# **Prof. Can Li's Laboratory**

# Heterogeneous chiral catalysis on surfaces, in nanopores and with emulsions

Chiral catalysis is of great industrial interest for the production of enantiomerically pure compounds. Although many homogeneous chiral catalysts have been developed, the difficulty of the product purification and catalyst recycle is one of the obstacles of the practical applications. The design and synthesis of efficient and recyclable heterogeneous chiral catalysts remain the challenges and attracted much research interests in the past decades. The present work focuses on the design, synthesis, characterization and application of high performance heterogeneous chiral catalytic systems for the synthesis of fine chemicals and chiral pharmaceuticals. Heterogeneous chiral catalysts were prepared by various strategies such as covalent grafting, encapsulation, ion interaction, chiral modification, copolymerization and interphase assembly of amphiphilic molecules etc. Chiral catalysis on the surfaces, in the nanopores and with emulsions have been investigated for the asymmetric epoxidation, hydrogenation, hydroformylation, transfer hydrogenation, Diels-Alder, Aldol, and biocatalysis reactions. Some heterogeneous chiral catalysts have been demonstrated to be highly active, enantioselective, and readily recyclable. Very interesting phenomena such as pore confinement, nano-size effect, ligand acceleration, configuration reversal, and cooperative activation have been observed and the heterogeneous chiral catalytic mechanisms have been studied.

#### 1.1 Chiral epoxidation

Chiral Sharpless catalysts and Mn(salen) catalysts have been immobilized onto mesoporous silicas (Fig.1). We found that in some cases heterogeneous Mn(salen) catalysts exhibit higher TOF, cis/trans ratio and enantioselectivity than those of the homogeneous catalysts for the asymmetric epoxidation of some unfunctionalized olefins. For examples, heterogeneous catalyst gives higher TOF ( $14.8 h^{-1} vs 10.8 h^{-1}$ ) and ee values (90.6% vs 80.1%) than those of the homogeneous catalyst for the asymmetric epoxidation of 6-cyano-2, 2-dimethylchromene. Also the heterogeneous catalyst shows higher cis/trans ratio (17.6 vs 0.38) and ee values (94.6% vs 54.8%) than those of the homogeneous catalyst for the asymmetric epoxidation of cis-methylstyrene. The pore confinement effects were studied by using mesoporous supports with different pore size and hydrophobicity, grafting linkages with different length and rigidity as well as auxiliary.



Fig.1 Chiral Sharpless catalysts and Mn(salen) catalysts immobilized onto mesoporous silicas

We present a novel method for the fabrication of immobilized polyoxometalate catalysts that directly use a self-assembled polyoxometalate solution without isolation and purification (Fig. 2). Specifically, self-assembled  $[WZn_3(ZnW_9O_{34})_2]^{12}$  catalyst can be selectively immobilized into layered double hydroxides in the presence of undesired anions. The material thus obtained shows high dispersions and good hydrothermal stability. The heterogenized catalyst exhibits excellent activity (turnover frequency up to 18 000 h<sup>-1</sup>, 50 °C) in the epoxidation of allylic alcohols with aqueous H<sub>2</sub>O<sub>2</sub> and can be readily recycled without apparent loss of activity.



Fig.2 Immobilized polyoxometalate catalysts into layered double hydroxides Participant: Song Xiang, Huidong Zhang, Peng Liu and Changhao Wang

# 1.2 Chiral hydrogenation

Cinchonidine-modified  $Pt/\gamma$ -Al<sub>2</sub>O<sub>3</sub> catalysts show excellent performance in the enantioselective hydrogenations of  $\alpha$ -ketoesters. For the enantioselective hydrogenations of ethyl pyruvate, the enantioselectivity as high as 99% ee is achieved on cinchonidine-modified  $Pt/\gamma$ -Al<sub>2</sub>O<sub>3</sub>. In the enantioselective hydrogenation of ethyl 2-oxo-4-phenylbutyrate (EOPB), the TOF can reach as high as 20,000 h<sup>-1</sup> with 86% ee (Fig. 3). The hydrogenation product, (R)-(+)-EHPB, is an important building block for the synthesis of several commercially

important A.C.E. inhibitors. We have cooperated with a chemical company in Jiangsu Province for the commercialization of this process for pharmaceuticals production. Our recent results show that Pt nanoparticles confined in the carbon nanotubes exhibits enhanced activity and enantioselectivity.



Fig.3 enantioselective hydrogenations of α-ketoesters on CD-modified Pt catalysts Participant: Xin You, Xiaohong Li and Zhijian Chen

#### **1.3 Chiral hydroformylation**

Heterogeneous chiral hydroformylation catalysts were prepared by chiral modification of supported rhodium catalysts Rh/SiO<sub>2</sub> and stabilization of rhodium nanoparticles with chiral diphosphorus ligand such as (R)-BINAP, (S,S)-DIOP, and (R,R)-Ph-BPE (Fig. 4). The chirally modified catalysts exhibit similar or even better catalytic performance than the homogeneous counterparts, and up to 90% ee and 100% branched regioselectivity can be obtained for the asymmetric hydroformylation of olefins. <sup>31</sup>P MAS NMR and CO-IR spectra indicate that the diphosphine ligands strongly adsorb on rhodium surface through coordination. A catalytic mechanism involving surface multi-site cooperation is proposed.



Fig. 4 Heterogeneous asymmetric hydroformylation on chirally modified/stabilized rhodium nanoparticles catalysts

# Participant: Difei Han

#### 1.4 Chiral transfer hydrogenation

Noyori's catalyst (RuTSDPEN) has been also successfully covalent-grafted on silica as well as supermagnetic nanoparticles (Fig. 5). The catalysts show high activity (> 99% conv.) and enantioselectivity (> 90%) for transfer hydrogenation of aromatic acetophenones and imines, and can be conveniently separated and recycled.



Fig. 5 Noyori's catalyst (RuTSDPEN) covalent-grafted on silica as well as supermagnetic nanoparticles

An amphiphilic polymer-based chiral diamino metal complexes emulsion catalyst also exhibits enhanced activity (30-fold rate acceleration) for the transfer hydrogenation of aryl aldehydes (Fig. 6). The excellent performance can be ascribed to the high local concentration of reactants resulting from the cooperative effects of both the hydrophilic and hydrophobic parts of the emulsion catalyst.



Fig. 6 Transfer hydrogenation by amphiphilic polymer-based chiral diamino metal complexes emulsion catalyst

# Participant: Jun Li

#### **1.5 Chiral Aldol reaction**

Chiral organic acid-base catalysts have been immobilized on alumina through adsorption. The configuration reversal was observed for chiral Aldol reactions on amino acids (e.g. L-Proline) adsorbed  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, which switches the enantioselectivity of the direct Aldol reaction of acetone with p-nitrobenzaldehyde from 68% ee (*R*, free L-proline) to 21% ee (*S*).



Fig. 7 The configuration reversal for chiral Aldol reactions on chiral organic acid-base catalysts modified alumina

Easy-to-handle chiral emulsion catalytic systems were developed by the self-assembly of amphiphilic chiral catalyst at the water-oil interphase (Fig. 8). Amphiphilic chiral emulsion catalysts derived from amino acid can catalyze asymmetric Aldol reactions with up to 99% ee (Fig. 2). Remarkable enhancement of reaction rate and selectivity was found for chiral emulsion catalysts.



Fig. 8 The configuration reversal for chiral Aldol reactions on chiral organic acid-base catalysts modified alumina

# Participant: Lin Zhong and Qiang Gao

#### **1.6 Chiral Diels-Alder reaction**

Chiral organic acid-base catalysts or ligands have been immobilized on silica or alumina through adsorption and reaction (Fig. 9). Metal bis(oxazoline) complexes supported on silica show up to 96% ee for Diels-Alder reactions and an interesting reversal of the absolute product configuration was observed for immobilized (*S*)-PhBOX-Cu(II) complex. Theoretical study clarifies the mechanism of this phenomenon.



Fig. 9 The configuration reversal for chiral D-A reactions on metal bis(oxazoline) complexes supported on silica

# **Participant: Hong Wang**

#### 1.7 Biocatalysis

A magnetically separable, highly efficient biocatalyst adsorbed in magnetic siliceous mesocellular foam was prepared for the kinetic resolution of secondary alcohols. The resulting heterogenized biocatalyst adsorbed in the magnetically separable, hydrophobic foam showed much better catalytic activity than that of the commercial lipase powder for the kinetic resolution of secondary alcohols, and can be readily recycled for at least seven times without significant loss of its catalytic performance.

#### Participant: Yanmei Zhang



Fig. 10 Kinetic resolution of secondary alcohols on magnetically separable, highly efficient biocatalyst adsorbed in magnetic siliceous mesocellular foam

