doi:10.2533/chimia.2007.470 CHIMIA **2007**, *61*, No. 7/8

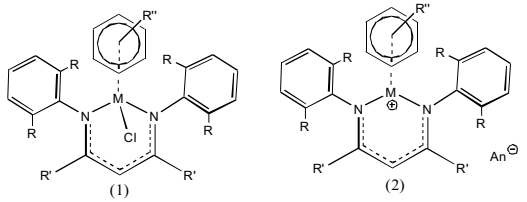
Inorganic and Coordination Chemistry **213**

## New Insights into the Reactivity of Arene Coordinated Ruthenium- and Osmium- β–Diketiminate Complexes

Paul J. Dyson, Aitor Moreno, Andrew D. Phillips, Paul S. Pregosin

Institut des Sciences et Ingénierie Chimiques, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland. Laboratorium für Anorganische Chemie, ETHZ HCI Hönggerberg CH-8093 Zürich.

The β-diketiminate class of ligands is renowned for the stabilization of coordinatively unsaturated main-group and transition metal complexes. We report on the synthesis, characterization and hydrogenation capabilities of a series of $\eta^6$-arene Ru- and Os-*β*–diketiminate complexes (1). Facile chloride exchange with different anions affords coordinatively unsaturated species (2) that readily undergo thermo-reversible [4+2] cycloaddition with alkenes, alkynes and $H_2$.[1] DFT calculations, in adjunction with high pressure NMR-deuterium labeling experiments, reveal a concerted heterolytic cleavage mechanism with a low energy barrier. Through steric and electronic variation of the β-diketiminate ligand, the efficiency of styrene and cyclohexene hydrogenation is shown to be highly tunable. $^{19}F$-$^{1}H$ HOESY and diffusion NMR experiments reveal different degrees of cation-anion interaction which has been demonstrated to influence catalytic activity.




M = Ru, Os. An = OTf, $BPh_4$, $BF_4$, $PF_6$, BArF. R = Me, iPr, OMe, H. R' = $^t$Bu, Me, $CF_3$, R'' = $C_6H_6$, $C_6H_5Me$, *p*-$MeC_6H_4{}^iPr$, $C_6Me_6$, etc.

1. Phillips, A. D.; Laurenczy, G.; Scopelliti, R.; Dyson, P. J. *Organometallics*, **2007**, *26*, 1120.

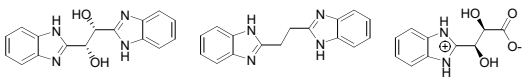
Inorganic and Coordination Chemistry **214**

## The Clash of the Synthons: Crystal Structures of Benzimidazole-alcohol carboxylic acids

Franck Delval, Alexandra Spyratou, Simon Verdan, Gerald Bernardinelli and Alan F. Williams

Département de Chimie minérale, analytique et appliquée, Université de Genève, 30 quai Ernest Ansermet, CH 1211 Genève 4.

Desiraju has introduced the notion of the supramolecular synthon to characterize a link (or predict an intermolecular interaction) between molecules in the solid state.[1] The identification of synthons can allow the rationalization of observed solid state structures. For molecules with several functional groups several synthons may be identified and the question arises as to which will be expressed. In this work we compare the structures of a number of compounds such as those shown below which we have used elsewhere as ligands.[2] They carry benzimidazole functions which can undergo stacking interactions,[3] alcohol and carboxylic acid functions able to undergo hydrogen bonding.




The results show that stacking interactions are less favorable than hydrogen bonding. Hydrogen bonds are formed preferentially between groups with similar $pK_a$.

[1] G. R. Desiraju, *Angew. Chem. Int. Ed. Engl.*, **1995**, *34*, 2311.
[2] K. Isele, F. Gigon, A. F. Williams, G. Bernardinelli, P. Franz, and S. Decurtins, *Dalton Trans*., **2007**, 332.
[3] C. J. Matthews, V. Broughton, G. Bernardinelli, X. Melich, G. Brand, A. C. Willis, and A. F. Williams, *New J. Chem.*, **2003**, *27*, 354.

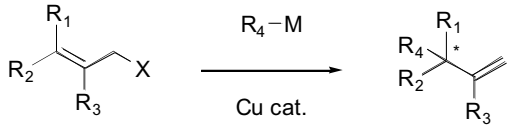
Organic Chemistry **215**

## Allylic Substrates for the Copper Catalyzed Asymmetric $S_N2'$ Reaction

Caroline A. Falciola, Alexandre Alexakis*

University of Geneva, Quai Ernest-Ansermet 30, 1211 Geneva 4, Switzerland

The formation of chiral centers via a copper catalyzed asymmetric allylic alkylation using external chiral ligands has already shown very good enantioselectivities. Our group has previously demonstrated that monodentate phosphoramidite ligands are good chiral inductors and alkyl functions through diverse organometallic reagents can be added to allylic substrates with excellent enantiomeric excess [1-2].




Herein we present that small functionalized allylic substrates can be versatile starting material and show good enantioselectivities for the copper catalyzed addition of organometallic reagents (up to >99% *ee*) with excellent regioselectivities [3-4]. 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 Lett.* **2004**, *45*, 7375-7378
[3] Falciola C. A., Tissot-Croset K., Alexakis A., *Angew. Chem. Int. Ed.* **2006**, *45*, 5995-5998
[4] Falciola C. A., Alexakis A., *Angew. Chem. Int. Ed.*, **2007**, *46*, 2619-2622

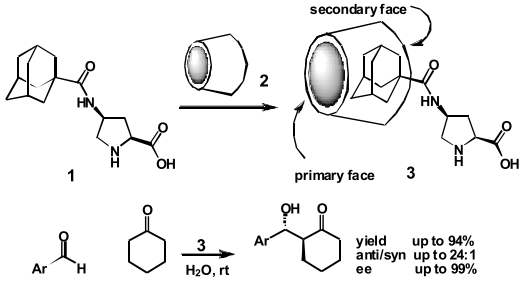
Organic Chemistry **216**

## Aldol reactions in water using a β-cyclodextrin-binding proline derivative

Kegang Liu, Daniel Häussinger, Wolf-D. Woggon*

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

The adamantoyl amide of S,S-4-amino proline **1** binds well to β-cyclodextrin **2** entering the cavity from the secondary face; the binding constant $K_a$= 1.4 x $10^4$ $M^{-1}$ was calculated from NMR-titration experiments. The water soluble inclusion complex **3** catalyzes aldol reactions of various aromatic aldehydes with cyclohexanone in good yield and high enantiomeric excess (ee). The catalyst can be easily recovered and reused with only small changes in reactivity and enantioselectivity.




The easy access and recycling of the catalyst and the high enantio- and diastereoselectivity of the reaction makes this procedure an attractive alternative to other methods for the synthesis of β-hydroxy ketones in water.

doi:10.2533/chimia.2007.470 CHIMIA **2007**, *61*, No. 7/8

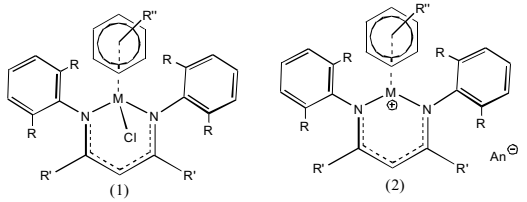
Inorganic and Coordination Chemistry **213**

## New Insights into the Reactivity of Arene Coordinated Ruthenium- and Osmium- β–Diketiminate Complexes

Paul J. Dyson, Aitor Moreno, Andrew D. Phillips, Paul S. Pregosin

Institut des Sciences et Ingénierie Chimiques, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland. Laboratorium für Anorganische Chemie, ETHZ HCI Hönggerberg CH-8093 Zürich.

The β-diketiminate class of ligands is renowned for the stabilization of coordinatively unsaturated main-group and transition metal complexes. We report on the synthesis, characterization and hydrogenation capabilities of a series of $\eta^6$-arene Ru- and Os-*β*–diketiminate complexes (1). Facile chloride exchange with different anions affords coordinatively unsaturated species (2) that readily undergo thermo-reversible [4+2] cycloaddition with alkenes, alkynes and $H_2$.[1] DFT calculations, in adjunction with high pressure NMR-deuterium labeling experiments, reveal a concerted heterolytic cleavage mechanism with a low energy barrier. Through steric and electronic variation of the β-diketiminate ligand, the efficiency of styrene and cyclohexene hydrogenation is shown to be highly tunable. $^{19}F$-$^{1}H$ HOESY and diffusion NMR experiments reveal different degrees of cation-anion interaction which has been demonstrated to influence catalytic activity.




M = Ru, Os. An = OTf, $BPh_4$, $BF_4$, $PF_6$, BArF. R = Me, iPr, OMe, H. R' = $^t$Bu, Me, $CF_3$, R'' = $C_6H_6$, $C_6H_5Me$, *p*-$MeC_6H_4{}^iPr$, $C_6Me_6$, etc.

1. Phillips, A. D.; Laurenczy, G.; Scopelliti, R.; Dyson, P. J. *Organometallics*, **2007**, *26*, 1120.

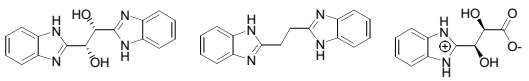
Inorganic and Coordination Chemistry **214**

## The Clash of the Synthons: Crystal Structures of Benzimidazole-alcohol carboxylic acids

Franck Delval, Alexandra Spyratou, Simon Verdan, Gerald Bernardinelli and Alan F. Williams

Département de Chimie minérale, analytique et appliquée, Université de Genève, 30 quai Ernest Ansermet, CH 1211 Genève 4.

Desiraju has introduced the notion of the supramolecular synthon to characterize a link (or predict an intermolecular interaction) between molecules in the solid state.[1] The identification of synthons can allow the rationalization of observed solid state structures. For molecules with several functional groups several synthons may be identified and the question arises as to which will be expressed. In this work we compare the structures of a number of compounds such as those shown below which we have used elsewhere as ligands.[2] They carry benzimidazole functions which can undergo stacking interactions,[3] alcohol and carboxylic acid functions able to undergo hydrogen bonding.




The results show that stacking interactions are less favorable than hydrogen bonding. Hydrogen bonds are formed preferentially between groups with similar $pK_a$.

[1] G. R. Desiraju, *Angew. Chem. Int. Ed. Engl.*, **1995**, *34*, 2311.
[2] K. Isele, F. Gigon, A. F. Williams, G. Bernardinelli, P. Franz, and S. Decurtins, *Dalton Trans*., **2007**, 332.
[3] C. J. Matthews, V. Broughton, G. Bernardinelli, X. Melich, G. Brand, A. C. Willis, and A. F. Williams, *New J. Chem.*, **2003**, *27*, 354.

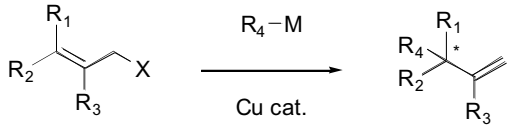
Organic Chemistry **215**

## Allylic Substrates for the Copper Catalyzed Asymmetric $S_N2'$ Reaction

Caroline A. Falciola, Alexandre Alexakis*

University of Geneva, Quai Ernest-Ansermet 30, 1211 Geneva 4, Switzerland

The formation of chiral centers via a copper catalyzed asymmetric allylic alkylation using external chiral ligands has already shown very good enantioselectivities. Our group has previously demonstrated that monodentate phosphoramidite ligands are good chiral inductors and alkyl functions through diverse organometallic reagents can be added to allylic substrates with excellent enantiomeric excess [1-2].




Herein we present that small functionalized allylic substrates can be versatile starting material and show good enantioselectivities for the copper catalyzed addition of organometallic reagents (up to >99% *ee*) with excellent regioselectivities [3-4]. 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 Lett.* **2004**, *45*, 7375-7378
[3] Falciola C. A., Tissot-Croset K., Alexakis A., *Angew. Chem. Int. Ed.* **2006**, *45*, 5995-5998
[4] Falciola C. A., Alexakis A., *Angew. Chem. Int. Ed.*, **2007**, *46*, 2619-2622

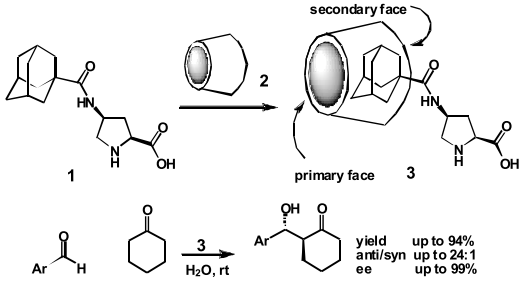
Organic Chemistry **216**

## Aldol reactions in water using a β-cyclodextrin-binding proline derivative

Kegang Liu, Daniel Häussinger, Wolf-D. Woggon*

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

The adamantoyl amide of S,S-4-amino proline **1** binds well to β-cyclodextrin **2** entering the cavity from the secondary face; the binding constant $K_a$= 1.4 x $10^4$ $M^{-1}$ was calculated from NMR-titration experiments. The water soluble inclusion complex **3** catalyzes aldol reactions of various aromatic aldehydes with cyclohexanone in good yield and high enantiomeric excess (ee). The catalyst can be easily recovered and reused with only small changes in reactivity and enantioselectivity.




The easy access and recycling of the catalyst and the high enantio- and diastereoselectivity of the reaction makes this procedure an attractive alternative to other methods for the synthesis of β-hydroxy ketones in water.

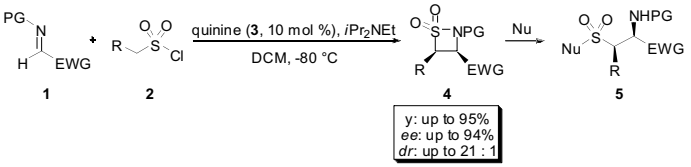
Organic Chemistry **217**

## Catalytic Asymmetric Formation of β-Sultams

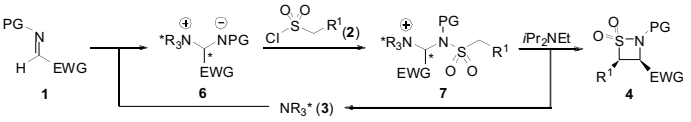
Marian Zajac, René Peters

ETH Zürich, Laboratory of Organic Chemistry, Wolfgang-Pauli-Str. 10, HCI E 110, CH-8093 Zürich, Switzerland

β-Sultams **4**, highly strained sulfonyl analogs of β-lactams, were prepared by a tertiary amine catalyzed asymmetric formal [2+2] cycloaddition reaction of electron-poor imines **1** with alkylsulfonylchlorides **2** in excellent yields and with high enantio- and diastereoselectivity.




According to our studies, the formation of product proceeds *via* a zwitterionic aminal intermediate **6**, resulting from nucleophilic addition of the tertiary amine catalyst **3** to the imine substrate **1**.
The title compounds are practical precursors of highly enantioenriched biologically interesting β-aminosulfonic acid (taurine) derivatives **5**, witch can be prepared by ring opening reactions with various nucleophiles.



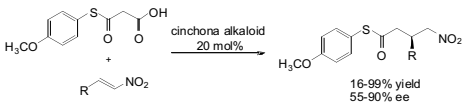

[1] M. Zajac, R. Peters, *Org. Lett.* **2007**, *in press*.

Organic Chemistry **218**

## Bioinspired 1,4-Addition Reactions Catalyzed by Derivatives of Cinchona Alkaloids

Jana Lubkoll and Helma Wennemers*

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




In the biosynthesis of fatty acids and polyketides malonic acid half thioester (MAHT) are used as ester enolate equivalents.[1] We were intrigued to investigate whether additions of MAHTs can also be catalyzed by metal-free

organocatalysts of low molecular weight. Here we present the first enantioselective 1,4-addition reactions of MAHTs to nitroalkenes catalyzed by derivatives of cinchona alkaloids. Using 20 mol% of the catalyst, γ-nitrothioesters were obtained in 16-99% yields and up to 90% enantioselectivity. The resulting γ-nitrothioesters are interesting precursors to, for example, chiral γ-butyrolactams.[2]

[1] Staunton, J.; Weissman, K.J. *Nat. Prod. Rep.* **2001**, *18*, 380.
[2] Lubkoll, J., Wennemers, H. **2007**, *manuscript submitted.*

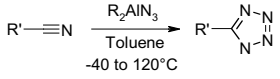
Organic Chemistry **219**

## Application of Click Chemistry for a Novel Synthesis of 5-Substituted Tetrazoles from Organo Aluminum Azides and Nitriles

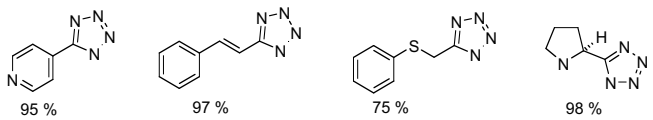
Valentina Aureggi [a,b], Gottfried Sedelmeier* [a], Reinhard Neier[b]

[a]Chemical & Analytical Development, Novartis Pharma AG
Klybecktrasse 141, CH- 4057 Basel, Switzerland
[b]University of Neuchatel, Av. de Bellevaux 51, CH-2000 Neuchatel, Switzerland

Tetrazoles are a class of heterocycles with a wide range of applications [1]. Although a versatile method to synthesize tetrazoles through safe protocols had not been really developed. We report here the discovery and development of a novel process for the efficient transformation of a wide variety of nitriles into the corresponding tetrazoles in high yield, using dialkylaluminum azides [2].




The cycloaddition occurs under mild conditions and the chemoselectivity allows the presence of a variety of different functional groups. In addition this methodology can be efficiently used for the synthesis of a novel class of pyrrolidin-tetrazole organocatalysts [2b].




[1] R. J. Herr, *Bioorg. Med. Chem.* **2002**, *10*, 3379.
[2] a) G. Sedelmeier, Novartis Pharma AG, **2005**, WO 2005/014602 A1; b) V. Aureggi, G. Sedelmeier, Novartis Pharma AG, **2007**, WO 2007/009716.

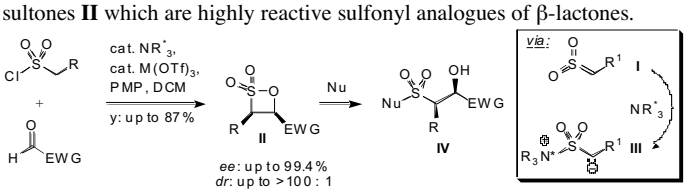
Organic Chemistry **220**

## Catalytical Asymmetric Synthesis of β-Hydroxysulfonyl Derivatives

Florian M. Koch, René Peters*

Laboratory of Organic Chemistry, ETH Zürich,
Hönggerberg HCI E 110, CH-8093 Zürich

Sulfenes **I** are the sulfonyl equivalents of ketenes.[1] An unsolved problem was prior to work by our group, the application of sulfenes as substrates in asymmetric catalysis, which would provide a tool to replace the chiral auxiliary controlled sulfonyl carbanion chemistry by more economical and time saving approaches. Since enantiopure sulfonyl analogs of carbonyl derivatives are playing an increasingly important role in medicinal chemistry, the development of catalytic asymmetric methods using sulfene substrates is an important undertaking. We were mainly interested in the formation of β-sultones **II** which are highly reactive sulfonyl analogues of β-lactones.




Our work was based on the hypothesis that it should be possible to carry out the β-sultone formation enantioselectively by the action of a catalytic amount of an enantiopure chiral nucleophile which would trap and at the same time activate the sulfene intermediate **I** by the formation of a zwitterionic sulfene-amine adduct **III**. The key to achieve both good yields and high enantioselectivities was the co-activation by a Lewis acid co-catalyst.[2] Ring opening reactions of the strained heterocycles with nucleophiles gave regioselective access to highly enantioenriched β-hydroxysulfonates, sulfonamides or sulfones **IV**.

[1] Zwanenburg, B. *Sci. Synth.* **2004**, *27*, 123.
[2] Koch, F. M.; Peters, R. *Angew. Chem. Int. Ed.* **2007**, *46*, 2685.

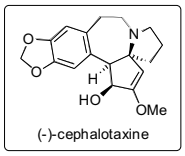
Organic Chemistry **221**

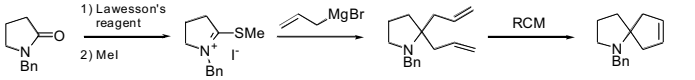
## Thioiminium Ions: Reaction With Organometallic Reagents and Their Use in the Synthesis of Aza-spirocycles

Alessandro Agosti, Britto Sebastian, Philippe Renaud*

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

Azaspirocycles represent an important subunit present in a wide range of natural products such as *Cephalotaxus* alkaloids. Many synthetic approaches to the core structure are described [1]. Here we wish to report a short and efficient synthesis of aza-spirocyclic compounds via *gem*-diallylation reaction of a thioiminium ion with allylmagnesium bromide followed by ring closing methatesis. The corresponding *gem*-dibenzylated heterocycles were prepared using the same procedure. The reaction with organocerium reagents allows the preparation of *gem*-dialkylated pyrrolidine derivatives.




[1] Dake, D.*Tetrahedron*, **2006**, *62*, 3467-3492.

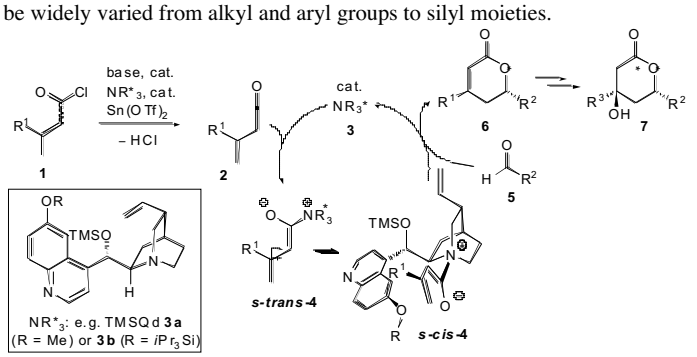
Organic Chemistry **222**

## Catalytic Asymmetric Formation of δ-Lactones by [4+2]-Cycloaddition of Zwitterionic Dienolates Generated from Acid Chlorides

Paolo. S. Tiseni, Prof. Dr. René Peters*

*ETH Zürich, Laboratory of Organic Chemistry, Wolfgang-Pauli-Str. 10, Hönggerberg HCI E 111, CH-8093 Zürich, Switzerland*

δ-Lactones are subunits of numerous highly bioactive compounds such as the cholesterol-lowering statin drugs. We have developed a tertiary amine catalyzed asymmetric [4+2]-cycloaddition of α,β-unsaturated acid chlorides **1** and electron poor aldehydes **5** such as chloral ($R^2 = CCl_3$), providing δ-lactones **6** in good yield and with up to 98% *ee* [1]. The substituent $R^1$ can be widely varied from alkyl and aryl groups to silyl moieties.




The versatile trichloromethyl moiety can be readily transformed into several valuable functionalities (e.g. $CO_2H$, $CHCl_2$, $CH_2Cl$, $CH_2OH$). β-Silyl-substituted δ-lactones **6** ($R^1 = R^3SiX_2$) were utilized to diastereoselectively prepare β-hydroxy-δ-lactones **7** with a quaternary carbon stereocenter.

[1] P. S. Tiseni, R. Peters, *Angew. Chem. Int. Ed.* **2007**, *in press.*

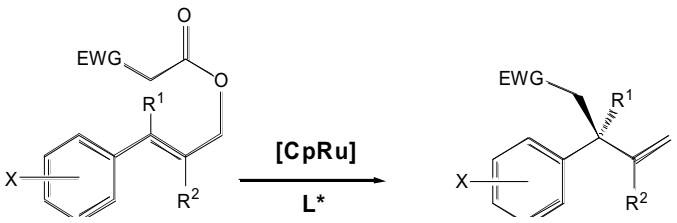
Organic Chemistry **223**

## Through the Looking-Glass of Ruthenium Catalyzed Enantioselective Carroll-like Allylic Rearrangements

David Linder, Simone Tortoioli, Frédéric Buron and Jérôme Lacour*

Department of Organic Chemistry, University of Geneva
30 Quai Ernest Ansermet, CH1211 Geneva Switzerland
e-mail: david.linder@chiorg.unige.ch

The stereoselective generation of tertiary and quaternary stereogenic centers by C-C bond forming reactions still represents a challenge in natural product and medicinal chemistry.[1] In this context, the decarboxylative Carroll rearrangement of secondary and tertiary allyl β-ketoesters is attractive as chiral γ,δ-unsaturated ketones are readily afforded.[2] Recently, we have found that CpRu(II) half-sandwich complexes can, in the presence of selected enantiopure diimine ligands, catalyze this transformation and afford complete conversions and decent level of enantiomeric excess (up to 80%).[3] We have also discovered that the same catalysts can perform the Carroll-like decarboxylative allylic rearrangement of allylic esters with other electron-withdrawing β-substituents with analogous yields and selectivity.




[1] Fuji, K. *Chem. Rev.* **2003**, *93*, 2037-2066,
[2] Tunge, J. A.; Burger, E. C. *Eur. J. Org. Chem.* **2005**, 1715-1726,
[3] Constant, S.; Tortoioli, S.; Müller, J.; Lacour, J. *Angew. Chem. Int. Ed.* **2007**, *46*, 2082-2085

Organic Chemistry **224**

## Screening of Chiral Catalysts by Mass Spectrometric Monitoring of Catalytic Intermediates

Antje M. Teichert and Andreas Pfaltz*

Department of Chemistry, University of Basel, St. Johanns-Ring 19,
CH-4056 Basel, Switzerland
Fax +41 61 267 1103, e-mail: antje.teichert@unibas.ch

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

We here report the retro-Diels-Alder reaction of mass-labelled quasi-enantiomers with chiral bis(oxazoline)copper(II) catalysts. Due to the different masses the catalyst-reactant complexes can be distinguished by ESI-MS. The ratio of the two catalyst-reactant complexes, which is determined by integration, reflects the efficiency for enantiodiscrimination of the chiral catalyst.
We were also able to extend this concept to the organocatalysed retro-Diels-Alder reaction by monitoring mass-labelled iminium ion intermediates.

[1] Markert, C. and Pfaltz, A. *Angew. Chem.* **2004**, *116*, 2552; *Angew. Chem. Int. Ed.* **2004**, *43*, 2498.

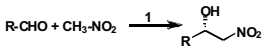
Organic Chemistry **225**

## A homochiral metal-organic framework catalyzes enantioselective Henry reactions in aqueous media

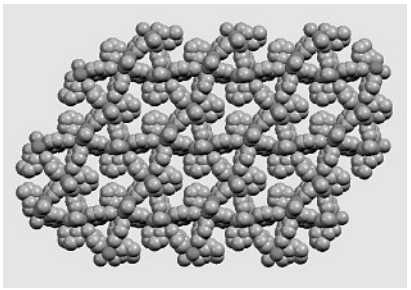
Guoqi Zhang, Wolf-D Woggon*

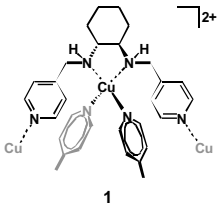
Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

The Henry reaction is one of the most efficient reactions for carbon-carbon bond formation, providing access to valuable functionalized structural motifs, such as 1,2-amino alcohols and α-hydroxy carboxylic acids. Recent efforts regarding catalytic, enantioselective Henry reactions have focused mainly on catalysts derived from small organic molecules and/or metal complexes and were normally carried out in non-aqueous media.




We discovered that self-assembly of 1R,2R-N,N'-bis(4-pyridylmethylene)-1,2-diaminocyclohexane and $Cu(OAc)_2$ led to a homochiral, two dimensional, lamellar coordination polymer **1** (see structure according to X-ray analysis). This material is remarkably soluble in water and catalyzes the Henry reaction of various aldehydes with nitromethane in 95% yield and up to 87% ee in ethanol/water (9:1) at 0°C.






**1**

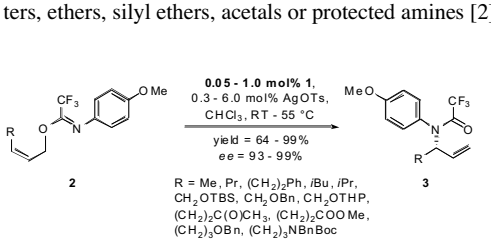
Organic Chemistry **226**

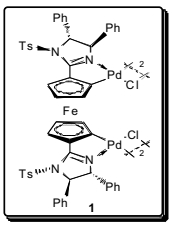
## Ferrocenyl Bisimidazoline Palladacycles (FBIP) as Highly Active and Enantioselective Catalysts for the Aza-Claisen Rearrangement of *Z*-Configured Allylic *N*-*para*-Methoxyphenyl Trifluoroacetimidates

Sascha Jautze and René Peters*

ETH Zürich, Laboratory of Organic Chemistry, Wolfgang-Pauli-Str. 10, Hönggerberg HCI E 111, CH-8093 Zürich, Switzerland

$Pd^{II}$-catalyzed aza-Claisen rearrangements of achiral allylic trifluoroacetimidates **2** enable the convenient formation of chiral enantioenriched allylic amines. The substrates are readily prepared from allylic alcohols in one step. Recently, we have developed macrocyclic ferrocenyl bisimidazoline palladacycle dimers (FBIP) of type **1** as efficient precatalysts for the title reaction [1]. Complex **1** is obtained in good yield *via* a four step synthesis and after activation with AgOTs exhibits the highest catalytic activity (catalyst loading: 0.05 - 1.0 mol%) for *Z*-configured trifluoroacetimidate substrates **2** providing protected allylic amines **3** in good (63%, R = *i*Pr) to excellent (86-100%, all other examples) yield and with generally very high enantioselectivity (*ee* 93-99%). Moreover, this catalyst system was found to be highly compatible with the most important functional groups such as ketones, esters, ethers, silyl ethers, acetals or protected amines [2].




[1] S. Jautze, P. Seiler, R. Peters, *Angew. Chem. Int. Ed.* **2007**, *46*, 1260.
[2] S. Jautze, R. Peters, unpublished results.

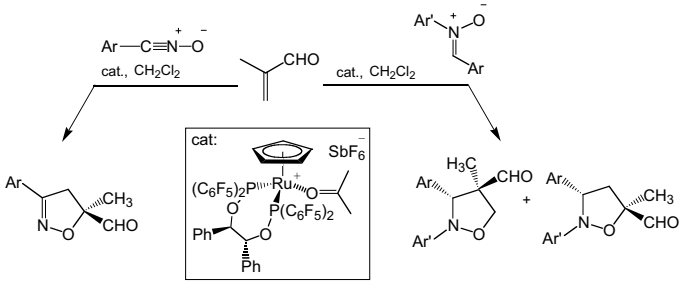
Organic Chemistry **227**

## Asymmetric Lewis Acid-Catalyzed 1,3-Dipolar Cycloadditions

Andrei Bădoiu, Yasmin Brinkmann, Florian Viton, E. Peter Kündig*

University of Geneva, Department of Organic Chemistry, Sciences II, 30 quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland
*peter.kundig@chiorg.unige.ch

Highly tuned, one-point binding chiral iron and ruthenium complexes selectively coordinate and activate $\alpha$, $\beta$-unsaturated carbonyl compounds towards asymmetric catalytic Diels-Alder cycloaddition reactions.[1] We have also reported the reactions between enals and nitrones, giving the corresponding isoxazolidines in good yields, moderate to high enantio- and regioselectivities and complete *endo*/*exo* selectivity.[2] We now present the extension of the work with nitrones and also report the first examples of one-point binding asymmetric catalytic 1,3-dipolar cycloaddition reaction of enals with aryl nitrile oxides.




[1] a) Kündig, E. P.; Saudan., C. M.; Viton, F. *Adv. Synth. Catal.* **2001**, *343,* 51. b) Rickerby, J.; Vallet, M.; Bernardinelli, G.; Viton, F.; Kündig, E. P. *Chem. Eur. J.* **2007**, *13*, 3354.
[2] Viton, F.; Bernardinelli, G.; Kündig, E. P. *J. Am. Chem. Soc.* **2002**, *124*, 4968.

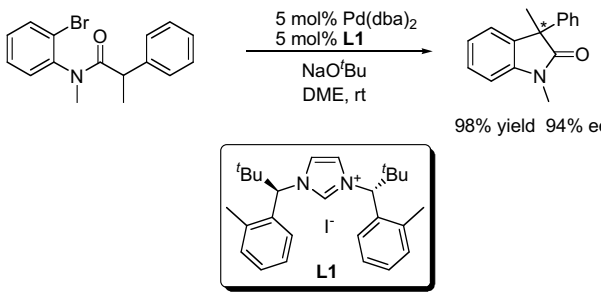
Organic Chemistry **228**

## Highly Enantioselective Palladium-Catalyzed Intramolecular α-Arylation Reaction Using New *N*-Heterocycle Carbene Ligands

Yi-Xia Jia, Thomas Seidel, E. Peter Kündig*

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

The palladium-catalyzed intramolecular α-arylation reaction of amides is an efficient synthetic access to oxindoles. Although many chiral ligands have been screened in this reaction, the best *ee* value was moderate and less than 76% [1].
Here, we report the synthesis of a new group of *N*-heterocycle carbene ligands from the chiral α-alkyl benzylamines and their successful application in the reaction mentioned above. The enantioselectivity is up to 94% with almost quantitative yield at room temperature when **L1** used as carbene precursor, which represents the best result so far.




1. [1] (a) S. Lee, J. F. Hartwig, *J. Org. Chem.* **2001**, *66*, 3402. (b) F. Glorius, G. Altenhoff, R. Goddard, C. Lehmann, *Chem. Commun.* **2002**, 2704. (c) T. Arao, K. Kondo, T. Aoyama, *Tetrahedron Lett.* **2006**, *47*, 1417.

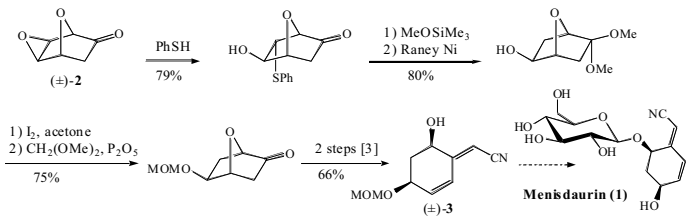
Organic Chemistry **229**

## Total Synthesis of the Aglycone of Menisdaurin

A. Walther, D. Josien-Lefebvre and C. Le Drian

Université de Haute-Alsace
Ecole Nationale Supérieure de Chimie de Mulhouse
3, rue Alfred Werner, 68093 Mulhouse, France.

Menisdaurin (**1**), was first isolated in 1978 from *Menispermum Dauricum* [1] and this natural non-cyanogenic cyanoglucoside posseses a strong inhibitor activity against the Epstein-Barr virus. Starting from epoxide (±)-(**2**) [2], a *Vogel's* "naked sugar" which is easily obtained optically pure, we report herein an original route for the first total synthesis of the protected aglycone (±)-(**3**) in 6 steps and 31% global yield.




Futhermore, this synthesis could be extended to the preparation of many other biologically active substances such as Menisdaurilide, Phyllanthurinolactone, Simmondsin, Lophirosides and Ehretiosides.

[1] K. Takahashi, S. Matsuzawa, M. Takani, *Chem. Pharm. Bull*. **1978**, *26*, 1677.
[2] C. Le Drian, P. Vogel, *Helv. Chim. Acta* **1987**, *70*, 1703.
[3] see D. Josien-Lefebvre, C. Le Drian, *Helv. Chim. Acta* **2007,** *90***,** 19.

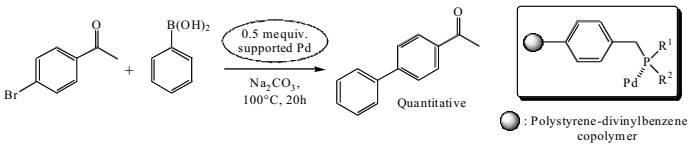
Organic Chemistry **230**

## Development of Efficient and Reusable Phosphinopolystyrene-Supported Palladium Catalysts for C-C Bond Forming Reactions

S. Schweizer, J.-M. Becht and C. Le Drian

Université de Haute Alsace
Ecole Nationale Supérieure de Chimie de Mulhouse
3, rue Alfred Werner, 68093 Mulhouse Cedex, France.

The Suzuki-Miyaura cross-coupling reaction of aryl halides with arylboronic acids is one of the very important palladium-catalyzed reactions in modern organic synthesis. During the last decade, considerable work has been devoted to the development of homogeneous catalysts from precious metals. However, since these catalysts are dissolved, they are usually almost impossible to recover for direct reuse, and the presence of the transition metal in the reaction products is often very difficult to avoid. We describe here very active, versatile, easy to prepare and reuse, polystyrene-supported palladium catalysts for the Suzuki and other C-C bond forming reactions.[1]




For example the above coupling afforded still a 86% yield in the presence of only 0.05 mequiv. of supported palladium. Furthermore, it should be noted that the recovered catalyst was reused four times without showing any loss of activity and that only less than 1% of the palladium initially present was leached in the reaction medium, which precludes the presence of sizeable amounts of palladium in the product.

[1] S. Schweizer, J.-M. Becht, C. Le Drian, *Adv. Synth. Catal*. **2007**, in press.

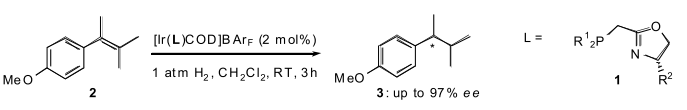
Organic Chemistry **231**

## Iridium Catalysed Asymmetric Hydrogenation of Unfunctionalised, Tetrasubstituted Olefins

Marcus G. Schrems, Eva Neumann and Andreas Pfaltz

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

Enantioselective hydrogenation of olefins has become a powerful tool in synthetic organic chemistry. Especially Ir-complexes with chiral N,P ligands have established themselves as efficient catalysts for the enantioselective hydrogenation of imines and unfunctionalised olefins, largely complementary to the scope of Rh and Ru catalysts.[1] Despite all advances in this field, suitable catalysts for the enantioselective hydrogenation of unfunctionalised, tetrasubstituted olefins have been elusive. Recently, we used N,P ligands **1** for synthesising new N,P Ir-complexes [Ir(**1**)COD]$BAr_F$ and subsequently applied these complexes in the enantioselective hydrogenation of various olefins, including olefin **2**, for which up to date, only moderate enantioselectivities have been reported.[2] With several catalysts Ir-**1** *ee*s higher than reported were obtained. These results encouraged us to further investigate this type of Ir-complexes in the enantioselective hydrogenation of unfunctionalised, tetrasubstituted olefins, and we subsequently found very high activity and selectivity for several classes of substrates.




[1] a) A. Pfaltz et al., *Adv. Synth. Catal*. **2003**, *345*, 33; b) X. Cui, K. Burgess, *Chem. Rev*. **2005**, *105*, 3272.
[2] A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem. Int. Ed.* **1998**, *37*, 2897; W. J. Drury III, N. Zimmermann, M. Keenan, M. Hayashi, S. Kaiser, R. Goddard, A. Pfaltz, *Angew. Chem. Int. Ed.* **2004**, *43*, 70; T. T. Co, T.-J. Kim, *Chem. Commun*. **2006**, 3537.

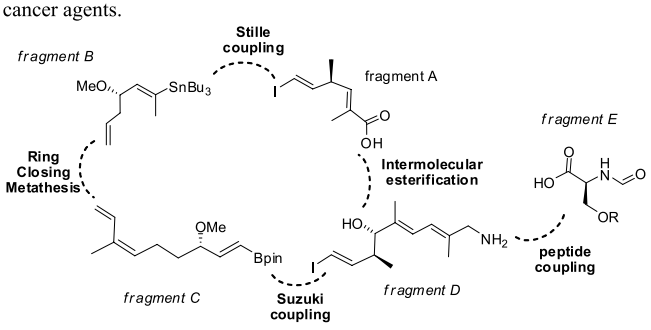
Organic Chemistry **232**

## Total Synthesis of Iejimalides A-D

Alois Fürstner*, Mario Waser, Martin Tremblay, Carine Chevrier, Filip Téply, Christophe Aïssa and Cristina Nevado

Max Planck Institut für Kohlenforschung, Kaiser Wilhelm Platz 1, D-45470, Mülheim an der Ruhr, Germany

A concise and convergent total synthesis of the highly cytotoxic marine natural products iejimalide A-D is reported, which relies on an effective ring closing metathesis (RCM) reaction of a cyclization precursor containing no less than 10 double bonds. Moreover, a series of non-natural "iejimalide-like" compounds has been prepared, differing from the natural lead in the polar head groups linked to the macrolide's N-terminus. With the aid of these compounds it was possible to uncover the hitherto unknown effect of iejimalide and analogues on different crucial biological processes in addition to their role as promising lead structures for the development of anti-cancer agents.




[1] Fürstner, A.; Nevado, C.; Tremblay, M.; Chevrier, C.; Téply, F.; Aïssa, C.; Waser, M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5838.

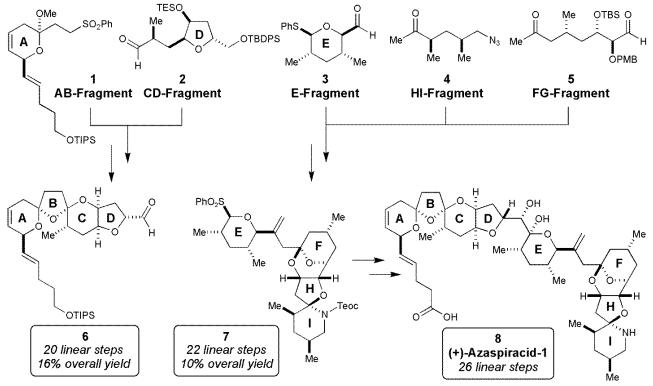
Organic Chemistry **233**

### Total Synthesis of (+)-Azaspiracid-1

Lisbet Kvaerno, Travis B. Dunn, Jason A. Mulder, André Beauchemin, Eward J. Olhava, Brian Raymer, Martin Juhl, Katsuji Kagechika, and David A. Evans*

Department of Chemistry & Chemical Biology, Harvard University, 12 Oxford Street, Cambridge, MA 02138, USA

(-)-Azaspiracid-1 (*ent*-**8**) is a marine neurotoxin implicated in seafood poisoning. A total synthesis of this structurally complex polyketide will be presented relying on catalytic asymmetric methodology for the construction of the desired key fragments: A carbonyl-ene reaction to furnish the CD-fragment **2**, a hetero-Diels-Alder reaction to afford the E- and HI-fragments **3** and **4**, and a Mukaiyama aldol reaction to deliver the FG-fragment **5**. The ABCD-tetracyclic aldehyde **6** and the EFGHI-sulfone **7** have both been achieved on a large scale (>800 mg). The final fragment coupling involved the addition of the sulfone anion of **7** to aldehyde **6** and allowed for a highly convergent synthesis of (+)-azaspiracid-1 (**8**) in only 26 linear steps.



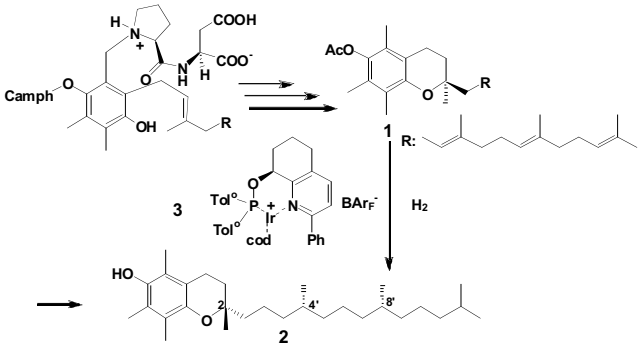

Organic Chemistry **234**

### Biomimetic syntheses of tocotrienols and tocopherols

Julien Chapelat, Antoinette Chougnet, Wolf-D. Woggon*

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

The biosynthetic chromanol ring closure is acid catalyzed proceeding by *si*-protonation of the double bond of phytylhydroquinone followed by *re*-attack of the phenolic oxygen yielding γ-tocopherol. A synthetic mimic of this reaction involves the use of a covalently attached pro-asp dipeptide which finally can be removed to provide α-tocopherol with 80-85 % de and overall 25% yield from commercially available material.[1] The configuration at C-2 depends on the absolute configuration of pro-asp (S-pro-S-asp → 2S; R-pro-R-asp → 2R). An alternative strategy, reported here, makes α–tocotrienol **1** accessible from which subsequently α-tocopherol **2** can be produced by enantioselective hydrogenation using the Ir catalyst **3**.[2] Accordingly two physiologically important members of the vitamin E family can be prepared in an enzyme–like fashion.




[1] Grütter, C.; Alonso, E.; Chougnet, A.; Woggon, W.-D. *Angew. Chem. Int. Ed.* **2006**, 45, 1126.
[2] Bell, S.; Wüstenberg, B.; Kaiser, S.; Menges, F.; Netscher, T.; Pfaltz, A. *Science* **2006**, 311, 642

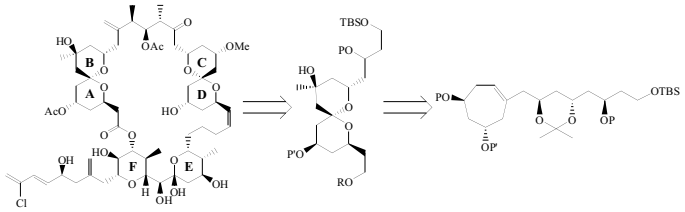
Organic Chemistry **235**

### New route toward the synthesis of AB-spiroketal of spongistatin 1

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

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

Discovered in 1993, spongistatin 1 is a complex marine macrolide that displays extraordinary antitumor activities against human cancer cell lines. Composed of two spiroketals units (AB and CD) and two densely substituted tetrahydropyran rings (E and F) this molecule represents a formidable synthetic challenge [1]. After the synthesis of the EF fragment [2], we report here an application of Vogel's non-iterative asymmetric methodology for the synthesis of fifteen-carbon 1,3-polyols [3] to the straightforward preparation of an advanced precursor of the AB spiroketal. In particular, taking advantage of an early desymmetrisation [4], new pathways have been developed for the orthogonal and selective protection of the hydroxyl groups allowing their complete differentiation and synthesis of analogues.




Spongistatin 1

[1] Yeung, K-S.; Paterson, I. *Chem. Rev.* **2005**, *105*, 4237.
[2] Lemaire-Audoire, S.; Vogel, P. *J. Org. Chem.* **2000**, *65*, 3346.
[3] Schwenter, M-E.; Vogel, P. *Chem. Eur. J.* **2000**, *6*, 4091.
[4] Meilert, K.; Pettit,G. R.; Vogel, P. *Helv. Chim. Acta.* **2004**, *87*, 1493.

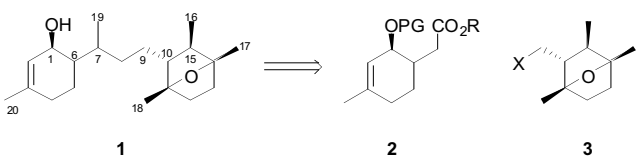
Organic Chemistry **236**

### Enantioselective Total Synthesis of Laurenditerpenol, a potent disruptor of cellular response to hypoxia

Christophe Braun, Karl-Heinz Altmann

Institute of Pharmaceutical Sciences, ETH Zurich, Wolfgang-Pauli-Strasse 10, 8093 Zurich, Switzerland

Laurenditerpenol **1** is a diterpene isolated from the extracts of the marine red algae *Laurencia intricata*. It has been reported to disrupt the cellular response to hypoxia in T47D cells by lowering cellular levels of the hypoxia-inducible factor HIF-1α ($IC_{50}$=0.4μM) [1], a key protein in the cellular regulation of oxygen homeostasis. HIF-1α is upregulated in hypoxic solid tumors associated with poor clinical prognosis, and is believed to play a key role in ischemic diseases and HIF-1α thus represents an attractive drug target [2].
We report on our progress toward the enantioselective total synthesis of Laurenditerpenol **1**, which involves a convergent stereoselective alkylation reaction between fragments **2** and **3**, possibly allowing the determination of the absolute configuration at C(6) and C(7). Various strategies toward the synthesis of Laurenditerpenol will be presented.




[1] K. A. Mohammed, C. F. Hossain, L. Zhang, R. K. Bruick, Y.-D. Zhou, D. G. Nagle, *J. Nat. Prod.* **2004**, *67*, 2002.
[2] G. L. Semenza, *Nat. Rev. Cancer* **2003**, *3*, 2003.

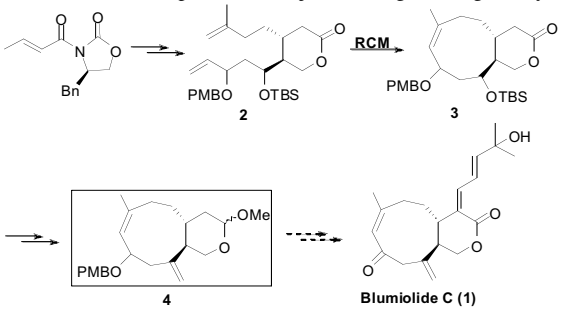
Organic Chemistry **237**

**Towards the first total synthesis of the natural product Blumiolide C**

Cotinica Hamel, Karl-Heinz Altmann*

Institute of Pharmaceutical Sciences, ETHZ, 8093 Zürich, Switzerland

Blumiolide C (**1**) was isolated from the soft coral *Xenia blumi* in 2005 and was shown to exhibit significant antiproliferative activity against different cancer cell lines [1]. Base on these interesting initial findings we are interested in the total synthesis of **1** for more extensive biological profiling and as a basis for future analog synthesis and SAR studies. To the best of our knowledge the total synthesis of blumiolide C has not been accomplished so far. The molecule incorporates a carbocyclic nine-mebered ring as a key structural feature, which represents a major challenge for organic synthesis.




Our approach to the formation of the nine-membered ring was based on ring closing olefin metathesis with diene **2**, which provided bicyclic intermediate **3** in up to 66% yield. **3** was then elaborated into protected lactol **4**. Current efforts are concentrated on the side chain introduction in order to complete the total synthesis.

[1] El-Gamal, A. A. H.; Chiang, C-Y.; Huang, S-H.; Wang, S-K.; Duh, C-Y, *J. Nat. Prod.* **2005**, *68*, 1336.

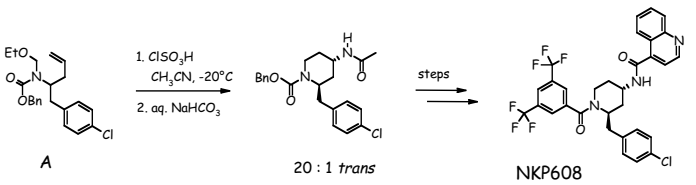
Organic Chemistry **238**

**Synthesis of 4-Aminopiperidines NK1 Antagonists via Acyliminium Intermediates**

Siem Veenstra, Priska Schmid, Peter Felber and Hinke Malda

Novartis Pharma AG, Werk Klybeck, Klybeckstrasse 141, CH-4057 Basel

We developed a short and practical synthesis for the selective NK1 antagonist **NKP608** based on acyliminium ion chemistry that is suitable for scale-up.




We investigated the scope of this cationic cyclisation reaction that produces selectively trans substituted 2-alkyl-4-aminopiperidines in terms of substituents, alternative precursors, stereo- and enantioselectivity.

[1] Vassout et al, *Regulatory Peptides* **2000**, *96*, 7-16.
[2] Papp et al, *Behavioural Brain Research* **2000**, *115*, 19-23.
[3] Veenstra S.J., Schmid P. *Tetrahedron Lett.* **1997**, *38*, 997.
[4] Veenstra et al, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 3029.

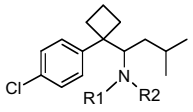
Organic Chemistry **239**

**A Hydrogenation Approach to Enantiopure di-desmethyl Sibutramin**

Ulrich Berens†, Oliver Dosenbach†, Hans-Jörg Kirner†, Oanh Mai-Huynh‡, Christophe Malan‡, Tanja Moessner†, Franz Schwarzenbach†

†Ciba Group Research, CH-4002 Basel, Switzerland
‡ Solvias AG, Postfach, CH-4002 Basel, Switzerland

Currently, racemic Sibutramine **1** is licensed for the treatment of obesity.[1] Preliminary preclinical studies suggest that the potent serotonin, norepinephrine, and dopamine re-uptake inhibitor (*R*)-**2** might be useful for the treatment of CNS disorders.[2] Also, the enantiomers of **3** have been claimed for the treatment of depression and related disorders.




**1** $R^1$, $R^2$ = Me, racemate
**2** $R^1$ = H, $R^2$ = Me, enantiopure
**3** $R^1$, $R^2$ = H, enantiopure

Sibutramine **1** and analogues

The synthesis of enantiopure **2** or **3** has remained a considerable challenge. Various approaches have been reported by Sepracor [2, 3] where resolution, a chiral auxiliary or in a catalytical variant the addition of a Grignard reagent to an imine in the presence of chiral ligands was used. Unfortunately, the resolution of **1**, **2** or **3** is tedious, and the catalytical approach gave the product only with an *ee* of 40%. The synthesis of enantiopure **3** *via* asymmetric hydrogenation of a readily accessible substrate will be presented.

[1] Scheinbaum, M. L PCT Appl WO 90/06110
[2] (a) Young J. W. PCT Application WO 94/00047 (b) Young J. W. PCT Application WO 94/00114.
[3] Han Z.; Krishnamurthy D.; Senananyake C. H. *Org. Proc. Res. Dev.* **2006**, *10*, 327 and references cited therein.

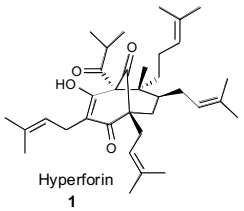
Organic Chemistry **240**

**Progress toward the total synthesis of Hyperforin**

Christian G. Bochet, Claire-Lise Ciana

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

Hyperforin **1** is thought to be responsible of biological activity of St-John's wort extracts (*Hypericum perforatum*) against mild to moderate depression [1]. The challenging polyoxygenated bicyclo[3.3.1]nonane core common to the polyprenylated acylphloroglucinol (PPAPs) family has attracted the attention of several research groups [2]. Total synthesis of closely related Garsubellin A [3] and Clusianone [4] were published recently but to our knowledge no total synthesis of Hyperforin **1** was achieved. Here we described our recent progresses toward the total synthesis of Hyperforin.




[1] J. Barnes, L.A. Anderson, J.D. Phillipson, *J. Pharm. Pharmacol.* **2001**, *53*, 583
[2] R. Ciochina, R.B. Grossman, *Chem. Rev.* **2006**, *106*, 3963
[3] A. Kuramochi, H. Usuda, K. Yamatsugu, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2005**, *127*, 14200; D.R. Siegel, S.J. Danishevsky, *J. Am. Chem. Soc.* **2006**, *128*, 1048
[4] P. Nuhant, M. David, T. Pouplin, B. Delpech, C. Marazano, *Org. Lett.* **2007**, *9(2)*, 287; V. Rodeschini, N.M. Ahmad, N.S. Simpkins, *Org. Lett.* **2006**, *8(23)*, 5283

Organic Chemistry **241**

**www.nmrdb.org : Resurecting and processing NMR spectra**

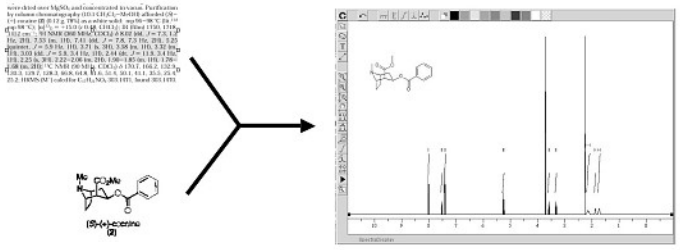
Damiano Banfi and Luc Patiny

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

NMR spectroscopy is certainly the analytical methodology that provides the most information about a molecule but most of the time spectra are not fully assigned and the result in not stored in a database. For this reason it is very rare in both academic and corporate environments to be able to query a database for all singulets at 3 ppm corresponding to protons next to a carbonyl.

In this poster we present a web-based approach implementing a new java applet that enables to assign a chemical structure to the corresponding NMR spectrum by simply drawing lines between atoms and automatically characterized signals.

We also provide a way to recreate NMR spectra from published in-line experimental parts, allowing to recover all this lost knowledge.



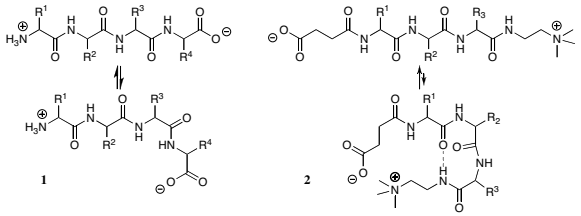
Organic Chemistry **242**

**Reversed-Polarity Peptides: A Novel Concept for the Design of β-Turns**

Damien Barbaras[1] and Karl Gademann*[1,2]

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

One of the most challenging problems in biological and medicinal chemistry remains the elucidation of the structure and function of every peptide and protein in metabolism [1]. Controlling the structure, *e.g.* the exact arrangement of functional groups in three-dimensional space, should allow controlling protein function. A key element of the protein structure is the β-turn, which is often involved in recognition and binding of different proteins [2]. Therefore, several successful strategies, such as the incorporation of unnatural amino acids (peptidomimetics) in the turn region, or the synthesis of cyclic peptides, have been developed to constrain and fold small peptides derivatives into β-turn structures [3].



In general, small peptides with a normal polarity **1** are conformationally flexible molecules. We propose an alternative approach for sequence-independent folding using linear, unconstrained reversed-polarity peptides **2** that fold into compact and well-defined secondary structures (foldamers). The synthesis and structural characterization will be discussed.

[1] Pandey, A.; Mann, M. *Nature* **2000**, *405*, 837.
[2] Rini, J. M.; Schulzegahmen, U.; Wilson, I. A. *Science* **1992**, *255*, 959.
[3] Venkatraman, J.; Balaram, P. *Chem. Rev*. **2001**, *101*, 3131.

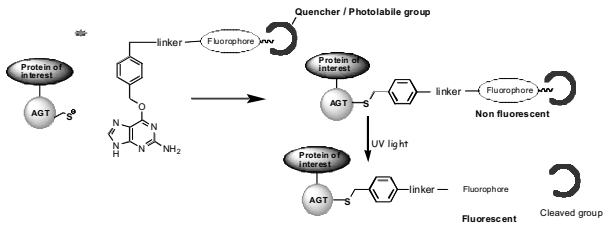
Organic Chemistry **243**

**Caged Fluorophores for Labeling of AGT Fusion Proteins**

Samba Shiva Banala, Helen O'Hare, Kai Johnsson*

Institute of Chemical Sciences and Engineering, EPFL
CH-1015 Lausanne, Switzerland

Fluorescent molecules are important tools in studying protein dynamics and other biological processes.[1] Despite recent improvements in the field, it is difficult to control the fluorescence in a spatial and temporal manner. Caged fluorophores offer the possibility to overcome this limitation. Here, we present caged fluorophores linked to Benzyl Guanine (BG) derivatives. Previous work proved that BG derivatives specifically react with mutants of human DNA repair protein $O^6$-alkylguanine –DNA alkyltransferase (AGT) and its fusion proteins.[2] We use two different approaches to mask the fluorescence, in the first model a photolabile protecting group (4,5-dimethoxy-2-nitrobenzyl) was used to cage the Rhodamine. The second approach uses the principle of Fluorescence Resonance Energy Transfer (FRET)[3] to quench the fluorescence with non fluorescent quenchers. Fluorescence was finely controlled using UV light in both models.




[1] B. N. G. Giepmans, S. R. Adams, M. H. Ellisman, R.Y. Tsien, *Science*, **2006**, *312*, 217. [2] A. Juillerat, T. Gronemeyer, A. Keppler, S. Gendreizig, H. Pick, H. Vogel, K. Johnsson, *Chemistry & Biology*. **2003**, *10*, 313. [3] K. E. sapsford, L. Berti, I. L. Medintz, *Angew. Chem. Int. Ed.* **2006**, *45*, 4562.

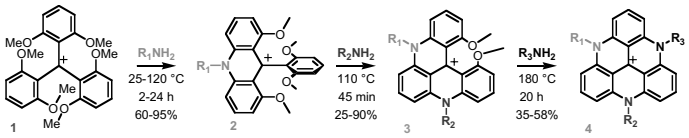
Organic Chemistry **244**

**Exceptionally Stable Carbenium Ions: Synthesis and Applications**

Cyril Nicolas[a], Christelle Herse[a], Benoît Laleu[a], Pierre Mobian[a], Gérald Bernardinelli[a], Eric R. Francotte[b], Thomas Burgi[c] and Jérôme Lacour[a,*]

[a] University of Geneva, Department of Organic Chemistry, 30 Quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland.
[b] Novartis Institutes for Biomedical Research, Discovery Technologies, Postfach, WKL-122.P.25, CH-4002 Basel
[c] University of Neuchâtel, Chemistry Institute, 51 Av de Belleveaux, 158 Postfach, CH-2009 Neuchâtel, Switzerland

Using simple organic synthetic transformations, a variety of highly stable nitrogen- and oxa-bridged heterocyclic carbenium ions of the acridinium and triangulenium families, compounds **2-4** (see below), have been synthesised in medium to excellent yields.




Their preparation is based on the facile nucleophilic aromatic substitution ($S_NAr$) of methoxy substituents of tris(2,6-dimethoxyphenyl)carbenium ion **1** by primary alkyl or aryl amines. Not only by virtue of its stepwise and irreversible nature, this process provides a powerful tool for the preparation of a wide variety of unsymmetrical heterocyclic carbenium salts [1] but it also affords synthetic targets/tools for many applications [2].

[1] Laursen. Bo. W, Krebs. F. C, *Chem. Eur. J.* **2001**, *7*, 1773.
[2] Nicolas. C. Lacour. J, *Org. Lett.* **2006**, *8*, 4343 and reference 18 therein; Mobian. P, Banerji. N, Bernardinelli. G, Lacour. J, *Org. Biomol. Chem.* **2006**, *4,* 224.

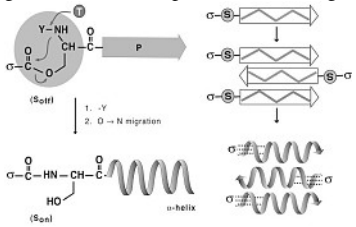
Organic Chemistry **245**

**Switch Peptides as Folding Precursors in Self-Assembling Peptides and Amyloid Fibrillogenesis**

Marie-Stephanie Camus, Richard Mimna, Adrian Schmid, Arunan Chandravarkar, Gabriele Tuchscherer, Hilal A. Lashuel, Manfred Mutter

Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland

Understanding the early event of protein misfolding is crucial to study its implication to neuronal death leading to neurodegenerative diseases. Here, we demonstrate that our new generation of switch peptides is able to control the induction of conformational transitions under physiological conditions using O, N-acyl migration *in situ* [1]. In combining switch-elements, which can be activated by chemical or enzymatic cleavage, the consecutive triggering of O,N-acyl migrations gives new insights into the role of peptide segments in early processes of polypeptide self-assembly and fibrillogenesis [2]. CD, TEM and ThT studies will be presented revealing conformational transitions relevant in degenerative diseases. In switching on helix-inducing peptidomimetics *in situ* (Figure), a so far unobserved reversal of type β to α paralleled by fibril disruption will be described [3]. The experimental access to early molecular events in degenerative diseases represents a starting point for the rational design of inhibitors of protein misfolding.



[1] M. Mutter et al., *Angew. Chem. Int. Ed.*, **2004**, *43*, 4172.
[2] G. Tuchscherer et al., *Biopolymers (Peptide Science)*, in press.
[3] R. Mimna et al., *Angew. Chem. Int. Ed.*, in press

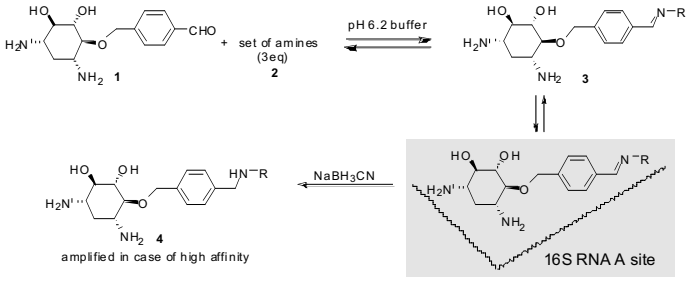
Organic Chemistry **246**

**Efficient routes for the discovery of new RNA binders**

Gérald Coste and Sandrine Gerber-Lemaire*

Ecole Polytechnique Fédérale de Lausanne, Laboratory of Glycochemistry and Asymmetric Synthesis, Batochime, 1015 Lausanne, Switzerland

Among the panel of biopolymers representing relevant therapeutic targets, RNA molecules constitute fascinating molecular hosts in view of their distinctive architecture, as well as the electrostatic field generated by their fold that create potential binding pockets for small molecules. [1] Among the various methods that might be applied to the rapid discovery of new ligands for RNA molecules, dynamic combinatorial chemistry [2] would offer an efficient and innovative strategy by combining different binding fragments around the RNA template that will select the best assemblies. Here we report the development of dynamic combinatorial libraries involving a 2-deoxystreptamine derived aldehyde, various polyamines and 16S A-site rRNA as triggering agent. LC-MS analysis of the composition of the libraries allowed the discovery of new RNA binders that will be evaluated for their potential antibacterial properties.




[1] *ChemBioChem* **2003**, Special Issue 4, RNA targeting.
[2] Corbett, P. T.; Leclaire, J.; Vial, L.; West, K. R.; Wietor, J. L.; Sanders, J. K. M.; Otto, S. *Chem. Rev.* **2006**, *106*, 3652.

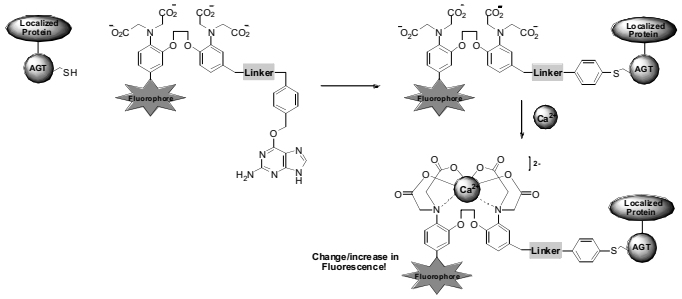
Organic Chemistry **247**

**$O^6$-benzylguanine-BAPTA fluorescent indicators for local Calcium sensing in living cells**

Ivan R. Corrêa Jr., Michael Bannwarth, Agostina Ruggiu, Kai Johnsson*

Institute of Chemical Sciences and Engineering, EPFL
CH-1015 Lausanne, Switzerland

Signal transduction events are known to be triggered and controlled by changes in the cytosolic concentration of free $Ca^{2+}$. Rational development of indicators for investigating $Ca^{2+}$ levels in living cells is therefore critical for understanding biological systems [1]. Several synthetic and protein-based indicators were designed for studying the dynamics of intracellular $Ca^{2+}$ concentrations. While synthetic fluorophores can offer advantages over genetically-encoded fluorescent proteins, such as superior brightness and higher photostability, they usually lack specificity for targeting a given subcellular compartment. Herein we would like to present the synthesis of $O^6$-benzylguanine-BAPTA fluorescent sensors for local $Ca^{2+}$ sensing in cells using covalent labeling of AGT fusion proteins [2].




[1] R. Rudolf, M. Mongillo, R. Rizzuto, T. Pozzan, *Nat. Rev. Mol. Cell Biol.* **2003**, *4*, 579. [2] A. Keppler, S. Gendreizig, T. Gronemeyer, H. Pick, H. Vogel, K. Johnsson, *Nat. Biotechnol.* **2003**, *21*, 86.

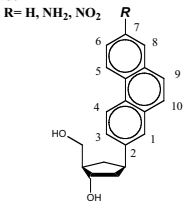
Organic Chemistry **248**

**Functionalized Phenanthrenes as DNA Base Surrogates**

Nikolay A. Grigorenko and Christian J. Leumann

University of Berne, Freistrasse 3, 3012, Berne, Switzerland

Hydrophobic DNA base surrogates are invaluable tools to probe the roles of hydrogen bonding and stacking interactions in DNA and RNA duplexes, and for probing the structural requirements of DNA-manipulating enzymes [1]. On the other hand, the phenomenon of charge transport through the DNA duplex is of great interest for both, fundamental and applied research [2, 3]. Replacing the natural bases with electronically tunable aromatic residues will allow modulation of the charge-carrier properties of DNA and thus provide new insights on the mechanism of this phenomenon and widen the opportunities for applications.




As an extension of our recent work on biphenyl DNA [4] we present here the synthesis of phenanthrenyl nucleosides, bearing substituents of different electronic nature, their incorporation into oligonucleotides and the studies of their pairing and fluorescence properties.

[1] E. T. Kool, *Acc. Chem. Res.* **2002**, *35*, 936.
[2] B. Giese, *Acc. Chem. Res.* **2000**, *33*, 631.
[3] B.M. Zeglis, J.K. Barton, *Nature Protocols* **2007**, *2*, 357.
[4] C. Brotschi, G. Mathis, C. J. Leumann, *Chem. Eur. J.* **2005**, *11*, 1911.

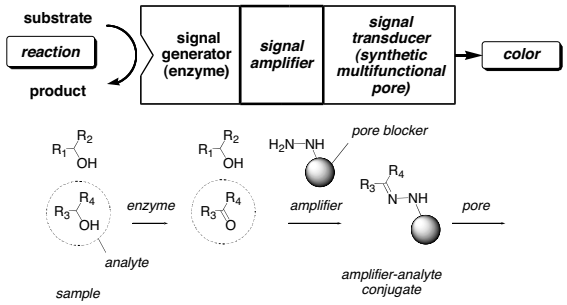
Organic Chemistry **249**

## Reactive Amplifiers for Multianalyte Sensing with Synthetic Pores

Sara Butterfield, Shinya Hagihara, Hiroyuki Tanaka, Svetlana Litvinchuk and Stefan Matile*

University of Geneva, Department of Organic Chemistry
Geneva - Switzerland

Synthetic pores have been introduced as optical transducers of chemical reactions and, in concert with enzymes, as universal biosensors [1,2]. Here, we describe reactive amplifiers to covalently capture otherwise elusive analytes after enzymatic signal generation and drag them into synthetic pores for blockage. Focus will be on reactive amplification for multicomponent sensing in samples from the supermarket or the hospital, for the development of inhibitor screening assays for otherwise problematic enzymes, and application to other transducers such as cell-penetrating peptides [3].



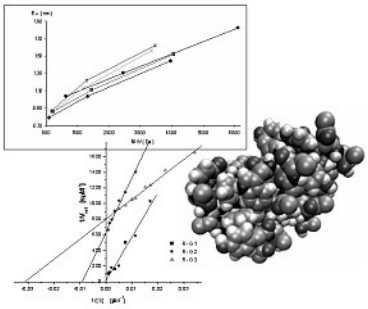

[1] G. Das, P. Talukdar, S. Matile, *Science* **2002**, *298*, 1600-1602
[2] S. Matile, H. Tanaka, S. Litvinchuk, *Analyte Sensing across Membranes with Artificial Pores*. In *Chemical Sensor Systems*, Schrader, T., Ed.; *Top. Curr. Chem.*, in press.
[3] T. Miyatake, M. Nishihara, S. Matile, *J. Am. Chem. Soc.* **2006**, *128*,12420-12421.

Organic Chemistry **250**

## Structure and Activity in Single Catalytic Site Peptide Dendrimers

Sacha Javor, Estelle Delort, Tamis Darbre, Jean-Louis Reymond*

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



We are investigating peptide dendrimers[1,2] as artificial enzyme models. We have reported a single site esterolytic peptide dendrimer[3] obtained by high throughput screening[4] of a combinatorial library. Here we report the first study of the sequence-structure-activity relationship of such enzyme mimics using PGSE diffusion NMR[5] combined with exhaustive kinetic studies.

[1] J. Kofoed, J.-L. Reymond, *Curr.Opin.Chem.Biol.* **2005**, *9*, 656-664.
[2] a) E. Delort, N.-Q. Nguyen-Trung, T. Darbre, and J-L. Reymond, *J.Org.Chem.* **2006**, *71*, 4468-4480. b) E. Delort, T. Darbre, J.-L. Reymond, *J.Am.Chem.Soc.* **2004**, *126*, 15642-15643.
[3] SCS Fall Meeting 2006, Poster Nr. 293
[4] A. Clouet, T. Darbre, J.-L. Reymond, *Angew.Chem.Int.Ed.* **2004**, *43*, 4612-4615.
[5] Y. Cohen, L. Avram, L. Frish, *Angew.Chem.Int.Ed.* **2005**, *44*, 520-554.

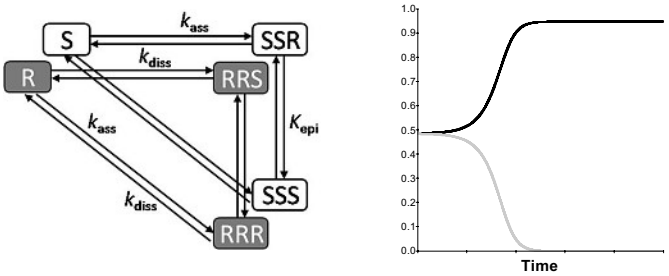
Organic Chemistry **251**

## Kinetic Scheme and Model for Chiral Amplification of Amino Acids

Déborah Mathis and Peter Chen

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

Emergence of homochirality in living systems remains an unresolved question for scientists. Hypotheses propose that it could have appeared via symmetry breaking of racemic mixtures followed by a chiral amplification mechanism. But no experimental evidence ever shows such behavior.
Inspired by the work of Plasson [1], we designed a new kinetic scheme which shows amplification of enantiomeric excess. The kinetic scheme consists of a reversible association step which forms a homo or heterochiral trimer. The second step epimerizes the heterochiral trimer into the homochiral trimer. The kinetic scheme was modeled with Powersim and the simulations are shown in the picture.




Cobalt complexes with amino acids ligands have the required properties to epimerize amino acids [2]. We are currently investigating *tris* amino acids cobalt complexes which could obey to our kinetic scheme and show chiral amplification of amino acids.

[1] R. Plasson, H. Bersini, A. Commeyras, *PNAS,* **2004***, 101*, 16733
[2] J. Chin, S. S. Lee, K. J. Lee, S. Park, D. H. Kim, *Nature,* **1999**, *401*, 254

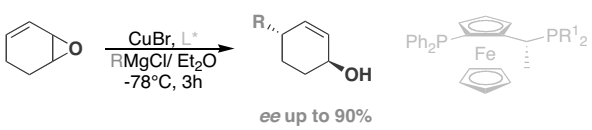
Organic Chemistry **252**

## Copper-catalyzed kinetic resolution of allylic epoxides

Millet Renaud, Alexakis Alexandre

University of Geneva, Department of organic chemistry, Quai E. Ansermet 30, 1211 Geneve 4, Switzerland.

Enantioselective copper catalyzed allylic substitution is a useful method for carbon-carbon formation [1]. Vinylic epoxides can be regarded as a subclass of allylic substrates affording useful allylic alcohols. The kinetic resolution of racemic epoxides can easily lead to chiral allylic alcohols. Zinc and aluminium reagents have already been sucessfully used for these reactions [2]. Recently, we reported the use of Grignard reagents for such a reaction on 1,3-cyclohexadiene monoepoxide [3].




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

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

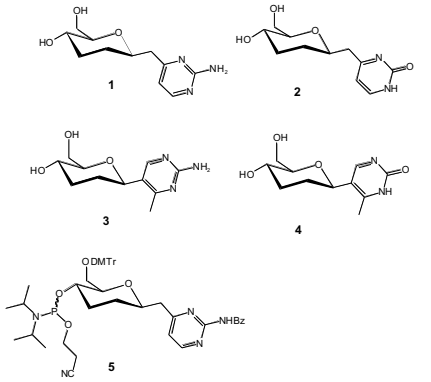
Organic Chemistry **253**

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

Michael Löpfe, Jay S. Siegel

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

For structural investigations of a recently proposed pyrimidine codon [1] a series of homo-DNA-*C*-nucleosides **1**-**4** were prepared according to a new method derived from the *Vorbrüggen* method of nucleoside synthesis [2]. Nucleoside **1** was converted to the phosphoramidite **5** to be used in oligonucleotide synthesis.



[1] J. S. Siegel, Y. Tor, *Org. Biomol. Chem.* **2005**, *9*, 1591.
[2] H. Vorbrüggen, G. Benua, *Chem. Ber.* **1981**, 114, 1279.

Organic Chemistry **254**

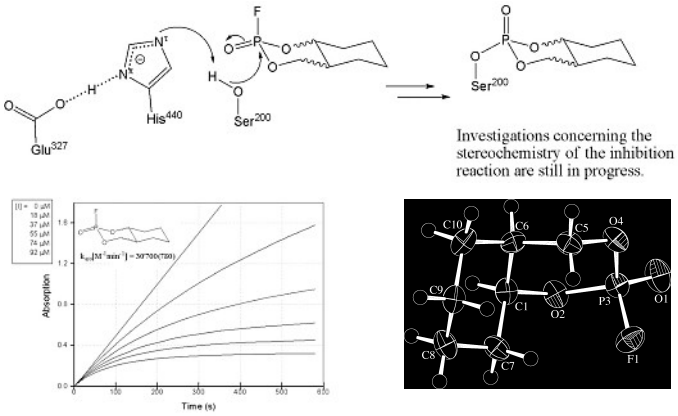
### Optically Active Dioxaphosphadecalins as Inhibitors of Acetylcholinesterase: Structural Observations and Enzyme Kinetic Investigations

Michael Wächter, Peter Rüedi*

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

The 2,4-dioxa-3-fluoro-3-phosphabicylco[4.4.0]decane-3-oxides (1,6-*cis*- and 1,6-*trans*-, 3-ax and 3-eq) are conformationally restricted irreversible inhibitors of acetylcholinesterase and related serine hydrolases (*e.g.* chymotrypsin).

In order to determine the inhibition constants ($k_{ass}$ or $k_i$) of the compounds, enzyme kinetic experiments with the enantiomerically pure dioxaphosphadecalins were performed.




In addition to the kinetic results we also present some particular structural observations of the 3-phosphadecalins in solution and in the solid state (double inversion of the equatorially substituted *cis*-decalins).

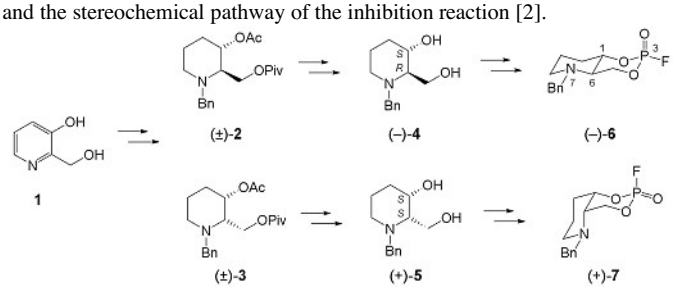
Organic Chemistry **255**

### Optically Active 7-Aza-2,4-dioxa-3-fluoro-3-phosphadecalins as Acetylcholine-Mimetics

Michael Wächter, Peter Rüedi*

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

Continuing our studies on the inhibition of acetylcholinesterase by organophosphates we have synthesized the eight stereoisomeric title compounds ((+)-**6ax**, (–)-**7eq** as representatives) with *ee* > 99%. Representing acetylcholine mimetics they are useful probes for the investigation of the physiologically active conformation of acetylcholine [1] and the stereochemical pathway of the inhibition reaction [2].



The inhibitors were prepared from the enantiomerically pure (+)- and (–)-, *cis*- and *trans*-1-benzyl-3-hydroxy-2-(hydroxymethyl)piperidines (**4** and **5**) by cyclization with $POCl_2F$ as summarized above. The complete procedure and the determination of the absolute configurations as well as first results of the enzyme kinetic characterization are presented.

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

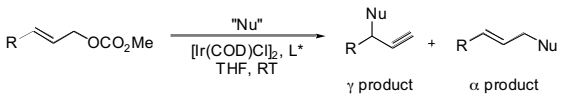
Organic Chemistry **256**

### Iridium-Catalyzed Asymmetric Allylic Substitution with Various Nucleophiles

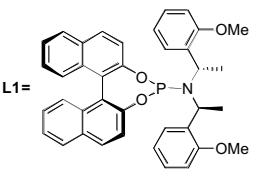
Xavier Rathgeb, Damien Polet, Alexandre Alexakis*

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

The allylic substitution is a fundamental reaction in organic chemistry. The reaction of carbon nucleophiles is usually catalyzed by a transition metal, and chiral ligands around this metal may allow the asymmetric version of this reaction. Iridium is well known to perform allylic substitution[1]. Using 2 mol% of $[Ir(CODCl]_2$, 4.4 mol% of chiral ligand and various nucleophiles, we are able to obtained on a large panel of substrates quantitative conversions and very high enantiomeric excesses for the γ products.




The best results were obtained with phosphoramidite ligands and especially with ligand L1 developed in our laboratory.




[1.] Polet, D.; Alexakis, A.; Tissot-Croset, K.; Corminboeuf, C.; Ditrich, K., *Chemistry--A European Journal* **2006,** 12, (13), 3596-3609.

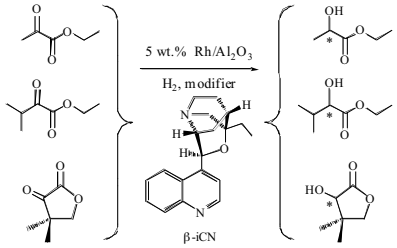
Organic Chemistry **257**

## Hydrogenation of α-ketoesters and ketopantolactone on rhodium modified by cinchona and isocinchona alkaloids

Fatos Hoxha, Tamas Mallat, Alfons Baiker *

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

Various Rh catalysts and cinchona type modifiers were tested in the hydrogenation of ethyl pyruvate, ethyl 3-methyl-2-oxobutyrate, and ketopantolactone. The experiments were completed with the study of the nonlinear behavior of modifier mixtures, and the UV and NMR analysis of the hydrogenation of the modifiers. From this study β-isocinchonine (β-iCN) emerged as an outstanding modifier of $Rh/Al_2O_3$ that gave up to 68% ee in the hydrogenation of ketopantolactone to (*R*)-pantolactone in toluene, at full conversion and without the formation of any detectable byproduct. In the weakly interacting solvent toluene only a few ppm of β-iCN related to ketopantolactone was sufficient to induce enantioselection. This unique feature of the conformationally rigid isocinchona alkaloid is attributed to the stronger adsorption on Rh and weaker adsorption on $Al_2O_3$, and to the higher resistance against hydrogenation of its quinoline ring "anchoring moiety", compared to the corresponding values of cinchonine and cinchonidine.




Organic Chemistry **258**

## New, Easily Accessible 1,2-Bisphosphinoferrocene Ligands for Asymmetric Hydrogenation

Björn Gschwend[a], Xiangdong Feng[b],
Felix Spindler[b], Martin Paas[b], Benoît Pugin[b]

[a]University of Basel, Department of Chemistry,
St. Johanns Ring 19, CH-4056 Basel, Bjoern.Gschwend@unibas.ch

[b]Solvias AG,
WRO-1055.631, PO-Box CH-4002 Basel, Benoit.Pugin@Solvias.com

In 2000 Kagan showed that chiral 1,2-bisphosphinoferrocenes provide active catalysts for the Rh-catalyzed hydrogenation, although most time with only moderate enantioselectivity.[1]

In our work on substituted Josiphos-ligands the lithiation next to a bromide-substituent published by Weissensteiner became a key step in the functionalisation of the ferrocene ring.[2] Applying this procedure, a multigram synthesis was developed to give access to structures which differ from the Kagan system only by the additional substituent next to one of the coordinating phosphine mojeties. These ligands gave very active and selective catalysts for the asymmetric hydrogenation using rhodium or iridium.


**Reagents and conditions: (a)** 1.) *s*BuLi, $Et_2O$, 0 °C, 1h, 2.) $(CF_2Br)_2$, -78 °C to rt, (91%); **(b)** 1.) LiTMP, THF, -40 °C, 3.5 h, 2.) $R_2PCl$, -78 °C, 2h, (59-95%); **(c)** 1.) *n*BuLi, TBME, 0 °C, 2h, 2.) $R'_2PCl$, -78 °C to rt, (37-74%).

[1] Argouarch, G.; Samuel, O.; Kagan, H., B., *Eur. J. Org. Chem.* **2000**, *16*, 2885.
[2] Streuer, M.; Tiedl, K.; Wang, Y.; Weissensteiner, W., *Chem. Comm.* **2005**, 4929.

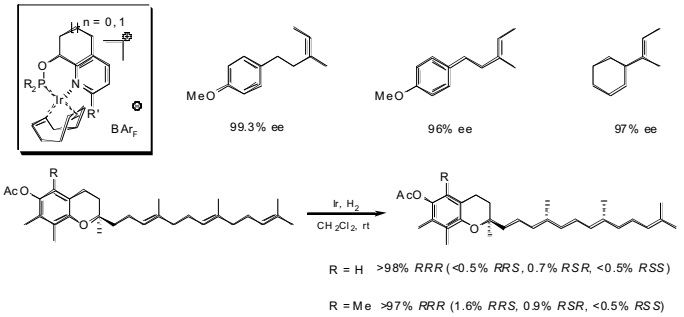
Organic Chemistry **259**

## Asymmetric Hydrogenation of Purely Unfunctionalized Trialkyl-Substituted Olefins

Aie Wang, Andreas Pfaltz*

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

Asymmetric hydrogenation of olefins is one of the most useful reactions for the synthesis of optically active compounds, especially in industry. However, the application range of the catalysts developed so far is limited to alkenes with a coordinating functional group or an aryl substituent next to the double bond. We have found a class of chiral iridium catalysts that give high enantioselectivity in the hydrogenation of unfunctionalized, trialkyl-substituted olefins [1]. Here we report the improved hydrogenation of these purely unfunctionalized trialkyl-substituted olefins under very mild conditions (0.5 mol% of catalyst, 5 bar of $H_2$). Hydrogenation of other pharmaceutically interesting substrates such as farnesol derivatives are ongoing.




[1] S. Bell, B. Wuestenberg, S. Kaiser, F. Menges, T. Netscher, A. Pfaltz, *Science,* **2006**, *311*, 642-644.

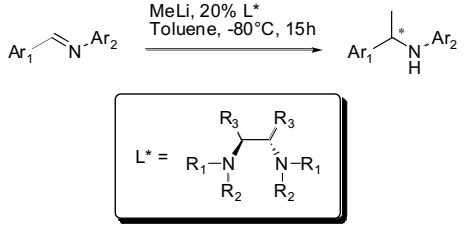
Organic Chemistry **260**

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

Quentin Perron and Alexandre Alexakis*

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

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




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

Organic Chemistry **261**

**Mass Spectrometric Screening of Chiral Catalysts**

Constanze A. Müller, Andreas Pfaltz*

Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland
Fax +41 61 267 1103, e-mail: andreas.pfaltz@unibas.ch

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

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

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

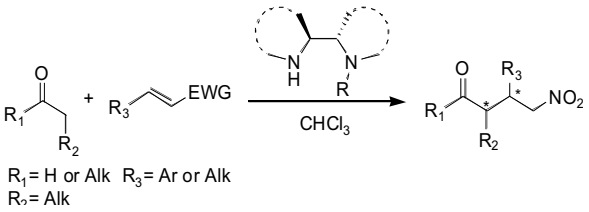
[1] C. Markert, A. Pfaltz, *Angew. Chem. Int. Ed.* **2004**, *43*, 2498.

Organic Chemistry **262**

**Organocatalysed Conjugate Addition**

S. Mossé, A. Alexakis*, S. Belot

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




Our group, specialized in $C_2$-symmetrical diamine and in conjugate addition, has recently developed their own organocatalysts for the enamine catalysis[1] (Among them the best one appeared to be the N-*i*Pr-2,2'-bipyrrolidine). They have been used for the conjugate addition of aldehydes or ketones on ß-nitro-olefines[2] and more recently with aldehydes on bis-vinyls sulfones.[3] Stereoselectivities for adducts are good to excellent in all cases.

[1] S. Mossé, A. Alexakis, *Chem. Comm.* **2007** Early View.
[2] O. Andrey, A. Alexakis, A. Tomassini, G. Bernardinelli, *Adv. Synth. Catal.* **2004**, *346*, 1147.
[3] S. Mossé, A. Alexakis, *Org. Lett.* **2005**, *7(20)*, 4361.

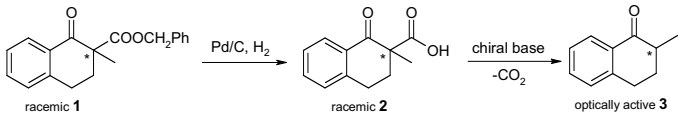
Organic Chemistry **263**

**Enantioselective decarboxylation of α-disubstituted benzyl β-ketoesters**

Pavel Kukula, Václav Matoušek, Tamas Mallat, Alfons Baiker

Institute for Chemical and Bioengineering, ETH Zurich, Hönggerberg, HCI, 8093 Zurich, Switzerland

The Pd-induced one-pot cascade reaction of racemic 2-methyl-2-benzyloxycarbonyl-1-tetralone **1** to the corresponding chiral 2-methyl-1-tetralone **3** was studied to clarify the reaction mechanism. The carboxylic acid intermediate **2** was synthesized and the kinetics of the debenzylation of **1** and the decarboxylation of **2** has been followed by NMR, UV, and IR. The studies revealed that deprotection of **1** occurs on the Pd surface, but the decarboxylation step is catalyzed homogeneously by the chiral amino alcohol. The enantioselective step is probably a kinetic resolution of the diastereomeric salt of racemic **2** and the chiral amino alcohol.




Organic Chemistry **264**

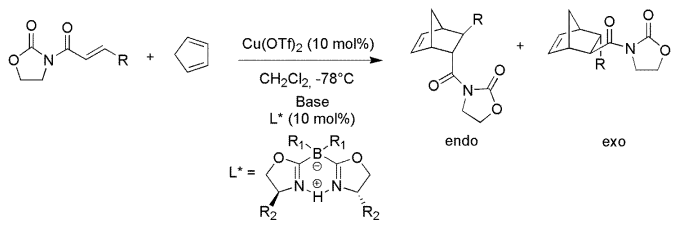
**BORON-BASED BISOXAZOLINES AND THEIR USE IN COPPER-CATALYZED ASYMMETRIC REACTION**

Aurélie Toussaint, Andreas Pfaltz*

Department of Organic chemistry, University of Basel
St. Johanns Ring 19, CH-4056 Basel, Switzerland
Fax: +41 / 61 / 267-1103, aurelie.toussaint@unibas.ch

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

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




[1] A. K. Ghosh, P. Mathivanan, J. Cappiello *Tetrahedron Asymmetry*, **1998**, *9*, 1-45.

[2] C. Mazet, V. Köhler, A. Pfaltz *Angew. Chem. Int. Ed.* **2005**, *44*, 4888-4891.

Organic Chemistry **265**

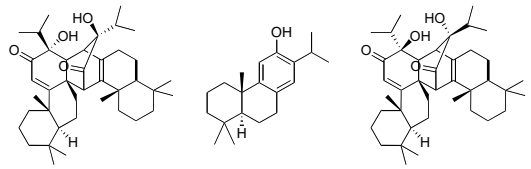
## Towards the Total Synthesis of the Heptacyclic Bisditerpenoid Maytenone and a Minor Constituent of Devil's Claw (*H. procumbens*)

Adrien K. Lawrence and Karl Gademann

Chemical Synthesis Laboratory, EPFL, 1015 Lausanne, Switzerland.

In 1961, Johnson *et al*. isolated maytenone (**1**), a heptacyclic bisditerpene from the root bark of the Australian tree *Maytenus dispermus*.[1] This natural product is thought to be formed by the oxidation of ferruginol (**2**) and dimerisation by a Diels-Alder reaction of the resulting α-hydroxycyclohexadienone. Over the last forty years, numerous attempts were tried in order to prepare this compound but all of them failed at the critical oxidation step.[2] In 2006, Jaroszewski and coworkers published a similar dimer (**3**) to maytenone but with opposite configuration at two centres. This compound was isolated from Devil's claw (*Harpagophytum procumbens*).[3]

We are currently pursuing synthetic studies on maytenone and have carried out promising model studies. Our goal is to unlock the mystery surrounding the oxidation step and access these compounds of complex architecture.



**1** **2** **3**

[1] A. W. Johnson, T. J. King, R. J. Martin, *J. Chem. Soc*. **1961**, 4420.
[2] C. P. Falshaw, A. W. Johnson, T. J. King, *J. Chem. Soc*. **1963**, 2422; *J. Chem. Soc*. **1967**, 2652; *J. Chem. Soc. Perkin Trans. I* **1984**, 95-100.
[3] C. Clarkson, D. Staerk, S. H. Hansen, P. J. Smith, J. W. Jaroszewski, *J. Nat. Prod*. **2006**, *69*, 1280-1288.

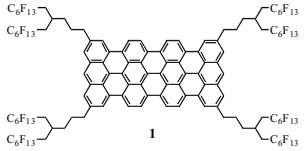
Organic Chemistry **266**

## New Polycondensed Aromatic Hydrocarbons for Supramolecular Self-assembly

Patrick Tondo, Titus A. Jenny*

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

Polycondensed aromatic hydrocarbons (PAHs) are known for their tendency to form conducting columnar assemblies, which could be used as molecular wires. Most of the work has been devoted so far to the study of hexa-*peri*-benzocoronene (HBC) [1]. As an alternative to the HBC's, a disk shaped highly symmetrical core structure, we are developing strategies for the synthesis of the so far unknown tetraanthryl core structure **1** surrounded by partially fluorinated branched aliphatic side chains. Preliminary calculations allow us to expect for this structure a further improved π-π stacking behavior as compared to the HBC's.



**1**

In the HBC series these side chains gave the best results in minimizing lateral interactions between columnar assemblies, maximizing the π-π stacking in the columnar axis, and simultaneously providing highest solubility of the molecules in appropriate solvents such as hexafluorobenzene. Due to the purification and sometimes synthetic difficulties associated with perfluorinated chains, the synthesis is first being optimized on building blocks bearing aliphatic chains.

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

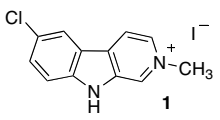
Organic Chemistry **267**

## New Bioactive Metabolites from Cyanobacteria

Cyril Portmann and Karl Gademann*

Chemical Synthesis Laboratory, EPFL,
1015 Lausanne, Switzerland

Cyanobacteria, also known as blue-green algae, are prokaryotic photosynthetic algae and they can be found in freshwater or marine environments. They are considered as a prolific source for new bioactive compounds [1]. Recently, we reported the isolation of nostocarboline **1** from *Nostoc* 78-12A as a cholinesterase inhibitor and also as a potent algicide [2] [3].



**1**

Our present efforts are concentrated on the optimization of the screening procedure for our cyanobacterial culture collection (>100 strains). The extracts are fractionated by HPLC in 96-well plate before being screened. The fractionation will reduce the time for the dereplication and the identification of new compounds, as well as reduce the number of false negative or false positive results [4]. By this procedure, interesting compounds with promising biological activity can be discovered.

[1] Review: Burja, A. M.; Banaigs, B.; Abou-Mansour, E.; Burgess, J. G.; Wright, P. C. *Tetrahedron* **2001**, *57*, 9347.
[2] Bercher, P. G.; Beuchat, J.; Gademann, K.; Jüttner, F. *J. Nat. Prod.* **2005**, *68*, 1793.
[3] Blom, J. F.; Brütsch, T.; Barbaras, D.; Bethuel, Y.; Locher, H. H.; Hubschwerlen, C.; Gademann, K. *Org. Lett.* **2005**, *8*, 737.
[4] Hostettmann, K.; Wolfender, J.-L.: Terreaux, C. *Pharm Biol.* **2001**, *39*, 18.

Organic Chemistry **268**

## Synthesis of Trioxatriangulene Derivatives

Fitore Kasumaj, Jay. S. Siegel

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

Trioxatriangulene is a rigid, bowl shaped molecule with a large surface area. Furthermore it is synthetically accessible and is used as a keystone for the synthesis of various structural entities. An important derivative of trioxatriangulene is 1, 5, 9-tribromotrioxatriangulene. It's synthesis was improved and X-Ray structures were obtained. This derivative will serve as a precursor for chiral catenanes. Possible applications of the resulting target molecules include host-guest interactions and surface chemistry.

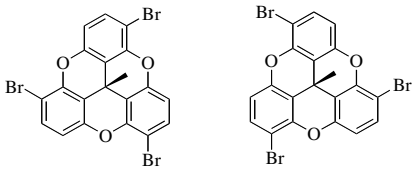


**Fig. 1**: Enatiomeres of 1, 5, 9- Tribromotrioxatriangulene

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

Organic Chemistry **269**

## Tunable Silyl Cationic Lewis Acids

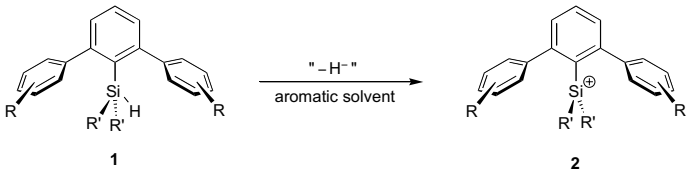
Simon Duttwyler, Paola Romanato, Kim Baldridge, Jay S. Siegel*

Organisch-chemisches Institut der Universitaet Zuerich, Winterthurerstrasse 190, CH-8057 Zuerich, Schweiz

Silylium ions $R_3Si^+$ are the period 3 analogues of carbenium ions. Their high reactivity towards almost all sources of electron density and halogen atoms makes it necessary to carefully choose reaction conditions and the counterion. It was only in 2002 when the the first free tri-coordinate $R_3Si^+$ system was synthesized.[1,2]

Our project deals with the preparation of a new class of silyl cations in which the partial positive charge on silicon can be tuned by structural modifications of the carbon skeleton. We chose **2** as our target cations, which can be made by hydride abstraction from the corresponding silanes **1**. In a series of cations **2** it was evidenced by $^{29}Si$ NMR spectroscopy that the silicon nucleus is more shielded with increasing electron donation ability of the flanking aryl rings and substituents R'.

NMR studies of molecules with different R and R' groups as well as the results of a reaction condition optimization will be presented.




**1** **2**

[1] J. B. Lambert, A. Zhao, S. M. Zhang, *J. Phys. Org. Chem.* **2001**, *14*, 370.
[2] K.-C. Kim, C. A. Reed, D. W. Elliot, L. J. Mueller, F. Tham, L. Lin, J. B. Lambert, *Science* **2002**, *297*, 825.

Organic Chemistry **270**

## Electrophilic Trifluoromethylation of Phenols

Kyrill Stanek, Raffael Koller, Antonio Togni

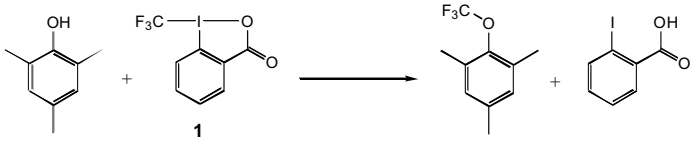
Department of Chemistry and Applied Biosciences, ETH Zurich.

Trifluoromethylated phenols play an important role in pharmaceutical and agrochemical products. The anticonvulsant Riluzole and the insecticide Triflumuron are examples of biologically active molecules bearing a trifluoromethoxy group.

Introduction of the $CF_3$ moiety by reacting the phenolate with a trifluorohalomethane was not successful up to now. Instead, harsh conditions and reagents such as HF, $SF_4$ or $SbF_5$ are needed at a very early stage of the synthesis. Clearly, a more versatile and fuctional group tolerant methodology is demanded.

We take advantage of our newly developed electrophilic, hypervalent iodine(III) trifluoromethylating agent **1**, which showed high selectivity and reactivity towards Sulfur nucleophiles[1], to transfer a $CF_3$ group onto a phenol.

First attempts gave the desired product in low yields, along with other interesting trifluoromethylated sideproducts.




**1**

[1] I. Kieltsch, P.Eisenberger, A.Togni, *Angew. Chem. Int. Ed.*, **2007**, 46, 754.

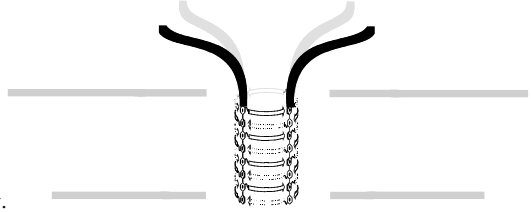
Organic Chemistry **271**

## Synthesis of Advanced Multifunctional Pores

Federico Mora, Santanu Maity, Hiroyuki Tanaka, Shinya Hagihara and Stefan Matile*[a]

University of Geneva, Departments of Organic Chemistry, Geneva, Switzerland

From diagnostics to drug discovery, the emerging potential of multifunctional pores as universal sensors for practical applications [1,2] invites for design and synthesis of advanced suprastructures with refined function. Recent attention shifted from internal multipoint ion pairing and external pore design [3] to internal π-clamping (sticky [4], slippery, fixed or floppy), "in-depth" molecular recognition [5] and, most recently, hydrophilic anchoring (Figure) as so far underrecognized approach to maximize



sensitivity.

[1] G. Das, P. Talukdar, S. Matile, *Science* **2002**, *298*, 1600-1602.
[2] S. Matile, H. Tanaka, S. Litvinchuk, *Analyte Sensing across Membranes with Artificial Pores*. In *Chemical Sensor Systems*, T. Schrader, Ed., *Top. Curr. Chem.*, in press.
[3] V. Gorteau, F. Perret, G. Bollot, J. Mareda, A. N. Lazar, A. W. Coleman, D.-H. Tran, N. Sakai, S. Matile, J. Am. Chem. Soc. **2004**, 126, 13592-13593.
[4] H. Tanaka, S. Litvinchuk, D.-H. Tran, G. Bollot, J. Mareda, N. Sakai, S. Matile, J. Am. Chem. Soc. **2006**, 128, 16000-16001.
[5] Y. Baudry, D. Pasini, M. Nishihara, N. Sakai, S. Matile, Chem. Commun. **2005**, 40, 4798-4800.

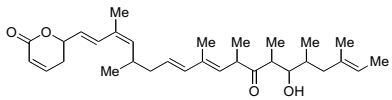
Organic Chemistry **272**

## Synthetic Studies on Anguinomycin C, a Tumor-Selective Polyketide

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

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

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




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

[1] (a) Y. Hayakawa, K.-Y. Sohda, K. Shin-Ya, T. Hidaka, H. Seto, *J. Antibiot.* **1995**, *48*, 954-961; (b) Y. Hayakawa, K. Adachi, N. Komeshima, *J. Antibiot.* **1987**, *40*, 1349-1352.
[2] Review: M. Kalesse, M. Christmann, *Synthesis* **2002**, *8*, 981-1003.

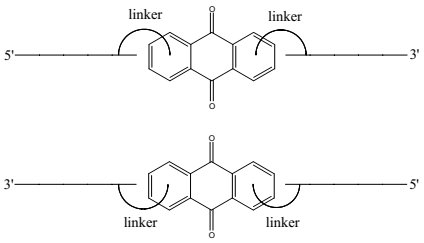
Organic Chemistry **273**

**Study of anthraquinones in DNA duplexes**

Nicolas Bouquin, Robert Häner.

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

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



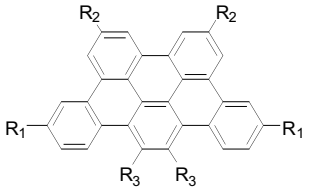

Organic Chemistry **274**

**Synthesis of tribenzo[*fg, ij, rst*]pentaphene derivatives as possible candidates for molecular electronics**

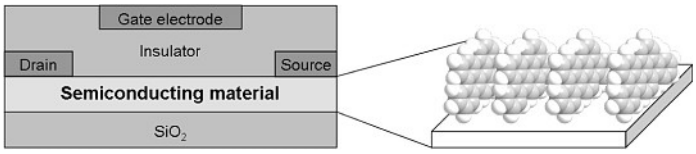
Mauro K. Schindler, Titus A. Jenny*

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

Organic semiconducting materials and molecular electronics are hot topics in material sciences. Possible candidates for these applications, such as field effect transistors (FET), are tribenzopentaphenes. Five tribenzopentaphene derivatives were synthesized using new straightforward strategies. The derivatives differ by the number and the position of the sidechains. So far the compounds have been investigated by $^{1}$H-NMR, $^{13}$C-NMR, UV and fluorescence spectra.




a) $R_1 = R_2 = R_3 = H$
b) $R_1 = C_8H_{17}$, $R_2 = R_3 = H$
c) $R_2 = C_8H_{17}$, $R_1 = R_3 = H$
d) $R_3 = C_8H_{17}$, $R_1 = R_2 = H$
e) $R_1 = R_2 = C_8H_{17}$, $R_3 = H$




The half-moon shape of the tribenzopentaphenes is ideal for edge-on stacking on flat surfaces, which orients the semiconducting stacks (c.f. insert) of the material in the desired direction.

Organic Chemistry **275**

**Helical arrangement of interstrand stacked pyrenes in a DNA framework**

Florent Samain,Vladimir Malinovskii, Robert Häner

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

A highly ordered structure observed with pyrene building blocks is reported. The system described herein represents the first example of an interstrand helical organization within an entirely artificial section embedded in a double stranded DNA.[1]
The construct is composed of achiral, non-nucleosidic pyrene building blocks (S), as illustrated in Figure1.

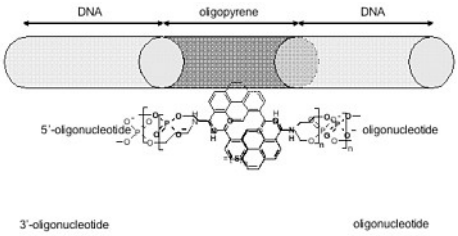



***Figure 1.*** Schematic representation of *oligopyrene-stacks* embedded in a DNA duplex.

[1] Vladimir Malinovskii, Florent Samain, Robert Häner *Angew. Chem.* **2007**, *accepted*

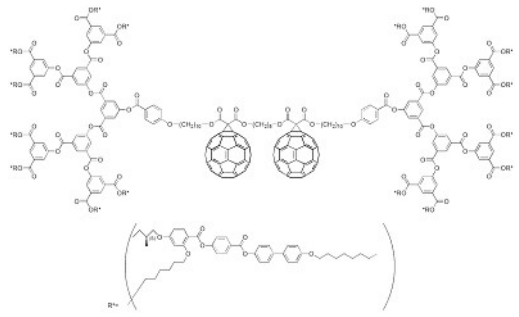
Organic Chemistry **276**

**Chiral Liquid-Crystalline Fullerodyads**

Sébastien Gottis and Robert Deschenaux*

Université de Neuchâtel, Institut de Chimie, Avenue de Bellevaux 51, Case postale 158, CH-2009 Neuchâtel, Switzerland.
*sebastien.gottis@unine.ch*

It was demonstrated that covalent functionalization of fullerene ($C_{60}$) with dendrimers prevented the formation of aggregates. The use of liquid-crystalline dendrimers allowed the design of thermotropic macromolecules with tailor-made mesomorphic properties.[1] Furthermore, the introduction of two $C_{60}$ units into liquid-crystalline materials is of interest with the aim to better our understanding of the "structure-supramolecular organization" relationship for this class of compounds, and could serve as a model for the subsequent construction of main-chain polymers.



Optically-active mesophases (our mesogen is chiral) open opportunities in the development of devices for optical-storage information.

[1] Chuard T., Deschenaux R., *J. Mater. Chem.* **2002**, *12*, 1944.

Organic Chemistry **277**

**Design and Synthesis of Oligoporphyrin Arrays with Exceptional Photophysical, Electronic, and Self-Assembly Properties**

Leslie-Anne Fendt, Fuyong Cheng, Hongjuan Fang, Davide Bonifazi and François Diederich

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

The photophysical, electrochemical, and self-assembly properties of two types of novel oligoporphyrin arrays comprising *meso,meso*-singly linked type and triply linked type porphyrins are investigated and compared with one another to look for trends within varied array lengths and different metal and free base combinations. Especially the triply fused, rigid, planar molecular porphyrin tapes exhibit unusually low HOMO-LUMO gaps and one-electron oxidation potentials, and may eventually serve as molecular wires within electronic devices[1,2]. Recently, triply fused porphyrin dimers have been covalently derivatized with two fullerene $C_{60}$ molecules (Fig. 1), resulting in a dyad structure capable of undergoing up to fifteen reversible electron transfer steps [3].

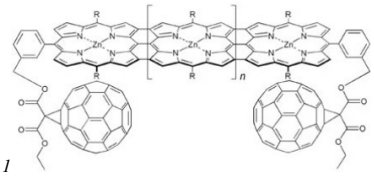


*Fig. 1*

[1] L. A. Fendt, H. Fang, S. Zhang, M. E. Plonska-Brzezinska, F. Cheng, L. Echegoyen, F. Diederich, *to be published*.
[2] F. Cheng, S. Zhang, A. Adronov, L. Echegoyen, F. Diederich, *Chem. Eur. J.* **2006**, *12*, 6062.
[3] D. Bonifazi, G. Accorsi, N. Armaroli, F. Song, A. Palkar, L. Echegoyen, M. Scholl, P. Seiler, B. Jaun, F. Diederich, *Helvetica Chimica Acta* **2005**, *88*, 1839.

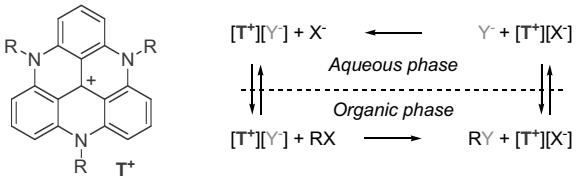
Organic Chemistry **278**

**Triazatriangulenium Salts: Exceptionally Stable Carbocations For Phase-Transfer Catalysis**

Cyril Nicolas, and Jérôme Lacour*

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

Since the pioneering work of Makosza almost forty years ago [1], phase transfer catalysis (PTC) has become a topic of great interest, as it provides many advantages, such as a simple reaction procedure, mild conditions, environmentally friendly reagents, absence of anhydrous or expensive aprotic solvents, ease of scale-up and (most often) metal free conditions.




All in all, PTC appears as a "green" alternative to many classical homogeneous reaction conditions. Many different catalysts have been used in the above mentioned context. However, carbenium ions have so far not been tested, due to their general reactivity with strong bases and nucleophiles. Recent reports have shown that exceptionally stable carbocations $\mathbf{T}^+$ ($pK_{R+}$ > 20) can be made by the simple reaction of primary alkyl amines with the readily available tris(2,6-dimethoxyphenyl)carbenium ion [2]. Herein, we report the first application of these very stable carbenium ions as phase-transfer catalysts in several classical organic reactions.

[1] Makosza. M, Serafin. B, *Rocz. Chem.* **1965**, *39*, 1223.
[2] Laursen. B. W, Krebs. F. C. *Chem. Eur. J.* **2001**, *7*, 1773.

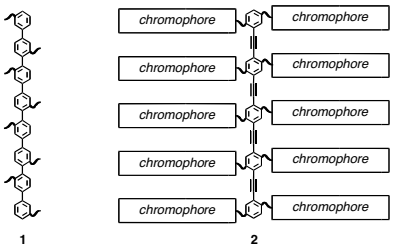
Organic Chemistry **279**

**Colorizing Rigid-Rod Scaffolds for Advanced Photoactive Nanoarchitecture**

Kishore Ravuri, Alejandro Perez-Velasco, Rajesh Bhosale, Naomi Sakai and Stefan Matile*

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

Recently, we have introduced rigid-rod π-stack nanoarchitecture with photosynthetic activity that can open up into into ion channels in response to chemical stimulation [1]. Rigid *p*-octiphenyl rods (**1**) were used in this study for strutural reasons only. To secure contributions of rigid-rod scaffolds also to function, we will describe synthetic efforts to replace the *p*-octiphenyls (**1**) by oligo(phenyleneethynylene)s (OPEs, **2**) and to facilitate the attachment of chromophores along the rigid-rod scaffolds. For photosynthesis in lipid bilayers and photovoltaics on conducting surfaces, the OPE scaffold is expected to contribute to high-energy light harvesting and to serve as semiconducting hole acceptor. These additional characteristics may afford nano-versions on n/p-heterojunctions, the most important part of solar cells.




[1] S. Bhosale, A. L. Sisson, P. Talukdar, A. Fürstenberg, N. Banerji, E. Vauthey, G. Bollot, J. Mareda, C. Röger, F. Würthner, N. Sakai, S. Matile, *Science* **2006**, *313*, 84-86.

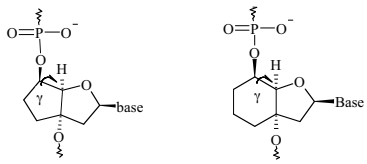
Organic Chemistry **280**

**Synthesis and properties of [4.3.0]-bicyclo-DNA oligonucleotides**

Andrea Stauffiger and Christian J. Leumann

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

In the last two decades, a variety of modified nucleosides have been developed to improve antisense oligodeoxynucleotide properties such as target affinity, nuclease resistance, and pharmacokinetics [1]. It is well established that conformational restriction leads to an enhancement in binding affinity and biostability due to an entropic advantage. In the context of conformational restriction our laboratory synthesized and characterized the analogue bicyclo-DNA (bc-DNA) [2]. In continuation of this work we now envisaged the synthesis of [4.3.0]-bicyclo-DNA. This novel analogue is expected to show improved geometry of the torsion angle γ compared to bc-DNA.
We present the synthesis of the DMT/phosphoramidite-protected thymidyl- and adenosyl-nucleosides starting from D-Glucose in 18 steps as well as their incorporation into oligonucleotides.




bicyclo-DNA (bc-DNA) [4.3.0]-bicyclo-DNA

[1] C.J. Leumann, *Bioorg. Med. Chem.* **2002**, *10*, 841-854.
[2] M. Tarköy, M. Bolli, B. Schweizer, C.J. Leumann, *Helv. Chim. Acta*, **1993**, *76*, 481-510.

doi:10.2533/chimia.2007.487 CHIMIA **2007**, *61*, No. 7/8

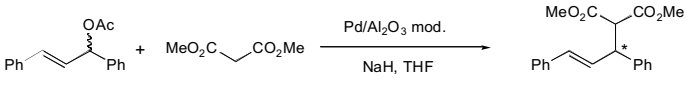
Organic Chemistry **281**

### Asymmetric allylic alkylation catalyzed by $Pd/Al_2O_3$ modified with chiral phosphines

Sven Reimann, Tamas Mallat, Alfons Baiker*

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

Soluble chiral Pd complexes afford excellent yields and enantioselectivities in asymmetric allylic alkylation reactions. Recently, the method has been extended to colloidal Pd modified by a chiral xylofuranoside diphosphite. This catalyst system affords up to 97% *ee* at medium conversions [1], and is one of the very few examples on highly enantioselective reactions on heterogeneous catalysts apart from the thoroughly investigated hydrogenation reactions. Here we report an extension of the method to other catalyst-modifier systems, using the same model reaction, the transformation of racemic **1** to **2**.




Allylic alkylation of **1** has been carried out on $Pd/Al_2O_3$ modified with various P-containing compounds such as (*S*,*S*)-chiraphos or (*R*)-BINAP. Several reaction parameters like the catalyst pretreatment, the reaction temperature and the concentrations of both the nucleophile and modifier have been studied. Under optimized reaction conditions high conversion and good chemo- and enantioselectivity were achieved at reasonably low catalyst/substrate and modifier/substrate ratios. Interestingly, the enantioselectivity of the homogeneous system with (*R*)-BINAP as ligand depends strongly on the reaction temperature, whereas the opposite holds for the heterogeneous system.

[1] S. Jansat, M. Gomez, K. Philippot, G. Muller, E. Guiu, C. Claver, S. Castillon, B. Chaudret, *J. Am. Chem. Soc.* **2004**, *126*, 1592.

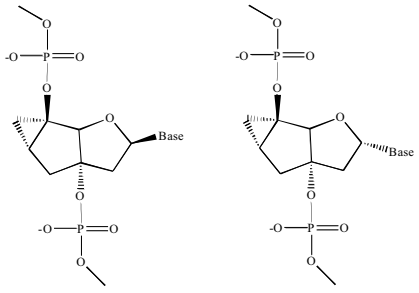
Organic Chemistry **282**

### Strand Invasion by α-tricyclo-DNA

Simon P. Scheidegger, Christian J. Leumann

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

β-tricyclo (tc) DNA is a third generation antisense oligonucleotide that has been extensively studied in our lab [1]. We recently became interested in the pairing properties of the α-anomeric form and observed parallel orientation in the duplexes with natural DNA and RNA complements [2]. Interrestingly, within its own backbone series α-tc-DNA exhibits poor thermal stability which makes it a candidate for strand invasion applications. We present recent results on the triplex forming and strand invasion properties of α-tc DNA.




β-tricyclo DNA α-tricyclo DNA

[1] D. Ittig, S. Liu, D. Renneberg, D. Schümperli, and C. J. Leumann, *Nucleic Acids Research*, **2004**, *32*, 346–353

[2] S. P. Scheidegger, C. J. Leumann, *Chem. Eur. J.,* **2006**, *12*, 8014-8023

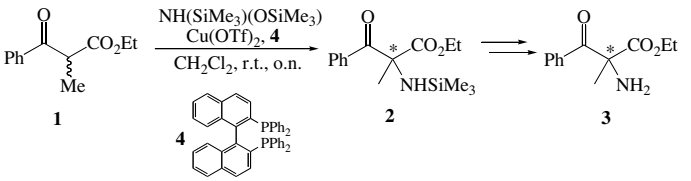
Organic Chemistry **283**

### Catalytic Electrophilic Amination of ß-Keto Ester

Aline Sondenecker, Antonio Togni*

Dept of Chemistry and Applied Biosciences, ETH Zürich, CH-8093 Zürich

Very few catalytic asymmetric syntheses of α-amino acid involving carbon-nitrogen bond forming reactions have been described in literature.[1] Our group recently reported an efficient electrophilic amination of ß-keto esters catalyzed by chiral copper(II)-bisoxazoline.[2] However, this method gives α-hydrazino ß-keto esters, which are difficult to convert to the desired amino acids.




We present now a new direct α-amination of ß-keto ester **1** catalyzed by a copper(II)-binap (**4**) complex with bis(trimethylsilyl)-hydroxylamine as the nitrogen source. The reaction gives ß-keto-ester **2**, which is a convenient precursor of the corresponding α-amino acid **3**. Our efforts are currently directed toward the optimization of the reaction conditions and the full characterization of the products.

[1] Marigo, M.; Juhl, K.; Jørgensen, K.A.; *Angew. Chem. Int. Ed.*, **2003**, *42*, 1367.

[2] Huber, D.P.; Stamek, K.; Togni, A., *Tetrahedron: Asym.*, **2006**, *17*, 658.

Organic Chemistry **284**

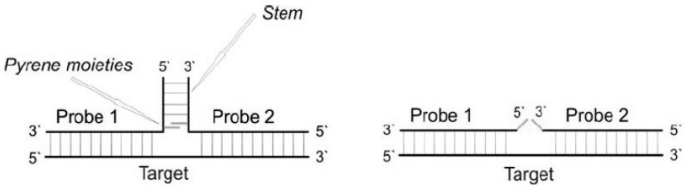
### A target assembled tandem oligonucleotide probe assay based on excimer formation

Daniel Wenger, Simon M. Langenegger, Robert Häner

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

The tetracyclic hydrocarbon pyrene is well known for its ability to form an excimer emission band and has been studied extensively as a reporter fluorophore[1]. This dual probe assay based on excimer formation of incorporated pyrene moieties with an additional stem is able to discriminate a single-base insertion much better than does the assay with the pyrene moieties terminally attached.

We have studied the use of non-nucleosidic pyrene building block in the context of a dual probe assay. Of particular interest was the discrimination of single base mismatches. The results will be presented.




[1] F.M. Mannik, *Chem. Revs.* **1993**, *93*, 587-614.