Inorganic and Coordination Chemistry **205**

Isolation and characterization of the first circular single-stranded polymetallic lanthanide-containing helicate

Jean-Michel Senegas,[a] Sylvain Koeller,[a] Gérald Bernardinelli[b] and Claude Piguet*[a]

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[b]Laboratory of X-ray Crystallography, University of Geneva, 24 quai E. Ansermet, CH-1211 Geneva 4, Switzerland

A thorough examination of the disassembly of bimetallic triple-stranded lanthanide helicates $[Ln_2(Li)_3]^{6+}$ in excess of metals shows the competitive formation of standard linear bimetallic complexes $[Ln_2(Li)_2]^{6+}$, and circular trimetallic single-stranded helicates $[Ln_3(Li)_3]^{9+}$.

[1] Jean-Michel Senegas, Sylvain Koeller, Gérald Bernardinelli and Claude Piguet, *Chem. Commun.*, **2005**, 2235-2237.

Inorganic and Coordination Chemistry **206**

Ion Pairing on $[(\eta^6\text{-Arene})Mn(CO)_3]^+$,$[X]^-$ Complexes

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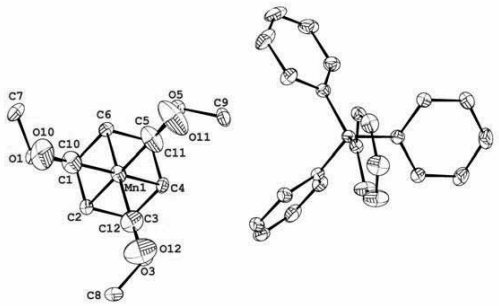
Significant differences in the ion pairing were found in a series of salts $[(\eta^6\text{-Arene})Mn(CO)_3]^+$, $[X]^-$ where the counter ion, X, is either BPh_4 or BArF.



PGSE diffusion measurements in different solvent and NOESY Spectra for those anions confirm these observations, providing unexpectedly strong ion pairing for $[(\eta^6\text{-Arene})Mn(CO)_3]^+$, $[BPh_4]^-$ in CD_2Cl_2.

Organic Chemistry **207**

The Cyanobacterial Iron Chelator Anachelin – From Fe(III) Binding to Surface Binding

Karl Gademann*, Yann Bethuel*, David Wäckerlin‡, Barbora Malisova‡, Samuele Tosatti‡, Stefan Zürcher‡ and Marcus Textor‡

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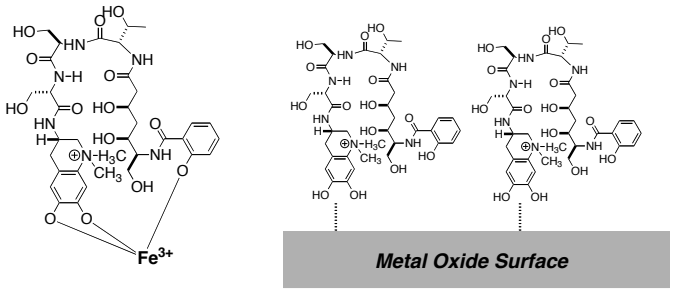
ETH Hönggerberg, 8093 Zürich

Cyanobacteria evolved sophisticated strategies for iron acquisition, transport and storage. The iron chelator anachelin[1] was evolutionarily optimized to effectively bind to Fe(III) ions. We wondered whether this exceptional phenomenon could be applied to bind to *metal oxide surfaces*.

Ion Binding *vs.* **Surface Binding**



We will present a biomimetic approach for surface modification utilizing tailor-made anachelin derivatives. The generation of self-assembled monolayers and their potential applications are discussed.

[1] For our own efforts in this area, see: K. Gademann, *ChemBioChem* **2005**, *6*, 913; K. Gademann, Y. Bethuel, *Org. Lett.* **2004**, *6*, 4707; K. Gademann, Y. Bethuel, *Angew. Chem., Int. Ed.* **2004**, *43*, 3327; K. Gademann, H. Budzikiewicz, *Chimia* **2004**, *58*, 212.

Organic Chemistry **208**

Enantioselective Hydrogen Transfer Reactions Catalyzed by Ruthenium(II) Amino Alcohol Complexes Attached to β-Cyclodextrin

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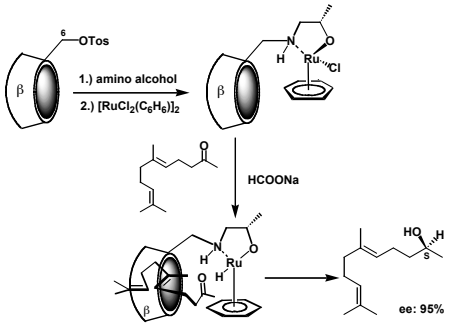
We have synthesized new water-soluble Ru complexes of -cyclodextrin-modified amino alcohols to serve as supramolecular catalysts in hydrogen transfer reactions in the presence of formiate. The reduction of aromatic and, for the first time, of aliphatic, unconjugated ketones was accomplished with ee-values as high as 97% in good to excellent chemical yields. In all cases, -cyclodextrin plays an important role on enantioselection through preorganization of the substrates in the hydrophobic cavity, see example below.



Organic Chemistry **209**

Total synthesis of the cyanoglucoside isolated from *Ilex Warburgii*

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Ecole Nationale Supérieure de Chimie de Mulhouse
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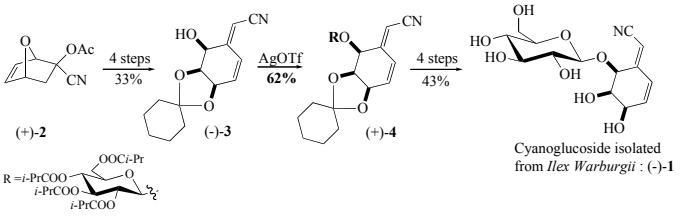
The non-cyanogenic cyanoglucoside (-)-**1** was first isolated in 1983 from the fruits of *Ilex Warburgii*, an endemic plant, collected in Iriomote Island (Okinawa, Japan) [1]. A number of non-cyanogenic cyanoglucosides of related structure, *e.g.* Simmondsin, Bauhinin, Purshianin and Lithospermoside, have been isolated from various medicinal plants and therefore they appeared us to be interesting targets. Taking advantage of the versatile methodologies developed during our syntheses of Bauhine and Lithospermoside [2], we report herein the first total synthesis of (-)-**1**.



The cyclohexylidene protecting group was chosen because of its relative stability towards acid-catalyzed isomerizations. Starting from the optically pure cycloadduct (+)-**2** [3], the protected all-*cis*-subsituted aglycone (-)-**3** was easily prepared. Carefully optimized *Koenigs-Knorr* glycosidation conditions [4] afforded then, in a very good yield (62%), the desired b-glucoside (+)-**4**.

[1] K. Ueda, K. Yasutomi, I. Mori, *Chem. Lett.* **1983**, 149
[2] D. Josien-Lefebvre, G. Desmares, C. Le Drian, *Helv. Chim. Acta* **2001**, *84*, 890 ; *Helv. Chim. Acta* **2003**, *86*, 661
[3] A. Warm, P. Vogel, *Helv. Chim. Acta* **1987**, *70*, 690
[4] G. Desmares, D. Lefebvre, G. Renevret, C. Le Drian, *Helv. Chim. Acta* **2001**, *84*, 880

Organic Chemistry **210**

New route towards functionalized polyamines and polyhydroxymacrolactones.

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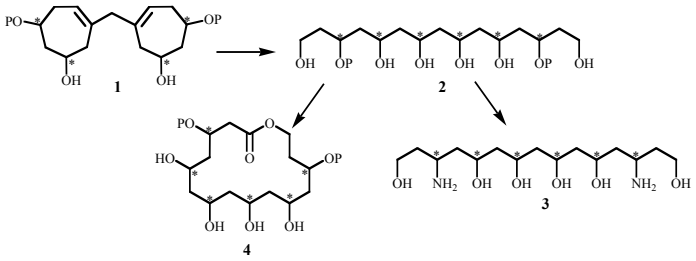
Institute of Chemical Sciences and Engineering
Ecole Polytechnique Fédérale de Lausanne (EPFL), BCH, CH-1015 Lausanne

Macrocyclic polyols are key fragments of various natural products of biological interest such as Leucascandrolide A and Bryostatin that exhibit potent antifungal and anti-cancer activities[1]. On the other hand, long-chain polyketides with amino-groups such as Zwittermycin A[2] are scarce; nevertheless they show antifungal and antibacterial properties. Recently, we reported a new efficient approach to long-chain polyols with 1,3-diol sub-units[3]. Starting from diolefin of type **1**, a large variety of stereoisomeric polyols were synthesized. These fragments were functionalized to get a library of new polyamines such as **3** and polyhydroxymacrolactones.



[1] D'Ambrosio, M.; Guerriero, A.; Debitus, C.; Pietra, F. *Helv. Chim. Acta* **1996**, *79*, 51-60. Pettit, G.R.; Herald, C. L.; Herald, D.L. *J. Am. Chem. Soc.* **1982**, *104*, 6846.
[2] Silo-Suh, L. A.; Stabb, E. V.; Raffel, S. J.; Handelsman, *J. Curr. Microbiology* **1998**, *37*,6.
[3] Gerber-Lemaire, S.; Vogel, P. *Eur. J. Org. Chem.* **2003**, 2959.

Organic Chemistry **211**

New asymmetric synthesis of polyketides and functionalized spiroketals

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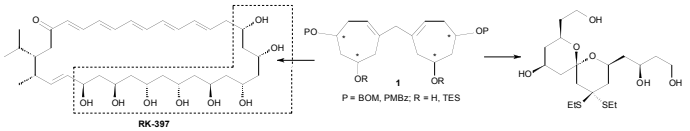
Recently, we developped an efficient route for the synthesis of long chain polyol fragments based on the stereoselective functionalization of dialkenes of type **1**.[1] This methodology was applied to the preparation of spiroketals[2] related to the spongistatin family[3] and to the polyolic subunit of the macrolide antibiotic RK-397.[4]



[1] Gerber-Lemaire, S.; Vogel, P. *Eur. J. Org. Chem.* **2003**, 2959.
[2] Gerber-Lemaire, S.; Vogel, P. *Eur. J. Org. Chem.* **2004**, 5040.
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[4] Kimie, K.; Hiroyuki, K; Takuji, K.; Kiyoshi, I.; Hiroyuki, O. *J. Antibiotics* **1993**, *46*, 1616.

Organic Chemistry **212**

A new Si-based chiral auxiliary for the stereoselective addition of organometallics to α- and β-silyloxy carbonyl compounds

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We have developed several chiral silyl groups that were shown to effect high degrees of chiral induction in a number of stereoselective transformations [1]. Since silyl groups are widely used as protective groups in organic synthesis, we intended to combine the "protective groups properties" and the "stereodirecting properties" of chiral silicon moieties. We report on the newly designed chiral silicon group **A** and its use as a chiral auxiliary for the stereoselective addition of organometallics to α- and β-silyloxy carbonyl compounds of the type **1**.

[1] S. Gassmann, B. Guintchin and S. Bienz, *Organometallics*, **2001**, *20*, 1849; M. Trzoss, J. Shao and S. Bienz, *Tetrahedron*, **2002**, *58*, 5885; B. Guintchin and S. Bienz, *Tetrahedron*, **2003**, *59*, 7527.

Organic Chemistry **213**

Synthesis of "Bioorganic" Rigid-Rod Molcules Beyond the Classical *p*-Octiphenyl

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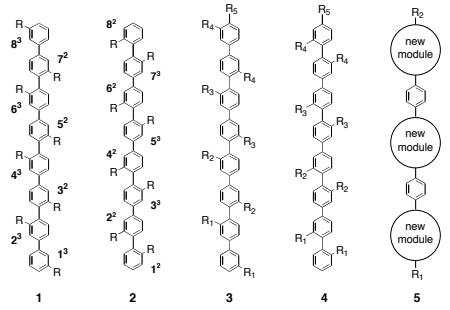
University of Geneva, Department of OrganicChemistry
1211 Geneva, Switzerland

The classical rigid-rod *p*-octiphenyl scaffold **1** has provided to access to refined supramolecular architecture such as artificial β-barrels with activities covering many variations of molecular translocation, molecular recognition and transformation [1]. The practical usefulness particularly of synthetic multifunctional pores made from **1** as detectors and sensors justifies efforts to synthesize new rigid-rod scaffolds for the discovery of new functions. Ongoing projects include efforts toward structural isomers with varied substitution pattern along the scaffold (**2**), chain-growth synthesis of refined classical (**3**) and isomeric (**4**) *p*-octiphenyls with up to five different significant substituents (peptides, higher arenes) [2] and rigid-rod molecules with modules other than phenyls (**5**).



[1] N. Sakai, J. Mareda, S. Matile, *Acc. Chem. Res.* **2005**, *38*, 79-87.
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Organic Chemistry **214**

Metal-catalyzed Hydrohydrazination and Hydroazidation of Olefins

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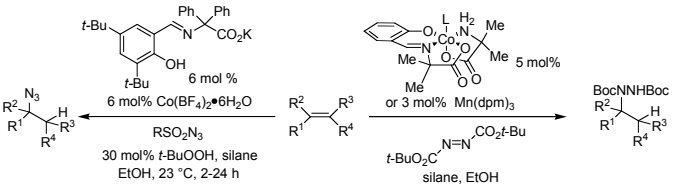
Laboratorium für Organische Chemie, ETH Hönggerberg, CH-8093 Zürich, Switzerland

Direct amination of olefins provides a fast access to synthetically useful building blocks. Whereas selective oxygen-transfer methods are now well established, amination methods are still scarce. We have developed the cobalt- and manganese- catalyzed reaction of an olefin with a silane as hydride transfer reagent and azodicarboxylates as nitrogen source to furnish protected hydrazine derivatives [1][2]. The use of sulfonyl azides as oxidizing nitrogen source allows us to extend this methodology to a convenient synthesis of alkyl azides [3].



The hydrohydrazination reaction is characterized by its ease of use, high Markovnikov selectivity, broad scope and good yield (66-94 %).
The azides obtained via the hydroazidation reaction (40-90% yield) present the added benefits of being easily converted to free amines and heterocycles.

[1] Jérôme Waser and Erick M. Carreira *J. Am. Chem. Soc.* **2004**, *126*, 5676.
[2] Jérôme Waser and Erick M. Carreira *Angew. Chem., Int. Ed.* **2004**, *43*, 4099.
[3] Jérôme Waser, Hisanori Nambu and Erick M. Carreira. *J. Am. Chem. Soc.* **2005**, in press.

Organic Chemistry **215**

Oxidations Catalyzed by a Manganese Complex Containing a Pentadentate Nitrogen Ligand Attached to β-Cyclodextrin

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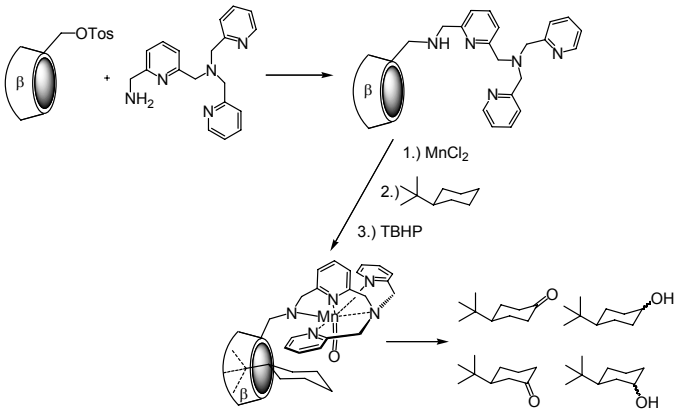
Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

We have developed a new water-soluble Mn complex consisting of a β-cyclodextrin-modified pentadentate nitrogen ligand. This complex reacts with oxygen atom transfer oxidants (e.g. TBHP) probably yielding the corresponding Mn-oxo complex. The high-valent Mn-oxo-complex is capable of oxidizing C-C double bonds, benzylic positions and non-activated C-H bonds in alkanes at room temperature, see example below. The β-cyclodextrin moiety of our supramolecular catalyst plays a role in the preorganization of the substrates by non-covalent interactions in the hydrophobic cavity of the cyclic sugar oligomer.



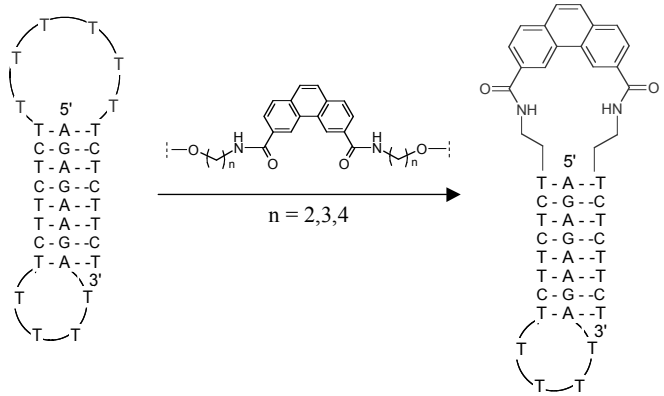
Organic Chemistry **216**

Stabilization of an intrastrand nucleic acid triplex by replacing the loop sequence with phenanthrene building blocks

Ivan Trkulja, Robert Häner

University of Berne, Freiestrasse 3, 3012 Bern, Switzerland

Phenanthrene building blocks with various linker lengths (ethylene, propylene and buthylene) [1] were successfully synthesized and used to replace the 6-T hairpin loop of an intramolecular triplex-forming DNA strand 5'- AGAGAAGA-TTTT-TCTTCTCT-**TTTTTT**-TCTCTTCT-3'. Influence of these replacements on the stability of the obtained triplex mimics at different pH values and Mg^{2+} concentrations was investigated. Introduction of the building block demonstrated a high increase of the binding affinity of the Hoogsten strand in the triplex. The results of this study will be presented and discussed.



[1] A. Stutz, S. M. Langenegger, R. Häner, *Helvetica Chimica Acta* **2003,** *86*, 3156.

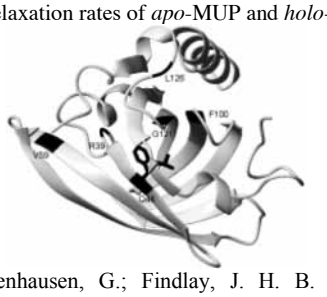
Organic Chemistry **217**

Effects of Protein-Pheromone Complexation on Correlated Chemical Shift Modulations

Chiara Perazzolo, Julien Wist and Geoffrey Bodenhausen

EPFL, SB-ISIC-BCH, 1018 Lausanne, Switzerland

Major Urinary Protein (MUP) is a pheromone-carrying protein of the lipocalin family. Previous studies on *fast internal motion* [1], *i.e.* faster than the correlation time, show that the change in backbone mobility upon binding of MUP with the pheromone 2-methoxy-3-isobutylpyrazine is not restricted to residues close the binding site. Further information can be extracted from changes in *slow internal motions*. Slow internal motions can lead to *correlated or anti-correlated modulations* of the isotropic chemical shifts of carbonyl C' and amide N nuclei [2]. Correlated chemical shift modulations in MUP have been determined by measuring differences of the transverse relaxation rates of zero- and double-quantum coherences ZQC{C'N} and DQC{C'N}. The effects of complexation on slow time-scale protein dynamics can be determined by comparing the temperature dependence of the relaxation rates of *apo*-MUP and *holo*-MUP.



Bingham, R.; Bodenhausen, G.; Findlay, J. H. B. C.; Hsieh, S.-Y.; Kalverda, A. P.; Kjellberg, A.; Perazzolo, C.; Phillips, S. E. V.; Seshadri, K.; Turnbull, W. B.; Homans, S. W. *J. Am. Chem. Soc.* **2004**, *126*, 1675.
Wist, J.; Frueh, D.; Tolman, J. R.; Bodenhausen, G. *J. Biomol. NMR* **2004**, *28*, 263

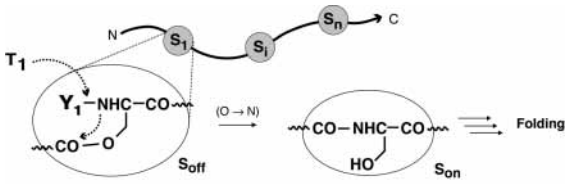
Organic Chemistry **218**

Switch on Amyloid β Peptide Self-Assembly by Enzyme-Triggered Acyl Migration

S. Dos Santos, A. Chandravarkar, B. Mandal, R. Mimna, K. Murat, L. Saucède, M. Camus, G. Tuchscherer, M. Mutter*

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

Conformational transitions as origin of peptide aggregation is considered as a fundamental molecular event in early processes of degenerative diseases. We have recently developed a new generation of switch-peptides for the controlled induction of conformational transitions at physiologic pH using O → N acyl migrations *in situ* [1]. Here, we explore the sequential triggering of O → N acyl migrations in amyloid β derived switch-peptides as a general tool to study the onset and inhibition of polypeptide folding, self-assembly and aggregation (Figure). As specific cleavage sites (**Y**) a series of orthogonal systems including chemical, photolytic and enzymatic triggers (**T**) are developed [2]. As shown by conformational and structural analyses, the sequential "switching on" of **S**-elements in Aβ 1-42 allows for evaluating the impact of individual peptide segments upon folding and self-assembly as well as its specific inhibition.



[1] Mutter, M., et al. *Angew. Chem. Int. Ed.* **2004**, *43*, 4172.
[2] Dos Santos S., Mutter, M., et al. *J. Am. Chem. Soc.*, **2005**, in press.

Organic Chemistry **219**

Synthetic Pores for Sugar Sensing in Soft Drinks and More

Svetlana Litvinchuk, Dario Pasini, Tomohiro Miyatake, Hiroyuki Tanaka and Stefan Matile*

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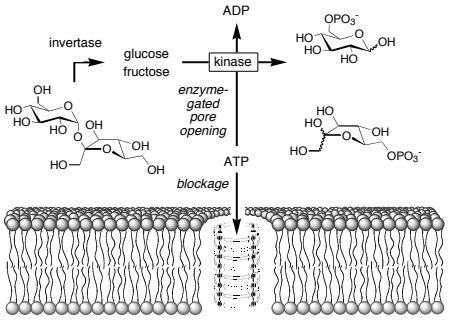
1211 Geneva, Switzerland

Recently, we discovered that chemical reactions can be detected fluorometrically with synthetic multifunctional pores in a universal manner comparable to chromatographic techniques [1]. Using enzymes as variable co-sensors to detect the analyte of choice, conceptual expansions of this method are first exemplified with sugar sensing in soft drinks [2] and then generalized toward multicomponent sensing in complex matrixes. Complementary studies focus on the developement of enzyme, substrate and inhibitor screening assays for medicinal applications such as drug discovery as well as the synthesis of pore sensors with orthogonal recognition sites.



[1] G. Das, P. Talukdar, S. Matile, *Science* **2002**, *298*, 1600-1602.
[2] S. Litvinchuk, N. Sordé, S. Matile, submitted.

Organic Chemistry **220**

Synthesis and Resolution of the First Non Racemic Diquats

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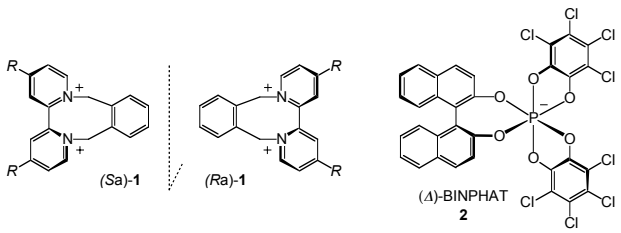
Quai Ernest Ansermet 30, CH-1211 Geneva, Switzerland

Tricyclic diquaternary salts (diquats), which have been mainly studied as electron transfer reagents, are noteworthy for their axial chirality. Their configurational stability – or the lack of it – has been strongly studied in the past [1]. So far, only racemic diquats have been reported due to (i) a high configurational lability or (ii) a lack of resolution attempts.



Resolution of diquats of type **1** (R = H, Me, *t*-Bu) was performed using BINPHAT (**2**) and TRISPHAT as temporary enantiopure counterions. The absolute configuration of **1** was assigned by X-ray structural analysis and correlated to the CD spectra. Rather high racemization barriers have been determined (R = *t*-Bu: $\Delta G^{\neq} = 25.1$ kcal.mol^{-1}, H_2O, 20 °C)

[1] (a) I.C. Calder, T.McL. Spotswood, C.I. Tanzer, *Aust. J. Chem.*, **1967**, *20*, 1195; (b) F.D. Popp, D.K. Chesney, *J. Heterocycl. Chem.*, **1972**, *9*, 1165; (c) F. Vögtle, D. Brombach, *Chem. Ber.*, **1975**, 1682; (d) C. Campà, J. Camps, J. Font, P. de March, *J. Org. Chem.*, **1987**, *52*, 521; (e) R.P. Thummel, F. Lefoulon, S. Chirayil, V. Goulle, *J. Org. Chem.*, **1988**, *53*, 4745; (f) C. Pasquini, V. Desvergnes-Breuil, J.J. Jodry, A. Dalla Cort, J. Lacour, *Tetrahedron Lett.*, **2002**, *43*, 423.

Organic Chemistry **221**

Analogs Synthesis Towards Target Fishing for C-Di-GMP

Nicolas Amiot, Karine Heintz and Bernd Giese*

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

Cyclic-di-guanylate monophosphate (C-Di-GMP) **1** is a biologically active compound that is gaining more and more attention.[1] Numerous examples have revealed that it is involved in the biofilm formation in the bacterial kingdom. It was shown that an increase of the cellular level of C-Di-GMP resulted in a gene over-expression and an increase of exopolysaccharide synthesis (EPS).[2] EPS being a mechanism taking place during biofilm formation. Although this molecule is biologically active, its mode of action is unknown to date and a target protein still remains to be found.

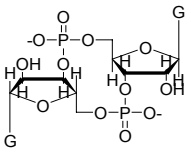


Figure 1. cyclic-di-(guanylic monophosphate) (C-Di-GMP) **1**.

We have started a research program dedicated to target fishing for C-Di-GMP. We wish to report here the synthesis of analogs designed towards this goal.

[1] Paul, R.; Weiser, S.; Amiot, N.; Chan, C.; Schirmer, T.; Giese, B.; Jenal, U. *Genes & Dev.,* **2004**, 18, 715
[2] Tischler, A. D.; Camilli, A. *Molecular Microbiology,* **2004**, 53(3), 857

Organic Chemistry **222**

Transmembrane Rigid-Rod π-Stack Architecture

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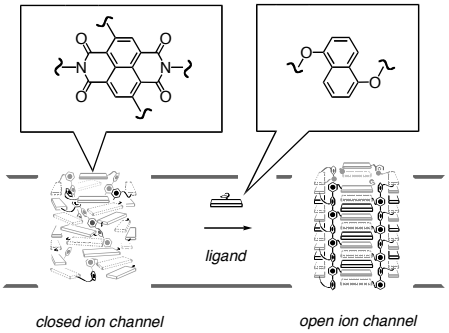
1211 Geneva, Switzerland

Supramolecular π-stack architecture is fundamental in DNA chemistry but absent in synthetic and biological ion channels and pores. Here, an electron-poor rigid-rod π-stack architecture is introduced to create synthetic ion channels that open rather than close in response to the intercalation of electron-rich ligands [1]. Highly cooperative and highly selective ligand gating is shown to give small, long-lived, weakly anion selective, ohmic ion channels with the purple color of charge transfer complexes. Current efforts focus on core substitution of the naphthalenediimide acceptors and on elongated perylenediimide acceptors to obtain transmembrane rigid-rod π-stack architecture with attractive spectroscopic characteristics.



[1] Talukdar, P.; Bollot, G.; Mareda, J.; Sakai, N.; Matile, S. *J. Am. Chem. Soc.* **2005**, *127*, 6528-6529.

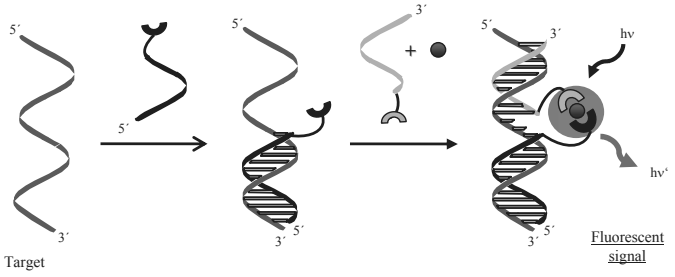
Organic Chemistry **223**

Nucleic acid duplex stabilisation and fluorescence detection by means of metal coordinating ligand conjugated to oligonucleotides.

Gapian Bianké[b], Valérie Chaurin[a]; Maxim Egorov[c]; Jacques Lebreton[c]; Edwin Constable[a] and Robert Häner[b]

[a]University of Basel, Spitalstrasse 51, 4056 Basel, Switzerland.
[b]University of Bern, Freiestrasse 3, 3012 Bern, Switzerland.
[c]Laboratoire de Synthèse Organique, 44322 Nantes, France.

Using the photophysical properties of polypyridine-metal complexes, we are investigating a new type of direct detection of DNA and RNA from biological analyte without used of label. To achieve this aim terpyridine, bipyridine and phenanthroline derivatives building blocks were incorporated into DNA-oligonucleotides. The metal coordination process on these polypyridine modified oligonucleotides should be capable of "reporting" the target DNA/RNA recognition hybridisation by fluorescent only if the ternary complex is formed. Prior to hybridisation induced fluorescent detection analysis, illustrated below, the stability of this complex was investigated in the presence and absence of metal. The results of these investigations will be shown and discussed.



Organic Chemistry **224**

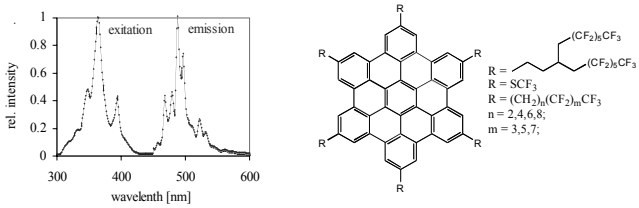
Synthesis of new Hexa-*peri*-hexabenzocoronenes and investigation of their self-organization properties

Olivier F. Aebischer, Titus A. Jenny

University of Fribourg, Chemistry Department, 1700 Fribourg, Switzerland

Discotic liquid crystals, composed of flat polycondensed aromatic cores bearing side chains in their periphery, have attracted considerable interest due to their self-organization. Hexa-*peri*-hexabenzocoronene (HBC) exhibits one of the highest charge carrier mobilities for a discotic mesogen, which make them promising components in electronic devices. The variation of the side chains in the corona of the HBC core influences the self-association and consequently the solubility and morphology of the self-assembled π-π stacks[1].

A new series of self-associating HBC derivatives have been synthesized and concentration dependent fluorenscence and UV/Vis experiments have been performed in order to gain deeper insight into the role of the lateral chain and the self-assembly behavior.



[1] T. A. Jenny, B. Alameddine, O. F. Aebischer, W. Amrein, B. Donnio, R. Deschenaux, D. Guillon, C. Savary, D. Scanu, O. Scheidegger, *J. Mater. Chem.* submitted

Organic Chemistry **225**

Total Synthesis of *Junionone* by the S_Ni' Reaction

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[a]University of Zurich , Winterthurerstrasse 190, 8057 Zurich, Switzerland
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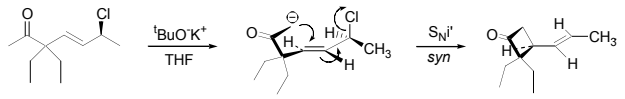
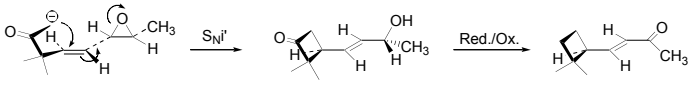
Recently, we reported a novel access to cyclobutanones by the S_Ni' reaction [1]. Ring closure of **1** by the S_Ni' reaction, leading to cyclobutanones **2**, was found to take place with retention of configuration, demonstrating selective *syn*-displacement of the leaving group.



(*E*)(*S*)-**1** (*E*)(*S*)-**2** (85%)

It was the goal of our research to apply these findings in the total synthesis of *Junionone*, an olfactorily interesting cyclobutane monoterpenoid from *Juniperus communis*, L. [2]. The intramolecular attack of a variety of different enolates on the allyl epoxide in compound **3** was the central object of investigation in this synthesis. The stereo electronic requirements, the role of Lewis acids in this reaction, and the final conversion of keto alcohol **4** to *Junionone* will be discussed.



(6*R*,7*R*)-(*E*)-**3** (3*S*,3'*R*)-(*E*)-**4** (*S*)-*Junionone*

[1] G. Fráter, A. Goeke, M. Lovchik, *SCS Fall Meeting*, **2004**, University of Zurich.
[2] A. F. Thomas, M. Ozainne, *J.C.S. Chem. Comm.*, **1973**, *19*, 746.

Organic Chemistry **226**

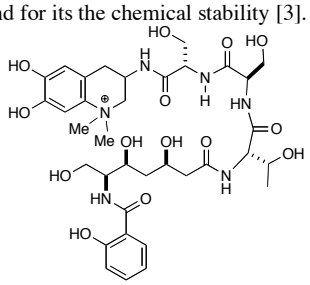
Diversity-Oriented Synthesis of Anachelin as a Tool to Study the Biological Function

Yann Bethuel[a], Judith F. Blom[b] and Karl Gademann[a]*

a) Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule Zürich, ETH Hönggerberg, CH-8093 Zürich
b) Limnological Station, Institute of Plant Biology University of Zürich, Seestr. 187, CH-8802 Kilchberg.

We recently achieved the first total synthesis of the cyanobacterial metabolite anachelin H, thus proving its relative and absolute configuration [1]. The strategy was based on the stereodivergent preparation of all possible diasteroisomers of the polyketide fragment and on a biomimetic Te-mediated oxidative aza-annulation yielding the tetrahydroquinolinium ring [2]. We also showed that quaternization of the anachelin chromophore is essential both for Fe complexation and for its the chemical stability [3].

Anachelin H



The biological function of this fascinating metabolite is still unknown. We will report on the use of diversity-oriented synthesis as a tool for profiling the biological activity of anachelin.

[1] Gademann, K.; Bethuel, Y. *Org. Lett.* **2004**, *6*, 25, 4706.
[2] Gademann, K.; Bethuel, Y. *Angew. Chem. Int. Ed.* **2004**, *43*, 3327.
[3] Bethuel, Y; Gademann, K. *J. Org. Chem.* manuscript submitted.

Organic Chemistry **227**

New Methodology towards *anti,syn* and *anti,anti* Stereotriads and its Application to the Synthesis of Naturally Occurring Polypropionates

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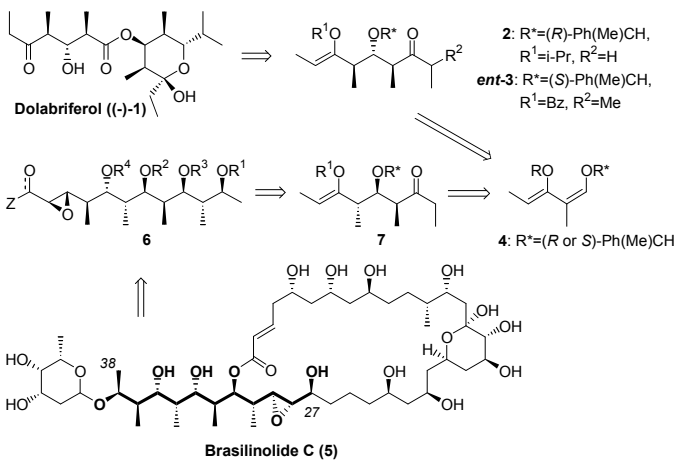
Laboratoire de glycochimie et de synthèse asymétrique, Ecole Polytechnique Fédérale de Lausanne, BCH, 1015 Lausanne, Switzerland

Among other targets, syntheses of Dolabriferol (**1**) and C(27)-C(38) fragment **6** of Brasilinolide C (**5**) will be discussed. Our approach is based on recently reported Vogel's oxyallylation cascade which employs 1,3-dioxydienes **4** [1]. This new methodology allows one to obtain either *anti,anti* or *anti,syn* stereotriads **2**, **3**, and **7** in very short and efficient way.



[1] Turks, M.; Huang, X.; Vogel, P. *Chem. Eur. J.* **2005**, *11*, 465.

Organic Chemistry **228**

Tripeptides as Efficient and Selective Aldol Catalysts

Jefferson D. Revell, Daniel Gantenbein, Roman Kovasy, Helma Wennemers

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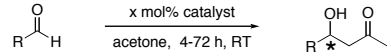
Interested in the discovery and development of peptidic catalysts for organic processes, we have developed a combinatorial screening technique known as Catalyst-Substrate Co-Immobilisation.[1] This methodology implicated H-Pro-Pro-Asp-NH_2 as a catalytically active tripeptide for asymmetric aldol reactions. Solution-phase studies revealed this to be both highly active and enantioselective for different aldol reactions.[2]



In order to elucidate the mechanism of this catalyst, both chemical modification of the basic tripeptide motif was made, and kinetic studies performed. We will present the specific properties of our novel catalysts, and the implications with regard to the mechanism.

[1] P. Krattiger, C. McCarthy, A. Pfaltz, H. Wennemers, *Angew. Chem. Int. Ed.* **2003**, *42*, 1722-1724.
[2] P. Krattiger, R. Kovasy, J. Revell, S. Ivan, H. Wennemers, *Org. Lett.* **2005**, *7* 1101-1103.

Organic Chemistry **229**

The Total Synthesis of (–)-Lepadiformine

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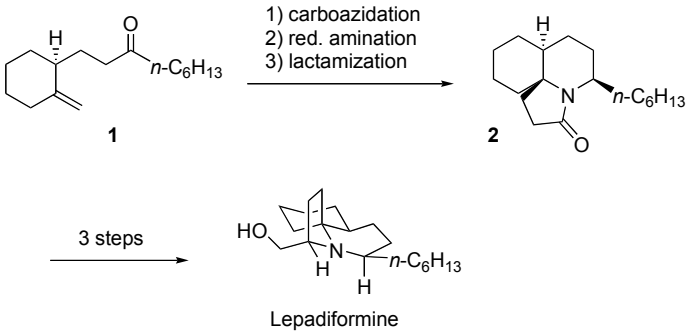
Universität Bern, Departement für Chemie und Biochemie, Freiestrasse 3, 3012 Bern, Switzerland

Lepadiformine is a marine alkaloid from *Clavelina lepadiformis* with a unique tricyclic structure, which displays interesting cytotoxic activities and cardiovascular effects [1]. By using the radical carboazidation developed in our group [2], we provided a particularly short synthetic route to lepadiformine and a series of other alkaloids. Thus, the carboazidation of optically pure olefin **1** followed by two cyclizations gave tricyclic lactam **2**, which was further elaborated to give (–)-lepadiformine.



[1] M. Jugé, N. Grimaud, J.-F. Biard, M.-P. Sauviat, M. Nabil, J.-F.Verbist, J.-Y. Petit, *Toxicon* **2001**, *39*, 1231.
[2] P. Panchaud, L. Chabaud, Y. Landais, C. Ollivier, P. Renaud, S. Zigmantas, *Chem. Eur. J.* **2004**, *10*, 3606.

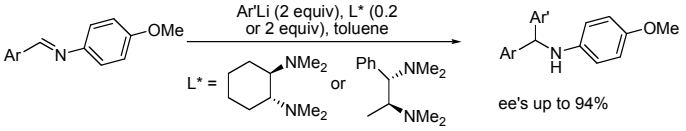
Organic Chemistry **230**

Simple 1,2-Diamine Ligands for Asymmetric Addition of Aryllithium Reagents to Imines

Ségolène Gille, Noemi Cabello, Jean-Claude Kizirian, Alexandre Alexakis*

Department of Organic Chemistry, University of Geneva, 30 quai Ernest Ansermet, CH-1211 Genève 4, Switzerland Fax: +41 22 379 32 15; e-mail: alexandre.alexakis@chiorg.unige.ch

Diarylmethylamines are compounds of great interest in organic synthesis since they constitute building blocks for complex structures of biologically active molecules. Since the first enantioselective addition of aryllithium compounds to aromatic imines promoted by an external chiral ligand described by Tomioka and coworkers in 1990,[1] some efficient arylation procedures of imines have been reported.[2] All of these are high-yielding and selective, but they suffer from the cost of the catalysts used. We report herein a low-cost and efficient catalytic arylation of aromatic imines using a wide diversity of aryllithium reagents activated by easy accessible chiral 1,2-diamines.[3] Enantiomeric excesses up to 94% were obtained.



[1] Tomioka. K.; Inoue, I.; Shindo, M.; Koga, K. *Tetrahedron Lett.* **1990**, *31*, 6681-6684.
[2] (a) Hermanns, N.; Dahmen, S.; Bolm, C.; Bräse, S. *Angew. Chem. Int. Ed.* **2002**, *41*, 3692-3694. (b) Otomaru, Y.; Tokunaga, N.; Shintani, R.; Hayashi, T. *Org. Lett.* **2005**, *7*, 307-310. (c) Weix, D.J.; Shi, Y.; Ellman, J.A. *J. Am. Chem. Soc.* **2005**, *127*, 1092-1093. (d) Kuriyama, M.; Soeta, T.; Hao, X.; Chen, Q.; Tomioka, K. *J. Am. Chem. Soc.* **2004**, *126*, 8128-8129.
[3] Cabello, N.; Kizirian, J.-C.; Alexakis, A. *Tetrahedron Lett.* **2004**, *45*, 4639-4642.

Organic Chemistry **231**

Synthesis of Sterically and Electronically Tunable Anionic C_2-symmetric Bisoxazoline Analogues and their Application in Asymmetric Catalysis

Clément Mazet, Valentin Köhler and Andreas Pfaltz

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

Bisoxazoline ligands (BOX) have proven to be highly versatile, very efficient ligands for a variety of enantioselective catalytic reactions such as cyclopropanation, Diels-Alder, aziridination, Mukaiyama-Michael reactions.[1]

We recently have developed a new class of C_2-symmetric bisoxazoline analogues that contain a tetrasubstituted boron atom bridging the two oxazoline rings (Bora-BOX). This allowed preparation of zwitterionic metal-complexes. Structural and electronic comparisons with their C-bridged analogues were carried out. Promising applications of these ligands in different enantioselective copper-catalyzed reactions will be presented.[2]

[1] R. J. S. Johnson, D. A. Evans, *Acc. Chem. Res.*, **2000**, *33*, 325-335.
[2] C. Mazet, V. Köhler, A. Pfaltz, *Angew. Chem. Int. Ed. accepted*

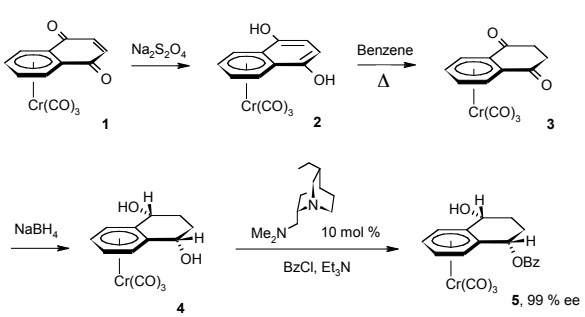
Organic Chemistry **232**

$[Cr(CO)_3(\ ^6$-5,8-Naphthoquinone)]: a New Entry into Highly Enantioenriched Planar Chiral Complexes

A. Enríquez, E. P. Kündig,* T. Lomberget.

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

Planar chiral [Cr(arene)$(CO)_3$] complexes are of interest because of their use as chiral synthons and chiral ligands [1]. We here report new findings in this area. Reduction of the naphthoquinone complex **1** [2] provides ready access to the dihydroxynaphthalene complex **2**. Remarkably, simple heating in benzene converts **2** into the tautomeric tetralindione complex **3**. Its reduction affords the syn-diol complex **4**, which was desymmetrized into **5** via a new chiral diamine acyl transfer catalyst.



[1] (a) Kündig E. P., Pache S. H. *Science of Synthesis* **2003**, *2*, 153.
(b) *Topics in Organometallic Chemistry*, Kündig E. P., Ed., Springer-Verlag: Berlin, **2004**, *Vol. 7.2*
[2] Kündig E. P., Lomberget T., Bragg R., Poulard C., Bernardinelli G. *Chem. Comun.* **2004**, 1548.

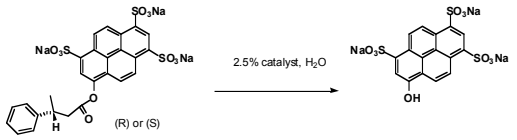
Organic Chemistry **233**

Discovery of New Functional Peptide Dendrimers, as Enantioselective Catalysts, and Host for Vitamin B_{12}

Anthony Clouet, Tamis Darbre, Jean-Louis Reymond*

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

Peptide dendrimers are new and attractive artificial proteins that adopt a globular shape as a consequence of topology rather than folding. Recently, we reported a combinatorial approach to peptide dendrimers based on split-and-mix synthesis and on-bead screening[1]. The method was exemplified by the discovery of catalytic and binding peptide dendrimers in a 65'536-member library. We developped this strategy to generate focused libraries leading to enantioselective catalysts with enzyme-like activity able to discriminate enantiomers of fluorogenic esters.



For binding studies, new peptide dendrimer libraries have been prepared, which contain N-terminal capping groups grafted onto the periphery of third generation peptide dendrimers. Screening for binding to vitamin B_{12} showed the ability to form stable complexes of either single- or multiple-vitamin B_{12} with peptide dendrimers in aqueous media. These experiments demonstrate a general strategy for the preparation of functional peptide dendrimers.

[1] A. Clouet et al., *Angew. Chem. Int. Ed.* **2004**, *43*, 4612 –4615; A. Clouet et al., *Adv. Synth. Catal.* **2004**, *346*, 1195 –1204; A. Esposito et al., *Angew. Chem. Int. Ed.* **2003**, 42, 1381; C. Douat-Cassassus et al., *JACS*, **2004**, *126*, 7817-7826; David Lagnoux et al., *Chem. Eur. J.* **2004**, *10*, 1–13

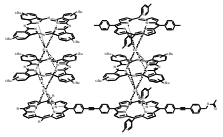
Organic Chemistry **234**

Porphyrin Based Systems for Molecular Information Storage

V.L. Malinovskii[1], J.S. Lindsey*

North Carolina State University, Dabney Hall 8204, 27695 Raleigh, USA

Multiple bits of information can be stored in a single molecule [where $\log_2$(number of states) = number of bits]. Information can be stored either in cationic or anionic states; however, because of the greater stability of cations under ambient conditions, we have focused on electron-rich molecules that more readily afford sets of cationic states than anionic states.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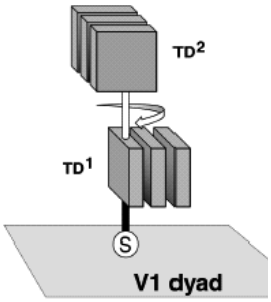


one of architectures example

Herein we report the design, synthesis, and characterization of thiol-derivatized porphyrins [1] [2], porphyrin-phthalocyanine triple deckers [3] [4] and dyads of triple deckers [3] [5] for examination as multistate counters.

[a] recent place: Department of Chemistry, University of Bern

[1] *J. Org. Chem.* **2004**, *69*, 1435–1443.
[2] *J. Am. Chem. Soc.* **2004**, *126*, 11944.
[3] *Inorg. Chem.* **2003**, *42*, 7431.
[4] *J. Mater. Chem.* **2002**, *12*, 808.
[5] *J. Porphyrins Phthalocyanines*, in preparation.

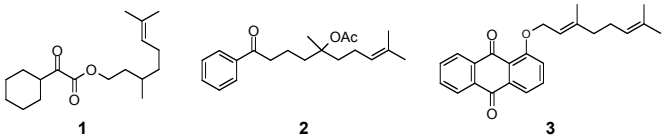
Organic Chemistry **235**

Photochemical Release of Bioactive Substances. Concepts and Applications for Controlled Fragrance Delivery.

Andreas Herrmann

Firmenich SA, Division Recherche & Développement, B.P. 239, CH-1211 Genève 8

Most biologically active substances are quite sensitive to various environmental conditions and often degrade before they fulfill their purpose of use. As an alternative to encapsulation techniques, the preparation of suitable precursors which release bioactive compounds under smooth reaction conditions have been developed. Whereas in the pharmaceutical area mainly hydrolysis or enzymatic reactions are used as the release trigger, much less has been reported on the controlled release of organic molecules using photochemical processes. Fragrances, being generally deposited onto surfaces from which they slowly evaporate, are exposed to visible light during application, and are thus suitable candidates for light-induced release [1].



1 **2** **3**

Different photolabile fragrance precursors such as α-keto esters (**1**), alkyl phenyl ketones (**2**) or alkoxy-anthraquinones (**3**) were prepared, and various parameters such as the influence of the light intensity on the release, substituent effects, the presence of oxygen, or the formation of side products were studied systematically. The concept was found to be generally applicable under everyday life conditions, using natural daylight as the release trigger.

[1] A. Herrmann, *The Spectrum (Bowling Green)* **2004**, *17(2)*, 10-13, 19.

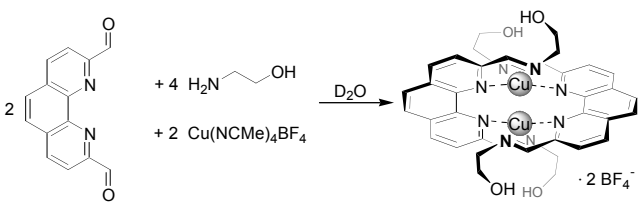
Organic Chemistry **236**

Selection Rules for Helicate Ligand-Component Self-Assembly: Steric, pH, Charge, and Solvent Effects

David Schultz, Jonathan R. Nitschke

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

Building upon the successes of the programmed self-assembly of preformed ligands with metals, ligand-component self-assembly is emerging as a powerful means to create new structures.
The reaction between 1,10-phenanthroline-2,9-dicarboxaldehyde, copper(I), and certain primary amines was found to give quantitatively a dicopper double-helicate product by imine self-assembly around Cu^{I} templates, bringing both ligands and supramolecular complexes into being at the same time [1].



The parameters of this reaction were investigated, and important roles were found to be played by the steric bulk of the amine, the charge of the amine, the solvent used, and the pH of the solution. Water was found to allow the broadest range of structures to form, and ligand-component exchange reactions were demonstrated to proceed readily in this solvent.

[1] J.R. Nitschke, D. Schultz, G. Bernardinelli, D. Gérard, *J. Am. Chem. Soc.* **2004**, *126*, 16538.

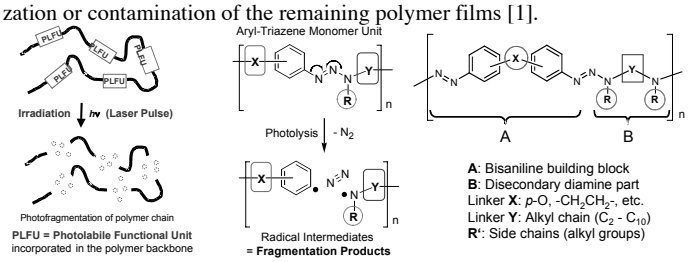
Organic Chemistry **237**

Photodecomposible Materials Designed for Laser Applications: Triazene-Based Polymers as Photodynamic Release Layers

Matthias Nagel,[a] Thomas Lippert*[b]

[a] Swiss Federal Laboratories for Materials Testing and Research (EMPA), Überlandstrasse 129, CH-8600 Dübendorf, Switzerland; [b] Paul Scherrer Institute, Materials Group, CH-5232 Villigen PSI, Switzerland

The concept of controlled laser-induced photolysis of designed polymeric materials is based on the covalent incorporation of photochemically active chromophores as photosensitive breaking points into the polymer backbone. Selective laser irradiation of the photolabile units in these functional polymers causes rapid decomposition of the photoactive groups into small fragments or gaseous products. This allows a controlled photodegradation of the polymeric material at low laser threshold fluences and also without carbonization or contamination of the remaining polymer films [1].



Polymers with incorporated triazene groups as photodegradable chromophores have been synthesized and studied in detail in UV-laser ablation experiments [2]. These triazene polymers were also successfully used as intermediate sacrificial photodynamic release layers in UV-laser-induced forward transfer (LIFT) experiments at low laser fluences.

[1] T. Lippert, J. T. Dickinson, *Chem. Rev.* **2003**, *103*, 453 – 485.
[2] T. Lippert, *Adv. Polym. Sci.* **2004**, *168*, 51 – 246.

Organic Chemistry **238**

Frictionless Cyclophanes from 2,6-Diaryltolan Derivatives

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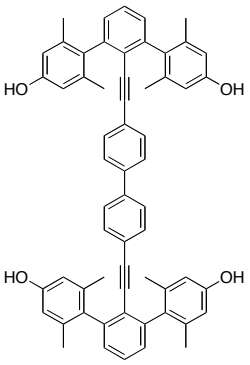
University of Zürich, Winterthurerstr. 190, CH-8057, Zürich, Switzerland

We have prepared 2,6-Diaryltolan and its pyridyl analogs in order to investigate conformational preference due to polar-pi interactions. It was determined that this effect is not significant enough to cause a strong conformational bias and there is essentially free rotation about the triple bond. These molecules are being used as model systems for the design of a frictionless cyclophane. Compounds of this type can be viewed as precursors for the rational design of molecular rotors. This series of compounds also allows for the study of photophysical effects in aryl-alkynes. The lifetime and quantum yields in these systems will be discussed. In combination, the novel dynamic and photonic properties provide a prototype for material design.



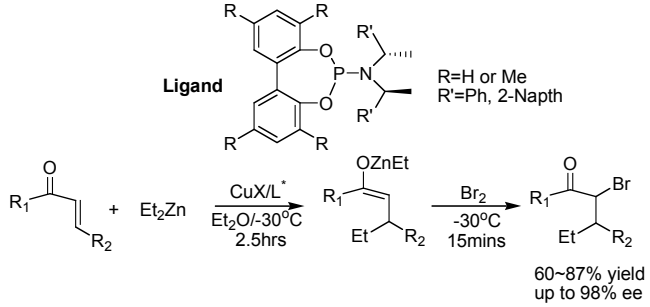
Organic Chemistry **239**

A Highly Efficient One Pot Reaction for the Synthesis of Chiral α-Brom-β-alkyl Ketones from α,β-Unsaturated Ketones

Kangying Li, Alexandre Alexakis*

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

α-bromination of carbonyl compounds is an important transformation in organic synthesis since the α-brominated productes are useful intermediates[1]. Herein, we present a highly efficient one pot reaction for the synthesis of chiral α-brom-β-alkyl ketones from α,β-unsaturated ketones catalyzed by copper and chiral phosphomidite ligands[2].



A series of cyclic and linear α,β-unsaturated ketones were tested. The final products were isolated as a mixture of two diastereomers with various ratios that depend on the substrate structure. The isolated yields were moderate to good and up to 98% enantiomer excess was achieved.

[1] R. C. Larock *Comprehensive Organic Transformations*, 2nd ed.; VCH: New York, **1999**, pp715-719.
[2] A. Alexakis, D. Polet, S. Rosset, S. March *J. Org. Chem.* **2004**, *69*, 5660.

Organic Chemistry **240**

A New Synthetic Modifier for the Pt-Catalyzed Enantioselective Hydrogenation of Fluorinated Ketones

S. Diezi, E. Orglmeister, T. Mallat, A. Baiker

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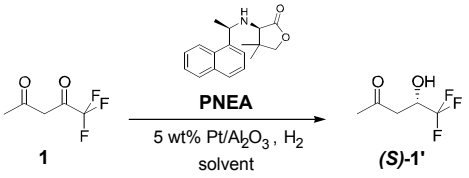
A viable and practical route to chiral fluorinated alcohols is the heterogeneous enantioselective hydrogenation of the prochiral ketones.
Here we used a combinatorial methodology to accelerate the research. The high-throughput screening under various reaction conditions involved eight trifluoromethyl ketones and eight chiral modifiers synthesized by reductive alkylation of (*R*)-1-(1-naphthyl)ethylamine with various aldehydes and ketones [1]. The chiral modifiers contained N-alkyl, cycloalkyl, hydroxyalkyl, or hydroxybenzyl groups, or an ester group in α-position to the N atom.



In the second stage of screening only the most promising substrate-modifier combinations were involved. The final optimization yielded 93% *ee* in the hydrogenation of **1** over Pt modified by **PNEA**, under mild conditions (10°C, 10 bar) [2]. The most influential parameters for the hydrogenation of **1** were the solvent, the Pt/modifier ratio, and the catalyst treatment before use. This is the first case that a metal–synthetic chiral modifier system affords over 90% *ee*.

[1] E. Orglmeister, T. Mallat, A. Baiker, *Adv. Synth. Catal.*, **2005**, *347*, 78.
[2] S. Diezi, M. Hess, E. Orglmeister, T. Mallat, A. Baiker, *Catal. Lett.* **2005**, *in press*.

Organic Chemistry **241**

Formation and stabilization of a three-way junction via the Diels Alder reaction

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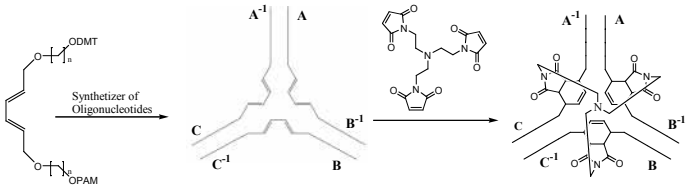
A diene building block was synthesized and incorporated into three oligonucleotides, which form a three-way junction. A trifunctional dienophile was synthesized, which is designed to react via Diels Alder reactions on this three-way junction. Thermal melting experiments and gel electrophoresis were used to charaterize this kind of structure. The results of these studies will be shown and discussed.



Organic Chemistry **242**

Immobilisation of Trypsin by Activated Tween 85™

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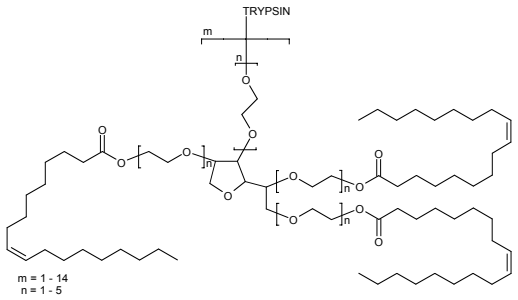
The immobilisation of enzymes for industrial applications is an important issue to facilitate product isolation. Trypsin was immobilised by Tween 85, a polyoxyethylene surfactant. It contains a single specific group (hydroxyl), which can be functionalised with various ligands. In particular an enzyme, an affinity ligand or other molecule [1]. We found that derivatized trypsin is in most cases less active than in its native form but more thermo stable [2].



Tween 85-Bioconjugates may be employed in enzymatic catalysis or affinity precipitation for down stream processing purposes in Biotechnology.

[1] Bharda D., Bharda S., Jain P., Jain N.K., *Pharmazie* **2002**, *57*, 5.
[2] Murphy A., Fágáin C.Ó., *Journal of Biotechnology* **1996**, *49,* 163.

Organic Chemistry **243**

Nonlinear Phenomenon in Heterogeneous Enantioselective Catalysis

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The nonlinear effect in asymmetric catalysis has been a topic of great interest [1]. Here we present a study of the nonlinear phenomenon in heterogeneous enantioselective hydrogenation. The transformation of ketopantolactone to pantolactone was investigated over Pt/Al_2O_3 and the catalyst was modified by mixtures of enantiomers, diastereomers, and chemically different chiral compounds possessing the same or different "anchoring moiety". Significant deviation from the ideal behavior was observed for all cases (see e.g. Fig.1) except when two enantiomers were applied.

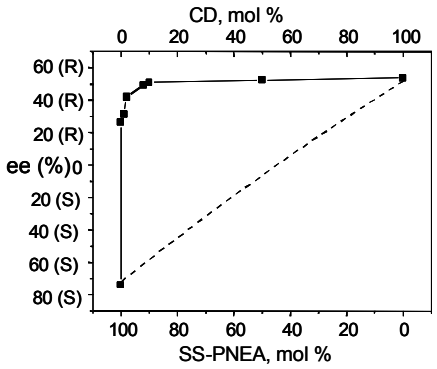

Figure 1. Non-linear behavior of the CD (cinchonidine) + (*S*,*S*)-PNEA ((1'*S*, 2*S*)-*N*-[1'-(1-naphthyl)ethyl]-2-amino-3,3-dimethyl-γ-butyrolacton) mixture. The dashed line indicates the ee calculated for an ideal behaviour of the modifier mixture.

[1] C. Puchot, O. Samuel, E. Dunach, S. Zhao, C. Agami, H.B. Kagan, *J. Am. Chem. Soc.* **1986**, *108*, 2353.

Organic Chemistry **244**

Synthesis of intermedidates between resorcinarenes and calixarenes

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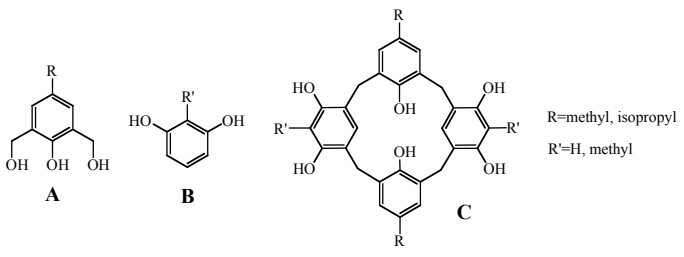
Calixarenes and resorcinarenes play an important role in supramolecular chemistry [1]. The synthesis, the structures, the complexing properties and thermal decomposition of some new resorcinarenes have recently been studied in our laboratory [2]. To our knowledge, intermediate structures between resorcinarenes and calixarenes, such as compound **C** were never described.



Compounds **A** can be brought to reaction with compounds **B** in hot, slightly acid aqueous medium to produce macrocycles of the type **C** in good yields. The ^{1}H-NMR spectra are perfectly in agreement with this structure. We currently continue this research in order to describe a maximum of mixed compounds and to optimize the synthesis.

[1] J. L. Irwin, M.S. Sherburn, *J. Org. Chem*, **2000**, 65, 602.
[2] J.-M. Bourgeois, H. Stoeckli-Evans, Synthesis of New Resorcinarenes Using Alkaline Conditions, currently submitted for publication in Helvetica Chimica Acta.

Organic Chemistry **245**

Photochemically Induced RNA Abasic Sites: A Study of their Stability and Influence on Reverse Transcriptases

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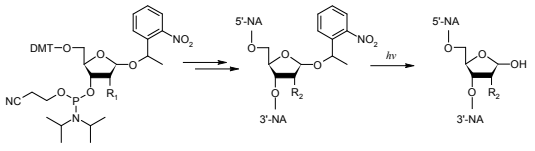
DNA abasic sites are highly mutagenic DNA lesions for which a dedicated cellular repair machinery exists. In contrary, RNA abasic sites and their biological impact are largely unknown. RNA abasic sites are e.g. the result of the action of RNA N-ribohydrolases and severely affect the vitality of a cell. We set out to study the biological impact of RNA abasic sites in more detail and developed a method for their synthesis.[1]



DMT: 4,4'-Dimethoxytriphenyl, TOM: [(Triisopropysilyl)oxy]methyl, NA: nucleic acid

Monomers **1a** and **1b** and the DNA analogue **1c** (as a reference) were synthesized and incorporated into oligomers to give protected oligonucleotides **2a-c**. UV irradiation of **2a-c** shows clean and fast deprotection to form abasic oligonucleotides **3a-c**. The stability of **3a-c** upon treatment with base was investigated and compared to each other. In addition a RNA abasic site was incorporated into a RNA template and reverse transcription activity was investigated with DNA primers. HIV and AMV RT readily showed trans-lesion synthesis. Both enzymes incorporate dNTPs according to the A-rule: A > G >> C ~ T.

[1] A similar approach was recently disclosed: J. D. Trzupek, T. L. Sheppard, *Org. Lett.* **2005**, *7*, 1493-1496.

Organic Chemistry **246**

Synthesis and Resolution of the First Enantiopure Bowl-Shaped Molecule

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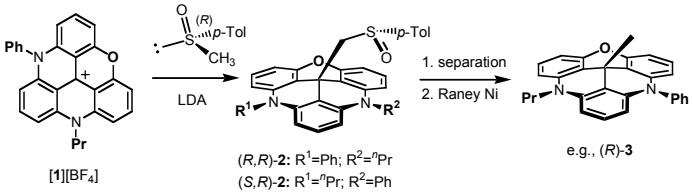
Bowl-shaped molecules have attracted attention due to a potential use as intermediates for the synthesis of fullerenes and other bent molecules.[1] Herein, we report a short stepwise synthesis of a chiral bowl-shaped derivative **3** and its resolution into single enantiomers using an enantiopure sulfoxide as chiral auxiliary.



[**1**][BF_4] (*R*,*R*)-**2**: R^1=Ph; R^2=^{n}Pr (*S*,*R*)-**2**: R^1=^{n}Pr; R^2=Ph

Reaction of salt [**1**][BF_4] with the lithium carbanion of (+)-(*R*)-methyl-*p*-tolylsulfoxide [2] results in neutral diastereomers (*R*,*R*)-**2** and (*R*,*S*)-**2** that can be separated by preparative HPLC. Upon treatment with Raney Ni, the enantiopure bowl-shaped molecule **3** was isolated and characterized.

[1] P.W. Rabideau, A. Sygula, *Acc. Chem. Res*. **1996**, *29*, 235-242.
[2] For a related study on [4]heterohelicinium cations, see B. Laleu, P. Mobian, C. Herse, B. W. Laursen, G. Hopfgartner, G. Bernardinelli, J. Lacour, *Angew. Chem. Int. Ed*, **2005**, *44*, 1879 and references therein.

Organic Chemistry **247**

C-Di-GMP: Biological Relevance and Revisited Synthesis

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PleD is a novel type of response regulator, presenting two receiver domains. The first containing a typical phosphorylation site whereas the second unusual domain is not phosphorylated. The output domain of PleD is composed of a so-called GGDEF domain, which is homologous to a large family of proteins. In our search concerning the biological relevance of this output domain, we have demonstrated that the enzyme processes the transformation of GTP to cyclic-di-(guanylic monophosphate) (C-Di-GMP) **1**, revealing at the same time the biological function of the GGDEF domain.[1]

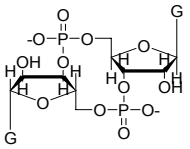

Figure 1. cyclic-di-(guanylic monophosphate) (C-Di-GMP) **1**.

Facing growing demands, since cyclic-di-GMP is now thought to be a secondary messenger involved in the biofilm formation in the bacterial kingdom,[2] we have decided to investigate a new synthetic route to replace the tedious existing one.[3] This new pathway, that is suitable for scale up and more flexible than previous ones, will also be useful in the preparation of derivatives required to investigate further C-Di-GMP's biological function.

[1] Paul, R.; Weiser, S.; Amiot, N.; Chan, C.; Schirmer, T.; Giese, B.; Jenal, U. *Genes & Dev.,* **2004**, 18, 715
[2] Tischler, A. D.; Camilli, A. *Molecular Microbiology,* **2004**, 53(3), 857
[3] Verdegaal, C. H. M.; Jansse, P. L.; de Rooij, j. F. M.; Veeneman, G.; van Boom, J. H. *J. of Biol. Chem.,* **1990**, 265, 31(5), 18933

Organic Chemistry **248**

Synthesis and Inhibition Studies of Bisubstrate Inhibitors of Porphobilinogen Synthase from *Pseudomonas aeruginosa*

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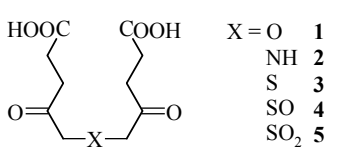
[1]Institut de chimie, Université de Neuchâtel, Av. de Bellevaux 51, 2007 Neuchâtel, Switzerland
[2]Institut für Mikrobiologie, Technische Universität Carolo-Wilhelmina, Spielmannstr. 7, 38106 Braunschweig, Germany

Porphobilinogen synthase synthesizes porphobilinogen, the commun precursor of all natural tetrapyrroles, through an asymetric condensation of two molecules of aminolevulinic acid [1] [2]. Symetrically linked dimers **1**-**5** derived from levulinic acid have been synthesized to mimic the assumed bisubstrate bound to the active site of the enzyme.



Their inhibition potential was caracterized determining the constant of inhibition K_I. The inhibition type was also determined when it was possible. The heteroatom used to link the two levulinic acid units has shown a strong influence on the inhibitor behaviour.

[1] R. Neier, *Advan. Nitrogen Heterocycles* **1996**, *2*, 135.
[2] J. Kervinen, E. K. Jaffe, F. Stauffer, R. Neier, A. Wlodawer, A. Zdanov, *Biochemistry* **2001**, *40*, 8227.

Organic Chemistry **249**

Highly Stable Chiral Atropisomers by Restricted Rotation about a Csp^2-Csp^3 Bond

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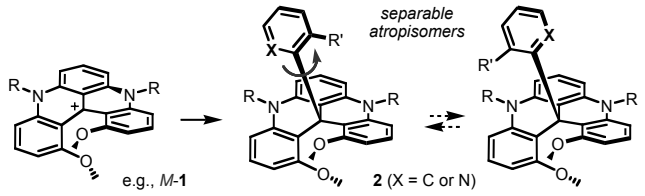
Previously, non-biaryl atropisomeric systems have been extensively studied for their "slow" rotation around Csp^2 and Csp^3 bonds [1]. Recently, the synthesis and resolution of dimethoxyquinacridinium dyes of type **1** have been reported [2]. These helical derivatives **1** (*P* or *M* enantiomers) react readily with organometallic reagents and generate chiral neutral adducts **2** [3].



Herein, we report the extremely slow rotational behavior of aromatic rings attached to the center of this novel chiral scaffold. In some cases, the diastereomers can be separated and very high barriers to rotation around the central Csp^2-Csp^3 bond were measured ($\Delta G^{\ddagger}$ up to 33 kcal.mol^{-1}, X = C; R' = SMe).

[1] M. Oki, *Top. Stereochem.* **1983**, *14*, 1.
[2] B. Laleu, P. Mobian, C. Herse, B.W. Laursen, G. Hopfgartner, G. Bernardinelli, J. Lacour, *Angew. Chem. Int. Ed.* **2005**, *44*, 1879 and references therein.
[3] a) M. Lofthagen, J.S. Siegel, R. VernonClark, K.K. Baldridge, *J. Org. Chem.* **1992**, *57*, 61; b) B.W. Laursen, F.C. Krebs, M.F. Nielsen, K. Bechgaard, J.B. Christensen, N. Harrit, *J. Am. Chem. Soc.* **1998**, *120*, 12255.

Organic Chemistry **250**

Catalytic Enantioselective Hydrogenolysis of [Cr(5,8-Dibromonaphthalene)$(CO)_3$]

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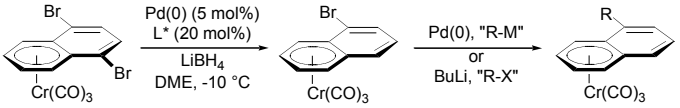
Due to their rich and varied chemistry, metal-arene π-complexes find application as catalysts, chiral ligands and starting materials for asymmetric synthesis [1]. Here we report our results on the efficient desymmetrisation of a dibromonaphthalene complex *via* Pd-catalysed asymmetric hydrogenolysis. Phosphoramidite ligands [2] performed better than phosphine ligands, affording the highly enantioenriched (1*R*)-5-bromonaphthalene complex in good yield. Initial results on the enantioselective hydrogenolysis of the analogous cationic CpRu complex will also be presented.



The planar chiral bromonaphthalene complex has been transformed by lithiation/quench and by Pd(0) catalysis. New conditions for a modified Suzuki reaction allow rapid alkynylation and vinylation of aryl bromides at room temperature with a commercially available catalyst/ligand combination.

[1] *Transition Metal π-Complexes in Organic Synthesis and Catalysis*, E.P. Kündig (Ed.), Topics in Organometallic Chemistry, Vol.7, Springer Verlag, Heidelberg, **2004**.
[2] B.L. Feringa, M. Pineschi, L.A. Arnold, R. Imbos, A.H.M. de Vries, *Angew. Chem., Int. Ed.* **1997**, *36*, 2620.

Organic Chemistry **251**

New Ene-Reactions of Allylgermanes and Allylboronates with Sulfur Dioxide. A New Synthesis of Enantiomerically Enriched Sulfoxides

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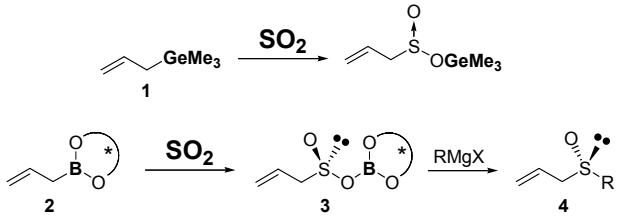
The use of sulfoxides has been growing over the last few years in many different areas of synthetic chemistry [1]. Continuing the development of organic chemistry of sulfur dioxide [2] we have discovered new ene reactions [3] of SO_2 with allylgermanes **1** and allylboronates **2**. Intermediate sulfinates **3** so-formed can be quenched with Grignard reagents to provide allyl sulfoxides **4**. Chirality transfer from boronate moiety to sulfur center and practical recovery of chiral auxiliaries will be discussed.



[1] Fernández, I.; Khian, N. *Chem. Rev.* **2003**, *103*, 3651.
[2] a) Narkevitch, V.; Megevand, S.; Schenk, K.; Vogel, P. *J. Org. Chem.* **2001**, *66*, 5080. b) Turks, M.; Fonquerne, F.; Vogel, P. *Org. Lett.* **2004**, *6*, 1053. c) Turks, M.; Huang, X.; Vogel, P. *Chem. Eur. J.* **2005**, *11*, 465.
[3] a) Bouchez, L.; Vogel P. *Synthesis* **2002**, 225. b) Huang, X.; Craita, C.; Awad, L.; Vogel, P. *Chem. Commun.* **2005**, 1297.

Organic Chemistry **252**

Asymmetric Dearomatization via (Arene)$Cr(CO)_3$ Complexes : Synthetic Studies Towards Novel Cyclic Enediynes

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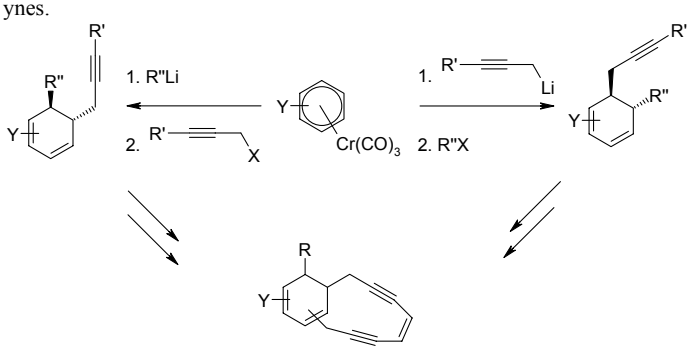
Switzerland

Enediynes have attracted much attention because of their potential as anticancer and antibiotic agents [1]. Novel cyclic enediynes have been synthesised using the dearomatization reaction developed in our group [2]. Activation of an arene by temporary complexation to the electrophilic $Cr(CO)_3$ group allows the sequential *trans* addition of two propargylic groups or other C-fragments across an arene double bond.

A variety of functionalized cyclohexadienes bearing propargyl units could be synthesized by this way. These were then elaborated into cyclic enediynes.



[1] K. C. Nicolaou, W. M. Da, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1387.
[2] A. Pape, K. P. Kaliappan, E. P. Kündig, *Chem. Rev.* **2000**, *100*, 2917.

Organic Chemistry **253**

Receptor-Ligand Driven Self-Assembly A Key-Lock Mechanism with a Diketopiperazine Receptor

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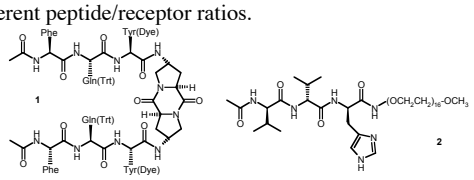
Physical Chemistry, University of Basel, Kingelbergstrasse 80, CH-4056 Basel, Switzerland

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. [1] To understand this highly selective host-guest interaction, we prepared the pegylated tripeptide **2** and tried to perform NMR binding studies. However, when we mixed tripeptide **2** with receptor **1** in $CHCl_3$, the formation of a gel was observed. The gel formed at different peptide/receptor ratios.



To gain insight into the properties of the gel, we are currently performing light scattering and isothermal calorimetry investigations.

[1] (a) H. Wennemers, M. Conza, M. Nold, P. Krattiger, *Chem. Eur. J.*, **2001**, *7*, 3342; (b) M. Conza, H. Wennemers, *J. Org. Chem.*, **2002**, *67*, 2696; (c) M. Conza, H. Wennemers, *Chem. Commun.*, **2003**, 866.

Organic Chemistry **254**

First Organocatalyzed Asymmetric Michael Addition of Aldehydes to Vinyl Sulfones

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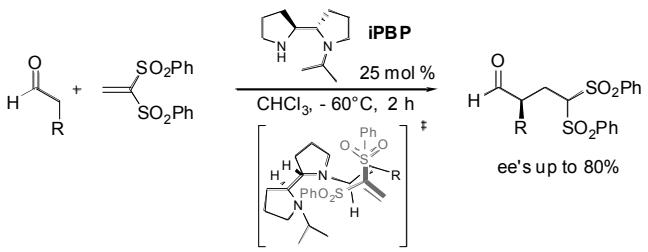
In the last few years, organocatalysis has become very attractive and the focus of intense research efforts [1]. After having developed an highly enantioselective Michael addition of aldehydes and ketones to nitroolefins catalyzed by N-*i*Pr-2,2'-bipyrrolidine (***i*PBP**) [2], we applied our catalyst on vinyl sulfones as Michael acceptors. We have disclosed the first direct asymmetric conjugate addition of aldehydes to vinyl sulfones catalyzed by diamine ***i*PBP**.



The reaction proceeds with good yields and enantioselectivities. The determination of absolute configuration allowed us to postulate a *Si,Si* transition state model as shown previously for nitroolefins.

[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.

Organic Chemistry **255**

Rationalisation of solvent effects in the Diels-Alder reaction between cyclopentadiene and methyl acrylate in room temperature ionic liquids

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a) Ecole Polytechnique Fédérale de Lausanne, EPFL-BCH, 1015 Lausanne, Switzerland

b) Novartis Pharma AG, WSJ-145.6.54, CH-4002 Basel, Switzerland

The Diels-Alder reaction between cyclopentadiene and methyl acrylate has been evaluated in ionic liquids. Anion, and in particular cation effects, have been investigated using an extensive series of air-stable room-temperature ionic liquids. Kinetic parameters have also been determined. It has been found that strongly interacting groups, particularly electrophilic moieties on the cation, accelerate the formation of the *endo* products. Long substituents on the cation lead to lower selectivities.[1] Substrate solubility is intimately connected to the selectivity, and was found to be mainly anion dependent. The effect of contamination of the ionic liquids by common impurities, *viz.* sodium and chloride ions, and water, on the selectivity has been investigated, and it has only a minor effect on the selectivity of the reaction.

[1] A. Vidiš, C. A. Ohlin, G. Laurenczy, E. Küsters, G. Sedelmeier, *Adv. Synth. Catal.* **2005**, *347*, 266.

Organic Chemistry **256**

Azidoproline as Structure-Directing Element in Polyproline

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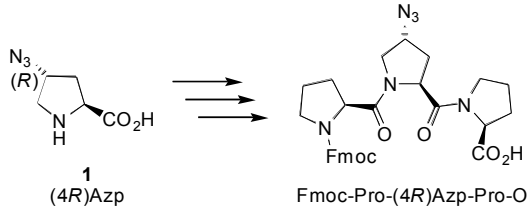
Poly-L-proline adopts two helical conformations. In the polyproline form I all peptide bonds are in an *s-cis* conformation whereas in polyproline type II they are in an *s-trans* conformation [1]. Previous studies in our lab have shown that the absolute configuration at (C4) of 4-azidoproline derivatives has an influence on the *s-cis*/*s-trans* equilibrium of the *N*-terminal tertiary amide bond [2]. We have now prepared oligo-proline derivatives up to a length of 18 amino acid residues with (4*R*)-azidoproline **1** or (4*S*)-azidoproline at every third position.



R^1-[Pro-(4*R*)Azp-Pro]$_n$-R^2; n = 2-6, R^1 =H or Ac; R^2 = OH or NH_2

Using CD and NMR spectroscopy the conformations and the stability of these modified polyprolines were studied with regard to the absolute configuration at (C4), the chain-length, the *C*- and *N*-terminal modification, the solvent and the temperature. A time-resolved interconversion from PPII to PPI was observed.

[1] W. Traub, U. Shumeli, *Nature* **1963**, *198*, 1165-1166.
[2] L.-S. Sonntag, S. Schweizer, D. Häussinger, C. Ochsenfeld, H. Wennemers, *in preparation*.

Organic Chemistry **257**

Total diastereoselective synthesis of substituted pyrrolidines

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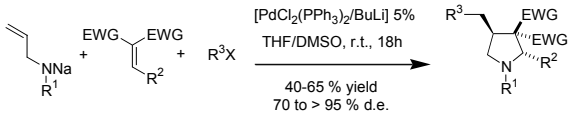
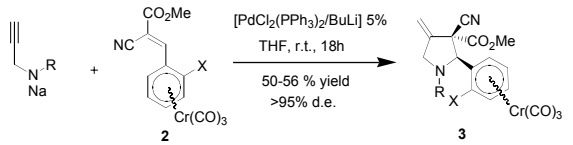
As part of our ongoing research aimed at the development of transition metal-mediated, multicomponent, five-membered heterocycle syntheses, we recently described a diastereoselective synthesis of highly substituted pyrrolidines (**1**) [1].



1

We have now found that the selectivity of a related one-pot palladium-catalysed reaction can be increased by coordinating the arene to a bulky chromium tricarbonyl fragment (**3**).



2 **3**

This also offers opportunities in asymmetric synthesis via an enantiopure planar chiral complex **2**.

[1] Martinon L., Azoulay S., Monteiro N., Balme G., Kündig E.P. *J. Organomet. Chem.* **2004**, *689*, 3831.

Organic Chemistry **258**

Ruthenium-Catalyzed Enantioselective Michael Addition and Robinson Annulation

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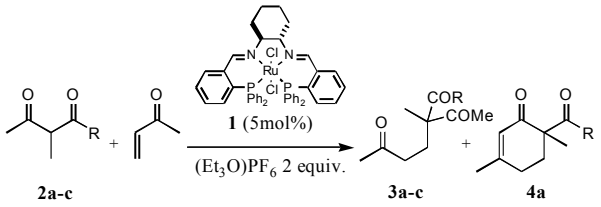
We previously reported the asymmetric fluorination of β-ketoesters catalyzed by **1** after activation with 2 eq. of $(Et_3O)PF_6$ [1]. Following the interest in ruthenium-based chiral Lewis acid catalysis, we focused on enantioselective C-C bond formation. We find now that **1** catalyzes also the asymmetric Michael addition of methyl vinyl ketone to β-ketoesters:



2a-c **3a-c** **4a**

a: R = OEt; **b**: R = OBz; **c**: R = Ph

Surprisingly, the reaction with substrate **2a** gave the product of the Robinson annulation **4a** as major compound along with a minor amount of **3a** (approximately 3:1 ratio). In these preliminary experiments, **3a** is formed with low enantioselectivity (ca. 10% ee was measured by polarimetry). Our efforts are currently focused on studying this unexpected reactivity and improving the reaction selectivity.

[1] C. Becker, Ph.D. Thesis no. 15699, ETHZ (Zürich), **2004**.

Organic Chemistry **259**

Photochemical Release of Aldehydes

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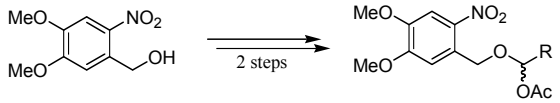
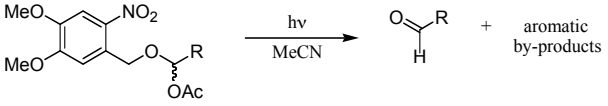
The photochemistry of 2-nitrobenzyl groups has been extensively studied in the past due to their utility as photoremovable protecting groups [1]. We expected to use this type of group to cleanly release several aldehydes under mild conditions. Indeed, slow and controlled release of substances is of great interest in many applications. For example, in the particular case of fragrance industry, the slow photo-release of odorant aldehydes has been studied on many instances (*e.g.* by Norrish-type II fragmentation) [2].
In this work, we first synthesized α-acetoxy ethers starting from 2-nitroveratrol (Scheme 1) in good yields.



Scheme 1: Synthesis of α-acetoxy ethers.

As expected, subsequent irradiation at 350 nm of these new compounds resulted in a smooth release of the corresponding aldehydes (Scheme 2).



Scheme 2: Photolysis of α-acetoxy ethers.

[1] Bochet, C. G. *J. Chem. Soc. Perkin Trans 1* **2002**, 125-142.
[2] Herrmann, A. *The Spectrum* **2004**, *17 (2)*, 10-13, 19.

Organic Chemistry **260**

Dearomatization of (Arene)$Cr(CO)_3$ Complexes and Synthetic Studies Towards the Core of the Phomoidrides and other Carbocycles

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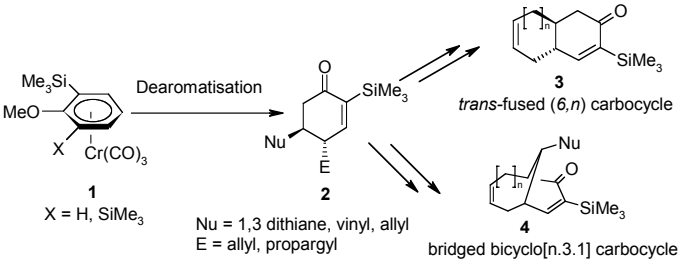
Dearomatization of anisole complexes **1** by regio-selective and diastereoselective addition of a nucleophile and an electrophile provides access to the highly functionalized cyclohexenones **2** [1].



1 X = H, $SiMe_3$ **2** Nu = 1,3 dithiane, vinyl, allyl; E = allyl, propargyl

Ring-closing metathesis (RCM) of unsaturated side chains furnished *trans*-fused carbocycles (e.g. **3**). Alternatively, diastereoselective α-alkylation in **2** and RCM provides a rapid route to the functionalized bicyclo[n.3.1] framework (e.g. **4**).
We will report on the progress of the application of these reactions towards the synthesis of bioactive molecules such as Phomoidride A [2].

[1] Kündig E. P., Quattropani A., Anderson G. *J. Am. Chem. Soc.* **1997**, *119*, 4773.
[2] Wood J. L., Spiegel D. A., Njardarson J. T., McDonald Ivar M. *Chem. Rev.* **2003**, *103*, 2691.

Organic Chemistry **261**

Synthesis of Metal Binding Combinatorial Peptide Dendrimer Libraries

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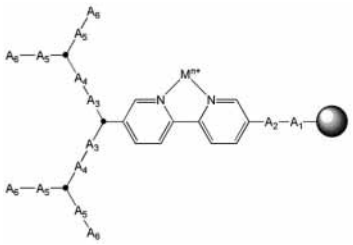
We have shown that peptide dendrimers are interesting models for enzymes and can display catalytic activity [1] when containing histidine. Their branched structure can mimic the globular shape of proteins arising from their folding. In this work we report our investigation of metal binding peptide dendrimers. Such compounds should be able to combine metal catalysis and substrate binding. Using the split-and-mix approach, combinatorial libraries of peptide dendrimers containing metal binding sites have been synthesized. Their ability to bind metal ions has been tested. Such metal containing libraries have been tested for catalytic activity.



[1] a) E. Delort, T. Darbre, J.-L. Reymond, *J. Am. Chem. Soc.* **2004**, *126*, 15642-15643. b) A. Clouet, T. Darbre, J.-L. Reymond, *Angew. Chem. Int. Ed.* **2004**, *43*, 4612-4615.

Acknowledgement: This work is financially supported by the European Marie Curie Resarch Training Network IBAAC, EC contrat no. 505020. 1.4.2004-1.4.2008.

Organic Chemistry **262**

Combinatorial Approaches to Aldolase Peptide Dendrimers

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Key to the efficiency of aldolase antibodies and class I aldolases is a lysine residue in the active site capable of forming the crucial enamine [1]. Small molecule aldolase peptides, on the other hand, rely on proline as the essential motif [2].

Dendrimeric architectures applied to peptide sequences provide a protein-like structure where catalysis appears by constructive interactions between amino acids. Recently, we have constructed combinatorial libraries of such peptide dendrimers and discovered esterase activity with histidine containing dendrimers [3].

Herein, we report two different on-bead assays for the screening for aldolase activity of combinatorial libraries of peptide dendrimers functionalized with lysine and proline. One assay is based on turn-over with a fluorogenic substrate that was found to give a very strong reaction with a known aldolase antibody. The other assay is based on covalent trapping of the essential lysine residue using a dye-functionalized diketone forming a stable enaminone.

[1] J. Wagner, R. A. Lerner, C. F. Barbas III, *Science* **1995**, *270*, 1797.
[2] J. Kofoed, J. Nielsen, J.-L. Reymond, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2445.
[3] a) A. Clouet, T. Darbre, J.-L. Reymond, *Angew. Chem. Int. Ed.* **2004**, *43*, 4612. b) E. Delort, T. Darbre, J.-L. Reymond, *J. Am. Chem. Soc.* **2004**, *126*, 15642.

Organic Chemistry **263**

New strategy to tune selective photochemical deprotections

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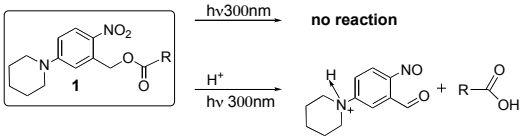
The concept of chromatic orthogonality in which two different photolabile protecting groups are cleaved selectively using two different wavelengths of irradiation has been recently developed in our group [1,2]. In order to find additional tools for the selective cleavage of photolabile protecting groups, we studied compounds which photochemical reactivity could be modulated by a chemical reagent. Our first study was focused on the photochemical reactivity of derivative **1**. This compound was photochemically inert, presumably due to the quenching of the reactive excited state by a charge transfer between the electron rich *para*-amino group and the electron withdrawing nitro group. We have demonstrated that photochemical reactivity could be restored by protonation of the aniline-type nitrogen.



We describe in details the photochemical properties of this derivative and its use in chromatic orthogonality strategy. We also describe our progress in modulating the photochemical reactivity using metal cations bound to a molecular recognition element.

[1] Bochet, C. G., *Synlett*, **2004**, 13, 2268.
[2] Blanc, A.; Bochet, C. G., *J. Org. Chem.*, **2002**, 16, 5567.

Organic Chemistry **264**

Intramolecluar [2+2] photocycloaddition between aromatic aldehydes and allenes. Formation of fused tricyclic compounds containing an exo-methylene oxetane.

Christian G. Bochet, Frederic Birbaum

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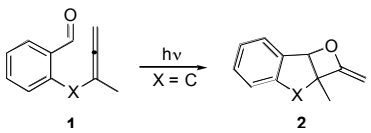
The intramolecular [2+2] photocycloaddition between aromatic aldehydes and allenes is a synthetically useful reaction as it provides a rapid and efficient method for accessing strained 2-methylene oxetane rings in polycyclic systems. Substituted benzaldehyde **1** was photochemically converted into compound **2**, in good yields.
We intend to study not only the formation of heterocycles such as hydrofurans and pyrrolidines (X = O, N), but also the subsequent ring opening and the thermal rearrangement of the 2-methylene oxetane entity [1].



[1] A. R. Howell, R. Fan, A. Truong, *Tetrahedron Lett.* **1996,** *48,* 8651-8654.

Organic Chemistry **265**

Supramolecular Stereocontrol of Biaryl Configuration and Translation into an Enantioselective [1,2]-Stevens Rearrangement

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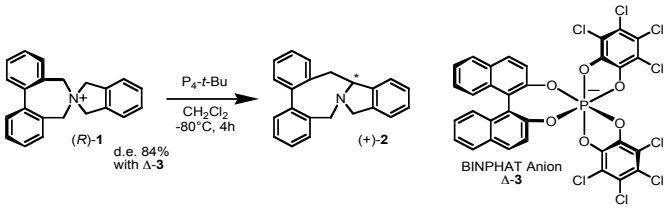
Recently, chiral diarylazepinium salts are strongly studied as catalysts in enantioselective phase-transfer reactions,[1] and hence the question of their stability under strongly basic conditions [2]. Herein, we report that diarylazepinium cation **1** reacts with a phosphazene base (P_4-*t*-Bu) following a [1,2]-Stevens rearrangement which sees the exclusive formation of *ring-expanded* amine **2**.



Enantioselective [1,2]-Stevens rearrangements have not been reported although highly diastereoselective or stereoretentive processes are known [3]. Herein, we also report that ion pairing of **1** with BINPHAT anion **3** leads to the preferred formation of one diastereomeric salt, [(*R*)-**1**][*Δ*-**3**], to the extent of a 84% diastereoselectivity. Treatment of this salt with P_4-*t*-Bu leads to the formation of (+)-**2** with a reproducible enantiomeric excess of 35%.

[1] K. Maruoka, T. Ooi, *Chem. Rev.* **2003**, *103*, 3013.
[2] L. Vial, M.-H. Gonçalves, P.-Y. Morgantini, J. Weber, G. Bernardinelli, J. Lacour, *Synlett.* **2004**, *9*, 1565.
[3] I. G. Stara, I. Stary, M. Tichy, J. Zavada, V. Hanus, *J. Am. Chem. Soc.* **1994**, *116*, 5084, F. G. West, *Org. Lett.* **2002**, *4*, 2813 and reference therein.

Organic Chemistry **266**

Design, preparation and evaluation of new families of chiral photosensitizers

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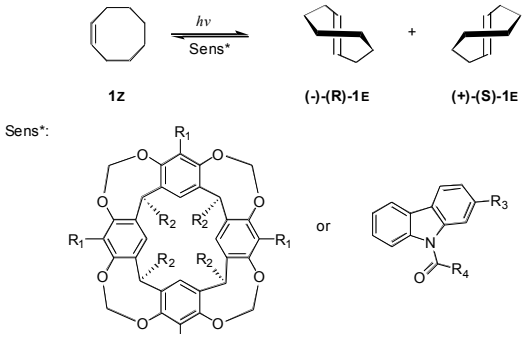
Chirality transfer from optically active sensitizers to prochiral substrates in the excited state is an intriguing and attractive process in photochemistry [1]. We are studying new families of chiral photosensitizers based on substituted calix[4]resorcinarenes and carbazoles.



We report our progress towards the preparation of such types of sensitizers and the evaluation of their efficiency in asymmetric photochemical reactions, such as the *Z-E* photoisomerization of cyclooctene [2].

[1] Inoue, Y.; Hoffmann, R. *J. Am.Chem. Soc.* **1999**, *121*, 10702.
[2] Inoue, Y. *Chem. Rev.* **1992**, *92*, 741.

Organic Chemistry **267**

New application of excited-state proton transfer in organic chemistry

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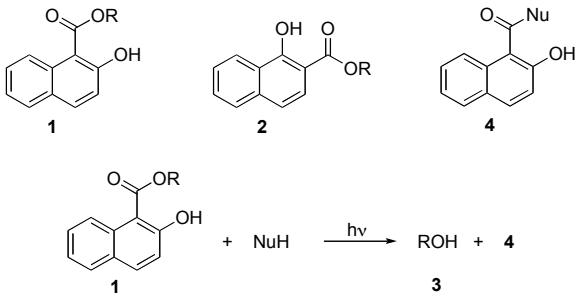
Departement of Chemistry, University of Fribourg, Ch. du Musée 9, CH-1700 Fribourg, Switzerland

Photoacids are molecules showing enhanced excited state acidity [1,2]. Only few organic reactions using photoacids have been described in the literature [3]. We propose to use excited state intra-molecular proton transfer to activate carbonyl group toward nucleophiles and therefore develop a new photolabile protecting group for alcohols [4].
Since naphthols are known as photoacids, we studied the reactivity of derivatives like **1** and **2** under several irradiation conditions. The identified reaction products are the released alcohol **3** and the substituted product **4**.



[1] T. Förster, *Naturwissenschaften* **1949**, *36*, 186
[2] L. M. Tolbert, K. M. Solntsev, *Acc. Chem. Res.* **2002,** *35*, 19-27
[3] H. J. P. de Lijser, N. A. Rangel, *J. Org. Chem.* **2004**, *69*, 8315
[4] C. G. Bochet, *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 2071-2073

Organic Chemistry **268**

Macrocyclic Precursors of [0_n]Paracyclophanes

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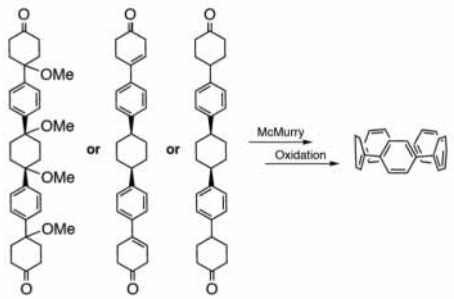
University of Fribourg, Chemistry Department, CH-1700 Fribourg, Switzerland

The interest for polyaromatic molecules, like cyclic oligoparaphenylenes, is increasing for a few years. This kind of aromatic products is difficult to synthesize and their preparation is one of the big challenge in this field of organic chemistry. This research started in the 90's with Vögtle [1] and Herges [2], but no synthetic way has been found until now.
The aim of our work is to find a good strategy to get [0_5]paracyclophane. For this purpose, we are using different precursors constituted of alternate phenyls and cyclohexyl rings. The macrocyclisation is attempted by a McMurry olefination at the terminal ketones, as shown in the scheme below. Once the cycle is obtained, the polyaromatic molecule will be prepared by oxydation of the cyclohexyl rings.



[1] R. Friederich, M. Nieger and F. Vögtle, *Chem. Ber.* **1993**, *126*, 1723.
[2] S. Kammermeier, P. G. Jones and R. Herges, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2669.

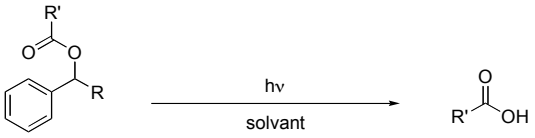
Organic Chemistry **269**

New and versatile photolabile protecting groups

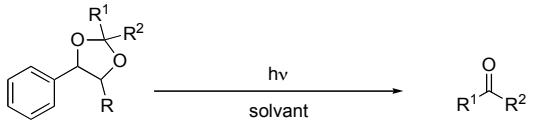
Aspasia Theodossiou and Christian G. Bochet

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

Protecting groups' chemical nature is unique in organic chemistry, since they solved the problem of chemical incompatibility during the synthesis of complex molecules. However, their use decreases the yield of the synthetic sequence and increases its length inevitably by two more steps: protection and deprotection. Therefore, photolabile protecting groups are a good alternative since they only need light for their deprotection [1]. We wish to report here a new type of photolabile protecting group:



This new type of protecting group is cheap and easily available. The mecanisme of its cleavage needs to be elucidated, as well as its protective application on other chemical functions such as the carbonyl group.



[1] Bochet, C. G. *J. Chem. Soc., Perkin Trans. 1,* **2002**, 125-42.

Organic Chemistry **270**

Chiral NHCs for the catalytic creation of quaternary carbon centers

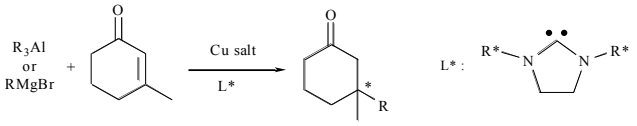
David Martin, Alexandre Alexakis*

Université de Genève, 30 quai Ernest Ansermet, 1211 Genève 4, Suisse

Diaminocarbenes (NHC)-metal catalysts have led to numerous breakthroughs in highly useful reactions such as the olefin metathesis, the Heck or Suzuki reactions[1]. Concerning the asymmetric catalysis, the use of NHCs is very recent, but the field has grown dramatically the last three years[2].

Meanwhile, excellent results have been obtained during the last decade for the asymmetric copper catalysed conjugate addition, in particular with dialkylzinc reagents in combination with chiral phosphoramidites ligands. However, the formation of chiral quaternary centers remains challenging with this methology. Recently, our group showed that the use of trialkylaluminum compounds, allows to overcome the lack of reactivity of β-trisubstituted enones with ee's up to 96%[3].

Here we report our preliminary results concerning the use of chiral NHCs as ligand for the asymmetric copper catalysed conjugate addition of Grignard reagents on β-trisubstituted enones.



[1] (a) D. Bourissou, O. Guerret, F. Gabbaï, G. Bertrand *Chem. Rev.* **2000,** 100, 39. (b) W. A. Herrmann, *Angew. Chem. Int. Ed.* **2002**, *41*, 1290. (c) Kirmse, *Angew. Chem. Int. Ed.* **2004**, *43*, 1767.
[2] V. Cesar, S. Bellemin-Laponnaz, L. H. Gade, *Chem. Soc. Rev.* **2004**, 33, 619.
[3] M. d'Augustin, L. Palais, A. Alexakis, *Angew. Chem. Int. Ed.* **2005**, 44, 2.

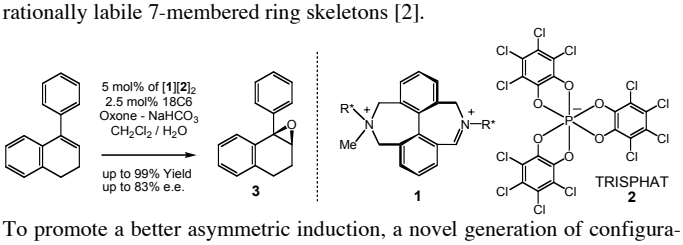
Organic Chemistry **271**

Doubly Bridged Biphenyl Azepinium Salts as Chiral Catalysts for Enantioselective Epoxidation Reactions

Alexandre Martinez, Jérome Vachon, Claire Marsol, Samuel Rentsch and Jérome Lacour*

Department of Organic Chemistry, University of Geneva, Switzerland

The epoxidation of olefins mediated by iminium salts was first reported by Lusinchi *et al* and proceeds *via* the *in-situ* formation with Oxone® of reactive oxaziridinium intermediates [1]. Recently, the groups of Page and our own have independently developed an enantioselective process using as catalysts iminium ions combining chiral exocyclic appendages and configurationally labile 7-membered ring skeletons [2].



To promote a better asymmetric induction, a novel generation of configurationally stable doubly bridged biphenyl azepinium salts was prepared – 4 steps from simple starting materials. Herein, we report their synthesis as well as their catalytic activity (conversion and e.e up to 99% and 83%).

[1] P. Milliet, A. Picot, X. Lusinchi, *Tetrahedron Lett.* **1976**, 1573.
[2] P. C. B. Page, G. A. Rassias, D. Barros, A. Ardakani, D. Bethell, E. Merifield, *Synlett* **2002**, 580; J. Lacour, D. Monchaud, C. Marsol, *Tetrahedron Lett.* **2002**, *43*, 8257; P. C. B. Page, D. Barros, B. R. Buckley, A. Ardakani, B. A. Marples, *J. Org. Chem.* **2004**, *69*, 3595; J. Vachon, C. Pérollier, D. Monchaud, C. Marsol, K. Ditrich, J. Lacour, *J. Org. Chem.* **2005**, in press.

Organic Chemistry **272**

Functionalized substrates for the copper catalyzed asymmetric allylic alkylation

Caroline Falciola, Alexandre Alexakis*

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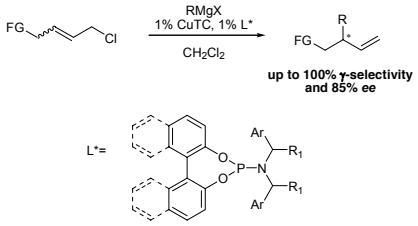
The formation of chiral centers via a copper catalyzed asymmetric allylic alkylation using external chiral ligands has already shown very good enantioselectivities. Monodentate phosphoramidite ligands are good chiral inductors and alkyl functions through organomagnesium reagents can be added to allylic substrates with excellent enantiomeric excess.



Herein we present that small functionalized allylic substrates can be versatile starting material and show good enantioselectivities for the copper catalyzed addition of Grignard reagents (up to 85% *ee*) with excellent regioselectivities, giving quantitatively the branched products. 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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Organic Chemistry **273**

Polymer-cyanine dye blends for photovoltaic applications

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The most efficient polymeric solar cells up to now use C60 derivatives as acceptors in bulk-heterojunction structures. One major limitation in the further improvement of these devices is the mismatch with Sun emission spectrum, since C60 absorbs in the ultraviolet region. Our approach is to use a cyanine dye as acceptor due to its very high absorption in the near-infrared (can also be tuned to the infrared), where the Sun emits most of its light. In these work we prepared thin films from blends of poly[2-methoxy-5-(2'-ethylhexyloxy)-*p*-phenylene vinylene] (MEH-PPV) and 2-(5-(1-Butyl-3,3-dimethyl-benzo[e]indol-2-ylidene)-penta-1,3-dien-yl)-1-butyl-3,3-dymethyl-benzo[e]indolium perchlorate, herein called CY680, using different concentrations of dye inside the polymer matrix. We also prepared films from blends of polystyrene (PS) and CY680. The optical absorbance spectra in the UV-vis from MEH-PPV/CY680 blends is formed by the superposition of the absorbance of the two components which are complementary and can harvest light up to 750 nm. Fluorescence measurements have shown that CY680 can efficiently (~99%) quench MEH-PPV emission when the blend has dye concentration of more than 1w%. However, quenching of CY680 emission due to charge transfer to the polymer is not clearly seen from the fluorescence spectra since this dye presents both re-absorption, due to a very small Stokes shift, and self-quenching. However, if we compare the dye emission in a blend with polystyrene with that in a blend with MEH-PPV, at the same dye concentration, a strong quenching (~85%) of the CY680 emission due to the MEH-PPV can be estimated. Our first results indicate that both MEH-PPV and CY680 could be used as active light harvesting materials in bulk-heterojunction solar cells.

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A fluorescence-based assay for Baeyer-Villiger monooxygenases, hydroxylases and lactonases.

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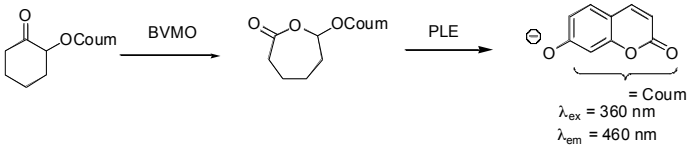
Enzyme assays are essential tools in drug discovery and enzyme engineering [1]. Since several years we developed fluorogenic enzyme substrates for high-throughput screening [2]. Herein we report the preparation and evaluation of cyclic and acyclic 2-coumaryloxy-ketones as fluorogenic substrates for detecting Baeyer-Villigerase activities in microbial cell cultures [3]. The use of the intermediate lactones as fluorogenic and chromogenic probes for esterases will also be discussed.



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[3] R. Sicard et al., *Adv. Synth. Catal*. **2005**, in press.

Organic Chemistry **275**

Radical azidation of *B*-Alkylcatecholborane

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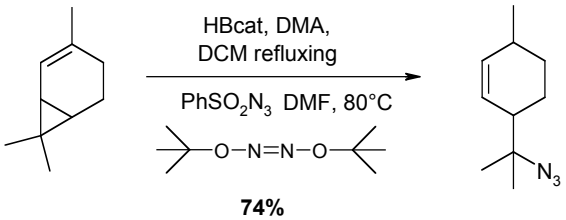
B-Alkylcatecholborane, easily prepared from hydroboration of alkenes, are excellent radical precursors[1]. We describe here a new methodology for their azidation based on the reaction of alkyl radicals with phenyl sulfonyl azide.



74%

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Organic Chemistry **276**

PORPHYRIN SUBSTITUTED NUCLEOTIDES

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Over the past years, modified nucleotides have become increasingly attractive to create supramolecular assemblies in aprotic solvents by using the Watson-Crick base-pairing motif. They also were used to incorporate various functionalities such as fluorophores or amino acid side chain mimics into the DNA itself. Using the appropriate substitution position, in particular the 5-postion in pyrimidines, these modified nucleotides retain their ability to selectively recognise the complementary base.
The goal of this project is the study of the electronic properties of a DNA based supramolecular porphyrin assembly. We present the synthesis of a tetramer porphyrin and the 21 oligomers incorporating one, two, three and more cental porphyrins. The incorporation of the porphyrin-modified deoxyuridines into DNA using a standard DNA synthesizer and the first results of the structural analysis will be discussed (UV-visible spectroscopy and mass spectrometry).

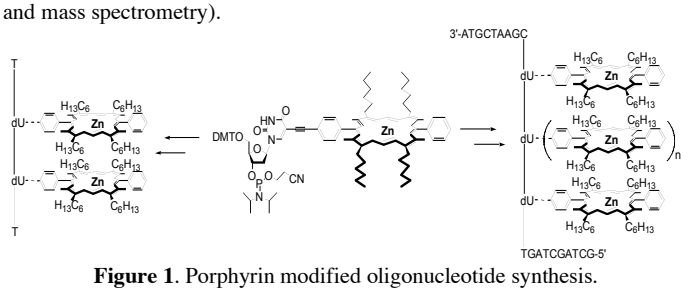

Figure 1. Porphyrin modified oligonucleotide synthesis.

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[2] Bouamaied, I.; Stulz, E. *Chimia* 2005, *59,* 101-104.

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Synthesis of the Polypropionate Fragment of Apoptolidinone

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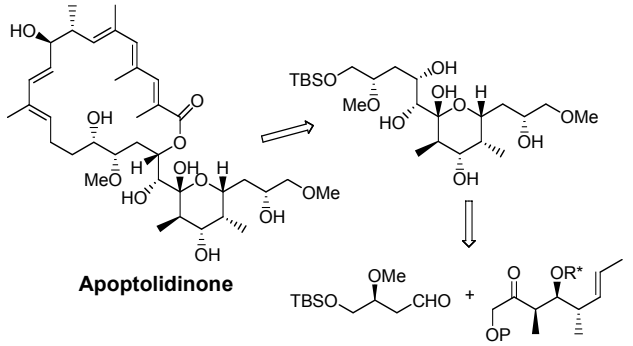
We present a new approach to the synthesis of the polypropionate fragment of **Apoptolidinone**. Apotolidinone is the aglycon of Apoptolidin [1], a natural product, isolated from *Nocardiopsis sp.*, which is capable to induce selectively apoptosis in tumour cells. Our approach for the synthesis of the polypropionate building block is based on two key reactions: the cascade oxyallylation of enoxysilanes with 1-oxy-1,3-dienes in the presence of sulfur dioxide of β,γ-insaturated sulfinic acids followed by retro-ene reaction developed in our group [2], and the aldol coupling.



[1] K. C. Nicolaou, Li Yiwei, K. Filaktakidou, H. J. Mitchel, H-X. Wei, B. Weyershausen, *Angew. Chem.* **2001**, 3849.
[2] V. Narkevitch, S. Megevand, K. Schenk, P.Vogel, *J.Org.Chem.* **2001**, 66, 5080; X.Huang, C. Craita, P.Vogel, *J.Org.Chem.* **2004**, 69, 4272.

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A New Type of Schmidt Rearrangement: Towards the Asymmetric Total Synthesis of (-)-Indolizidine 167B

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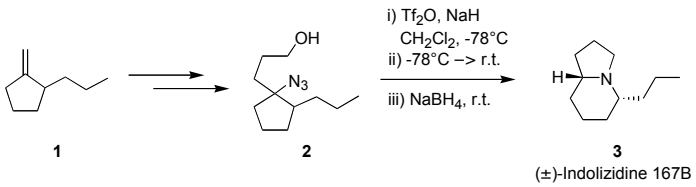
Azidoalcohol **2** is readily available as a 1:1 mixture of diastereomers in 2 steps from terminal olefin **1** via radical carboazidation [1] and subsequent reduction. Triflation and warming up leads to a spontaneous Schmidt type rearrangement [2] to the imminium salt which is then stereoselectively reduced to obtain racemic Indolizidine 167B **3**. This result represents the first example of a Schmidt rearrangement initiated by a nucleophilic substitution onto a primary carbon center. Regioselectivity problems of the rearrangement originating from the diastereomeric mixture of **2** will be discussed.



Currently we are working on the asymmetric synthesis of **3**. We expect that the configuration of the chiral center α to the olefin doesn't epimerize during the rearrangement, so it should be possible to obtain natural (-)-Indolizidine 167B by starting from optically pure **2**.

[1] P. Panchaud, L. Chabaud, Y. Landais, C. Ollivier, P. Renaud, S. Zigmantas, *Chem. Eur. J.* **2004**, *10*, 3606
[2] W. H. Pearson, R. Walavalkar, J. M. Schkeryantz, W.-K. Fang, J. D. Blickensdorf, *J. Am. Chem. Soc.* **1993**, *115*, 10183

Organic Chemistry **279**

Structural Analysis of a DNA Duplex containing a Non-Hydrogen-Bonding and Non-Shape Complementary Base Couple by NMR

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Hydrogen bonding and stacking interactions between nucleobases are considered as the major non-covalent interactions that stabilize the DNA and RNA double helix[1]. The relative contribution of each factor to the stability has been a matter of debate since the discovery of the structure of double helix.

5'- GTGAC**N**GCAG - 3'
3'- CACTG**O**CGTC - 5'

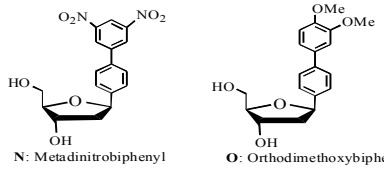

Figure 1: The DNA sequence and the structure of non-hydrogen bonding base analogues.

In order to analyze the influence of stacking in the absence of hydrogen bonding, the solution structure of a non self-complementary decamer duplex with one central biphenyl-deoxyribose unit (N/O) on each strand was detemined by NMR. The structure calculations were performed with XPLOR-NIH[2] version 2.0.4 using distance restraints generated from NOESY (mixing time 300 msec) with the aid of SPARKY[3].

[1] C. Brotschi, A. Haberli and C. J. Leumann, *Angew. Chem. Int. Ed.* **2001**, *40*, 3012.
[2] C. D. Schwieters, J. J. Kuszewski, N. Tjandra, and G. M. Clore, *J. Mang. Res.* **2003**, *160*, 65.
[3] T. D. Goddard, D. G. Kneller, 'Program SPARKY v3.110', University of California, San Francisco, 2004.

Organic Chemistry **280**

Synthetic Approach Toward the Natural Product Family of Frondosins

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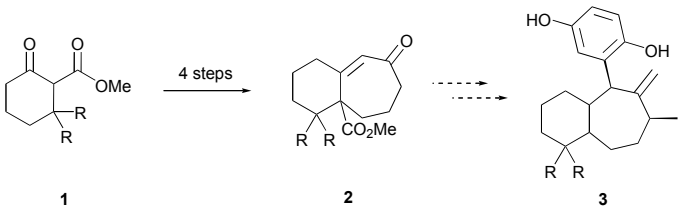
Frondosins were isolated from the marine sponge *Dysidea frondosa*. [1] IL-8 receptor antagonists such as the Frondosins represent a promising target for the development of novel pharmacological agents against autoimmune hyperactivity.
They are new, unusual members of marine bicyclic sesquiterpene quinones with a unifying bicyclo[5.4.0]undecane sesquiterpene framework.



In order to synthesise the bicyclo[5.4.0]undecane sesquiterpene framework we prepared key intermediate **2** in a four step sequence starting from *β*-keto ester **1**. Different strategies to finish the sesquiterpene framework are currently under investigation.

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