor and weak π-acceptor properties, NHCs have appeared as attractive and versatile alternatives to the ubiquitous tertiary phosphine ligands in many metal-catalyzed processes. The one area of research where NHCs have lagged behind is their application in asymmetric catalysis in comparison to phosphine ligands.[2] As an extension of our previous work,[3] herein we report new chiral carbene ligands that are derived from chiral backbone and substituted naphthyl side chains.

[1] (a) *N-Heterocyclic Carbenes in Synthesis*; Nolan S. P., Ed.; Wiley-VCH: Weinheim, Germany, 2006. (b) *N-Heterocyclic Carbenes in Transition Metal Catalysis*; Glorius, F., Ed.; Topics in Organometallic Chemistry, Vol 21; Springer: Berlin, Germany, 2007.
[2] (a) Perry, M. C.; Burgess, K. *Tetrahedron: Asymmetry* **2003**, *14*, 951. (b) César, V.; Bellemin-Laponnaz, S.; Gade, L. H. *Chem. Soc. Rev.* **2004**, *33*, 619. (c) Douthwaite, R. E. *Coor. Chem. Rev.* **2007**, *251*, 702. (d) Mata, J. A.; Poyatos, M.; Peris, E. *Coor. Chem. Rev.* **2007**, *251*, 841.
[3] Luan, X. J.; Mariz, R.; Gatti, M.; Costabile, C.; Poater, A.; Cavallo, L.; Linden, A.; Dorta, R. *J. Am. Chem. Soc.* **2008**, *130*, 6848.

Organic Chemistry **331**

## Synthesis of substituted 2-aminonorbornane-2,3-dicarboxylic acids: Potent virtual hits for glutamate transporter GLT1

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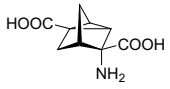
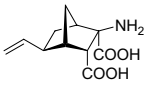
Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, 3012 Bern, Switzerland

Glutamate transporter proteins play an essential role in neurotransmission of glutamate in the mammalian CNS. Because of their putative importance in numerous neurodegenerative diseases[1], they have become attractive targets in medicinal chemistry. So far, only few potent and selective ligands have been found, among them the tricyclic glutamate analog WAY-855.[2]
For the discovery of new ligands for glutamate transporters, an exhaustive virtual library of glutamate and aspartate analogs up to 17 atoms of C, N, O, F was generated in our group. Docking experiments of this library at the crystal structure of bacterial glutamate transporter GLT1 resulted in a structurally diverse library of molecules with better binding energies (BE) than the native ligand glutamate.[3]
Different stereoisomers of 2-aminonorbornane-2,3-dicarboxylic acids with a vinyl group at C5 or C6 showed very high binding scores. In the present work, the synthesis of different stereo- and regioisomers of this potent ligand as well as of its phenethyl-substituted analog is presented.




WAY-855
BE = -10.7 kcal/mol




BE = -11.0 kcal/mol

[1] Maragakis, N. J.; Rothstein, J. D., *Neurobiology of Disease* **2004**, *15*, 461.
[2] Dunlop, J. et al., *Br. J. Pharmacol.* **2003**, *140*, 839.
[3] Nguyen, K. T.; Reymond, J.-L., *J. Chem. Inf. Model.* **2008**, submitted.

Organic Chemistry **332**

## Allylic Bissulfones as Coupling Reagents

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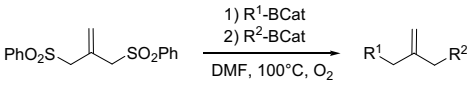
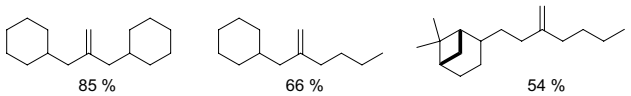
Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

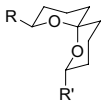
The hydroboration-allylation process discovered in our laboratory [1] is efficiently extended to a bisallylation reaction. The involved allylic bissulfone serves as a coupling reagent for two alkyl radicals.



85 % 66 % 54 %

This bisallylation approach can be applied to short syntheses of naturally occurring, enantiomerically pure spiroketals. This target structure is found in products from various natural sources, including insects, microbes, fungi, and marine organisms and a broad spectrum of biological activities is attributed to it.




[1] A.-P. Schaffner, P. Renaud, *Angew. Chem. Int. Ed.* **2003**, *42*, 2658.

Organic Chemistry **333**

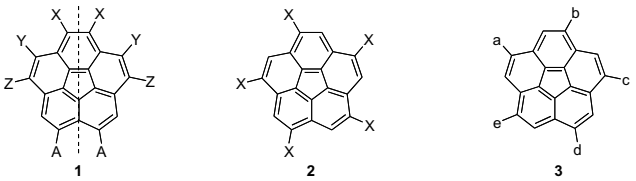
**Synthesis of 1,3,5,7,9-penta-Substituted Corannulene**

Roman Maag, Jay S. Siegel*

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.




[1] Seiders, T. J.; Elliot, E. L.; Grube, G. H.; Siegel, J. S. *J. Am. Chem. Soc.* **1999,** *121*, 7804.; Sygula, A.; Rabideau, P. W. *J. Am. Chem. Soc*. **2000**, *122*, 6323.
[2] Grube, G. H.; Elliot, E. L.; Steffens, R. J.; Jones, C. S.; Baldridge, K. K.; Siegel, J. S. *Org. Lett*. **2003**, *5*, 713.

Organic Chemistry **334**

**Off-Beads High-Throughput Screening For Functional Dendrimers**

Noélie Maillard, Tamis Darbre, Jean-Louis Reymond*

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

Our group investigates peptide dendrimers as artificial enzymes. We recently reported single site esterolytic peptide dendrimers identified by direct functional selection in a solid supported combinatorial library.[1] Closer examination of on-bead screening assays showed a high frequency of false positive results. To circumvent this limitation, we have developed an alternative screening protocol that allows one to assay catalytic reactions "off-beads" with soluble dendrimers, using a photolabile linker as reported for the identification of the binding between terbium (III) and peptides.[2] Using this method the occurrence of false positives was greatly reduced. Application of the method to search for enantioselective esterase dendrimers will be presented.


[1] a) S. Javor, E. Delort, T. Darbre, J.-L. Reymond *J.Am.Chem.Soc.* **2007**, *129*, 13238-13246. b) A. Clouet, T. Darbre, J.-L. Reymond *Angew.Chem.Int.Ed.* **2004**, *43*, 4612-4615.
[2] L. J. Martin, B. R. Sculimbrene, M. Nitz, B. Imperiali *QSAR Comb.Sci.* **2005**, *24*, 1149-1157.

Organic Chemistry **335**

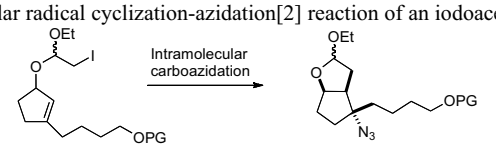
**A New Access to Azaspirocyclic Core of Pinnaic Acid**

Nathalie Mantrand, Philippe Renaud*

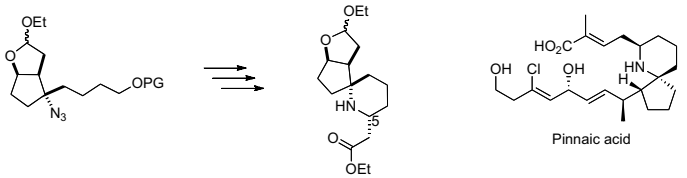
University of Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

The marine alkaloid pinnaic acid was isolated in 1996 from the marine sponge *Pinna Muricata*[1] by Uemura and co-workers. This alkaloid bears a unique highly functionalized spiranic core representing the main synthetic challenge towards this natural product.

We envisioned that the azaspirocyclic core could be prepared via the intramolecular radical cyclization-azidation[2] reaction of an iodoacetal.




With this intermediate in hand we explored different strategies to obtain the 1-azaspirocycle core of pinnaic acid with control of the stereochemistry at C5.




[1] Chou, T.; Kuramoto, M.; Otani, Y.; Shikano, M.; Yasawa, K.; Uemura, D.; *Tetrahedron Lett.* **1996**, *37*, 3871.
[2] For carboazidation reaction see: Panchaud, P.; Ollivier, C.; Renaud, P.; Zigmantas, S. *J. Org. Chem.* **2004**, *69*, 2755-2759.

Organic Chemistry **336**

**Structural Studies of Short Pyrene-modified Oligonucleotides**

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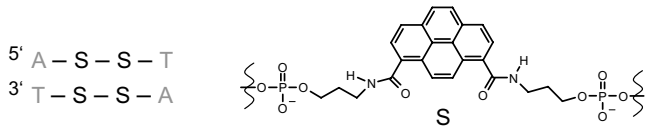
Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3012 Bern

Polyaromatic compounds, such as 1,8-pyrenedicarboxamides, have proven to be excellent building blocks for the assembly of □-stacked oligomers.[1] The interaction between the pyrene residues in single and double stranded oligonucleotides had been intensively analyzed by spectroscopic methods in our group.[1,2] Thus far, all models of interstrand-stacked polyaromatic residues are derived from spectroscopic data. With the aim to further analyze such systems by x-ray crystallography, the crystallization of short pyrene-modified oligonucleotides is attempted. The synthesis of such model systems is described and results of spectroscopic investigations as well as crystallization experiments will be shown.




[1] V.L.Malinovskii, F. Samain and R. Häner, *Angew. Chem. Int. Ed.* **2007**, 46,
4464-4467.
[2] F. Samain, V.L. Malinovskii, S. M. Langenegger and R. Häner, *Bioorg. Med. Chem*. **2008**, 16, 27-33.

Organic Chemistry **337**

## A New Family of Planar Chiral Posphine Ligands

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30 Quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland
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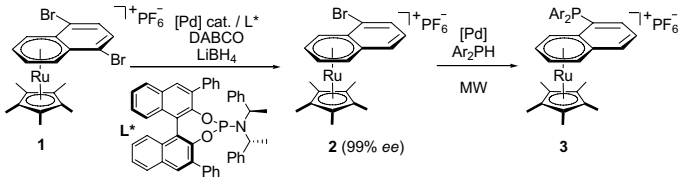
Chiral ruthenium arene complexes are of interest for their potential as chiral ligands in asymmetric catalysis. They have received much less attention than planar chiral ferrocenes and chromium based ligands [1]. We here report on an easy access via desymmetrization of [Ru($\eta^5$-Cp*)(5,8-dibromonaphthalene)][$PF_6$] complex **1**. The very attractive catalytic route adopted is the asymmetric hydrogenolysis of the *meso*-complex using a chiral catalyst [2], followed by a microwave-assisted reaction to the enantioenriched phosphine ligand **3**.




We will also detail the extension of this sequence to [Ru($\eta^5$-Cp*)(indenyl)] complexes.

[1] (a) Mũniz, K. *in Transition Metal π-Complexes in Organic Synthesis and Catalysis*, Kündig E. P. Ed., Topics in Organometallic Chemistry, Vol 7, Springer Verlag, Heidelberg, **2004**. (b) *Ferrocenes*, Hayashi, T.; Togni, A. Eds., VCH: Weinheim, Germany, **1995**.
[2] Cr-complexes : (a) Kündig E. P.; Chaudhuri, P. D.; House, D.; Bernardinelli, G. *Angew. Chem. Int. Ed.* **2006**, *45*, 1092. (b) Cumming, G. R.; Bernardinelli, G.; Kündig, E. P. *Chem. Asian J.* **2006**, *1*, 459.

Organic Chemistry **338**

## Synthesis of Shape Switchable Azo Functionalized Macrocycles

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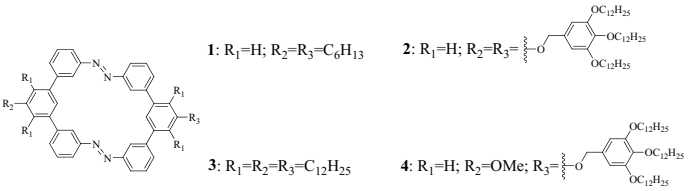
University of Basel, St. Johanns-Ring 19, 4056 Basel, Switzerland

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 *trans/cis* 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. The optical addressability of the joints gives access to two conformations with large differences in exterior form, namely a flat cycle in the *trans* form and a bent cycle in the *cis* form.




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.

Organic Chemistry **339**

## Enantioselective epoxidation of prochiral olefins using axially chiral biaryl azepinium salts as catalysts.

Roman Novikov, Gérald Bernardinelli, and Jérôme Lacour

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e-mail: roman.novikov@chiorg.unige.ch, jerome.lacour@chiorg.unige.ch

Two series of novel biaryl (axially chiral) iminium salts were prepared to be used as catalysts in enantioselective epoxidation of unfunctionalized alkenes[1]. These species combine ($R_a$)-dimethylbiphenyl (**1**) or ($R_a$)-5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl (**3**) skeletons with chiral exocyclic appendages derived from commercially available (*S*)- or (*R*)-3,3-dimethylbutan-2-amine and (*S*)- or (*R*)-1-phenylpropan-1-amine. Under biphasic reaction conditions[2], *in-situ* generated bromide iminium salts of these derivatives have shown similar or better asymmetric efficiency then widely-used binaphthyl derivatives of type (**2**). A structural analysis was performed in search of a correlation between the origin of the stereocontrol/ level of enantioselectivity in the products, and the dihedral angle around the biaryl (binaphthyl) twist of the catalyst. Care was taken to compare the results obtained with these "new" *in-situ* generated iminium bromide salts with that of more "classical" fully-isolated iminium salts which have displayed similar of better asymmetric efficiency [3].

Organic Chemistry **340**

## Copper-Catalyzed conjugate Addition With Chiral SimplePhos Ligands

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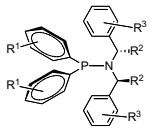
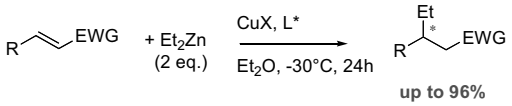
University of Geneva, Department of Organic Chemistry,
30 quai Ernest Ansermet 1211 Geneva 4 Switzerland

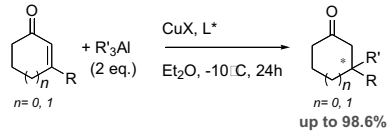
SimplePhos ligands represent a novel class of monodentate chiral ligands, based on chiral amine moiety and flexible diaryl groups on the phosphorus atom. They are easily prepared by two different pathways and they are highly functionalized.



Herein, we report the copper-catalyzed asymmetric conjugate addition of diethylzinc reagent with SimplePhos ligands, which give high enantioselectivity with cyclic enones up to 96% ee. Others substrates as acyclic enones and nitroolefine were also tested.




The main efficiency of these ligands was showed with the use of trialkylaluminium reagents to a wide range of 3-substituted enones in presence of various copper salts. After some optimizations of experimental conditions, stereogenic quaternary carbon centres were obtained with enantioselectivity up to 98.6%.




L. Palais, I. S. Mikhel, C. Bournaud, L. Micouin, C. A. Falciola, M. Vuagnoux-d'Augustin, S. Rosset, G. Bernardinelli, A. Alexakis, *Angew. Chem. Int. Ed.* **2007**, *119*, 7606-7609

Organic Chemistry **341**

**Addition of Methyl lithium to imines, catalyzed by a new chiral diamine.**

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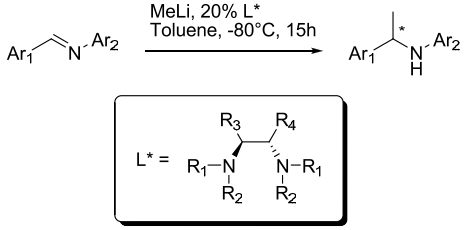
The discovery of new ligands for enantioselective reactions is one of the major goals in asymmetric synthesis. In our previous papers, we described conceptually new $C_2$ and pseudo $C_2$ symmetric tertiary diamines in which nitrogen atoms could become stereogenic in the reactive species [1]. Following those previous studies we design a new chiral diamine for addition of methyl lithium on aromatic imines [2].




[1] (a) Gille, S.; Cabello, N.; Kizirian, J.-C.; Alexakis, A. *Tetrahedron Asymmetry*, **2006**, *17*, 1045. (b) Kizirian, J.-C.; Cabello, N.; Pinchard, L.; Caille, J.-C.; Alexakis, A. *Tetrahedron*, **2005**, *61*, 8939. (c) Kizirian, J.-C.; Caille, J.-C.; Alexakis, A. *Tetrahedron Lett*. **2003**, *44*, 8893.
[2] Perron, Q.; Alexakis, A. *Tetrahedron Asymmetry*, **2007**, *18*, 2503.

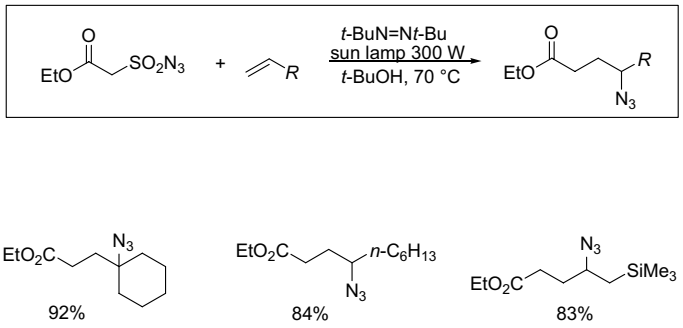
Organic Chemistry **342**

**A New Reagent for the Tin-free Radical Carboazidation Reaction**

Karin Weidner, André Giroult, Philippe Renaud*

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

A highly efficient addition-azidation procedure to terminal alkenes was accomplished using ethyl 2-(azidosulfonyl)acetate as carboazidating reagent. The combination of radical precursor and azidating reagent into a single compound allows the formation of 3-azidoesters that give access to mono- and polycyclic lactams. The reaction was performed by visible-light irradiation of 1,2-di-*tert*-butyldiazene (DTBD) in *tert*-butanol to afford the desired product in high yields.




Organic Chemistry **343**

**New Toxic Ribosomal Heterocyclic Peptides from Cyanobacteria**

Cyril Portmann[a], Judith F. Blom[b], Friedrich Jüttner[b] and Karl Gademann[a,]*

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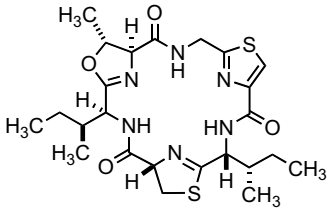
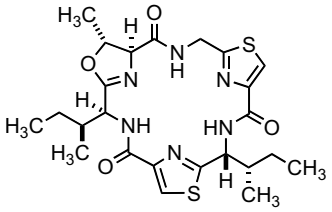
[b] Limnological Station, University of Zürich, 8802 Kilchberg, Switzerland

Cyanobacteria (formerly called blue-green algae) are prokaryotic photoautotrophs and can be found in freshwater or marine environments. They are considered as a prolific source for new bioactive compounds.[1] In this communication, we report the isolation of aerucyclamides A (**1**) and B (**2**) [2] from *Microcystis aeruginosa* PCC7806.



Aerucyclamide A (**1**)



Aerucyclamide B (**2**)

These ribosomal heterocyclic peptides [3] display moderate toxic activity against the freshwater crustacean *Thamnocephalus platyurus* and their ecological and therapeutic properties will be discussed.

[1] Review: Burja, A. M.; Banaigs, B.; Abou-Mansour, E.; Burgess, J. G.; Wright, P. C. *Tetrahedron* **2001**, *57*, 9347.
Gademann, K.; Portmann, C. *Curr. Org. Chem.* **2008**, 12, 326.
[2] Portmann, C.; Blom, J. F.; Gademann, K.; Jüttner, F. *J. Nat. Prod.* **2008**, in press.
[3] Ziemert, N.; Ishida, K.; Quillardet, P.; Bouchier, C.; Hertweck, C.; Tandeau de Marsac, N.; Dittmann, E. *Appl. Environ. Microbiol.* **2008**, *74*, 1791.

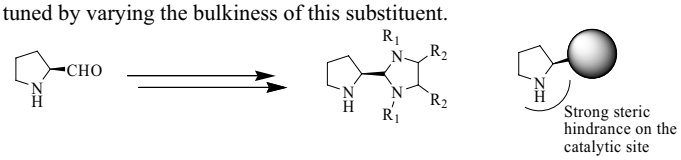
Organic Chemistry **344**

**New Chiral Catalysts for Organocatalysed Enamine Asymmetric Conjugate Additions**

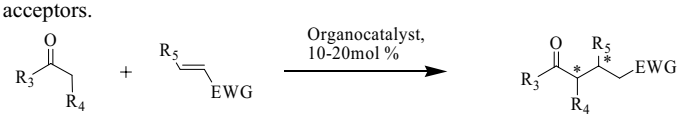
Alexandre Alexakis, Adrien Quintard

Department of Organic Chemistry, University of Geneva, Switzerland.

Recently, different pyrrolidine based organocatalysts have been developed for the activation of aldehydes or ketones towards various Michael acceptors.[1] Among them, several powerful catalysts were designed by looking on the major part on steric hindrance.[2] Herein, we wish to report the synthesis of a family of new highly modular organocatalysts by playing on the bulkiness of the substituent of the pyrrolidine. The catalyst's properties could easily be tuned by varying the bulkiness of this substituent.




These catalysts give good results in terms of diastereo- and enantioselectivity on the Michael addition of both aldehydes and ketones on various Michael acceptors.




**1.a**. S. Sulzer-Mossé, A. Alexakis, Chem. Commun, **2007**, 3123. **1.b**. S. Mukherjee, J. W. Yang, S. Hoffmann, B. List, Chem. Rev. **2007**, 107, 5471. **2.a**. Y. Hayashi, H. Gotoh, T. Hayashi, M. Shoji, Angew. Chem. Int. Ed, **2005**, 44, 4212. **2b**. T. Mandal, C-G. Zhao, Tetrahedron Letters, **2007**, 48, 5803.

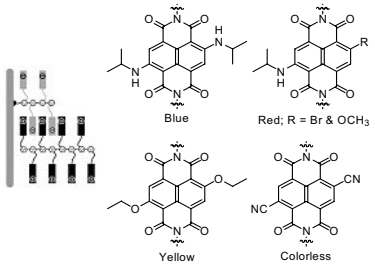
Organic Chemistry **345**

**Syntheses of Rainbow Naphthalendiimide-*p*-Oligophenyl Architectures**

Velayutham Ravikumar, Kishore Ravuri, Aude Violette, Shin-ichiro Sakurai, Rajesh Bhosale, Santanu Maity, Marco Lista, Natalie Banerji, Oksana Kel, Eric Vauthey, Naomi Sakai and Stefan Matile*

University of Geneva, Department of Organic Chemistry
Geneva, Switzerland

In order to create smart photosystems on a conducting surface, zipper assembly is developed [1]. Using *p*-oligophenyls (POP) or oligophenylenethynylenes (OPE) with mismatched length, zipping up of n-semiconducting and chromophoric naphthalenediimide (NDI) π-stacks along p-semiconducting rigid-rod scaffolds is feasible. To secure access to the advanced multicomponent rainbow architectures, a full set of NDI-POP systems that are blue, red and yellow and emit red, orange and green respectively has been developed together with exceptionally strong NDI electron acceptors.




[1] (a) Sakai, N.; Sisson, A. L.; Bürgi, T.; Matile, S. *J. Am. Chem. Soc.* **2007**, *129*, 15758-15759. (b) Sisson, A. L.; Sakai, N.; Banerji, N.; Fürstenberg, A.; Vauthey, E.; Matile, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 3727-3729.

Organic Chemistry **346**

**Peptide-Based Di- and Tetraethynylethenes: Switchable Scaffolds to Control the Process of Peptide Self-Assembly**

Dirk T.S. Rijkers [1,2] and François Diederich[1,*]

[1]Laboratorium für Organische Chemie, ETH-Hönggerberg, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich, and [2]Medicinal Chemistry and Chemical Biology, Department of Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands

The tetraethynylethene (3,4-diethynylhex-3-ene-1,5-diyne; TEE) moiety provides a unique carbon-rich framework with unusual structural, electronic and optical properties.[1] In the last decade our laboratory reported versatile synthesis routes toward a diverse set of TEEs in which the Pd-catalyzed Sonogashira cross-coupling was used for the introduction of electron donating/accepting aryl functionalities.[2,3] In the present work, the TEE framework was decorated with peptide sequences with an intrinsic tendency for self-recognition. The peptides were based on either the Val-Phe recognition motif of the Alzheimer Aβ peptide or on the Val-Thr sequence because of its high β-sheet propensity. The peptide derivatives were N-terminally modified with a suitable aryl functionality for their conjugation on the TEE molecule via the Sonogashira reaction. The switchable TEE scaffold enabled the control over the peptide-induced self-assembly since different morphologies (peptide nanotubes, helical ribbons, lamellar sheets) of the supramolecular assemblies were observed. In this poster, the rationale for design, details of the synthesis, spectroscopic data, and switching properties of the peptide-TEE derivatives will be presented.

[1] M.Brondsted Nielsen, F. Diederich, *Chem. Rev.* **2005**, *105*, 1837.
[2] J. Anthony, A.M. Boldi, Y. Rubin, M. Hobi, V. Gramlich, C.B. Knobler, P. Seiler, F. Diederich, *Helv. Chim. Acta* **1995**, *78*, 13.
[3] R.R. Tykwinski, M. Schreiber, R. Pérez-Carlón, F. Diederich, V. Gramlich, *Helv. Chim. Acta* **1996**, *79*, 2249.

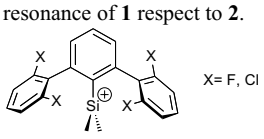
Organic Chemistry **347**

**Synthesis of Organosilicon Ions stabilized by Cabon Halogen Bonds.**

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

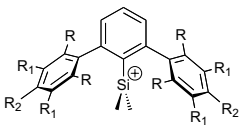
Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland.

Carbocations $R_3C^+$ have been known for more than 100 years. The evidence for the existence of a free, planar $R_3Si^+$ ion was provided only in 2002 by the crystal structure of $[(Mes)_3Si][H\text{-}CB_{11}Me_5Br_6]$ (where Mes is 2,4,6-trimethylphenyl).[1] The main issue in the synthesis of silylium ions is to avoid the interaction of solvent, counterion or neighboring groups with the electropositive center.
This project deals with the synthesis of organosilicon ions where silicon carries a 1',3'-terphenyl residue with electron-withdrawing lateral rings (**1**). The idea comes from a previous work developed in this group where a 1',3'-terphenyl residue with electron-rich lateral rings (**2**) was choosen as a suitable system because silicon is sterically protected by the two flanking rings as well as electronically stabilized by $\pi_{ring}$–$3p_{Si}$ interaction.[2] Fluorine and chlorine substituents in **2** withdraw electrons from the preferred position of interaction of silicon with the flankink rings: the ortho carbon. The result is an enhancement of the silicon cation character of **1** as demonstrated by the more downfield shifted resonances in the $^{29}Si$ nuclear magnetic resonance of **1** respect to **2**.




X= F, Cl

1




R = $CH_3$
$R_1$,$R_2$= $CH_3$, H

2

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

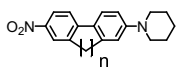
Organic Chemistry **348**

**A universal synthetic route towards torsion angle restricted biphenyl based push-pull-systems**

Jürgen Rotzler, Marcel Mayor

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

In the last fifty years materials which exhibit optical nonlinearity attracted considerable attention.[1-3] A novel universal synthetic route towards biphenyls based push-pull-systems, which are suitable molecules for investigations in this ongoing research area, is reported.




n = 0, 1, 2, 3, 4, 5

**1a - 1f**

These biphenyls **1a** – **1f** are model compounds to investigate the influence of π-conjugation, dictated by the torsion angle in the backbone on the non-linear optical properties. Therefore they are bridged between 2 and 2' position by a variable number of methylene groups, giving them a defined and fixed torsion angle between the two phenyl rings.
The target molecules are synthesized starting by converting dibromobiphenyl derivatives into their diamine analogons, followed by a chemoselective azacycloalkylation and in a closing oxidation of the remaining amino functionality.

[1] K. S. Thanthiriwatte, K. M. Nalin de Silva, *Theochem* **2002**, *617*, 169.
[2] D. R. Kanis, M. A. Ratner, T. J. Marks, *Chem. Rev.* **1994**, *94*, 195.
[3] D. J. Williams, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 690.

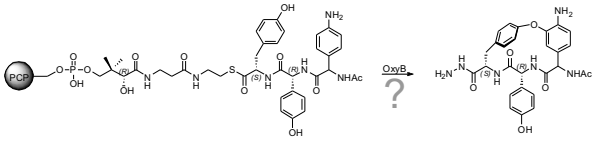
Organic Chemistry **349**

**Attempted Phenol Coupling Reaction with an Anilino-Analogue of a Tripeptide Substrate Catalyzed by the Enzyme OxyB from the Vancomycin Biosynthetic Pathway**

Patrick Schmartz[1], Ernst Freund[2], Khaled Abou Hadeed[1], John A. Robinson[1]

[1]Institute of Organic Chemistry, University of Zurich, Winterthurerstr. 190, CH-8057 Zurich, Switzerland
[2]CARBOGEN AMCIS AG, Schachenallee 29, CH-5001 Aarau, Switzerland

In a first step, the racemic non-proteinogenic amino acid *p*-aminophenylglycine (Apg) with side chain Boc-protection was synthesized using a straightforward palladium catalyzed α-arylation methodology. The enantiomers were separated by chiral phase HPLC.
Before resolution, racemic *N*-Alloc protected *p*-(Boc)aminophenylglycine was incorporated into the tripeptide AcHN-Apg-(*R*)-Hpg-(*S*)-Tyr-OH. This tripeptide was tested towards OxyB activity in a standard *in vitro* activity assay developed in our group [1,2]. This required the conversion into the corresponding diastereomeric tripeptide phenyl- and coenzyme A thioesters, which could effectively be separated at the stage of the phenyl thioesters by semipreparative reverse phase HPLC. The CoA-thioesters were loaded onto PCP-7bCS, which was produced in *E.coli* strain Rosetta2(DE3)pLysS. Assay products were analyzed by analytical HPLC and ESI-MS.




Although the corresponding tripeptide containing (*R*)-Hpg as an N-terminal residue is effectively converted into the monocyclic product, no turnover could be detected with both investigated epimeric tripeptides.

[1] K. Zerbe, K. Woithe, D. B. Li, F. Vitali, L. Bigler, J. A. Robinson, *Angew. Chem. Int. Ed. Engl.* **2004**, *43*, 6709.
[2] K. Woithe, N. Geib, K. Zerbe, D. B. Li, M. Heck, S. Fournier-Rousset, O. Meyer, F. Vitali, N. Matoba, K. Abou-Hadeed, J. A. Robinson, *J. Am. Chem. Soc*. **2007**, *129*, 6887.

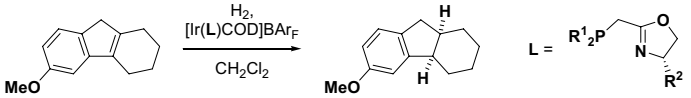
Organic Chemistry **350**

**Asymmetric Hydrogenation of Unfunctionalized, Tetrasubstituted Olefins: Synthesis, Structure and Application of Phosphinomethyl-Oxazoline-Iridium Complexes**

Marcus G. Schrems, Eva Neumann and Andreas Pfaltz

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

Iridium-catalyzed enantioselective hydrogenation has become the method of choice for the enantioselective reduction of unfunctionalized olefins.[1] In particular, tetrasubstituted olefins are interesting substrates, which allow the generation of two adjacent stereocenters in a single hydrogenation step. We have recently shown, that cationic iridium(COD) complexes with chiral phosphinomethyl-oxazolines are very efficient catalysts for the enantioselective hydrogenation of various classes of tetrasubstituted olefins.[2]
We show a short and practical synthesis of differently substituted phosphinomethyl-oxazolines and their corresponding iridium(COD) complexes. The crystal structures of iridium catalysts and our latest results in the asymmetric hydrogenation of tetrasubstituted olefins will be presented.[3]




91% ee, full conv.

[1] S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res.* **2007**, *40*, 1402; K. Källström, I. Munslow, P. G. Andersson, *Chem. Eur. J.* **2006**, *12*, 3194; X. Cui, K. Burgess, *Chem. Rev.* **2005**, *105*, 3272.
[2] M. G. Schrems, E. Neumann, A. Pfaltz, *Angew. Chem*. **2007**, *119*, 8422; *Angew. Chem. Int. Ed.* **2007**, *46*, 8274.
[3] M. G. Schrems, E. Neumann, A. Pfaltz, *Heterocycles* **2008**, *76*, in press.

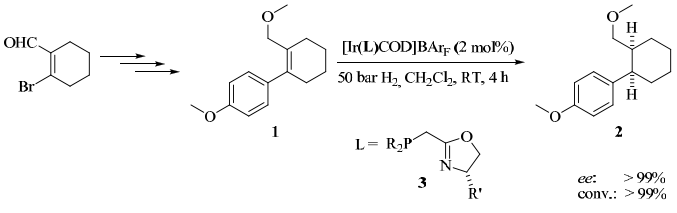
Organic Chemistry **351**

**Iridium Catalyzed Asymmetric Hydrogenation of Cyclic, Tetrasubstituted Olefins**

Andreas Schumacher, Marcus G. Schrems, Wei Liu, Markus Neuburger and Andreas Pfaltz*

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

Establishing two adjacent chiral centers in one step by enantioselective hydrogenation of tetrasubstituted olefins opens up new synthetic pathways in organic synthesis. First investigations using iridium-complexes with chiral P,N-ligands have shown excellent results for tetrasubstituted, unfunctionalized olefins.[1, 2] These results encouraged us to extend our method to new tetrasubstituted olefins. We developed a protocol for synthesizing cyclic, tetrasubstituted, functionalized olefins using *Suzuki-Miyaura* cross-coupling methodology. Very high activity and selectivity was obtained in the enantioselective hydrogenation of methyl ether **1** using iridium-complexes with chiral P,N-ligands.




[1] M. G. Schrems, E. Neumann, A. Pfaltz, *Angew. Chem*. **2007**, *119*, 8422; *Angew. Chem. Int. Ed.* **2007**, *46*, 8274.
[2] M. G. Schrems, E. Neumann, A. Pfaltz, *Heterocycles* **2008**, in press.

Organic Chemistry **352**

**Synthesis of cholesteryl-(3, 4-Dihydroxy-5-methoxy-tetrahydro-furan-2-yl)-methanone**
**A potential cholesterol substitute for studies in membranes**

Sedaghat Soheila; Poormand Sanaz; Saber Tehrani Mandana

Department of Chemistry, Islamic Azad University- North Tehran branch, post code, 19136-74711 – TEHRAN- IRAN

Cholesterol is an integral component of various biological membranes and it affects the fluidity of biological membranes . Previous work proved that a free hydroxyl group in cholesterol is not necessary for the normal cholesterol-associated properties observed in model membranes [1].
In this study, cholesteryl-(3, 4-Dihydroxy-5-methoxy-tetrahydro-furan-2-yl)-methanone was obtained from multi step organic synthesis. At first, we prepared N-methoxy-N-methyl amide compound that react with organolithium species in THF [2, 3]. N-methoxy-N-methyl amide as effective acylating agent (weinreb amide) is routinely prepared from N-O-dimethyl hydroxylamine hydrochloride and the activated derivative of riboside compound [4]. We have reported the cholesteryl glucoside ketones are as effective as cholesterol in supporting the growth of the membrane and have been successfully used to study the role of sterol in natural membranes. we used a glucoside moiety in cholesterol molecule that increasing the hydrophobic bulk, decreases its ability to condense membranes.

[1] . Sedaghat .S, Desaubry L., Streiff S, Ribeiro N, Micheals B., Nakatani Y.,Ourisson G.; Chemistry and biodiversity –vol.1( 2004 ) 124
[2] . Duvold T. et al. ; ; tetrahedron letter ,vol. 36 , no. 18 ,pp.3153 ( 1995 ); "
[3] . Dumitru Petru Iga and et al. ,Carbohydrate research ,vol.340,pp. 2052 (2005 )
[4] . Steven Nahm , Steven Wrinreb , tetrahedron letters , vol 22 , no 39 , 3815-3818, ( 1981 ) ,

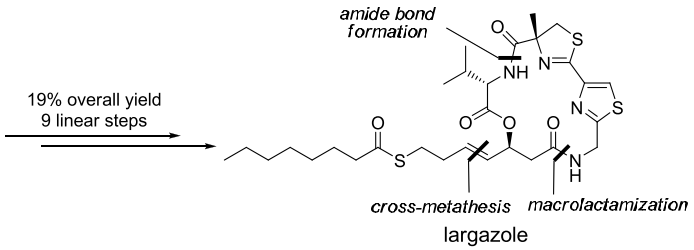
Organic Chemistry **353**

**Synthesis and Biological Activity of Largazole and Derivatives**

Tobias Seiser, Faustin Kamena, Nicolai Cramer*

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

The search for new pharmaceutically relevant lead structures still has a focus on natural products. In particular, cytotoxic compounds isolated from marine sources display a rich structural diversity. However, the often highly potent compounds frequently lack selectivity for cancer cells compared to the non-transformed wild type cells. An exemption of this pattern seems to be largazole, which has been recently isolated in scarce amounts by Luesch *et al.* from cyanobacteria of the genus *Symploca* [1]. The proliferative inhibitory activity of largazole is remarkably higher for cancer cell lines compared to the corresponding non-transformed cells (7.7 nM *vs* 122 nM).




We will describe a short and modular synthesis of largazole and related synthetic analogs [2]. Furthermore the necessity of the thiobutenyl moiety for an antiproliferative activity is demonstrated in activity tests.

[1] K. Taori, V. J. Paul, H. Luesch, *J. Am. Chem. Soc.* **2008**, *130*, 1806.
[2] T. Seiser, F. Kamena, N. Cramer, *Angew. Chem.* **2008**, accepted.

Organic Chemistry **354**

**Molecular Characterization of the NCoA-1/STAT6 Interaction**

Markus Seitz[1], Ludovic T. Maillard[1], Daniel Obrecht[2] and John A. Robinson[1]

[1]Institute of Organic Chemistry, University of Zurich, Winterthurerstr. 190, CH-8057 Zurich, Switzerland
[2]Polyphor AG, Gewerbestrasse 14, CH-4123 Allschwil, Switzerland.

Many protein-protein interactions involved in cell signalling, cell adhesion and regulation of transcription are mediated by short α-helical recognition motifs with the sequence Leu-Xaa-Xaa-Leu-Leu (LXXLL, where Xaa = any amino acid). Originally observed in cofactors that interact with hormone-activated nuclear receptors, LXXLL motifs are now known to occur in many transcription factors, including the STAT family, which transmit signals from activated cytokine receptors at the cell surface to target genes in the nucleus. STAT6 becomes activated in response to IL-4 and IL-13, which regulate immune and anti-inflammatory responses. Structural studies have revealed how an LXXLL motif located in 2.5 turns of an α-helical peptide derived from STAT6 provide contacts through the Leu side chains to the coactivator of transcription NCoA-1 [2,3]. However, since many protein-protein interactions are mediated by LXXLL motifs, it is important to understand how specificity is achieved in this and other signalling pathways. Here we show that energetically important contacts between STAT6 and NCoA-1 are made in residues that flank the LXXLL motif, including the underlined residues in the sequence LLPPTEQDLTKLL. We also demonstrate how the affinity for NCoA-1 of peptides derived from this region of STAT6 can be significantly improved by optimizing knobs-into-holes contacts on the surface of the protein. The results provide important new insights into the origins of binding specificity, and might be of practical value in the design of novel small molecule inhibitors of this important protein-protein interaction[1].

[1] M. Seitz, *ChemBioChem* **2008**, *9*, 1318.
[2] A. Razeto et al., *J. Mol. Biol.* **2004**, *336*, 319.
[3] C.M. Litterst et al., *J. Biol. Chem.* **2002**, *277*, 36052.

Organic Chemistry **355**

**Synthetic Analogs of Telomestatin**

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

Telomestatin, a molecule identified in 2001 by Shin-Ya[1] from *Streptomyces anulatus* during a telomerase inhibition screen, is one of the best quadruplex ligands reported to date and is showing very promising anti-cancer activities in vivo. Telomestatin has a good, but not ideal, shape for binding the stacked G-tetrads that constitute G-quadruplex DNA. Due to the presence of a single thiazoline unit, as well as severe macrocyclic ring strain, telomestatin is not a planar molecule. Our design efforts have been directed towards the synthesis of telomestatin analogs that are fully planar. These efforts have resulted in a series of macrocyclic polyzoles containing a thiazole unit at every second position and imidazole or oxazole units at the remaining positions. Here we describe the design and synthesis of these analogs.

1. K. Shin-ya, K. Wierzba, K.-I. Matsuo, T. Ohtani, Y. Yamada, K. Furihata, Y. Hayakawa and H. Seto, *J. Am. Chem. Soc.* **2001**, *123*, 1262.

Organic Chemistry **356**

**Tröger Base: a new Reactivity Towards Novel Configurationally Stable Derivatives**

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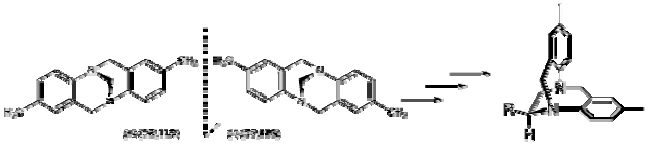
Tröger bases were discovered ca. 130 years ago, and since their resolution into single enantiomers, these compounds have been strongly studied for a variety of purposes[1]. Tröger bases, that is to say methano-bridged Tröger moieties, can unfortunately undergo facile racemization under acidic conditions[2]. This drawback can for instance be overcome by the synthesis of ethano-bridged derivatives[3]. 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. Discovery: J. Tröger, *J. Prakt. Chem.* **1887**, *36*, 225. Structure: M.A. Spielman, *J. Am. Chem. Soc.* **1935**, *57*, 583. Mechanism: E. C. Wagner, *J. Am. Chem. Soc.* **1941**, *63*, 832. Resolution: V. Prelog, P. Wieland, *Helv. Chim. Acta* **1944**, *27*, 1127. Configuration: S.H. Wilen, J.Z. Qi, P.G. Williard, *J. Org. Chem.* **1991**, *56*, 485.
[2] A. Greenberg, N. Molinaro, M. Lang, *J. Org. Chem.* **1984**, *49*, 1127. O. Trapp, G. Trapp, J. Kong, U. Hahn, F. Vögtle, V. Schurig *Chem. Eur. J.* **2002**, *8*, 3629.[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.

Organic Chemistry **357**

## Towards Chiral Trifluoromethylphosphines for Asymmetric Catalysis

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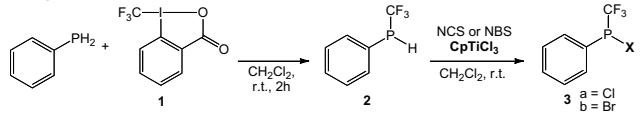
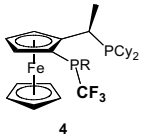
We recently reported a simple method for the synthesis of trifluoromethylphosphines.[1] Both secondary and primary phosphines smoothly react with a hypervalent iodine(III)-$CF_3$ reagent (**1**) developed in our laboratory.[2] During our studies aimed at exploiting this methodology for the synthesis of more complex trifluoromethylphosphines we found that secondary mono(trifluoromethyl)phosphines (**2**) can be converted to the corresponding chlorides or bromides (**3**) upon reaction with NCS or NBS, respectively. Surprisingly, these reactions require the presence of catalytic amounts of $CpTiCl_3$.[3]




We will show how halophosphines of type **3** may be used for the synthesis of Josiphos derivatives such as compound **4**.




1. Eisenberger P., Kieltsch I., Armanino N., Togni A., *Chem. Commun.*, **2008**, 1575.
2. Kieltsch I., Eisenberger P., Togni A., *Angew. Chem. Int. Ed.*, **2007**, *46*, 754.
3. Hintermann L., Togni A., *Helv. Chim. Acta*, **2000**, *83*, 2425.

Organic Chemistry **358**

## De Novo Synthesis of D-Galacturonosyl Glycosphingolipids

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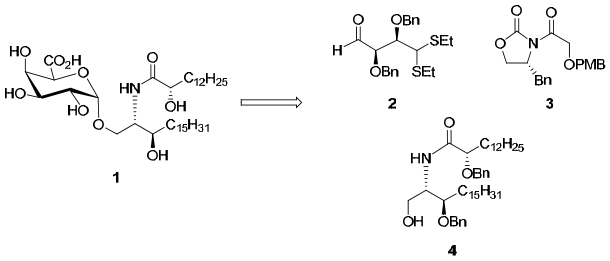
ETH Zurich, Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland

A concise de novo synthesis of a differentially protected D-galacturonic acid (D-GalA) thioglycoside and the construction of a potent immunomodulating glycosphingolipid are described [1]. Glycosphingolipids (e.g. **1**), with the sugar moiety forming an α-glycosidic linkage to a ceramide, exhibit an intriguing biological activity, since they are recognized by human natural killer T (NKT) cells, after binding to CD1d, thus inducing immune response.




The key steps of the synthesis are an Evans aldol reaction between C4 aldehyde **2** and PMB-protected glycolyl-oxazolidinone **3** as well as a tandem-PMB-deprotection/cyclization to thioglycosides. The key glycosylation step between ceramide **4** and the galacturonosyl donor is carefully optimized by varying the nature of the anomeric leaving group, the activating agent and the solvent system.

[1] P. Stallforth, A. Adibekian, P.H. Seeberger, *Org. Lett.* **2008**, *10*, 1573.

Organic Chemistry **359**

## Electrophilic Trifluoromethylation of Phenols using Hypervalent Iodine(III)-$CF_3$ Reagents

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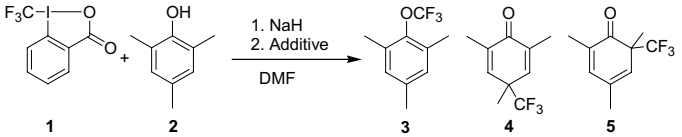
[a]Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology, ETH Zurich, CH-8093 Zurich, Switzerland.

For the introduction of a $CF_3$ moiety, harsh conditions and reagents such as HF, $SF_4$ or $SbF_5$ are needed at a very early stage of the synthesis. Clearly, a more versatile and fuctional group tolerant methodology is demanded.
We take advantage of our newly developed electrophilic, hypervalent iodine(III) trifluoromethylating agent **1**, which showed high selectivity and reactivity towards sulfur[1] and phosphorus[2] nucleophiles, to transfer a $CF_3$ group onto a phenol.
We were able to obtain the desired O-trifluoromethylated product **3** as a minor product in the special case of trimethylphenol **2**, along with trifluoromethylated cyclohexadienones **4** and **5**. We optimized the conditions, investigated the reaction mechanism and extended the reaction to other phenolic substrates.




[1] Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem. Int. Ed.* **2007**, 754.
[2] Eisenberger, P.; Kieltsch, I.; Armanino, N.; Togni, A. *Chem. Commun.* **2008**, 1575.

Organic Chemistry **360**

## Synthesis of a Water Soluble Cyclic Selenosulfide for Electrochemical and Radiationchemical Studies

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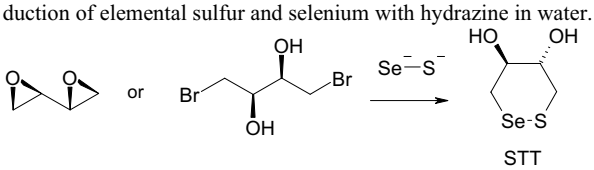
The redox chemistry of selenosulfides plays a vital role in selenoenzymes [1], nevertheless, fundamental electrochemical and radiation-chemical studies are rare. Inspired by [2,3], we synthesized *trans*-1,2-selenathiane-4,5-diol (STT): DL-1,3-butadiene diepoxide or DL-1,4-dibromobutane-2,3-diol was converted to STT in water by $SeS^{2-}$, which was prepared *in situ* by reduction of elemental sulfur and selenium with hydrazine in water.




STT is considered a suitable model compound for investigating selenosulfide oxidations states due to its high solubility in water, simplicity (no effects from other functional groups) and cyclic nature (minimal rearrangement to diselenides and disulfides during redox cycling).
The reduction potential of the STT/$STT^{2-}$ couple is being determined via the Nernst equation, by measuring redox equilibria with redox couples having known reduction potentials, and by cyclovoltammetry. The reduction potential is being compared with the disulfide and diselenide analogues. The radical anion and radical cation species are being studied by pulse radiolysis.

[1] S. Gromer, J. K. Eubel, B. L. Lee, J. Jacob, *Cell. Mol. Life. Sci*, **2005**, *62*, 2414
[2] M. Iwaoka, T. Takahashi, S. Tomoda, *Heteroatom Chemistry* **2001**, *4*, 293.
[3] E. N. Deryagina, V. A. Grabel'nykh, N. V. Russavskaya, O.V. Alekminskaya, *Russain Journal of General Chemistry* **2001**, *71*, 11, 1825

Organic Chemistry **361**

### Asymmetric Intramolecular Diels-Alder Reactions Using a Chiral Ruthenium catalyst

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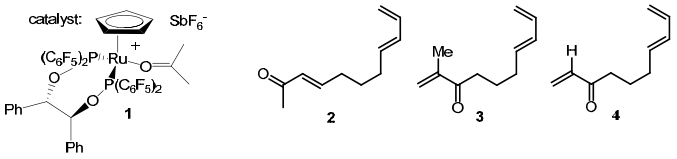
The intramolecular Diels-Alder (IMDA) reactions of 1,6,8-nonatrienes and 1,7,9-decatrienes are classic methods for the synthesis of the hexahydro-1*H*-indene and octahydronaphthalene substructures that occur in a wide range of natural products. [1] The first IMDA type II substrate using [CpRu(*R,R*-BIPHOP-F)(acetone)][$SbF_6$] (**1**) as chiral Lewis acid catalyst has been very successful.[2]
We here report on the continuation of these studies with the type I substrates **2**, **3** and **4**.




[1] (a) Roush, W. R. In *Comprehensive Organic Synthesis*; B. M. Trost,, Ed.; Pergamon Press: Oxford, **1991**, *5*, 513 (b) Roush, W. R.; Yakelis, N. A. *Org. Lett.* **2001**, *3*, 957. (c) Roush, W. R.; Dineen, T. A. *Org. Lett.* **2003**, *5*, 4725.
[2] Rickerby, J.; Vallet, M.; Bernardinelli, G.; Viton, F.; Kündig, E. P. *Chem. Eur. J.* **2007**, *13*, 3354..

Organic Chemistry **362**

### Design and Synthesis of Triphenylene Dimer: Towards Ordered Hexagonal Columnar Mesophases

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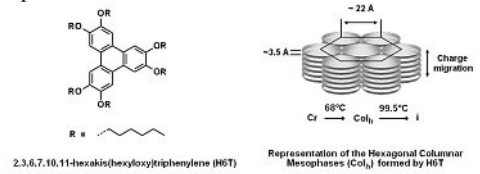
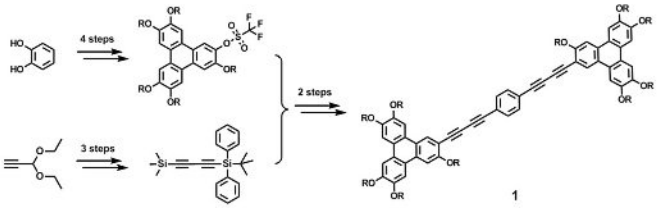
2,3,6,7,10,11-hexakis(alkoxy)triphenylene (**HAT)** are the most widely studied compounds in the field of discotic liquid crystals[1,2]. They are of interest because of their potential application as one dimensional conducting materials in photovoltaic devices.




This project aims to control the molecular alignment in the columnar mesophases with intermolecular interactions, in order to improve the electronic properties of the materials. The synthetic methodology leading to **1** and the liquid crystalline properties will be presented.




[1] Billard, J., Dubois, N. H., Zann, A., *Nouv. J. Chim.,* **1978**, *2,* 535-540
[2] Laschat, S., *et al*, *Angew. Chem. Int. Ed.,* **2007**, *46*, 4832-4887

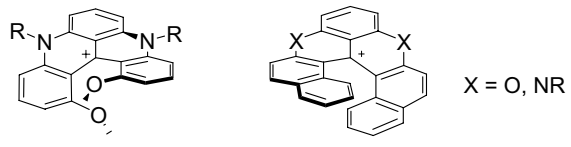
Organic Chemistry **363**

### Towards the synthesis of extended cationic helicenes

Franck Torricelli, Jérôme Lacour *

University of Geneva, Dept. of Organic Chemistry, Geneva, Switzerland.

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




(*M*) - **1** (*P*) - **2**

Herein, we report on the synthesis of novel extended [6] cationic helicenes of type **2** and discussed their resolution and optical properties.

[1] Urbano, A. *Angew. Chem. Int. Ed. Engl.* **2003**, *42*, 3986 and ref. therein.
[2] Hellwinkel, D.; Schmidt, W. *Chem. Ber.* **1980**, *113*, 358. Arai, S.; Ishikura, M.; Yamagishi, T. *J. Chem. Soc., Perkin Trans I*, **1998**, *9*, 1561.Laursen, B. W.; Krebs, F. C. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 3432. Laali, Kenneth K.; Chun, Joong-Hyun; Okazaki, Takao; Kumar, Subodh; Borosky, Gabriela L.; Swartz, Carol *J. Org. Chem*., **2007**, *72*, 8383 and ref. therein.
[3] Herse, C.; Bas, D.; Krebs, F. C.; Bürgi, T.; Weber, J.; Wesolowski, T.; Laursen, B. W.; Lacour, J. *Angew. Chem. Int. Ed. Engl.* **2003**, *42*, 3162; Laleu, B.; Mobian, P.; Herse, C.; Laursen, B. W.; Hopfgartner, G.; Bernardinelli, G.; Lacour, J. *Angew. Chem. Int. Ed. Engl.* **2005**, *44*, 1879.

Organic Chemistry **364**

### Vitamin $B_{12}$ Binding to Peptide Dendrimers and Cyclic Peptides

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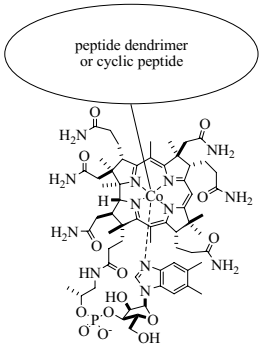
Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

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 aquocobalamine.[1] Presently, also cyclic peptides are under investigation. The binding interactions were explored by $^1$H NMR studies, ligand-ligand exchange reactions and UV/Vis titrations.




[1] P. Sommer, N. A. Uhlich, J.-L. Reymond and T. Darbre *ChemBioChem* **2008**, *9*, 689-693.

Organic Chemistry **365**

## MECHANISTIC ASPECTS OF ELECTROPHILIC FLUORINATION

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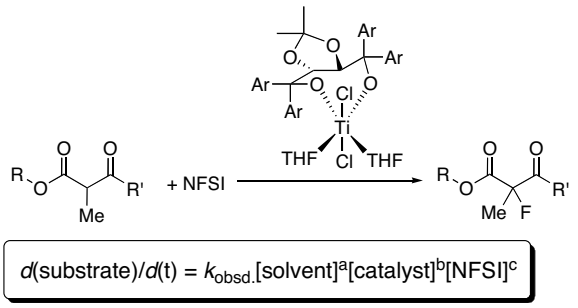
Department of Chemistry and Applied Biosciences

Swiss Federal Institute of Technology

ETH Zürich, CH-8093 Zürich, Switzerland

Enantioselective electrophilic fluorination mediated by chiral titanium Lewis acids is historically the first metal mediated fluorination. We like to present the recent results for the fluorination of ß-ketoesters with NFSI mediated by titanium taddolato complexes. The mechanistic approach is based on complementary spectroscopic and kinetic analyses. The effects of the solvent, catalyst, substrate and NFSI are used to draw a detailed picture of the rate law and intricacies of this catalytic system. The mechanistic data are the basis for the development of new and more efficient Taddol-based catalysts in a rational way.




$$d(\text{substrate})/d(t) = k_{obsd.}[\text{solvent}]^a[\text{catalyst}]^b[\text{NFSI}]^c$$

Organic Chemistry **366**

## Improving the Ru-Catalyzed Olefin Metathesis Reactions: Use of N,N'-binaphtyl substituted *N*-Heterocyclic Carbenes (NHC) as a new Class of Ligands

Ludovic Vieille-Petit, Reto Dorta*

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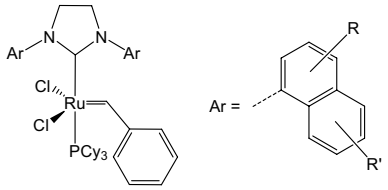
Olefin metathesis has attracted widespread attention as a versatile carbon-carbon bond-forming method.[1] Many new applications have become possible because of major advances in catalyst design. State-of-the-art ruthenium catalysts are not only highly active but also compatible with most functional groups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

We report herein on the preparation of N,N'-binaphtyl substituted *N*-heterocyclic carbenes as a new class of ligands for the Ru-catalyzed olefin metathesis reaction. The discussion includes ongoing work to improve activity, stability, and selectivity of this family of (NHC)(L)$X_2$Ru=CHR complexes.




[1] For reviews on olefin metathesis, see: (a) Trnka, T.M.; Grubbs, R. H. *Acc. Chem. Res*. **2001**, *34*, 18. (b) Fürstner, A. *Angew. Chem. Int. Ed*. **2000**, *39*, 3012.
[2] Scholl, M.; Ding, S.; Lee, C.W.; Grubbs, R.H. *Org. lett*. **1999**, 953.

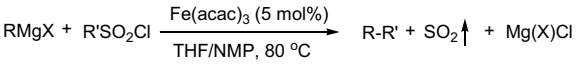
Organic Chemistry **367**

## Recent developments in Iron-catalyzed Carbon-Carbon bond forming reactions

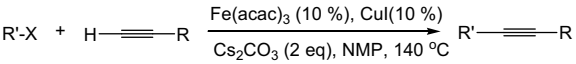
Chandra M. Rao Volla and Pierre Vogel*

Swiss Federal Institute of Technology (EPFL), Batochime, BCH-5418, CH-1015, Lausanne, Switzerland

Transition-metal-catalyzed reactions are among the most powerful methods of organic synthesis.[1] Although there has been major emphasis on palladium, there are some major drawbacks, toxicity, cost and sometimes the requirement of expensive and/or toxic ligands. So there is an increasing attention towards developing new reactions using iron catalysts, which are cheap, non-toxic and environmentally benign.[2] We present here a novel desulfinylative C-C cross-coupling reaction using inexpensive sulfonyl chlorides and Grignard reagents.[3] The reaction proceeds under mild conditions in the presence of catalytic amount of iron(III) salts.




We also found that aryl iodides can be coupled with terminal alkynes in the presence of catalytic amounts of iron salt and CuI. These new methodologies do not require any ligands.




[1] Tsuji, J. *Palladium Reagents and Catalysts,* 2nd ed., Wiley, Chichester, **2004**.; Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359.
[2] Bolm, C; Legros, J; Le Paih, J; Zani, L, *Chem. Rev*. **2004,** *104,* 6217; Fürstner, A; Martin, R, *Chem. Lett.* **2005**, *34*, 624.
[3] Volla, C. M. Rao; Vogel, P, *Angew. Chem. Int. Ed.* **2008***, 47*, 1305.

Organic Chemistry **368**

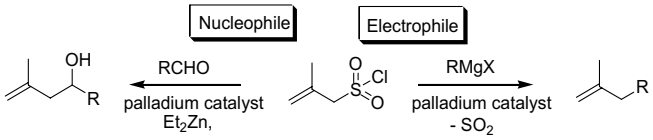
## New reactions of organosulfur compounds : Allylsulfonyl derivatives as new Electrophilic and Nucleophilic C-C Allylating agents

Chandra M. Rao Volla, Srinivas Reddy Dubbaka and Pierre Vogel*

Swiss Federal Institute of Technology (EPFL), Batochime, BCH-5418, CH-1015, Lausanne, Switzerland.

Transition-metal-catalyzed carbon-carbon and carbon-heteroatom bond forming reactions are among the most powerful methods of organic synthesis.[1] We have shown previously that aromatic sulfonyl chlorides can be coupled with all kinds of nucleophiles, in the presence of a palladium catalyst.[2] Now we have successfully extended this concept to allyl systems.

Allylsulfonyl chlorides have been synthesized by the three component ene-reaction of allylsilanes and $SO_2$ in the presence of a Lewis acid followed by chlorination.[3] They were successfully used both as electrophiles towards Grignard reagents and as nucleophiles towards aldehydes by umpolung in the presence of transition metal catalysts.




Application of Nozaki-Hiyama-Kishi reaction to sulfonyl chlorides was also investigated. Allyl sulfonylchlorides reacted with aldehydes in the presence of $CrCl_2$ to give the corresponding homoallylic alcohols in moderate to good yields.

[1] Tsuji, J. *Palladium Reagents and Catalysts,* 2nd ed., Wiley, Chichester, **2004**.
[2] Dubbaka, S. R.; Vogel, P. *Angew. Chem. Int. Ed.* **2005**, *44*, 7674.
[3] Bouchez, L.; Vogel, P. *Synthesis* **2002**, 225; Dubbaka, S. R.; Turks, M.; Vogel, P. *J. Org. Chem.* **2004**, *69*, 6413.

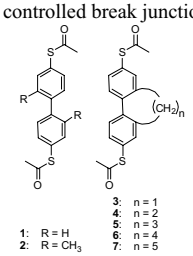
Organic Chemistry **369**

### Tricyclic Biphenyls: Conformation under Control

David Vonlanthen,[1] Mark Elbing,[2] Markus Neuburger,[1] and Marcel Mayor*[1,2]

1.) Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland
2.) Forschungszentrum Karlsruhe GmbH, Institute for Nanotechnology, P.O.Box 3640, D-76021 Karlsruhe, Germany

The understanding of electronic transport through a single molecule is a scientific challenge, which became experimentally addressable only recently.[1] The conductance of biphenyl structures on molecular level is expected to change with the relative twist angle between the two phenyl rings due to the change of the π-overlap. Self-assembled monolayers (SAMs) and molecular conformation of the biphenyl-derived dithiols (BDDTs) **1-4** have been described before.[2] A series of mixed and heteroatom-substituted biphenyldiamines have been recently investigated by mechanically controlled break junction (MCB).[3]




The torsion angle of the consistent bridged but difficult to access BDDTs **4-7** is adjusted by the number of inserted C-Atoms. The attached thiol moieties allow immobilization in a MCB, whereby the I/V characteristics can be obtained. The correlation between the back bone conformation (adjustment of the torsion angle by choosing the number of C-Atoms) and conductance on molecular level may lead to a new perception regarding electronic transport mechanism in conjugated systems.

[1] C. Joachim, J. K. Gimzewski, A. Aviram, *Nature* **2000**, *408*, 541.
[2] A. Shaporenko, M. Elbing, A. Blaszczyk, C. vonHanisch, M. Mayor, M. Zharnikov, *J. Phys. Chem. B* **2006**, *110*, 4307.

Organic Chemistry **370**

### Antimicrobial Surfaces Through Natural Product Hybrids

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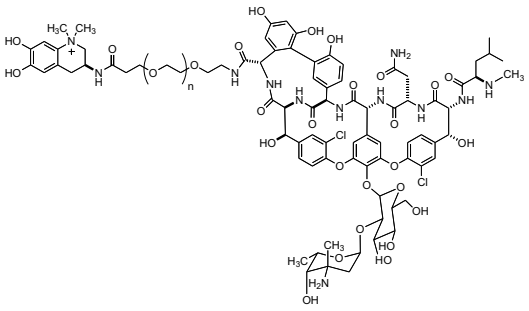
Hybridization of natural products is a strategy which employs covalent linkage of two natural products (or fragments) to obtain compounds with combined biological activity[1] and sometimes superior properties compared to the fragments resulting from synergetic effects.[2]



In this communication, we present a hybrid combining the chromophore of anachelin and the antibiotic vancomycin allowing for the preparation of antimicrobial and cell-resistant surfaces through a mild dip-and-rinse procedure.[3]

[1] Review: Gademann, K., *Chimia* **2006**, *60*, 841-845.
[2] Review: Tietze, L. F., Bell, H. P., Chandrasekhar, S., *Angew. Chem., Int. Ed.* **2003**, *42*, 3996.
[3] Wach, J.-Y., Bonazzi, S., Gademann, K., *Angew. Chem. Int. Ed.*, **2008**, *in press.*

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### *In vitro* selection of novel Diels-Alder Ribozymes

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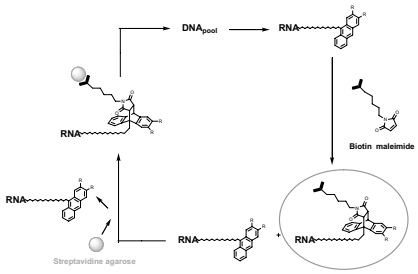
Since the discovery of the catalytic activity of RNA, many natural Ribozymes have been reported. *In vitro* selection and evolution have become powerful tools for discovering new artificial Ribozymes that catalyse chemical reactions like hydrolysis or peptide bond forming reactions.
Our laboratory has reported a Ribozyme catalysing carbon-carbon bond formation, in a **Diels-Alder reaction** between maleimide and anthracene under ambient conditions.[1,2] Our in vitro synthetic approach is now being extended to ribozymes with the ability to process sterically more demanding substrates, function at elevated temperatures and to identify potential alternatives to the original 49mer structure.




[1] A. Serganov *et al*, Structural Basis for Diels-Alder ribozyme-catalyzed carbon-carbon bond formation, *Nat. Struct. Mol. Biol.* **2005**, *12,* 218.
[2] J. J. Agresti *et al*, Selection of ribozymes that catalyse multiple-turnover Diels–Alder cycloadditions by using in vitro compartmentalization, *PNAS*, **2005**, *102*, 16170.

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### Conformational change of oligopyrenes induced by a DNA B-to-Z transition

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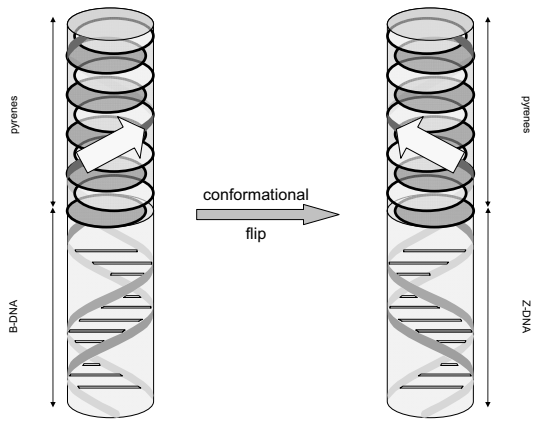
The arrangement of a non-nucleosidic oligopyrene part embedded between two natural oligonucleotide sequences was shown to be helical, following the arrangement of the natural part [1]. Based on these findings we developed a molecular system that allows the conformational change of the pyrene segment by manipulating the DNA part.




[1]V.L. Malinovskii, F. Samain and R. Häner, *Angew. Chem. Int. Ed*, **2007,** *46***,** 4464.

Organic Chemistry **373**

**Synthesis, Fluorescence Properties, and Incorporation into DNA of Triazolylpyrenes**

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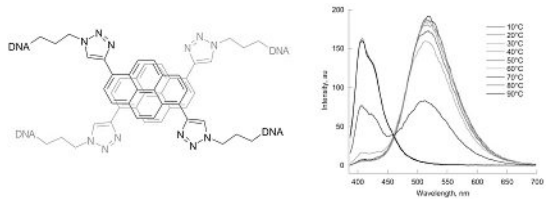
Pyrene and its derivatives are promising candidates for use in DNA-based diagnostics and applications in material sciences[1,2]. The synthesis of 1,6- and 1,8-triazolylpyrenes and their incorporation into oligonucleotides will be presented[3].




In hybrids, triazolylpyrenes adopt interstrand stacking interactions. For the duplex containing a pair of the 1.6-isomer exciton coupling is observed by CD-spectroscopy that indicates a well-defined helical arrangement of the triazolylpyrene building blocks. The substitution of pyrene with triazole results in pronounced red-shifts of monomer as well as excimer fluorescence. Furthermore, quantum yields of the formed excimers are remarkably high[3]. UV/Vis-, fluorescence- and CD-spectra as well as thermal denaturation experiments will be shown.

[1] R. T. Ranasinghe, T. Brown *Chem. Commun.* **2005**, 5487–5502.
[2] V. L Malinovskii, F. Samain, R. Häner *Angew. Chem., Int. Ed.* **2007**, *46*, 4464.
[3] S. Werder, V.L. Manlinovskii, R. Häner *Org. Lett.* **2008**, *10*, 2011-2014

Organic Chemistry **374**

**Synthesis and Biological Evaluation of the Neuroactive Steroid Withanolide A**

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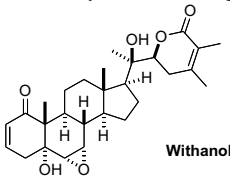
Neurodegenerative dieases such as Alzheimer's and Parkinson's are becoming more prevelant in society due to an ageing population. Therefore, the need for drugs capable of treating these dieases is becoming more urgent. Neuritic atrophy is considered one of the major causes for the loss of cognitive function in sufferers of neurodegenerative dieases. [1]
The dried roots of *Withania Somnifera* (Ashwagandha) have been used in herbal medicine for many years, particularly in Ayurvedic medicine. [2] Moreover, it has been shown that the methanol extracts of Ashwagandha are capable of inducing neurite outgrowth. [3] Subsequent isolation and structural elucidation identified the highly oxygentated steroid Withanolide A as one of the active species in Ashwagandha. [4]
As part of a program aimed at synthesising potent neuroactive natural products in our laboratories we propose to synthesise Withanolide A and derivatives thereof and test their activity in neurite outgrowth assays.



**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] Mishra, L-C.; Singh. B. B; Dagenais, S. *Alt. Med. Rev.* **2000**, *5,* 334.
[3] a) Kuboyama, T.; Tohda, C.; Komatsu, K. *NeuroReport.* **2000**, *11*, 1981. b) Kuboyama, T.; Tohda, C.; Komatsu, K. *NeuroReport.* **2002**, *13*, 1715.
[4] Kuboyama, T.; Tohda, C.; Komatsu, K. *Br. J. Pharm.* **2005**, *144,* 961.

Organic Chemistry **375**

**Assay development for the discovery of novel DNA base-pairs**

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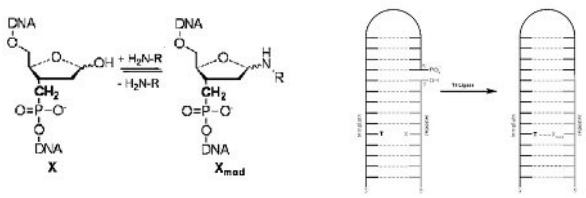
We are interested in finding novel DNA bases or base-pairs, e.g. for use as universal bases, or for the expansion of the genetic code. However, the synthesis of the requisite nucleosides is time-consuming, and design rules for bases interacting with each other or with natural bases different from the Watson-Crick base-pairing rules are largely elusive. We therefore developed a combinatorial assay which allows for fast and easy evaluation of novel DNA base candidates. The assay is based on the use of a chemically stable and functional abasic site analogue (X) in an oligonucleotide duplex having identical functionality to a natural abasic site which is, however, resistant towards β- and δ-elimination. [1] A library of diversely substituted amines reversibly forming hemiaminals with X is used to investigate the interactions of the amines with the opposite base in the duplex, by determining ligation rates in a template/ reporter system. (Figure)
We have screened a library of 34 amines and we have identified novel aromatic amines recognizing T.




[1] Mosimann, M.; Küpfer, P. A.; Leumann, C. J. *Org. Lett.* **2005**, *7*, 5211-5214

Organic Chemistry **376**

**A Layered Red-Emitting Chromophoric Organic Salt**

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Careful selection of molecules containing functional groups which assemble in the solid state allows the construction of robust molecular architectures exhibiting a diverse variety of motifs[1-2].

We have investigated the synthesis as well as the self-assembly and the optical properties of a novel π-conjugated system (Figure 1). Through the combined actions of directional hydrogen bonds and Coulombic interactions, a two-dimensional molecular topology is realized whereby the extended layers of strongly chromophoric π-conjugated anions are spatially isolated by tetrabutylammonium cations. The sandwich type structural motif suppresses the quenching of the solid state emission and gives reliable geometrical parameters to probe the excited states by the theoretical molecular exciton approximation.

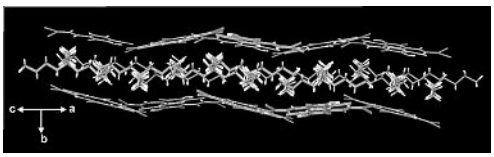

Figure 1. Crystal structure of the salt

[1] Desiraju, G. R. *Angew. Chem. Int. Ed.* **2007**, *46*, 8342.
[2] Yi, C. Y.; Blum, C.; Liu, S. X.; Ran, Y. F.; Frei, G.; Neels, A.; Stoeckli-Evans, H.; Calzaferri, G.; Leutwyler S.; Decurtins, S. *Cryst. Growth Des.* **2008**, *Accepted.*

doi:10.2533/chimia.2008.652 CHIMIA **2008**, *62*, No. 7/8

Organic Chemistry **377**

## Pd/NHC-Catalyzed Asymmetric Intramolecular α-Arylation Reactions

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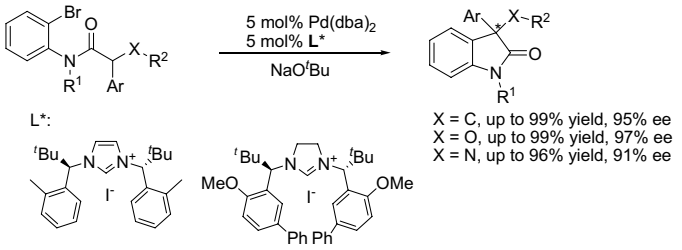
The palladium-catalyzed intramolecular α-arylation reaction of amides provides an efficient synthetic access to oxindoles. For the asymmetric version, many chiral ligands have been screened in the reaction and, prior to our study, the highest enantioselectivity reached was 76%. [1]
We have developed new chiral *N*-heterocyclic carbene ligands (NHCs) for this reaction. Their application in Pd-catalyzed reactions allows asymmetric oxindoles to be accessed efficiently and with high asymmetric induction. This includes, for the first time, also products with heteroatoms at the stereogenic center.[2,3]




[1] (a) S. Lee, J. F. Hartwig, *J. Org. Chem.* **2001**, *66*, 3402. (b) F. Glorius, G. Altenhoff, R. Goddard, C. Lehmann, *Chem. Commun.* **2002**, 2704. (c) T. Arao, K. Kondo, T. Aoyama, *Tetrahedron Lett.* **2006**, *47*, 1417.
[2] (a)E. P. Kündig, T. M. Seidel, Y.-X. Jia, G. Bernardinelli. *Angew. Chem., Int. Ed.* **2007**, *46*, 5565. (b) Unpublished results.
[3] In collaboration with the group of Dr. S. Marsden, Leeds, UK.

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## A Novel Strategy towards the Total Synthesis of Rhazinilam Analogue

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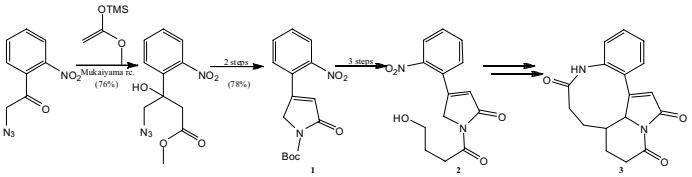
The alkaloid rhazinilam shows significant *in vitro* cytotoxicity, but no activity was found *in vivo* [1]. Our synthetic strategy is to replace, in the first time, the pyrrole ring by a corresponding pyrrole-2(5*H*)-one ring [2] using Mukaiyama crossed aldol reaction followed by Staudinger reaction.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




[1] O. Baudoin, D. Guénard, F. Guéritte, *Mini-Rewiews in Organic Chemistry* **2004**, *1*, 333-341.

[2] O. Vallat, A.-M. Buciumas, A. Neels, H. Stoeckli-Evans and R. Neier (2008. in preparation).

[3] M.G. Banwell, D.A.S. Beck and A. Willis, *ARKIVOK* (Gainesville, FL, U. S.) **2006**, 163-174.

Physical Chemistry **379**

## Competition between Charge Injection and Reductive Quenching at the Surface of Dye-Sensitized Semiconductors

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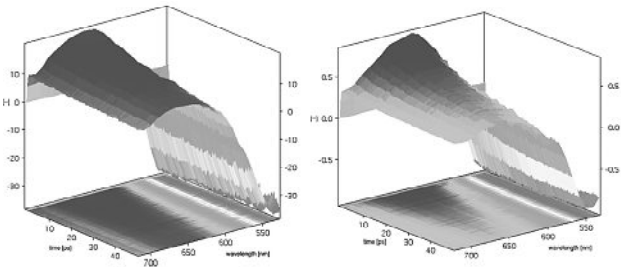
Aiming at the development of dye sensitized solar cells, photoinduced electron transfer at the surface of dye-sensitized semiconductors has been widely studied. Kinetic heterogeneities of the charge injection have been revealed and related, among other, to dye aggregation [1].



Comparison of the dynamics of Ru(II) complex dye excited states on alumina films (into which the dye doesn't inject) in the presence of reducing species (right) and in pure solvent (left), confirms that reductive quenching of the excited dye state by iodide does constitute an independent electron transfer pathway.
The time scale for such a process is in the order of tens of picoseconds and can indeed efficiently compete kinetically with other reactions involving the dye excited state, like the electron injection in titanium dioxyde.

[1] Wenger B., Grätzel M., Moser J.-E., *J. Am. Chem. Soc.*, **2005**, *127*, 12150.
[2] Thorsmølle V. K., Wenger B., Teuscher J., Bauer C., Moser J.-E., *Chimia*, **2007**, *61*, 631.

Physical Chemistry **380**

## From Radical Chemistry to Autoxidation Catalysis

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The liquid-phase oxidation of hydrocarbons such as cyclohexane and *p*-xylene are important processes in the chemical industry.[1] Despite their importance, the fundamental chemistry was not yet fully understood. Under the reaction conditions, the slow direct reaction of $O_2$ with the hydrocarbon is outrun by a much more efficient radical chain mechanism. It is generally accepted that the hydroperoxide is formed in a fast propagation reaction of chain carrying peroxyl radicals with the hydrocarbon substrate, whereas the alcohol and ketone were assumed to be formed in the slow termination reaction between two peroxyl radicals. This established vision is however at odds with several experimental observations. Based on a jointly combined theoretical and experimental study,[2-5] the hitherto overlooked, but very fast propagation of the hydroperoxide was recently identified as the predominant source of the ketone and alcohol product. The product distribution of various hydrocarbons can be readily rationalized by the rate of ROOH propagation, and the efficiency of the subsequent activated cage reaction.[3] During the presentation, several examples of catalyst design, based on this revised mechanism, will be discussed.

**references**

[1] R.A. Sheldon, J.K. Kochi, *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, **1981**.
[2] I. Hermans, T.L. Nguyen, P.A. Jacobs, J. Peeters, *ChemPhysChem* **2005**, *6*, 637.
[3] I. Hermans, J. Peeters, P.A. Jacobs, *J. Org. Chem.* **2007**, *72*, 3057.
[4] I. Hermans, P. Jacobs, J. Peeters, *Chem. Eur. J.* **2007**, *13*, 754.
[5] I. Hermans, P.A. Jacobs, J. Peeters, *Chem. Eur. J.* **2006**, *12*, 4229.