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Asymmetric Catalysis

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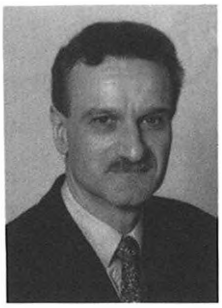
Abstract: Our main research interests are in the areas of homogeneous and heterogeneous asymmetric catalysis, focusing on the development of new classes of chiral ligands for the enantiocontrol of metal-catalyzed reactions.



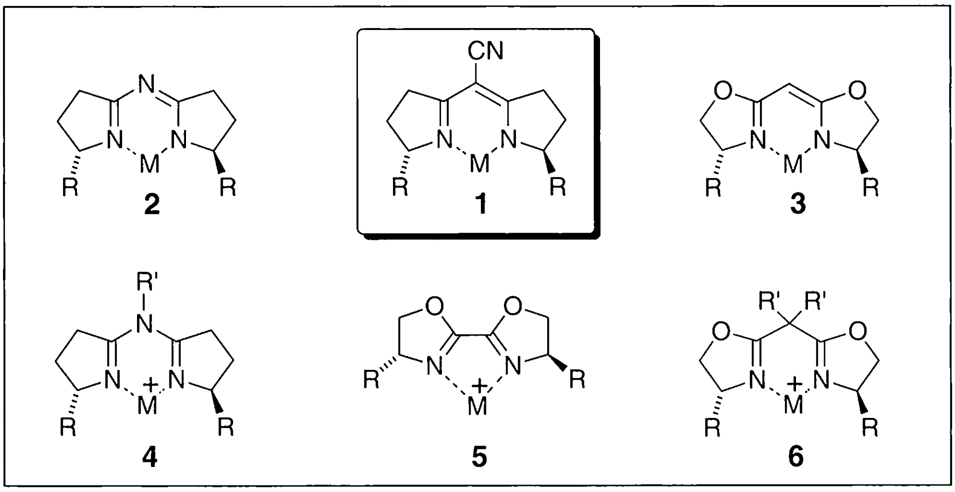
Andreas Pfaltz was born 1948 in Basel. He completed his Ph.D. in 1978 under the guidance of *A. Eschenmoser* at the ETH-Zürich and spent 1978–79 as a postdoctoral associate with *G. Stork*, Columbia University. He returned to the ETH-Zürich to study for his Habilitation (1980–86) and was Privatdozent there until 1990 when he moved to the University of Basel as Professor of Organic Chemistry. Between 1995 and 1998, he was director at the *Max-Planck*-Institut für Kohlenforschung, Mülheim an der Ruhr, and in 1999, he returned to Basel as Professor of Organic Chemistry.

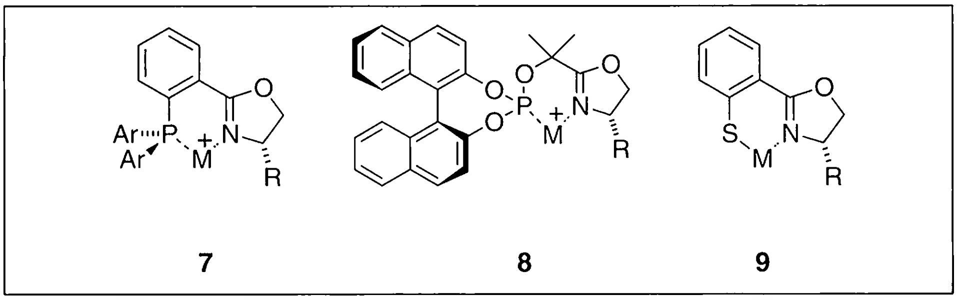
Catalytic methods for the synthesis of enantiomerically pure compounds are of great importance for the preparation of biologically active substances such as pharmaceuticals, fragrances, or crop-protecting agents. One of our research goals is the development of new and generally useful classes of chiral ligands that allow a metal-catalyzed process to be controlled in such a way that one of two enantiomeric products is formed with high preference over the other. By studying the effect of chiral ligands on a metal-catalyzed process, we also hope to learn more about the reaction mechanism and the specific interactions between the catalyst and the substrate that are necessary for stereochemical control. An additional, more general objective of our research is to develop some rational guidelines for the design of suitable chiral ligands for a given application. Although we focus primarily on homogeneous processes, we are also interested in enantioselective heterogeneous catalysis [1].

Semicorrins and Related C_2-Symmetric Nitrogen Ligands

In the mid 1980's, we developed a new class of chiral bidentate nitrogen ligand for asymmetric catalysis, the C_2-symmetric semicorrins **1**. In these compounds, the two substituents at the stereogenic centers are located in close proximity to the metal center and, therefore, are expected to have a distinct, direct effect on a reaction taking place in the coordination sphere. Semicorrins of this type were found to induce high enantioselectivities in the copper-catalyzed cyclopropanation of olefins with diazo compounds and in cobalt-catalyzed conjugate reductions of α,β-unsaturated carboxylic esters and amides [2].

These results prompted us and a number of others, including the groups of *Masamune*, *Evans*, *Corey*, *Helmchen*, and *Lehn*, to develop structurally related ligands such as aza-semicorrins **2** and **4** or bisoxazolines **3**, **5**, and **6**. The bisoxazolines of type **6**, especially, have proven to be extraordi-





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narily, highly versatile ligands for the enantiocontrol of a variety of metal-catalyzed processes [2][3].

Phosphinooxazolines and Other Chiral *P,N*- and *S,N*-Ligands

More recently, during the course of our studies on Pd-catalyzed allylic substitution, we changed the direction of our work toward unsymmetrical *P,N*-ligands such as **7**. We hoped that the different electronic *trans*-influences of the P- and N-atoms in these ligands could be exploited for controlling the stereochemical course of allylic alkylations [4], and, indeed, phosphinooxazolines of this type were found to be highly efficient controller ligands [5–7]. The different *trans* influences of the P- and N-atoms is reflected in the different bond lengths between Pd and the allylic termini (*Figure*).

Pd complexes of type **7** (R = *t*-Bu) are also excellent enantioselective catalysts for *Heck* reactions (*Scheme 1*) [8]. The dihydrofuran **12** as well as other cyclic products could be obtained in excellent yield with very high enantiomeric excess (*ee*).

Analogous iridium complexes were found to be promising catalysts for the enantioselective hydrogenation of imines [9] and olefins (*Scheme 2*) [10]. These are the only catalysts known so far that hydrogenate unfunctionalized olefins with high *ee* and such high turnover numbers and turnover frequencies (TOF).

In addition, we are studying various other catalytic reactions, including Cu-catalyzed 1,4-additions to α,β-unsaturated carbonyl compounds [11] using phosphinooxazolines **7** or related ligands such as phosphite- and mercapto-oxazolines **8** [11b][12], and **9** [11a].

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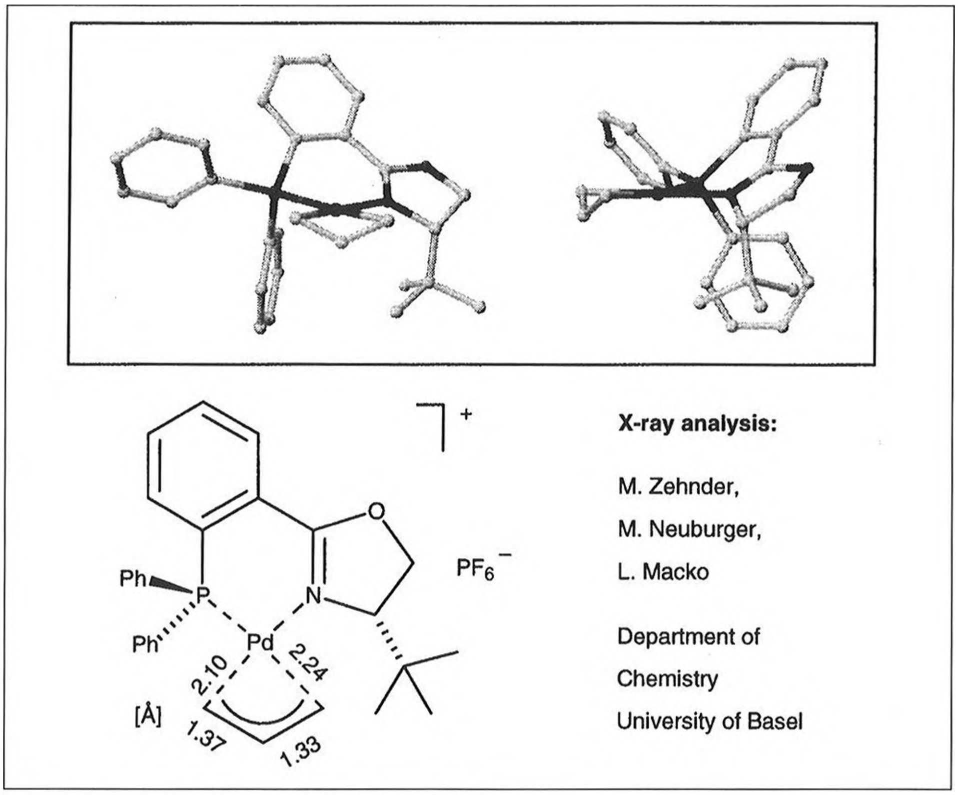

X-ray analysis:

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M. Neuburger,
L. Macko

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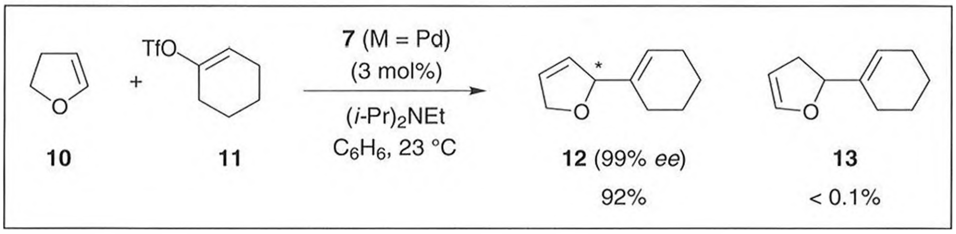
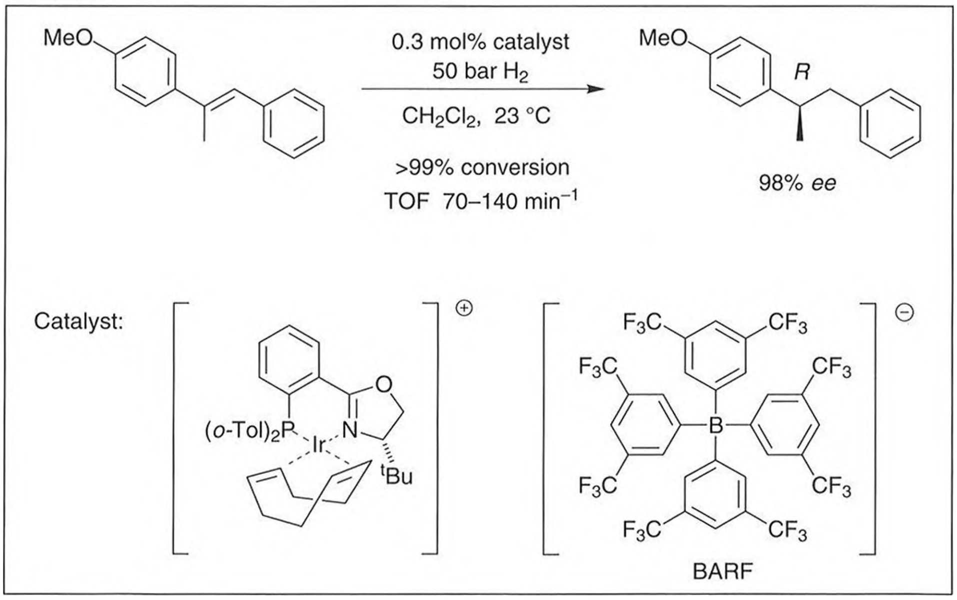
Figure. *X-Ray analysis of a Pd complex of type* **7**

Scheme 1



Scheme 2



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