

# Heidelberg Forum of Molecular Catalysis

June 22, 2007

## Program & Poster session

Jointly organized by the University of Heidelberg, BASF Aktiengesellschaft  
and Sonderforschungsbereich 623 "Molekulare Katalysatoren"

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# Program

- 9 a.m.**                    **Opening**
- 9.30 a.m.**                **Prof. Dr. Dr. h.c. mult. Ryoji Noyori**  
Riken Institute of Physical and Chemical Research, Saitama and  
Department of Chemistry and Research Center for Materials Science,  
Nagoya University, Japan  
**“Asymmetric Catalysts: Structural and Functional  
Engineering”**
- 10.30 a.m.**                **Poster session**
- 11 a.m.**                    **BASF’s 2007 Catalysis Award ceremony**  
**Lecture by the prizewinner Prof. Dr. F. Dean Toste**  
University of California, Department of Chemistry,  
Berkeley, USA  
**“Gold(I) Catalysts for Organic Synthesis:  
Development, Applications and Asymmetric Catalysis”**
- 12.30 p.m.**                **Poster session**
- 4 p.m.**                    **Prof. Dr. Steven V. Ley**  
University of Cambridge, Department of Chemistry,  
Cambridge, England  
**“Development of New Catalysts and Methods for Organic  
Synthesis”**
- 5 p.m.**                    **Prof. Dr. Richard R. Schrock**  
Massachusetts Institute of Technology, Department of  
Chemistry, Cambridge, Massachusetts, USA  
**“Catalytic Reduction of Dinitrogen to Ammonia at Room  
Temperature and One Atmosphere with Protons and  
Electrons”**
- 6 p.m.**                    **Poster session/ social get-together and dinner**



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## **Lectures**



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## Asymmetric Catalysts: Structural and Functional Engineering

Ryoji Noyori

*RIKEN and Nagoya University, Japan*

Asymmetric catalysis lies outside the realm of traditional organic synthesis. It is a pervasive, global endeavor involving synthetic organic chemistry, catalytic chemistry, structural chemistry, inorganic and coordination chemistry, physical chemistry, and theoretical chemistry, as well as chemical engineering.

Asymmetric (transfer) hydrogenation uses inexpensive hydrogen gas or other organic hydrogen donors and a very small amount of a chiral catalyst, providing the most powerful way to produce a wide array of enantio-enriched compounds in a large quantity without forming hazardous wastes. Currently, efficient asymmetric catalysis primarily uses a molecular catalyst that consists of a metallic element and chiral organic ligand(s). Practical asymmetric catalysis requires a high turnover number and high turnover frequency, but the best way to generate high catalytic activity is not immediately apparent. High efficiency can be achieved only by a combination of both an ideal three-dimensional structure and suitable kinetics. The means of developing efficient asymmetric hydrogenations is discussed from a mechanistic point of view.

## Gold(I) Catalysts for Organic Synthesis: Development, Applications and Asymmetric Catalysis

F. Dean Toste

Department of Chemistry, University of California,  
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Berkeley, California, USA 94705

This lecture will focus on the use of cationic phosphinegold(I) complexes as catalysts for cycloisomerization, rearrangement, ring expansion and addition reactions.

The development of these reactions stemmed from the hypothesis that the strong relativistic effects governing the electronic structure of gold render it unique among the electrophilic late transition metals, and, specifically, that the 5d orbitals might be accessible for backbonding to stabilize cationic intermediates in the course of Au(I)-catalyzed reactions. Thus, a number of reactions which proceed by mechanisms in which gold(I) serves to activate  $\pi$ -bonds towards nucleophilic addition and in some cases to donate electron density back into an electron deficient  $\pi$ -system will be presented.

In addition, strategies towards developing gold(I) complexes for enantioselective catalysis will be presented. Most prominently the use of dinuclear bisphosphine digold(I) complexes as catalysts. The application of these complexes as catalysts for enantioselective olefin cyclopropanation, allene hydroamination, and cycloaddition reactions will be discussed.

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## Development of New Catalysts and Methods for Organic Synthesis

Steven V. Ley  
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The development of new catalytic systems is a key component of modern synthesis design. These systems need to be robust, cheap to operate and, where possible, very general in their application.

Recent work on catalyst encapsulation, mixed metal perovskites and the development of new organic catalysts will be presented together with their application in the context of flow chemistry.

See also:

<http://leygroup.ch.cam.ac.uk/>

Asymmetric Organocatalysis, S.V. Ley, in "Asymmetric Synthesis - The Essentials". M. Christmann and Ed. S. Bräse. Wiley-VCH. 2006 ISBN-978-3-527-31399-0

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ISBN: 0080445136

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## „Catalytic Reduction of Dinitrogen to Ammonia at Room Temperature and One Atmosphere with Protons and Electrons“

Richard R. Schrock

We have been able to reduce dinitrogen selectively and catalytically to ammonia at 1 atm and room temperature with protons and electrons. Reduction takes place at a single molybdenum center that is sterically protected against bimetallic decomposition reactions with *meta*-terphenyl-substituted triamidoamine ligands such as  $[(\text{HIPTNCH}_2\text{CH}_2)_3\text{N}]^{3-}$  where HIPT is hexaisopropyl-metaterphenyl. The proton source is  $(\{2,6\text{-lutidinium}\}\{\text{BAr}'_4\})$ ;  $\text{Ar}' = 3,5\text{-}(\text{CF}_3)_2\text{C}_6\text{H}_3$  and the reductant is decamethyl chromocene. The reducing equivalents make either ammonia (~60% from dinitrogen) or dihydrogen. All evidence suggests that  $\text{N}_2$  is being reduced at a single Mo center in which the oxidation state of the metal varies between Mo(III) and Mo(VI). Recent studies concern complexes that contain a variety of “Hybrid” ligands, in which only two HIPT groups are present in the ligand, with the third group being a sterically less demanding aryl. Attempts to reduce dinitrogen catalytically led to little or no ammonia being formed from dinitrogen. The cause is likely to be a rapid decomposition of intermediate  $[\text{Hybrid}]\text{Mo}=\text{N}-\text{NH}$  species, a decomposition that was shown to be accelerated dramatically by 2,6-lutidine, the conjugate base of the acid employed in the attempted catalytic reduction.  $[(\text{HIPTNCH}_2\text{CH}_2)_3\text{N}]^{3-}$  complexes of tungsten, chromium, and vanadium all failed to yield any catalytic turnover of dinitrogen to ammonia.

## **Abstracts**





## Reactivity of Zinc(II)-bound O- and S-Nucleophiles: Novel Insights into the Modes of Action of Zinc Enzymes

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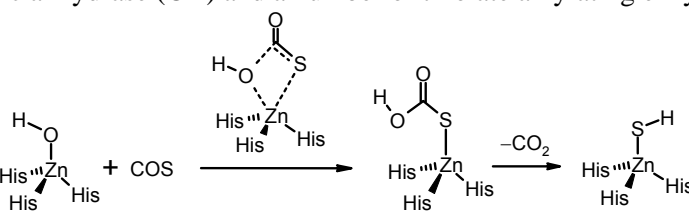
We recently investigated the reactivity of zinc-bound oxygen and sulfur bound nucleophiles towards a variety of heterocumulenes and other electrophilic substrates. This topic is of high interest within the scope of biomimetic chemistry, as it is closely related to the modes of action of a variety of different zinc(II) containing metalloenzymes, such as carbonic anhydrase (CA) and a number of thiolate alkylating enzymes.

The mechanism of the CA-mediated COS-fixation has been elucidated using density functional calculations (Figure 1).<sup>1a-c</sup> In the course of the reaction, which proceeds in close analogy to the catalytic path of CO<sub>2</sub> hydrolysis, a hydrosulfide analogue of the enzyme is formed. We also proposed a mechanism for the regeneration step which restores the zinc hydroxide moiety.<sup>1d</sup>

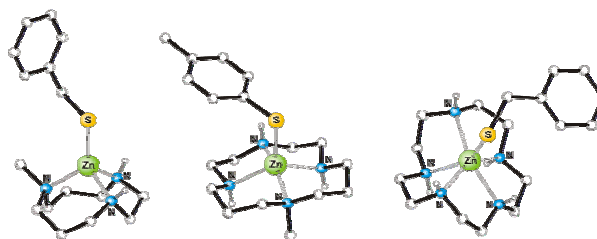
Recently, we synthesized a variety of zinc thiolate complexes with azamacrocyclic ligands (Figure 2).<sup>2a-d</sup> Their reactions with hetero-cumulenes (COS, CS<sub>2</sub>) proceed via four-centered transition states in mechanistic analogy to the CA-mediated CO<sub>2</sub> and COS fixation (Figure 3). Moreover, a similar mechanism is observed for the interconversion of the thiolates with methyl iodide (Figure 4), which serves as functional model for thiolate alkylating enzymes, e.g. methionine synthases, betaine-homocysteine methyl transferases etc.

From all these investigations we conclude that zinc-bound O- and S- nucleophiles (particularly hydroxide or thiolate) generally attack their substrates in the zinc-bound state, the reaction proceeding via a four-centered cyclic transition structure.

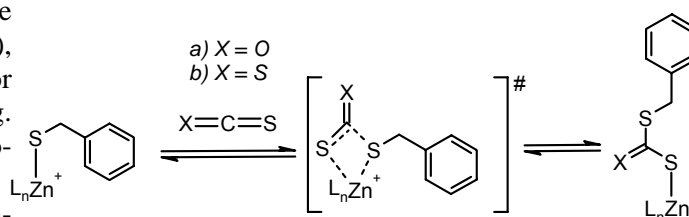
Applications in syntheses via novel metal mediated (catalytic) reaction principles are discussed.



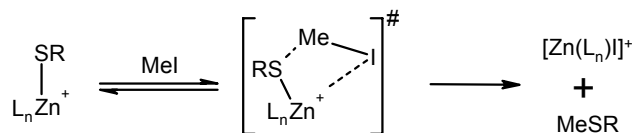
**Figure 1.** Fixation of COS by Carbonic Anhydrase



**Figure 2.** Zinc thiolate complexes with azamacrocyclic ligands



**Figure 3.** Reaction of a zinc thiolate complex with CS<sub>2</sub>



**Figure 4.** Reaction of a zinc thiolate complex with methyl iodide

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<sup>2a-d</sup> (a) J. Notni, E. Anders et al., *Eur. J. Inorg. Chem.* **2007**, 985; (b) **2006**, 1444; (c) **2006**, 2783; (d) S. Schenk, J. Notni, U. Köhn, K. Wermann, E. Anders, *Dalton Trans.* **2006**, 4191.



## “Small Molecule Activation & Functionalization with Uranium Coordination Complexes”



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The hexadentate tris-aryloxy triazacyclononane ligand,  $({}^t\text{BuArO})_3\text{tacn}^{3-}$ , and its sterically more demanding adamantyl derivative have provided access to trivalent coordination compounds of uranium,  $[({}^R\text{ArO})_3\text{tacn}]\text{U}^{\text{III}}$  ( $R = t\text{-Bu}, \text{Ad}$ ). These electron-rich precursor complexes display a pronounced reactivity toward small molecules of industrial and biological relevance. Reaction of diphenyldiazomethane,  $\text{Ph}_2\text{C}=\text{N}=\text{N}$ , with  $[({}^R\text{ArO})_3\text{tacn}]\text{U}^{\text{III}}$  resulted in two unique species highlighting key structural differences. The tert-butyl functionalized complex produced a U(IV) radical anion compound with the diazoalkane coordinated to the uranium in an  $\eta^2$  fashion,  $[({}^t\text{BuArO})_3\text{tacn}]\text{U}^{\text{IV}}(\eta^2\text{-NNCPh}_2)$ . The more bulky adamantane complex resulted in nitrogen insertion into an *sp* hybridized C-H bond to produce a 5-membered heterocyclic closed-shell indazole complex,  $[({}^{\text{Ad}}\text{ArO})_3\text{tacn}]\text{U}^{\text{IV}}(1,2\text{-}\eta^2\text{-3-phen(Ind)})$ .

The coordination chemistry of both U(III) complexes was studied with small nitrogen-containing molecules as potential catalytic intermediates for actinide mediated hydroamination. Addition of neutral amines, such as tert-butyl amine, produced uranium(III) amine complexes,  $[({}^R\text{ArO})_3\text{tacn}]\text{U}^{\text{III}}(\text{NH}_2{}^t\text{Bu})$ , which have unusual bent geometries. Both, pyridine and 2-aminopyridine, furnished uranium(III) pyridine adducts,  $[({}^R\text{ArO})_3\text{tacn}]\text{U}^{\text{III}}(\text{C}_5\text{H}_4\text{NR})$  ( $R = \text{H}, \text{NH}_2$ ). Allowing the 2-aminopyridine product to react further at room temperature produced the U(IV) amide complex via N-H activation. This process is more facile in the case of phenylhydrazine, which forms a U(III) amine adduct followed by immediate N-H activation of the more acidic hydrogen to produce the amide complex,  $[({}^R\text{ArO})_3\text{tacn}]\text{U}^{\text{IV}}(\text{NPhNH}_2)$  and  $\text{H}_2$ . Further reactivity of these molecules as well as those of U(V) and U(VI) imido complexes will be discussed.

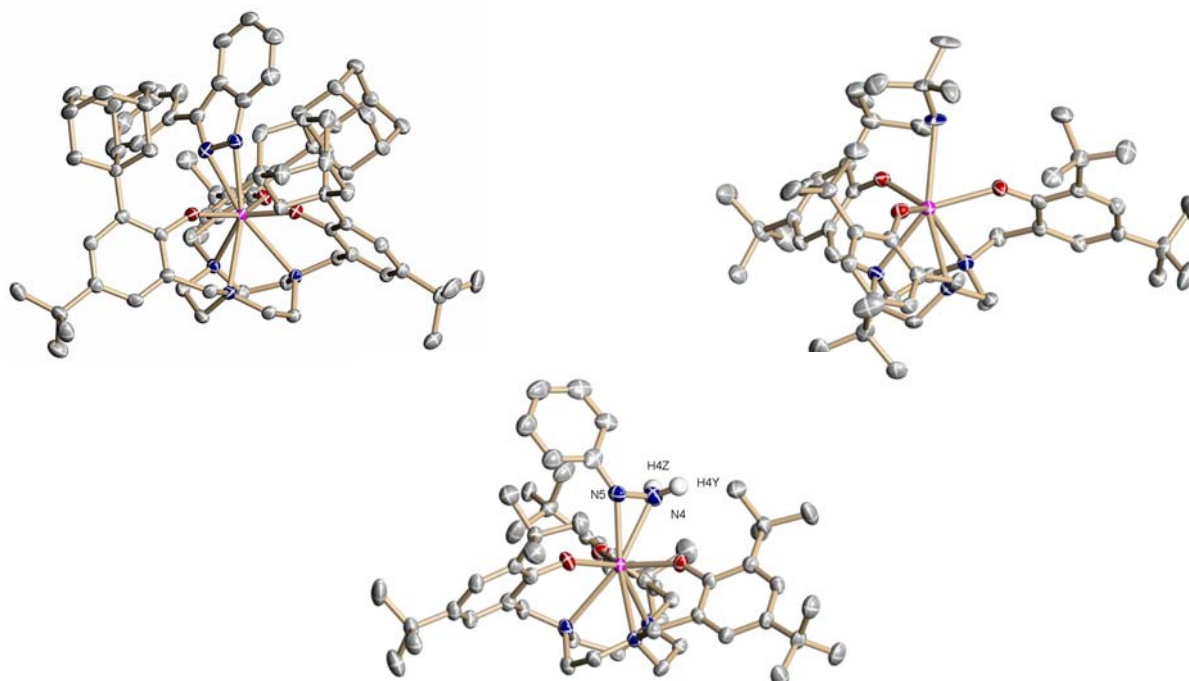


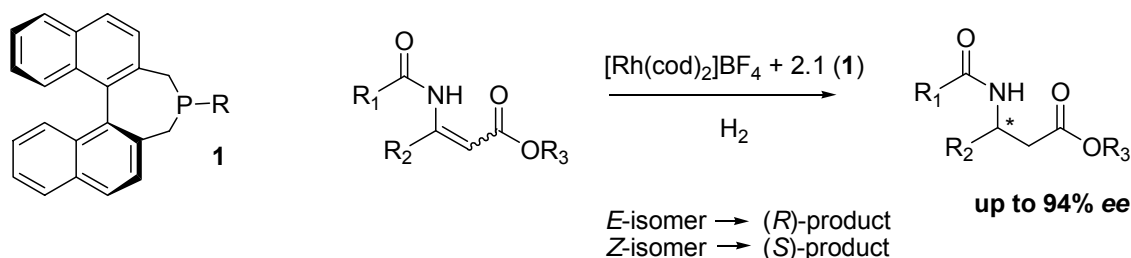
Figure 1. Molecular Structure of  $[({}^{\text{Ad}}\text{ArO})_3\text{tacn}]\text{U}(1,2\text{-}\eta^2\text{-3-phen(Ind)})$  (top left),  $[({}^t\text{BuArO})_3\text{tacn}]\text{U}(\text{NH}_2{}^t\text{Bu})$  (top right), and  $[({}^t\text{BuArO})_3\text{tacn}]\text{U}(\text{NPhNH}_2)$  (center).

## Rhodium Phosphine Catalysts for the Hydrogenation of $\beta$ -Dehydroamino Acid Derivatives

Stephan Enthaler<sup>[a]</sup>, Giulia Erre<sup>[a]</sup>, Kathrin Junge<sup>[a]</sup>, Jens Holz<sup>[a]</sup>, Armin Börner<sup>[a]</sup>, Elisabetta Alberico<sup>[b]</sup>, Ilenia Nieddu<sup>[c]</sup>, Serafino Gladiali<sup>\*[c]</sup>, and Matthias Beller<sup>\*[a]</sup>

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The discovery of new effective drugs is an important challenge for industrial and academic research. More recently, significant attention was directed to non-natural  $\beta$ -amino acids, which are interesting building blocks for the synthesis of biologically active compounds. In view of the growing demand of chiral  $\beta$ -amino acids an increasing number of synthetic methods have been established for their preparation. Within these methodologies, asymmetric catalytic hydrogenation constitutes the most attractive and versatile technology among industrial applications due to its remarkable improvements achieved in the last few years. Good to excellent enantioselectivities have been obtained in this reaction applying rhodium-catalysts with chiral diphosphines. However, a current trend in asymmetric catalysis is to switch from chiral bidentate to chiral monodentate phosphines because the latter ones are more easily accessible and tuneable than the bidentate counterparts. In this regard we demonstrated the usefulness of monodentate phosphine ligands based on the 4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1',2'-*e*]phosphepine scaffold **1** in several asymmetric hydrogenations of C–C double bonds with enantioselectivities up to 96% *ee*.<sup>[1],[2]</sup> With respect to the reduction of  $\beta$ -dehydroamino acids derivatives no detailed study has been reported on the influence of monodentate phosphines. Herein we wish to report our recent results in the asymmetric hydrogenation of challenging  $\beta$ -dehydroamino acids derivatives using rhodium catalysts containing ligand class **1**.<sup>[3]</sup> Excellent conversions and enantioselectivities up to 94% *ee* have been obtained after optimization of reaction conditions. Significant influences on enantioselectivity were caused by solvent, temperature, pressure, variation of the ligand and different substitutions on the substrate structure. Noteworthy, contradictory performance was obtained for the *E*- and *Z*-isomer and different reaction conditions were necessary to achieve best enantioselectivity. In addition a switch of product configuration was observed depending on the nature of the double bond (*E*- and *Z*-isomers), which has been scarcely reported before.



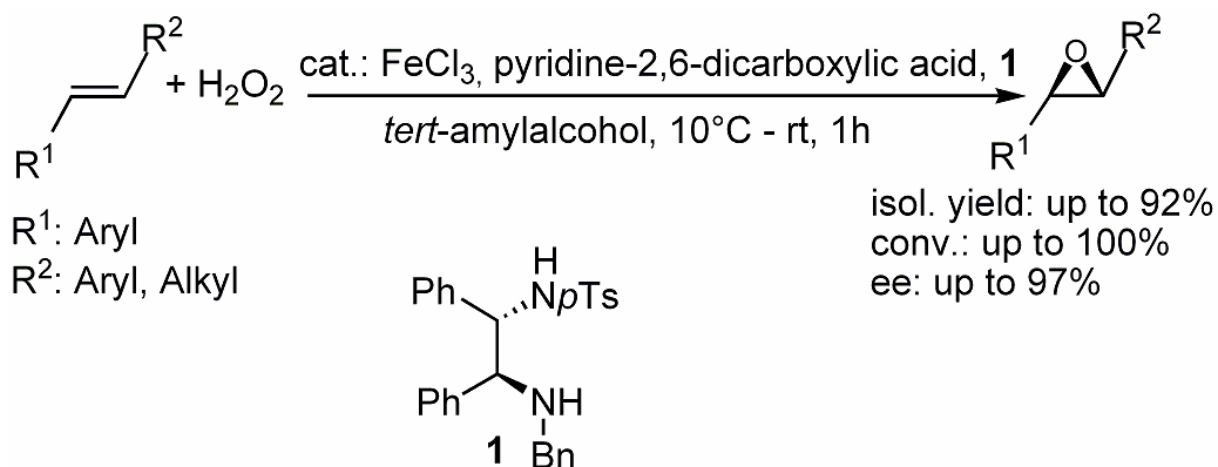
**Scheme 1.** Asymmetric hydrogenation of  $\beta$ -dehydroamino acid derivatives.

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## Asymmetric epoxidation of aromatic alkenes using hydrogen peroxide in the presence of an iron catalyst and novel chiral diamine ligands

Feyissa Gadissa Gelalcha, Anilkumar Gopinathan, Bianca Bitterlich, Man Kin Tse, Matthias Beller, E-Mail: Matthias.Beller@catalysis.de, Leibniz-Institut für Katalyse an der Universität Rostock, e. V. Albert Einstein Str. 29a, D-18059 Rostock, Germany.

A general epoxidation of aromatic alkenes with hydrogen peroxide using a convenient in situ catalyst consisting of ferric chloride hexahydrate ( $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ ), pyridine-2,6-dicarboxylic acid, and organic bases at room temperature has been described by us recently.<sup>1</sup> In this presentation we report the asymmetric version of this reaction which represents the first promising non-heme iron-catalyzed asymmetric epoxidation of aromatic alkenes using hydrogen peroxide and important factors that affect the selectivity as well as preliminary mechanistic studies. The reaction not only gives good to excellent isolated yields of epoxides but also enantioselectivities up to 97% within 1hr. The key to this success are the use of novel chiral *N-p*-toluenesulfonyl-*N'*-benzylsubstituted ethylenediamine ligands such as **1**.<sup>2</sup>



<sup>1</sup> Anilkumar, G.; Bitterlich, B.; Gelalcha, F. G.; Tse, M.-K.; Beller, M. *Chem. Commun.*, **2007**, 289; Bitterlich, B.; Anilkumar, G.; Gelalcha, F. G.; Spilker, B.; Grotevendt, A.; Jackstell, R.; M.- K. Tse, Beller, M. *Chem. Asian J.* 2007, 2, 521.

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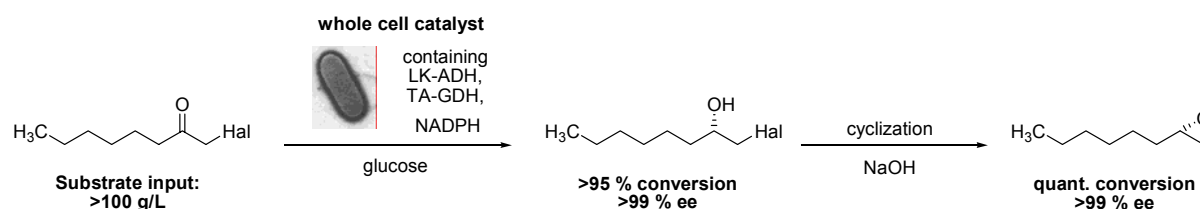
## Practical Aliphatic Terminal (*S*)-Epoxide Synthesis Based on Reduction with a Whole Cell-Biocatalysts as the Key Step

Albrecht Berkessel<sup>a</sup>, Claudia Rollmann<sup>b</sup>, Françoise Chamouleau<sup>b</sup>, Stefanie Labs<sup>a</sup>,  
Oliver May<sup>b</sup>, Harald Gröger<sup>b,c</sup>

<sup>a</sup>Institute of Organic Chemistry, University of Cologne, Greinstraße 4, 50939 Cologne, Germany; <sup>b</sup>Degussa AG, Service Center Biocatalysis, P.O. Box 1345, 63403 Hanau, Germany; <sup>c</sup>Institute of Organic Chemistry, University of Erlangen-Nuremberg, Henkestr. 42, 91054 Erlangen

Enantiomerically pure terminal (*S*)-epoxides are important chiral building blocks, widely used e.g. as intermediates in the synthesis of pharmaceuticals.<sup>1</sup> Whereas numerous asymmetric transformations comprising chemocatalytic<sup>2</sup> and biocatalytic<sup>3</sup> techniques have been developed for the enantioselective synthesis of aromatic terminal epoxides, there is still comparatively little methodology available for the preparation of enantiomerically pure aliphatic terminal epoxides.

A practical biocatalytic method for the synthesis of aliphatic  $\beta$ -halogenated (*S*)-alcohols as epoxide precursors by means of an enantioselective reduction of the corresponding ketones with recombinant whole cells, bearing an alcohol dehydrogenase and a glucose dehydrogenase, was developed. The biotransformations operate at high substrate concentrations of up to 208 g/L, and afford the (*S*)- $\beta$ -halohydrins with both high conversions of >95 % and enantioselectivities of >99 % ee. Base-induced cyclization of the  $\beta$ -halohydrin intermediates gave the desired (*S*)-epoxides in high yield and enantiomeric purity (>99 % ee) (see Scheme).



**Scheme:** Practical aliphatic terminal (*S*)-epoxide synthesis

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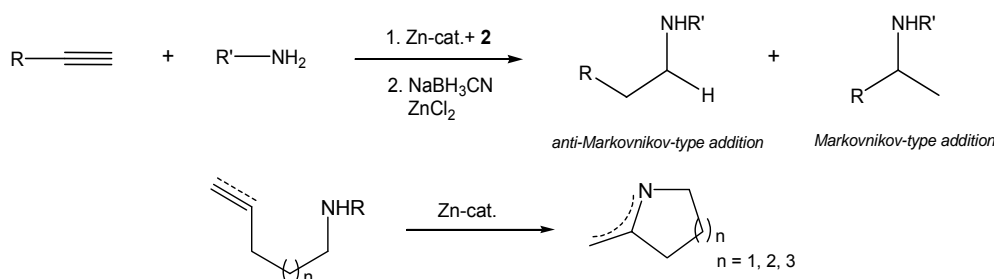
# Zinc-catalyzed Intermolecular Hydroamination and New Homogeneous Zinc-Catalysts for the Hydroamination of Non-activated Olefins

Jens-Wolfgang Pissarek, Maximilian Dochnahl and Siegfried Blechert

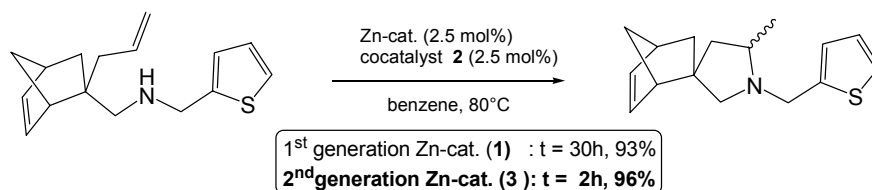
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D-10623 Berlin, Germany, [blechert@chem.tu-berlin.de](mailto:blechert@chem.tu-berlin.de)

Amines are often made in multi-step syntheses and therefore hydroamination offers an attractive alternative to yield nitrogen-containing molecules that are important for fine chemicals, pharmaceuticals as well as chiral building blocks. The catalyzed addition of an organic amine N-H bond to alkenes or alkynes (hydroamination) to furnish nitrogen containing molecules is of great interest for academic and industrial researchers<sup>[1]</sup>. We have developed *N*-isopropyl-2-(isopropylamino)troponimate zinc methyl,  $[(iPr)_2ATI]Zn-Me$  (**1**), as a new catalyst for the homogenous intramolecular hydroamination reaction<sup>[2]</sup>. Further investigations showed its applicability in the intermolecular hydroamination reaction with the addition of  $[PhNHMe_2][B(C_6F_5)_4]$  (**2**).



In order to improve the catalytic system different modifications on the aminotroponimate were tested. The variation of the N-substitution delivered a tremendous effect on the reaction rates towards the intramolecular hydroamination and so we were able to introduce  $[(Cy)_2ATI]Zn-Me$  as a new, even more reactive catalyst (**3**)<sup>[3]</sup>.



Beside sterical modifications we set our attention on the influence of acceptors and donors attached to the ATI's seven-membered ring. Furthermore these different substitutions leading to enormous differences in reactivity are currently under investigation.

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<sup>[2]</sup> A. Zulys, M. Dochnahl, D. Hollmann, K. Löhnwitz, J.-S. Herrmann, P. W. Roesky, S. Blechert, *Angew. Chem. Int Ed.* **2005**, 44, 7794-7798

<sup>[3]</sup> M. Dochnahl, J.-W. Pissarek, S. Blechert, K. Löhnwitz, P. W. Roesky, *Chem. Commun.* **2006**, 3405-3407

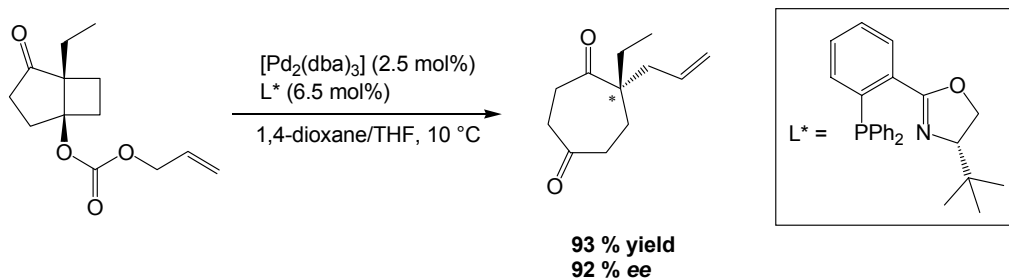
## Asymmetric Ring-Expanding Allylation (AREA): A new Approach to Substituted Carbocyclic 1,4-Diketones

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Oxygenated seven-membered carbocycles are a common motif in many natural products. These molecules are of potential interest as they display interesting biological and pharmaceutical properties.<sup>[1]</sup> Thus, much effort has been made especially towards their asymmetric synthesis.<sup>[2]</sup>

Recently, the asymmetric transition metal catalyzed decarboxylative allylation of ketone- or  $\beta$ -ketoester-derived enolates has provided an extremely valuable tool for the construction of stereocenters adjacent to carbonyl groups.<sup>[3]</sup> During the course of the *de Mayo* reaction a ketone enolate is formed which is normally protonated.<sup>[4]</sup> We planed to intercept this reaction by trapping the enolate with a chiral  $\pi$ -allyl palladium complex, to give enantioenriched 5-allylated cycloheptane-1,4-diones. In particular we wished to target allylated cycloheptanediones bearing quaternary stereocenters.



Following this concept we have developed an asymmetric decarboxylative ring-expanding allylation.<sup>[5]</sup> This method allows for the first time a preparation of enantioenriched substituted cycloheptane-1,4-diones and cyclooctane-1,5-diones. The latter compounds are valuable intermediates for the synthesis of functionalized medium-sized carbocycles which can be further elaborated to important natural product classes.

The reaction was demonstrated to proceed under mild conditions in high yield and with reasonable to very good enantiomeric excesses. Diketones with both tertiary and quaternary stereocenters were accessible and the reaction was shown to have a broad substrate spectrum.

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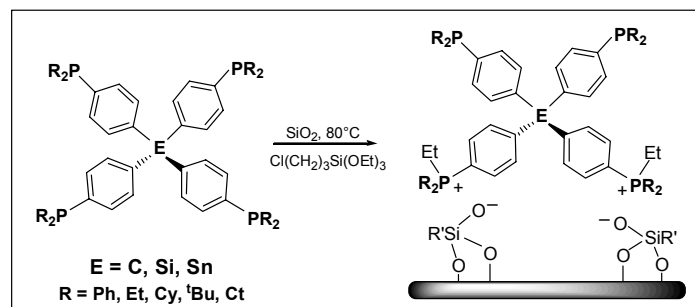
## Scaffolds of Di- and Tetraphosphine Linkers that Diminish Interactions of Immobilized Catalysts with Oxide Supports

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Phosphines bound to oxide surfaces are important as linkers for immobilizing catalysts, or as scavengers for metal complexes after catalysis. The success is always crucially dependent on the nature of the phosphine. For prolonging the lifetime of immobilized catalysts, the primary goal is to prevent any contact of the metal center with the aggressive oxide surface.



Phosphines with a rigid backbone, such as the tetraphenylelement scaffold shown above, prevent any metal/surface contact mechanically in an ideal way. Unfortunately, we could not attach two or three  $(EtO)_3Si$  groups to the molecule selectively.

However, based on our previous finding [1] that phosphines can also be attached to silica as ethylphosphonium salts by treating them with ethoxysilanes at higher temperatures, we could cleanly and irreversibly immobilize the phosphines in the shown way. With the help of  $^{29}Si$ ,  $^{31}P$ , and  $^{119}Sn$  CP/MAS NMR we could also prove that in the presence of an excess of ethoxysilane all the tetraphosphines are bound with two "ionic feet" to the support, and not by one or three. This way, two monodentate phosphine groups per linker molecule remain for binding two metal complexes [2].

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E-mail: bluemel@tamu.edu

## THE IMMOBILIZED SONOGASHIRA CATALYST SYSTEM: A CP/MAS AND HRMAS NMR STUDY

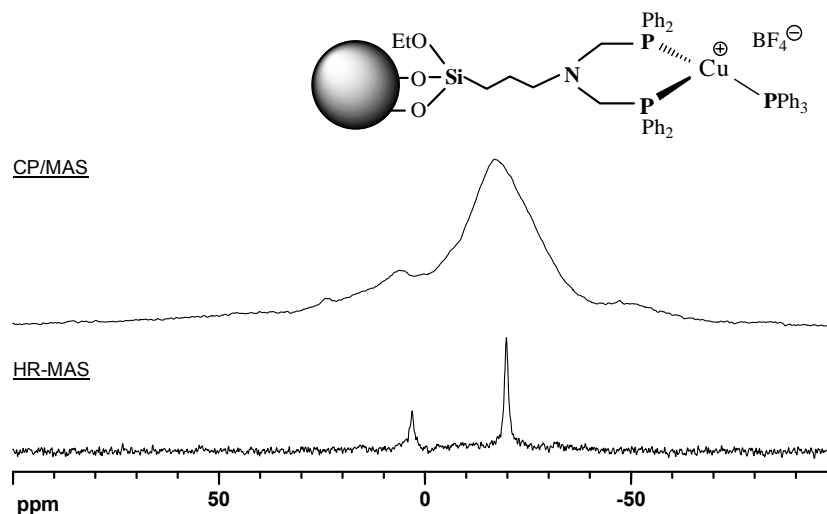
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Palladium and its complexes represent one of the most important groups of catalysts for organic reactions, especially in connection with Cu salts. However, the immobilized versions of the Pd(0)/Cu(I) Sonogashira catalyst system for cross-coupling reactions are still not very well understood.

Here, we will demonstrate that both, classical <sup>31</sup>P, <sup>13</sup>C, and <sup>29</sup>Si CP/MAS, as well as one- and two-dimensional HRMAS NMR can provide new and important insights into the reaction processes and dynamics on surfaces [1]. For binding the metal complexes to the support we use chelate phosphines incorporating ethoxysilane functions, such as the one shown below.



The spectra above (top: <sup>31</sup>P CP/MAS, bottom: <sup>31</sup>P HRMAS) also demonstrate that HRMAS gives narrower lines and allows the characterization of all surface species. The catalytic activity of the immobilized Sonogashira catalysts was checked, and we could obtain many interesting and crucial results that will be presented and interpreted [2].

[1] T. Posset, J. Blümel, *J. Am. Chem. Soc.* **2006**, *128*, 8394-8395.

[2] T. Posset, T. Oeser, J. Blümel, *Organometallics* **2007**, in preparation.

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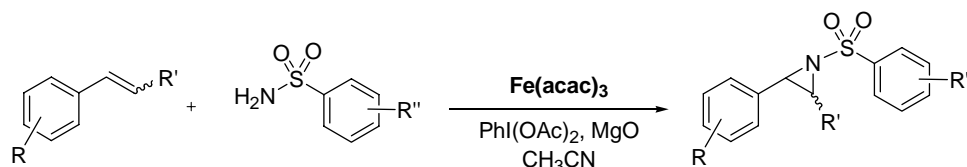
## Iron-Catalysed Nitrene Transfer Reactions: Aziridination of Styrene and Styrene Derivatives

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Aziridines are important building blocks in organic synthesis.<sup>[1]</sup> Among other synthetic approaches like the addition of imines to carbenes,<sup>[2]</sup> the heterocyclic moiety can be efficiently established using the transition metal catalysed nitrene transfer to olefins.<sup>[3]</sup> The best results reported to date were obtained with copper and rhodium complexes.<sup>[4]</sup> Despite the impressive application profile of these methodologies, there is a need for cheap and non-toxic catalysts that are readily available and show similar efficiency. Given the fact that many iron salts meet these requirements,<sup>[5]</sup> we were pleased to find that commercially available Fe(acac)<sub>3</sub> catalyses the aziridination of styrene and styrene derivatives (Scheme).



There are two distinct advantages of this newly developed method. First, the olefin can be used in as little as twofold excess over the nitrene source. Second, the tedious preparation of the iminoiodinane is circumvented as it is formed *in situ* from sulfonamide and PhI(OAc)<sub>2</sub>. The substrate scope of this method as well as the applicability of different acac-type iron complexes will be presented.

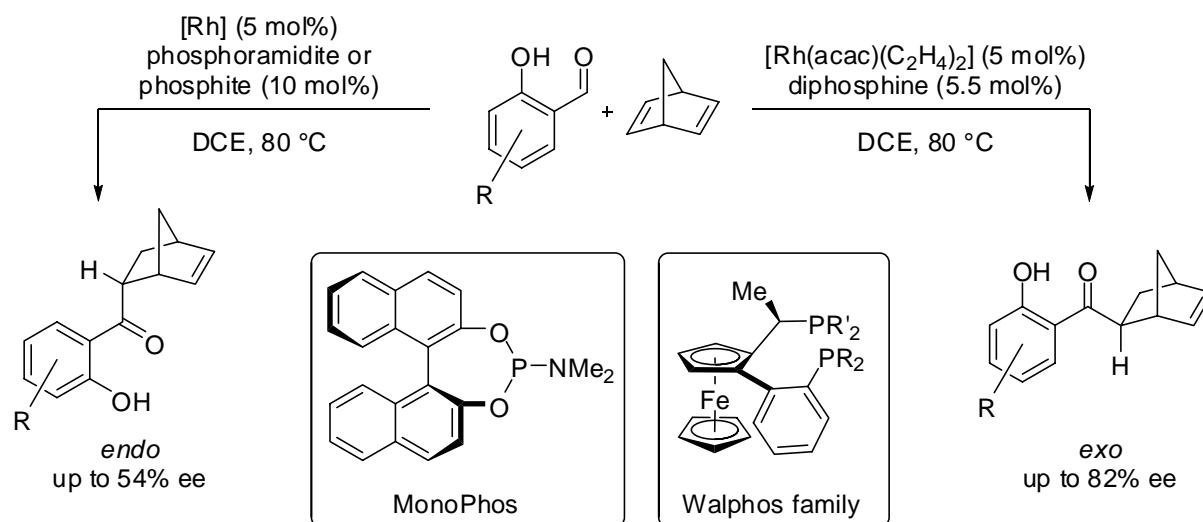
- 1 Reviews: (a) Tanner, D. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 599. (b) Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247.
- 2 (a) Hansen, K. B.; Finney, N. S.; Jacobsen, E. N. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 676. (b) Wulff, W. D.; Antilla, J. C. *J. Am. Chem. Soc.* **1999**, *121*, 5099.
- 3 Halfen, J. A. *Curr. Org. Chem.* **2005**, *9*, 657.
- 4 (a) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742. (b) Müller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905, and references cited therein. (c) Du Bois, J.; Guthikonda, K. *J. Am. Chem. Soc.* **2002**, *124*, 13672.
- 5 For a review on iron-catalysed reactions in organic synthesis, see: Bolm, C.; Legros, J.; Le Pailh, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217.

# An Unprecedented Rhodium-Catalyzed Asymmetric Intermolecular Hydroacylation with Salicylaldehydes

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The development of transition-metal catalysts for carbon-carbon bond forming reactions via the C–H bond activation strategy still remains a significant challenge.<sup>1</sup> The rhodium-catalyzed hydroacylation furnishes ketones from olefins and aldehydes in a highly atom-economic reaction. The *intermolecular* reaction has been studied much less than its *intramolecular* counterpart.<sup>2</sup> Due to the competitive rhodium-catalyzed decarbonylation, chelation-assisted intermolecular reactions have been developed almost exclusively. Herein we report the first asymmetric intermolecular hydroacylation of norbornenes with salicylaldehydes. After the screening of several catalyst systems it was found that monodentate phosphoramidite or phosphite ligands give rise to *endo* products while bidentate phosphine ligands catalyze the reaction to form *exo* products predominantly. The corresponding ketones were isolated in high yields with up to 54% and 82% ee, respectively.<sup>3</sup>



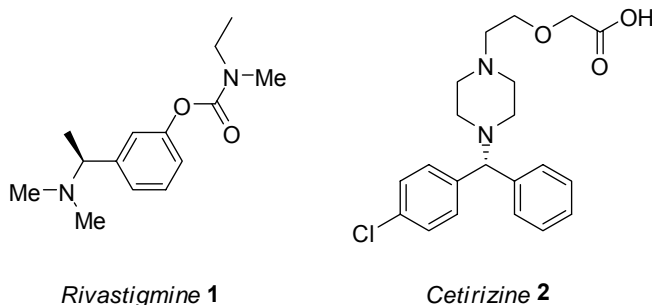
- (1) (a) *Handbook of C-H Transformations: Applications in Organic Synthesis* (Ed.: G. Dyker), Wiley-VCH, Weinheim, **2005**; (b) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev.* **2002**, *102*, 1731–1769; (c) F. Kakiuchi, S. Murai, *Acc. Chem. Res.* **2002**, *35*, 826–834; (d) J. A. Labinger, J. E. Bercaw, *Nature* **2002**, *417*, 507–514; (e) G. Dyker, *Angew. Chem.* **1999**, *111*, 1808–1822; *Angew. Chem. Int. Ed.* **1999**, *38*, 1699–1713. (f) F. Kakiuchi, S. Murai, in *Activation of Unreactive Bonds and Organic Synthesis* (Ed.: S. Murai), Springer, Berlin, **1999**, pp 47–79.
- (2) For a recent review on intermolecular hydroacylation reactions see: C.-H. Jun, E.-A. Jo, J.-W. Park, *Eur. J. Org. Chem.* **2007**, 1869–1881.
- (3) R. T. Stemmler, C. Bolm, *Adv. Synth. Catal.* **2007**, *345*, in press.

## *Synthesis of $\alpha$ -branched Amines by 1,2-Addition of Organoaluminium Reagents on Ketimines*

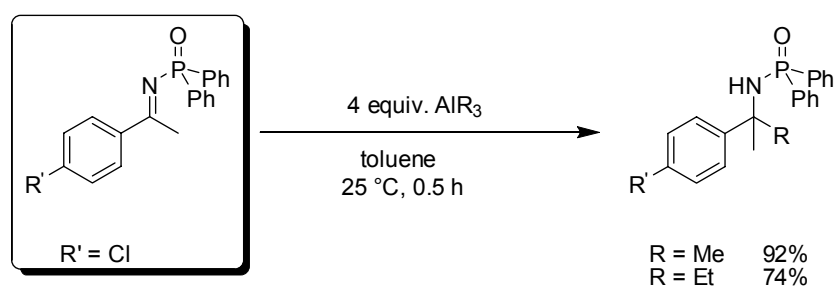
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Abstract: Due to their interesting properties the synthesis of  $\alpha$ -branched amines is a highly attractive field, as these compounds inhibit particular biological activity as for example the anti-Alzheimer drug *Rivastigmine* (**1**) or the non-sedative antihistaminic *Cetirizine* (**2**).<sup>[1,2]</sup>



Using the reactive *N*-diphenylphosphinoyl-ketimines,<sup>[3]</sup> we are investigating the asymmetric 1,2-addition of trialkylaluminium reagents catalysed by miscellaneous chiral ligands. Performing an efficient and flexible strategy, we should be able to achieve the chiral products in high yield as well as high enantiomeric access.



We report our results concerning this reaction and further improvements.

References:

[1] D. A. Evans, G. Helmchen, M. Rueping in *Asymmetric Synthesis The Essentials*, M. Christmann, S. Bräse, Eds., Wiley-VCH, Weinheim **2006**. [2] a) M. J. Bishop, R. W. McNutt, *Bioorg. Med. Chem. Lett.* **1995**, *5*, 1311; b) C. M. Spencer, D. Foulds, D. H. Peters, *Drugs* **1993**, *46*, 1055. [3] a) Y. Chu, Z. Shan, D. Liu, N. Sun., *J. Org. Chem.* **2006**, *71*, 3998; b) S. Masumoto, H. Usuda, M. Suzuki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2003**, *125*, 5634.

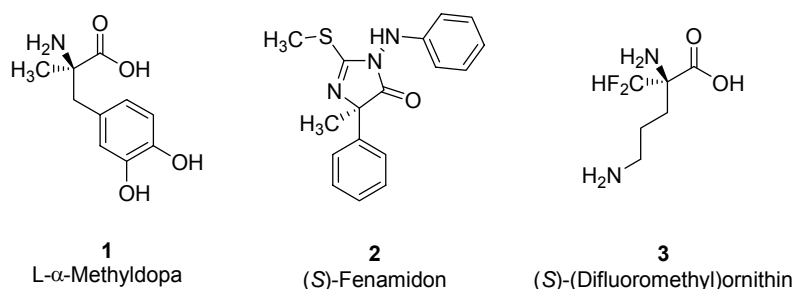
## Aymmetric Synthesis of $\alpha,\alpha$ -Disubstituted Amino Acids

**Caroline Hartmann** and **Stefan Bräse\***

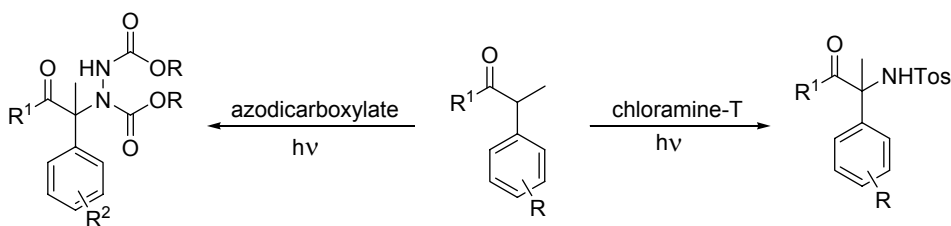
*Institute for Organic Chemistry, University of Karlsruhe, Germany*

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Abstract: The class of non-proteinogenic  $\alpha,\alpha$ -disubstituted amino acids and their derivatives is of high interest to biochemical and pharmacological research. This predicts on their ability to alter certain chemical and physicochemical properties of peptides and related structures. Moreover, the close structural relatedness to biologically relevant endogenous amino acid derivatives qualifies them in many cases to act as enzyme inhibitors or receptor antagonists.<sup>[1,2]</sup>



In the *Bräse* group, a series of aliphatic and aromatic carbonyl compounds has been transformed into the corresponding amino acid precursors by means of amine-catalyzed nitrene transfer.<sup>[3]</sup> Applying microwave conditions, good to excellent yields under significantly reduced reaction times could be obtained, thus providing a facile access to diverse  $\alpha,\alpha$ -disubstituted amino acids.<sup>[3b,4]</sup> The limit and scope of these reactions are to be investigated. Unfortunately the addition of the *N*-nucleophile chloramine-T to aldehydes with enantiomerically pure L-proline as a catalyst only delivered the racemic product.<sup>[4]</sup> Using chiral alkaloid-catalysts<sup>[5]</sup> we are now investigating the asymmetric addition of chloramine-T to  $\alpha$ -substituted aldehydes and ketones.



We report our results concerning these reactions and further improvements.

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[2] Sourkes, T. L. *Arch. Biochem. Biophys.* **1954**, *51*, 444.

[3] a) T. Baumann, H. Vogt, S. Bräse, *Eur. J. Org. Chem.* **2007**, 266. b) T. Baumann, M. Bächle, S. Bräse, *Org. Lett.* **2006**, *8*, 3797.

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## Combined Transition Metal and Organocatalysis

### Domino Hydroformylation/Proline-Catalyzed Aldol Coupling

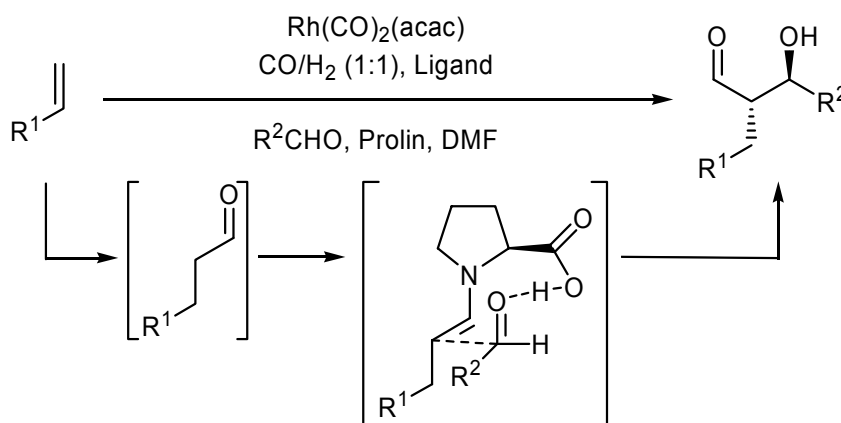
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Domino reactions allow the replacement of multiple sequenced transformations into one single synthetic operation, avoiding time and yield loss as well as unnecessary purifications and isolations. The search for reaction efficiency should head for the development of tandem processes in which one reaction has a cooperative effect to one another.

Herein we report the first enantioselective domino reaction by combining transition metal and organocatalysis. Recently a direct diastereo- and enantioselective aldol coupling between two discrete aldehydes has been described by MacMillan et al<sup>1</sup>. Our investigations led to the application of this aldol reaction in a tandem process under hydroformylation conditions.

In the present study, alkenes are converted into aldol adducts with moderate to high diastereoselectivity and high enantioselectivity in a one step operation through regioselective hydroformylation combined with a concomitant proline catalyzed aldol coupling.



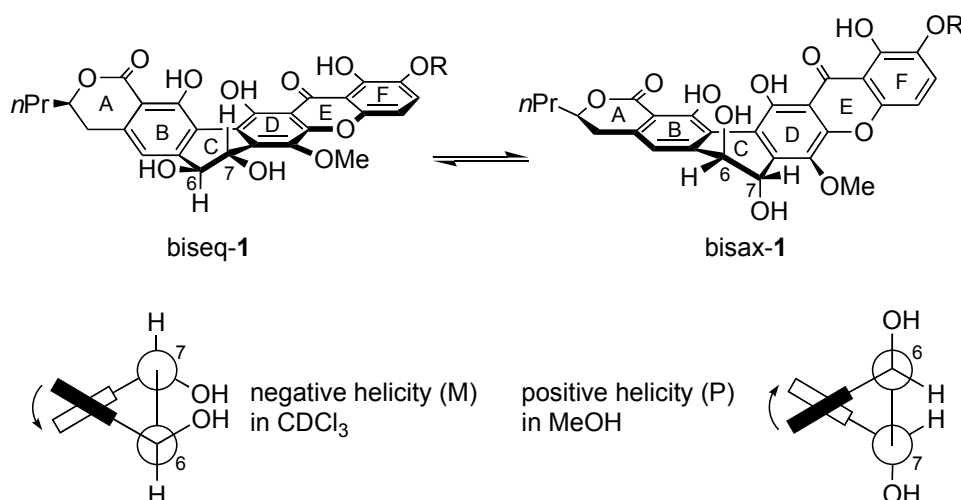
<sup>1</sup> MacMillan, D. W.; Northrup, A. B. *J. Am. Chem. Soc.* **2002**, *124*, 6798-6799.

## Development of an Axial Chirality Switch

Stefan Reichert, Bernhard Breit\*

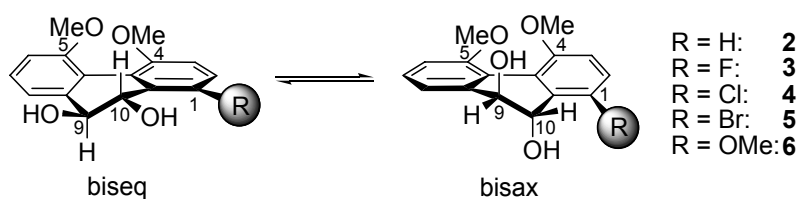
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Molecular switches are characterized as systems, which due to the action of an external stimulus, can change reversibly between two distinct states. In many cases processes known from nature have served as role models for the design of artificial systems. In this context we became interested in the natural product FD-594 which, dependent on the polarity of the solvent, can exist in two conformations having opposite helicity (solvent dependent atropisomerism).<sup>[1]</sup>



The helicity of the biaryl axis is connected to the preferred conformation of the central six-membered ring C. Thus, the two hydroxy-substituents at carbon atoms 6 and 7 can occupy either a pseudobisequatorial (biseq-1) or a pseudobisaxial position (bisax-1), which is a function of the solvent polarity. According to proton NMR experiments in chloroform FD-594 (**1**) prefers the biseq-1 conformation ( $^3J_{6,7} = 9.2$  Hz) in order to allow the formation of a stabilizing intramolecular hydrogen bond between the hydroxyl groups on C6 and C7. However, when switching to methanol as the solvent, the intramolecular hydrogen bond is broken, and minimization of gauche interaction of the hydroxy substituents at C6/C7 now favours the bisax-1 conformation ( $^3J_{6,7} = 3.6$  Hz), and induces a switch in helicity of the biaryl axis. If it were possible to mimic this behaviour with a smaller, simpler molecule, this could lead to interesting new applications. For example, one could think of using such a molecule as a switchable analogue of BINOL with potential applications in asymmetric catalysis.

Herein we wish to report on the synthesis of several model systems **2-6** and their conformational behaviour in different solvents.



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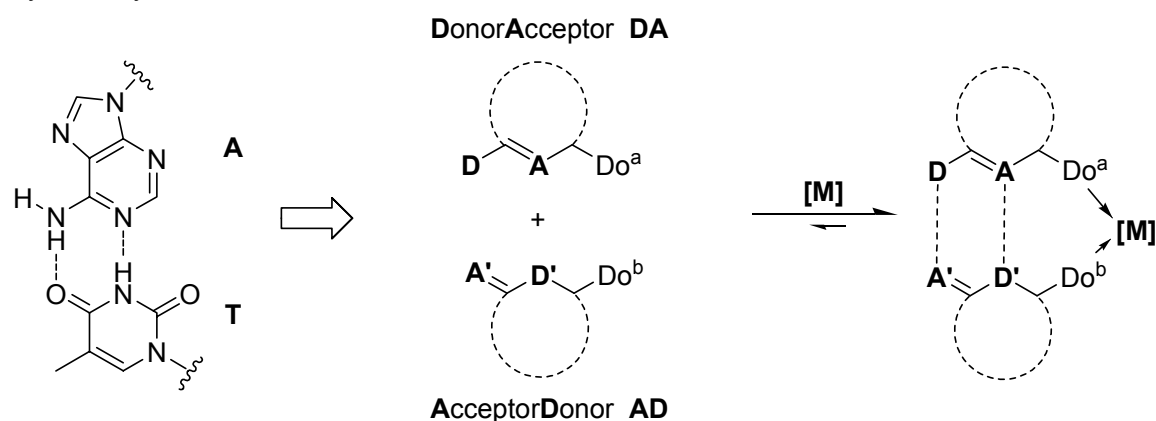


## Self-Assembly of Bidentate Ligands for Combinatorial Homogeneous Catalysis: New A–T Base Pair Analogous Platforms Stable in Methanol

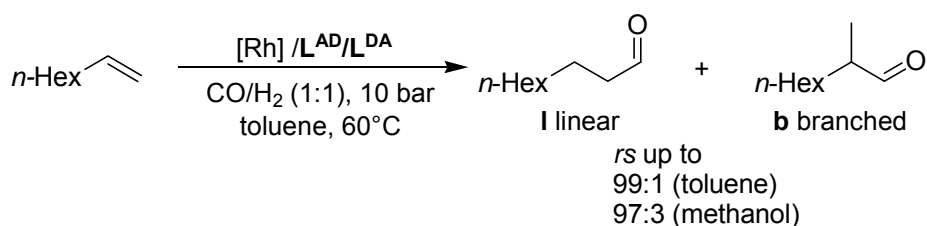
Jörg Wieland, Christoph Waloch, Bernhard Breit\*

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The control of selectivity in homogeneous metal complex catalysis relies in many cases on tailor-made bidentate ligands. The quest for the ultimate ligand giving rise to a catalyst with optimal activity and selectivity is a difficult task. We previously reported on an alternative to the classical covalent bidentate ligand, based on an aminopyridine-isoquinolone platform, interacting via complementary hydrogen bonds, analogous to A–T base pairing in DNA.<sup>[1]</sup> In all cases combinatorial ligand variations were achieved by changing the donor site (Do<sup>a/b</sup>) on the aminopyridine-isoquinolone system. This combinatorial approach identified a highly regioselective ligand combination for the rhodium-catalyzed hydroformylation of terminal alkenes.



We herein report on an alternative approach to generate a diverse ligand library. Instead of changing the donor functionality we have developed a series of ligands incorporating different heterocyclic backbones. This new library, based on the self-assembly of these novel phosphine ligands was employed in the hydroformylation of terminal alkenes. We were able to identify a ligand combination, which showed extremely high regioselectivities in an aprotic solvent such as toluene. Furthermore we also obtained very high regioselectivities in methanol. This latter observation was somewhat surprising, because protic solvents were expected to interfere with the formation of the hydrogen bonds necessary for self-assembly.<sup>[2]</sup>



[1] B. Breit, W. Seiche, *Angew. Chem.* **2005**, *117*, 1666-1669; *Angew. Chem. Int. Ed.* **2005**, *44*, 1640-1643.

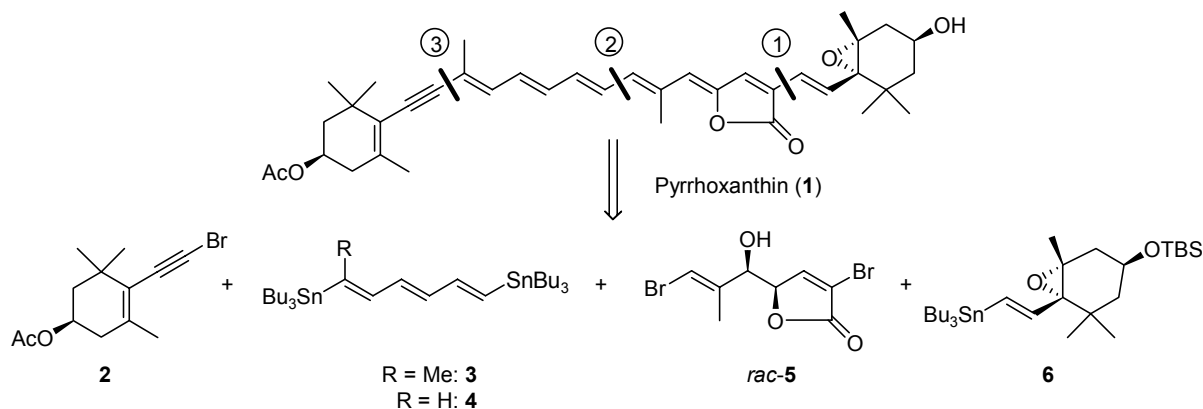
[2] C. Waloch, J. Wieland, M. Keller, B. Breit *Angew. Chem.* **2007**, *119*, 3097-3099; *Angew. Chem. Int. Ed.* **2007**, *46*, 3037-3039.

# Approach to the Total Synthesis of Pyrroloxanthin

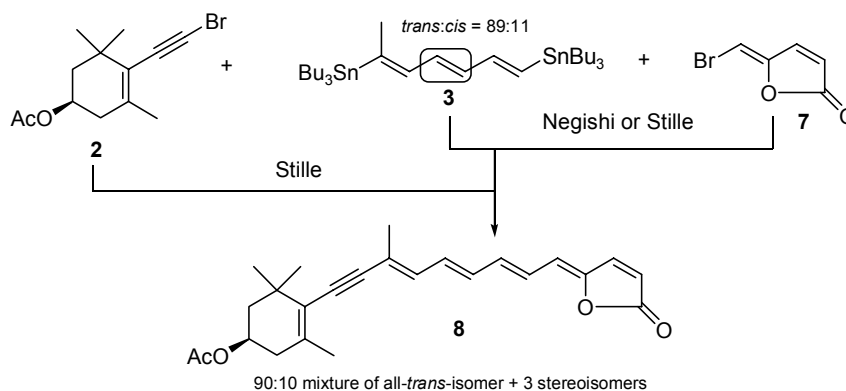
Jochen Burghart and Reinhard Brückner\*

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Transition-metal catalyzed cross-coupling reactions represent the method of choice for the synthesis of natural products containing polyene moieties. The tolerance of such coupling reactions for a broad range of functional groups combined with mild reaction condition, especially the STILLE REACTION, have proven superior to C=C-bond forming olefinations. Using bifunctional building-blocks makes C-C coupling strategies convergent. Distannylated building blocks e. g., **3** or **4**, are available via the RAMBERG-BÄCKLUND REARRANGEMENT with moderate to high *trans*-selectivity. The 1,6-bis(tributylstannyl)hexatriene building block **4** was first employed for the total synthesis of xerulonic acid by Sorg from our group.<sup>[1]</sup> Based on this result the methylated building block **3** should open the door for a highly convergent approach for the C<sub>37</sub>-carotenoid pyrroloxanthin (**1**).



Our retrosynthetic analysis dissects pyrroloxanthin (**1**) into four building blocks, all of which are designed to be joined via a STILLE REACTION:



To verify the key step, the connection of **2** and **3**, we choose a model. We were able to differentiate both ends of the unsymmetrical polyene building block **3** starting either with a STILLE or, after Sn→Li→Zn exchange, with a NEGISHI COUPLING. Fortunately, under both conditions the polyene chain isomerized from an initial *trans:cis* ratio = 89:11 to the all-*trans* structure. The final STILLE REACTION with bromoalkyne **2** delivered the target model compound **8** in good overall yield. In the second coupling the sterical homogeneity was not completely conserved: We detected a mixture of 90% of the all-*trans* compound **8** besides 3 stereoisomers. It was also possible to couple **2**, **3** and **7** in a one-pot procedure.

[1] A. Sorg, R. Brückner *Angew. Chem.* **2004**, *116*, 4623-4626; *Angew. Chem. Int. Ed. Engl.* **2004**, *43*, 4523-4526.

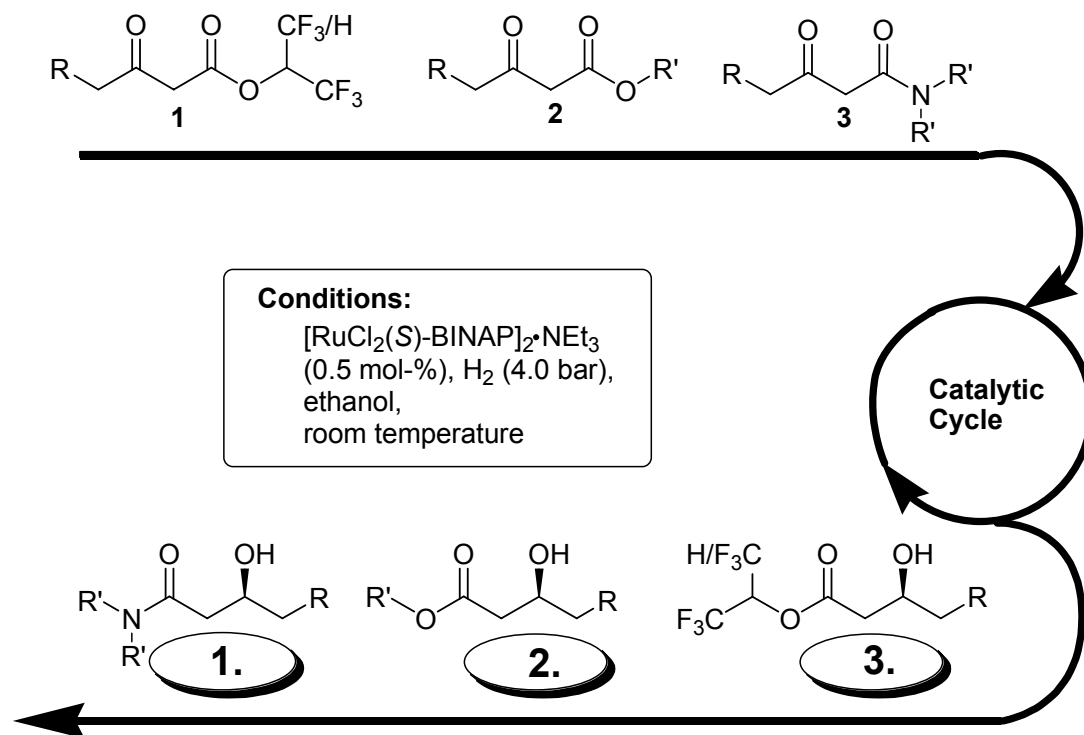
## REDUCTIONS ONE BY ONE: KINETIC DIFFERENTIATION OF $\beta$ -KETOESTERS AND $\beta$ -KETOAMIDES BY RU-CATALYZED ASYMMETRIC HYDROGENATION

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Asymmetric hydrogenation of  $\beta$ -ketoesters is most successfully achieved by using Ru(II)-BINAP catalysts.<sup>[1]</sup> These reductions deliver the corresponding  $\beta$ -hydroxyesters in high yields and enantioselectivities. The present study shows for the first time that the widely used hydrogenation catalyst  $[\text{RuCl}_2(\text{S})\text{-BINAP}]_2 \cdot \text{NEt}_3$ <sup>[2]</sup> moreover allows the kinetic differentiation of a series of derivatives of  $\beta$ -keto-carboxylic acids. As a general trend we observed that in a mixture of derivatives **1**, **2**, and **3** the compound with the most electron-rich carboxyl group, i. e. the  $\beta$ -ketoamide **3**, is reduced first. Only after complete conversion of this compound, the  $\beta$ -ketoester **2** ( $\text{R}' = \text{alkyl}$ ) is consumed, and thereafter the fluorinated  $\beta$ -ketoester **1**. These differentiations are effective under relatively mild conditions and proceed without any loss of enantioselectivity.



Seemingly, the reason for this selectivity is the different basicity of the respective carboxyl moiety: The most basic compound is processed selectively by the catalyst until it is completely consumed. However, the described reactivity order does not reflect the intrinsic reactivities of these substrates. For instance, control experiments established that the consumption of hydrogen by amide **3** needs approx. 16 h while ester **2** is reduced within 6-7 h.

[1] Reviews: a) T. Ohkuma, M. Kitamura, R. Noyori, in *Catalytic Asymmetric Synthesis* (Ed. I. Ojima), 2<sup>nd</sup> ed., Wiley-VCH, Weinheim, **2000**, 1-111. b) T. Ohkuma, R. Noyori, in: *Comprehensive Asymmetric Catalysis I* (Eds. E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, 199-245. c) D. J. Ager, S. A. Laneman, *Tetrahedron Asym.* **1997**, *8*, 3327-3355.

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**Research at the Catalysis Research Laboratory (“CaRLa”)**

Oleg Bondarev<sup>a</sup>, Patrick Crewdson<sup>a</sup>, Angelica Marson<sup>a</sup>, Vladimir Romakh<sup>a</sup>, Benjamin Ward<sup>a</sup>, Zhirong Zhao-Karger<sup>a</sup>, Pierre Croizat<sup>a</sup>, Belén Diaz<sup>a</sup>, Anders Gabrielsson<sup>a</sup>, Daniel Serra<sup>a</sup>, Caroline Taylor<sup>a</sup>, Marie-Alice Virolleaud<sup>a</sup>, Lutz H. Gade<sup>a,b</sup>, A. Stephen K. Hashmi<sup>a,c</sup>, Peter Hofmann<sup>a,c</sup> and Christoph Jäkel<sup>a,d</sup>

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Last year, BASF and the University of Heidelberg set up a joint laboratory devoted to homogeneous catalysis, CaRLa. The laboratory is funded by both partners and the federal state of Baden-Württemberg. In this laboratory, 12 postdocs working together on various projects in the area of homogeneous catalysis, each 6 are funded by each partner. An overview on the projects pursued at CaRLa will be given.

**Catalysis Research Laboratory (“CaRLa”)**

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Last year, BASF and the University of Heidelberg set up a joint laboratory devoted to homogeneous catalysis, CaRLa. Contrary to classical industry-academia partnerships, the concept of this lab relies on bringing academic and industrial researchers as close as possible together, fostering technology transfer from basic research to potential industrial applications. The laboratory is funded by both partners and the federal state of Baden-Württemberg. In this setting, 12 postdocs working together on various projects in the area of homogeneous catalysis, each 6 are funded by the partners. The concept and structure of CaRLa will be presented.

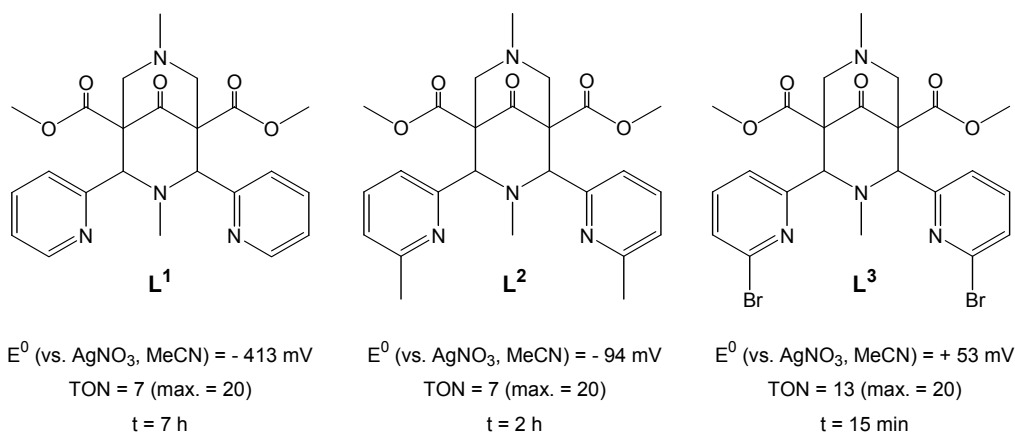
## Experimental and DFT based mechanistic studies of the copper-catalyzed aziridination

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Aziridines are interesting molecules, mainly as electrophilic building blocks in organic synthesis<sup>[1]</sup> and biomolecules with attractive properties.<sup>[2]</sup> One of the most promising synthetic routes to aziridines is the copper-catalyzed addition of nitrenes to olefins.<sup>[3]</sup> Here, bispidines<sup>[4]</sup> (3,7-diazabicyclo[3.3.1]nonane derivatives) are used as ligands for the copper-catalyzed aziridination with copper in both, the +I and +II oxidation states. Ligands L<sup>1</sup> to L<sup>3</sup> (see Figure) show large differences in catalytic activity: the reaction time is reduced from seven hours to a few minutes and the turnover number (TON) increases from 7 to 16 (TON<sub>max</sub> = 20), i.e. to essentially quantitative yields.

While attempting to produce catalytically more active bispidine complexes, we probe the mechanistic pathways of the entire reaction using DFT, which not only increases our understanding but ultimately will help us to tune the efficiency of our catalysts.



We will discuss details of a thorough investigation into the mechanism of aziridination with Cu<sup>I/II</sup>-bispidine catalysts using DFT. The DFT studies provide a deeper insight into issues such as reactive intermediates and the oxidation and spin state of the Cu center, the denticity of the nitrene source, which directly influence the efficiency of the catalytic process. Different pathways are explored for the formation of aziridine, where the two N-C bonds are formed either in a concerted or consecutive manner. Along the mechanistic pathways, interesting features such as spin-crossover and two-state reactivity are also addressed. The difference in the catalytic activity among different Cu bispidines is also rationalised based on the mechanistic features.

[1] D. Tanner, *Angew. Chem. Int. Ed. Engl.*, **1994**, 33, 599-619.

[2] R.S. Coleman, J.-S. Kong, *J. Am. Chem. Soc.*, **1998**, 120, 3538-3539.

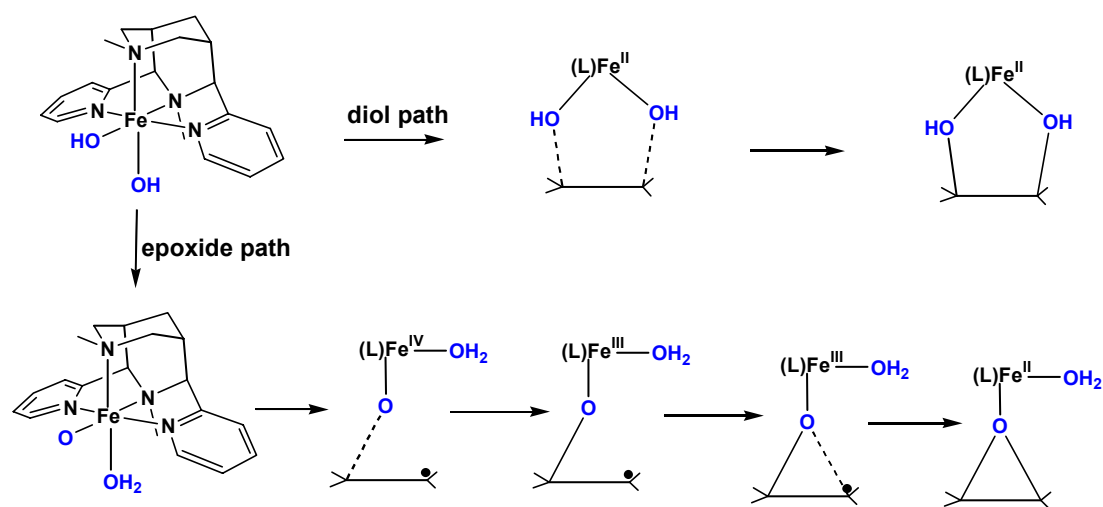
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## Oxidation of olefins by non-heme bispidine Fe(IV) complexes - a computational and experimental study

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 Heidelberg, Germany

Bispidine Fe(II) complexes oxidise olefins in presence of  $\text{H}_2\text{O}_2$ , to yield epoxide as well as *cis*-diol [1]. Experimental and computational studies indicate the formation of a  $\text{Fe}^{\text{IV}}=\text{O}$  species, that acts as the catalytically active complex [2]. The epoxide is formed via a carbon centered radical, while the diol is formed through a different reaction pathway (see figure 1). DFT calculations support the involvement of a novel  $\text{Fe}^{\text{IV}}(\text{OH})_2$  oxidant responsible for *cis*-hydroxylation. Moreover, the  $\text{Fe}^{\text{IV}}(\text{OH})_2$  oxidant also acts as precatalyst for the formation of a  $\text{Fe}^{\text{IV}}(\text{O})(\text{OH}_2)$  species, which is responsible for the formation of epoxide. Labeling studies and the increased yield of epoxide under aerobic conditions by autoxidation correspond to the proposed mechanism. Here we will discuss the catalytic mechanism according to experimental and computational results.



**Figure 1:** Mechanism of the catalysed formation of epoxide and diol

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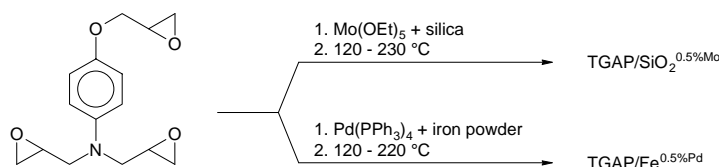
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## Organic-inorganic hybrid catalysts based on metal-doped epoxy resins

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Thermosetting epoxy resins are high-performance plastics with widespread applications, e.g. coatings, composites or adhesives.<sup>[1]</sup> Apart from these material applications, a series of catalysts based on commercially available epoxy resins was recently described.<sup>[2,3]</sup> Resins such as the triglycidyl derivative of 4-aminophenol (TGAP) can be polymerized in the presence of metal compounds that act simultaneously as polymerization initiators and precursors of catalytically active species in the resulting polymers. The catalysts can be prepared in a convenient one-step procedure by heating of resin/initiator mixtures and inorganic components such as silica or iron powder can be added affording organic-inorganic hybrid catalysts:



The properties of the catalysts can easily be adjusted by choice of the resin, initiator, inorganic filling material, component ratio and polymerization conditions. A TGAP/silica composite material with a molybdenum content of 0.5% was employed as catalyst in the epoxidation of propene with *tert.*-butyl hydroperoxide (TBHP) as oxidant and a hybrid system containing 0.5% palladium based on TGAP/iron powder was tested in the hydrogenation of crotonaldehyde. The latter catalyst can be easily removed from the reaction mixtures by magnetic separation and used repeatedly. Catalytic performances of the catalysts in five consecutive reactions are as follows:

Run no.	$\xrightarrow[\text{toluene, 90 }^\circ\text{C, 24 h}]{\text{TGAP/SiO}_2^{0.5\%}\text{Mo, TBHP}}$		$\xrightarrow[\text{toluene, 60 }^\circ\text{C, 24 h}]{\text{TGAP/Fe}^{0.5\%}\text{Pd, H}_2}$	
	Yield (%) <sup>a</sup>	Metal leaching (%) <sup>b</sup>	Yield (%) <sup>c</sup>	Metal leaching (%) <sup>b</sup>
1	35	< 0.004	> 99	0.022
2	62	0.02	> 99	0.010
3	56	0.02	> 99	0.010
4	52	0.02	> 99	0.007
5	43	0.02	> 99	< 0.006

<sup>a</sup>Reaction conditions: 8 bar propene, 50 mmol TBHP (3.0M in toluene/dodecane), 1 g catalyst; yields are based on TBHP consumption. <sup>b</sup>Percentage of metal initially loaded on the polymer determined by metal enrichment and atomic spectroscopy. <sup>c</sup>Reaction conditions: 10 mmol aldehyde, 20 ml toluene, 2.5 bar H<sub>2</sub>, 0.5 g catalyst.

Metal losses of the catalysts are extremely low and they can be employed over periods of months without deactivation.<sup>[3]</sup> This concept is highly versatile and can easily be adapted to other metals and catalytic reactions.

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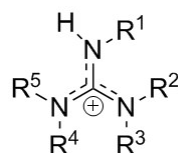
## Catalytic epoxidation of olefins by hydrogen peroxide in guanidinium salts

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Due to their broad spectrum of physicochemical properties, Ionic Liquids have gained increasing popularity in recent years. Extremely different properties like polarity, charge density and miscibility can be realized and make them interesting alternative solvents in organic synthesis.<sup>[1]</sup>

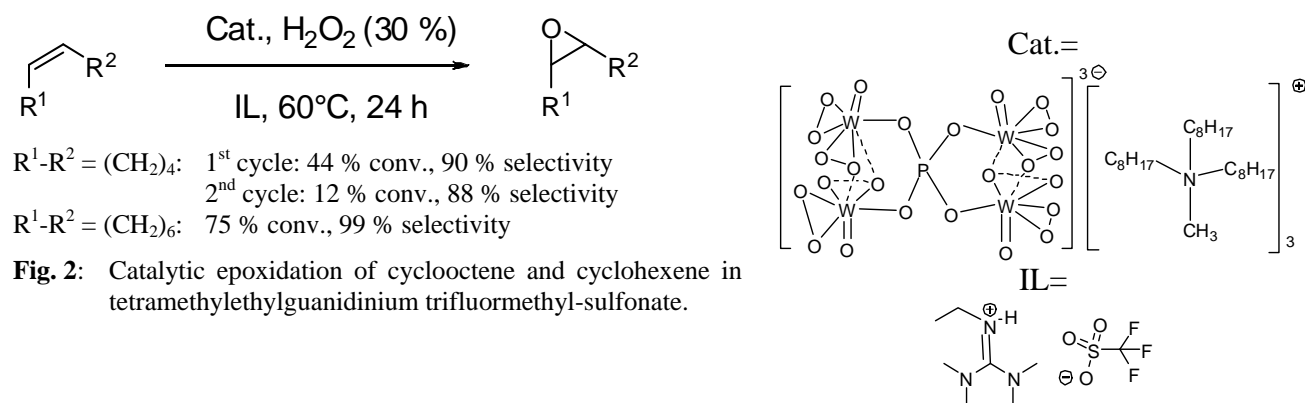
One group of less explored room temperature ionic liquids (RTILs) are guanidinium based salts (GILs), with a core structure as shown in Fig. 1.



**Fig. 1:** The core structure of guanidiniumsalts.

The aim of this work is the efficient epoxidation of alkenes, using aqueous hydrogen peroxide (30 %) as oxidant and guanidinium salts as reaction media. In this context, known organometallic catalysts based on W, Mn, Mo, and Re were synthesized and applied as homogeneous catalysts.

One model system to examine the applicability is the epoxidation of cyclooctene and cyclohexene with the tungsten based “Venturello catalyst”.<sup>[2]</sup> High epoxide selectivities were already achieved, even after recovery and reuse of the dissolved catalyst.



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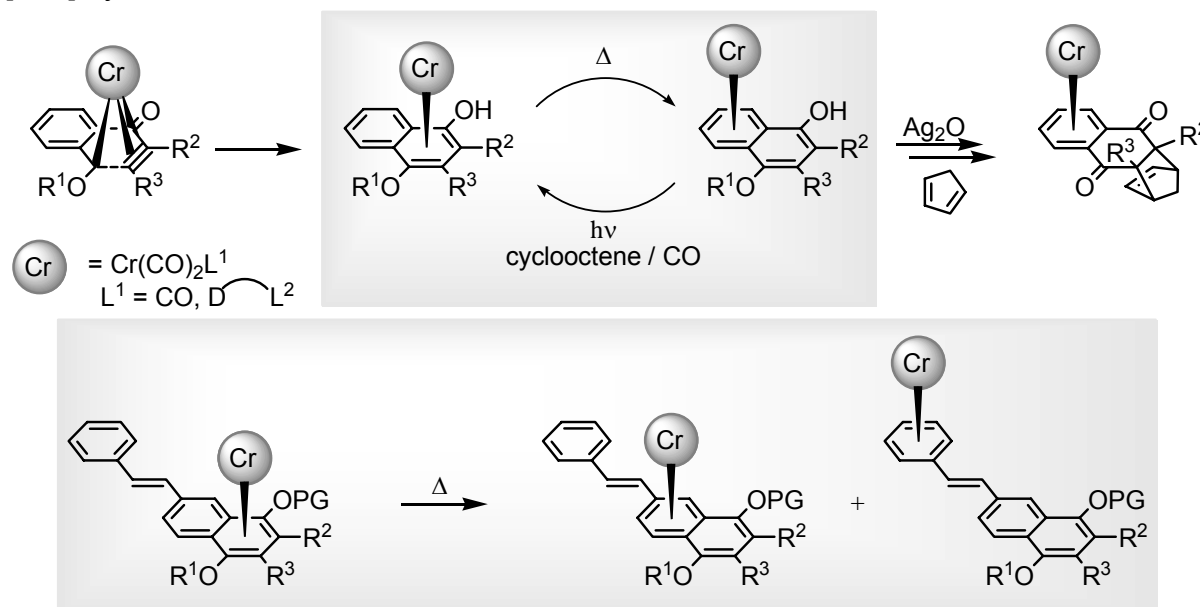
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## Coligand-Controlled Haptotropic Metal Migration in Arene Chromium Complexes

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The chromium-templated [3+2+1]-benzannulation provides a regio- and stereoselective synthesis of densely substituted  $\eta^6$ -arene  $\text{Cr}(\text{CO})_3$  complexes [1]. The chromium template may undergo a haptotropic migration along the aromatic platform or an acyclic conjugated  $\pi$ -system [2] which allows to activate a selected ring for subsequent synthetic transformations [3] as demonstrated for stereoselective [4+2]-cycloaddition reactions.



The haptotropic migration can be controlled by adjustment of the coligand sphere. Substitution of a CO ligand for a variety of phosphorus [4] and hemilabile chelating phosphorus ligands [5] reveals the role of steric and electronic properties of the ligand applied.

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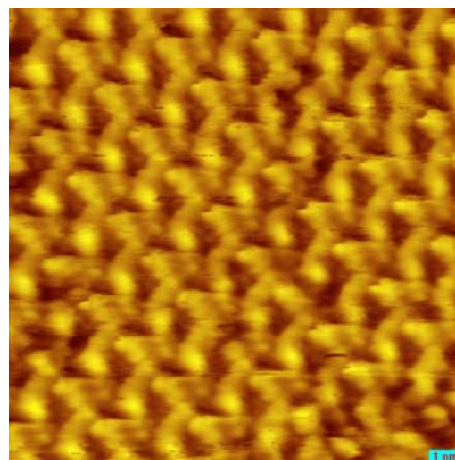
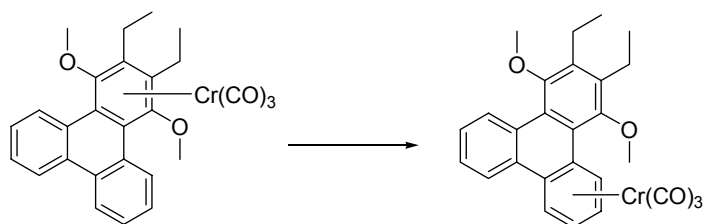
## Synthesis, Haptotropic Migration and STM Investigation of a Triphenylene-Cr(CO)<sub>3</sub>-Complex

Carola Rang,<sup>1</sup> Christoph H. Schmitz,<sup>2</sup> Iordan Kossev,<sup>2</sup> Moritz Sokolowski,<sup>2</sup>  
Karl Heinz Dötz<sup>1</sup>

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Arene tricarbonyl chromium complexes play an important role in enantioselective synthesis and catalysis due to their reactivity towards nucleophiles [1]. The chromium templated [3+2+1]-benzannulation allows for a regioselective synthesis of highly substituted fused arenes in which a specific benzene ring is labeled by Cr(CO)<sub>3</sub>-coordination [2]. We focus on a controlled haptotropic migration of the chromium tricarbonyl fragment [3]. This rearrangement involves an intramolecular shift along one face of the arene ligand [4] aiming at a stereospecific organometallic switch [5]. Here we present the regioselective synthesis and the haptotropic metal migration of a triphenylene complex in which the Cr(CO)<sub>3</sub> fragment is shifted from the hydroquinoid to an unsubstituted terminal arene ring. STM investigations of a monolayer of this complex on Ag(111) and Ag(100) surfaces under ultra-high vacuum at room temperature and low temperatures (80-100 K) reveal long-range ordered structures.



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## An Air-Stable Organometallic Low-Molecular-Mass Gelator: Aggregation and Catalytic Application of a Palladium Pincer Complex

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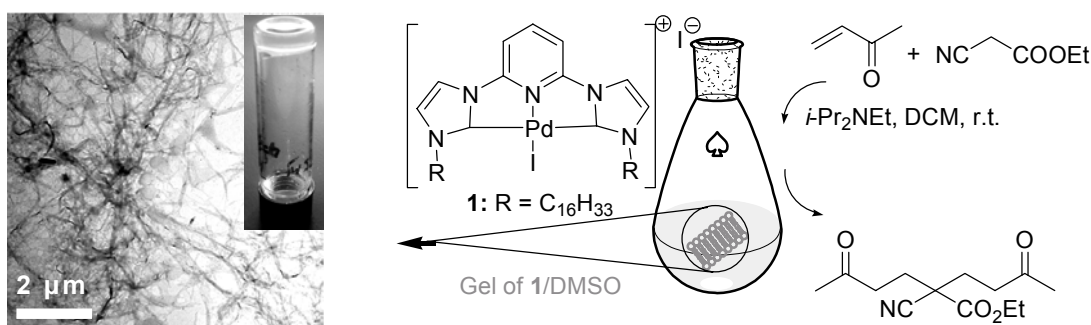
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Gels derived from low-molecular-mass compounds attract increasing interest resulting from the simplicity of the gelator molecules, their physical properties and potential applications [1]. Whereas organometallic compounds are well-established in organic synthesis, catalysis and material chemistry, only two recent examples of organometallic low molecular gelators have been reported to date which efficiently gelate customary organic solvents [2]. The unique role of the organopalladium compounds in organic synthesis encouraged us to develop pincer complexes into robust organogelators.

Palladium pincer bis-carbene complex **1** is an efficient gelator for a variety of organic solvents even in concentrations as low as 0.2 wt%.  $\pi$ -Stacking of the heteroarene moieties, van-der-Waals interactions between the alkyl chains and metal-metal interaction may be regarded responsible for the aggregation. It represents the first air-stable organometallic low-molecular-mass gelator which reveals promising catalytic activity in the gel state.



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## HI-Catalyzed Hydroamination and Hydroarylation of Alkenes<sup>[1]</sup>

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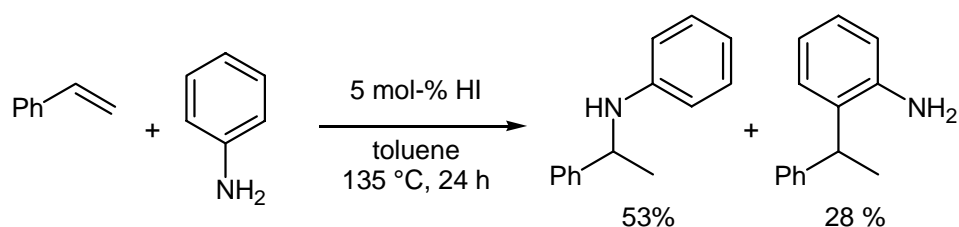
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Aromatic amines react with alkenes in the presence of catalytic amounts of aqueous HI to give mixtures of the corresponding hydroamination and hydroarylation products.<sup>[2]</sup> While the hydroamination reaction is the preferred pathway for aliphatic alkenes the hydroarylation reaction becomes more important when styrenes are used as substrates. In general, the electronic properties of the alkene and the amine strongly influence the efficiency and the selectivity of the reaction.



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## Neutral Ti-Catalysts for the Intramolecular Hydroamination of Alkenes<sup>[1]</sup>

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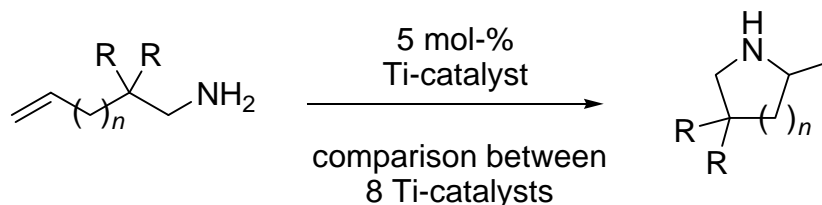
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Neutral titanium complexes are well known precatalysts for the inter- and intramolecular hydroamination of alkynes.<sup>[2]</sup> Our poster describes the capability of several neutral titanium complexes to catalyze intramolecular hydroaminations of alkenes.<sup>[3]</sup> The corresponding pyrrolidine and piperidine products are formed in yields up to 97%. Among the substrates used, only geminally disubstituted aminoalkenes are successfully cyclized.



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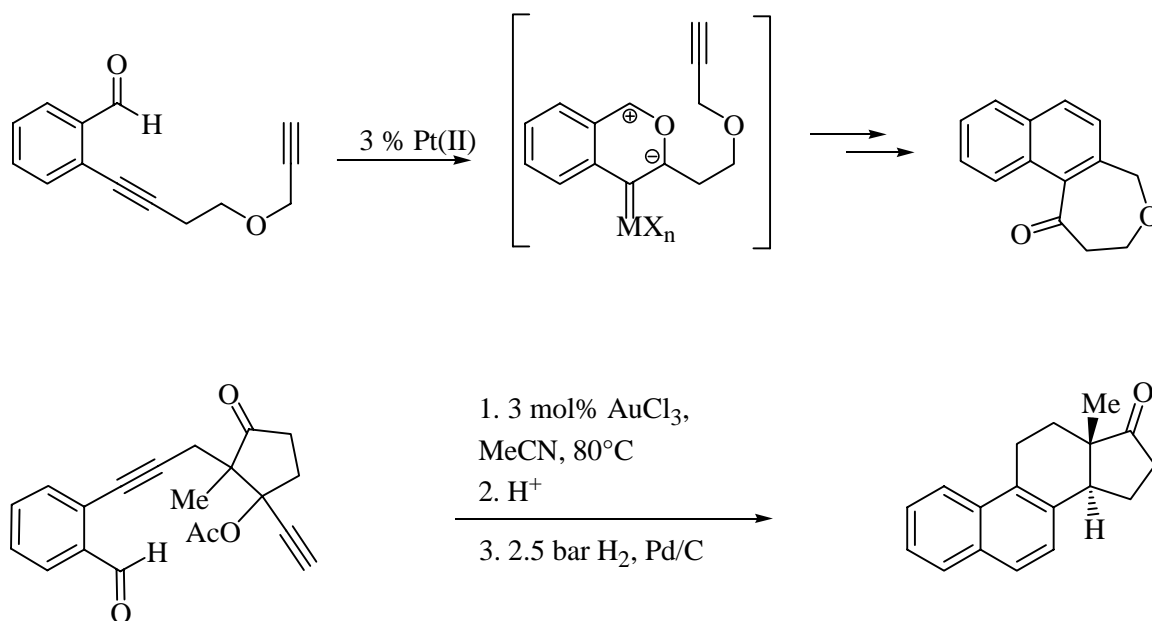
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## Gold- and Platinum-Catalyzed Cyclization Reactions

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Gold(III) chloride and similarly platinum(II) chloride are soft Lewis acids, which activate alkynes for the attack of nucleophiles under very moderate conditions. For instance, the formation of intermediary dipolar benzopyrylium units is the initializing key step for preparative useful domino processes, which are highlighted by the successful synthesis of various targets: 7 to 15-membered rings and the tricyclic natural product heliophenanthrone as well as the steroid equilenine (both racemic). Other remarkable reactions presented: domino processes with additional nucleophiles and a gold-catalyzed Friedel-Crafts-type macrocyclization.



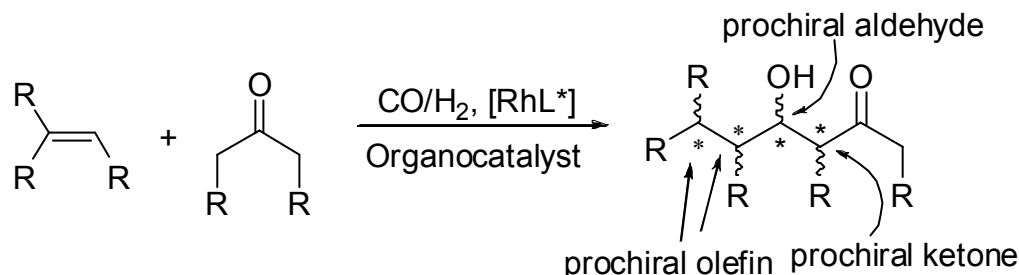
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**TANDEM METAL- AND ORGANOCATALYSIS IN ENANTIOSELECTIVE  
SEQUENTIAL HYDROFORMYLATION AND ALDOL REACTIONS**

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Control of stereochemistry during aldol addition reactions has attracted considerable interest over the last decades, as the aldol reaction is one of the most powerful and versatile methods in modern carbonyl chemistry<sup>1</sup>. Simple chiral organic molecules have been found to catalyse the direct aldol addition of unmodified ketones to aldehydes with relatively high chemical and stereochemical efficiency<sup>2</sup>. On the other hand, hydroformylation of olefins, one of the largest industrially applied homogeneous catalysed processes, provides the synthetically useful aldehyde function for further transformations, *e.g.* aldol addition.

Following a general trend in organic chemistry to combine several individual reaction steps to a single synthetic procedure<sup>3</sup>, we have developed hydroformylation and aldol reaction sequences<sup>4</sup> and here now report an enantioselective version with chiral phosphorous ligands and chiral organocatalysts<sup>5</sup>.

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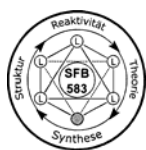
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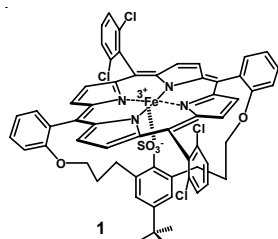
## Low Temperature Rapid-Scan Detection of Reactive Intermediates in Epoxidation Reactions Catalyzed by a New Enzyme Mimic of Cytochrome P450

Natalya Hessenauer-Ilicheva,<sup>a</sup> Alicja Franke,<sup>a</sup> Dominik Meyer,<sup>b</sup> Wolf-D. Woggon<sup>b</sup> and Rudi van Eldik<sup>a,\*</sup>

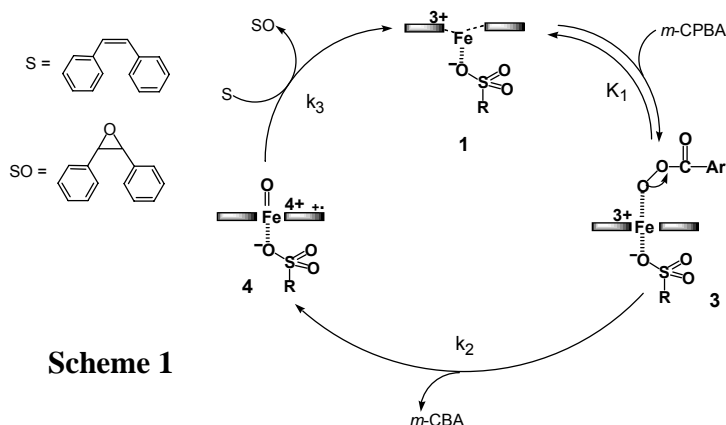
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Since the synthetic iron(III) porphyrins appeared to be good models for the heme-type catalysts found in nature, their use in biomimetic cytochrome P450 research has provided valuable information about nature and reactivity of the intermediates produced via “peroxide shunt” pathways. Extensive mechanistic studies on the oxygenation reactions of the biomimetic models with typical oxygen donors such as iodosylbenzene, peroxy acids and hydroperoxides resulted in proposing the oxoiron(IV) porphyrin  $\pi$ -cation radical as a reactive intermediate responsible for oxygen atom transfer to the organic substrates. Recently, Woggon et al. synthesized a new enzyme mimic of cytochrome P450 (**1**) in which the



$RS^-$  ligand is replaced by a  $RSO_3^-$  group.<sup>[1]</sup> Substitution of the  $S^-$  donor in P450 by a  $RSO_3^-$  ligand in this complex, remarkably tunes the redox potential of  $Fe^{III/II}$  to that measured for the resting state of P450<sub>cam</sub>. Moreover, although  $RS^-$  ligation was changed to the  $RSO_3^-$  group, **1** has been shown to display a rather broad spectrum of P450-type reactions.<sup>[1]</sup> In the present study,<sup>[2]</sup> we report spectroscopic and kinetic studies on the formation of the reactive iron(IV)-oxo porphyrin radical cation ( $(1^{*+})Fe^{IV}=O$ ) in the reaction of complex **1** with *m*-chloroperoxybenzoic acid (*m*-CPBA) in acetonitrile. With the use of low temperature rapid-scan stopped-flow techniques we were able to determine equilibrium ( $K_1$ ) and rate constants ( $k$  for the formation and decay of all intermediates in the catalytic cycle of **1** (Scheme 1), including the rate constant for the oxygen atom transfer from **4** to substrate ( $k_3$ ), a reaction that leads to almost complete reformation (95 %) of the starting complex **1**. We can conclude that complex **1** is a valuable catalyst with very promising properties for further application. Studies focused on the determination of the activation parameters and elucidation of the mechanism of  $(1^{*+})Fe^{IV}=O$  formation from **1** in various organic solvents are currently underway in our laboratory.



Scheme 1

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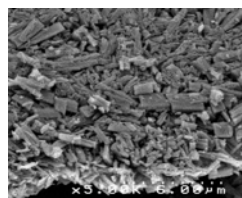
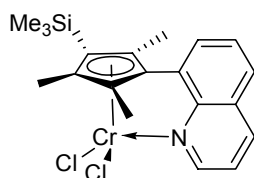
## New Mesoporous Hybrid Silicas and Molecular Chromium Catalysts for Olefin Polymerisation

Katrin Schuhen<sup>a</sup>, Michel Wong Chi Man<sup>b</sup>, Markus Enders<sup>a</sup>

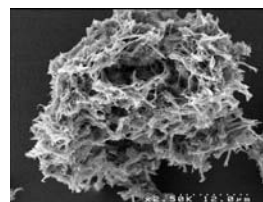
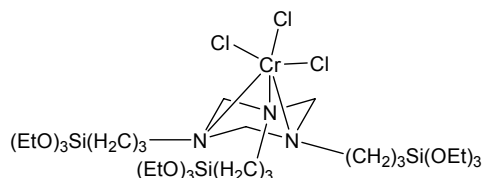
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F-34296 Montpellier CEDEX 5

Regularly structured solid materials like mesoporous silicas of the MCM-41 type can be used as supports for molecular catalysts. We developed a new method to self-direct the structuring of bridged silsesquioxanes on the molecular scale by hydrolysing newly designed molecular precursors bearing additional organic groups. These groups are capable to create the self-assembly through hydrogen bonding leading to crystalline materials. Although such self-organised hybrids are not as highly porous as the periodic mesoporous silsesquioxanes, the surface areas (around  $100 \text{ m}^2 \text{ g}^{-1}$ ) may be sufficiently porous enough for catalysis to proceed. Following two concepts for the attachment of catalytic centres we are interested in **a)** grafting of hybrid silicas with the molecular pre-catalysts or **b)** incorporation of suitable ligands or complexes during sol-gel-formation of structured materials.



route a) lamellar structured organic-inorganic hybrid silica with physisorbed chromium polymerisation catalyst



route b) new hybrid silica by co-condensation of self-structuring organo-silicon precursors and siloxy functionalized chromium compounds

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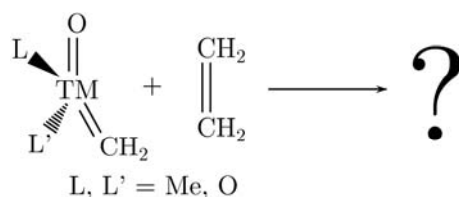
K. Schuhen, M. Wong Chi Man, M. Enders, Manuscript in preparation.

## Reactions of Transition Metal Carbenes with Ethylene

**Robin Haunschild and Gernot Frenking**

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Transition metal carbene complexes are often active for the metathesis reaction. The complex  $\text{ReO}_2(\text{CHCMe}_3)(\text{CH}_2\text{CMe}_3)$  was synthesized and detected to be inactive for the metathesis of olefins.<sup>[1]</sup> We performed quantum chemical calculations for the model system  $\text{ReO}_2\text{MeCH}_2$ , its isomers, and its products with ethylene.<sup>[2]</sup> Focussing on the [3+2] and [2+2] cycloadditions, we extended our research by investigating the reactions of transition metal carbenes in high oxidation states of the heavy elements of the 6<sup>th</sup> ( $\text{WOME}_2\text{CH}_2$ )<sup>[3]</sup>, 8<sup>th</sup> ( $\text{OsO}_3\text{CH}_2$ )<sup>[2]</sup> and 9<sup>th</sup> ( $\text{IrO}_2\text{MeCH}_2$ ) group of the periodic table with ethylene.



All geometry optimizations were done on the B3LYP density functional level of theory combined with Ahlrichs TZVP basis set<sup>[4]</sup> for the elements C, H and O. For the transition metals, we employed the Stuttgart/Köln relativistic effective core potentials replacing 60 core electrons for computational reasons and to include relativistic effects into our calculations. For the remaining electrons, we used a (311111/22111/411) valence basis.<sup>[5]</sup> All minima and transition structures were optimized at this level of theory without symmetry constraints. Analytic Hessians were computed to characterize the nature of the stationary points. All connectivities of minima and transition structures were verified by either IRC or DRP following calculations. On the B3LYP structures we performed additional B3LYP and CCSD(T) singlepoint calculations with Dunning's correlation consistent cc-pVTZ basis set<sup>[6]</sup> for the elements C, H and O and augmented our transition metal basis set by two sets of *f* and one set of *g* functions derived by Martin and Sundermann<sup>[7]</sup>.

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## Are Carbodiphosphoranes Better Ligands than NHCs for Grubb's Catalysts?

### Theoretical Investigations of the Key Intermediates in Olefin Metathesis

**Ralf Tonner, Gernot Frenking**

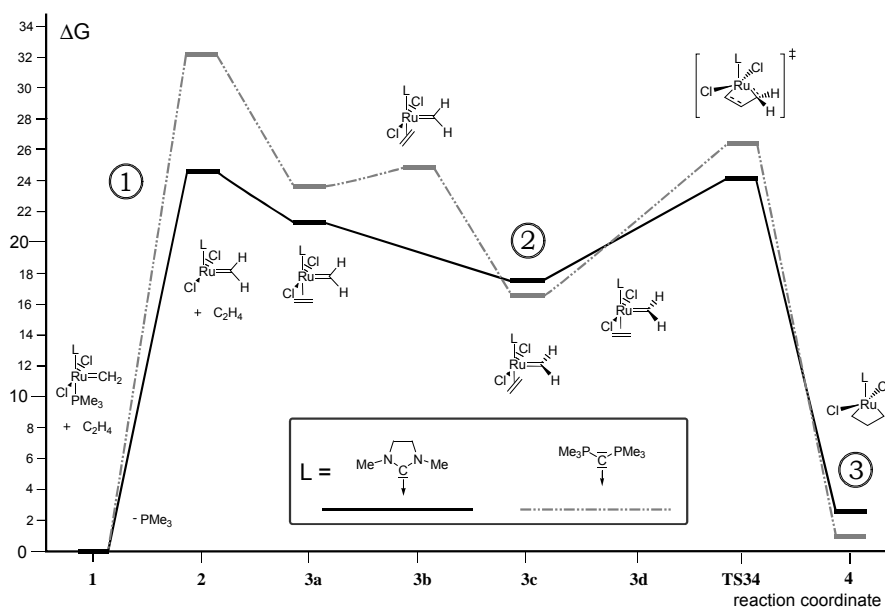
*Fachbereich Chemie, Philipps-Universität Marburg, 35032 Marburg, Germany*

The research about carbodiphosphoranes  $C(PR_3)_2$  has recently been revitalized due to experimental and theoretical studies which shed new light on the chemistry of a neglected class of compounds.[1-3] Based on the description of carbodiphosphoranes as carbon(0) compounds stabilized by two phosphine groups,[2] we studied the implications of this concept on the reactivity of carbodiphosphoranes. As this compound class has often been compared with carbenes but has to be distinguished from them in many respects we choose the well-known reaction profile of olefin metathesis as an application using model and real ligands.

An appealing theoretical explanation for the enhanced reactivity of 2<sup>nd</sup> generation Grubb's catalysts based on ligand rotation has been given recently by Straub.[4, 5] We calculated the corresponding energy profile based on the key steps for the olefin metathesis focussing on three main factors for reactivity:

1. Barrier for the dissociation of phosphine in the first step
2. Stabilisation of the reactive conformation in the p-complex with the olefin
3. Formation of a stable ruthenacyclobutane

It will be shown that carbodiphosphoranes reveal promising energetics regarding all three factors (see Figure) and could be an interesting choice for future experimental investigations.



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## Transition Metal-Carbon Complexes. A Theoretical Study

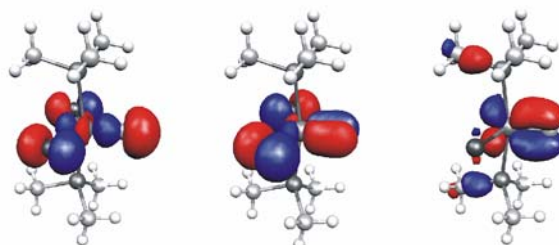
Andreas Krapp, Gernot Frenking

Philipps-Universität Marburg, Fachbereich Chemie, Hans-Meerwein-Strasse, 35032 Marburg, Germany

Transition metal (TM) complexes with a terminal carbon atom as ligand can be regarded as the endpoint in the series TM-alkyl (TM-CR<sub>3</sub>) → TM-carbene (TM=CR<sub>2</sub>) → TM-carbyne (TM≡CR) complexes. The first TM complex with a singly coordinated carbon atom<sup>[1]</sup> was synthesized by Cummins and coworkers in 1997.<sup>[2]</sup> They fully characterized the 14 valence electron (VE) anion [(NRAr)<sub>3</sub>Mo(C)]<sup>-</sup> which is isoelectronic with the previously known nitrido complex [(NRAr)<sub>3</sub>Mo(N)]. The first synthesis and X-ray structure analysis of a neutral transition metal compound with a terminal carbon ligand was recently reported by Heppert and co-workers.<sup>[3]</sup> They isolated the diamagnetic 16VE ruthenium complexes [(PCy<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>Ru(C)] (**I**: L= PCy<sub>3</sub>; **II**: L= 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene; Cy = Cyclohexyl) by a metathesis facilitated reaction. Shortly later, Grubbs and his group showed that **I** can act as a σ-donor towards Mo(CO)<sub>5</sub> and Pd(SMe<sub>2</sub>)Cl<sub>2</sub> via the terminal carbon atom.<sup>[4]</sup>

The synthesis of **I** and **II** and of the coordination compounds raises the question about the metal-carbon bonding situation in the compounds<sup>[5]</sup> and about their donor/acceptor capabilities<sup>[6]</sup>. In order to address the question about the bonding situation we calculated the geometries (BP86/TZ2P) and bond dissociation energies (BP86/TZ2P; CCSD(T)/TZ2P) of the 16 VE carbon complex [(PMe<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>Ru(C)] (**1Ru**). We also theoretically studied related 18VE carbon complexes and complexes in which a CO molecule binds instead of the terminal carbon atom. In all cases we also studied the analogue iron compounds. The bonding situation in the molecules was investigated with the energy decomposition analysis (EDA) and the NBO method. The calculations show that the ruthenium-carbon bond in the 16VE complex **1Ru** is very strong., the theoretically predicted BDE is D<sub>e</sub> = 146.5 kcal/mol. This is much higher than the BDE of the related CO complex [Cl<sub>2</sub>(PMe<sub>3</sub>)<sub>2</sub>Ru(CO)] which has a BDE of D<sub>e</sub> = 44.6 kcal/mol. The 16VE ruthenium complexes have larger bond dissociation energies for the C and CO ligands than the 16VE iron complexes. The opposite trend is calculated for the 18VE complexes. The Ru-C and Fe-C bonds in **1Ru** and the iron analogue are best described in terms of interactions between a carbon atom with the electron configuration (2s)<sup>2</sup>(2p<sub>z</sub>(σ))<sup>1</sup>(2p<sub>x</sub>(π))<sup>1</sup>(2p<sub>y</sub>(π))<sup>0</sup> and a metal fragment with the corresponding electron configuration at the metal atom d<sub>z</sub><sup>2</sup>(σ)<sup>1</sup>d<sub>xz</sub>(π)<sup>1</sup>d<sub>yz</sub>(π)<sup>2</sup>. This yields two electron sharing bonds with σ and π symmetry and one donor-acceptor π bond. The bonding situation in the 18 VE complexes of ruthenium and iron is better described in terms of closed shell donor-acceptor interactions between carbon atom possessing the electron configuration 2s<sup>2</sup>2p<sub>z</sub>(σ)<sup>2</sup>2p<sub>x</sub>(π)<sup>0</sup>2p<sub>y</sub>(π)<sup>0</sup> and metal fragments with the configuration d<sub>z</sub><sup>2</sup>(σ)<sup>0</sup>d<sub>xz</sub>(π)<sup>2</sup>d<sub>yz</sub>(π)<sup>2</sup>.

A comparative analysis of the bonding situation in which complexes with a terminal carbon atom bind via the carbon atom to a Lewis acid will be given as well.



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## New Ti(IV) Complexes with 2-Aminopyrroline Ligands and their Application as Hydroamination Catalysts

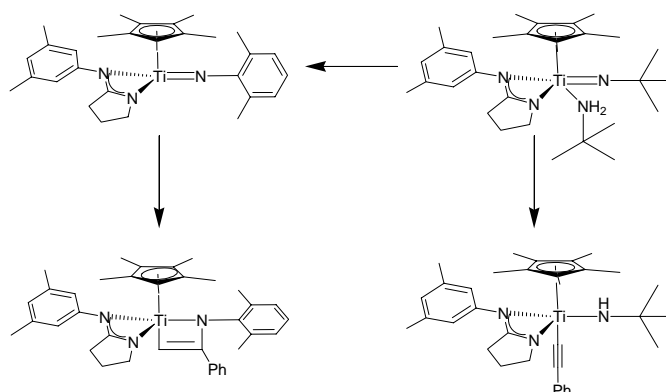
Katharina Weitershaus,<sup>a</sup> Benjamin D. Ward,<sup>a</sup> Carsten Müller,<sup>b</sup> Sven Doye,<sup>b</sup>, Hubert Wadepohl<sup>a</sup> and Lutz H. Gade<sup>a\*</sup>

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The addition of amines across carbon-carbon multiple bonds, the hydroamination reaction, is a fundamental, yet highly important reaction in synthetic organic chemistry, affording compounds which are building blocks for a wide variety of compounds in both academia and industry. Titanium in particular has shown much promise in hydroamination catalysis, and the Ti-catalysed hydroamination of C-C double and triple bonds has attracted significant attention in recent years.<sup>1</sup> Although many Group 4 complexes are known to catalyse the hydroamination reaction, a general catalytic system remains elusive. In order to achieve this objective, it is important to increase our knowledge of the catalytic system, especially regarding catalytic intermediates; such studies will ultimately lead us closer towards a general catalytic system which will be of immense importance for all branches of synthetic organic chemistry.

Inspired by the work of Bergman,<sup>2</sup> we focused our attention on half sandwich complexes of Ti(IV) containing 2-aminopyrrolines as rigid ancillary amidinate ligands.<sup>3</sup> We report on the synthesis and characterisation of a series of amido- and imido-supported complexes, and their employment as catalysts for the hydroamination of various substrates; in addition we report on the synthesis and characterisation of complexes arising from stoichiometric reactions with alkynes, of which some may be regarded as important catalytic intermediates, allowing the furtherance of our understanding of this reaction.



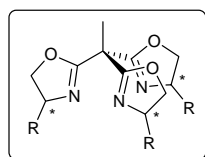
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## C<sub>3</sub>-symmetrical Chiral Trisoxazoline Ligands in Asymmetric Catalysis

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Stéphane Bellemin-Laponnaz,<sup>b</sup> and Lutz H. Gade<sup>a,\*</sup>

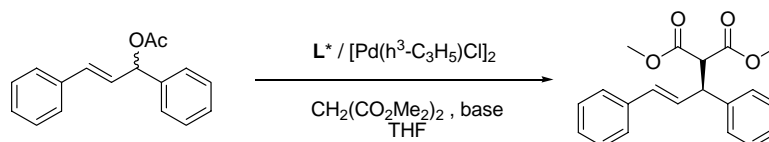
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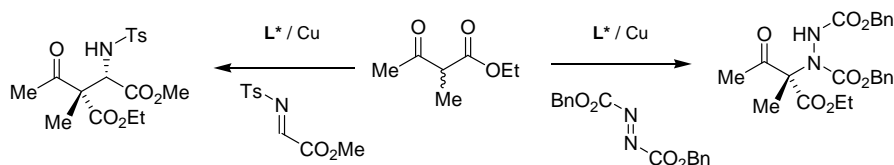


In contrast to the large number of C<sub>2</sub>-symmetric chiral ligands which are employed in asymmetric catalysis, the chemistry of C<sub>3</sub>-chiral polydentate ligands remains poorly developed. In this context, we recently reported a new class of chiral trisoxazoline tripod ligands and have begun studying their properties in asymmetric catalysis.<sup>1</sup>

The C<sub>3</sub>-symmetry was exploited in the dynamic coordination of a chiral trisoxazoline to palladium(0) and (II). Dynamic exchange between three symmetry-equivalent binding sites is observed for precatalysts of allylic alkylations. The third ligating unit in the C<sub>3</sub>-chiral stereodirecting ligands leads to superior catalyst performance compared to the bisoxazoline analogues.<sup>2</sup>



Promising results were obtained in the case of copper(II)-mediated transformations. The asymmetric Mannich reaction and the enantioselective  $\alpha$ -amination of  $\beta$ -ketoesters were investigated.<sup>3</sup> In both cases, the Cu(II)-trisoxazoline system showed good activities and high enantioselectivities.<sup>4</sup>



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# Peripherally Functionalised Dendritic Bisphosphines and their Application as Ligands for Asymmetric Hydrogenation and Hydrosilylation Reactions

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Enantioselection in a stoichiometric or catalytic reaction is governed by small increments of free enthalpy of activation, and such transformations are thus in principal particularly suited to assess "dendrimer effects" which result from the immobilisation of the catalyst. Chiral dendrimer catalysts, which possess a high level of structural regularity, molecular monodispersity and well defined catalytic sites, have been generated by the immobilisation of chiral catalysts onto the established non chiral dendrimers.<sup>[1]</sup>

In our investigation into the enantioselective induction of dendrimer-fixed catalytic systems we choose two different types of diphosphine, the known ligand Pyrphos<sup>[2]</sup> and H-AMINAP, a functionalised BINAP<sup>[3]</sup> ligand. These diphosphine ligands were attached to the amino-end groups of PPI- and PAMAM-dendrimers using glutaric acid as a linking unit (Figure 1).

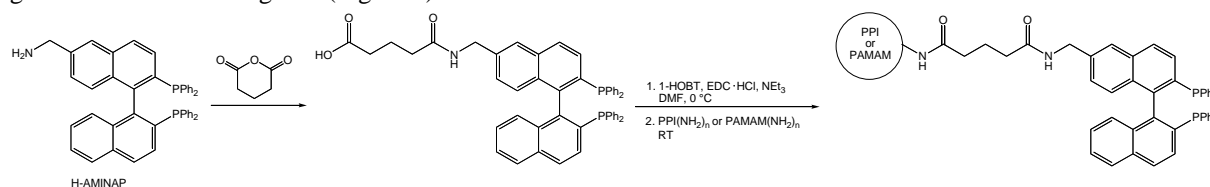


Figure 1: Synthesis of the dendritic AMINAP-ligands.

In the case of the dendritic Pyrphos-systems we studied the asymmetric hydrogenation of *Z*-methyl- $\alpha$ -acetamidocinnamate catalysed by rhodium(I) complexes. Generally, a decrease in activity and selectivity of the dendrimer catalysts was observed on going to higher generations of the dendrimers.<sup>[4]</sup> By changing the rhodium precursor from  $[\text{Rh}(\text{COD})_2]\text{BF}_4$  to  $[\text{Rh}(\text{NBD})_2]\text{BF}_4$  we obtained catalysts with enhanced activity, without changing the selectivity,<sup>[5]</sup> which may also be exploitable under heterogeneous conditions.

The immobilised AMINAP-systems were tested as ligands in the copper(I) catalysed hydrosilylation of acetophenone. In this case the observed activity and selectivity of the dendritic catalysts was unchanged compared to the monomeric system (Figure 2), but slightly enhanced compared to the unfunctionalised BINAP.

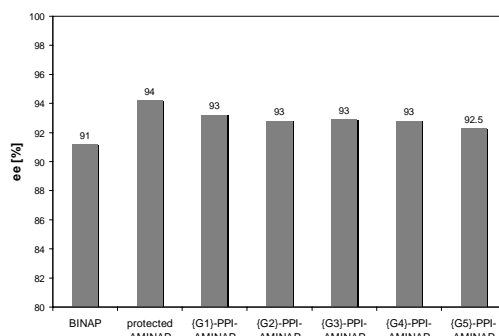


Figure 2: Selectivity of the dendritic AMINAP-ligands in the hydrosilylation of acetophenone.

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## A Modular Synthesis of Oxazoline / N-heterocyclic Carbene Ligands and their Application in Asymmetric Catalysis.

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Hubert Wadepohl<sup>a</sup> and Lutz H. Gade<sup>a,\*</sup>

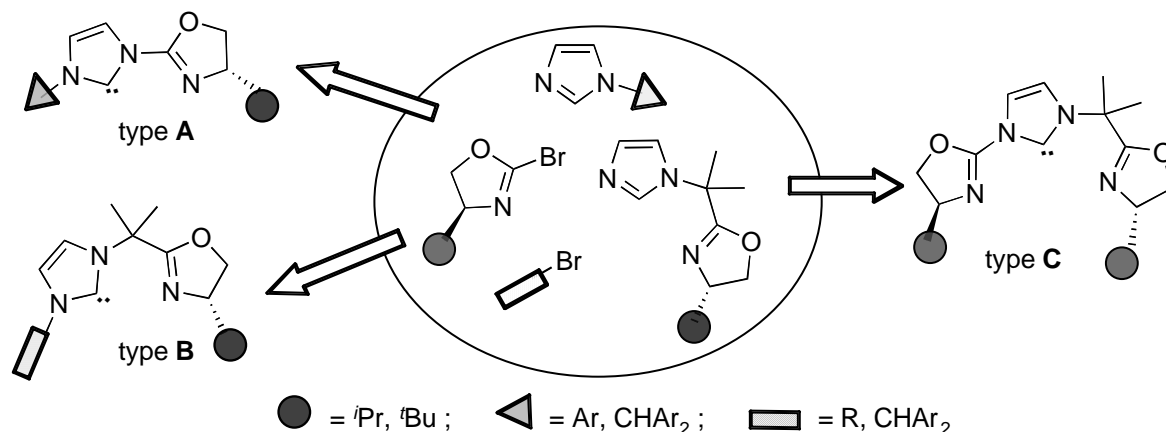
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Since the first isolation of a free N-heterocyclic carbene by Arduengo in 1991, the chemistry of these compounds, especially their coordination chemistry, has been intensively investigated.<sup>1</sup> Although some very active molecular catalysts containing these ligands have been developed, relatively few chiral derivatives are known to date which induce high enantioselectivity in catalytic transformations.<sup>2</sup>

The modular coupling of oxazolines and N-heterocyclic carbenes leads to chelating C,N ancillary ligands for asymmetric catalysis that combine both an “anchor” unit and a stereodirecting element.<sup>3</sup> Having established these building blocks, we have generated bidentate<sup>4</sup> (type **A** and **B**) as well as tridentate<sup>5</sup> (type **C**) ligands in simple one-step processes.

In particular, the coordination of bidentate (type **A**) ligands to rhodium (I) has been explored, and the complexes have been successfully employed in the catalytic asymmetric hydrosilylation of ketones.<sup>6</sup>



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3. For review on mixed oxazoline-carbenes as stereodirecting ligands in asymmetric catalysis, see : L.H. Gade, S. Bellemin-Lapponnaz, *Coor. Chem. Rev.*, **2007**, *251*, 718.

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## Isotactic Polymerisation of $\alpha$ -Olefins Catalysed by $C_3$ -Symmetric Lanthanide Complexes

Lenka Lukešová,<sup>a</sup> Benjamin D. Ward,<sup>a</sup> Stéphane Bellemin-Laponnaz,<sup>b</sup>  
Hubert Wadepohl,<sup>a</sup> and Lutz H. Gade<sup>a,\*</sup>

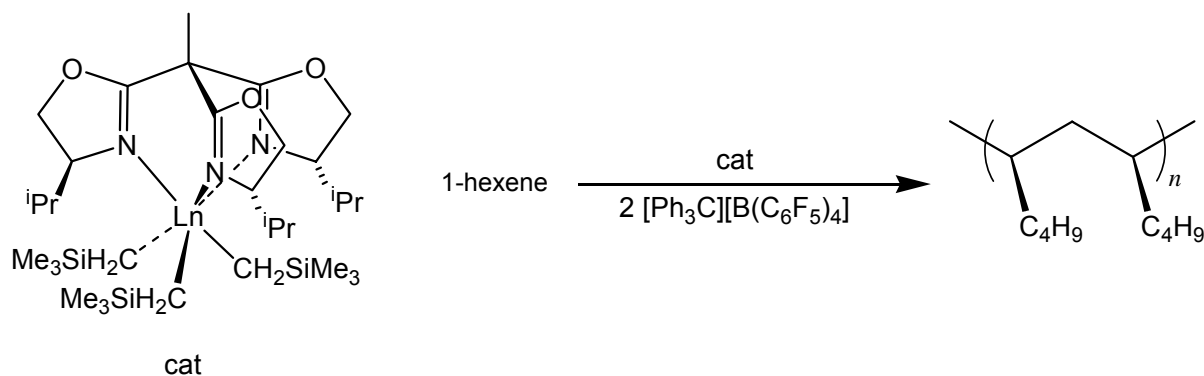
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Olefin polymerisation by “post-metallocene” Group 4 complexes has been studied extensively over the last 15 years,<sup>1</sup> whereas in contrast the corresponding Group 3 and lanthanide systems have received relatively little attention. Although reports of ethylene polymerisation catalysts are more numerous,<sup>2</sup> the employment of Group 3 and lanthanide catalysts for the stereospecific polymerisation of higher  $\alpha$ -olefins remains scarce.

As part of our ongoing research programme into asymmetric catalysis using the 1,1,1-tris(oxazolinyl)ethane (“trisoX”) ligand, we have prepared a series of lanthanide complexes of the form  $[\text{Ln}(\text{iPr-trisoX})(\text{CH}_2\text{SiMe}_3)_3]$  (**1**, Ln = Sc, Y, lanthanide). On activation with trityl borate, cationic complexes (**2**) were formed, which were employed as catalysts for the polymerisation of 1-hexene, 1-heptene, and 1-octene.<sup>3</sup>

In some cases, extremely active catalysts were obtained, with activities comparable to those of post-metallocene Group 4 complexes.<sup>4</sup> The resulting polymers were obtained with a high degree of isotacticity, up to 95%, of the *mmmm* pentad.



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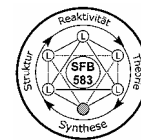
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## Applications of Phosphines in Cage Construction for $L_nM$ Rotators and Catalysis of Cycloadditions

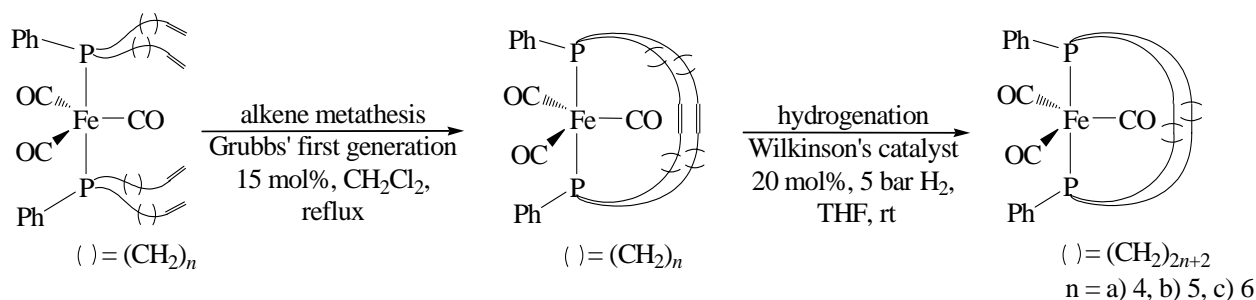


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91054 Erlangen, Henkestraße 42, Germany.*

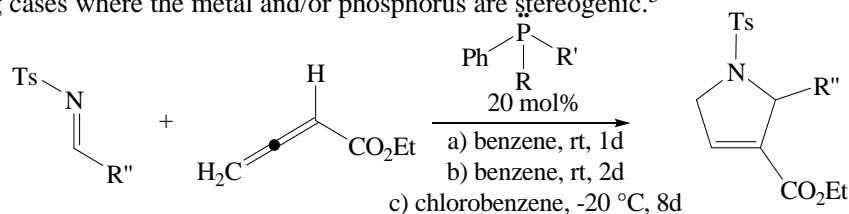
Phosphines are widely used in organic and organometallic chemistry. This poster will highlight two recent applications from our research group.<sup>1,2</sup>

The first involves the synthesis of gyroscope-type molecules. These consist of a rotator – a  $L_nM$  metal center – and a stator – a cage-like shielding enclosure derived from a P-M-P axis. As shown in the representative sequence in Scheme 1, alkene metathesis is first used to join two *trans* phosphine ligands that bear  $(CH_2)_nCH=CH_2$  groups, in this specific example coordinated to trigonal bipyramidal iron. Subsequent hydrogenation with Wilkinson's catalyst gives the two-spoked target molecule.<sup>3</sup>



**Scheme 1:** Representative Synthesis of Gyroscope-like Molecules.

The second involves metal-containing "organocatalysts". Over the last decade, there has been intense interest in phosphine-catalyzed reactions.<sup>4</sup> However, with the exception of ferrocenyl-containing systems; catalysts that feature "spectator" transition metal fragments have been ignored. These offer numerous architectural possibilities. Furthermore, it is well established that in eighteen-valence-electron complexes, the Lewis basicities and nucleophilicities of heteroatoms  $\alpha$  and  $\beta$  to the metal are markedly enhanced. As shown in Scheme 2, a variety of rhenium- and manganese-containing phosphines have been examined as catalysts for [3+2] cycloadditions of imines and allenes, including cases where the metal and/or phosphorus are stereogenic.<sup>5</sup>



R/R' = (*S*)- or (*rac*)- $(\eta^5-C_5H_5)Re(NO)(PPh_3)(CH_2-)/Ph-$ ;  
 $(\eta^5-C_5H_4-)Re(CO)_3$  or  $(\eta^5-C_5H_4-)Mn(CO)_3/t-Bu-, i-Pr-, Cy-, Ph-$  | R'' =  $C_6H_5-, p-C_6H_4NO_2-, p-C_6H_4OMe-, p-C_6H_4Me-,$   
 $p-C_6H_4F-, p-C_6H_4Cl-, p-C_6H_4Br-, 2-furyl, CH=CHC_6H_5$

**Scheme 2:** Manganese and Rhenium-containing Phosphines as Catalysts for [3+2] Cycloadditions.

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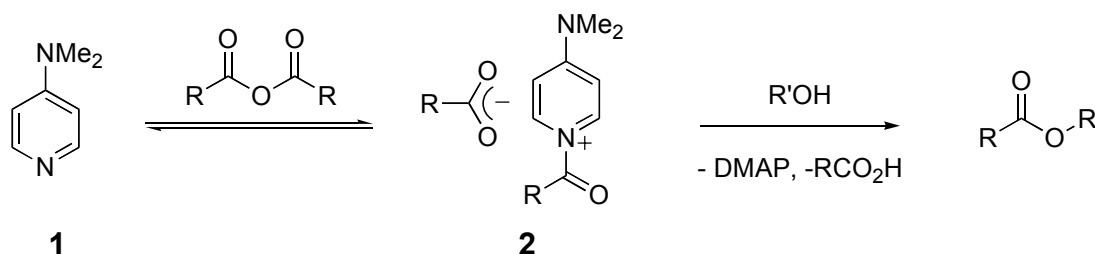
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## New Aspects of Dimethylaminopyridine Catalysis

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Dimethylaminopyridin (DMAP) **1** and analogues are highly active organocatalysts for the acylation of alcohols, amines and amino acids.<sup>[1]</sup> Recently, efforts were put into the development of stereoselective variants<sup>[2]</sup> that demand deeper insight into the reaction mechanism.<sup>[3]</sup> In this context we focus on the unexplored role of the counterion in dimethylaminopyridinium salts **2**, which are supposed to represent the catalytically active species.<sup>[3]</sup>



To study these organocatalytic reactions a new matrix isolation protocol was developed. A frozen matrix was prepared by co-deposition of **1**, various anhydrides, and an organic solvent at 40 K. By slowly raising the temperature the formation of **2** was initiated and progress was monitored by IR spectroscopy. The 70 – 200 K range also allows direct comparison with low temperature IR and NMR experiments in solution.

Depending on the nature of the anhydride, the reaction begins at unexpectedly low temperatures and **2** forms almost quantitatively. As a function of the anion the geometry of **2** changes with increasing temperature under conversion to the thermodynamically most favored ion pair.

### Literature

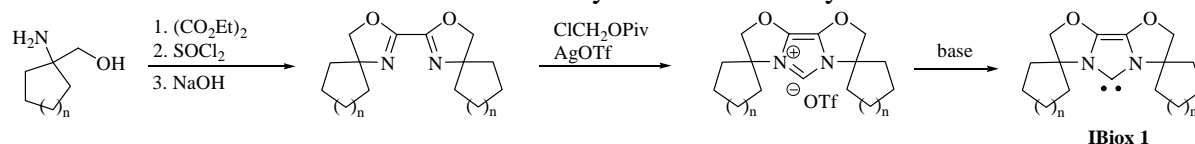
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## Novel bioxazoline derived N-heterocyclic carbenes (NHC) as ligands for palladium-catalyzed cross-coupling reactions

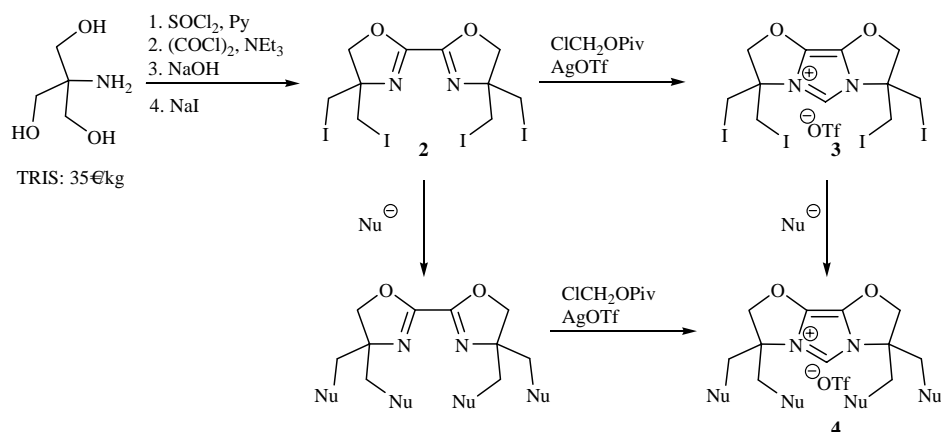
Sebastian Würtz, Frank Glorius\*

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35032 Marburg

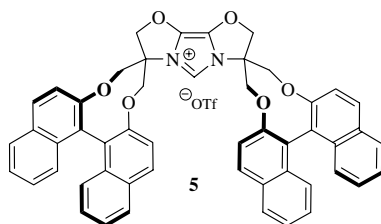
The number of N-heterocyclic carbene-ligands is rapidly growing. Classic phosphane ligands are increasingly replaced by carbenes in transition metal catalyzed reactions. Carbene-metal complexes are distinguished from phosphane-metal complexes by their higher thermal stability and superior tolerance to acidic conditions with simultaneously increased activity in numerous reactions.<sup>[1]</sup>



Based on a rigid tricyclic backbone we designed chiral  $C_2$ -symmetric NHCs<sup>[2]</sup> as well as achiral NHCs **1**<sup>[3,4]</sup> with flexible steric demand (IBiox). The steric flexibility may be beneficial for the high catalyst activity of the corresponding palladium-complexes in cross-coupling reactions of sterically hindered substrates. By varying the ring-size of the carbocycles of NHCs **1** we are able to create a family of ligands with different steric demand without affecting the electronic character. The results of Suzuki<sup>[3,4]</sup> and Sonogashira coupling reactions<sup>[5]</sup> catalyzed by palladium-complexes of these ligands will be presented.



Moreover, we followed an alternative synthetic strategy starting from commercially available TRIS to get access in only few easy steps to the synthetic building block **3**. After nucleophilic substitution the IBiox-salt **3** or the bioxazoline precursor **2** respectively, can be converted into a multitude of IBiox-salts **4**. This new strategy allows for the synthesis of novel  $C_2$ -symmetric ligands with axial chirality **5**, for instance.



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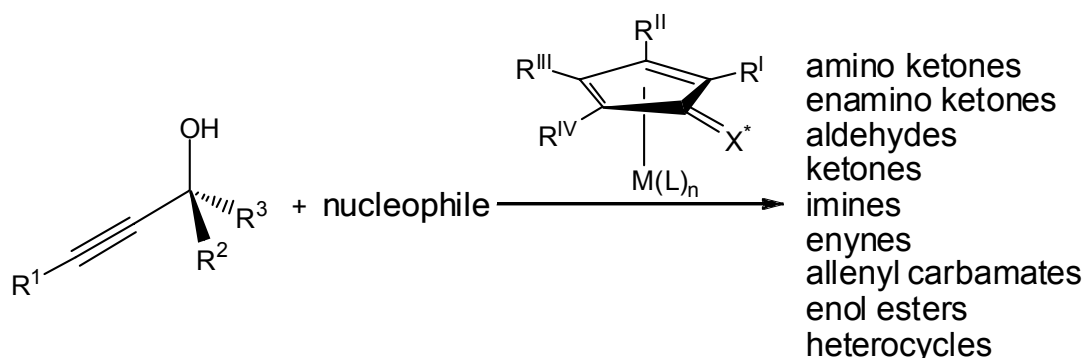
## Ruthenium Complexes of Redox-Coupled Cyclopentadienone Ligands - Catalysts in Transformations of Propargyl Alcohols

Haak, E., Braunschweig/D

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Hagenring 30, D-38106 Braunschweig

The development of new flexible methods to obtain substance classes of biological relevance is of high interest. The homogeneous transition metal catalysis delivers various processes and a brought range of new mechanisms to this field. We investigate transition metal catalyzed processes using complexes of redox-coupled ligands to obtain relevant especially nitrogen containing substance classes. New ligand systems that are suitable for electronic coupling are developed and their corresponding transition metal complexes are generated. Especially ruthenium derivatives are easily accessible, stable and show interesting catalytic activities towards various transformations of propargyl alcohols. Catalytic procedures to obtain  $\alpha$ -, or  $\beta$ -amino ketones, enamino ketones, aldehydes, ketones, imines, enynes, allenyl carbamates, enol esters or heterocycles could be archived.<sup>[1]</sup>

The formation of neutral vinyliden- and allenyliden-species as central intermediates is of major interest since these complexes cyclize after regioselective addition of functionalized nucleophiles.<sup>[2]</sup> New ligand systems that are suitable for electronic coupling and studies about the influence of their electronic and steric nature on the catalytic mechanisms are presented besides new catalytic transformations.



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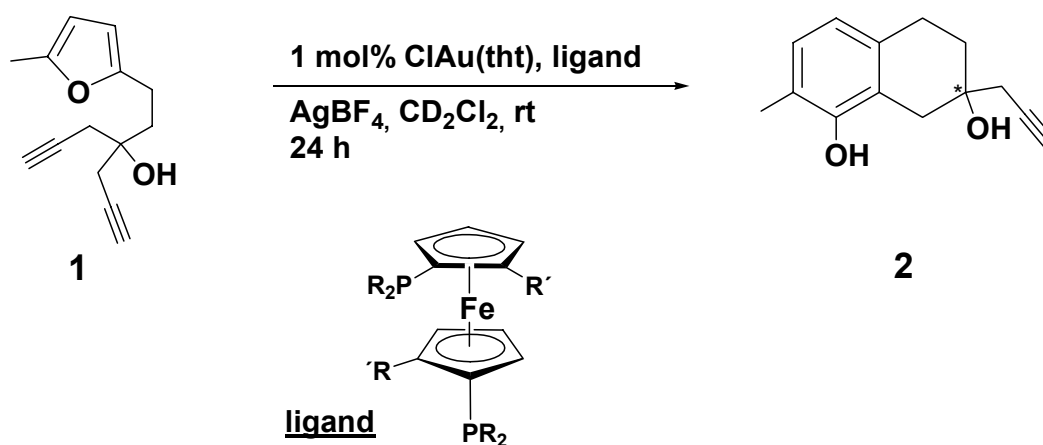
## The Application of Chiral Ferrocenyldiphosphane-Gold(I) Complexes in Enantiotopos Differentiating Arene Synthesis

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Melissa.Hamzic@oci.uni-heidelberg.de

In 1986, Ito and Hayashi reported an elegant synthesis of oxazolines utilizing a gold(I)-catalyzed aldol reaction in the presence of chiral amino-ferrocenyldiphosphane ligands that possess both planar and central chirality.<sup>1,2</sup>

21 years after this initial finding, we now try to revive research on this type of chiral catalysts. The influence of similar chiral ferrocenyldiphosphane ligands in the gold-catalysed arene synthesis<sup>3</sup> is investigated.

Furan **1** with enantiotopic alkynyl groups can easily be prepared in few chemical transformations starting from 5-methyl-2-furaldehyde. The results of the subsequent cycloisomerization reaction, catalyzed by gold complexes of these ligands, will be discussed at the poster.



### References:

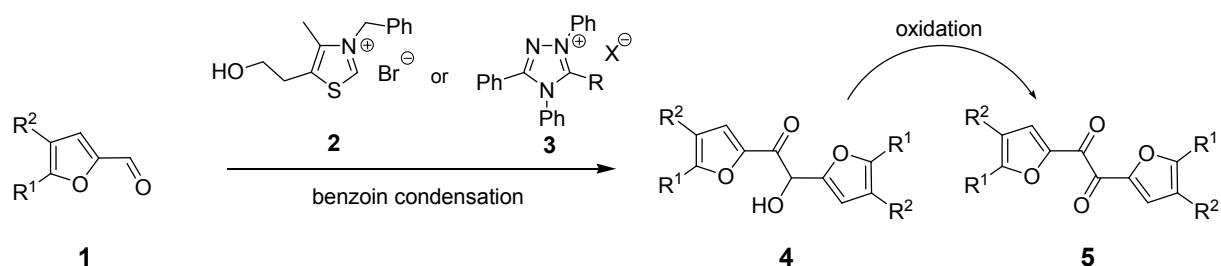
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## Gold-Catalysis with Substrates from Organocatalysis

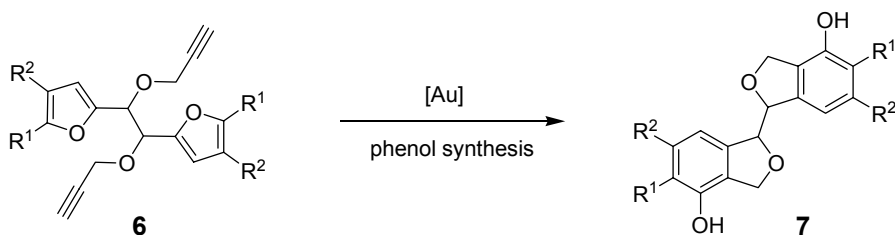
Michael Wölfle, A. Stephen K. Hashmi, Institut für Organische Chemie,  
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The gold catalyzed phenol synthesis presents a versatile method to generate annelated phenols from substituted furans.<sup>[1,2]</sup>

For the synthesis of highly substituted furan derivatives **5**, the benzoin condensation of aldehydes was used catalyzed by nucleophilic carbenes generated from thiazolium salts **2** and triazolium salts **3**.<sup>[3,4]</sup> Only few examples for diverse furan derivatives are hitherto known.<sup>[5]</sup> Thus we prepared more complex furan derivatives from different substituted furyl aldehydes.



Reduction and subsequent propargylation of **4** or **5** leads to substrate **6**, which was transferred to dihydroisobenzofuran **7** by gold catalysis.



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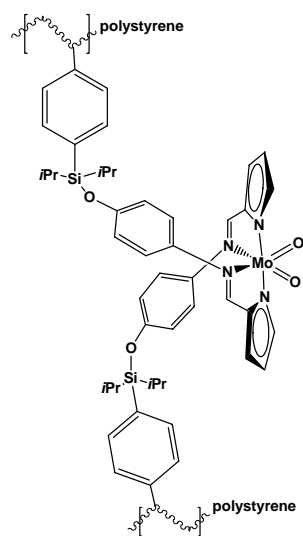
## Polymer-supported truly functional Molybdenum Oxotransferase Model System

**Andreas Fischer, Katja Heinze**

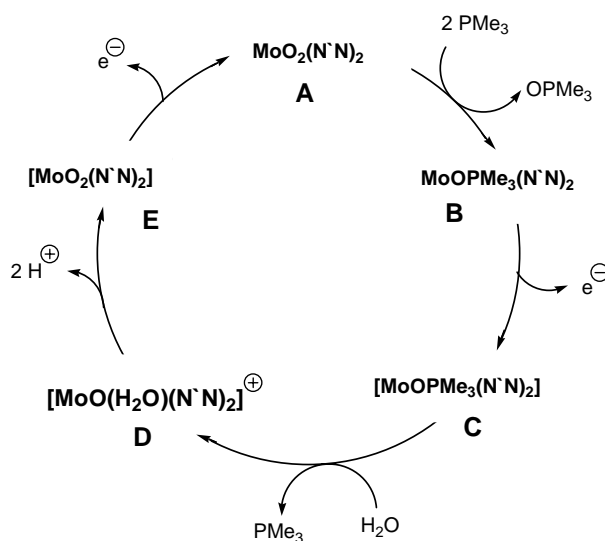
Department of Inorganic Chemistry, University of Heidelberg, Im Neuenheimer Feld 270,  
69120 Heidelberg, Germany. e-mail: [andreas.fischer@aci.uni-heidelberg.de](mailto:andreas.fischer@aci.uni-heidelberg.de)

The aim of this project is to employ polymers as support for biomimetic catalysts (benchmark reaction: oxygen atom transfer to phosphanes). On the basis of doubly immobilised dioxomolybdenum complexes (*two-point-fixation*) it is possible

- to isolate the active sites thus preventing deactivation via condensation and electron transfer,
- to minimise leaching, i.e. the loss of catalytic active species and
- to observe the active species during catalysis in situ on the polymeric support.



**Immobilised complex A**



**Suggested catalytic cycle**

The immobilised complex **A** catalyses the net transfer of an oxygen atom from water to trimethylphosphane with diacetylferrocenium-tetrafluoroborate as one-electron oxidant and phosphazene base P<sub>1</sub>-*t*Bu as proton acceptor. This model complex mimics the full catalytic cycle of a Molybdenum Oxotransferase. Mononuclear paramagnetic Mo(V)-species **C**, **D** and **E** relevant to the catalytic cycle are observed by EPR spectroscopy<sup>[1]</sup>.

<sup>[1]</sup> K. Heinze, A. Fischer, *Eur. J. Inorg. Chem.* **2007**, 1020-1026.

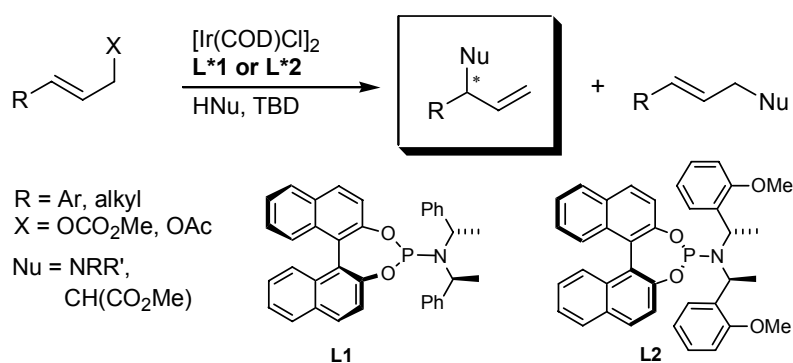
## Intermolecular Enantioselective Iridium-Catalyzed Allylic Amination as Key Step in the Synthesis of Tobacco Alkaloids

Carolin Welter and Günter Helmchen

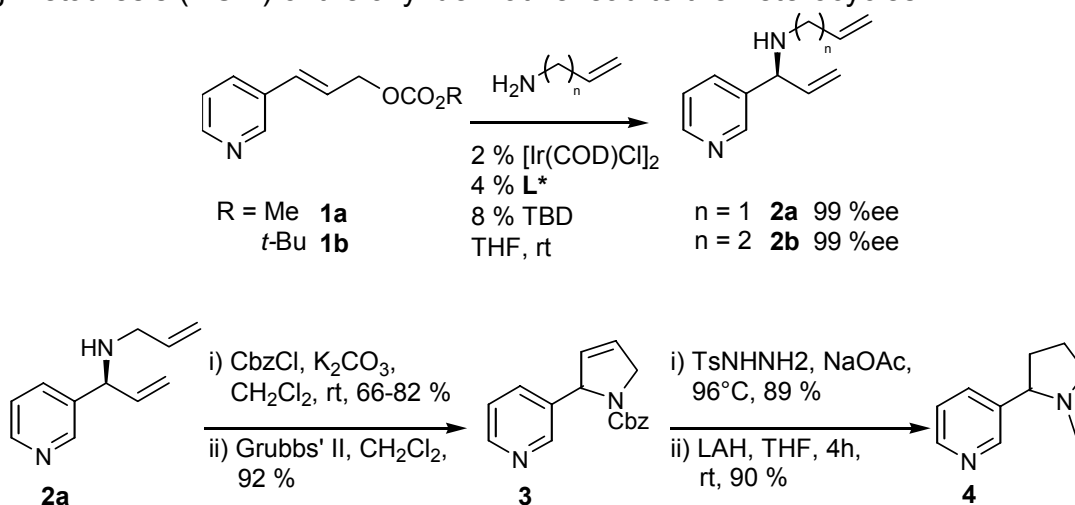
Organisch-Chemisches Institut der Ruprecht-Karls-Universität Heidelberg, Im Neuenheimer Feld 270,  
D-69120 Heidelberg, Germany; E-mail: carolinwelter@yahoo.de

In 1999, our group discovered that phosphorus amidites based on enantiomerically pure BINOL are particularly effective ligands<sup>1</sup> in Iridium catalyzed enantioselective alkylations and aminations.

It was previously found that active Ir-catalysts are generated by C-H activation promoted by the nucleophile or base.<sup>2</sup> Good results with respect to enantioselectivity were obtained upon activation with 1,5,7-triazabicyclo[4.4.0]undec-5-ene (TBD).<sup>3</sup>



In recent years nicotine (**4**) and related tobacco alkaloids (e.g. nor nicotine and anabasine), acting as agonists on nicotinic acetylcholine receptors (nAChR), have received considerable attention. Our synthesis strategy of **4** was based on Ir-catalysed allylic aminations, which proceeds with unusually high regio- and enantioselectivity, following ring closing metathesis (RCM) of the allyl derivative lead to the heterocycles.<sup>4</sup>



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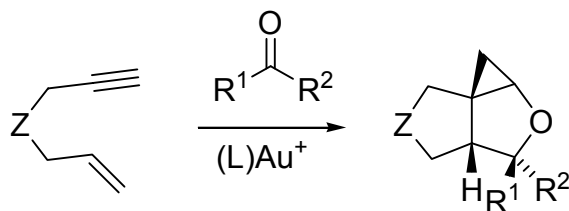
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## Gold-Catalyzed Intermolecular Addition of Carbonyl Compounds to 1,6-Enynes

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The study of transition-metal catalyzed cycloisomerization reactions of 1,6-enynes has led to innovative new reactions in organic synthesis. In this context, cationic Au(I) complexes have found increasing use as homogeneous catalysts and offer access to a variety of complex polycyclic systems.<sup>1</sup> Recently, we have found a novel and surprising Gold(I)-catalyzed intermolecular addition of carbonyl compounds to enynes leading to 2-oxabicyclo[3.1.0]hexanes with high stereoselectivity.<sup>2</sup>



As observed with many enyne cyclizations before, in the present case the catalyst [AuCl(PPh<sub>3</sub>)]/AgSbF<sub>6</sub> showed particularly high activity. A variety of aldehydes and ketones were reacted with high degrees of diastereoselectivity. Optimization, scope and mechanistic aspects of the reaction are presented.

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## Enantioselective Ir-Catalyzed Allylic Alkylations - Improvements and Applications Based on Salt-Free Reaction Conditions<sup>1</sup>

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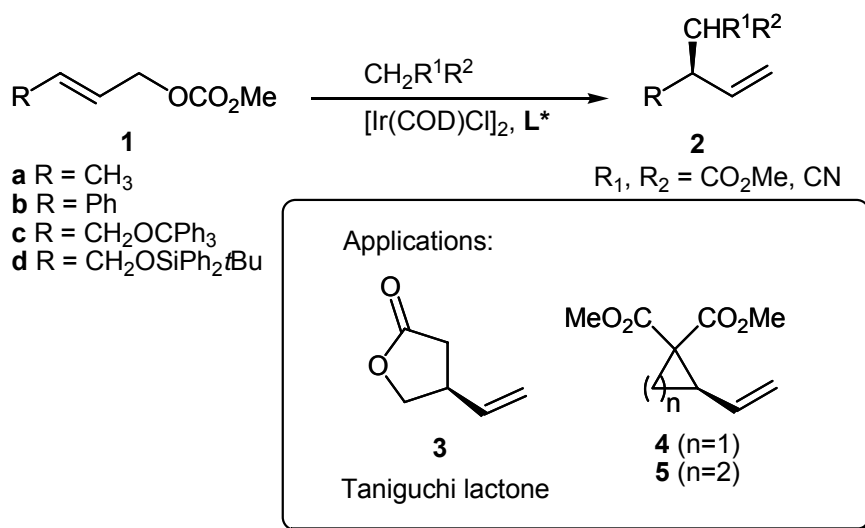
In recent years, the Ir-catalyzed allylic substitution has become a reliable method to synthesize chiral compounds **2** with high degrees of regio- and enantioselectivity from easily available monosubstituted allylic carbonates **1**.<sup>2</sup>

Scale-up ( $\geq 10$  mmol) disclosed a number of problems: (a) Highest selectivities were generally obtained with THF as solvent. Difficulties arose because of generally low solubility of alkali metal salts of  $\beta$ -dicarbonyl compounds. (b) Ir-catalysts usually employed, which are prepared from  $[\text{Ir}(\text{COD})\text{Cl}]_2$  and a phosphorus amidite by base induced CH-activation, are not stable against base in the long term. (c) In cyclizations, deprotonation of the malonate gives rise to the competitive non-catalyzed reaction pathway, which leads to reduced enantioselectivity.

Salt-free reaction conditions<sup>3</sup> were particularly effective in the case of methyl cyanoacetate. With the sodium salt no reaction occurred due to its very low solubility in THF. Under salt-free conditions, the carbonate **1c** and **1d** were alkylated with high degrees of regio- and enantioselectivity.

As one of several applications of this salt-free variant, we have carried out a highly enantioselective synthesis of Taniguchi lactone (**3**), the starting material of Stork's quinine synthesis and other natural product syntheses.

Furthermore, salt-free conditions allowed the known vinylcyclopropane **4** as well as the so far unknown vinylcyclobutane **5** to be prepared with high enantioselectivity.



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## Direct observation of complex formation and dissociation of single 2,2'-bipyridene-4,4'-dicarboxylic acid copper(II) complexes by single-molecule fluorescence spectroscopy

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In many catalytic reactions the first reaction step consists of formation of a complex of at least one component with a metal ion, lowering the activation energy and thus accelerating the reaction. As it is difficult to observe all reaction steps in one experiment we first focused on the development of a probe that allows us to follow the formation and dissociation of a copper(II) bipyridine complex with single-molecule fluorescence spectroscopy (SMFS). The probe design exploits the effect that some fluorescent dyes, like ATTO620 or TMR, are influenced in their fluorescence emission in presence of different metal ions or metal ion complexes. We designed dye-ligand conjugates that can be immobilized on glass surfaces to study metal-ion-binding by time-resolved SMFS. The probes consist of double stranded DNA-oligonucleotides as a rigid scaffold carrying 2,2'-bipyridene-4,4'-dicarboxylic acid as chelating ligand and a fluorescent dye as reporter, placed in close vicinity to the ligand. While the free probes show high fluorescence intensity, we observed strong fluorescence quenching upon binding of Cu<sup>2+</sup>-ions. Time-resolved single-molecule measurements revealed stochastic switching between a high-fluorescent (“on”) and a low-fluorescent (“off”) state. A linear dependency of the on-time duration from the copper(II) concentration was observed and attributed to individual association and dissociation events of copper(II)-ions to the ligand. Rate constants of the underlying association and dissociation kinetics of the copper(II)-complex in thermodynamic equilibrium were extracted from fluorescence fluctuations. Since copper(II)-complexes efficiently catalyze ester hydrolysis, we envisage the use of fluorescent substrates allowing to investigate reactions of copper complexes applying SMFS.

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## Cleavage of the N<sub>2</sub> Triple Bond by the Ti Dimer: A Route to Molecular Materials for Dinitrogen Activation?

Olaf Hübner, L. Manceron, W. Klopper, H.-J. Himmel

The dimer Ti<sub>2</sub> was prepared with the aid of the matrix isolation technique and the electronic properties in its electronic ground state (<sup>3</sup>Δ<sub>g</sub>) and several excited electronic states studied by a combination of spectroscopy and quantum chemical (CASSCF and MRCI) calculations.<sup>[1]</sup> Excited states of dimers and clusters are generally involved in their chemical reactions<sup>[2]</sup> and therefore their characterization is of vital importance to obtain a detailed understanding of the reactivity and selectivity of cluster species. Ti<sub>2</sub> turns out to be highly reactive. Thus reaction with N<sub>2</sub> in noble gas matrices leads to complete cleavage of the strong N≡N triple bond and formation of a cyclic, D<sub>2h</sub> symmetric Ti(μ-N)<sub>2</sub>Ti molecule. This result poses the question if it is possible to use small Ti clusters stabilized e.g. in carbon nanotubes for N<sub>2</sub> activation and fixation. This possibility was further tested by quantum chemical calculations performed on formation of NH<sub>3</sub> from N<sub>2</sub> and H<sub>2</sub> using the model catalyst C<sub>60</sub>Ti<sub>2</sub>.<sup>[4]</sup>

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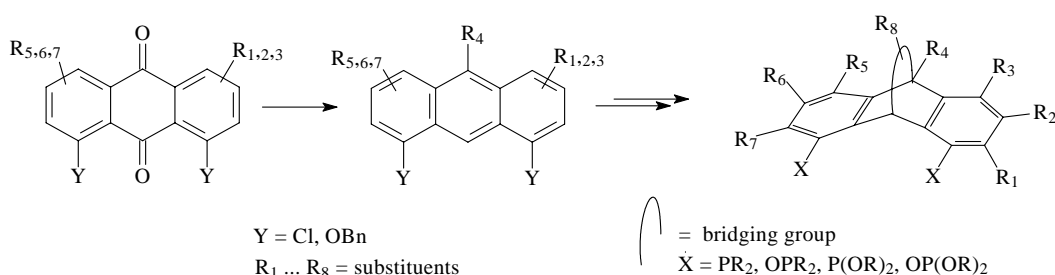
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## A New Class of Modular, Phosphorus Based Chelate Ligands for Nickel-Catalyzed Hydrocyanation and Pentene Nitrile Isomerization

M. E. Tauchert, F. Rominger and P. Hofmann

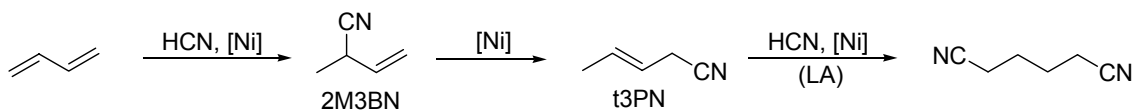
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We recently developed a new class of modular, easily accessible phosphorus based chelating ligands. These ligands can be prepared in three to six steps with broad structural diversity in up to 80% overall yield (Fig. 1).<sup>[1]</sup>



**Fig. 1:** General synthesis and substitution pattern for the novel ligand systems.

The most prominent industrial application of homogeneous hydrocyanation is the so-called adiponitrile process (Fig. 2), in which butadiene is converted into adiponitrile - an important building block for nylon production - in a three step process.<sup>[2]</sup>



**Fig. 2:** Nickel-catalyzed adiponitrile process.

Our new ligand systems, using in particular bisphosphine and bisphosphonite derivatives, was successfully applied in the isomerization of 2M3BN into t3PN, and in the hydrocyanation of styrene.

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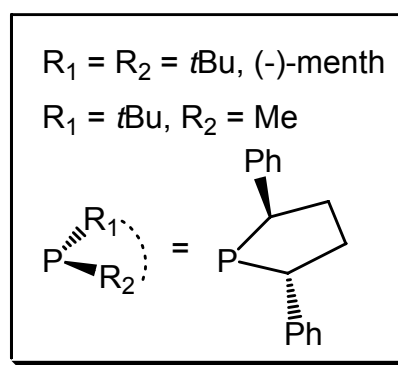
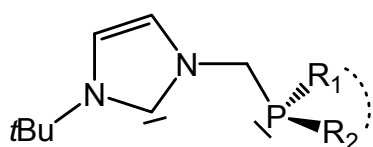
## NHCP Ligands: Group 10 Metal Complexes of a New Class of Bulky, Electron-Rich Phosphinomethyl Functionalized N-Heterocyclic Carbenes

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We describe a new class of chelating N-heterocyclic carbene ligands, in which an imidazolylidene ring is N-functionalized with achiral or various types of chiral phosphinomethyl substituents (NHCP ligands).



Only a few examples of related ligand systems have appeared in the literature<sup>1</sup>. None of them features a dialkyl substitution pattern at the phosphine moiety, which makes the P-donor atom sterically bulky and electron rich. By variation of the phosphorus substitution pattern it is possible to introduce chirality adjacent to metal centers in five-membered chelate structures and to fine-tune the steric bulk.

Reaction of these ligands with different group 10 metal precursors leads to various neutral and cationic complexes which are characterized by X-ray structure analysis and which provide access to interesting chemistry.

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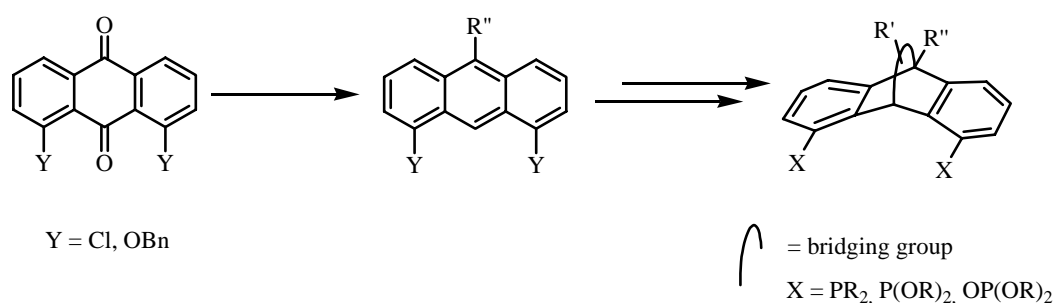


## NOVEL CHELATING DIPHOSPHOROUS LIGANDS IN RHODIUM-CATALYSED HYDROFORMYLATION

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New highly modular bisphosphine-, bisphosphonite- and bisphosphite chelate ligands, starting from commercially available or easily accessible 1,8-disubstituted anthraquinones<sup>[1]</sup> have been developed. In Rh-catalysed low pressure hydroformylation of 1-octene this new lead structure (the TTP ligand family) provides highly active (TOF > 10000) and highly *n*-selective (> 99%) catalysts.



Until now, no detailed and consistent understanding of activity and selectivity control in hydroformylation by steric and/or electronic effects of ligands has emerged. Therefore three analogs of one of our ligands with electronically modifying substituents at the *para*-positions of their diphenylphosphino moieties have been synthesised and their performance in low-pressure hydroformylation has been tested. The reaction rate is substantially enhanced by electron-withdrawing and decreased by electron-donating substituents, as predicted by a DFT study of the complete catalytic cycle.

In order to investigate the validity of the Wilkinson mechanism<sup>[2]</sup> for these systems, a model compound for elusive alkyl monocarbonyl intermediates of the catalytic cycle has been synthesised and its reactivity towards CO and H<sub>2</sub> has been studied by *in situ* IR- and NMR-techniques. Deuterioformylation experiments have been carried out with representative members of our ligand family. For all of them alkene insertion into the Rh-H bond is not irreversible. Thus a pure kinetic control of *n/i*-selectivity has to be discarded. Olefin insertion reversibility, however, is much more pronounced for *i*-insertions than for *n*-insertions, which ultimately leads to the observed, extremely high *n*-selectivity through thermodynamic control, as opposed to expectations based upon DFT computations assuming pure kinetic control via irreversible insertion steps.

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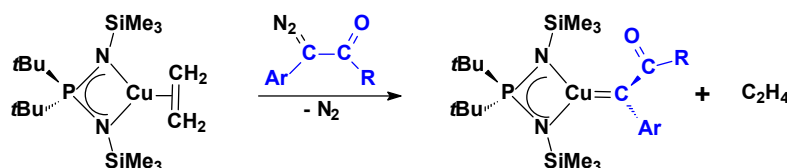
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## Stable Copper(I) Carbenes: Synthesis, Structure, Electronic Structure and Cyclopropanation Reactivity

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Cu(I)  $\alpha$ -carbonyl carbene complexes, postulated over more than 40 years<sup>[1]</sup> as intermediates in copper-catalyzed cyclopropanation with  $\alpha$ -diazo carbonyl compounds, have been isolated utilizing a tailor-made anionic, small bite-angle PNP-chelate ligand. Based upon our earlier report of the synthesis in solution and the spectroscopic characterization of Cu(I) carbenes<sup>[2]</sup> and guided by DFT<sup>[3]</sup> studies, a proper variation of the carbene substituents has enabled us for the first time to characterize an  $\alpha$ -carbonyl copper(I) carbene by X-ray<sup>[4]</sup>. The reaction of  $[t\text{Bu}_2\text{P}(\text{NSiMe}_3)_2-\kappa^2\text{N}]\text{Cu}(\eta^2\text{-C}_2\text{H}_4)$  with various diazo esters afforded the corresponding  $\alpha$ -carbonyl copper(I) carbenes.



The compound  $[t\text{Bu}_2\text{P}(\text{NSiMe}_3)_2-\kappa^2\text{N}]\text{Cu}=\text{C}[p\text{-OCH}_3\text{-C}_6\text{H}_4][\text{C}(\text{O})\text{OCH}(p\text{-Cl-C}_6\text{H}_4)_2]$  was isolated in analytically pure form. We will discuss its molecular structure, its electronic structure (DFT) and reactivity, its dynamic behavior (VT-NMR) and the kinetics for its reaction with styrene to give a *trans*-cyclopropane (1<sup>st</sup> order in both carbene and the alkene) and the associated activation parameters [ $\Delta H^\ddagger = 51.5(9)$  kJ/mol and  $\Delta S^\ddagger = -127.1(28)$  J/(mol·K)]. We will comment upon the cyclopropanation transition state geometry in relation to the Pfaltz-model<sup>[5]</sup> as well as upon copper carbene decomposition pathways, and we will describe the results of a cyclopropanation Hammett parameter study ( $\rho = -1.06(19)$ ) using *p*-substituted styrene substrates.

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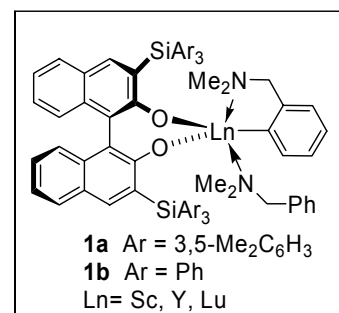
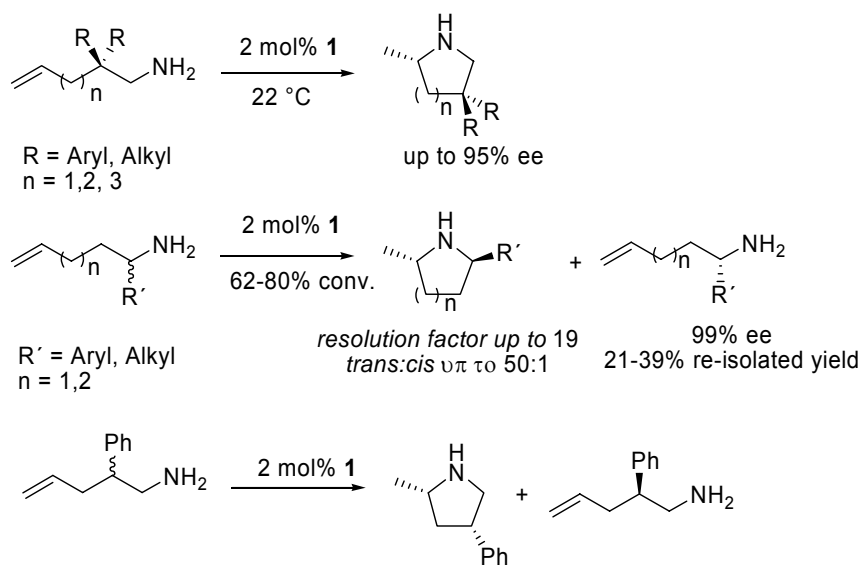
## Rare Earth Metal-Catalyzed Asymmetric Hydroamination/Cyclization of Aminoalkenes (AHA)

Alexander L. Reznichenko, Denis V. Gribkov, Kai C. Hultzsch\*

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The catalytic hydroamination of unsaturated carbon-carbon multiple bonds is an atom-efficient and highly desirable process.<sup>[1]</sup> In particular asymmetric hydroamination reactions have remained challenging. Increased interest in this reaction has led to significant progress utilizing a variety of transition metal catalysts, with rare earth metal based catalyst systems being among the most active and enantioselective as well.<sup>[2]</sup> Recently, our group has developed highly active and highly efficient catalysts based on trisarylsilyl-substituted binaphtholate rare earth metal complexes **1**. Cyclization of aminoalkenes proceed with enantioselectivities of up to 95% ee and high efficiencies in the kinetic resolution of chiral aminoalkenes were observed.<sup>[3]</sup>

In this poster we will discuss in particular recent kinetic investigations of the cyclization involving chiral aminoalkenes, which provide a deeper insight into the mechanism of the kinetic resolution process.



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## **Phosphodiester hydrolysis catalyzed by the restriction enzyme EcoRV: a computational study**

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The restriction enzyme *EcoRV* catalyzes the phosphodiester hydrolysis of the DNA backbone at a specific sequence. AM1d/CHARMM calculations were performed to elucidate the underlying reaction mechanism. A common feature of the computed reaction pathways is the combination of proton transfer and local conformational change, preparing and accompanying the nucleophilic attack as well as the leaving group departure. Dissociative and associative mechanisms are simulated. The rate determining step in both cases is found to be the leaving group departure. The nucleophile is a magnesium activated water molecule positioned in-line for attack at the scissile phosphate.

## **Molecular Simulation on the Ribozyme-Catalyzed Diels-Alder-Reaction**

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### Molecular Simulation on the Ribozyme-Catalyzed Diels-Alder Reaction

Understanding the catalytic mechanisms of a ribonucleic acid enzyme that catalyzes C-C bond formation between anthracene and maleimide derivatives by means of computer simulations is the aim of the project. On basis of experimental results the catalytic reaction mechanism is suggested as the Diels-Alder reaction mechanism [1].

The Molecular Dynamics simulations with classical force fields are used to study RNA - substrate interaction in solvent (H<sub>2</sub>O). Those components which are important for catalysis and their catalytic impact – like the active side shape complementarity with the transition state, in combination with electronic contributions such as stacking of the anthracene substrate and hydrogen bonding to one carboxyl oxygen of the maleimide [1] - are theoretically investigated.

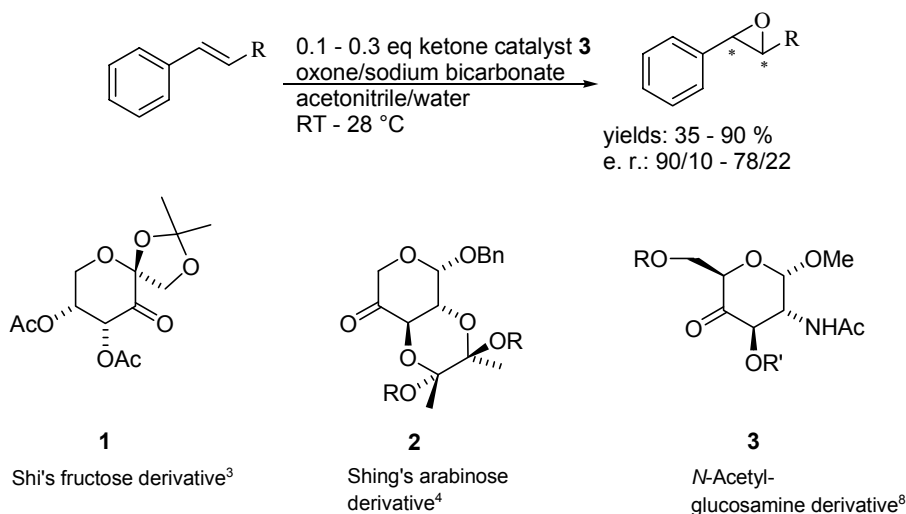
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# ASYMMETRIC ORGANOCATALYSTS FOR EPOXIDATIONS OF OLEFINS AND $\alpha,\beta$ -UNSATURATED ESTERS

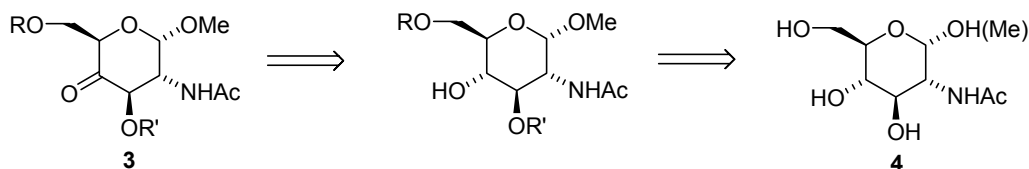
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Recently it was shown that dioxiranes generated *in situ* from chiral ketones can be used as highly enantioselective reagents for epoxidation of alkenes.<sup>1-4</sup> The epoxidations usually are carried out at room temperature with a catalytic amount of ketone and oxone as the oxidizing agent in acetonitrile/water with sodium bicarbonate buffer.



Very efficient catalysts are sugar derivatives like **1** introduced by Shi<sup>3</sup> and **2** reported by Shing et al.<sup>4</sup> We now present a new catalyst, the GlcNAc-derived ketone **3** which was developed in the course of studies concerning the synthesis of glycosidase inhibitors.<sup>5-8</sup> Several aminoketones of type **3** available in a few steps starting from *N*-acetylglucosamine or its glycoside **4**, were prepared.<sup>8</sup> Evaluation of these catalysts for epoxidation of a variety of alkenes and  $\alpha,\beta$ -unsaturated esters will be presented.



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## Anatomy of an RNA active site – dissecting structure and function of a Diels-Alderase ribozyme

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At the atomic level, not much is known about how RNA accelerates chemical reactions. The recently solved X-ray crystal structures of a ribozyme that catalyzes Diels-Alder reactions, both with and without bound reaction product (Serganov et al., *Nat. Struct. Mol. Biol.* 2005, 12, 218), suggest a rich tertiary architecture responsible for catalysis. Systematic probing of structural elements now reveals unexpected structural and mechanistic principles. We used a combination of site-specific atomic mutagenesis, combinatorial substitutions (nucleotide analog interference mapping), and rescue experiments in combination with chemically modified substrates and photoaffinity cross-linking.

The arguably most important single structural element is the “spine”, an extended cross-strand stack that runs through the catalytic pocket. The strand junction is stabilized by one hydrogen bond (G9-2'OH vs. U17-HN3) and by specific coordination of a magnesium ion. A single sensitive hydrogen bond attaches a two-base-pair minihelix to the spine (U17-O2 vs. C10-HN4), and the breakage of this bond leads to catalytic inactivity, likely due to disintegration of the active site. A sharp and unusual 360° turn inside the RNA structure allows the precise positioning of another minihelix and is found to be crucially important. The hydrogen bonds between catalyst and reaction product



observed in the crystal structure are not required for substrate binding and catalysis, ruling out dienophile activation by electron withdrawal as the catalytic mechanism. Photoaffinity cross-linking confirmed the importance of critical positions for RNA-product interactions in solution.

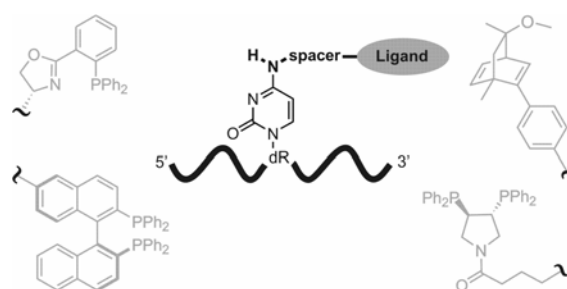
## DNA-Based Ligands for Transition Metals and Use in Asymmetric Catalysis

Mihaela Caprioara, Pierre Fournier, Roberto Fiammengo, and Andres Jäschke

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The catalytic potential of nucleic acids is being revealed by engineering of novel ribozymes and DNAzymes *in vitro*.<sup>1</sup> SELEX technique, that combines the repeated selection of active species from nucleic acid libraries and enzymatic amplification of the enriched library, has emerged as useful tool to design catalytic sequences.<sup>2</sup> Recently it has been demonstrated for the first time that DNA can be employed as chirality source in asymmetric transformations, e.g. Cu<sup>2+</sup>-catalyzed Diels-Alder reactions.<sup>3</sup>

Inspired by the pioneering work of Whitesides,<sup>4</sup> who showed that asymmetric catalytic hydrogenations could be performed by anchoring an achiral Rh<sup>I</sup> complex in a chiral cavity of the protein avidin,<sup>5</sup> we aim at embedding transition metal complexes in nucleic acids folds and generate *hybrid catalysts* that can perform asymmetric catalysis in aqueous medium. We have established an efficient post-synthetic strategy for the site-specific incorporation of metal chelators into DNA sequences. A number of DNA conjugates bearing bisphosphine (pyrphos, BINAP), phosphinooxazoline (PHOX), or conformationally constrained diene moieties have been prepared, affording new DNA-based ligands for transition metal coordination.<sup>6</sup>



Preliminary results on use of DNA-diene and PHOX appended conjugates in asymmetric Rh-catalyzed 1,4-addition and Ir-catalyzed allylic amination, respectively, will be discussed.

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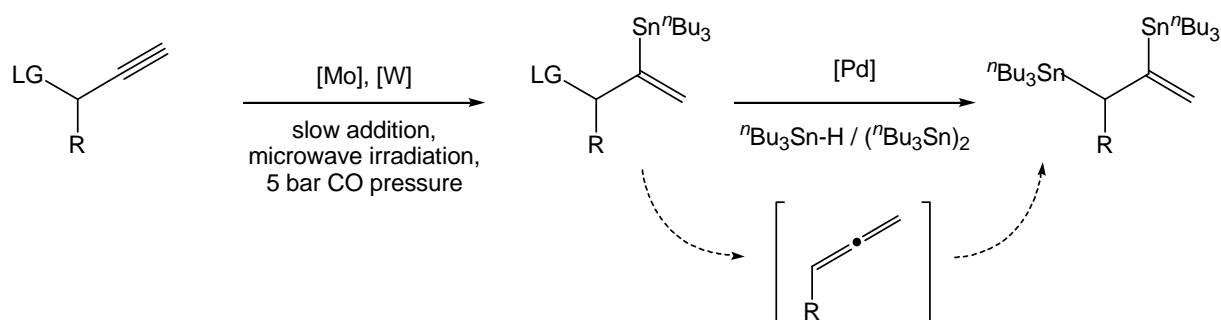
## Investigation of Stannylation Reactions: Improved Protocols for the Hydrostannation of Alkynes and Stannylation of *in situ* generated allenes

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The C-C cross coupling reaction according to Stille<sup>[1]</sup> is a widely used and important method in modern organic synthesis. Vinyl stannanes, the organometallic compounds for this type of reaction, are easily available by transition metal catalyzed hydrostannation of alkynes.

In this context Molybdenum complexes are very interesting. In contrast to Palladium catalyzed hydrostannation reactions, they selectively deliver the more hindered *cis* product.<sup>[2][3]</sup> In this Molybdenum catalyzed hydrostannation of alkynes the addition mode of tin hydride has a strong effect on the outcome of the reaction. Slow addition increases the yield, even if the amount of tin hydride is reduced to only one equivalent. Furthermore, microwave irradiation speeds up the reaction significantly. The regioisomeric ratio can be influenced by the addition of CO pressure. With the use of tungsten complexes distannylated products can also be obtained.<sup>[4]</sup>

At this point, recent results of the improved hydrostannation of alkynes by the use of microwave irradiation and slow addition of tin hydride are presented.<sup>[5]</sup> Furthermore, a short overview of the stannylation of *in situ* generated allenes yielding allyl and vinyl stannylated products is given.



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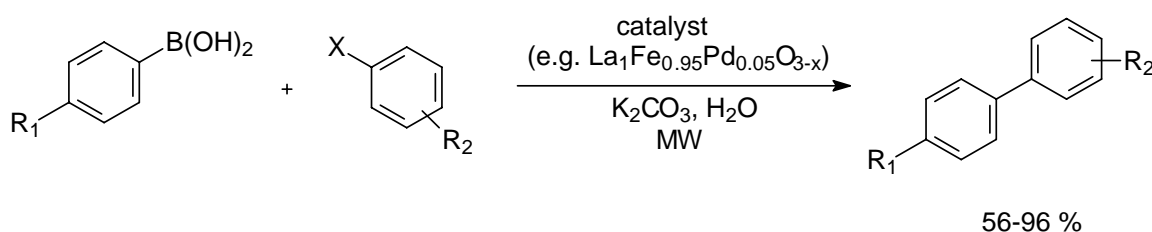
## Palladium-doped Sol Gel Materials as Efficient Catalysts for Suzuki Couplings

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The Suzuki coupling is one of the most popular cross coupling reactions, as illustrated with a wide range of synthetic applications.<sup>[1]</sup> The special charm results from its high reliability, broad functional group tolerance, as well as low toxicity associated with the boron compounds. In the last few years heterogeneous catalysts become more and more popular for this reaction. The heterogeneous catalysts do not only simplify the separation of the catalyst, but also allow a reuse of the removed material, thus reducing process costs. Therefore, numerous supported Pd catalysts have been reported in the literature, e.g. Pd/C,<sup>[2]</sup> Pd/zeolite<sup>[3]</sup> as well as Pd on several metal oxides.<sup>[4]</sup> Recently, Ley *et al.* reported on the application of palladium-containing perovskites,<sup>[5]</sup> a heterogeneous catalyst originally developed for automatic emission control.<sup>[6]</sup>

Our interest was to find out if the perovskite structure is essential for the catalysis. So we synthesized amorphous mixed oxides by sol gel process. Several Palladium-doped sol gel materials, such as  $\text{La}_1\text{Fe}_{0.95}\text{Pd}_{0.05}\text{O}_{3-x}$  were identified as effective catalysts for the Suzuki coupling in water by use of microwave irradiation. It was also possible to show that under these conditions the heterogenous catalyst released catalytically active palladium species into solution.



### Literature:

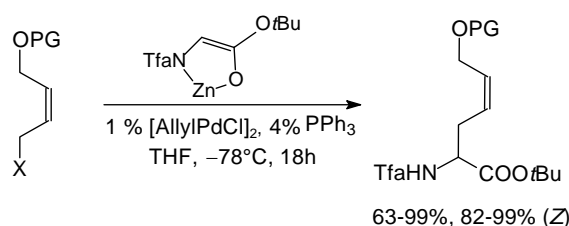
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## Isomerization-free Allylic Alkylations of Terminal $\pi$ -Allyl Palladium Complexes

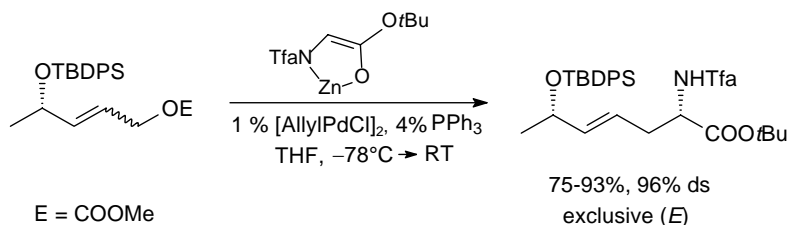
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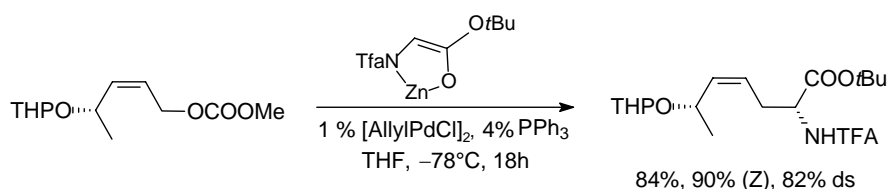
Chelated amino acid ester enolates are excellent nucleophiles for allylic alkylations. With these enolates, even terminal  $\pi$ -allyl palladium complexes react without significant isomerization. This allows a transfer of the *cis*-olefin geometry from the substrate into the product.<sup>[1]</sup>



Very recently, we could show that in reactions of chiral substrates the nucleophilic attack on the terminal  $\pi$ -allyl intermediate could be controlled by the stereogenic center in the substrate. Best results were obtained with the sterically high demanding *tert*-butyldiphenylsilyl protecting group (TBDPS). Herein the diastereoselectivity was 96% ds, independent of the olefin geometry, what is a clear indication for a rather fast  $\pi$ - $\sigma$ - $\pi$ -isomerization.<sup>[2]</sup>



Switching to smaller protecting groups conservation of the (*Z*)-olefine geometry of chiral substrates was also possible with a reasonably good 1,5-induction.



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## A quantum dynamical investigation of olefin-insertion and hydrogen elimination in late transition-metal complexes

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The  $[\text{CpM}(\text{L})\text{H}(\text{C}_2\text{H}_4)]^+$  complexes have been investigated theoretically for  $\text{M}=\text{Co}$  and  $\text{Rh}$  and various ligands ( $\text{L}=\text{PH}_3$ ,  $\text{PF}_3$ ,  $\text{PMe}_3$  and  $\text{P}(\text{OMe})_3$ ). Electronic structure and also quantum dynamical methods were employed. The sets of stationary points relevant to ethylene insertion and hydrogen elimination, namely the ethylene, ethyl, and agostic structures as well as the interconnecting transition states, have been determined through DFT calculations. For the  $\text{Rh}$  complex, the ethylene structure is always found to be the global minimum, while the barrier for insertion increases with electron richer ligands. In the same series, the agostic structure becomes less stable energetically. In agreement with experiment, the agostic structure is calculated to be the global minimum for  $\text{M}=\text{Co}$ . The subsequent quantum dynamical calculations rely on the method of wave packet propagation, considering 1-3 nuclear degrees of freedom. These are selected according to the most relevant structural parameters of the various stationary points, focussing on the  $\text{Rh}$  complex. The corresponding potential energy surfaces including all relevant minima and transition states have been calculated and characterized. Also, one-dimensional (1D) reaction path energy profiles were calculated and used for companion calculations [1]. 1D-3D wave packet studies have been performed for these potential energy surfaces which model the hydrogen transfer and its inverse, the  $\beta$ -hydrogen elimination. Typical vibrational periods for motion along the reaction coordinate are found to be  $\sim 350$  fs for both the  $\text{Co}$  and  $\text{Rh}$  (agostic) complexes. Lifetimes of 0.1 – 1 ps emerge, depending on the initial structure probed [2]. The comparison of the various ligands is expected [3] to shed new light on the real-time behaviour of these important elementary catalytic reaction steps.

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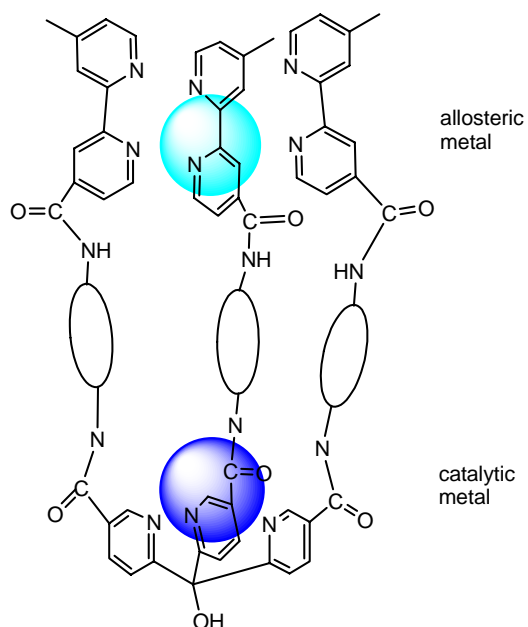
## Bioinspired phosphorylation catalysts: allosteric control of reactivity

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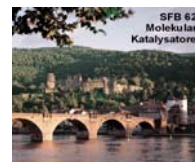
General aim of the project is to mimic allosteric reaction control in enzymatic reactions by synthetic small-molecule catalysts [1]. We report on the design and synthesis of a ditopic ligand which displays two distinct binding sites: a tridentate tris(2-pyridyl)methane site for incorporation of a catalytic metal ion, and a hexadentate tris(2,2'-bipyridyl) site for binding of an allosteric metal ion. The latter controls the conformation of the catalyst by defining a small hydrophobic cavity for substrate binding. Solution characterization of dinuclear metal complexes will be presented, together with preliminary studies of (phospho)esterase activity.

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## New 2,2'-Bipyridine-bridged *N*-Heterocyclic Biscarbenes – Structural Features of a Free Biscarbene and Silver(I) Complexes



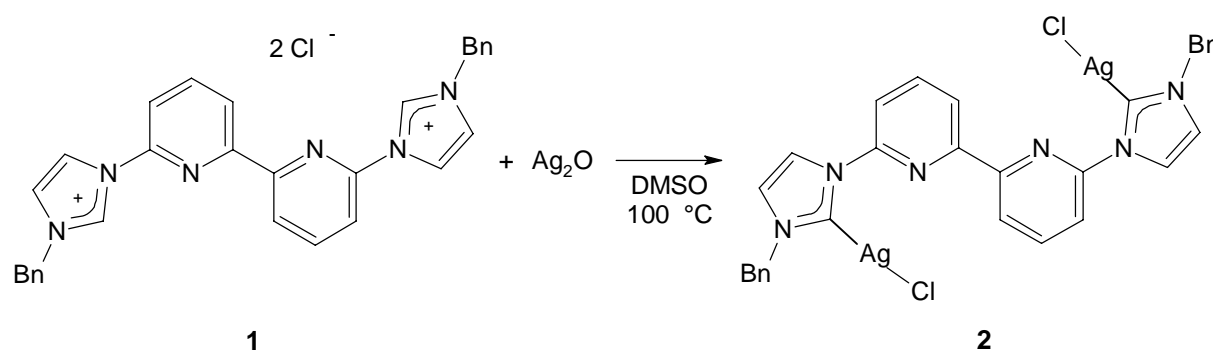
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*N*-heterocyclic carbenes (NHCs) have become a very attractive ligand class due to their steric and electronic properties.<sup>1</sup> Chelating bis-NHCs are yielding more stable metal complexes and are allowing for “fine tuning” of topological features.<sup>2</sup> The utilization of 2,2'-bipyridine as an ancillary donor ligand gives additional stabilization.

Imidazolium salts of type **1** can be easily prepared by alkylation of 6,6'-di-1*H*-imidazol-1-yl-2,2'-bipyridine with benzyl chloride (BnCl) or *Meerwein's* salts. Deprotonation of an ethyl-substituted imidazolium salt (X = BF<sub>4</sub>) provides an isolable free biscarbene and crystals suitable for single-crystal X-ray diffraction can be obtained.

Reactions of the imidazolium salts **1** with silver oxide at high temperatures give dinuclear silver(I) NHC complexes of type **2** which are characterized by spectroscopic methods and X-ray structure analysis.



Silver NHC compounds are useful reagents for transmetalation reactions.<sup>3</sup> First palladium complexes of this ligand could be synthesized by this method which were not accessible by *in situ* deprotonation in presence of the corresponding Pd precursor. These complexes will be subsequently tested in catalytic reactions.

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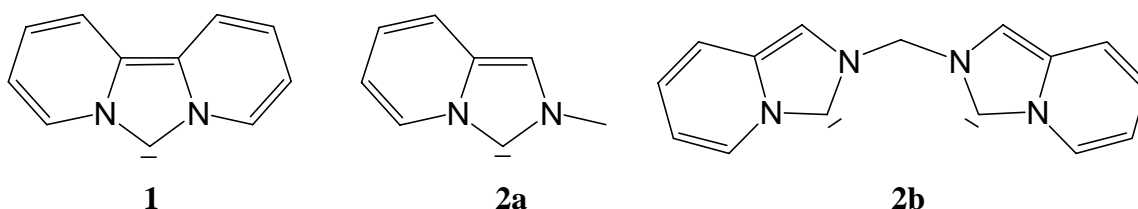
## $\pi$ -Electron Rich Pyrido Annelated N-Heterocyclic Carbenes in Catalysis

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N-heterocyclic carbenes have gained remarkable interest in coordination chemistry and catalysis in the past decade.<sup>[1]</sup> Structural and electronical differences but similar coordination abilities make NHCs supplementary to phosphines in many applications. In that context, our contribution is engaged with the synthesis and study of pyrido-<sup>[2]</sup> and dipyrido-annelated<sup>[3]</sup> imidazolynylidenes of the types **1** and **2**.



Metal complexes bearing these ligands could be synthesised and tested in catalysis<sup>[4]</sup> and in addition, two free carbenes could be isolated and structurally characterised. The spectroscopic data shows that there is a relation between the N-C-N carbene angle and the <sup>13</sup>C-NMR chemical shift of the unsaturated carbon atom. A thorough literature screening confirmed that correlation.<sup>[5]</sup>

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## SYNTHETIC GLYCOPEPTIDES FROM PSGL-1 AND ESL-1 AS SELECTIVE LIGANDS OF SELECTINS IN CELL ADHESION PROCESSES

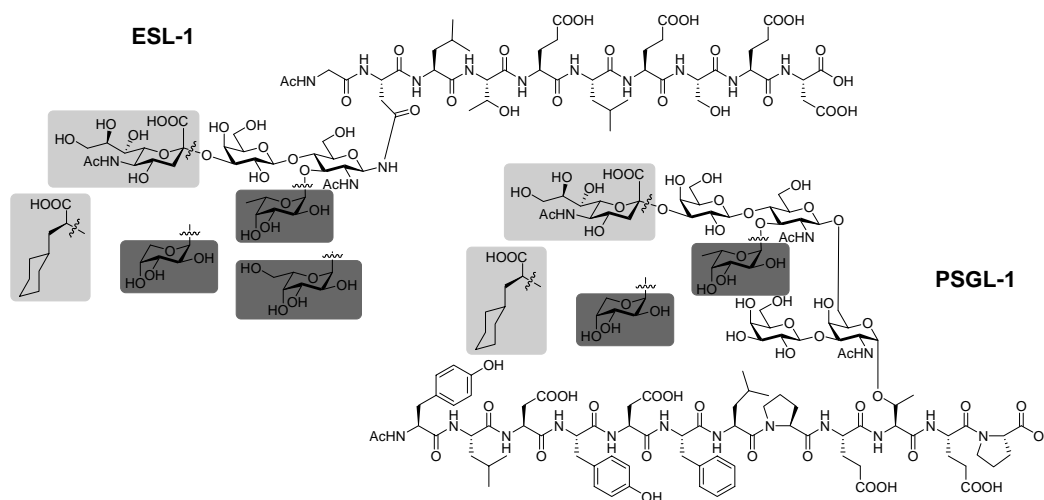
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Selectin-mediated cell adhesion is of major importance during the inflammatory cascade. At the beginning of the adhesion process, P- and E-selectin both expressed on the endothelium interact with their ligands PSGL-1 and ESL-1 on leukocytes. These initial interactions enable a firm attachment which finally results in the migration of leukocytes from the blood vessel into the inflamed tissue.

In order to competitively inhibit undesired cell adhesion events which occur in chronic inflammatory diseases such as rheumatoid arthritis, and in tumor metastasis, glycopeptides comprising all structural elements for binding to selectins were synthesized. The synthetic strategy exclusively relies on chemical methods. Thus, it allows for parallel production of potential mimetics and provides gram quantities of the required glycosylated amino acids.

The glycopeptides derived from the E-selectin ligand-1 contain sialyl Lewis<sup>x</sup> or a mimetic of the tetrasaccharide, which is *N*-glycosidically linked to L-asparagine within the peptide backbone. Flow-cytometry experiments revealed that the inhibitory potential of these conjugates towards E-selectin is generally higher than that of the sialyl Lewis<sup>x</sup> tetrasaccharide.<sup>1</sup>



Within the synthesized mucin-type glycopeptides from the *N*-terminal domain of the P-selectin glycoprotein-ligand-1 sialyl Lewis<sup>x</sup> or its mimetic is bound to an *N*-acetyl- $\alpha$ -D-galactosamine unit which, in turn, is connected to the hydroxyl function of L-threonine.

<sup>1</sup> C. Filser, D. Kowalczyk, C. Jones, M. K. Wild, U. Ipe, D. Vestweber, H. Kunz, *Angew. Chem. Int. Ed.* **2007**, *46*, 2108-2111.



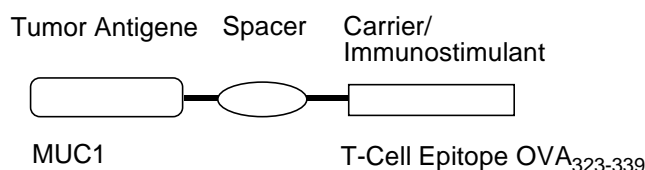
## Synthesis of Epithelial Mucin MUC1 Glycopeptide Antigens for the Development of Antitumor Vaccines

Ulrika Westerlind\*, Sebastian Dziadek, Simone Di Pietro, Nicola Gaidzik, Kai Groh, Anton Kaiser, Fauziya Syed and Horst Kunz

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Selective attack on tumor cells using non-toxic anticancer vaccines would be an attractive alternative to the cancer therapies used today. In contrast to normal cells, the glycoprotein profiles on epithelial tumor cells are distinctly altered. Incomplete formation of the glycan structure, by down-regulation of glycosyltransferases and premature sialylation, result in the exposure of the peptide backbone and additional epitopes become accessible to the immune system. These tumor-associated structure alterations constitute the basis for a selective immunological attack on cancer cells. Glycopeptide structures that mimic the 20 amino acid tandem repeat region of the extracellular domain of the tumor-associated epithelial mucin MUC1 have been synthesized. Recently a Sialyl T<sub>N</sub> monoglycosylated MUC1 peptide was conjugated with a T-cell epitope from ovalbumin (OVA<sub>323-339</sub>) in order to induce a humoral immune response<sup>1,2</sup>. This vaccine construct together with Freund's adjuvant was injected in transgenic mice (DO11.10), whose T-cells express a receptor for the OVA<sub>323-339</sub>. After booster immunization, one third of the mice, showed a high titer of MUC1 specific antibodies, indicative of an IgG response. Due to these promising results, Sialyl T<sub>N</sub> and T<sub>N</sub> di- and triglycosylated peptides containing the whole MUC1 tandem repeat and the OVA T-cell epitope, have also been synthesized. Glycopeptides conjugated to other immunostimulants, like the tetanus toxin T-cell epitope and the Pam<sub>3</sub>Cys mitogen are other promising vaccine constructs that are synthesized in our group.



**Scheme 1.** Illustration of the MUC1-OVA T<sub>H</sub>-cell epitope vaccine.

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## Mechanistic Studies of Catalytic Polyethylene Chain Growth in the Presence of Water

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Aqueous emulsion polymerization is among the most important polymerization processes. As a product, dispersions with polymer particle sizes of ca. 50 nm to 1  $\mu$ m are obtained. In comparison to traditional free radical techniques<sup>1</sup>, catalytic polymerization is complimentary in terms of polymers accessible, and it provides a much broader scope of control of polymer microstructures. The emulsion polymerisation of ethylene has found particular interest, recently<sup>2</sup>. Catalytic polymerizations are achieved using late transition metal based catalyst precursors that tolerate aqueous environments.

These versatile polymerizations in aqueous systems raise the question of fundamental underlying reaction steps, namely the competition of monomer and water for binding sites (that is reversible blocking of active sites), chain growth in the presence of water, and the reactivity of alkyl species M–R (R  $\geq$  Me) occurring during polymerization towards water in general. Recent theoretical studies indicate that ethylene binding is preferred over water coordination in various catalyst systems, namely Grubbs neutral salicylaldiminato nickel and Brookhart's cationic diimine palladium or nickel complexes<sup>3</sup>. Furthermore, it is conceivable that the presence of water has an influence on the migratory insertion step.

To gain insight into the various processes that underlay the observed macroscopic behaviour of the above mentioned catalytic systems we first investigated the direct observation of ethylene migratory insertion chain growth in homogeneous aqueous THF solution<sup>4</sup>. As the model system for experimental studies we chose the cationic  $\alpha$ -diimine palladium system studied by Brookhart, [ArNC(Me)(Me)CNArPdMe(OEt<sub>2</sub>)] [BAr<sub>4</sub><sup>F</sup>] (BAr<sub>4</sub><sup>F</sup> = B(3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>)<sub>4</sub>, Ar = 2,6-iPr<sub>2</sub>C<sub>6</sub>H<sub>3</sub>)<sup>5,6</sup>. Higher alkyl species [(N $\curvearrowright$ N)PdR(OH<sub>2</sub>)<sup>+</sup>] (R > Me, ArNC(Me)(Me)CNAr = N $\curvearrowright$ N) were prepared cleanly in the NMR tube and their reactivity towards water was studied at low temperatures, < 0°C. Surprisingly, water can compete with ethylene coordination in the system studied, in cationic Pd–Me species and also in higher Pd–alkyl species, the latter being the relevant species in chain growth. Noteworthy, the insertion rate constants of monomer into the Pd–Me bond are not affected by the presence of water.

Going from the cationic palladium diimine model system towards the neutral nickel salicylaldiminato complexes additional challenges arise. The catalytically active species is assumed to be the metal alkyl olefin complex which is formed from the catalyst precursor [(N $\curvearrowright$ O)NiMe(L)] by dissociation of a stabilizing labile ligand L. The ligands L studied to date bind much stronger than ethylene which hampers direct determination of binding equilibria.

We present here primary studies on the stability of the catalyst precursor complexes towards protic media in the presence and absence of excess monomer. Hydrolysis or methanolysis of the Ni–Me bond of the precursor complex leads to the formation of methane and known nickel bischelate complexes<sup>3,7</sup>. Noteworthy, half life times of protolysis are dependent on the coordinating labile ligand, ranging from 1/2 hour to more than 5 days with increasing binding ability of the labile ligand.

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## Polymerization of Ethylene with Water-soluble Salicylaldiminato Ni(II)-Methyl Complexes to Nanoparticles and their Use as Switchable Containers

Qiong Tong, Brigitte Korthals, Inigo Göttker-Schnetmann and Stefan Mecking\*

Salicylaldiminatonickel(II)complexes  $[(N^{\wedge}O)NiMe(L)]$  featuring different water-soluble ligands L (L = TPPTS [tri(sodiumphenylsulfonate)phosphine], TPPDS [di(sodiumphenylsulfonate)phenylphosphine], H<sub>2</sub>N-PEG, [H<sub>2</sub>N(CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub>Me, n = ca. 52] for the polymerization of ethylene were prepared. Under conditions where catalyst deactivation is retarded, the activity in water is higher than that in toluene. The catalyst precursors  $[(N^{\wedge}O)NiMe(L)]$  are designed in such a way, that they are water soluble but the actual active sites are not. This results in an enhanced dissociative self-activation in the aqueous system due to the compartmentalization of the dissociating stabilizing water-soluble ligand L into the aqueous phase, and of the active site into the formed polymer particles. Under organic solvent-free aqueous conditions extremely small particles of high molecular weight polyethylene are formed. This colloiddally stable dispersions with a volume average size of ca. 10 nm consist of semicrystalline polyethylene. The branching (and molecular weight) of the polymer, and thus the crystallinity of the obtained polyethylene particles, could be varied over a wide range via the remote substituents on the complex. Upon cooling of the dispersions in DSC studies, high extent of supercooling of crystallization is observed. This is due to crystallization of individual droplets, vs. heterogeneous nucleation in the bulk.

This provides an approach for reversible switching of nanoscale containers via melting and crystallization occurring in the individual dispersed particles. Beyond fundamental interest in the properties of very small compartments, this is also relevant for applications such as, for example, delivery of poorly soluble drugs, controlled release of active molecules, or as carriers in aqueous multiphase catalysis. Fluorescence studies of lipophilic probe molecules show that in the low-crystallinity particles they experience a more apolar environment. As the crystalline particles consist of a single lamella, the amorphous portions which can accommodate guest molecules are at the periphery of the particle, such that the probe experiences the water-particle interface to some extent. The polarity experienced by the probe molecules can be switched reversibly by melting and crystallization of the individual dispersed particles. The temperature at which this occurs can be adjusted via the microstructure, that is degree of branching, of the polymer.

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# Synthesis of aqueous polyethylene dispersions with electron-deficient neutral nickel (II) catalysts with enolatoimine ligands

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Catalyst activity is an issue in polymerization with neutral Ni (II) complexes in general, and in aqueous systems in particular.<sup>1</sup> An increased electrophilicity of the Ni center, brought about by electron withdrawing substituents in the bidentate N, O- or P, O- coordinating ligand, substantially increases the polymerization rates.<sup>2</sup> Neutral Ni(II) complexes based on enolatoimine ligands with strongly electron-withdrawing trifluoromethyl and trifluoroacetyl groups were studied as catalyst precursors for ethylene polymerization.<sup>3</sup> Despite the electron deficient nature of the metal centers, which enhances deactivation reactions such as hydrolysis or coordination of water, polymerizations can be carried out in aqueous systems to afford polyethylene dispersions.<sup>4</sup> Even at high temperatures of 70 °C catalyst stability is sufficient for the polymerization to continue for hours. Catalyst activities of up to  $1.9 \times 10^4$  TO h<sup>-1</sup> (70 °C polymerization temperature) were observed in aqueous systems. This rivals the highest activities reported for neutral Ni(II) salicylaldiminato complexes, which were the only complexes reported to date to afford polyethylene dispersions of higher molecular weight material ( $M_n \geq 10^4$  g mol<sup>-1</sup>). The substitution pattern of the N-bound aryl group (N-C<sub>6</sub>H<sub>3</sub>R<sub>2</sub>) influences the degree of branching of the polymer formed and correspondingly its crystallinity and melt temperature.

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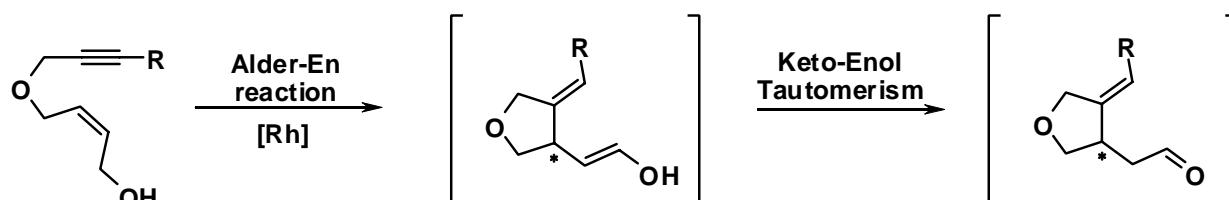
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## Catching Two Birds with One Stone – A Novel Sequentially Rhodium Catalyzed Process Initiated by *Alder-En-Cycloisomerization*

Nadine Körber, and Thomas J. J. Müller\*

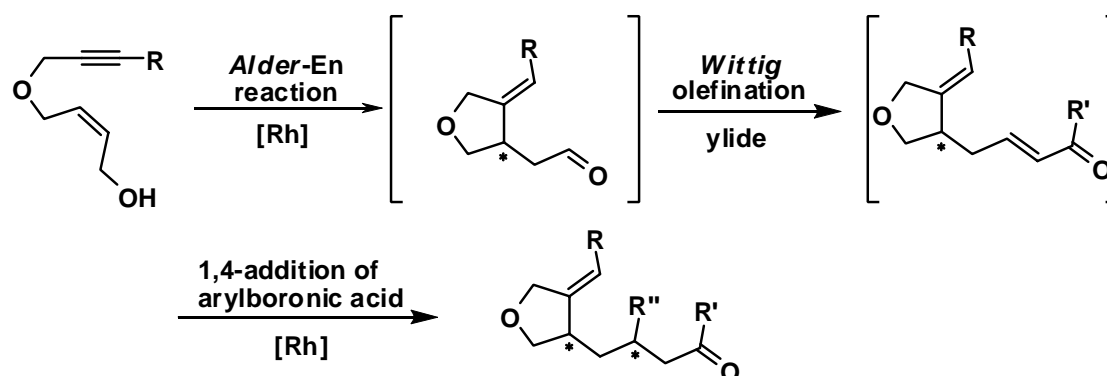
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The transition metal-catalyzed cycloisomerization of enynes offers a diversity oriented method for accessing complex cyclic structures from easily accessible acyclic precursors.<sup>1</sup> The rhodium-catalyzed *Alder-ene* reaction works on the basis of a cationic rhodium complex in combination with chelating phosphane ligands and transforms acyclic substrates into five membered rings with a 1,4-diene functionality.<sup>2</sup> In our special case alkynyl allyl alcohols do not to give 1,4-dienes but rather tautomerized  $\gamma,\delta$ -unsaturated aldehydes (Scheme 1).



Scheme 1

Furthermore, the *Alder-ene* reaction to enals was intended as a first catalytic step in sequential one-pot reactions. Therefore, the transient enal was further reacted with phosphonium ylides in *Wittig-olefinations*<sup>3</sup> and a subsequent rhodium-catalyzed 1,4-addition of arylboronic acids in a one-pot fashion (Scheme 2).



Scheme 2

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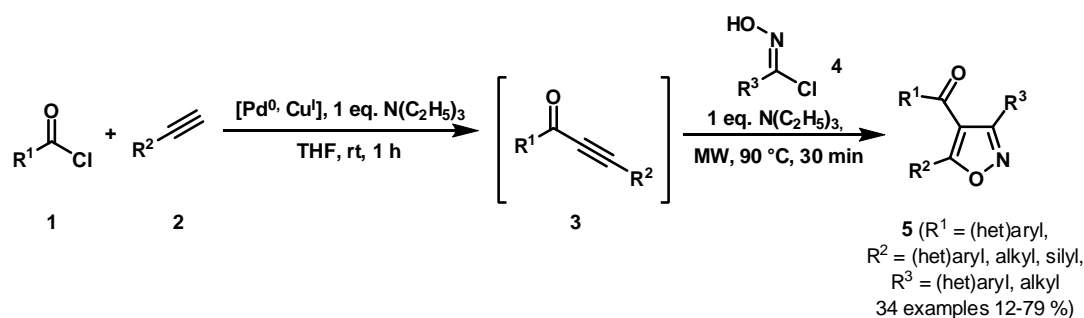
## Novel One-Pot Three-Component-Coupling-Cyclization Reactions

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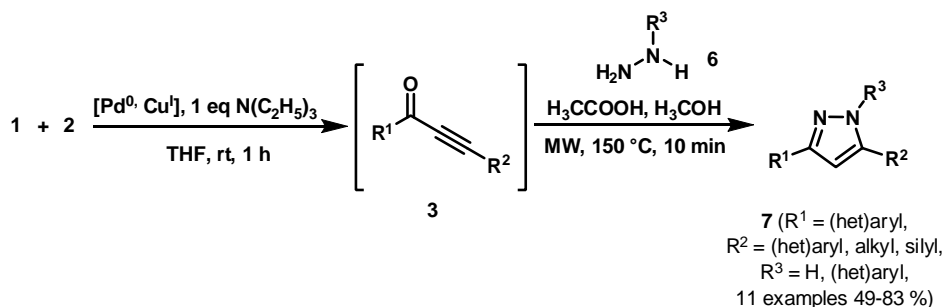
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Alkynones **3** are valuable synthetic intermediates for the preparation of a wide range of nitrogen-containing aromatic heterocycles. They are easily prepared via modified *Sonogashira*-coupling reaction of aromatic acid chlorides **1** and terminal alkynes **2**.<sup>1</sup> Subjecting alkynones **3** directly and without further isolation to microwave assisted reactions with 1,3-dipoles such as nitroxides (generated in situ from hydroxyiminoyl chlorides **4**) furnishes isoxazoles **5** in a one-pot fashion (Scheme 1).<sup>2</sup>



**Scheme 1:** Formation of isoxazoles **5** after coupling-addition-cycloaddition reactions.

The reaction with binucleophiles such as hydrazines **6** leads to the formation of pyrazoles **7**. 3,5-Diaryl pyrazoles are known to reversibly inhibit monoamine oxidase-A (MAO-A) and monoamine oxidase-B (MAO-B) at nanomolar concentrations.<sup>3</sup> Therefore, the intermediate alkynones **3** were reacted under microwave irradiation with hydrazines **6** to form pyrazoles **7** in good to excellent yields (Scheme 2).



**Scheme 2:** Formation of pyrazoles **7** after coupling-addition-cyclocondensation reactions.

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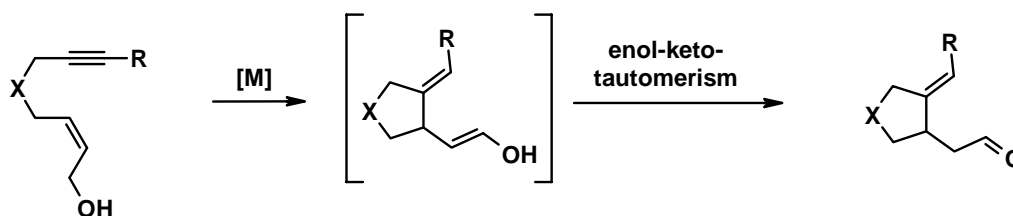
## One-pot Reactions based upon *Alder-ene* Cycloisomerizations – Scope and Mechanism of Iridium and Palladium catalysis

Manuela Kummeter\* and Thomas J. J. Müller\*\*

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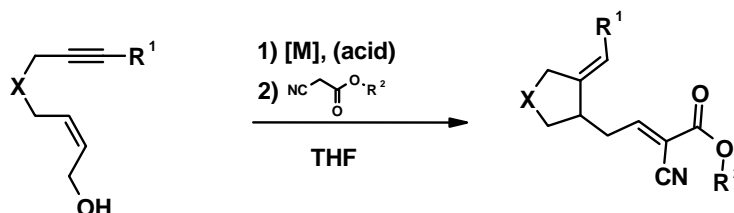
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Sequential transformations and multi-component reactions have come to utmost importance during the last years. Economically and ecologically these reactions work with high efficiency attracting the attention of both academic and industrial research.<sup>1</sup> In our group the intramolecular transition-metal catalyzed *Alder-ene* reaction has been well established as a successful entry to different sequences based upon enyne derivatives.<sup>2</sup> The intermediate enal, formed by enol-keto-tautomerism can be transformed by various reactions in a one-pot fashion.



X = O, NTs, C(COOMe)<sub>2</sub>  
R = Me, CH<sub>2</sub>OCH<sub>3</sub>, Ph, Si(CH<sub>3</sub>)<sub>3</sub>

Recently, we have established the intramolecular Pd and Ir catalyzed<sup>3</sup> *Alder-ene* reactions, as a successful entry to a novel sequence. The intermediate enal was transformed by a *Murahashi* reaction in a one-pot fashion. This sequence excels in its simplicity and diversity potential.



The iridium catalyzed version of the cycloisomerization has gone along with researches into mechanism and reactive species.

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R. Paciello<sup>a</sup>, C. Jäkel<sup>b</sup>, J. Rudolph<sup>a</sup>

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e-mail: [christoph.jaekel@basf.com](mailto:christoph.jaekel@basf.com)

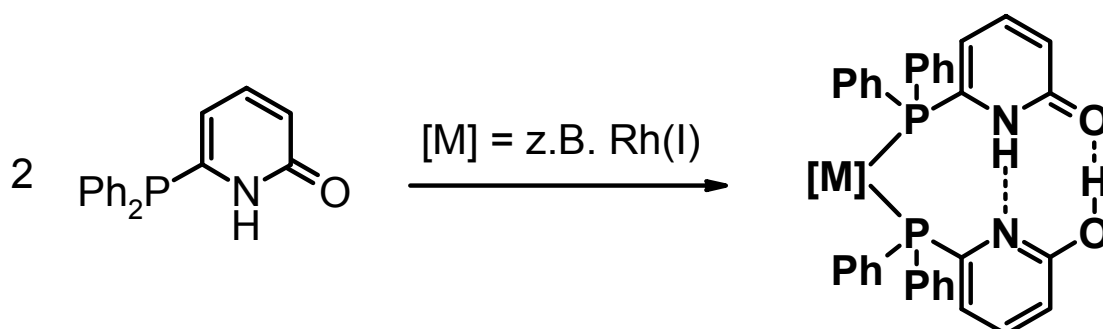
## New Ligands for Homogeneous Catalysis

Homogeneous catalysis is an important area of interest for the chemical industry. For example, 9 Mio tons of chemicals are produced per year *via* homogeneous catalyzed hydroformylation.

To enhance activity and selectivity, ligands, especially chelating ligands, are widely used. The ligands coordinate to the metal, which is the catalytically active center, and direct coordination of the substrate, which makes the process more selective. For example, in the low pressure hydroformylation of olefins, a significantly higher selectivity to terminal products can be achieved using chelating ligands, as compared to monodentate ligands.

Prof. Breit et al. recently introduced a new ligand concept, which lies conceptionally between monodentate and bidentate (chelating) ligands.<sup>1</sup> The monodentate ligands used are able to form dimeric species by formation of hydrogen bonds, thus yielding chelating species. This type of organisation is similar to that observed in the base-pair interaction in DNA.

The first example of this type of “pseudo-chelating” ligands, 6-DPPon, was originally investigated in discontinuous hydroformylation reactions of linear olefins. Here, activity and n-selectivity were of particular interest. However, as large scale industrial processes are usually conducted continuously, the tests on the investigated ligand system were extended to continuous experiments. This work and supporting discontinuous experiments are reported in this poster.



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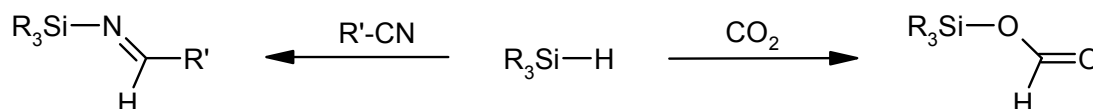


## How (un)reactive are C,O and C,N Bonds towards Hydrosilylation?

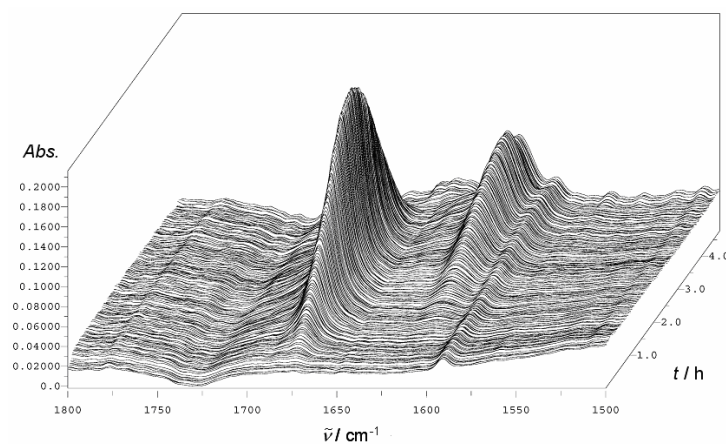
Stephan Pitter

Forschungszentrum Karlsruhe, Institute of Technical Chemistry (ITC-CPV), Karlsruhe (Germany)

The hydrosilylation represents the formal addition of an Si-H bond to an unsaturated organic substrate, and is one transformation that is still receiving much attention. Late transition metal complexes are traditionally employed as catalysts for a variety of such transformations. Hydrosilylation of various functional groups, such as  $R_2C=CR_2$ ,  $R_2C=O$  or  $R_2C=NR'$  provides facile routes to important organosilicon reagents and synthetic intermediates in organic syntheses as well as a unique method for the selective reduction of carbon-heteroatom bonds. In our initial work we studied the hydrosilylation at the C,O double bond of  $CO_2$  in the presence of ruthenium complexes.<sup>1</sup> This approach offers an efficient access to formic acid silyl esters.<sup>2</sup> Our studies promoted us to investigate in more detail the molecular steps of the catalytic reaction indicating a unique silane activation at the ruthenium catalysts used.<sup>3</sup>



In this work we present our recent studies on  $CO_2$  hydrosilylation, underlining in particular the benefit of *in situ* IR techniques. The catalysts of the general types  $RuX_2(MeCN)_4$  or  $RuX_3(MeCN)_3$  are also suitable to enable for hydrosilylation of the C,N



triple bond of organic nitriles. Results are therefore presented for the synthetic approach to a variety of N-silylated imines. The usability of this approach particularly depends on the degree of consecutive reactions observed for some substrates. Another key question is, how the silane is activated at the active ruthenium

centre. Theory predicts an uncommon activation dependent on co-ordinating halide ligands.<sup>3</sup> Isolation of new complexes is discussed in order to clarify the mechanistic pathway.

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<sup>2</sup> S. Pitter, A. Jansen, E. Dinjus (Forschungszentrum Karlsruhe G.m.b.H.), DE 19911616, **2000** [*Chem. Abstr.* **2000**, 133, 164169]

<sup>3</sup> P. Deglmann, E. Ember, P. Hofmann, S. Pitter, O. Walter, *Chem. Eu. J.* **2007**, 13, 2864.

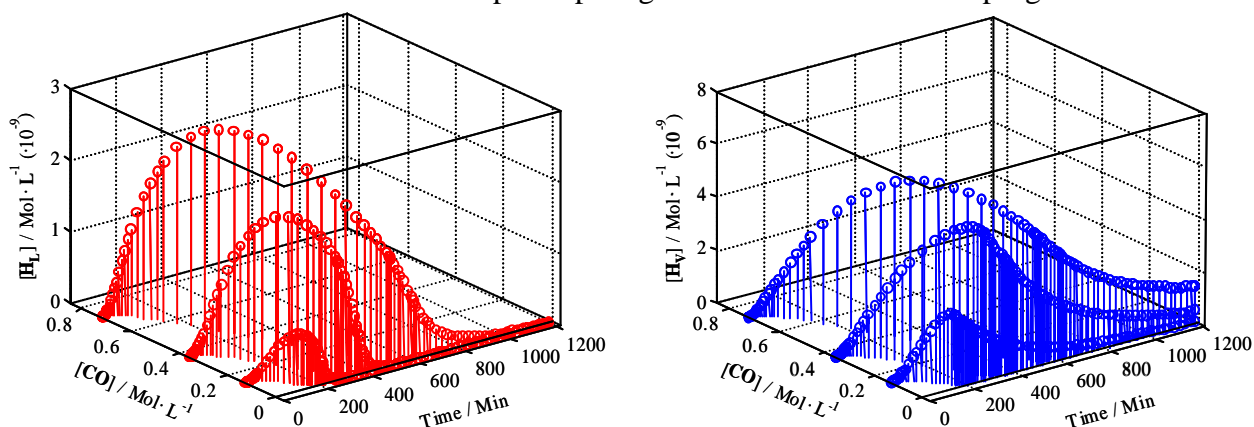
## A Kinetic Model for Hydroformylation of 1-Octene in supercritical CO<sub>2</sub>

Constantin Maniut and Stephan Pitter

*Forschungszentrum Karlsruhe, Institute of Technical Chemistry (ITC-CPV), Karlsruhe (Germany)*

Due to its environmental advantages, use of supercritical carbon dioxide (scCO<sub>2</sub>) has been investigated widely as alternative medium replacing organic solvents in chemical reactions. scCO<sub>2</sub> is nontoxic, does not form air-polluting daughter products, and is relatively cheap and plentiful. The physical-chemical properties of scCO<sub>2</sub> are between those of liquids and gases. In catalysis applications, its tunable solvent properties can result in a variety of effects, such as affecting kinetic rates by both temperature and pressure, shifting equilibrium constants in favor of the desired products, and increasing selectivity and yields.<sup>1</sup> One of the benefits of scCO<sub>2</sub> for homogeneous catalysis is that interface diffusion does not take place. As the hydroformylation of olefins for the synthesis of aldehydes is one of the most important industrial homogeneously catalyzed reactions, since the pioneering work by Rathke's group,<sup>2</sup> several research groups have investigated hydroformylation in scCO<sub>2</sub>. To exploit the whole potential of scCO<sub>2</sub> for catalysis, in particular by using the described switchable properties, the fundamental principles underlying the observed effects must be understood.

Recently we became interested in developing catalyst recycling strategies for hydroformylation.<sup>3</sup> In this work we present our recent studies on Co<sub>2</sub>(CO)<sub>8</sub> catalyzed hydroformylation of 1-octene in scCO<sub>2</sub>. Experimental work has been carried out in special parallel reactor system allowing for faster exploration of process parameters up to 350 bar pressure. Based on results of the mechanistically determined microkinetics, we have created a non-linear kinetic model describing the effects of initial concentrations of participating reactants on the reaction progress.



This model describes the experimental data much better than usual macrokinetics, as for example the influence of the initial CO partial pressure on the *n/i* ratio (see figure, left: *n*, right: *i*). It also allows for the prediction of process parameters on a satisfying level of accuracy.

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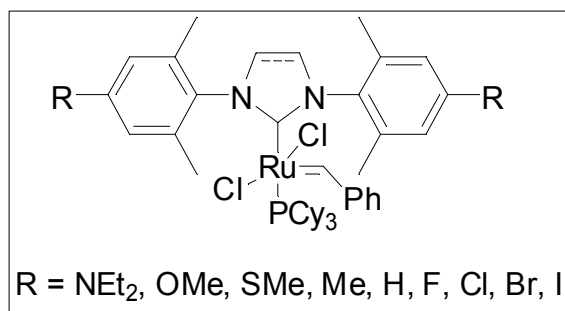
<sup>3</sup> F. Patcas, C. Maniut, C. Ionescu, S. Pitter, E. Dinjus, *Appl. Catal. B* (2007) 630.

## Tuning the electronic Properties of N-heterocyclic Carbenes

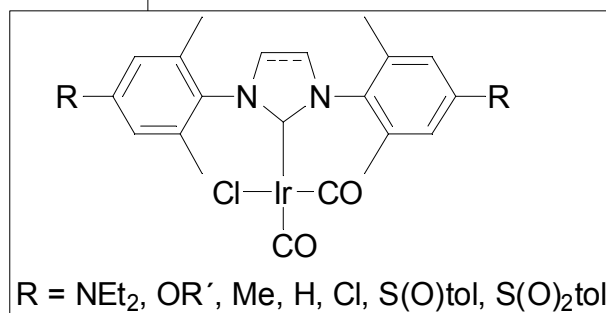
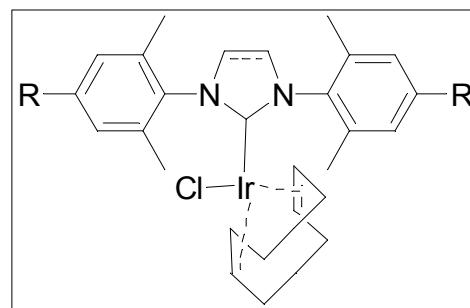
Leuthäuser, S., *TU Darmstadt/DE*, Plenio, H., *TU Darmstadt/DE*

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In a preliminary study we have determined the redox potentials of Grubbs II complexes with substituents R in the 4-position of the mesityl flaps. It was found that the electronic nature of the 4-substituents has a strong influence on the Ru(II)/(III) redox potentials<sup>[1]</sup>. For a better understanding of this effect and its implications for olefin metathesis a set of saturated and unsaturated NHC ligands was prepared in order to cover a large range of electronic effects in Grubbs II complexes. The redox potential of the Ru center varies from 0.20 V (R=NEt<sub>2</sub>) to 0.54 V (R=Cl). No difference between the saturated and unsaturated analogues concerning the redox potential was observed. In order to determine the effect of the electronic variation on the catalytic activity six Grubbs II complexes (R=NEt<sub>2</sub>, H, Cl; saturated and unsaturated) were tested in standard RCM and CM reactions. We found that the electron donating group R=NEt<sub>2</sub> leads to the best catalytic performance.<sup>[2]</sup>



Using this set of ligands we prepared (NHC)IrCl(cod) complexes to study the electronic behaviour by cyclic voltammetry. Comparing these results with the carbonyl stretching frequencies obtained from (NHC)IrCl(CO)<sub>2</sub> complexes we found that: (1) cyclic voltammetry of (NHC)IrCl(cod) may serve as a precise measure for the electron donating properties of the NHC ligand; (2) variation of the 4-position allows tuning of the electron donating properties as indicated by the redox potentials and stretching frequencies, respectively; (3) the results obtained for the iridium complexes bearing NHC ligand R=S(O)<sub>2</sub>tolyl show that this ligand has virtually the same electron donating capacity as tricyclohexylphosphine.<sup>[3]</sup>



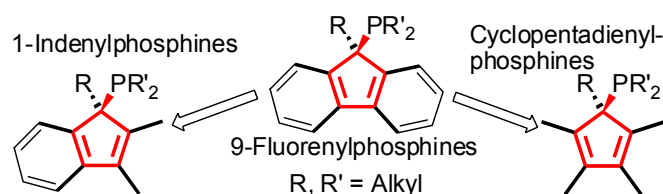
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## ***CataCXium F* – a new Class of tuneable Phosphines for Pd-catalyzed Cross Coupling Reactions in Water and organic Solvents**

*Fleckenstein, C.A., TU Darmstadt/DE, Plenio, H., TU Darmstadt/DE*

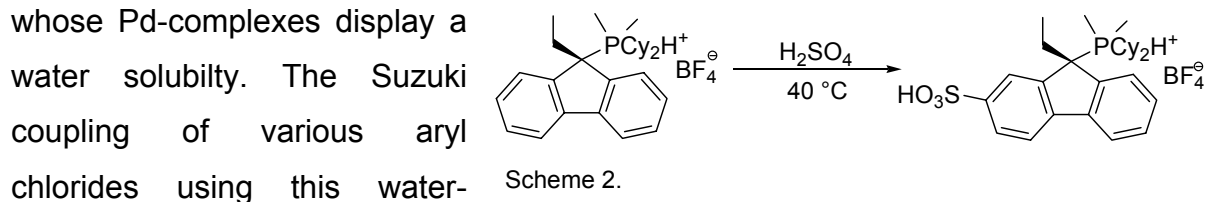
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With *cataCXium F* we have developed a new class of highly variable, electron-rich and sterically demanding trialkyl-phosphines bearing a 9-fluorenyl-, 1-indenyl- or cyclopentadienyl moiety, respectively.<sup>[1,2]</sup> The enhanced CH-acidity of the central cyclopentadienyl ring, enables the selective formation of the carbanions, allowing the facile ligand construction.



The in-situ formed  $[Pd-PR_3]$  complexes ( $Na_2PdCl_4$ , phosphonium salt, base, substrates) were tested in Sonogashira, Suzuki and Buchwald-Hartwig reactions of aryl chlorides and bromides in organic solvents displaying excellent activities. The Sonogashira coupling of aryl chlorides at 100-120°C leads to >90% yields with 1 mol% of Pd catalyst. The Suzuki coupling of aryl chlorides typically requires 0.05 mol% of Pd catalyst at 100 °C in dioxane for quantitative product formation.

The high variability of *CataCXium F* allows easy modification, e.g. phase-tagging. Sulfonation of that class generates the respective monosulfonated phosphonium salt, whose Pd-complexes display a water solubility.



soluble catalyst requires only 0.01 to 0.5 mol% of Pd catalyst for quantitative conversion in pure water, even when applying notoriously difficult substrate combinations such as *N*-heterocycles or sterically demanding substrates (aryl chlorides or boronic acids).

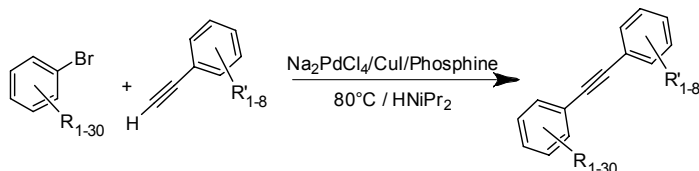
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*This work was supported by DEGUSSA AG.*

## Insights in Sonogashira Cross-Coupling via High Throughput Kinetics

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**Scheme:** Parallel Sonogashira reactions.

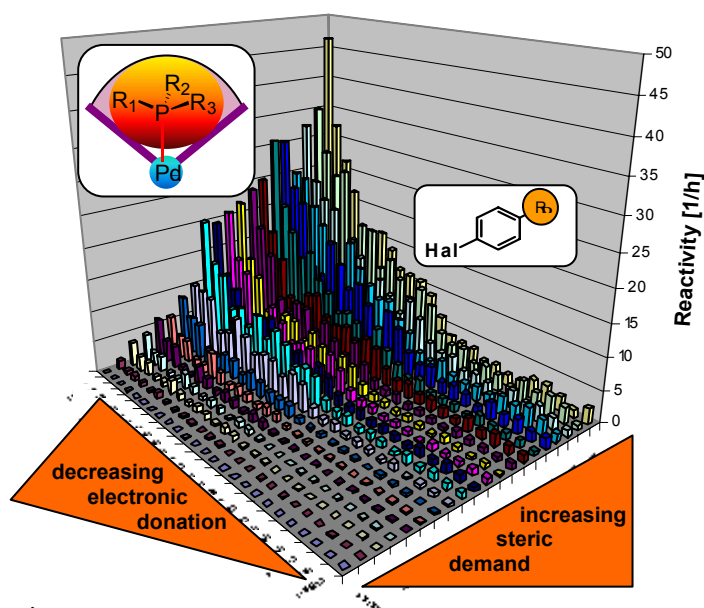
The increasing use of high throughput techniques underlines this basic problem. The enormous progress in cross coupling reactions during the last decade resulted in a few rules of thumb, which aid the design of new phosphine ligands for palladium. While the a posteriori rationalisation of a successful catalyst is possible, the rational design of catalysts remains the exception.

The optimisation of catalysts for a given chemical transformation is an extremely time consuming task. However, uncovering the “best” catalyst for a certain reaction primarily relies on an empirical trial-and-error approach; the

We want to demonstrate here the use of high throughput techniques to obtain a better understanding of the factors governing carbon-carbon coupling, especially that of the Sonogashira reaction. Our approach makes use of a technique, termed one-pot multisubstrate screening, introduced by Kagan. In this HTS approach a single catalyst acts upon numerous substrates to simultaneously effect a large number of coupling reactions in a single reaction vessel.

We have now extended and modified this method in order to allow the collection of a large number of kinetic data in a short time. The advantages of this approach are obvious:

- all reactions are carried out under *truly identical reaction conditions*, a requirement urgently needed to understand subtle catalytic effects, which is only met with difficulty in standard procedures;
- the large number of reactions carried out simultaneously result in enormous time savings, concerning the coupling reactions as well as the quantitative analysis of the reaction products by gas chromatography.



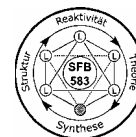
### Using One-Pot-Parallel-Multisubstrate-Screening

we want to demonstrate how systematic variation of *steric* and *electronic parameters* in both substrate and catalyst influence the rates at which the individual coupling products are formed. With this parallel screen - combined with an optimised analytic - we are able to screen up to 1000 reactions/week to obtain valid rates for these individual reactions.<sup>[1,2]</sup>

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## Why does $[\text{IrH}_2(\text{R}_2\text{PCH}_2\text{CH}_2\text{NH}_2)_2]^+$ favour Transfer Hydrogenation over direct $\text{H}_2$ -Hydrogenation? – A Computational Approach



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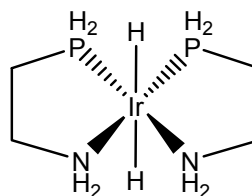
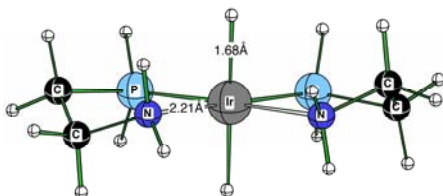
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Among the most efficient known catalysts for the transformation of ketones to secondary alcohols with dihydrogen as a reductant are bis(phosphane)/diamine-coordinated ruthenium(II) complexes  $[\text{Ru}(\text{X})(\text{Y})(\text{PR}_3)_2(\text{H}_2\text{N}\cap\text{NH}_2)]$  (X, Y, = Cl, H), where  $\text{H}_2\text{N}\cap\text{NH}_2$  stands for a chiral or achiral chelating 1,2-diamine and  $(\text{PR}_3)_2$  represents two monodentate or one chiral bidentate phosphane, especially the BINAP ligand.  $\text{H}_2$ -hydrogenations supported by such systems are exceptional with because of their consistently high enantioselectivity, their chemoselectivity for carbonyl over olefin reduction and the very large substrate-to-catalyst ratios (up to  $10^6$ ) that can be attained.[1] In contrast, the isoelectronic Ir(III) hydrido complexes do not catalyze the direct hydrogenation by molecular  $\text{H}_2$ , but rather the transfer hydrogenation of the C=O bond.[2]



Structure (RB3LYP/LACV3P+\*\*) of the catalyst's model

Based on DFT (RB3LYP/LACV3P+\*\* and RPW91PW91/LACV3P+\*\*) and *ab initio* (MP2) calculations for a model of the Ir-based catalyst, we have explored the reaction mechanism in order to explain why direct hydrogenation cannot be observed.

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## Towards Organocatalytical Applications of Polyisocyanates

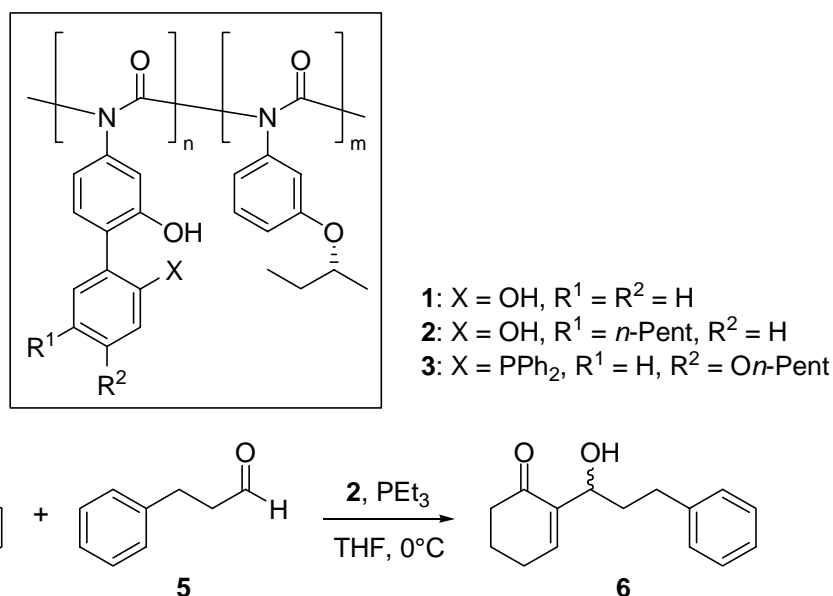
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Macromolecular catalysts do not only offer process-related advantages compared to conventional small-molecule catalysts. They also provide the possibility of activation and mutual orientation of two reaction partners by concerted action of two functional groups being apart in sequence but close in space.<sup>[1]</sup> Additionally helically chiral polymeric catalysts offer the opportunity to establish and maintain a chiral and uniform microenvironment at the active site.<sup>[2]</sup>

As we already demonstrated, metal coordinated polyisocyanates are active catalysts for asymmetric hydrogenations.<sup>[3]</sup> To adopt the concept of polymeric catalysts to organocatalysis we are about to develop biphenol-substituted polyisocyanates. These polymers are expected to act like multiple copies of small-molecule catalysts in a chiral environment established by their helical superstructure.

We were able to synthesise biphenol-substituted “sergeant and soldier”<sup>[4]</sup> polyisocyanates **1** and **2** and applied the latter in the Morita-Baylis-Hillman-Reaction of 2-cyclohexen-1-one **4** and 3-phenylpropionaldehyde **5** with triethylphosphane as cocatalyst. Unfortunately until now the results were unsatisfactory. Therefore we decided to synthesise the bifunctional phosphane-substituted phenolic polyisocyanate **3** that combines an advantageous phosphane-moiety with Brønsted-acidic properties in one molecule.



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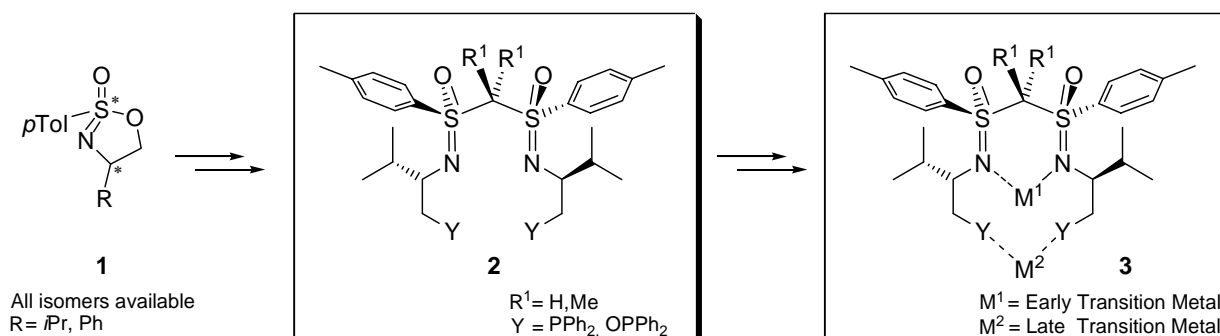
Towards *Heterobimetallic Asymmetric Catalysis Using Chiral Bis(sulfoximine)s*

Spohr V., Reggelin M.\*

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Since their first application in asymmetric catalysis in 1992,<sup>[1]</sup> chiral sulfoximines attracted increasing attention as ligands. The synthetic potential of this class of ligands has been outlined in a number of reviews.<sup>[2,3]</sup>

We recently reported on  $C_2$ -symmetric bis(sulfoximine)s **2** ( $R^1 = H, Y = PPh_2$ ) and demonstrated their principal suitability for asymmetric metal mediated transformations.<sup>[4]</sup> These ligands are easily prepared starting from (commercially available) cyclic sulfonimidate **1**. These new S–(C)–S linked bis(sulfoximine)s **2** offer the opportunity to complex two different metals by exploitation of the different coordination capabilities of the sulfoximine nitrogen and the phosphorus atoms in the N-bound sidechains. This in turn makes them interesting candidates for the development of *heterobimetallic* catalysts.<sup>[5,6]</sup>



Preliminary experiments revealed selective complexation of titanium by the N-donors without measurable effects (<sup>31</sup>P-NMR) on the P-atoms. Conversely, P-complexation of rhodium was possible without interference of the nitrogen atoms.

Progress along these lines, including structural investigations and first applications in asymmetric catalysis will be presented.

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## Functionalized, Helical Chiral Polyquinoxalines – Potential Organocatalysts

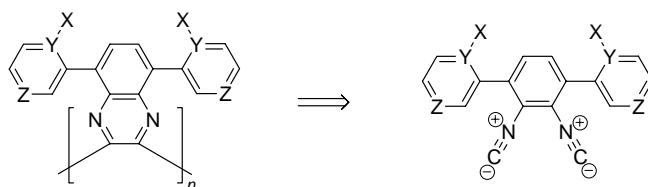
Hamburger, M.; Scholz, J.; Reggelin, M.\*

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Macromolecular catalysts based on helical chiral polymers offer the opportunity to combine process advantages (catalyst separation and recycling) with stereochemical function. In the ideal case these polymers display multiple copies of the active site in an uniform, chiral environment.

Beside polymethacrylates<sup>[1-3]</sup> and polyisocyanates<sup>[2]</sup> which have been proven to be active catalysts for the Pd-complex catalyzed allylic substitution reaction and asymmetric hydrogenation, respectively, polyquinoxalines appear to be interesting candidates as well. The functional group tolerance resulting from the Pd-complex mediated screw-sense-selective polymerization together with a pronounced configurational stability makes them very attractive.<sup>[4]</sup> Moreover, the possibility to incorporate biaryl motifs (**1** – **4**) into the polymer should entail the generation of diastereomorphic conformations at the active site which, in turn may result in a more effective “chirality transfer” from the polymeric backbone.

In the course of our efforts to prepare chiral polymeric organocatalysts, a number of new diisocyanide monomers have been prepared. Polymerization studies were undertaken and monitored by MS of the propagating oligomeric Pd-complexes.



- 1 X = NR<sub>2</sub>, Y = C, Z = N  
 2 X = O<sup>-</sup>, Y = N<sup>+</sup>, Z = CH  
 3 X = OH, Y = C, Z = CH  
 4 X = OH, PPh<sub>2</sub>, Y = C, Z = CH

Polyquinoxalines **1** represent polymeric chiral versions of the well known acylation catalyst DMAP. *N*-oxides of polyquinoxalines **2** may be catalytic in asymmetric allyl transfer reactions. Polyquinoxalines **3** with phenolic functions in the aryl groups may behave as chiral Brønsted acids like the well known organocatalyst TADDOL. Substitution of one hydroxyl function per monomer unit against a phosphorous donor may result in an organocatalyst **4** possibly suited for the Morita-Baylis-Hillman-Reaction.

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# First-Principles Investigation of the Schrock Mechanism of Dinitrogen Reduction

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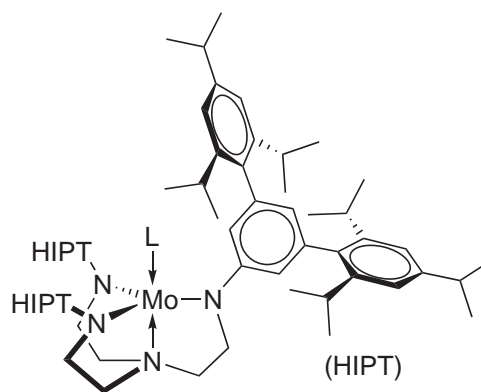
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The reduction of dinitrogen to ammonia is a very important reaction both for the living organisms and chemical industry. Most of the synthetic ammonia is used in the production of fertilizers which greatly enhance world food production. The reduction is performed using the Haber-Bosch process — a heterogeneous catalysis at elevated pressure and temperature. However, in nature, primitive bacteria and some blue-green algae are able to fix nitrogen at ambient conditions employing nitrogenases as efficient catalysts.<sup>1</sup> For decades an elegant way of reducing dinitrogen has been much sought-after by chemists.

Recently, Schrock *et al.* synthesized several well defined mononuclear molybdenum complexes that were shown to be capable of catalytically reducing dinitrogen to ammonia in the presence of both an electron and a proton source.<sup>2,3</sup> However, it turned out that efficient catalysis can only be achieved with very bulky ligands, i. e. hexaisopropylterphenyl substituents (HIPT, **Mo** complex). This system seems to be very finely balanced and already subtle changes to the ligands can result in a complete breakdown of the catalysis.<sup>4</sup>

In the past, several theoretical studies have been reported which investigated energetical details of the individual steps in the catalytic cycle. Most of the authors used model systems where the HIPT moiety is approximated by smaller substituents.<sup>5,6</sup> Our previous investigations are the only ones employing the full HIPT ligand.<sup>7,8</sup> We were able to demonstrate that the nature of the substituent does have a profound influence on the reaction energies — even with such subtle changes as replacing the remote isopropyl by methyl groups. Calculations incorporating models of the HIPT ligand were found to give significantly different results.<sup>7</sup>

Our present studies focus on the  $\text{NH}_3/\text{N}_2$  replacement step. For the reaction of the neutral species, ample evidence is provided that excludes a unimolecular loss of  $\text{N}_2$  from  $\text{Mo}(\text{N}_2)$ .<sup>9</sup> Instead, the reaction follows second order kinetics. Up to now it is unclear whether the exchange is a two step reaction with formation of a six-coordinated intermediate or a one step process similar to  $\text{S}_{\text{N}}2$  reactions. On the poster, we will present our latest results from density functional calculations as well as Car-Parrinello molecular dynamics simulations.<sup>10</sup>



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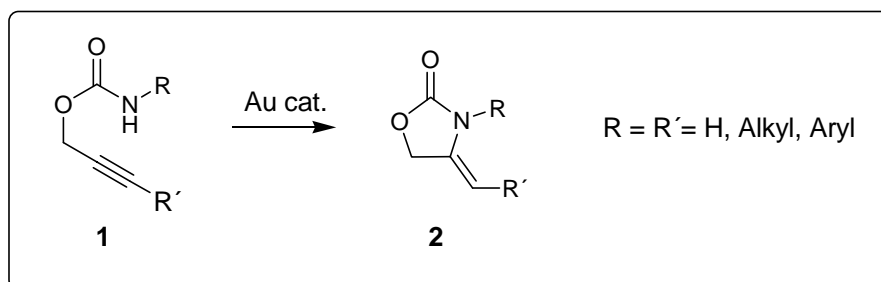
## Gold-Catalyzed Cyclization of O-Propargyl Carbamates: A Modular Access to Functionalized 4-Alkylidene-2-oxazolidinones

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In recent years, gold-catalysis [1] has evolved as a powerful concept for addition reactions of nitrogen nucleophiles to alkynes especially in intramolecular cases [2].

We have recently shown that, on treatment with catalytic amounts of gold(I) chloride (AuCl) and a base co-catalyst, O-propargyl carbamates (**1**) smoothly undergo a 5-exo dig cyclization at moderate temperatures to afford (Z)-4-alkylidene-2-oxazolidinones of type **2** in high yield [3]. As the substrates are readily accessible, this method opens a convenient, flexible and operationally simple route towards (Z)-4-alkylidene-2-oxazolidinones.



During our investigations, we discovered cases of metal-free hydroamination, depending on the electronic properties of R and R', in the presence of larger amounts of strong bases (such as KOH or *t*BuOK). Also, the class of 4-alkyl-oxazol-2-ones is accessible applying these reaction conditions. Currently, we are aiming at the application of this methodology in the synthesis of pharmacologically relevant compounds.

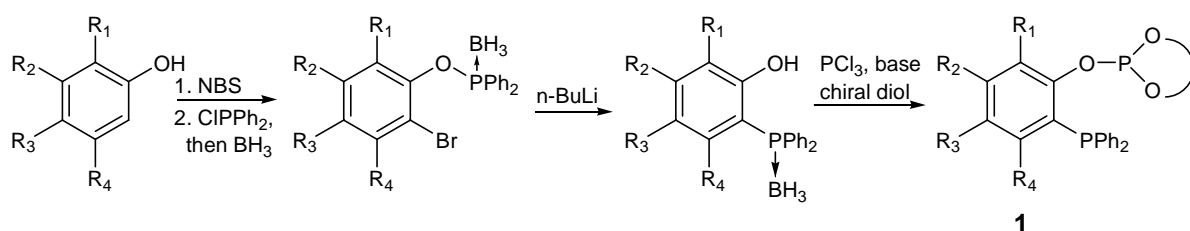
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## New Modular Chiral Phosphane-Phosphite Ligands and their Application in the Enantioselective 1,4-Addition of Grignard Reagents

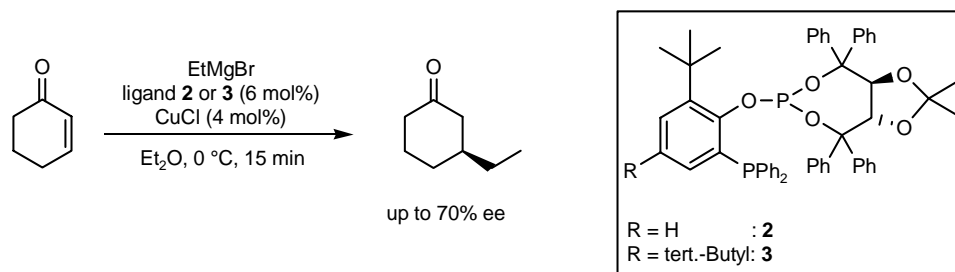
Tobias Robert, Janna Velder, Ingo Weidner and Hans-Günther Schmalz\*  
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An improved scheme for the synthesis of modular phosphane-phosphite ligands of type **1** was elaborated. Such ligands had previously been shown in our laboratories to give high enantioselectivities in the Rh-catalysed hydroboration of styrene [1].

As a key step of our Ligand synthesis, the BuLi-mediated Fries-type rearrangement of a boron-protected *ortho*-bromo aryl phosphinite is exploited. Chirality is introduced in the last step by using a chiral diol such as TADDOL or BINOL.



By screening a library of various ligands in the asymmetric Cu<sup>I</sup>-catalyzed 1,4-addition of ethylmagnesium bromide to cyclohexenone [2] we identified ligands **2** and **3**, with a bulky *ortho*-substituent, as particularly effective.



Thus, ligands of type **1** represent a new and promising class of phosphorous ligands for the direct enantioselective conjugate addition reaction of Grignard reagents. The modular nature of the synthesis opens various options for a further optimization of the ligand structure. Their application in the synthesis of bioactive compounds is under current investigation.

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# A Catalytic Enantioselective Approach to Some Bioactive Marine Natural Products

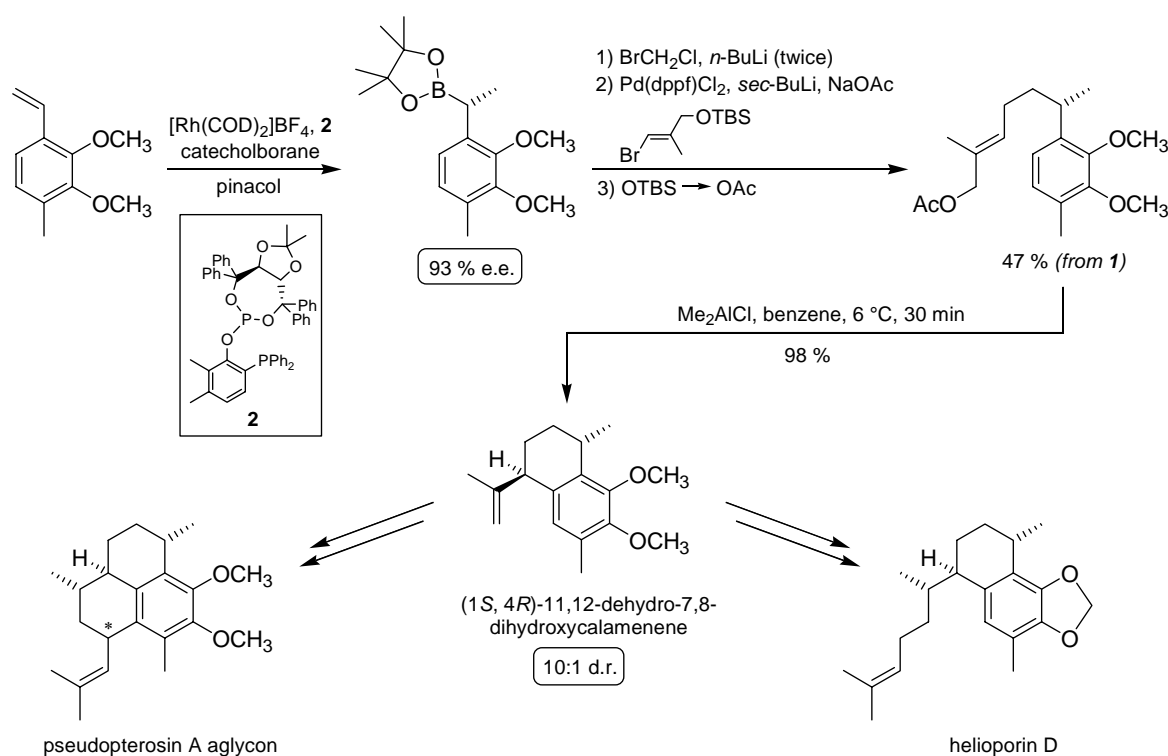
Susen Werle, Janna Velder, Hans-Günther Schmalz

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As part of our research programme concerning the use of organo-transition metal chemistry in the synthesis of bioactive compounds<sup>[1]</sup>, we have elaborated a methodology for the stereoselective preparation of the *trans*-calamenene **5**, which we consider as a key intermediate for the total synthesis of several marine natural products, such as pseudopterosins<sup>[2]</sup> and the helioporins<sup>[3]</sup>.

Our synthesis of **5** comprises

- (1) a Rh-catalyzed enantioselective hydroboration of the styrene **1** using the novel Taddol-derived chiral ligand **2**<sup>[4]</sup>,
- (2) a double homologation<sup>[5]</sup> of the resulting organoboron intermediate with subsequent Suzuki coupling,
- (3) a remarkably selective cationic cyclization of the allylic acetate **4** using Me<sub>2</sub>AlCl.



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## Asymmetric Bioreduction with Enoate-reductases

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The *trans*-specific asymmetric reduction of activated C=C bonds by flavin-dependent enoate reductases of the 'old yellow enzyme' family leads to the formation of up to two chiral centres and is thus of high interest for the synthesis of chiral compounds.

During our search for durable and oxygen-stable enoate reductases, we aimed at candidates possessing a desired broad-substrate spectrum which accept a wide range of C=C bonds bearing an electron-withdrawing activating group. We discovered that three Old Yellow Enzyme homologs, YqjM from *Bacillus subtilis* and the two isoenzymes OPR1 and OPR3 of 12-oxo-phytodienoate reductase (OPR) from *Lycopersicon esculentum* (tomato) displayed not only excellent chemo- but also high stereo-selectivities (up to 99% e.e.) in the asymmetric bioreduction of a broad range of activated alkenes, by accepting NADH and NADPH equally well. Depending on the activating substituent (carboxylic acid, imide, nitro-group), significant differences in reactivity and stereoselectivity were observed. Using nitroalkenes, a striking *switch of stereopreference* was observed between OPR1 and OPR3/YqjM. Modeling data based on the crystal structure of OPRs will help to explain this rare case of stereo-complementary behaviour. Using  $\alpha,\beta$ -unsaturated carboxylic acids, OPR1 and YqjM showed excellent stereoselectivities, whereas OPR3 was inactive towards this class of substrates.

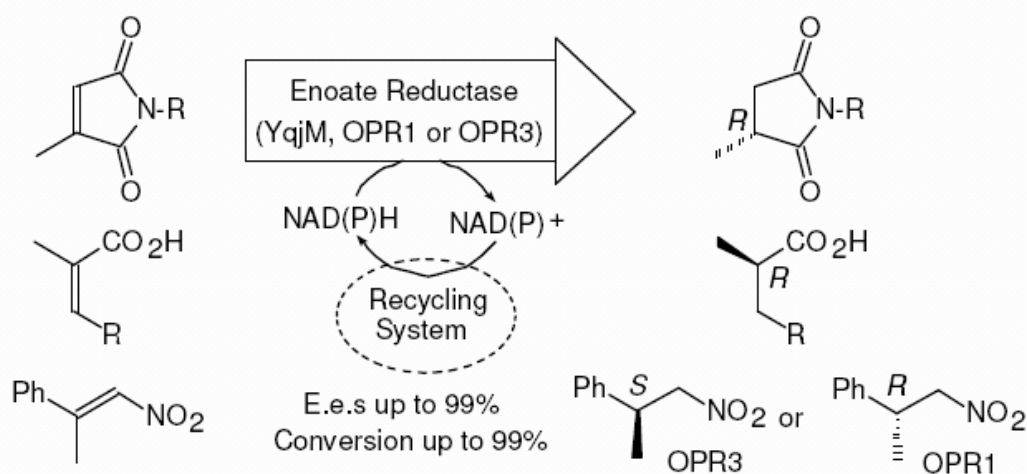


Figure 1.

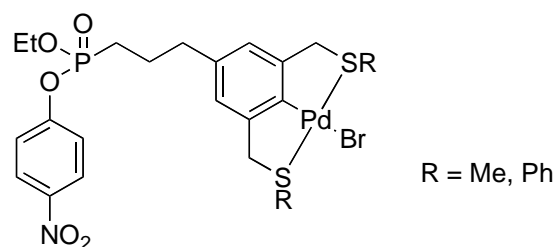
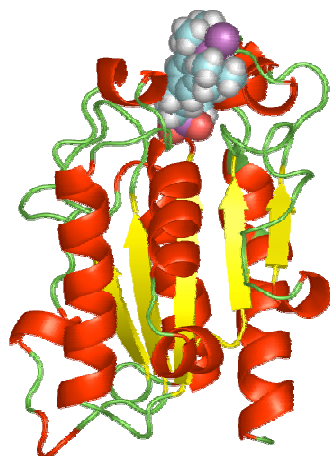
## CRYSTAL STRUCTURES OF 'ECE PINCER' COMPLEXES ANCHORED TO LIPASES

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The development of novel anchoring strategies for transition-metal complexes to proteins has high potential for future applications in the fields of protein structure elucidation (NMR, X-Ray, mass spectrometry), medicinal chemistry (biomarkers, MRI contrast agents, radiopharmaceuticals), biomaterials and catalysis (enantioselectivity, catalysis in aqueous media).

In our approach we have developed a selective anchoring method by which an organometallic pincer moiety is covalently attached to the active site of a lipase in a single reaction step, without the need of elaborate purification procedures. This approach is based on the inhibitory activity of nitrophenyl phosphonate esters to the catalytic triad (serine, histidine and asparagine) of lipases. Here we will present our immobilization method and describe the crystal structures we obtained. The crystal structure data show in detail how the pincer is attached to the enzyme. Depending on the crystallization conditions, pincer metal-induced monomeric and dimeric enzyme structures were found.



Left: cutinase modified by palladium pincer complex; Right: a lipase active site directed pincer complex

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## Novel (A)chiral Phosphite Orthopalladated and –platinated Complexes

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P-donor ligands have been widely studied and used in transition metal catalyzed organic transformations, especially in asymmetric synthesis. However, the high oxophilicity of phosphine ligands restricts their synthesis and application. Thus, the development of (a)chiral phosphite ligands and corresponding metalated complexes have become an interesting area in modern chemistry. [1]

For instance, complexes 1-3 showed reasonable to high catalytic activity in Suzuki coupling reactions. [1] These interesting results prompted us to develop the analogous chiral complexes 4, 5 as well as the (a)chiral phosphite PCP pincer complexes 6, 7 following reported synthetic procedures of orthopalladated phosphite complexes [2], [3] (Figure 1).

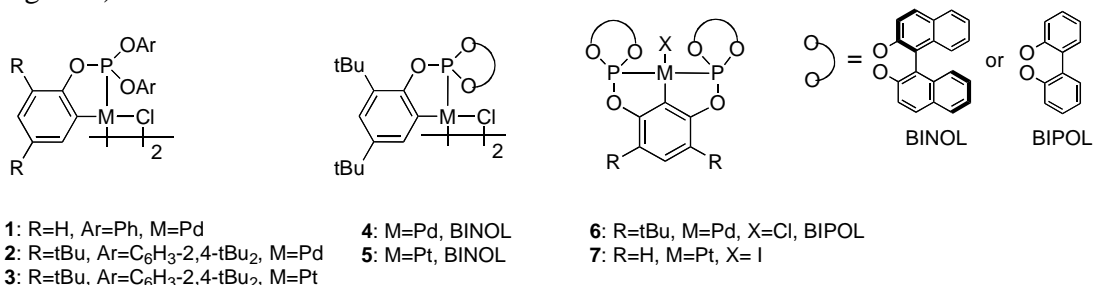


Figure 1

Finally, the applications and reactivities of obtained complexes will be also reported.

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- [1] R.B. Bedford, S.L. Hazelwood, M.E. Limmert, D.A. Albisson, S.M. Draper, P.N. Scully, S.J. Coles, M.B. Hursthouse, *Chem. Eur. J.*, 2003, 3216.  
 [2] R.A. Baber, R.B. Bedford, M. Betham, M.E. Blake, S.J. Coles, M.F. Haddow, M.B. Hursthouse, A.G. Orpen, L.T. Pilarski, P.G. Pringle, R.L. Wingad, *Chem. Commun.*, 2006, 3880.  
 [3] O. A. Wallner, V. J. Olsson, L. K. Eriksson, K. J. Szabo, *Inorg. Chim. Acta*, 2006, 1767.

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## QM/MM Simulations of ATP Hydrolysis in Myosin: Effect of Protonation States on the Barrier of Hydrolysis

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The molecular motor myosin converts chemical energy from ATP hydrolysis into mechanical work, thus driving essential motility processes such as cytokinesis, vesicle transport, or muscle contraction. The details of the chemical mechanism of ATP hydrolysis and its mechanochemical coupling to actin binding are poorly understood. Here, combined quantum mechanical/molecular mechanical (QM/MM) reaction path calculations are presented.<sup>1</sup> Three reaction routes (Figure 1a) differing in the activation mechanism of the attacking water molecule were found to be associative. However, the computed barriers are still significantly higher than those measured experimentally. It has been shown that the protonation state influences the barriers of pyrophosphate hydrolysis in vacuum.<sup>2</sup> It will be investigated whether this effect is important for the reaction in myosin.

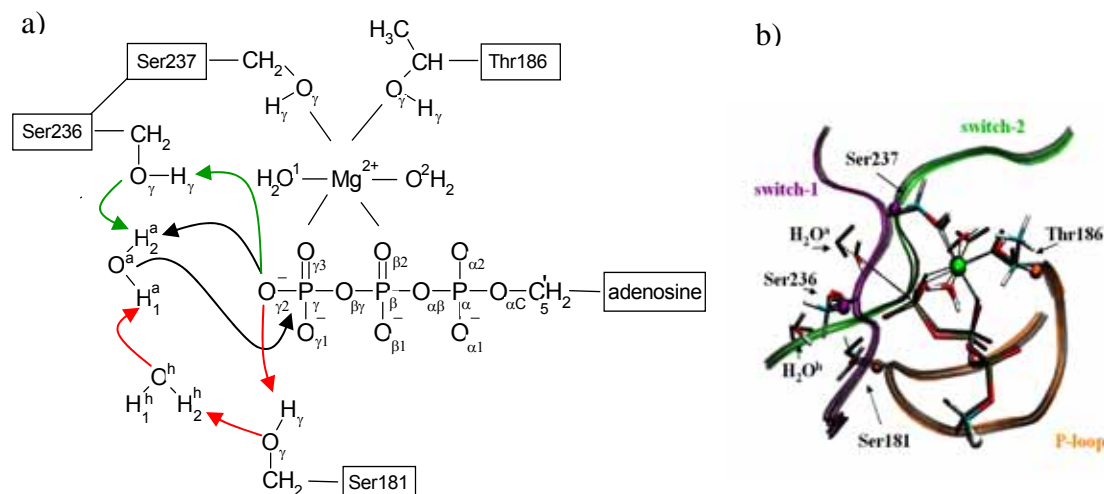


Figure 1: Reaction site in myosin. a) In the direct, Ser236, and Ser181 paths the attacking water is activated respectively by the  $\gamma$ -phosphate moiety itself (black arrows), the side chain of Ser236 or the side chain of Ser181 (grey arrows). b) The close overlap of the QM/MM minimized structure of ATP in myosin is almost identical to the crystal structure.

<sup>1</sup> Schwarzl, S. M.; Smith, J. C.; Fischer, S. *Biochemistry*, **2006**, 45, 5830-5847.

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