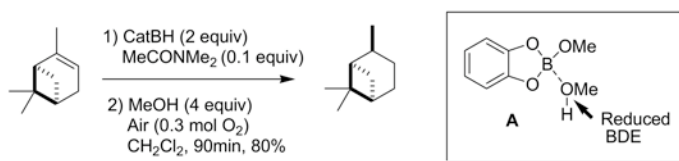


Alcohols and Water as Reducing Agents in Radical Reactions

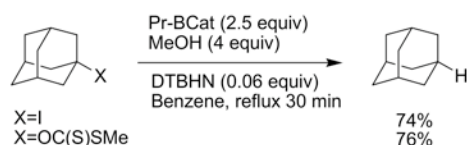
Davide Pozzi and Philippe Renaud*

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

Very recently we discovered that alkyl radicals, generated by decomposition of *B*-alkylcatecholboranes under dioxygen or peroxide initiation, can be reduced using methanol (other alcohols and water work similarly) as radical reducing agent [1]. The MeO-BCat activates methanol by formation of a Lewis acid-base complex **A** resulting in a decrease of the O-H bond dissociation energy.



The same procedure was applied for the deoxygenation of alcohols and the reduction of halides using propylcatecholborane (Pr-BCat) as radical chain propagator.



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

Polymerization and Dehydrogenation of Acetylene with an Iron(0)/DIBAH Catalyst on an Appropriated Template: Toward a Rational Synthesis of Carbon Nanotubes

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Since their discovery, carbon nanotubes became a major research subject in nanoscience and nanotechnology. Their particular mechanical and electronic properties are promising for many applications in different fields of science. Carbon nanotubes preparation has been very much improved, using many physical procedures as HiPco or PLV, but only moderate control on geometry, length or diameter is possible up to now. Contamination of bulk nanotubes by catalytic particles, nanocapsules or amorphous carbon is the other main disadvantage of synthesis under physical conditions.

The development of catalytic systems able to polymerize and dehydrogenize acetylene under mild conditions to form graphitic structures is the starting point of this work.

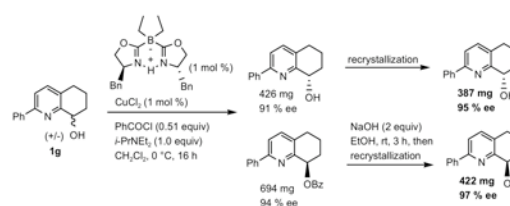
On the one hand, this procedure is applied on carbon nanotube pieces, beforehand cut by mechanical treatment. This short tubule part must act as a template for the growth of nanotubes under polymerization conditions. In the other hand, synthesis of well defined templates, such as [0₅]paracyclophane and [0₆]paracyclophane, is in progress. The synthetic route involves first a cyclization of a precursor, followed by aromatization. Indeed, such macrocycles are ideal templates as starting point for a carbon nanotubes growing process, because they offer the possibility to choose the diameter and the geometry of carbon nanotubes.

Iridium-Catalyzed Asymmetric Hydrogenation: Synthetic and Mechanistic Studies

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Switzerland

Enantioselective hydrogenation of simple, alkyl-substituted olefins is possible using iridium catalysts incorporating chiral P,N- ligands, derived from bicyclic pyridyl alcohols.¹ In connection with that work, kinetic resolution of pyridyl alcohols by Cu(II)(borabox)-catalyzed acylation has been investigated and the results of this study will be presented. Access to both enantiomers of a ligand precursor is possible using this method due to the high selectivity of the resolution.²



Deuterium labeling studies and DFT (Density Functional Theory) calculations are being used to obtain information about the mechanism of enantioselective hydrogenation and related processes. The latest results will be presented.

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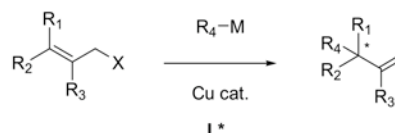
[2] C. Mazet, S. Roseblade, V. Kohler, A. Pfaltz, *Org. Lett.*, **2006**, *8*, 1879-1882.

Allylic Substrates for the Copper Catalyzed Asymmetric S_N2' Reaction

Caroline A. Falcicola, Alexandre Alexakis*

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The formation of chiral centers via a copper catalyzed asymmetric allylic alkylation using external chiral ligands has already shown very good enantioselectivities. Our group has previously demonstrated that monodentate phosphoramidite ligands are good chiral inductors and alkyl functions through diverse organometallic reagents can be added to allylic substrates with excellent enantiomeric excess [1-3].



Herein we present that small functionalized allylic substrates can be versatile starting material and show good enantioselectivities for the copper catalyzed addition of organometallic reagents (up to >99% ee) with excellent regioselectivities. Various reactions can then be carried out with no loss of the optical purity for the further derivatization of these products.

[1] Alexakis A., Croset K., *Org. Lett.*, **2002**, *4*, 4147-4149

[2] Tissot-Croset K., Alexakis A., *Tetrahedron*, **2004**, *45*, 7375-7378

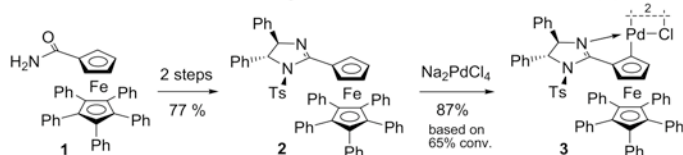
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FIP: a Practical Catalyst for Aza-Claisen Rearrangements

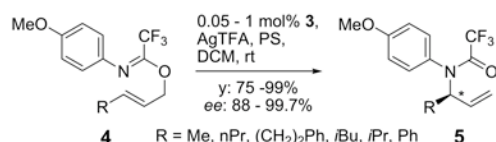
Daniel F. Fischer, Matthias E. Weiss, Zhuo-qun Xin, Sascha Jautze, René Peters*

Laboratorium für Organische Chemie, ETH Zürich, HCI, CH-8093 Zürich

The Pd(II) catalyzed aza-Claisen (Overman) rearrangement allows the transformation of achiral allylic imidates (readily prepared in one step from allylic alcohols) into chiral protected allylic amine derivatives, which are e.g. valuable intermediates for the synthesis of unnatural amino acids.[1]



The novel ferrocenyl imidazoline palladacycle **3** is easily prepared by a practical three-step synthesis starting from amide **1** using a direct diastereoselective cyclopalladation as the key step, and is unprecedentedly active and enantioselective tolerating a broad range of imidate substrates **4** possessing branched / unbranched aliphatic or aromatic groups R.[2]



- [1] S. F. Kirsch, L. E. Overman, M. P. Watson, *J. Org. Chem.* **2004**, *69*, 8101.
 [2] E. Weiss, D. F. Fischer, Z. Q. Xin, S. Jautze, W. B. Schweizer, R. Peters, *Angew. Chem. Int. Ed* **2006**, *accepted*.

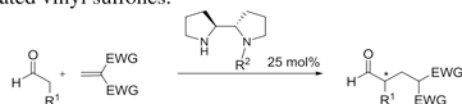
Organocatalyzed Asymmetric Michael Addition using 2,2'-Bipyrrolidine Derivatives

S. Mossé, A. Alexakis*

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

In the last few years, organocatalysis has become very attractive and the focus of intense research efforts [1]. After having developed a highly enantioselective Michael addition of aldehydes and ketones to nitroolefins catalyzed by *N*-*i*-Pr-2,2'-bipyrrolidine (*i*BPB, R²=*i*Pr) [2], we applied our catalyst on vinyl sulfones as Michael acceptors.

We have disclosed the first direct asymmetric conjugate addition of aldehydes to vinyl sulfones catalyzed by diamine *i*BPB in good yields and enantioselectivities up to 80% ee [3]. Unlike the impressive reactivity of vinyl geminal bis-sulfones (EWG = SO₂Ph), no reaction was observed with mono-activated vinyl sulfones.



Consequently, we are currently interested in synthesizing and testing other Michael acceptors bearing geminal bis-electron-withdrawing groups (EWG) to confirm our hypothesis of double activation.

- [1] For a recent review, see Dalko, P. I.; Moisan, L. *Angew. Chem. Int. Ed.* **2004**, *43*, 5138.
 [2] Andrey, O.; Alexakis, A.; Tomassini, A.; Bernardinelli, G. *Adv. Synth. Catal.* **2004**, *346*, 1147 and references cited therein.
 [3] Mossé, S.; Alexakis, A. *Org. Lett.* **2005**, *7*, 4361.

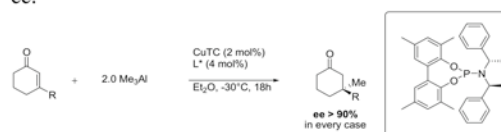
Enantioselective Cu-Catalyzed Conjugate Addition to Trisubstituted Cyclohexenones. Construction of Chiral Quaternary Carbon Centers.

Magali d'Augustin and Alexandre Alexakis

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

The copper-catalyzed asymmetric conjugate addition has found an impressive success, and many authors have described over 600 chiral ligands to do this transformation.[1] Moreover, the all-carbon quaternary stereogenic centers is an important challenge for organic chemist.[2]

We report here a highly efficient catalytic asymmetric conjugate addition of Me₃Al and Et₃Al to various trisubstituted cyclic enones, with up to 96.6% ee.[3]



Substrates bearing various functionalities are well tolerated, again with high yields and enantioselectivities.

The synthetic application of such functionalized 1,4-adduct is the straightforward construction of chiral building blocks for more elaborated natural products, such as axamide and axisonitrile.

- [1] Alexakis, A., Benhaim, C. *Eur. J. Org. Chem.* **2002**, 3221.
 [2] (a) Denissova, I., Barriault, L. *Tetrahedron* **2003**, *59*, 10105. (b) Douglas, C.J., Overman, L.E. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5363.
 [3] d'Augustin, M., Palais, L., Alexakis, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 1376.

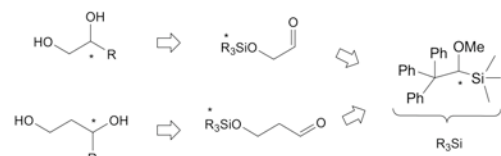
A New Si-based Auxiliary for Stereospecific Addition of Organometallics to α - and β -Hydroxy Carbonyl Compounds

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Various functionalized chiral 1,2- and 1,3-alkanediols are important fragments of natural products and bioactive molecules. Enantioselective synthesis of these structures by addition of organometallics to the corresponding α - or β -hydroxy carbonyl compounds remains an interesting challenge [1], and several chiral catalysts as well as auxiliaries have already been employed to effect stereoselectivity [2].

In this field remarkable results have been achieved using a silicon moiety to control the stereochemical course of the reactions [3]. We present a newly designed silicon auxiliary which acts concurrently as a protective and "stereodirecting" group in the above mentioned transformations.



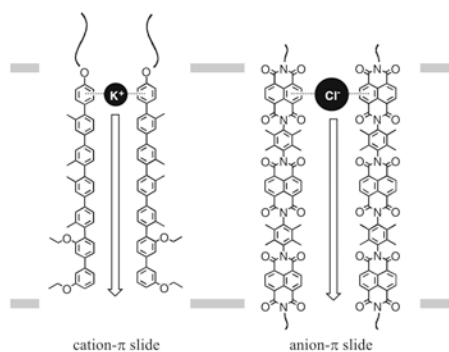
- [1] Timothy B. Durham, Nicolas Blanchard, Brad M. Savall, Noel A. Powell, and William R. Roush, *J. Am. Chem. Soc.* **2004**, *126*, 9307.
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 [3] Michael Trzoss, J. Shao, and Stefan Bienz, *Tetrahedron* **2002**, *58*, 5885.

Rigid Naphthalenediimide Rods as Anion- π Slides in Lipid Bilayer Membranes

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1211 Geneva, Switzerland

The rigid *p*-oligophenyl rods have served well as privileged scaffolds in synthetic nanoarchitecture in bilayer membranes that can function as porous sensors or smart photosystems [1]. The only example for a functional rather than structural role of rigid *p*-oligophenyl rods is a transmembrane π -slide, where potassium cations are thought to hop from cation- π to cation- π site along the scaffold to cross a bilayer membrane [2]. Here, the inverted quadrupole moment of the naphthalenediimide module is reported to provide access to the complementary rigid-rod anion- π -slides.

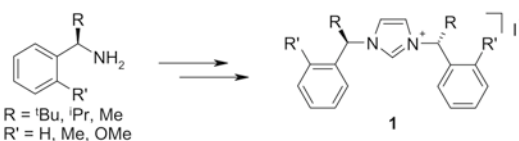


- [1] N. Sakai, J. Mareda, S. Matile, *Acc. Chem. Res.* **2005**, *38*, 79-87.
[2] M. M. Tedesco, B. Ghebremariam, N. Sakai, S. Matile, *Angew. Chem. Int. Ed.* **1999**, *38*, 540-543.

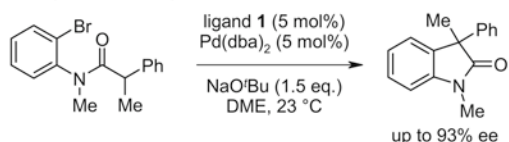
Chiral 2-(1-Aminoalkyl)phenols as Building Blocks for New Chiral Ligands

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Department of Organic Chemistry, University of Geneva,
30, Quai E. Ansermet, 1211 Geneva, Switzerland



2-(1-aminoalkyl)phenol building blocks¹ have been applied to the synthesis of new chiral ligands. The most promising class of the bulky carbene ligands **1** were applied successfully to an asymmetric Pd-catalyzed intramolecular amide arylation, affording oxindoles. Its use strongly improved the enantioselectivity of the reaction (see below) when compared to literature precedent (max. 65% ee).²



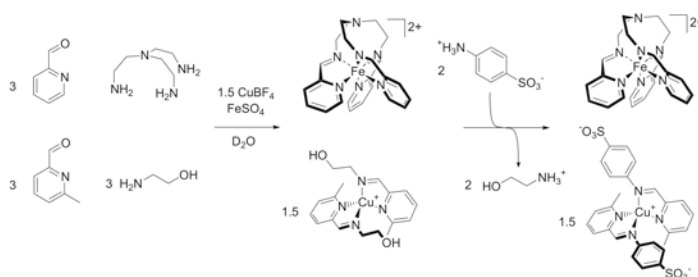
- [1] a) Kündig, E. P.; Botuha, C.; Lemercier, G.; Romanens, P.; Saudan, L.; Thibault, S. *Helv. Chim. Acta* **2004**, *87*, 561. b) Bernardinelli, G.; Fernandez, D.; Gosmini, R.; Meier, P.; Ripa, A.; Schupfer, P.; Treptow, B.; Kündig, E. P. *Chirality* **2000**, *12*, 529.
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Dynamic Assembly And Reassembly of Metallo-Organic Complexes from Subcomponents

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The field of subcomponent self-assembly is emerging as a means to rapidly build up new structures. Dynamic self-assembly processes are based on reversible reactions, therefore thermodynamic factors direct the syntheses of our products. Such reactions were combined to create a new kind of cascade reaction operating at both covalent and supramolecular levels [1]. We were also able to form selectively two complexes from a dynamic combinatorial library of ligand subcomponents, where iron (II) and copper (I) cooperatively selected those subcomponents best able to form stable complexes [2]. This thermodynamically stable mixture can undergo a selective ligand-component substitution on the copper complex leaving the iron complex untouched.



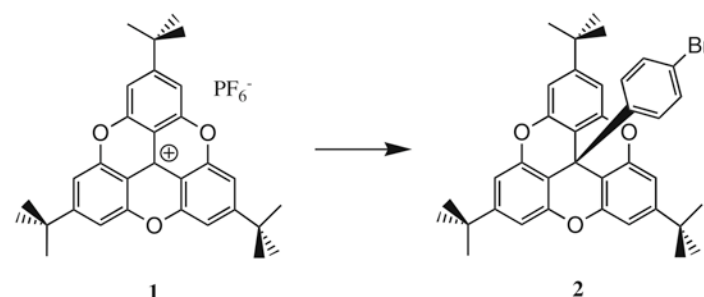
- [1] D. Schultz, J.R. Nitschke, *Proc. Nat. Acad. Sci. USA* **2005**, *102*, 11191.
[2] D. Schultz, J.R. Nitschke, *Angew. Chem. Int. Ed.* **2006**, *45*, 2453.

Trioxatricornan derivatives: Reactivity and Building Blocks

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The polycyclic aromatic *t*-butyl trioxatricornan **1** will be used as the base molecule due to the facile modification at the central position, large surface area and solubility. The 8-step synthesis of the *t*-butyl trioxatricornan **1** begins with 2,6-dimethoxyphenol [1] [2]. Nucleophilic addition to the central position with 1,4-dibromobenzene provides the molecular base for additional modifications **2** [3].



The central position has been functionalized in order to investigate the reactivity of a series of compounds. This series of compounds also allows for the study of photophysical effects. Moreover, the molecular base can provide a platform to supermolecular structures, e.g. rotaxanes or dendritic structures.

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[2] A. Faldt, F.C. Krebs, N. Thorup, *J. Chem. Soc., Perkin Trans. 2*, **1997**, 2219.
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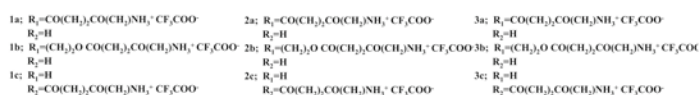
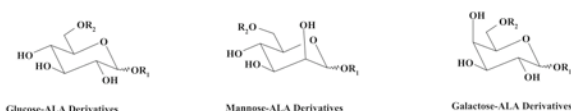
Sugar ALA (5-Aminolevulinic acid) derivatives -A Sweet Alternative for ALA in PDT (Photodynamic therapy)?

Ramakrishnan Vallinayagam, Schmitt Frédéric,
Juillerat-Jeanneret Lucienne, Neier Reinhard *

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University Institute of Pathology, CHUV, CH-1011, Lausanne, Switzerland

5-Aminolevulinic acid (ALA) is the first intermediate in heme biosynthesis. ALA can be used as a precursor of a photosensitizing agent in the photodynamic detection and therapy (PDT) of cancer. [1] To improve the target specificity and efficacy for PDT, we synthesized and evaluated sugar derivatives of ALA as sugars may help to increase the uptake and the target specificity of our ALA-derivatives.

Stable ALA derivatives of glucose, galactose and mannose were synthesized. ALA linked as an ester to the C1 hydroxyl group of sugars and ALA linked as an ester to the C6 hydroxyl group of sugars were synthesized. The synthesis of these compounds and their efficiency to function as precursors for PDT using various cancer cell lines will be presented.



[1] Jain et al; *Nature Reviews-Cancer*, **2003**, 3, 380-387.

[2] Berger et al; *Bioorganic & Medicinal Chemistry*, **2003**, 11, 1343-1351.

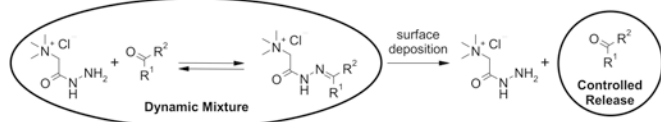
Controlled Fragrance Release from Dynamic Mixtures Obtained by Reversible Reaction of Hydrazides with Volatile Aldehydes or Ketones

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^b ISIS, Université Louis Pasteur, B.P. 70028, F-67083 Strasbourg, France

The performance of flavours and fragrances is often limited by their high volatility and/or their inherent instability during storage or application. To increase the long-lastingness of fragrance perception, we investigated the evaporation of volatiles from dynamic mixtures generated by reversible covalent reaction of aldehydes and ketones with hydrazides to form an equilibrium with their corresponding acylhydrazones [1]. Once deposited on a surface, the equilibrium is shifted towards the free hydrazide as a result of the evaporation of the unreacted fragrance molecules from the mixture which results in a gradual hydrolysis of the acylhydrazones.



The performance of the new delivery systems was studied by dynamic headspace analysis. This demonstrated that the presence of hydrazides in the perfume results in higher fragrance concentrations in the headspace as compared to the case when they were absent. The slow formation and hydrolysis of acylhydrazones in a dynamic mixture gives rise to a pronounced increase in the duration of fragrance perception and thus represents an efficient delivery system for the controlled release of volatile organic molecules [2].

[1] B. Levrant, Y. Ruff, J.-M. Lehn, A. Herrmann, *Chem. Commun.* **2006**, in press (DOI:10.1039/B602312F).

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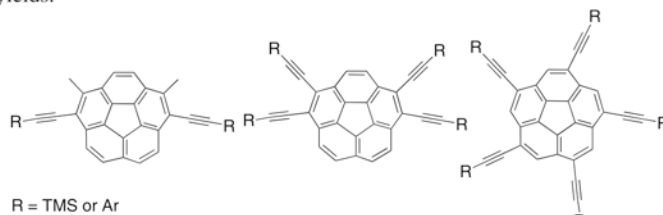
Multithiynyl Substituted Corannulene Derivatives

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^aUniversity of Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

^bNational Cheng-Kung University, 1 Ta-Hsue Rd., Tainan, Taiwan, R.O.C.

Multisubstituted corannulene derivatives, like 1,3,5,7,9-pentaaryl and pentaalkyl substituted, were previously prepared and their photophysical properties were investigated.[1] Recently, Wu, *et al.* reported an efficient procedure to prepare *peri*-ethynyl substituted derivatives.[2] In the present work, corannulene derivatives of the type **1**, **2** and **3** were prepared in good yields.



All derivatives absorb light between 310 – 390 nm. Those with R = Ar are red shifted compared to R = TMS. A similar effect is seen in their emission spectra. Compounds of type **2** show the highest fluorescence quantum yield. Compounds of series **3** show a dramatic decrease in quantum yield compared to their analogs of type **2**. Even compounds **1** have quantum yield higher than **3**. Crystal structures analyses show a bowl-in-bowl packing.

[1] Grube, G. H.; Elliott E. L.; Steffens, R. J.; Jones, C. S.; Baldrige, K. K.; Siegel, J. S. *Org. Lett.* **2003**, 5, 713-716.

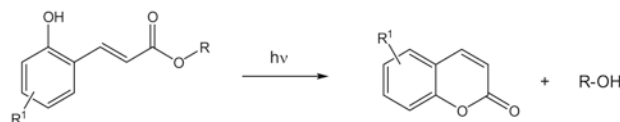
[2] Wu, Y.-T.; Hayama, T.; Baldrige, K. K.; Linden, A.; Siegel, J. S. *J. Am. Chem. Soc.* **2006**, 128, 6870-6884

Studies on *o*-Hydroxy Cinnamates as Traceless, Light-Cleavable Precursors for Perfumery Ingredients

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8600 Dübendorf, Switzerland

Efficient release of coumarins and an alcohol R-OH is observed, when *o*-hydroxy cinnamic esters **1** are irradiated with ultraviolet light [1-3]. Such compounds are therefore interesting for the controlled release of fragrance ingredients. The process involves light-induced *E/Z*-isomerization of the cinnamate double bond, followed by lactonization of the *Z*-isomer.



The rate of lactonization can be greatly influenced by substitution at strategically important sites of either R-OH or the *o*-hydroxy cinnamic acid moiety.

Domino-precursor strategies based on the parent structure **1** as well as synthetic routes for the preparation of *o*-hydroxy cinnamic esters will be discussed.

[1] B. B. Dey, T. H. R. Rao, T. R. Seshadri, *J. Ind. Chem. Soc.* **1934**, 11, 743.

[2] A. D. Turner, S. V. Pizzo, G. Rozakis, N. A. Porter *et al*, *J. Am. Chem. Soc.* **1999**, 121, 7716.

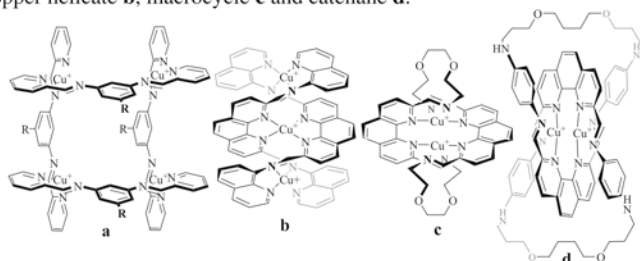
[3] a) D. Anderson, G. Frater, EP 0 936 211 A2, 1998. b) F. Flachsmann, J.-P. Bachmann, WO 2005077881 A1, 2005.

Complex Architectures From Simple Building Blocks Through Sub-component Self-Assembly

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University of Geneva, quai Ernest Ansermet 30, 1211 Geneva 4, Switzerland

A self-assembly methodology has been developed that allows unusual structures to be created in excellent yield [1]. Amines and aldehydes are held together by reversibly-formed imine (C=N) bonds that self-assemble around copper(I) templates. We were thus able to build [2x2] grid complex **a**, three-copper helicate **b**, macrocycle **c** and catenane **d**.



We are investigating ways to allow us to switch from one structure to a other topologically different one: this goal was achieved by changing the nucleophilicity [2], the pH or the rigidity of the subcomponents [3].

[1] J. R. Nitschke, M. Hutin, G. Bernardinelli, *Angew. Chem. Int. Ed.* **2004**, *43*, 6724

[2] M. Hutin, R. Frantz, J. R. Nitschke, *Chem. Eur. J.*, **2006**, *12*, 4077

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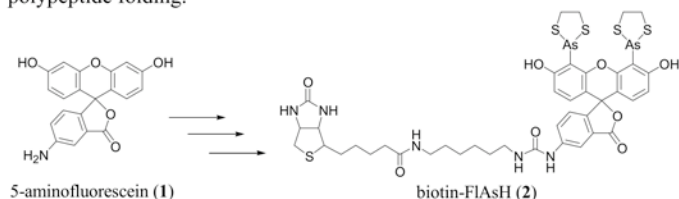
Fluorogenic Detection and Capture of Well-Folded Proteins

Nathan W. Luedtke,¹ Daniel Fried,² Rachel Dexter,² and Alanna Schepartz^{2*}

¹Organic Chemistry Institute, University of Zürich, CH-8057, Switzerland

²Department of Chemistry, Yale University, New Haven, CT 06520, USA

The biarsenical fluorescein derivative FIAsh was developed in the Tsien Laboratory to label recombinant proteins containing a six-residue tetracysteine motif CCXXCC [1]. We have found that FIAsh can be used to report protein folding by replacing the variable residues XX with small proteins that, upon proper folding, bring the two sets of cysteines into close proximity [2]. Rapid thiol-arsenic exchange reactions liberate 1,2-ethanedithiol from FIAsh to produce fluorescent protein complexes with apparent affinities and quantum yields proportional to the abilities of cysteine-modified proteins to fold into their native structures [2]. Here we show that 5-aminofluorescein (**1**) can be converted into a biotin-FIAsh derivative (**2**) in 5 steps, with yields ranging from 31 – 87 % per step. The resulting derivative (**2**) can fluorogenically report protein folding, and when used in conjunction with a streptavidin-containing solid support, it can capture well-folded proteins from a mixture of folded and misfolded species. Together, these new tools may help decipher the principles and requirements of proper polypeptide folding.



[1] Griffin, B.A.; Adams, S.R.; Tsien R.Y. *Science*, **1998**, *281*, 269.

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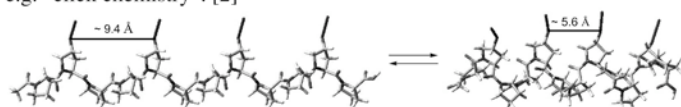
Functionalized Polyprolines – Switchable and Conformationally Well-defined Molecular Scaffolds

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Conformationally well-defined scaffolds which allow for facile decoration with functionalities at desired positions have become increasingly important for applications ranging from the generation of materials with defined properties to the development of cell penetrating compounds, antibiotics and inhibitors for specific protein-protein interactions. [1]

We envisioned polyproline as a versatile molecular template since it adopts two well-defined helical conformations that can be interconverted simply by changing the solvent. We will present oligo-proline derivatives with (4S)- or (4R)-azidoprolines at every third position and show that they adopt already at short chain lengths two distinct helical conformations depending on the solvent. For applications the azido groups allow for further functionalisation by e.g. “click chemistry”. [2]



We will also demonstrate that incorporation of (4R)-azidoprolines into polyproline stabilizes the biologically relevant polyproline II structure. [2]

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Porphyrim Substituted Oligonucleotides: Synthesis And Spectroscopy

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Modified nucleotides are becoming increasingly attractive, e.g. to create supramolecular assemblies by using the Watson-Crick base pairing motif. We report the synthesis of porphyrin substituted DNA strands starting from modified phosphoramidite nucleosides **1** and **2**, and applying standard procedures. First results on the thermodynamic stabilities and structural investigations of the duplexes will be presented. The UV-Visible and fluorescence spectroscopic properties of the different multiporphyrin arrays will be discussed, which show enhanced electronic interactions between the different porphyrin units in the DNA strands.

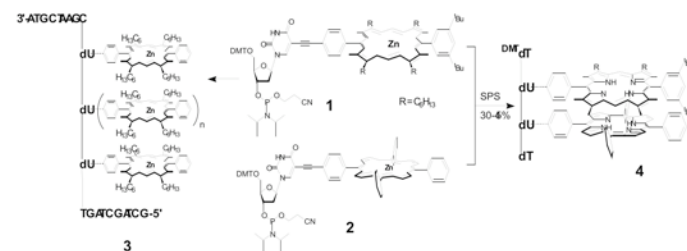


Figure 1. Solid phase synthesis of oligonucleotides.

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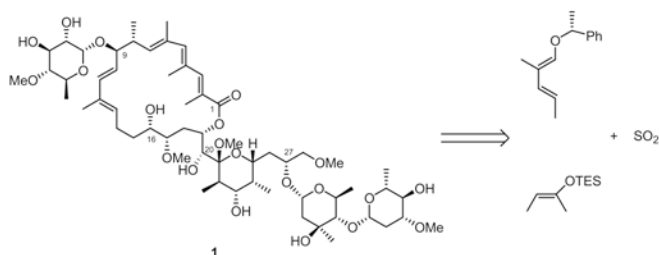
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Studies Towards the Total Asymmetric Synthesis of Apoptolidin and Analogues. Application of the Vogel's Cascade

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Drugs that can selectively sensitize cancer cells to apoptosis induction are of extreme interest for cancer therapy. Apoptolidin (**1**), isolated from *Nocardia* sp. by Hayakawa and co-workers, selectively induces apoptosis in rat glia cells transformed with E1A oncogene (IC₅₀ = 11 ng/mL).¹



Applying the Vogel's one-pot, four component synthesis of polyfunctional sulfones, an efficient synthesis of the C₁-C₁₁ fragment of apoptolidin has been developed recently.² Our efforts are currently concentrated on a short synthesis of the C₁₆-C₂₈ fragment of apoptolidin.

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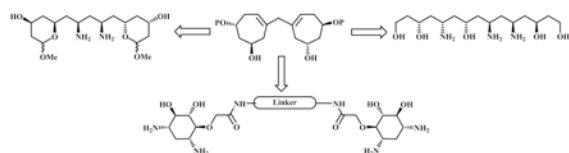
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New Efficient Synthesis of Long Chain di- and tri-Aminopolyols.

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Aminopolyols belonging to the large family of amino sugars and deoxyamino sugars are molecules of high importance in medicinal chemistry and glycobiology. Despite many efforts, few synthetic routes toward linear aminopolyols have been reported thus far and are mostly limited to short sequences. We report here a further application of the non-iterative asymmetric synthesis of fifteen-carbon 1,3-polyols developed in Vogel's group [1], allowing the efficient preparation of long chain di- and tri-aminopolyols [2] as potential aminoglycosides mimetics. A library of 2-deoxystreptamine dimers linked by our aminopolyols was synthesised for biological properties evaluation. The generation of new RNA-binding compound was investigated by selection and amplification from a dynamic combinatorial library.



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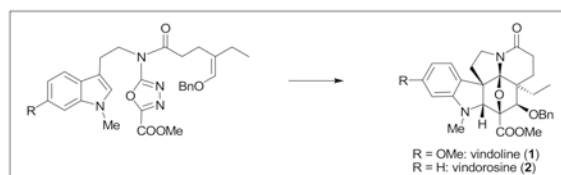
Total Synthesis of Vindoline and Vindorosine by Tandem [4+2]/[3+2]-Cycloaddition

Juraj Velcicky,^a Hayato Ishikawa, Gregory I. Elliott, Younggi Choi, YongKai Li, Michael M. Miller and Dale L. Boger*

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Vindoline (**1**) represents the highly substituted pentacyclic portion of biologically important anticancer therapeutics vinblastine and vincristine [1]. Our approach to the total synthesis of vindoline (**1**) and its C-16 *des*-methoxy derivative vindorosine (**2**) is based on a tandem intramolecular Diels-Alder/1,3-dipolar cycloaddition of a 1,3,4-oxadiazole [2].



The efficiency of this unique cascade is clearly illustrated by its ability to construct three rings, four C-C bonds and all six stereocenters within the central ring including four quaternary centers in a single step.

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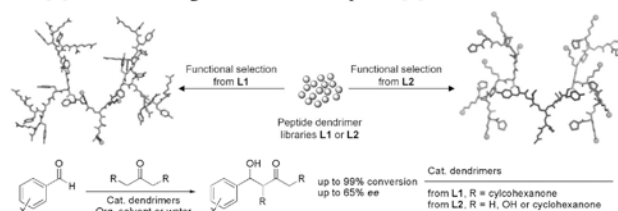
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Aldolase Peptide Dendrimers from Combinatorial Libraries

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Peptide dendrimers are attractive as models for enzymes because they are easily prepared by solid phase peptide synthesis and given their globular shape omit the difficult problem of protein folding[1]. Combinatorial peptide dendrimer libraries[2] were probed for aldolase activity using a dye-labeled 1,3-diketone suitable for covalent trapping of enamine-reactive side-chains[3], and a fluorogenic enolization probe[4].



Dendrimers from library **L1** containing core encapsulated lysines catalyzed the aldol reaction of cyclohexanone with 4-nitrobenzaldehyde. Dendrimers obtained from a second library **L2** featuring multivalent display of *N*-terminal catalytic residues (e.g. prolines) catalyzed aldol reactions with either acetone, cyclohexanone or dihydroxyacetone. In general, the aldolase dendrimers were more active in water than in organic solvent, and showed positive dendritic effects.

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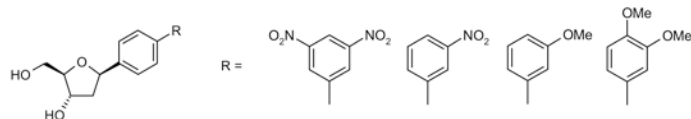
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Biphenylic DNA

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Recently we observed that oligonucleotide duplexes can accommodate biphenylic nucleoside pairs in a zipper-like structure without compromising with duplex stability[1-3]. Such a structural scaffold is of considerable interest in the context of the material properties of DNA. To determine the influence of the electronic character of the biphenyl residues on their mutual recognition properties we designed biphenylic nucleoside analogs containing electron rich and electron poor aromatic rings. All of these compounds are accessible from a common p-bromophenyl-nucleoside precursor by *Suzuki* coupling with suitably substituted phenylboronic acids. We present the detailed synthesis of the building blocks as well as thermodynamic properties and structural data of modified oligodeoxynucleotides.



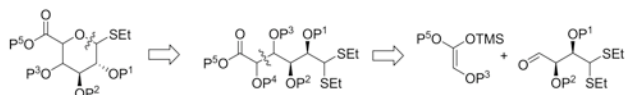
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Stereoselective Synthesis of Fully Functionalized Uronic Acids

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A typical monosaccharide building block used in oligosaccharide assembly is equipped with different protecting groups to mask the hydroxyl and amine functions and an anomeric leaving group that can be activated to induce the formation of a glycosidic linkage [1]. These differentially protected and functionalized monosaccharides have traditionally been accessed from naturally occurring sugar starting materials through a series of protection-deprotection maneuvers in order to establish the desired protecting group pattern. We reported a convergent route to orthogonally protected D-glucuronic and L-iduronic acid thioglycoside building blocks, which are commonly used in the assembly of heparin oligosaccharides [2]. This approach relies on the selective Mukaiyama-type aldol reaction [3] that unifies a silyl enol ether and a thioacetal-containing aldehyde.

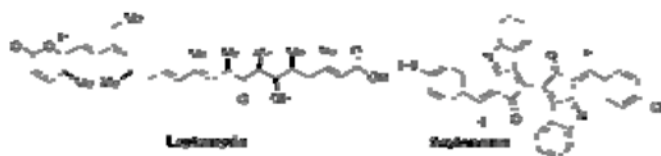


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Controlling Cellular Pathways by Synthetic Natural Products

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Natural products contain the evolutionary wisdom of ages and only synthetic organic chemistry can unlock their full potential. These compounds have been evolved for the specific control of cellular function and their use thus allows for a detailed understanding of key biological processes on a fundamental level. In this communication, we will present our recent efforts concerning two natural products, leptomycin and scytonemin.



Leptomycin[1] (LMB) is a potent inhibitor of nucleocytoplasmic transport and is frequently used as a tool compound in cell biology. Its mode of action is unknown on a molecular level. Scytonemin,[2] a sheath pigment of cyanobacteria, was reported to possess inhibitory activity on polo-like kinase 1, an emerging target in cancer research.[3] We will report on chemical and biological studies related to these targets. The ability of both natural products for the generation of chemical lead structures will be discussed.

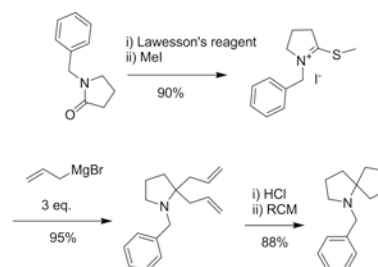
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Synthesis of 1-Azaspirocycles via Facile gem-Dialkylation of Thioiminium Ion and Ring Closing Metathesis

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1-aza-spirocycles [1] represent an important sub-structure of many natural products. We developed the synthesis of the 1,1-bis-allylated pyrrolidine (see Scheme) and piperidine precursors *via* the reaction of a thioiminium salt [2][3] with a suitable Grignard reagent. The ring closing metathesis then leads to the corresponding aza-spirocycle in good overall yields.



The procedure used for the preparation of gem-dialkylated species was extended to other gem-disubstituted cyclic amines.

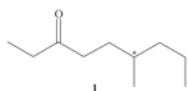
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Asymmetric Hydrogenation of Unfunctionalised Olefins

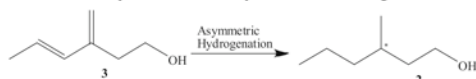
Rui Fraga, Andreas Pfaltz*

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Recent advances in iridium based hydrogenation catalysts, using various P,N-ligands, allowed for hydrogenation of substrates bearing unfunctionalised olefins with high conversion and ee [1]. In this work we envisage to broaden the scope of application for these catalysts, by aiming for a natural product **1** in which asymmetric hydrogenation can be a key synthetic step.



Another class of substrates in which we focused our attention is unfunctionalised conjugated olefins, for which a recent study by Burgess [2] brings evidence for the complexity of the hydrogenation mechanism. Branched alcohols like **2** are compounds with specific interest as building blocks in natural product chemistry, like in the synthesis of Amphidinol A [3].



Herein we will describe the synthesis of **3** as well as the results in asymmetric hydrogenation of this substrate.

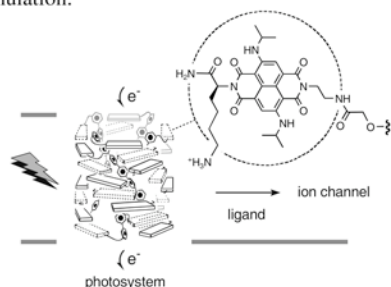
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Artificial Photosynthesis with Rigid-Rod π -Stack Architecture in Lipid Bilayer Membranes

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 Jiri Mareda,^a Alexandre Fürstenberg,^b Nathalie Banerji,^b Eric Vauthey,^b
 Naomi Sakai,^a and Stefan Matile^{a*}

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 1211 Geneva, Switzerland

Design, synthesis and photosynthetic activity of blue, red-fluorescent rigid-rod π -stack architecture are reported [1]. Femtosecond fluorescence and transient absorption spectroscopy revealed that quantitative ultrafast and relatively long-lived charge separation as origin of photosynthetic activity. Supramolecular self-organization was confirmed to account for photoactivity, ligand intercalation for the transformation into ion channels in response to chemical stimulation.



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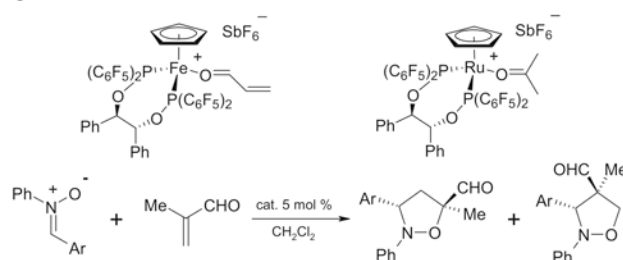
Chiral Lewis Acid Catalyzed Asymmetric 1,3-Dipolar Cycloaddition Reactions Between Methacrolein and Diarylnitrones

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

Highly tuned, one-point binding iron and ruthenium complexes selectively coordinate and activate α,β -unsaturated aldehydes towards cycloaddition reactions.[1] These chiral Lewis acid complexes show preference of enal over nitron coordination and reversibility of coordination of both substrates.[2]

The catalyzed asymmetric 1,3-dipolar cycloaddition reaction of methacrolein with a series of diarylnitrones gave the corresponding isoxazolines in good yields, moderate to high enantio- and regioselectivities and complete endo/exo selectivity. Regioselectivity is shown to be correlated to the electronic properties of the *p*-substituent of the nitron C-aryl group.



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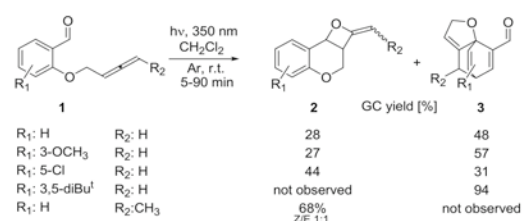
Intramolecular [2+2] and [4+2] photocycloadditions between aromatic aldehydes and allenes.

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Switzerland.

The intramolecular photocycloaddition between aromatic aldehydes and allenes is a synthetically useful reaction as it provides a rapid and efficient method for accessing strained 2-methylene oxetane rings [1] and bicyclo[2.2.2]octane [2]. Substituted benzaldehyde **1** was photochemically converted into compounds **2** and **3**, in good yields.

We study not only the formation of such compounds, but also the control of the regiochemistry by changing the substituents, either on the aromatic ring, or on the terminal part of the allene moiety.



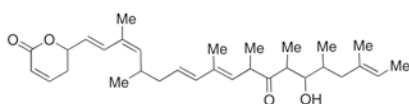
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Synthetic Studies on the Antitumor Anguinomycin C, a Tumor-Selective Polyketide

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Cancer remains a major disease worldwide and many of the currently used chemotherapeutics are of natural origin. This warrants the investigation of natural products with anticancer properties. Anguinomycin C, an antitumor antibiotic isolated from *Streptomyces*, possesses a unique mode of action. [1] This compound selectively targets retinoblastoma tumor suppressor protein (pRB) inactivated cancer cells and exerts only growth arrest on normal cells.



Anguinomycin C

Anguinomycin, a member of the leptomycin family,[2] has not prepared in synthetic form, and the relative and absolute configuration remain unknown. Moreover, the interesting biological activity and in particular the selectivity for transformed cells warrant biological studies for the identification of the molecular mode of action. All these questions can be addressed by total synthesis. We will report on synthetic studies of anguinomycin C featuring modern metal-mediated transformations.

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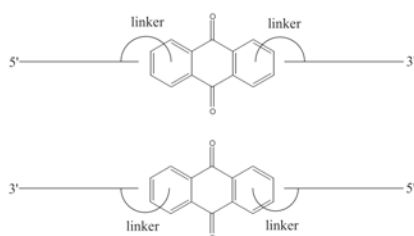
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Incorporation and study of different anthraquinones in DNA

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Various anthraquinones and other polyaromatic residues were synthesized and incorporated into duplex forming oligonucleotides. The effect of the modified building block on duplex stability was investigated. We examined the influence of the length as well as the site of attachment of the linkers. Thermal melting experiments and fluorescence measurements were used to characterize the duplexes. Furthermore, we investigated the spectroscopic properties of the so-obtained DNA mimics. The results of these studies will be presented and discussed.

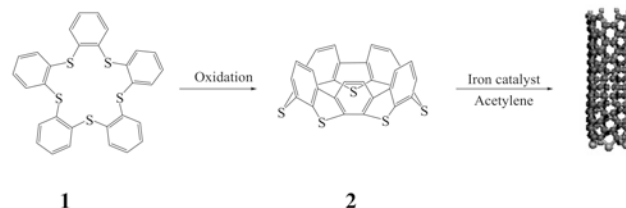


Towards Sulfur Terminated Carbon Nanotubes

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Carbon nanotube research is a very hot topic and there is still a vast research activity on this subject. Fabrication of different types of carbon nanotubes has meanwhile become a mature industrial task. However, all fabrication processes and nanotubes syntheses use physical methods for producing this material, no rational chemical synthesis exists so far.



There is evidence for an iron catalyst capable of polymerizing and dehydrogenating acetylene to graphitic structures. Provided that an appropriate template such as compound 2 could be obtained, one could expect carbon nanotubes growth on this template. Therefore, the problem consists in finding a route for the synthesis of the macrocycle 1 formed by five aromatic rings linked by five sulfur atoms, since the aromatic rings of compound 1 could be linked oxidatively by a known procedure. Such a template would allow for a uniformity of diameter, orientation and length of the nanotubes formed. First steps towards the synthesis of 1 are presented.

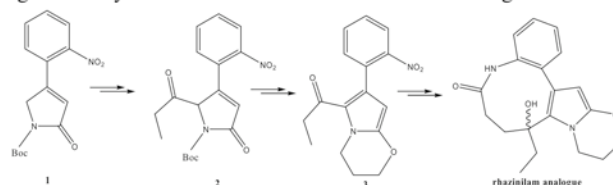
Towards the Total Synthesis of Rhazinilam Analogue

Ana-Maria Buciumas, Olivier Vallat and Reinhard Neier*

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Rhazinilam is a natural product with antitumoral properties[1].

The starting material for our planned synthesis of rhazinilam and derivatives of rhazinilam is 2-nitroacetophenone. Bromination, replacing the halogen by the azido group, followed by Mukaiyama reaction and cyclisation to the five membered ring by Staudinger reaction gave compound 1 in good yield. Our next goal is to synthesize the additional nine membered ring.



Starting with compound 1 the next steps were the addition of propionaldehyde followed by a Dess-Martin oxidation, obtaining the product 2. After cleavage of the protecting group and cyclisation to the six membered ring will be achieved by the addition of ethyl propiolate[2] followed by hydrogenation and cyclisation to obtain compound 3. Methods to achieve the cyclisation to the nine membered ring are the next challenge of our project.

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Automated Synthesis of Complex Carbohydrates

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Laboratory for Organic Chemistry, ETH Zurich, 8093 Zurich, Switzerland

With the growing interest in the precise nature of carbohydrate interactions with other bio-molecules, there is a growing interest for well-defined oligosaccharide structures. Synthetic carbohydrates are not only well-defined single compounds, but can also be easily modified or conjugated to markers, proteins and surfaces in order to study their interactions. Solid-phase carbohydrate synthesis has proven to be amenable to automation, simplifying greatly the assembly of oligosaccharides from simple building blocks [1]. Our progress towards the efficient automated synthesis of a broader scope of complex structures and challenging linkages will be presented as well as the post-synthetic manipulations, namely purification, deprotection and functionalization of the linker moiety. The α -Galactosidic linkage is common in nature and is found in the human cancer antigen Globo-H. Our effort towards the development of a method for efficient automated synthesis of α -galactose-containing carbohydrates such as Globo-H and other cis-glycosidic linkages will also be described.

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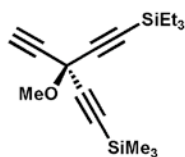
Asymmetric Synthesis of a Differentially Silyl-protected Tris(alkynyl)methyl Methyl Ether

Vito Convertino, François Diederich

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In view of the current interest in new and fascinating three-dimensional acetylenic scaffold, the synthesis of monomers from which to build these networks is now a major goal and a considerable challenge.

For an improved synthesis of the recently described expanded octamethoxycubane [1, 2] with a central C_{56} core, formally obtained by inserting buta-1,3-diyne moieties into all $C(sp^3)-C(sp^3)$ bonds of octamethoxycubane, the preparation of the optically pure methyl ether of a differentially silyl-protected trispropargylic alcohol was required. The key step of the preparation involved a diastereoselective addition of a lithium acetylide to an optically active alkynylketone under *Cram* chelation control [3].



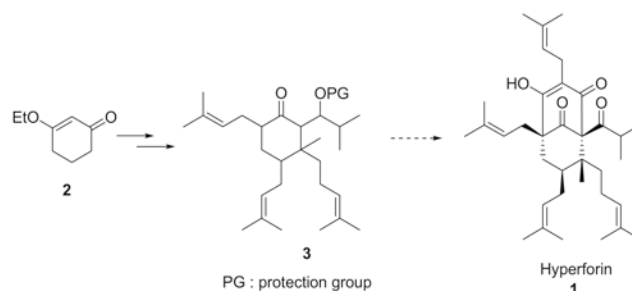
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Progress toward the total synthesis of Hyperforin

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Hyperforin **1** is a polyprenylated bicyclo-[3.3.1]-nonane product isolated from St-John's wort [1]. It is supposed to be responsible of *Hypericum perforatum's* activity in the treatment of mild to moderate depression [2]. From the best of our knowledge, total synthesis of Hyperforin has not been achieved yet in spite of intensive efforts toward the key bicyclic core construction [3,4].



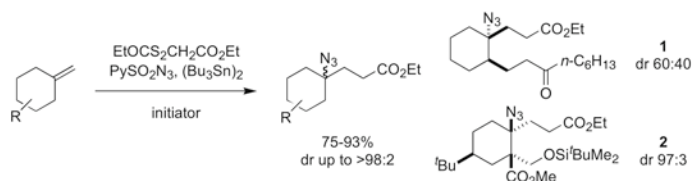
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Controlling the Diastereoselectivity of the Radical Carbooxidation - Studies Towards the Synthesis of Natural Alkaloids

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The radical carbooxidation has proved a very useful tool to synthesise complex molecules by forming a C-C bond and a C-N bond in a single step [1]. This reaction constitutes a very attractive method to prepare building blocks bearing an amino-substituted quaternary carbon centre and has been successfully applied to the synthesis of natural alkaloids. However, the level of diastereoselectivity reached in the process is not always satisfactory as shown in our recent synthesis of (\pm)-lepadiformine (see intermediate **1**) [2].



Here is described the radical carbooxidation of a series of methylene cyclohexane derivatives. This study leads to a better understanding of the reaction and allows the prediction and the control of the diastereoselective outcome of the reaction (see compound **2** for example). These results are currently being applied to the synthesis of natural products.

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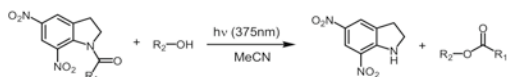
Preparation of Esters under Neutral Conditions by Photochemical Acylation of Alcohols

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Recently, our group described the smooth and neutral acylation of amines to form amides by photoactivation of *N*-acyl-5,7-dinitroindolines [1]. An improved acylation of nitroindolines allowed the convenient preparation of *N*-acyl-5,7-dinitroindolines making possible the recycling of the nitroindoline released during the photoactivation.

Based on this previous work, we decided to try to synthesize esters with alcohols much less nucleophile than amines, by photoactivation of *N*-acyl-5,7-dinitroindolines using LED as light source in our photoreactor (scheme 1). The reaction conditions were optimized by using a convenient primary alcohol, the undecen-1-ol. The major problem, which occurred during the photoacylation of alcohols, was the competition between the weak nucleophiles that are alcohol and water. In order to obtain good to excellent yields with a large variety of alcohols, it was important to keep the medium strictly anhydrous. It is interesting to note that certain functionalities like olefins, ketones, aldehydes and alkynes are tolerated.



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Synthesis and Investigation of Terphenylsilylium Ions

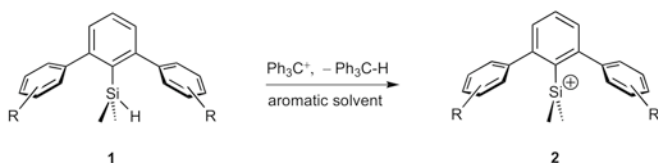
Simon Duttwyler, Kim Baldrige, Jay S. Siegel

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

Silylium ions R_3Si^+ are the period 3 analogues of carbenium ions. They are of fundamental interest to organosilicon chemistry, and it was only in 2002 when the planar, three-coordinate structure of a free R_3Si^+ system was confirmed by X-ray crystallography.^{1,2}

This project deals with the synthesis and characterization of a new class of silyl cations, where silicon carries a 1',3'-terphenyl residue. The hydride abstraction methodology is used to convert the neutral silane precursors **1** into the target ions **2**. The idea behind the system **2** is that the Si center is sterically protected by the two flanking rings as well as electronically stabilized by $\pi_{ring}-3p_{Si}$ interactions. The electronic stabilization, as measured by the ^{29}Si NMR shift, should increase with more electron-rich ring π systems.

Several silyl cations of the general structure **2** have been prepared, and the results of NMR studies and an X-ray diffraction analysis will be presented.



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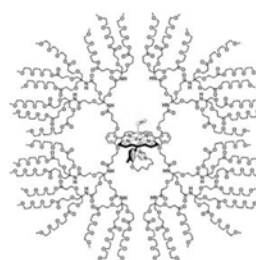
Dendritic Model Compounds for Heme Proteins

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Dendritic encapsulated iron porphyrins are synthesized in order to obtain complete models of heme proteins. Thus, not only the active sites of the proteins are considered, but also the protein shell around them is mimicked by the dendrons. The influence of this microenvironment on the porphyrin properties can be quite substantial. [1, 2]

The model compounds for hemoglobin and myoglobin consist of an elaborate iron porphyrin core, which bears the proximal base as well as a distal hydrogen bond donor covalently attached to it. *Newkome* type dendrons are used to mimic the proteinic environment.

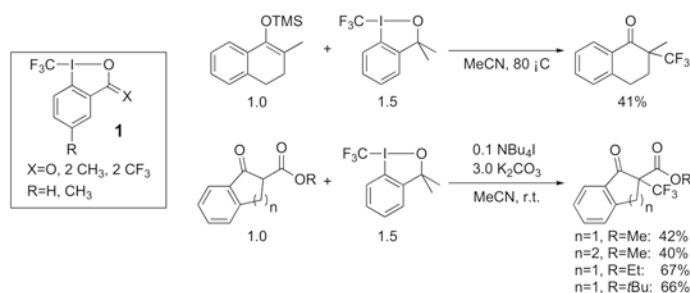


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Electrophilic Trifluoromethylation with Hypervalent I- CF_3 Iodine(III) Reagents

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Fluorine containing molecules and materials are gaining increasing interest in pharmaceutical-, agrochemical-, and material sciences since they show altered physical- and physiological properties compared to their hydrocarbon relatives. Thus, efficient methods to introduce fluorine and perfluorinated functional groups into organic molecules are eagerly sought. Direct transfer of a trifluoromethyl moiety in an electrophilic fashion onto nucleophiles still constitutes a major challenge.^[1] Recently we prepared new reagents based on the hypervalent iodine scaffold **1** and showed their potential in trifluoromethylating carbon nucleophiles.^[2] Here, we wish to present results of our ongoing effort to elucidate the scope of these reagents as mild electrophilic CF_3 -transfer reagents in reactions with organic nucleophiles.

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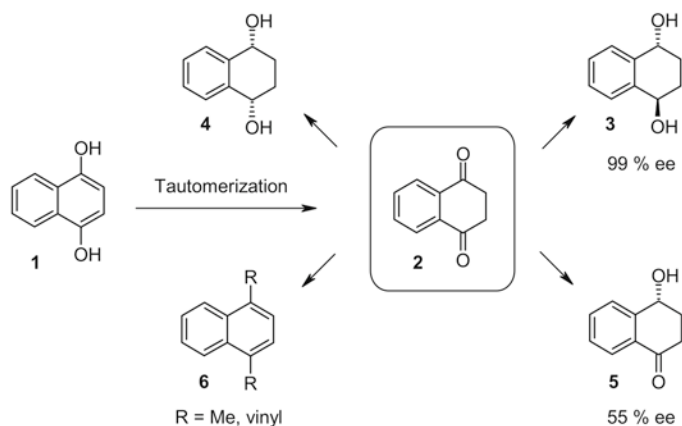
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Rediscovery, Isolation and Synthetic Potential of 1,4-Tetralindione

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Quai E. Ansermet 30, CH-1211 Geneva 4, Switzerland

Dihydroxynaphthalene **1** converts into its tautomer **2** in neat CF_3COOH [1]. The dione **2** is kinetically stable at room temperature but reverts to the phenolic form in polar media. Surprisingly, to our knowledge, no chemistry of isolated **2** has ever been reported. We here detail our results on an efficient access to crystalline diketone **2** in multigram scale and its use as an attractive and promising starting material for organic synthesis.



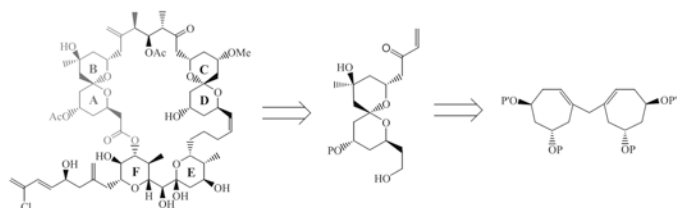
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New route towards the synthesis of AB-spiroketal of spongistatin I

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Ecole Polytechnique Fédérale de Lausanne (EPFL), Batochime
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Discovered in 1993, the spongistatins comprise an important family of architecturally complex marine macrolides that display extraordinary antitumor activities against a variety of human cancer cell lines. Composed of a 42-membered macrolactone ring, two spiroacetals units (AB and CD) and two densely substituted tetrahydropyran rings (E and F) this class of molecule represent a formidable synthetic challenge [1]. After the synthesis of the EF fragment, we report here an application of Vogel's group non-iterative asymmetric methodology for the synthesis of fifteen-carbon 1,3-polyols [2] to the rapid preparation of an advanced intermediate of the spongistatin AB spiroketal [3]. In particular, pathways have been developed for the orthogonal protection of the hydroxyl groups allowing synthesis of analogues.



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Design and screening of mannosylated peptides dendrimers libraries for the discovery of high affinity ligands for lectins.

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Lectins are carbohydrate-specific binding proteins that are found throughout nature.¹ Since they are widely involved in many endogenous and exogenous biological phenomena (glycoproteins clearance, inflammation processes, intercellular interactions, host-guest adhesion...), an efficient method of modulating lectin activity is of significant relevance.² Moreover, one can assume that such supramolecular phenomena could be reinforced by taking advantage of the « Cluster Effect » characterizing some multivalent systems.³ Therefore, we underline herein the versatility of mannose-coated peptide dendrimers from combinatorial libraries, as tuneable probes allowing to select for high affinity ligands. Libraries were designed on solid phase by *split-and-mix* strategy.⁴ These libraries provide dendrimers with exceptional backbone and structural diversity. This approach takes advantage of cheap and easily available model plant lectins and represents an elegant way to inhibit carbohydrate-protein interactions utilizing glycopeptide dendrimers as interesting pharmacophores.

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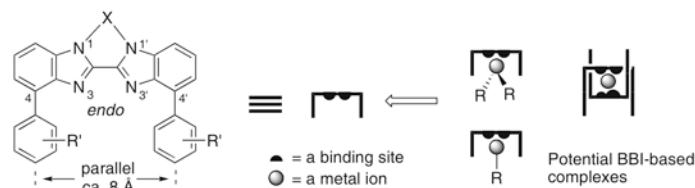
N,N'-Bridged Derivatives of 4,4'-Bisaryl-2,2'-bisbenzimidazoles as Building Blocks for Supramolecular Structures

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4,4'-Bisaryl-2,2'-bisbenzimidazoles have the potential to be building blocks for supramolecular structures. Although 2,2'-bisbenzimidazoles (BBIs) have been studied extensively, the chemistry of substituted BBIs is limited.²

Bridging of the N(1) and N(1') nitrogen atoms fixes the bisbenzimidazole (BBI) framework into an inverted U-shape that allows the *endo* binding sites to complex with metal ions, leading to interesting structural arrangements. Using our method for employing Negishi conditions to produce 4,4'-bisaryl-BBI's,¹ a series of N,N'-bridged BBIs have been and will be synthesized and their complexation properties will be analyzed.



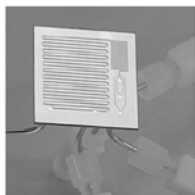
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Microreactors in Organic Synthesis

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Microreactors offer many advantages for synthetic chemists such as high through-put, fast 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 [1-4].



A silicon-based microreactor was chosen for proof-of-principle and kinetic studies of glycosylation reactions as well as for large scale production of oligosaccharides.

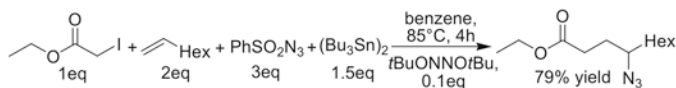
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A Polymer-supported Carboazidation Reaction

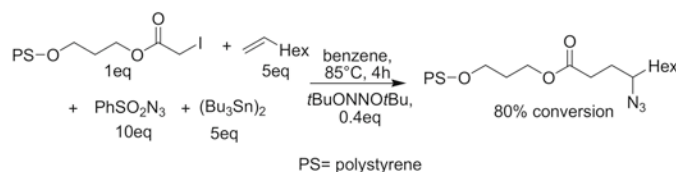
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A few years ago, our group developed a novel intermolecular carboazidation reaction [1]. This efficient reaction presents a great versatility and enables the creation of two interesting functionalities on a carbon skeleton.



Its greatest limitations are the use of toxic tin reagents, and the difficulty to purify and isolate the products. To overcome these problems, we have devised a polymer-supported iodoacetate reagent. At the end of the reaction, the products are attached to the polymer, allowing us to wash away all the unwanted material.



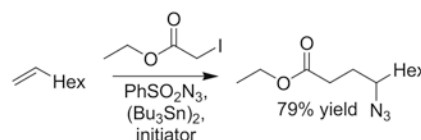
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A Novel Reagent for Tin-Free Carboazidation of Alkenes

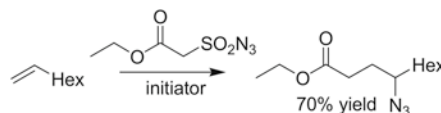
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A few years ago, our group developed a novel intermolecular carboazidation reaction [1]. This efficient reaction presents a great versatility and enables the creation of two interesting functionalities on a carbon skeleton.



Despite its usefulness, it requires the use of toxic tin derivatives [2]. We report here that sulfonyl azide (A) represents an efficient reagent for tin-free carboazidation. It is acting as a radical precursor and azidating agent.



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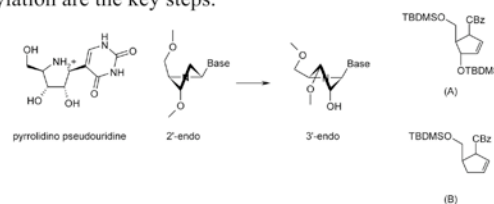
Towards the Synthesis of Pyrrolidino Pseudouridine

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Pyrrolidino nucleotides as third strand constituents are expected to stabilize DNA triplexes because of salt-bridge formation between target DNAduplex 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. Two different approaches were chosen. The key steps in the first synthesis are the Heck coupling of pyrrolidino sugar (A) with the base followed by epoxidation to introduce the 2'-hydroxyl function. In the second approach, the Heck coupling of the pyrrolidino sugar (B) with the base followed by dihydroxylation are the key steps.



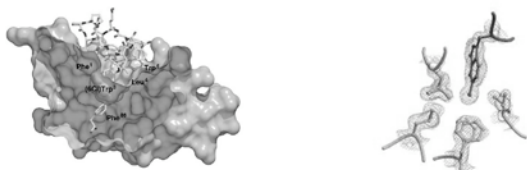
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Thermodynamic Studies on Peptidic Inhibitors of p53 and HDM2

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Protein-protein interactions play key roles in the control of many molecular events involved in cell proliferation, cell death and signal transduction. The interaction between the tumour suppressor protein p53 and its negative regulator Human Double Minute Protein 2 (HDM2) is one of these interactions that are challenging to control by small drug-like molecules. Cyclic β -hairpin peptides are an interesting tool to mimic protein epitopes and display hot spot residues in the optimal geometry to interact with a protein surface. High affinity cyclic peptides have been found to bind to HDM2 and inhibit the interaction to p53. The essential amino acid residues Leu, Trp and Phe of the p53 α -helix are displayed in the optimal positions in the mimetics



Peptido-mimetic binding to HDM2 6-Cl-Trp and HDM2 residues

Mimetics containing a Cl- and Me-substitution at the Trp-6 position were synthesized and characterized. K_d -determinations by surface plasmon resonance experiments show that a substitution from 6-H-Trp to 6-Cl-Trp leads to a high increase in binding affinity. The Cl-atom fits well into a hydrophobic cleft in the HDM2 binding pocket. The introduction of a Cl-atom is also much more effective than the methyl group at the 6-Trp position. Determined K_d -values were confirmed by isothermal titration calorimetry.

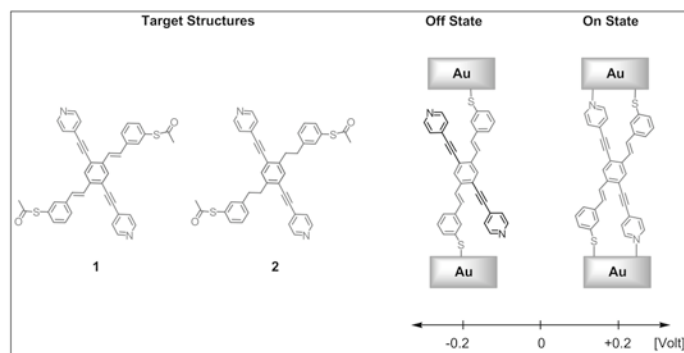
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Electrochemical Molecular Switching Device

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Single molecule switches have attracted considerable attention in the last few years. Here we propose a new switching concept, based on the interplay between electrodes and molecule. The switching molecules consist of two crossing rod-like substructures. While the first rod-like substructure (blue in the figure below) consists of rather "insulating" subunits and sulphur anchor groups in *meta*-position, the second rod-like substructure (red and black in the figure below) consists of well "conducting" delocalised π -systems as subunits and potential dependant pyridine anchor groups in *para*-position.

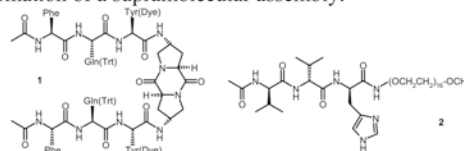


We present synthetic endeavours towards the proposed target structure to investigate the hypothesized switching behaviour in further details.

Diketopiperazine Receptor – Peptide Complexes Self-Assembly in Aqueous Solution Driven by Selective Non-covalent Interactions

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The Wennemers group has recently developed two-armed diketopiperazine receptors that bind peptides with high binding selectivities and affinities. These receptors consist of a diketopiperazine scaffold and two tripeptidic recognition elements that allow for facile structural and functional modifications. Combinatorial binding studies revealed that for example, diketopiperazine receptor **1** binds to the tripeptide Ac-D-Val-D-Val-D-His-resin in CHCl_3 -solution with high selectivity and a binding affinity of $\Delta G = -5.8$ kcal/mol. [1] Due to the low solubility of the non-resin bound peptide, we prepared the pegylated tripeptide **2**. Upon mixing the receptor **1** with the pegylated peptide **2** in CHCl_3 , the formation of a gel was observed, demonstrating the formation of a supramolecular assembly.



When a THF solution of receptor **1** was added to the aqueous solution of peptide **2**, the vesicles formed as revealed by Dynamic Light Scattering (DLS), Transmission Electron Microscopy (TEM), Atomic Force Microscopy (AFM) and Langmuir-Blodgett (LB) techniques.

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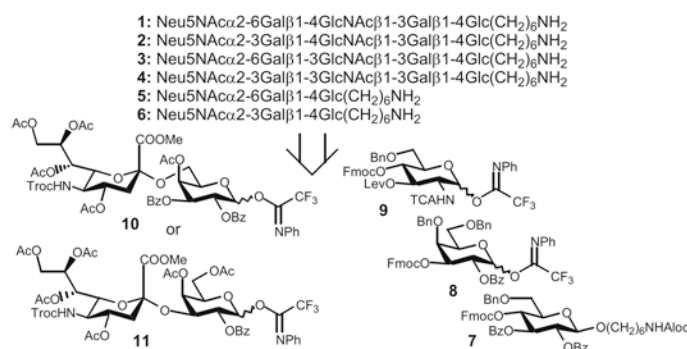
Synthesis of Sialylated Glycans Related to Influenza Virus Infection

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

Influenza virus constitutes a severe world pandemic threat. Avian influenza virus is not thought to infect humans directly, however, it has clearly been spreading in Asia and Europe and is a cause for great concern. The issue with viruses is rapid mutation prevent efficient immunization, and increase risk of changing host from bird to human.

Sialylated glycans on the surface of host cell play an essential in virus infection. Specifically, sialyl lacto and neolacto glycans are readily recognized by virus hemagglutinins. It has been reported that potency of virus binding is significantly related to the glycan sequences. For example, avian viruses recognize more α -2-3 sialyl galactose sequence than α -2-6, and human virus prefer α -2-6 sequence. We intend to develop a rapid and trustworthy method to determine the virus host by using a microarray system with immobilized sialylated glycans. Sialylated glycans **1-6** were systematically synthesized from the 5 building blocks **7-11**.



New Approach for the Synthesis of c-di-GMP and its Analogs

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Cyclic bis(3'-5')diguanylic acid (c-di-GMP) **1** has been recently identified as a universal bacterial secondary messenger.[1-5] It has been shown to be involved in the biofilm formation in different bacteria. It is believed that c-di-GMP represents an excellent platform for drug design in medicinal chemistry and especially in the field of antibiotics where compounds with new modes of action are required. However, the mechanisms of c-di-GMP dependent signaling remain unknown, mainly because very little data is available on c-di-GMP targets.[1,4]

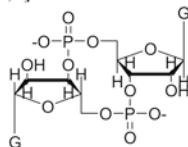


Figure 1. Cyclic bis(3'-5')diguanylic acid 1.

In order to study the biochemistry of this molecule in more details we have started a research program dedicated to the synthesis of c-di-GMP and its analogs. We have developed a new approach where a cyclic sugar backbone was synthesized first and the base was introduced at the latest stage.[6]

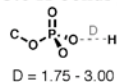
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A Quantitative Study on Phosphate Hydrogen Bonding in Proteins

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Phosphate groups are ubiquitous in biology and fulfill a number of crucial functions in organisms. To gain a better understanding of the way they are bound within enzymes, a search of the RCSB Protein Data Bank was performed using the program Relibase focusing on the H-bonding pattern [1-3]. **14590** entries matching the structural features were found. Out of these, **3004** structures matched the distance constraint. These showed **19713** H-bonds to **5520** phosphate groups with a distance lower than **3.2 Å**, corresponding to an average of **3.6** H-bonds per phosphate group.



A closer examination of these entries with respect to the amino acids involved in H-bonding was performed for the whole group and for interesting subsets. While the whole group shows a special distribution of amino acids participating in phosphate binding, the subgroups show highly characteristic patterns of amino acids. The kinases and phosphatases were examined in more detail due to their importance in medicinal chemistry.

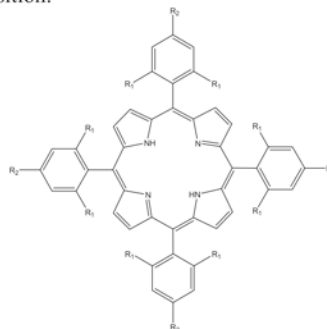
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Synthesis of New Substituted Tetraphenylporphyrin Derivatives as Precursors for Extended Porphyrins

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The aim of this work is to synthesize a series of *tetraphenylporphyrin* (TPP) derivatives which bear different substituents on the meso-phenyl position:



These molecules serve as precursors for the production of new annulated porphyrins. In view of their application in molecular electronics (*solar panels, LED's*) we will test the final products for their properties as liquid crystals.

The annulated porphyrins should form *columnar discotic mesophases* and that π -stacking of their aromatic core should allow efficient electron transfer processes.

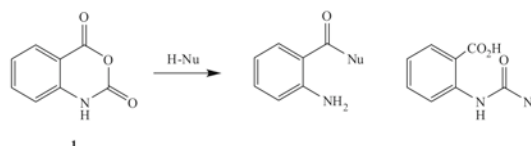
Facilitated Screening of Reaction Conditions Using Microreaction Systems

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The benefits of using microreaction systems for organic synthesis have been demonstrated several times before [1]. In addition to leading to higher yields and selectivities in many cases, microreactors also facilitate the screening of different reaction conditions and allow the safe handling of hazardous reactions.

To demonstrate this, we studied the addition of different nucleophiles to isatoic anhydride (**1**) and compared the yields and selectivities to published data and results obtained under batch conditions [2][3].



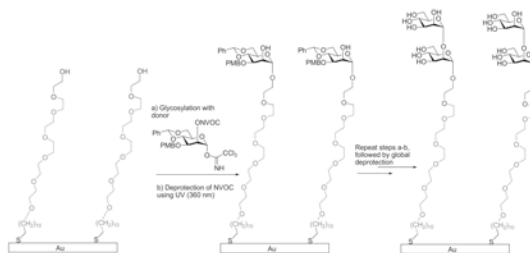
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On-Chip Oligosaccharide Synthesis

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Microarrays for biological assays are an efficient means of using precious material obtained from biological or synthetic sources for biological assays [1][2]. This holds especially true for oligosaccharides where the material is difficult to obtain from biological sources or by organic synthesis.



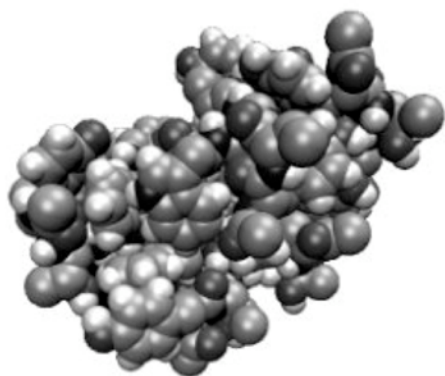
We here present the development of 'on-chip' synthesis of oligosaccharides. The 'on-chip' synthesis requires the use of a building block with protecting groups and glycosylation conditions which are compatible with the chip surface. The glycosylations must be first optimized in solution before being used on the chip. MALDI-TOF MS will be used to analyze the compounds on the chip [3].

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Single catalytic site peptide dendrimers as artificial esterases

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We are investigating peptide dendrimers^[1] as artificial enzyme models. We have reported esterase activity in peptide dendrimers that were obtained by rational design bearing multiple catalytic residues^[2]. However the same approach failed in designing a single catalytic site enzyme mimic. We report here a single site catalytic peptide dendrimer obtained by high throughput screening^[3] of a combinatorial library.

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Enantioselective hydrogenation of ketones on platinum: The critical role of adsorption of the modifier.

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Cinchona alkaloid-modified Pt used for the hydrogenation of ketones represents one of the most successful heterogeneous enantioselective catalysts. A general trend was observed in the hydrogenation of activated ketones in the presence of ether derivatives of cinchonidine (CD) [1,2]: with increasing bulkiness of the ether groups the enantioselectivity decreased and even the opposite enantiomer was formed in excess. The aim of the present study was to show that electronic effects are also critical in controlling the adsorption mode of the modifier on the Pt-surface, and thus its interaction with the substrate. The steric bulkiness of the two modifiers, PhOCD- and *o*-PyOCD, are almost identical but in the hydrogenation of various ketones they afforded mostly the opposite enantiomers in excess. This observation demonstrates that even subtle changes in the modifier structure can lead to striking changes in the output of the reaction and these changes cannot be understood without considering the adsorption of the reaction components on the metal surface.



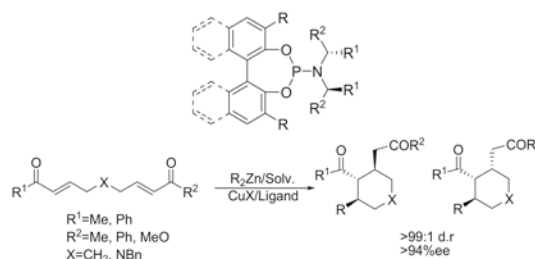
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Cu-Catalyzed Highly Enantioselective Conjugate Addition-trapping Reactions: Synthesis of Chiral Cyclic Compounds

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The intramolecular asymmetric conjugate-trapping reaction of dialkylzinc to bis α,β -unsaturated carbonyl compounds catalyzed by copper/chiral phosphorimidate ligands was investigated. Cyclic and heterocyclic compounds with multi-chiral centers were obtained with excellent diastereoselectivities (up to 99:1) and enantioselectivities (up to 94%ee).

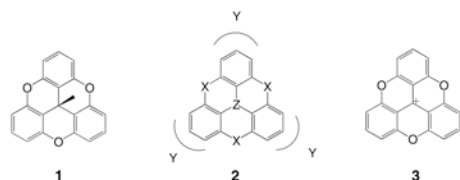


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Synthesis of Trioxatricornan Derivatives

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Trioxatricornan (**1**) is an easily accessible derivative¹⁻³ of triangulene (**2**). It can be derived from the known triangulene (**3**).Fig. 1: Triangulene **2** and derivatives **1** and **3**This trioxatricornan precursor cation (**3**) can be derivatized in either the flanking aromatic region or in the central cation position. This project focuses on both derivatization possibilities.

References

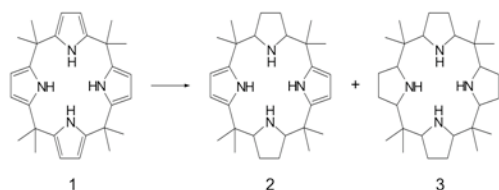
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Synthesis, Structure and Complexation Properties of Partially and Totally Reduced meso-Octamethyl Porphyrinogens (calix[4]pyrroles)

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Compared to the wealth of metal-porphyrin complexes described in the literature the metalation of the meso-octaalkylporphyrinogens proved to be experimentally much more challenging and therefore only comparatively few reports have been published.^[1] In view of the ease and the simplicity of the access to the meso-octaalkylporphyrinogens chemical modifications of this macrocyclic system have been studied to create better ligands.^[2] To the best of our knowledge no report of a successful reduction of meso-octaalkylporphyrinogen has appeared in the literature so far. We will report the results of our broad screening with the goal to find experimental procedures for the reduction of meso-octamethylporphyrinogens. Using optimized conditions we have been able to synthesize two new classes of reduced ligands obtained from meso-octamethylporphyrinogens by catalytic reduction. Exploratory experiments allowed to isolate and to characterize a series of metal complexes of the totally reduced ligand **3**.



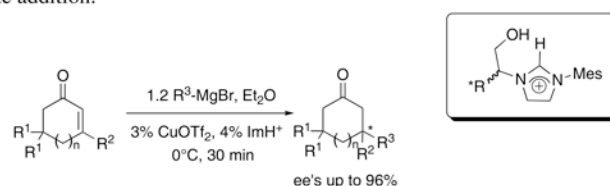
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Cu catalyzed asymmetric conjugate addition of Grignards to trisubstituted enones. Formation of all carbon quaternary chiral centers

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The use of the asymmetric conjugate addition to create enantioenriched all-carbon quaternary centers have been recently disclosed.[1] After using R₃Al reagents [2], our group tried Grignard reagents on the Cu-catalyzed asymmetric 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.



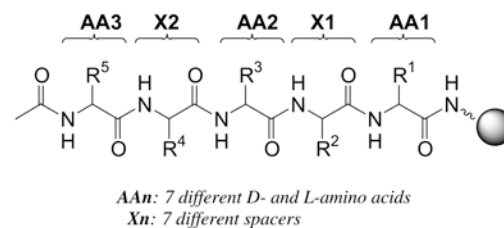
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Towards the Selective Non-Enzymatic Cleavage of Peptides

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A major challenge is the selective and efficient cleavage of esters and non-activated peptide bonds for which nature utilizes esterases and proteases. Only a few practical reagents are able to cleave such bonds selectively. Recently we demonstrated that acid-rich peptides are damaged under Fenton conditions to a greater extent than others as revealed by combinatorial screenings.^[1] Our new approach is based on the proteolytic activity of the serine protease "charge-relay" system known as the catalytic triad which consists of the amino acids Asp, His and Ser. We synthesized an encoded split-and-mix peptide library containing the amino acids of the catalytic triad and spacers (including turn elements) in alternating sequence (Figure 1). In this context we are examining peptides and metal complexes of peptides for their proteolytic activity.



AA_n: 7 different D- and L-amino acids
 X_n: 7 different spacers

Figure 1: Split-and-mix library tested for phosphate-, ester- and amide bond hydrolysis.

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Towards the Automated Solid-Phase Synthesis of Biologically Relevant Mannose-Rich and Complex Oligosaccharides

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N-Glycans are important for the biological function of cell-surface receptors, cell-adhesion molecules, immunoglobulins and tumor antigens. Mannose-rich **1a** and complex type **2a** are two major classes of *N*-Glycans. The goal of the discussed project is the development of the automated solid-phase synthesis of *n*-pentenyl functionalized branched mannose-rich undecasaccharide **1b** and complex type nonasaccharide **2b**. The targeted modular approach applies only monomeric building blocks. The main challenges lie in the synthesis of beta-mannosidic bonds on solid support and the high degree of branching inherent to the structures. Both challenges and opportunities especially with respect to a general automated oligosaccharide synthesis as well as preliminary results will be discussed on the poster.

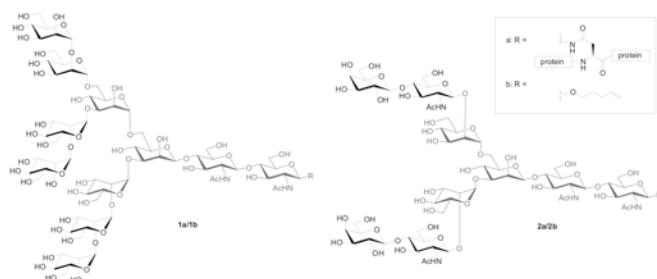


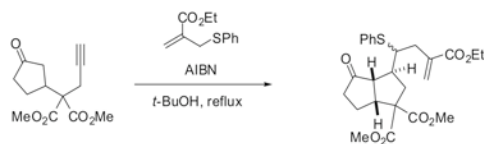
Figure 1. Structures of the mannose-rich (1a) and complex (2a) classes of *N*-Glycans and of the mannose-rich (1b) and complex (2b) oligosaccharide targets.

Tandem 1,5-Hydrogen Transfer – Cyclization – Alkylation Mediated by Thiyl Radicals

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Recently, we developed a tin-free process to run alkenyl radical mediated 1,5-hydrogen transfer - cyclization processes.¹ This reaction has been used for short and efficient synthesis of erythrodiene² and uses thiophenol as a reagent. We report here an extension of this reaction to allylsulfides. This tandem process allows to create two C–C bonds and one C–S bond in a single operation.



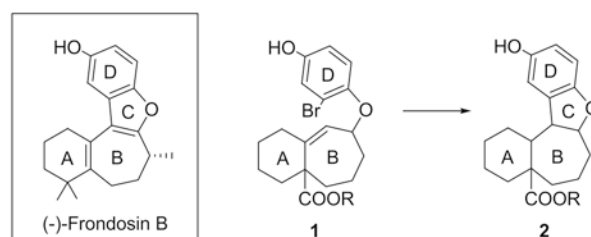
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New Approach towards the Synthesis of Frondosin B

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Freiestrasse 3, 3012 Bern

(-)-Frondosin B belongs to a family of related marine sesquiterpenoid, the frondosins A-E, recently isolated from a marine sponge *Dysidea frondosa*. Each of them inhibits the binding of IL-8 to its receptor in the low micromolar range [1]. Therefore, an IL-8 receptor antagonist represents a promising target for the development of novel pharmacological agents against autoimmune hyperactivity. In this work we propose a new synthetic approach in which the key step will be the radical cyclization for the formation of the furan ring C. A model system (**1**) for the cyclization has been investigated.



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New Applications of Chromium Mediated Dearomatisation Reactions

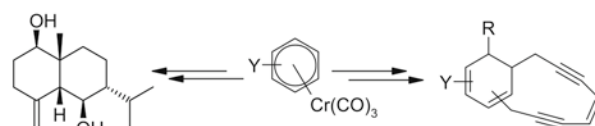
Séverine Lavy, Alejandro Pérez Luna,
Laxmisha Mundrupady, E. Peter Kündig*

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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. This dearomatization reaction provides a rapid access to stereoselectively substituted cyclohexadienes. This dearomatization sequence is used to reach bioactive natural products [1].

We here report progress in the application of this one-pot dearomatization sequence in the synthesis of a rare member of the eudesmane family of natural products: 5-*epi*-eudesma-4(15)-ene-1 β ,6 β -diol [2].

We have also applied the nucleophile/electrophile addition reaction to the elaboration of novel cyclic enediynes introducing a propargyl group either as a nucleophilic or electrophilic reagent.

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

novel cyclic enediynes

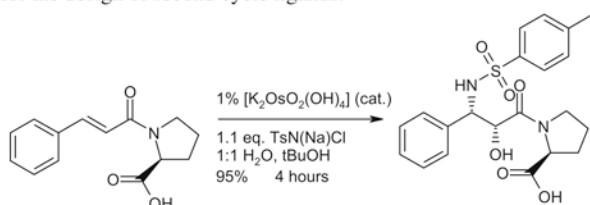
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Cinnamoyl-Proline Amides Exhibit Unforeseen Enhanced Reactivity in "Special" 2nd Cycle Osmium Catalysed Amino Hydroxylation

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Ligand-independent osmium catalysed aminohydroxylation of olefins has been the subject of intense investigation. Our goal was to further expand the scope and application of this important reaction and to uncover hitherto unknown characteristics such as rate, diastereoselective and regioselective effects of the 2nd cycle. During these studies, we discovered that cinnamoyl-proline amides exhibit unforeseen enhanced reactivity. It was rationalised that the planar 5-membered ring system combined with the hydrophilic carboxylic acid constituent in cinnamic-proline amides was optimal for accelerating the 2nd cycle aminohydroxylation. This accelerated 2nd cycle "special" aminohydroxylation of cinnamic-proline amides is believed to be general, with complete conversion even being observed after only 4 hours. We consider that these structure-reactivity-relationships, observed in 2nd cycle "special" aminohydroxylation, may provide pivotal new principles for the design of second cycle ligands.



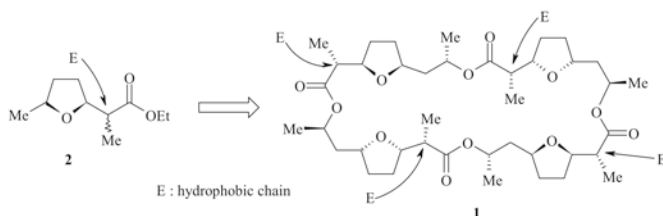
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Preparation of hydrophobic ionophore derivatives

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Antibiotic ionophore nonactin **1** is a natural product produced by a variety of *Streptomyces*. Nonactin **1** is used in ion selective electrodes because of its selectivity in favor of ammonium and potassium cations [1]. The use of these electrodes is limited due to the loss of nonactin through bleeding. Our goal is to modify **1** adding hydrophobic chains [2], to increase the life time of nonactin in the semi permeable membrane.



Model compounds such as **2** were synthesized and successfully transformed into more hydrophobic derivatives. The challenge of this transformation is not to affect the chiral centers of the *cis* ring junctions.

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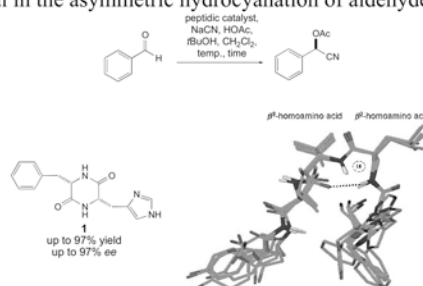
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Designed α/β -Mixed Oligopeptidic Catalysts with Stable Hairpin-Turn Structure

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Inoue's diketopiperazine **1** is one of the most effective catalysts for the asymmetric hydrocyanation of aromatic aldehydes.^[1] The origin of the asymmetric induction is supposed to be a kind of "enzymatic" pocket formed by the aromatic side-chains.^[2] We chose to incorporate a central \square^2/\square^3 -amino acid control element^[3] in an \square -hexapeptidic backbone to form a hairpin-turn secondary structure. The termini of the peptide-chain converge to form a pocket. "Designed" peptides^[4] of this type are tested for their potential in the asymmetric hydrocyanation of aldehydes.



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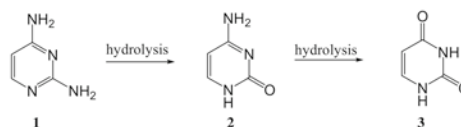
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Synthesis of Homo-DNA-C-Nucleosides (2',3'-dideoxy- β -D-glucopyranosyl-C-nucleosides)

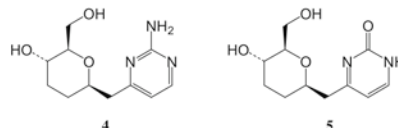
Michael Löpfe, Jay S. Siegel

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Chemistry can rationalise DNA by a systematic chemical synthesis and structure investigation of possible but not naturally occurring alternative structures. [1] We recently proposed a possible pyrimidine codon derived from 2,4-diaminopyrimidine **1** and its hydrolysis products cytosine **2** and uracil **3**. [2] By forming a glycosidic bond with the exocyclic amino group, cytosine **2** can form an additional nucleoside. Therefore 2,4-diaminopyrimidine **1** would act as a single source for all nucleobases of that codon.



For structural investigation, a synthesis of the two 2',3'-dideoxy- β -D-glucopyranosyl-C-nucleosides **4** and **5** was developed.



[1] A. Eschenmoser, A. Dobler, *Helv. Chim. Acta* **1992**, 75, 218.

[2] J. S. Siegel, Y. Tor, *Org. Biomol. Chem.* **2005**, 9, 1591.

Organocatalysts for Decarboxylative Aldol-Type Reactions

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

The biosynthesis of polyketides and fatty acids is based on an enzymatic activation of a malonic acid mono thioester to generate selectively a thioester enolate via decarboxylation.¹ The following cross-Claisen condensation with a second thioester elongates then the carbon chain by a C₂-unit. In the case of fatty acids the resulting alcohol is then reduced or eliminated before a next reaction cycle can occur.

According to the biosynthesis we will present a synthetic approach for the key step of the metabolism of polyketides and fatty acids. We will show an enantioselective reaction between a malonic acid mono thioester² and different electrophiles catalysed by several organocatalysts which gives access to several interesting chiral substrates and building blocks.

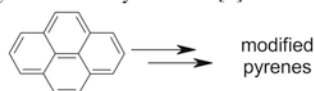
- [1] Staunton, J.; Weissman, K.J. *Nat. Prod. Rep.* **2001**, *18*, 380.
[2] Imamoto, T.; Masahito, K.; Yokoyama, M. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2303.

Modification of Pyrene: New Developments and New Properties.

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Freiestrasse 3, CH-3012 Bern, Switzerland

During the last decade the use of pyrene derivatives as components of new materials is well recognized. Because of the richness of photophysical properties of pyrene the number of research articles as well as patents in different fields of its studies is growing extremely (microenvironment sensors, liquid crystals, OLEDs, fluorescent polymers and dendrimers, genetic probes). Such modern applications are based typically on quite aged synthetic developments that bring advantages (price and simplicity etc) and disadvantages (characterization, purity etc as well as some limitation of available compounds) [1]. Needs of new properties of pyrene ring promoted various groups to pyrene organic chemistry research [2].



Herein, we report our recent developments on synthesis of pyrenes with tuned spectroscopic properties [3]. Analysis of synthetic developments, as well as NMR, UV-Vis and fluorescence data will be presented and discussed.

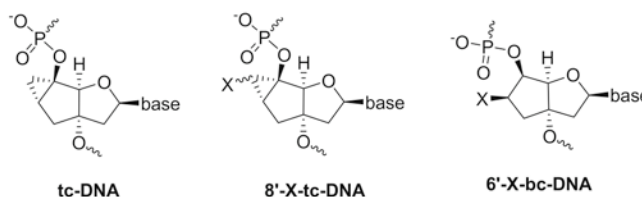
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[2] e.g. see articles by groups of Geerts, Y.H.; Yamana, K.; Schlüter, A.D.
[3] Malinovskii, V. L., Häner, R. *Eur. J. Org. Chem.* **2006**, accepted.

Synthesis of conformationally constrained nucleotides with improved lipophilicity

Luisier Samuel, Christian Leumann

Department of chemistry and biochemistry, University of Bern, Freiestrasse
3, 3012 Bern, Switzerland

Tricyclo (tc)-DNA shows promising properties as an antisense oligonucleotide^{1,2}. Due to the anionic character of the sugar-phosphate backbone, oligonucleotides and modified oligonucleotides show restricted cellular uptake. The attachment of a lipophilic rest to the sugar analogue of tc-DNA is expected to increase the membrane permeability of the modified oligonucleotide³. In this context, we synthesized two different bicyclo- and tricyclo-DNA, with lipophilic side chains at the carbocyclic rings.



¹ D. Ittig, S. Liu, D. Renneberg, D. Schümperli, C. J. Leumann, *Nucleic Acids Res.*, **2004**, *32*, 346

² Renneberg, Leumann, *JACS*, **2002**, *124*, 5993

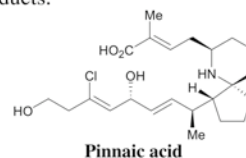
³ Chaltin, Margineanu, Marchand, Van Aerschot, Rozenski, De Schryver, Herrmann, Mül-
len, Juliano, Fisher, Kang, De Feyter, Herdewijn, *Bioconjugate Chem.*, **2005**, *16*, 827

Toward a New Synthesis of Azaspirocyclic Core of Pinnaic Acid

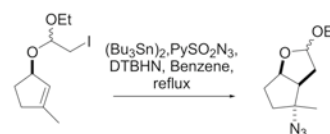
Nathalie Mantrand, Philippe Renaud*

University of Berne, 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. The structurally related halichlorine was isolated at the same time from the marine sponge *Halichondria okadai* Kadota. These two alkaloids bear a unique highly functionalized spiranic core representing the main synthetic challenge towards these natural products.



We are currently developing a novel synthesis of the azaspirocyclic core via a radical carboazidation-cyclization reaction[2]. The diastereoselective formation of the quaternary centre bearing a nitrogen atom is investigated on a model substrate (see scheme).



[1] Chou, T.; Kuramoto, M.; Otani, Y.; Shikano, M.; Yasawa, K.; Uemura, D.; *Tetrahedron Lett.* **1996**, *37*, 3871.

[2] Panchaud, P.; Ollivier, C.; Renaud, P.; Zigmantas, S. *J. Org. Chem.* **2004**, *69*, 2755-2759.

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Synthesis and Crystal Engineering of Halogenated Fluorostilbenes

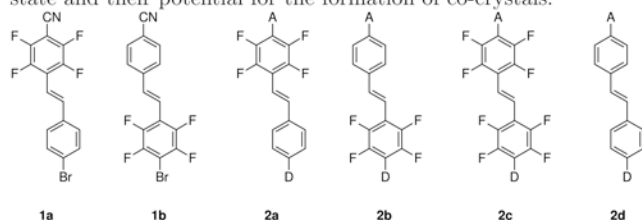
Raul Mariaca, Fabien Helbling, Norwid-Rasmus Behrnd, Patrick Eggli, Helen Stoeckli-Evans* and Jürg Hulliger**

*Institut de Microtechnique, Université de Neuchâtel, Rue Emile-Argand 11, 2009 Neuchâtel.

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

Polyfluorinated (*E*)-4-(4-bromostyryl)-benzonitriles are suitable building blocks for the preparation of solid-state 1:1 complexes with corresponding H counterparts. In crystal engineering, F-aromatic/H-aromatic interactions are highly significant. Previous work showed that **1a** and **1b** can conveniently be synthesized and used as building blocks to form solid solutions with polar properties [1].

Present efforts are concentrated on the synthesis of acceptor (A) / donor (D)-model stilbenes of type **2a–2d**, the study of interactions in the solid state and their potential for the formation of co-crystals.



D = F, Cl, Br, I
A = CN, NO₂

- [1] R. Mariaca, N. Behrnd, P. Eggli, H. Stoeckli-Evans, J. Hulliger, *CrystEngComm*, **2006**, *8*, 222–232.

Organic Chemistry

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Solid-Phase Synthesis of *N*-Hydroxypolyamines Derivatives

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The venom of the spider *Agelenopsis potteri* contains a complex mixture of linear polyamine derivatives, e.g. *N*-hydroxypolyamine derivatives. These biologically active compounds interact for example with ion channels in mammalian central nervous system and thus have a therapeutically interest for studies of brain disorders such as Parkinson's and Alzheimer's diseases. Construction of orthogonally protected *N*-hydroxypolyamines can be performed on solid phase. The required *N*-hydroxyl group is introduced during the cleavage of the polyamine derivative from the resin through a Cope elimination reaction [1]. Selective deprotection of either of the two terminal amino functions allows the derivatisation of the *N*-hydroxypolyamines. The synthesized acyl-*N*-hydroxypolyamines are used as reference compounds for the study and identification of constituents of authentic venom samples of *Agelenopsis potteri*, applying high performance liquid chromatography coupled with mass spectrometry (HPLC-MS).

- [1] J. Seo et al. *Tetrahedron* **2005**, *61*, 9305

Organic Chemistry

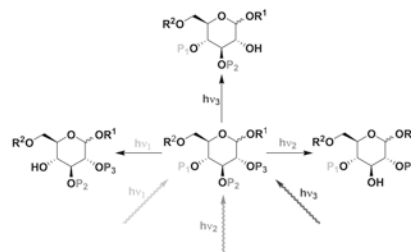
314

Orthogonal protection of glycosides with photolabile protecting groups

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Recently, our group developed the concept of chromatic orthogonality which consists in the selective cleavage of two different photolabile protective groups using two different wavelengths [1]. The conditions of cleavage only requiring light and no additional reagents could apply as an appropriate answer to the challenges of the oligosaccharide synthesis.



Our goal is to develop methods using known orthogonal photolabile protective groups to protect hydroxyl groups of glucose as ethers and/or carbonates to obtain a potential orthogonal two-dimensional wavelength system [2] [3] coupled with a third sequential photo-deprotection. We will in particular show the strategies and problems involved with such type of protection using photolabile protective groups.

- [1] C.G. Bochet, *Synlett* **2004**, *13*, 2268–2274.

- [2] U. Zehavi, B. Amit, A. Patchornik, *J. Org. Chem.* **1972**, *37*, 2281–2284.

- [3] A. Blanc, C.G. Bochet, *J. Am. Chem. Soc.* **2004**, *126*, 7174–7175.

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Organic Chemistry

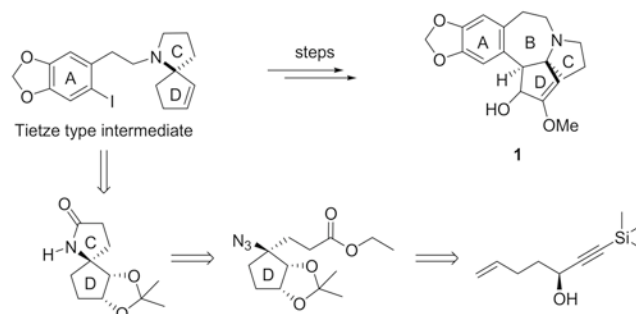
316

A Novel Strategy for the Synthesis of Optically Pure of *Cephalotaxus* Alkaloids

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

Recently our group has developed a procedure for one-pot intermolecular radical addition [1]. To study the control of the relative and absolute stereochemistry of the spirocenter we decided to synthesise cephalotaxine **1** according to the retrosynthetic analysis shown above.



The spirocenter of cephalotaxine is stereogenic and the control of its absolute configuration is a key feature. To achieve this stereocontrol we are working with bicyclic compounds.

- [1] P. Renaud, C. Ollivier, P. Panchaud, *Angew. Chem. Int. Ed.* **2002**, *41*, 3460

Radical Azidation of Organoboranes

F. Montermini, P. Renaud*

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Organoboranes are very useful reagents for organic synthesis. They are easily prepared by hydroboration of alkenes and are very efficiently converted into alcohols by oxidative treatment.⁽¹⁾ This reaction sequence represents one of the most efficient ways of achieving anti-Markovnikov addition of water to alkenes. In 1972, Davies and Roberts demonstrated that benzenesulfonyl bromide is a suitable reagent for the bromination of tri-*n*-butylborane.⁽²⁾ They assumed that this reaction is a radical chain process in which a benzenesulfonyl radical displaces an alkyl radical from tri-*n*-butylborane. Recently, we discovered that *B*-alkylcatecholboranes are extremely useful radical precursors that can participate in efficient carbon-carbon and carbon-oxygen bond formation.⁽³⁾ To the best of our knowledge, no conversion of organoboranes into azides has been reported. We describe here the radical azidation of organoboranes using benzenesulfonyl azide.



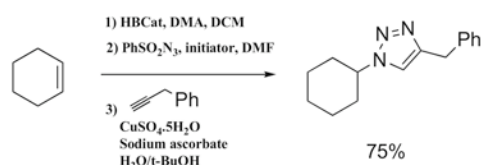
- (1) : G.C Fu, C.E. Garrett, *J. Org. Chem.*, **1996**, *61*, 3224.
 (2) : Davies, A. G.; Roberts, B. P. *Acc. Chem. Res.* **1972**, *5*, 387.
 (3) : C. Ollivier, P. Renaud, *Chem. Rev.* **2001**, *101*, 3415-3434.

Sequential Radical Azidation – 1,3 Dipolar Cycloaddition
Rapid access to 1,4 disubstituted 1,2,3 triazoles.

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University of Bern, Freiestrasse 3, 3012 Bern, Switzerland.

Copper(I) catalyzed regioselective ligation of azides and terminal alkynes by Huisgen cycloaddition process is well described in mild conditions to furnish the regioselective 1,4 disubstituted 1,2,3 triazoles⁽¹⁾. Here, we describe radical azidation of organoboranes followed by a 1,3 dipolar cycloaddition process starting from different olefins.



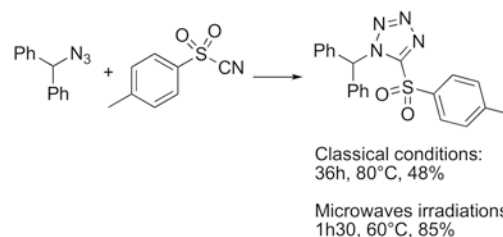
- (1) : Vsevolod V. Rostovtsev, Luke G. Green, Valery V. Folkin, K. Barry Sharpless, *Angew. Chem. Int. Ed.*, **2002**, *41*, 14, 2596-2599.

Preparation of Tetrazoles using Microwave Technology
Synthesis of 5-Sulfonyl Tetrazoles from Azides and Sulfonyl Cyanides

F. Montermini, P. Renaud

University of Bern, Freiestrasse 3, 3012 Bern, Switzerland.

Tetrazoles have gained increasing attention since early 1980s, mainly due to pharmaceutical applications. Recently⁽¹⁾, click chemistry reactions, in neat conditions, between toluenesulfonyl cyanide with various alkyl and aryl azides were very efficient. But reaction time is the main drawback of this process. Due to the dipolar properties of sulfonyl cyanides and alkyl azides, we describe here the [2+3] cycloaddition process under Microwaves irradiations.



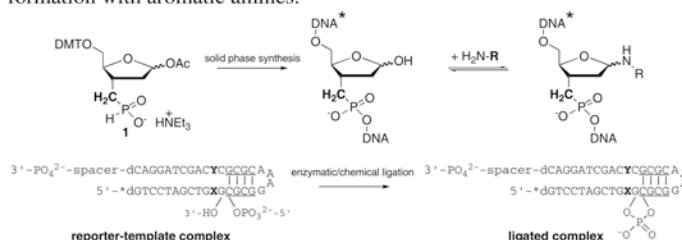
- (1) : Zachary P. Demko, K. Barry Sharpless*, *Angew. Chem. Int. Ed.* **2002**, *41*, 12, 2110- 2113.

A Combinatorial Method for Selecting Novel Interacting DNA Base Analogues

Markus Mosimann, Christian J. Leumann

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Freiestrasse 3, 3012 Bern, Switzerland

There is considerable need for new nucleobases or base-pairs, e.g. for use as universal bases, or for the expansion of the genetic code. Design and synthesis of such new potential nucleobases is a time consuming process and design rules for those interacting by hydrophobic forces only are missing. Here we present a novel assay for fast and easy screening of potential nucleobases. The assay is based on the recently developed [1] chemically stable and functional abasic site analogue **1**, capable of reversible hemiaminal formation with aromatic amines.



Aromatic residues **X** that correspond to a match with its opposing partner **Y** in a duplex are expected to increase the ligation rate between a labeled (*) reporter oligonucleotide with its corresponding hairpin template (see Figure), which in turn can be measured by optical or electroforetic techniques.

- [1] M. Mosimann, P. A. K pfer, C. J. Leumann, *Org. Lett.* **2005**, *7*, 5211.

Mass Spectrometric Screening of Chiral Catalysts

Constanze A. Müller, Andreas Pfaltz*

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Fax +41 61 267 1103, e-mail: andreas.pfaltz@unibas.ch

High-throughput parallel screening of chiral catalysts is an important area of research in asymmetric catalysis. Electrospray mass spectrometry can be used as an analytical tool to measure the intrinsic enantioselectivity of chiral catalysts directly from examining catalyst-reactant complexes. [1]

In our group the efficiency of chiral Pd-catalysts in the kinetic resolution of allylic esters was determined directly by mass spectrometric monitoring of allyl-Pd-intermediates derived from quasinantiomeric substrates.

Here we report on the application of this technique in asymmetric allylic alkylation reactions. According to the principle of microscopic reversibility, we analysed the retro reaction. We therefore used leaving groups, which are normally applied as nucleophiles in the forward reaction.

[1] C. Markert, A. Pfaltz, *Angew. Chem. Int. Ed.* **2004**, *43*, 2498.

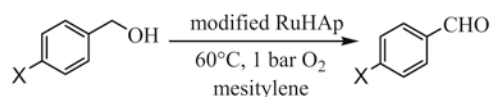
Fast and highly selective heterogeneous catalytic oxidation of benzylic alcohols to aldehydes with oxygen

Z. Opre, D. Ferri, F. Krumeich, T. Mallat, A. Baiker

Institute for Chemical and Bioengineering, Department of Chemistry and Applied Biosciences, ETH Zurich, Hönggerberg, HCI, 8093 Zurich

Aerobic oxidation of alcohols to aldehydes and ketones over solid catalysts is an important transformation in "green" chemistry.

The activity of ruthenium-hydroxyapatite (RuHAp) in the oxidation of benzylic alcohols with molecular oxygen was enhanced remarkably by incorporation of Ru into organically modified HAp and no detectable product beside the aldehydes formed.



X = H, Me, MeO, Cl, NO₂

Yield: 98-99%, Selectivity: 100%, TOF: 72-242 h⁻¹

On the basis of catalytic, DRIFT, SEM, STEM-EDX, ICP-OES, and BET measurements we assume that the major reason for the activity enhancement is the higher intrinsic activity of Ru species due to their different location and coordination in organically modified HAp. It is very probable that incorporation of Ru is not an ion-exchange but rather an adsorption process which is controlled by the polar organic compounds (prolinol, proline, benzoic acid, and hexanoic acid) and, interestingly, during this process the modifiers leach out and thus do not disturb the catalytic oxidation of alcohols.

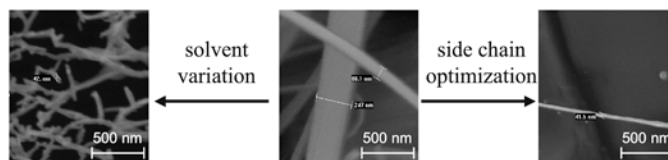
[1] Z. Opre, D. Ferri, F. Krumeich, T. Mallat, A. Baiker, *J. Mol. Catal.* in press

Control of the lateral aggregation of perfluoroalkylated hexa-*peri*-hexabenzocoronene columnar stacks by side chain and medium engineering

Olivier F. Aebischer, Titus A. Jenny

University of Fribourg, Chemistry Department, 1700 Fribourg,
Switzerland

The ability of molecules to self-assemble into highly ordered architectures has gained increasing importance in the past decade, as these nano-objects are applicable in the field of optical and electronic devices. Hexa-*peri*-hexabenzocoronene (HBC) self-assembles into columnar architectures, by π -stacking, with an outstanding degree of order. Alkylated¹ or perfluoroalkylated² side chains bestow the HBC with a liquid crystalline property, unfortunately their crystallization and hence aggregation with the side chains of neighboring stacks hinders the formation of very long micrometer sized freestanding filaments, a highly valued property for certain applications. This undesired lateral aggregation can be influenced by appropriate solvents and by subtle modifications of the lateral chains as shown by optical fluorescence spectroscopy and cryo-SEM investigations.



[1] M. Kastler, W. Pisula, D. Wasserfallen, T. Pakula, K. Müllen, *J. Am. Chem. Soc.*, **2005**, *127*, 4286-4296.

[2] B. Alameddine, O. F. Aebischer, W. Amrein, B. Donnio, R. Desche-
naux, D. Guillon, C. Savary, D. Scanu, O. Scheidegger, T. A. Jenny, *J. Mater. Chem.*, **2005**, 4798-4807.

New chiral ligands for Cu-catalyzed asymmetric conjugate addition

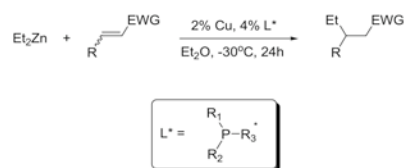
Laëtitia Palais, Alexandre Alexakis*

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Ansermet, CH-1211 Geneva, Switzerland

The conjugate addition reaction has received an impressive interest in the past decades. Many efforts have been made in designing efficient systems and identifying new ligands to improve enantioselectivities with specific families of substrates [1].

We have demonstrated that phosphoramidite ligands based on atropoisomerically flexible biphenol unit are also excellent ligands (ee's up to 99.5%) [2].

Consequently, we have synthesized a new class of phosphorous ligands and applied them in the copper-catalyzed 1,4 addition of diethylzinc to various Michael acceptors (ee's up to 91%).



[1] Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, 3221-3236

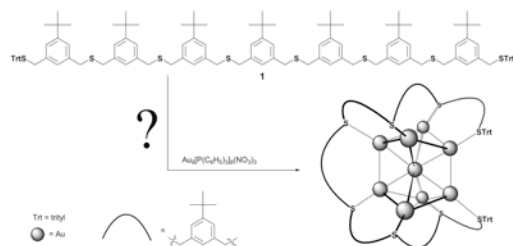
[2] Alexakis, A.; Polet, P.; Benhaim, C.; Rosset, S. *Tetrahedron Asymmetry*, **2004**, *15*, 2199-2203

A Ligand for the Inclusion of Au₉ Nanoparticles

Torsten Peterle, Marcel Mayor

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The selective inclusion of gold nanoparticles into organic ligands should allow to control the spatial arrangement of nanoparticles. This allows the creation of new functions like directed energy or electron transport, which give rise to future applications in the field of Single Electronics [1].



The heptameric ligand **1** containing eight thioether groups was developed for selective binding of the surface atoms of Au₉ nanoparticles. Other ligands or dyes for the above mentioned functions can easily be attached to **1** by replacement of the acid labile trityl protection group. Currently, the complexation properties of ligand **1** and Au₉ nanoparticles are under investigation.

[1] G. Schmid, U. Simon, *Chem. Commun.* **2005**, 697.

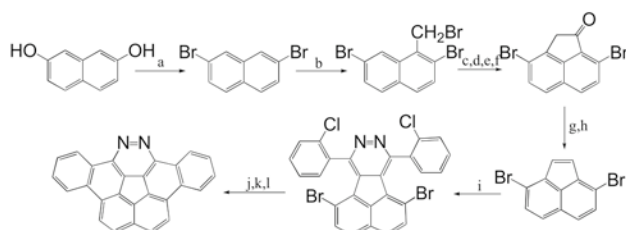
Synthesis of azacorannulene and diazacorannulene

Jay Siegel, Tony Linden, Nelli Rahanyan

Institute of Organic Chemistry, Winterthurerstrasse 190
8057 Zürich, Switzerland

Azacorannulene and diazacorannulene - nitrogen analogs of the corannulene molecule, which was first synthesized in 1966 by Lawton and Barth and has generated intense research activity in recent years.¹ Introduction of nitrogen into the corannulene framework will be based on the chemistry of triazines and tetrazines. Using the cycloaddition reaction of 1,2,4,5-tetrazines with acenaphthylene derivatives, different varieties of diazafluoranthene derivatives have been synthesized.

Current work:



a) P(Ph)₃, Br₂, acetonitrile, 250°C b) (HCHO)_x, HBr, H₃PO₄, CH₃COOH, HBr gas, 100°C, 8 h, 86%
c) NaCN, CH₃OH, reflux, 24 h, 92% d) H₂SO₄ (75%), CH₃COOH, reflux, 24h, 92% e) SOCl₂,
reflux, 6h f) AlCl₃, PhNO₂, 50°C, 8h, 78% (2 steps) g) LiAlH₄, HCl, THF h) AcOH i) 3,6-Bis(2-chlorophenyl)-1,2,4,5-tetrazine j) n-BuLi, k) ZnCl₂ l) CuCl₂

[1] Seiders, T. J.; Baldrige, K. K.; Grube, G. H.; Siegel, J. S.; *J. Am. Chem. Soc.*, **2001**, 123, 517-525.

[2] Iyoda M.; Kabir H.; Vorasingha A.; Kuwatani Y.; Yoshida M.; *Tetrahedron Letters*, **1998**, 39, 5393-5396.

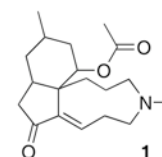
Identification and molecular modeling of a new anabaenopeptin and Investigation of the lycopodium alkaloids of *Huperzia serrata* from Hawaii

Cyril Portmann, Wesley Yoshida, Thomas Hemscheidt*

University of Hawaii at Manoa, 2545 McCarthy Mall, 96822 Honolulu, USA
University of Fribourg, Chemin du musée 09, 1700 Fribourg, Switzerland

A new anabaenopeptin extracted from *Planktothrix agardhii* CYA 126/8 was identified by different 2D NMR techniques. Its stereochemistry was determined by using Marfey's method and chromatography on chiral stationary phase of the hydrolyzed peptide. Molecular modeling [1] using NMR restraints reveals a surprising conformation of this molecule in solution (MeOH).

The alkaloids of *Huperzia serrata* from Hawaii were studied for the first time. Three already known lycopodium alkaloids were isolated and formally identified, lobscurine, huperzine J and flabellidine. A new lycopodium alkaloid **1** was isolated and identified. Its structure and its relative stereochemistry were established by NMR spectroscopy (DEPT, COSY, HSQC, HMBC).



[1] Fuhrmans, M.; Milbradt, A. G.; Renner, C. *J. Chem. Theory Comput.* **2006**, 2, 201-208

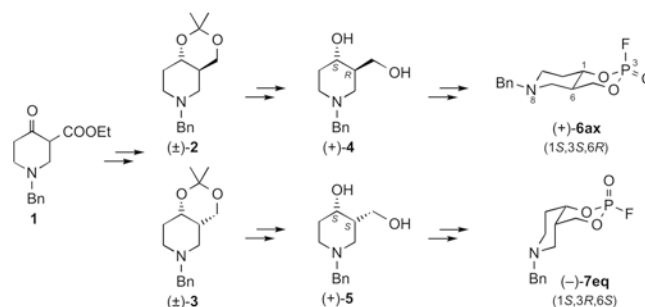
[2] Ma, X.; Gang, D. R. *Nat. Prod. Rep.* **2004**, 21, 752-772

Optically Active 8-Aza-2,4-dioxo-3-fluoro-3-phosphadecalins as γ -homo-Acetylcholine-Mimetics

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

In continuation of our studies on the irreversible inhibition of acetylcholine-esterase by organophosphates—in particular the investigation of the physiologically active conformation of acetylcholine [1] and the stereochemical course of the inhibition reaction [2]— we have synthesized the eight stereoisomeric, 3-fluoro substituted title compounds ((+)-**6ax**, (-)-**7eq** as representatives) with *ee* > 99%.



The heterocycles were prepared from the enantiomerically pure *cis*- and *trans*-1-benzyl-4-hydroxy-3-(hydroxymethyl)piperidines (**4** and **5**) by cyclization with POCl₂F as summarized above. The complete procedure and the determination of the absolute configurations as well as first results of the enzyme kinetic characterization are presented.

[1] S. Furegati, F. Gorla, A. Linden, P. Rüedi, *Chem. Biol. Interactions* **2005**, 157-158, 415.

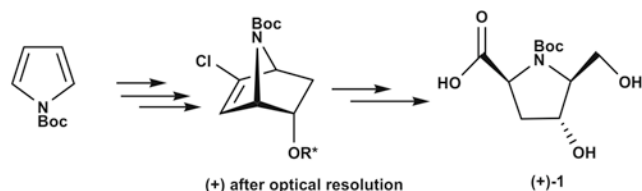
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Synthesis of 5-epi-Bulgecinine, a New Aminoacid derivative of Proline.

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D and L-prolines and derivative have been found to be excellent catalysts for asymmetric aldol and Mannich reactions, α -amination and α -aminoxylation of carbonyl compounds [1]. In addition L-proline and derivatives play a particular role in protein structure and peptide conformation and they are used to prepare new peptide-based drugs [2].



The synthesis of (\pm) and (+)-2,4-*trans*-4,5-*trans*-*N*-(Boc)-5-hydroxymethyl-4-hydroxy-proline was performed from azanobornene systems which have been stereoselectively functionalized following the "naked sugar" methodology [3].

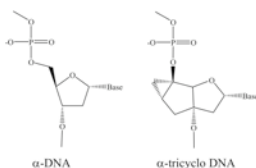
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Synthesis and Pairing Properties of β -tricyclo-DNA

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β -tricyclo(tc)-DNA is a DNA-analogue with a conformationally constrained sugar backbone that was designed in our group to enhance duplex stability via entropic stabilization [1]. It was found to be a promising candidate for antisense applications [2]. We now became interested in the α -anomeric form. We present the synthesis of the corresponding phosphoramidites bearing all four natural bases as well as oligomers thereof. Pairing properties of α -tc-DNA with natural DNA and RNA complements in parallel and anti-parallel orientation were investigated by UV-melting analysis and CD spectroscopy. We found that β -tcDNA behaves similar to β -DNA and binds natural nucleic acid complements preferably in the parallel mode via Watson-Crick base-pair formation [3]. Interestingly, within its own backbone series β -tc-DNA exhibits poor thermal stability. This among other properties makes it an interesting candidate for DNA double-strand invasion.



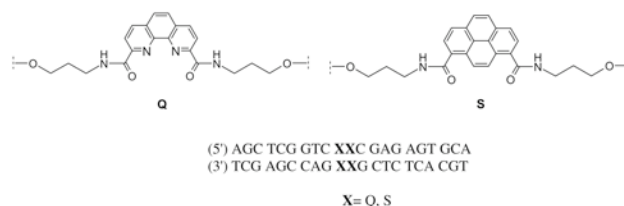
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Synthesis and Properties of DNA Mimics Containing Stretches of Non-Nucleosidic Building Blocks

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Simple, non-nucleosidic phenanthroline (Q) and pyrene (S) derivatives have been synthesized and incorporated into DNA. The hybrids containing stretches of phenanthroline or pyrene in opposite positions have been studied by thermal denaturation experiments. Furthermore, fluorescence properties of oligomers containing pyrene derivatives have been investigated and the results will be discussed.

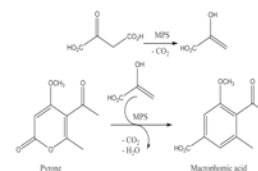


Macrophomate Synthase – a true Diels-Alderase?

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Macrophomate synthase catalyses a highly complex multi-step reaction from oxaloacetate and alpha-pyrone to benzoates [1], involving the formation of two new C-C bonds. The key step has been proposed to be a 4 + 2 Diels-Alder cycloaddition [2].



However, this conclusion is controversial [3], since an alternative 2-step Michael-aldol sequence is also possible. We have investigated this enzyme kinetically and by NMR spectroscopy. We will report our mechanistic findings together with the results of site-directed mutagenesis experiments probing the residues that line the active site.

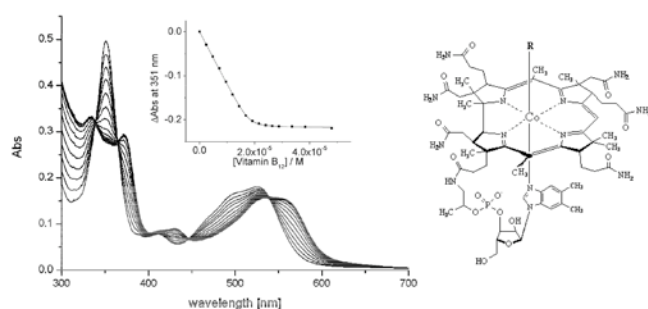
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Combinatorial Approach to Vitamin B₁₂ and Hemin Binding Peptide Dendrimers

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Peptide dendrimers are attractive models for enzymes because they can adopt a globular shape due to their branched structure. Rationally designed peptide dendrimers with histidine residues at their surface display esterase-like activities [1]. A combinatorial approach to peptide dendrimers was recently reported in our group [2]. Here we report orthogonal peptide dendrimers binding either to vitamin B₁₂ or to hemin. The dendrimers were discovered by direct functional selection from combinatorial libraries. Structure-activity relationships as well as binding affinities and the mode of coordination of the dendrimers to their ligands will be presented.



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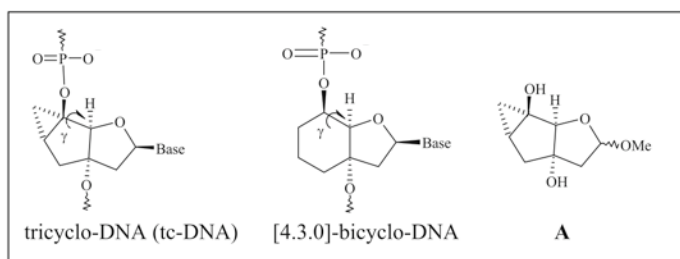
Synthesis of [4.3.0]-bicyclo-DNA nucleosides

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

In the last decade, a variety of modified nucleosides have been developed to improve antisense oligodeoxynucleotide properties such as target affinity, nuclease resistance and pharmacokinetics. The concept of conformational restriction has widely been used to enhance binding affinity and biostability. In this context our laboratory developed the analogue tricyclo-DNA (tc-DNA) [1]. In order to correct for non-optimal orientation of torsion angle γ in tc-DNA, we evaluated the analogue [4.3.0]-bicyclo-DNA by computer modeling. One of the low energy conformations of this analogue indeed showed preferential gauche orientation of angle γ .

We present the synthesis of the thymidyl-nucleoside starting from compound **A**, a precursor of tc-DNA, via Pd(II)-mediated ring-expansion. In addition we report on a *de novo* synthesis of [4.3.0]-bicyclo-DNA nucleosides starting from D-glucose using Nielsen's strategy [2].



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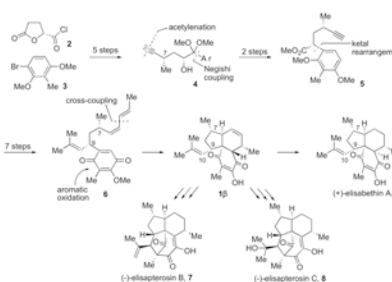
Synthetic Studies Towards the Elisabethae Family of Natural Products

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The objective of the project was to develop an efficient route to the structurally challenging Elisabethae family of natural products, which are generating much pharmacological interest due to their interesting biological activities including anti-inflammatory, antibacterial, analgesic, and cytotoxic properties [1]. The unique and complex framework, the multiple rings, and the various peripheral functionalizations of these natural products pose formidable challenges to the development of an efficient, convergent approach to this set of molecules.

Efforts were directed towards the asymmetric total synthesis of (+)-elisabethin A (**1**), which is believed to be a precursor to several other members of the family. A key step in the synthesis was construction of the tricyclic elisabethin framework (**1**) by an intramolecular Diels-Alder reaction of a *E,Z*-diene onto a quinone (**6**), a transformation that created three of the five chiral centers of (+)-elisabethin A [2]. Compound **6** was synthesized from (*R*)-5-oxo-2-tetrahydrofuran-carboxylic acid chloride (**2**), through a 14-step sequence that featured a diastereoselective methylation to introduce the C7 methyl group and a stereospecific pinacol-type ketal rearrangement to set the C9 center. The Diels-Alder reaction proceeded as planned to yield the intramolecular cycloadduct **1b**, which after further transformation followed by epimerization gave the desired natural product (+)-elisabethin A (**1**) [3]. Additionally, the (+)-elisabethin A precursor **1b** nicely underwent a biosynthesis inspired oxidative cyclization to yield (-)-elisapterosin B (**7**) and (-)-elisapterosin C (**8**) [2][3].



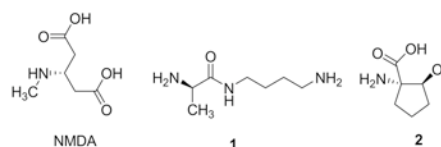
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Synthesis of Candidate NMDA-Receptor Ligands from the Chemical Universe Database

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Our group recently reported a database of all synthetically feasible small organic molecules up to 11 atoms, containing 13.9 million molecules with an average MW of 153 Da, including a very large number of drug-like molecules [1]. Herein we report the synthesis of 21 compounds from the chemical universe database. The compounds were selected from the database for their potential affinity to the glycine site of the NMDA-receptor by virtual screening and 3D-docking. [11] 9 of these newly synthesized molecules were previously known, as indicated by the indexing in the CAS, but were never evaluated for NMDA binding. All the other 21 ligands, including **1** and **2** shown below, are new, previously unknown molecules. The syntheses involve straightforward and high-yielding synthetic steps. This work demonstrates the first synthesis of new molecules from the chemical universe database, and exemplified the potential of this database for delivering new molecules of interest.



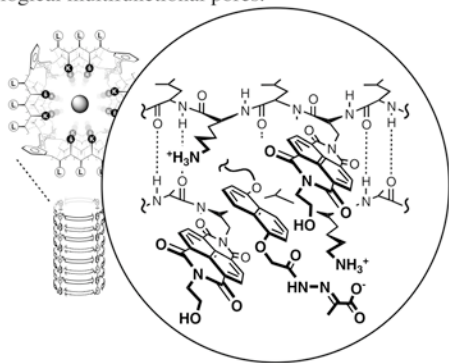
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Adhesive π -Clamping within Synthetic Porous Biosensors

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We report design, synthesis and evaluation of synthetic multifunctional pores with electron-poor naphthalenediimide (NDI) π -clamps at the inner surface for molecular recognition by aromatic electron donor-acceptor interactions. Synthetic multifunctional pores have been introduced as optical transducers of chemical reactions and, in concert with enzymes, as universal biosensors [1,2]. However, the molecular recognition motifs elaborated so far for the closing and the opening of synthetic multifunctional pores in response to chemical stimulation focus exclusively on multiple ion pairing. Here, we introduce ion-pair-assisted, adhesive π -clamping as attractive concept for interactions that are orthogonal to ion pairing and without reach for biological multifunctional pores.

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Synthesis and Reactivity of Novel Benzofuran Scaffolds

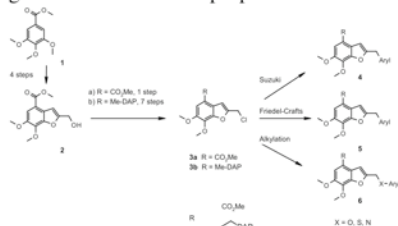
S.Greiveldinger-Poenaru, S.Teixeira-Fouchard, S.Michel, M.Muhmenthaler,
K. Burri, D. Gillissen, K. Islam

ARPIDA AG, Dammstrasse 36, CH-4142, Münchenstein, Switzerland

In order to explore the potential of benzofuran scaffolds in the search of novel antibacterial agents, we studied and developed the synthesis of common intermediates suitable for further chemical modification/diversification via parallel synthesis.

Here we wish to report on the synthesis of two novel 2-chloromethylbenzofuran^[1] scaffolds and on their use for the development of new chemical entities. The first type of scaffold **3a** (R = CO₂Me) was obtained in 5 steps starting from methyl 3,4,5-trimethoxybenzoate, whereas, the second type **3b** (R = methyl-diaminopyrimidine, Me-DAP) could be obtained after 7 subsequent steps starting from the intermediate **2**. Both scaffolds were tested for their reactivity in several types of reactions such as alkylations^[2], Suzuki or Friedel-Crafts couplings, reactions which were not described until now with chloro-methylbenzofurans.

Scaffolds like **3a** and **3b** allowed the preparation of several small libraries of novel and well diversified aryl- or heteroaryl-methylbenzofuran derivatives for the screening of their antibacterial properties.

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Screening of Chiral Catalysts by Mass Spectrometric Monitoring of Catalytic Intermediates

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Developing high-throughput screening methods for an accelerated discovery of catalysts for asymmetric synthesis has been the subject of much attention lately. It is possible to determine the intrinsic enantioselectivity of a chiral catalyst directly from detecting catalyst-reactant complexes, which can be observed by electrospray ionisation mass spectrometry (ESI-MS). This concept has been demonstrated previously by Markert and Pfaltz by examining the kinetic resolution of allylic esters with quasisantiomeric substrates.[1]

We here report the retro-Diels-Alder reaction of mass-labelled quasi-enantiomers with a chiral catalyst. Due to the different masses the catalyst-reactant complexes can be distinguished by ESI-MS. The ratio of the two catalyst-reactant complexes, which is determined by integration, reflects the efficiency for enantiodiscrimination of the chiral catalyst.

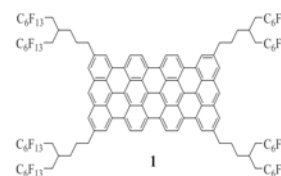
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New Polycondensed Aromatic Hydrocarbons for Supramolecular Self-assembly

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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) [1]. As an alternative to the HBC's, a disk shaped highly symmetrical core structure, we developed strategies for the synthesis of the so far unknown tetraanthryl core structure **1** surrounded by partially fluorinated branched aliphatic side chains. Preliminary calculations allow us to expect for this structure a further improved π - π stacking behavior as compared to the HBC's.



In the HBC series these side chains gave the best results in minimizing lateral interactions between columnar assemblies, maximizing the π - π stacking in the columnar axis, and simultaneously providing highest solubility of the molecules in appropriate solvents such as hexafluorobenzene.

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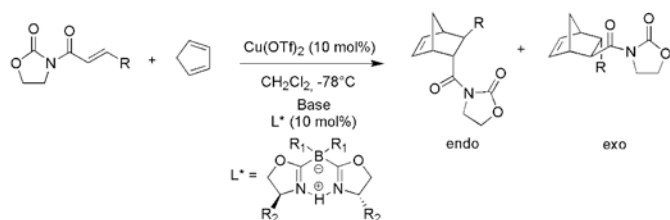
BORON-BASED BISOXAZOLINES AND THEIR USE IN COPPER-CATALYZED ASYMMETRIC REACTION

Aurélie Toussaint, Andreas Pfaltz*

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Bisoxazoline (BOX) have established themselves as privileged chiral ligands in asymmetric catalysis.¹ Boron-based variants of these ligands (Bora-BOX) have been recently developed in our group.²

Herein, we describe their use as effective catalysts in enantioselective Copper-catalyzed Diels-Alder and Henry reactions.



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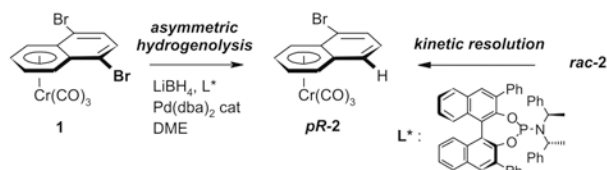
Catalytic Desymmetrization and Kinetic Resolution of Chromiumtricarbonyl and RutheniumCp Complexes of Substituted Naphthalenes

Xavier Urbaneja, Jingyu Chou, Piyali Datta-Chaudhuri,
Graham Cumming, E. Peter Kündig*

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Highly enantioenriched (η^6 -arene)tricarbonylchromium(0) complexes whose chirality originates from the 1,2-disubstitution pattern of the arene and the coordination of the metal to one enantiotopic face of the arene are powerful chiral centers in asymmetric synthesis. Robust, planar chiral arene complexes also increasingly find application as chiral ligands in asymmetric catalysis.[1] A potentially very attractive catalytic route is the desymmetrization of *meso*-complexes by a chiral catalyst.

We here detail ongoing studies of catalytic asymmetric hydrogenolysis and kinetic resolution to obtain highly enantioenriched planar chiral π -complexes. The bulky chiral phosphoramidite ligand L* has been found best for these Pd-catalyzed transformations.[2]



We also report results on desymmetrization of the more robust and air stable complex [*meso*-Ru(5,8-dibromonaphthalene)(Cp)]⁺.

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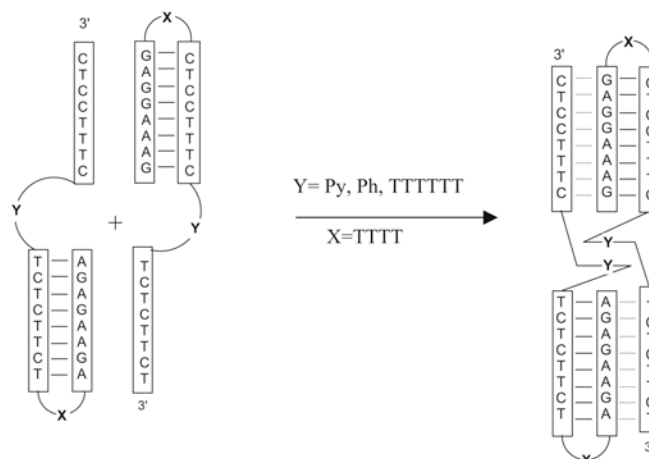
DNA mimics: Formation of modified interstrand triplex dimers

Ivan Trkulja, Robert Häner

University of Berne, Freiestrasse 3, 3012 Bern, Switzerland

Pyrene and phenanthrene non-nucleosidic building blocks were synthesized and used to study the formation of a novel "triplex dimer" through Hoogsteen binding between the two complementary sequences.

Dimer formation was followed by monitoring excimer formation between the two pyrene moieties that were used to modify natural DNA. Influence of different substituents on the thermal stability of this structure and its fluorescence properties have been studied and will be discussed.

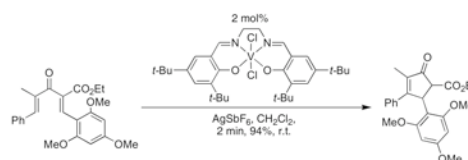


Catalytic Nazarov Cyclization promoted by Dichloro Vanadium(IV) Complexes

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The Nazarov reaction [1] represents a versatile approach to the synthesis of functionalized five-membered carbocycles. In general, the substrates are subjected to Lewis acid catalysis [2]. Here, we report a highly effective cyclization catalyzed by a V(IV) salen complex. The catalytically active species is prepared by the treatment of a known oxovanadium complex [3] with SOCl₂, followed by *in situ* activation with AgSbF₆. Under these conditions, divinyl ketones bearing α -ester groups react at room temperature, some within minutes, to afford cyclopentenones.



Cyclized products are isolated in up to 94% yield and high diastereoselectivities using 2 mol% of the V(IV) catalyst. The development of an enantioselective version of the Nazarov cyclization with chiral V(IV) complexes is underway in our laboratory.

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