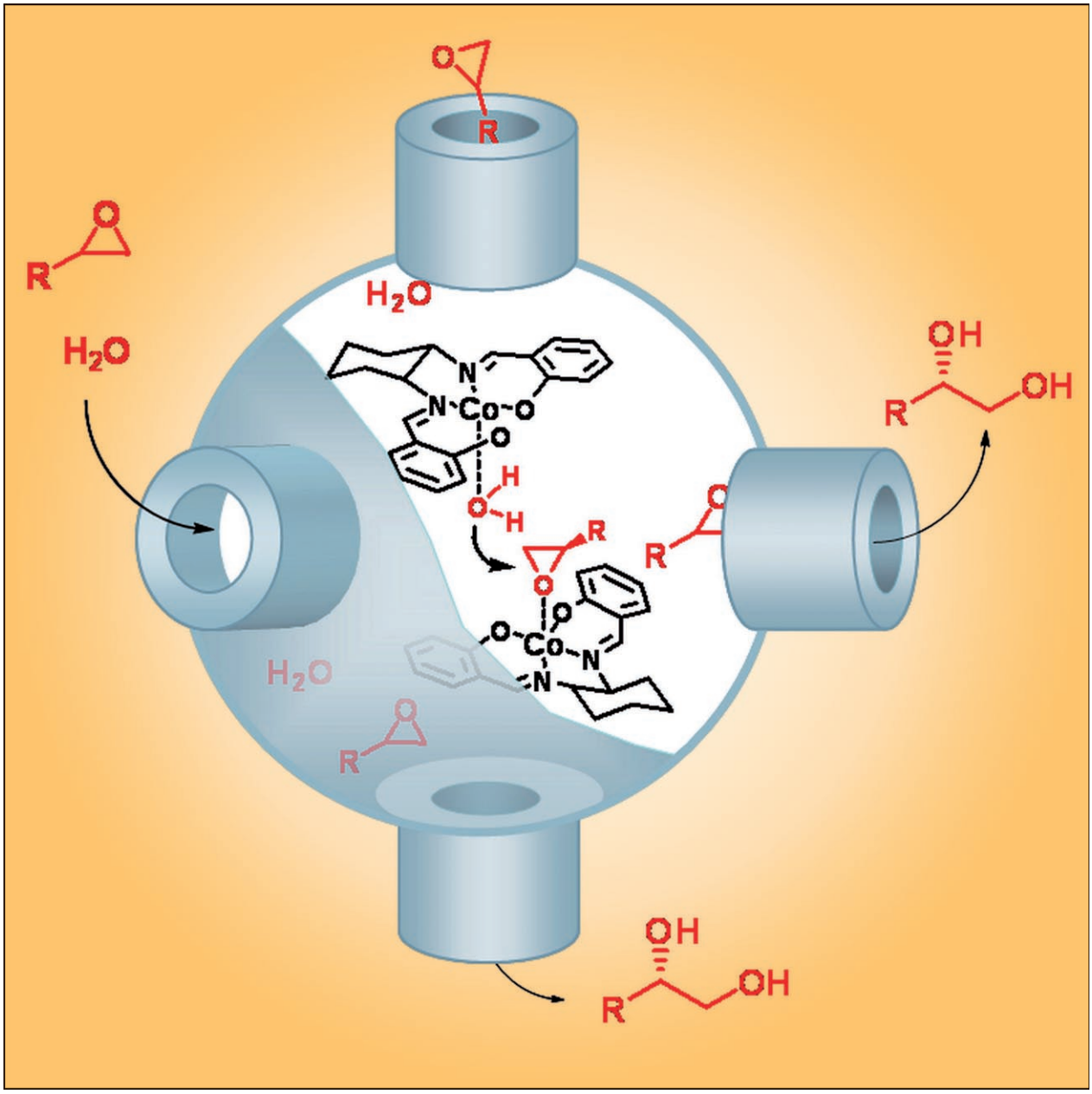
DOI: 10.1002/asia.200800110

Asymmetric Catalysis with Metal Complexes in Nanoreactors

Qihua Yang, Difei Han, Hengquan Yang, and Can Li*[a]

Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday



Abstract: Recently, the field of heterogeneous asymmetric catalysis, generally using chiral solid catalysts, has attracted much attention in the production of single enantiomers. Among versatile chiral solid catalysts, chiral metal complexes confined in nanoreactors often exhibit very unique enantioselectivity and catalytic activity compared to homogeneous catalysts. In this Focus Review, we summarize the recent advances in asymmetric reactions on chiral metal complexes confined in nanoreactors with an emphasis on the confinement effect and cooperative activation effect of the nanoreactor and new strategies for the preparation of chiral solid catalysts, such as the encapsulation of chiral metal complexes in the nanocages of mesoporous silica and incorporation of chiral ligands in the network of mesoporous organosilicas.

Keywords: asymmetric catalysis · epoxidation · heterogeneous catalysis · nanoreactors · organosilicas

1. Introduction

Single enantiomers have attracted much research attention because of their importance in the pharmaceutical industry and other applications such as agricultural chemicals, flavors, fragrances, and materials. Asymmetric catalysis, synthesis from chiral compounds, and resolution of racemates have been widely used for obtaining single enantiomers. Among these methods, asymmetric catalysis is the most attractive because it uses a relatively small amount of chiral catalyst to transform large amounts of substrate containing prochiral elements into chiral products.[1]

Since the pioneering work of enantioselective hydrogenation of olefinic substrates on rhodium complexes containing chiral phosphine ligands by William Knowles and colleagues in the early 1970s,[2a] tremendous progress has been made in the field of homogeneous asymmetric catalysis to generate enantiomerically enriched compounds. A major breakthrough came in 1980 when Noyori et al. initiated their pioneering work on chiral ligands, particularly axially chiral 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (binap), which are still used in the manufacture of β-hydroxy esters, for the synthesis of carbapenems and the Lipitor side chain, for example. Because of their milestone contributions to asymmetric catalysis, Knowles, Noyori, and Sharpless were awarded the 2001 Nobel Prize in Chemistry.[2b] Versatile asymmetric reactions and chiral catalysts have been developed.[3] Among various kinds of chiral catalysts, transition-metal complexes are most often used for homogeneous asymmetric catalysis. More and more elegant chiral catalysts have been synthesized which can catalyze asymmetric reactions with enantiomeric excesses approaching 100 %.[4]

However, compared with thousands of papers published and great advances made in the field of homogeneous asymmetric catalysis, only a few dozen processes have been industrialized.[5] The main reasons include the difficulty in the separation of the catalyst, the purification of the product, and the recovery of the expensive catalysts. Heterogeneous asymmetric catalysis, mostly using solid catalysts, has attracted much research attention because it has the advantages of easy separation of the catalyst and product, recycling of the recovered catalyst, and easy handling for the large-scale production.

Many research efforts have been made to develop asymmetric synthesis using heterogeneous catalysts, such as assembling the chiral catalysts in emulsion and phase-separation media,[6] heterogenization of the chiral catalyst by polymerization,[7] immobilization of chiral catalysts onto solid supports, and so on.[8] The immobilization of chiral catalysts onto solid supports is the most popular method to prepare heterogeneous asymmetric catalysts. Both the surface and porous matrix of a solid support could be used to anchor the asymmetric active center. The metal complexes can be supported on oxide surfaces, such as by chiral self-dimerization, to create asymmetric oxidative coupling catalysis and surface functionalization with achiral reagents to promote asymmetric catalysis.[9] Moreover, the inner pore of a solid support immobilized with chiral catalysts provides a novel chiral space for asymmetric catalysis. Four main approaches have been commonly used to immobilize the chiral catalyst: 1) adsorption of chiral modifiers onto an active metal surface; 2) covalent tethering of homogeneous catalysts;

[a] Prof. Dr. Q. Yang, Dr. D. Han, Dr. H. Yang, Prof. Dr. C. Li
State Key Laboratory of Catalysis
Dalian Institute of Chemical Physics
Chinese Academy of Sciences
457, Zhongshan Road, Dalian (China)
Fax: (+86) 411-84694447
E-mail: canli@dicp.ac.cn

3) electrostatic interaction between a negatively charged framework and a cation; and 4) encapsulation. Organic and inorganic materials, such as metal oxides,[10] clays,[11] zeolites,[12] activated carbon,[13] porous silica,[14] mesoporous silicas,[15] and polymers[16] have been employed as supports for immobilizing the chiral catalyst. The inorganic materials usually have advantages over organic polymers in view of chemical, mechanical, and thermal stabilities.

Mesoporous silicas with high surface area, tunable and large pore diameter (2–50 nm), and ordered pore arrangement are excellent support materials for chiral catalysts.[15] The tunable mesopores provide a large space to immobilize chiral catalysts and allow free diffusion of reactants and products. The ordered pore arrangement of mesoporous materials can make the microenvironment of immobilized chiral catalysts uniform and isolated. The rich amount of hydroxyl groups available on the surface of mesoporous silicas offers the anchoring sites for the immobilization of various metal complexes. In some cases, the heterogeneous catalysts based on mesoporous support can exhibit better performance than the homogeneous counterpart because of the uniform distribution, site isolation, pore confinement effect, and so on.[17] A chiral catalyst with the ligand 1,1′-bis(diphenylphosphino)ferrocene (dppf) anchored to the inner walls of the mesoporous support MCM-41 and coordinated to Pd^{II} exhibits an enantioselectivity as high as 99% in the allylic amination of cinnamyl acetate, which is far superior to that of its homogeneous counterpart or that of a surface-bound analogue attached to a nonporous silica.[18]

The nanopore of the mesoporous silicas immobilized with chiral catalysts can be regarded as a nanoreactor for asymmetric synthesis. The microenvironment of the nanoreactor could be finely modified to meet the requirement of a given reaction, such as the surface hydrophobicity/hydrophilicity, surface polarity, and electrostatic properties through direct cocondensation or postsynthesis.[19] Recently, periodic mesoporous organosilicas (PMOs) built from bridged organosilane precursors, $(R'O)_3Si\text{-}R\text{-}Si(OR')_3$, wherein an organic group R is an integral part of the mesoporous wall, opened up a new approach for the modification of the microenvironment of the nanopore.[20–22] The bridging organic groups in the pore wall of PMOs not only modify the surface properties of the materials but also endow the PMOs with novel physical and mechanical properties, such as improved hydrothermal and mechanical stability.[23–26] The chemical and physical properties of PMOs, especially the microenvironment of the nanopore, can be tuned towards specific appli-

Abstract in Chinese:

多相不对称催化是解决手性合成工业化的重要途径之一。本文综述了在多孔材料纳米孔道内引入手性有机金属配合物的制备方法和纳米反应器限阈的催化剂上手性催化反应的最新研究进展，特别介绍了将手性有机金属配合物引入有机-无机杂化介孔材料和限阈在纳米反应器中的新方法，并深入探讨了纳米反应器中手性催化反应的限阈效应及双中心活化耦合加速反应的效应。

Qihua Yang *(born in 1969) obtained her PhD in inorganic chemistry at Northeast Normal University in 1997. She was a posdoctoral fellow at the Dalian Institute of Chemical Physics (1997–1999) and Laboratory COMS-CNRS/CPE, France (1999–2001). She then worked at Toyota Central R&D Labs. Inc., Japan from 2001–2003 as a visiting scientist. She was promoted to professor at the Dalian Institute of Chemical Physics in 2003, and her research interests include the synthesis of hybrid organic–inorganic mesoporous materials and their application in heterogeneous asymmetric catalysis.*

Difei Han *(born in 1974) obtained his PhD degree under the supervision of Prof. Can Li from the Dalian Institute of Chemical Physics, Chinese Academy of Sciences. His research interests include heterogeneous chiral catalysis for the synthesis of fine chemicals and chiral pharmaceuticals, especially heterogeneous asymmetric hydrogenation and hydroformylation.*

Hengquan Yang *(born in 1976) obtained his PhD degree from Wu Han University in 2004. From 2004 to 2007, he worked as a postdoctoral fellow under the supervision of Prof. Can Li and Prof. Qihua Yang at the Dalian Institute of Chemical Physics, Chinese Academy of Sciences. He is now a professor at Shanxi University and his research interests include the synthesis and application of mesoporous materials in fine chemical synthesis, especially heterogeneous asymmetric catalysis.*

Can Li *(born in 1960) obtained his PhD at the Dalian Institute of Chemical Physics in 1988. He became a full professor in 1993, and was elected as a member to the Chinese Academy of Sciences in 2003 and to the Third World Academy of Sciences in 2005. He is currently the chairman of the Catalysis Society of China and the Vice President of the International Association of Catalysis Societies. He received the International Catalysis Award in 2004 and Hong Kong HLHL Prize in 2005. His research areas span physical chemistry, catalysis, applied spectroscopy, heterogeneous chiral synthesis, and photocatalysis.*

CHEMISTRY
AN ASIAN JOURNAL

cations by adjusting the organic species in the network. It was demonstrated that PMOs with enhanced surface hydrophobicity exhibited higher catalytic activity than the mesoporous silica either for acid-catalyzed esterification[27] or asymmetric transfer hydrogenation.[28] Similar to mesoporous silicas, the PMOs also have high surface area and tunable and well-ordered mesopores. If the chiral ligand or chiral catalysts are incorporated in the pore walls of the PMOs, a new class of chiral solid catalysts could be developed.

Though versatile methods have been used to immobilize chiral catalysts in the nanopores of mesoporous silicas, such as chemical grafting, ion exchange, adsorption, and encapsulation, among others, only limited numbers of efficient heterogeneous asymmetric catalytic systems have been reported to date. The development of efficient chiral solid catalysts is still one of the main objectives in the field of heterogeneous asymmetric catalysis.

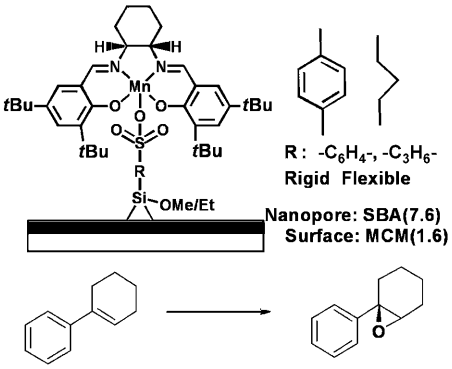
In many cases, the catalysts in nanopores show lower activity and enantioselectivity than those of homogeneous catalysts in asymmetric reactions under the same conditions. Our recent studies show that metal complexes confined in nanoreactors could give higher enantioselectivity and activity than their homogeneous counterparts in the asymmetric catalysis.[17b] Some other research groups have also observed the similar phenomena that a significant enhancement of the enantioselectivity was observed for the chiral catalysts immobilized in the nanopores of mesoporous silica.[18]

The improved catalytic performance of the chiral catalysts in nanoreactors could be generally attributed to the pore confinement effect. The pores of mesoporous silica may increase the rigidity of the overall catalytic structure because of the rigid structure of the pore and the weak interactions possibly involved in the chiral reactions in pores, such as van der Waals forces, hydrogen bonding, and physical adsorption.[17a] The energy range of these interactions is in the same magnitude of the energy difference between the transition states of the *R* product and the *S* product. This suggests that the weak interactions are able to affect or even to alter the energy difference between the two transition states accordingly to change the enantioselectivity or even reverse the chiral selectivity. Because the energy difference between the two transition states is very small, the enantioselectivity is very sensitive to the surface/pore environment of the immobilized catalysts.[17a] Through adjusting the pore size, the length of linkage groups, and surface properties of the nanopore, the confinement effect of the nanoreactor could be enhanced.[17b] Asymmetric catalysis in the nanoreactor is promising and provides opportunities to develop more efficient asymmetric synthesis systems based on solid chiral catalysts. In this Focus Review, we mainly summarize the recent advances of asymmetric catalysis in nanoreactors. The supported chiral catalysts and the asymmetric catalysis on other inorganic or organic supports can be found in recent reviews.[17,29]

2. Chiral Metal Complexes Immobilized in Mesoporous Materials

Heterogeneous chiral metal catalysts immobilized in the nanopores of mesoporous materials have been synthesized and applied for asymmetric hydrogenation, epoxidation, alkylation, and nitroaldol reactions, among others.[30] These immobilized catalysts exhibit inferior catalytic performance compared with their homogeneous analogues, and the effects of mesoporous materials on chiral catalysis are not well investigated in these cases. However, in some cases, the catalysts confined in nanopores show comparable or even higher conversions and *ee* values than the homogeneous catalysts.

Recently, immobilization of chiral [Mn(salen)] catalysts in mesoporous silicas have been investigated for the asymmetric epoxidation of unfunctionalized olefins.[31] Various factors influencing the heterogeneous catalysts were investigated in detail. Several chiral [Mn(salen)] catalysts were axially immobilized in the nanopores and on the external surface of mesoporous materials through phenoxy groups and organic sulfonic groups. The [Mn(salen)] catalysts immobilized in the nanopores generally exhibit higher chemical selectivity and enantioselectivity than those immobilized on the external surface of supports for the asymmetric epoxidation of unfunctionalized olefins.[17b] The [Mn(salen)] catalysts grafted through flexible propyl sulfonic groups generally give higher chemical selectivity and enantioselectivity than those grafted through rigid phenyl sulfonic groups (Scheme 1).

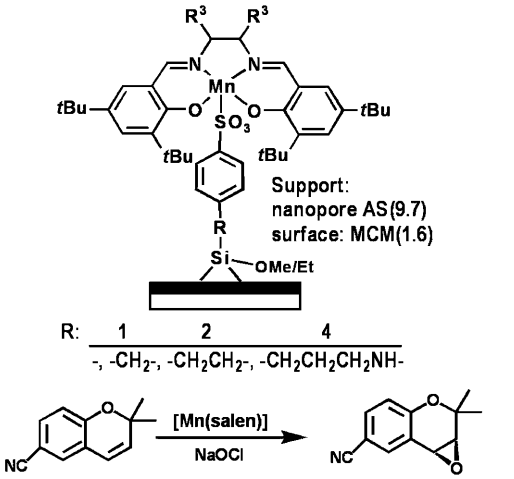


Catalyst	*t*	Conv. [%]	*ee* [%]
Mn(salen)Cl	6	95.5	82.3
$C_6H_4SO_3$Mn(salen)/MCM(1.6)	24	87.9	22.1
$C_3H_6SO_3$Mn(salen)/MCM(1.6)	24	90.2	44.9
$C_3H_6SO_3$Mn(salen)/SBA(7.6)	24	93.1	60.1

Scheme 1. [Mn(salen)] grafted in nanopores of mesoporous silica through flexible propyl groups results in higher *ee* values for the asymmetric epoxidation of 1-phenylcyclohexene than that grafted through rigid phenyl groups;[31] *t* is given in hours.

This is probably due to the electronic and steric factors of the linkages, which may affect the configuration of the transition state for the asymmetric reactions.

For chiral [Mn(salen)] catalysts immobilized in the nanopores of supports, an increase in conversion, chemical selectivity, and enantioselectivity was observed with increasing the axial linkage lengths for the asymmetric epoxidation of unfunctionalized olefins (Scheme 2). However, for [Mn-



En	Catalyst	Conv. [%]	*ee* [%]	TOF[h^{-1}]
1	[Mn(salen)Cl]	97.0	80.1	10.8
2	9.7AS-2-$C_6H_4SO_3$Mn(salen)	88.8	78.7	2.47
3	9.7AS(Me)-2-$C_6H_4SO_3$Mn(salen)	98.3	86.5	10.9
4	9.7AS-4-$C_6H_4SO_3$Mn(salen)	87.3	82.6	2.43
5	9.7AS(Me)-4-$C_6H_4SO_3$Mn(salen)	100	90.6	14.8
6	1.6MCM-4-$C_6H_4SO_3$Mn(salen)	76.8	71.1	2.14

Scheme 2. Asymmetric epoxidation on [Mn(salen)] immobilized in the nanopores of AS(9.7) and on the external surface of MCM(1.6) with different linkage lengths. Modification of nanopores with methyl groups can further improve the TOF and *ee* values.[33]

(salen)] catalysts immobilized on the external surface of the support, the conversion and chemical selectivity increased, but the enantioselectivity remained unchanged for the asymmetric epoxidation of unfunctionalized olefins with increasing the axial linkage lengths.

It is noteworthy to mention that the modification of nanopores of the heterogeneous [Mn(salen)] catalysts with methyl groups can further increase the TOF, chemical selectivity, and enantioselectivity because of the increased surface hydrophobicity of the nanopore (Scheme 2). Generally, organic molecules are hydrophobic and the silica-based mesoporous nanopores are hydrophilic. The difficulty in the diffusion of reactants and products in nanopores may reduce the reaction conversions.[17a] To improve the conversion, the nanopores of the mesoporous materials can be modified with organic groups.[32] More importantly, the change of the reaction microenvironment in nanopores may affect the enantioselectivity of asymmetric reactions in nanopores.[33] In homogeneous asymmetric catalysis, the reaction microenvironment has been found to be very important because the different solvent environments generally lead to different reaction results. Therefore, the increased TOF, chemical selectivity, and enantioselectivity of [Mn(salen)] supported on mesoporous silica modified with methyl groups is mainly attributed to the improved surface hydrophobicity of the microenvironment in the nanopore.

The above examples show that asymmetric reactions in nanopores, compared to those on the surface and in homogeneous media, can improve the enantioselectivity for some asymmetric transformations. When the nanopore size of the support or the tether length is tuned to a suitable value, the chiral catalysts in the nanopores can show higher *ee* values for some cases. Moreover, hydrophobic modification of the inner wall of mesoporous silica can also result in improved catalytic activity and enantioselectivity.

Malek et al.[34] studied the asymmetric epoxidation reaction of *cis*- and *trans*-methylstyrene on oxo-Mn(salen) in the mesopore of MCM-41 using molecular dynamic simulations (Figure 1). The calculations provide new insights in the importance of electronic and steric effects of the salen ligand, substrate, immobilizing linker, and MCM-41 confinement. Based on the assumption that the formation of a radical intermediate is the key step along the reaction pathway, the calculations were performed on a catalytic surface with triplet spin state, comprising no Mn–salen spin-crossing. The effect of immobilization was rationalized and correlated with the linker and substrate choices. The immobilized linker influences the enantioselectivity of the catalyst owing to increasing chirality content of the [Mn(salen)] complex. Simulations with docked olefin (β-methylstyrene) suggest that *cis* and *trans* substrates have different levels of asymmetric induction to the [Mn(salen)] catalyst. A *trans* substrate induces higher chirality to the immobilized [Mn(salen)] complex than a *cis* olefin. Although a *trans* substrate has a higher level of asymmetric induction to the immobilized [Mn(salen)] complex than that to a homogeneous catalyst, the reaction path is more in favor of the *cis* substrate (Figure 2). The MCM-41 channel reduces the energy barriers and enhances the enantioselectivity by influencing geometrical distortions of the [Mn(salen)] complex.

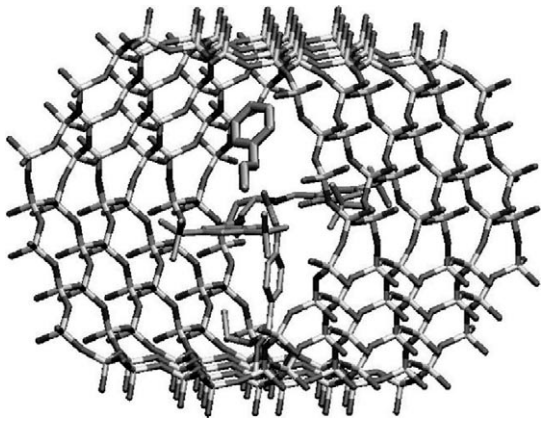


Figure 1. An oxo-Mn^{III}(salen) complex anchored in a MCM-41 channel along with a docked *trans* olefin [OACM(tr) system].[34a]

CHEMISTRY
AN ASIAN JOURNAL

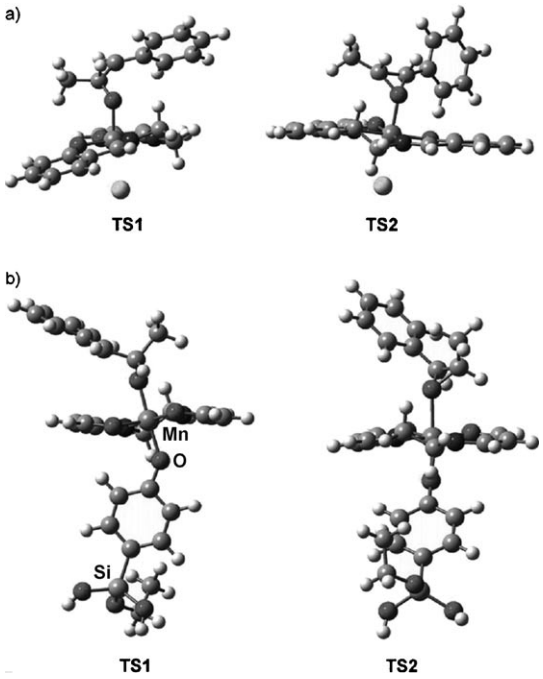
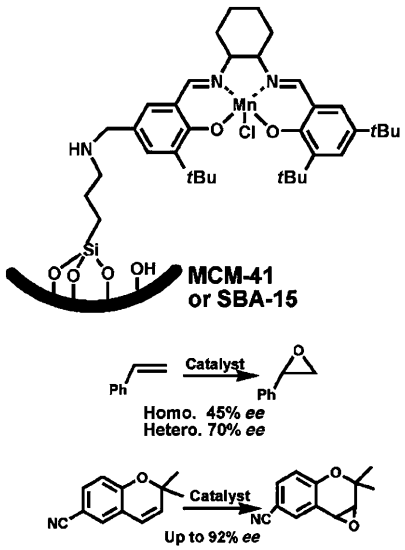


Figure 2. Optimized geometry of TS1 (transition state 1) and TS2 (transition state 2) for a) homogeneous and b) heterogeneous [Mn(salen)] catalyst.[34b]

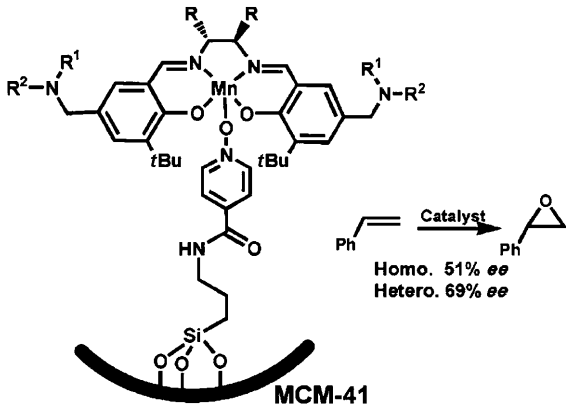
The confinement effect of the mesoporous material in asymmetric catalysis was also explored by Kureshy et al.[35] A chiral [Mn(salen)] catalyst immobilized in the nanopores of MCM-41 and SBA-15 (Scheme 3) showed higher chiral



Scheme 3. Asymmetric epoxidation on a chiral [Mn(salen)] catalyst immobilized in the nanopores of MCM-41 or SBA-15.[35]

induction (70% *ee*) than its homogeneous counterpart (45% *ee*) for the enantioselective epoxidation of styrene with aqueous NaOCl as oxidant. In addition, bulkier alkenes such as 6-cyano-2,2-dimethylchromene were also efficiently transferred into their epoxides on these supported [Mn(salen)] catalysts (up to 92% *ee*), and the reaction results were comparable to those of the homogeneous counterparts. The heterogeneous catalyst can be used for four times without obvious loss of activity and enantioselectivity.

A [Mn(salen)] catalyst was also axially immobilized in the nanopores of MCM-41 through pyridine *N*-oxide by the Kureshy group (Scheme 4). These immobilized catalysts

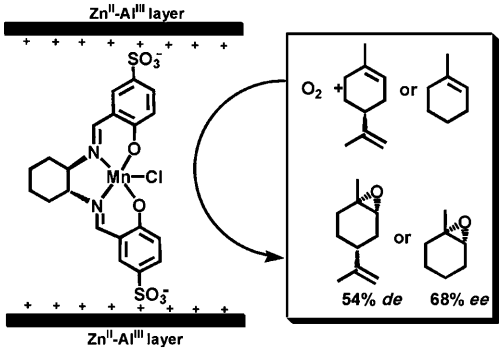


Scheme 4. Asymmetric epoxidation on a chiral [Mn(salen)] catalyst axially immobilized in the nanopores of MCM-41 through pyridine *N*-oxide.[35]

showed higher enantioselectivity (69% *ee*) than their homogeneous counterparts (51% *ee*) for the asymmetric epoxidation of styrene. These catalysts were also effective for the asymmetric epoxidation of bulkier substrates such as indene and 2,2-dimethylchromene (conversion: 82–98%; 69–92% *ee*). The catalysts could be recycled for at least four times without loss of performance. The increase in *ee* values was attributed to the unique spatial environment constituted by the chiral salen ligand and the surface of the support.

A series of mesoporous MCM-41 and MCM-48 materials with different pore sizes were synthesized and used as supports to immobilize a chiral [Mn^{III}(salen)] complex.[36] The confinement effect of the pore size on the catalytic performance of the heterogeneous catalysts was studied for the asymmetric epoxidation of unfunctionalized olefins with *m*-chloroperoxybenzoic acid as an oxidant. It was found that the conversions and enantiomeric excess (*ee*) values were closely correlated with the pore sizes of the supports. The catalysts immobilized on mesoporous silica with large-pore size exhibited higher conversions, and the *ee* values increased with increasing pore size for the catalysts immobilized on MCM-41 materials. However, for catalysts supported on MCM-48, the compatible pore size of the support with the substrate was found to be beneficial for obtaining higher enantioselectivity in olefin epoxidation.

Bhattacharjee and Anderson[37] incorporated a chiral sulfonato-salen-Mn^{III} complex into cationic Zn–Al-layered double hydroxides (Scheme 5). This heterogeneous [Mn(salen)] catalyst was found to be highly active and enantio-



Scheme 5. Chiral sulfonato-salen-Mn^{III} complex immobilized in cationic Zn–Al layered double hydroxides for the asymmetric epoxidation of various substituted styrenes and cyclic alkenes.[37]

selective for the asymmetric epoxidation of various substituted styrenes and cyclic alkenes. Up to 94% conversion, 68% *ee*, 90% selectivity, and a TOF of 234 h^{-1} were obtained for the asymmetric epoxidation of 1-methylcyclohexene. The catalysts immobilized on the layered supports are as effective as the homogeneous catalysts, and they can be separated and recycled.

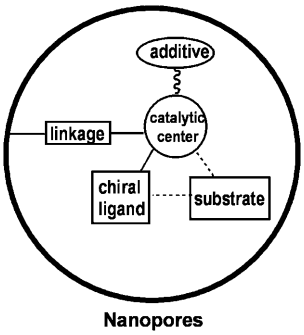
Thomas and co-workers[38] reported that a chiral Rh^{I} complex could be confined in nanopores by an ion-exchange method for the heterogeneous asymmetric catalytic hydrogenation of α-ketones. The chiral catalyst confined in nanopores of silicas showed up to 77% *ee* for asymmetric hydrogenation, while the homogeneous chiral catalyst gave essentially the racemic products. Their results assumed that the confinement effect originating from the nanopores could enhance the chiral induction for asymmetric hydrogenation in nanopores.

Similar heterogeneous chiral catalysts were prepared by impregnation of mesoporous Al-MCM-41, Al-MCM-48, and Al-SBA-15 with rhodium diphosphine organometallic complexes and were tested for the hydrogenation of dimethyl itaconate, methyl α-acetamidoacrylate, and methyl α-acetamidocinnamate.[39] The immobilized catalysts showed high activities and excellent chemo- and enantioselectivities, up to greater than 99% conversion, 99% selectivity, and 98% *ee*.

Caps et al.[40] demonstrated that the heterogenization of the achiral cluster $[Os_3(CO)_{12}]$ on the internal space of MCM-41 using simple chemical vapor deposition (CVD) could generate a new chiral species in situ from achiral catalyst precursors, and lead to improved stereoselectivity towards the *S*,*S* configuration of 1,2-diphenyl-1,2-ethanediol in the dihydroxylation of *trans*-stilbene using *N*-methylmorpholine *N*-oxide (NMO) as an oxidant without adding any chiral ligand. Up to 90% *ee* for the *S*,*S* isomer was obtained when surface Al sites were introduced into the silicate. Spontaneous symmetry breaking of achiral $[Os_3(CO)_{12}]$ during CVD on the MCM-41 may result in a new surface-chiral catalytic species.

Hutchings and co-workers reported that a Cu catalyst modified with chiral bis(oxazoline) ligand could be introduced into the pores of zeolite Y by ion exchange.[41] This catalyst showed an *ee* value of 77%, higher than the homogenous catalyst (28% *ee*), in the asymmetric aziridination of styrene. The confinement effect of the zeolite cages was regarded to improve the asymmetric induction of the chiral modifier. The heterogeneous catalyst also exhibited a superior enantioselectivity (93% *ee*) compared to the homogeneous catalyst (57% *ee*) for the reaction of methylenecyclopentane and ethyl glyoxylate.

Thomas et al.[38] proposed that the confinement effect of the nanopores could improve the chiral induction for asymmetric catalysis in nanopores by strengthening the interaction between the incoming reactants and the chiral ligand as well as the catalytic metal center in the nanopores (Scheme 6). Besides the confinement effect originating from



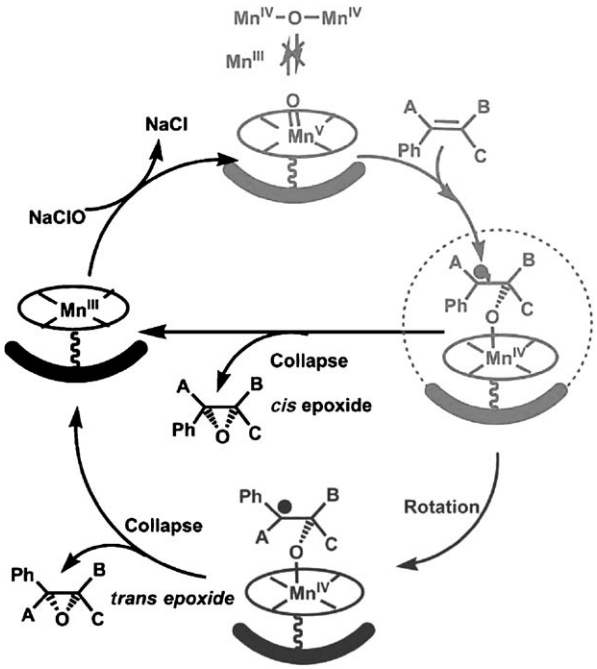
Scheme 6. The factors originating from the pores that influence the chiral catalysis.[38]

the nanopores, electronic and steric factors from the linkage may also have some effect on the chiral induction in the nanopores. In addition, the reaction microenvironment in the nanopores may also have an important influence on the catalytic performance.[33] However, the factors originating from the pores that influence the chiral catalysis have not been thoroughly studied so far. It is generally believed that tuning the steric and electronic properties of chiral ligands can alter the enantioselectivity for homogeneous asymmetric catalysis. For heterogeneous chiral catalysts in nanopores, the pore effect can provide another alternative to improve the asymmetric induction by employing the nanopores with suitable pore structures and sizes.

The mechanism of asymmetric catalysis in nanopores might be different from that in homogeneous systems owing to the effects of the nanopores, the linkages, and the reaction microenvironment in the nanopores. Here we give the [Mn(salen)]-catalyzed asymmetric epoxidation in nanopores as an example to discuss the asymmetric epoxidation mechanism in nanopores.

According to the reported mechanism of the homogeneous [Mn(salen)]-catalyzed asymmetric epoxidation[42] and the experimental results of the catalysis in nanopores,[31] a mechanism for the asymmetric epoxidation in nanopores can be proposed in Scheme 7. The olefin approaches the im-

CHEMISTRY
AN ASIAN JOURNAL



Scheme 7. A proposed mechanism for asymmetric epoxidation in nanopores.[31b]

mobilized Mn^V active sites to form the radical intermediate, which directly collapses to form the *cis* epoxide or first rotates and then collapses to form the *trans* epoxide.

Several points should be emphasized on the asymmetric epoxidation mechanism in nanopores. The immobilization of Mn^V complexes on the surface of nanopores effectively prevents the formation of inactive Mn^{IV}-O-Mn^{IV} dimers, which are reported to be generally formed in the homogeneous asymmetric epoxidation.[42] Therefore, the isolated active sites immobilized in the nanopores result in higher apparent TOF values for the immobilized [Mn(salen)] catalyst than that for the homogeneous catalyst in the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene (14.8 vs. 10.8 h^{-1}, 90.6 vs. 80.1% *ee*; Scheme 2).[31] The chiral recognition between chiral ligand and the prochiral olefin may be enhanced or weakened owing to the stereo effect of the nanopores. The surface and the axial grafting modes may retard the coordination of some axial additives to the Mn atom, which may reduce the asymmetric catalytic performance. The reaction microenvironment, including the nanopores and the grafting modes, may have an influence on the stability and lifetime of the radical intermediate in the nanopores. Notably, the rotation of the radical intermediate may be greatly retarded by the nanopores, which results in the production of more *cis* epoxide (higher *cis*/*trans* ratio) compared to that of the homogeneous reaction.

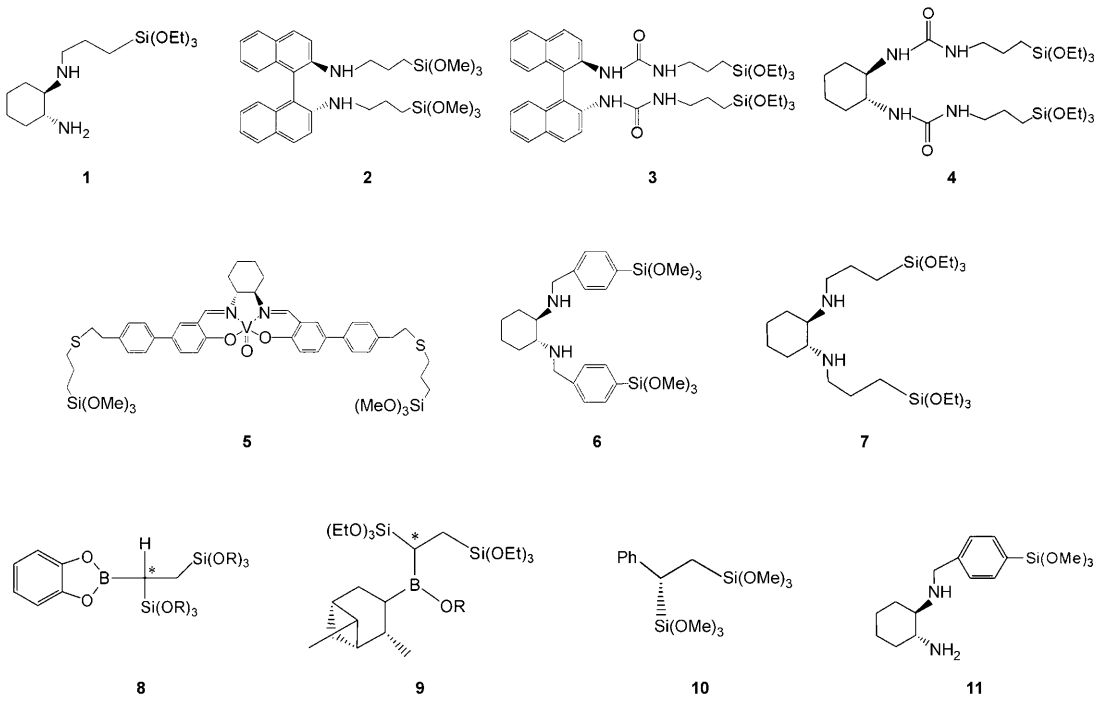
The factors influencing the chiral catalysis in nanopores clearly suggest that the confinement effect from the nanopores can improve the chiral induction for the asymmetric catalysis compared to that on the surface and in homogeneous media for many examples. The chiral catalysts in the nanopores can give higher *ee* values in some cases when the pore size of the support is optimized. The linkage groups of the heterogeneous chiral catalysts have a remarkable effect on the performance of asymmetric catalysis. The electronic and steric properties of the linkages may affect the configuration of the transition state for the asymmetric reactions. More importantly, the microenvironment of the nanoreactor is crucial for asymmetric reactions in the nanoreactor. An appropriate microenvironment may increase the conversion and enantioselectivity for chiral reactions in nanopores.

3. Chiral Metal Complexes Immobilized in Mesoporous Organosilicas

Mesoporous silicas have been used as unique supports for immobilizing chiral catalysts. A recent advance in mesoporous materials is the successful synthesis of the periodic mesoporous organosilicas (PMOs) using $(R'O)_3SiR(OR')_3$ as the precursor.[20–22] Compared with mesoporous silicas, PMOs with organic groups distributed uniformly in the framework exhibit higher mechanical and hydrothermal stability. The surface hydrophilicity and hydrophobicity of nanopores in PMOs could be easily tuned by incorporating different kinds and different amounts of organic groups in the pore walls. Moreover, the chiral catalysts could be incorporated in the pore walls of PMOs. The chiral catalysts in the pore walls could have homogeneous microenvironments and not block the pores, which are important for chiral synthesis in the nanopores. The immobilization of chiral metal complexes in the nanopores of PMOs may provide more opportunities for the development of efficient solid chiral catalysts.

3.1. PMOs with Chiral Ligands Bridging in the Framework

Though PMOs with chiral channels have been synthesized,[43] introducing chiral functionalities into PMOs is more adaptable for applications in asymmetric catalysis. In 2004, García and co-workers reported the incorporation of chiral moieties in the pore walls of PMOs by cocondensation of bis-silylated binaphthyl (compound **2** or **3** in Scheme 8) or cyclohexadiyl (compound **4** in Scheme 8) precursors with TEOS in basic medium using CTAB as a structure-directing agent.[44] The materials with ordered pore structure could be synthesized with the amounts of chiral precursor in the initial mixture at less than 15 mol%. The confirmatory proof for the presence of chiral units in the solid was obtained by observing the behavior of the solid toward plane-polarized light. Also, a certain degree of chiral discrimination was observed for the asymmetric enhancement of the binaphthyl fluorescence by adding enantiomerically pure 1,2-cyclohexadiamine. The material synthesized with cyclohexadiyl precursors (compound **4** in Scheme 8) showed an enantioselectivity of 24% at 11% conversion in the di-π-methane rearrangement of 11-formyl-12-methyldibenzobarrelene (Figure 3).[44b]



Scheme 8. Potential organosilane precursors containing chiral ligands.

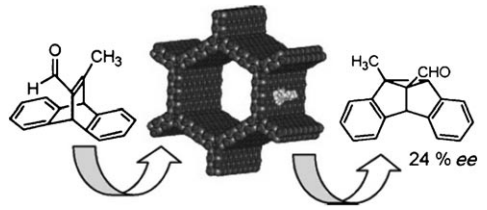


Figure 3. Photoreactivity of dibenzobarrelene in chiral PMOs synthesized by cocondensation of compound **4** with TEOS.[44b]

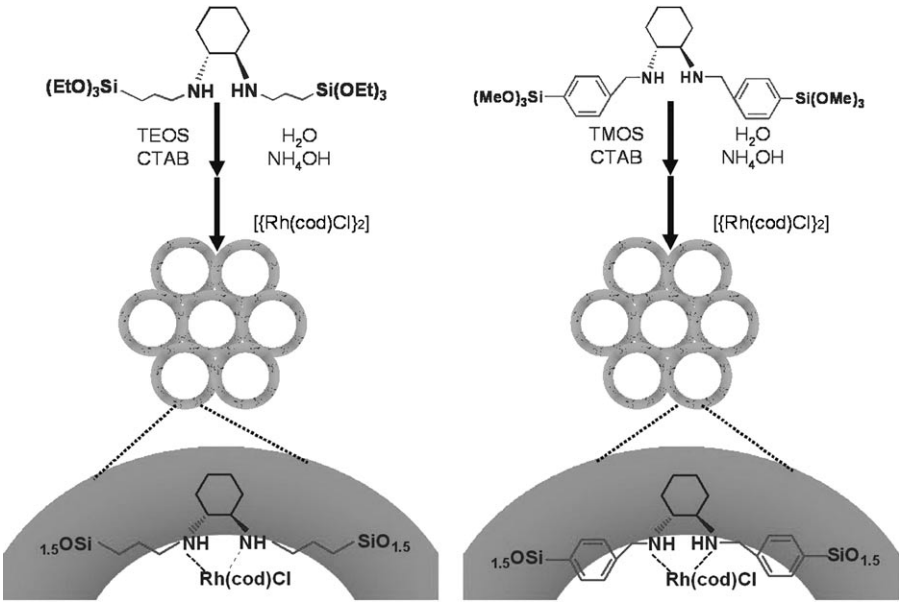
Corma's group tried to integrate the chiral vanadyl salen complex in the pore walls of MCM-41 by cocondensation of the bis-silylated precursor (compound **5** in Scheme 8) and TEOS in basic medium.[45] The catalytic properties of the material were investigated in the asymmetric cyanosilylation of benzaldehyde. This catalyst gave 30% *ee*, which was lower than that obtained for the corresponding catalyst synthesized by a grafting method. The decrease in enantioselectivity could be induced by the steric constraints imposed on the catalyst by the surrounding pore wall. Moreover, the accessibility of the chiral ligands bridged in the framework may also affect the activity and enantioselectivity of the catalysts.

Recently, Li and co-workers reported the synthesis of mesoporous organosilicas by cocondensation of *N*,*N*′-bis[4-(trimethoxysilyl)benzyl]-(−)-(1*R*,2*R*)-diaminocyclohexane (compound **6** in Scheme 8) with TMOS under basic conditions using CTAB as the template (Scheme 9).[46]

Under similar synthetic conditions, the mesoporous organosilica was also synthesized using a mixture of TEOS and *N*,*N*′-bis[4-(trimethoxysilyl)propyl]-(−)-(1*R*,2*R*)-diaminocyclohexane (Scheme 9).[46] An active catalyst was generated after coordinating $[\{Rh(cod)Cl\}_2]$ to the mesoporous organosilicas with chiral ligands. In the asymmetric transfer hydrogenation (ATH) of acetophenone using *i*PrOH as a hydrogen source, mesoporous organosilica with benzyl as a linker exhibited 93% conversion with 27% *ee*. In contrast, the mesoporous organosilica with propyl as a linker showed 16% conversion with 8% *ee*. The higher activity and *ee* value observed for mesoporous organosilica with benzyl as a linker were mainly attributed to the presence of the rigid and electron-withdrawing benzyl group attached to the N atoms of (1*R*,2*R*)-diaminocyclohexane. Different kinds of ketones could be converted into the corresponding alcohols on the catalysts with benzyl as a linker. The highest enantioselectivity of 61% *ee* was obtained for 2-acetylnaphthalene. The chiral reactions in the nanopores of mesoporous organosilicas may occur in a different way from those in homogeneous processes because the coordination and rigidity properties of the chiral moiety bridged in the pore wall may be altered by the steric constraints of the surrounding pore. Through adjusting the pore size and mesostructure of the material, the catalytic activity and enantioselectivity of the chiral catalysis in the nanoreactor may be improved. However, it still remains a challenge to finely tuning the mesoporous structure of the chiral organosilicas because the large and flexible chiral moieties bridged between two silicon atoms may inhibit the formation of well-ordered mesostructures.

The incorporation of higher amounts of chiral ligand in the pore walls is desirable in the view of chiral inductivity. A well-defined chiral PMO was synthesized by using 100%

CHEMISTRY
AN ASIAN JOURNAL



Scheme 9. Preparation procedure for Rh-containing mesoporous silicas with *trans*-(1*R*,2*R*)-diaminocyclohexane in the wall under basic conditions.[46] cod = 1,5-cyclooctadiene.

of a chiral bis-alkoxysilane sol–gel precursor (compound **8** in Scheme 8) as the building block; unfortunately, C–B bond cleavage and C–Si bond cleavage were observed in the chiral PMO.[47] Thomas's group also reported the synthesis of porous chiral amine-functionalized organosilicas by varying the molar ratio of chiral TEOS/organosilane in the range of 0–8.[48] The chiral organosilane precursors (compound **9** in Scheme 8) were formed by a convenient enantioselctive hydroboration route using (*S*)-monoisopinocampheylborane on an ethylene-bridged silica precursor. The chirality of the materials was proven using circular dichroism measurements. The materials showed strong optical activity because of the chiral amines in the framework.

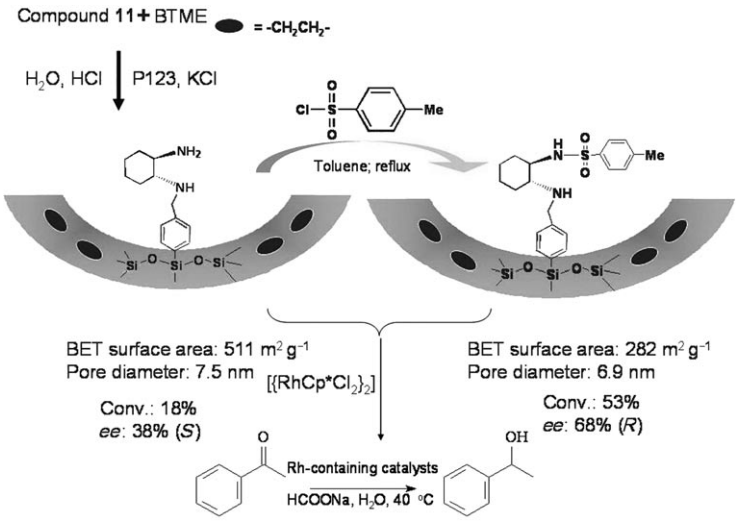
Inagaki and co-workers reported the synthesis of chiral PMOs from a newly designed chiral (*R*)-(+)-1,2-bis(trimethoxysilyl) phenylethane precursor (compound **10** in Scheme 8) by a surfactant-mediated self-assembly approach in either basic or acidic medium.[49] The most interesting point of the work is that the enantiomeric purity (95% *ee*) of the chiral ligand can be maintained in the solid material as determined by eluting the organic groups from the solid. However, the chiral PMOs synthesized by using 100% of chiral bis-alkoxysilane have not yet been used in asymmetric catalysis.

Among the various PMOs reported, only a limited numbers of PMOs have chiral moieties incorporated in the mesoprous framework. The synthesis and applications of chiral PMOs are still in their infant stage. The enantioselectivity, albeit not yet high enough, demonstrates the possibility for synthesizing a new kind of chiral solid catalysts for potential applications in asymmetric reactions. Some PMOs with chiral catalysts in the framework exhibit lower catalytic activity and enantioselectivity than the homogeneous catalyst. One of the reasons is due to the steric constraints imposed on the chiral catalyst by the surrounding pore wall. In future investigations, much research efforts should be focused on the synthesis of chiral PMOs with different kinds of chiral moieties incorporated in the framework and the control of the microenvironment of chiral PMOs through changing the pore size, the surface hydrophilicity/hydrophobicity, and the linker groups connected with the chiral moieties.

3.2. Mesoporous Organosilicas with Chiral Moieties Protruding in the Pores

Introduction of hydrophobic bridging groups in the pore walls of PMOs may endow the materials with special adsorption properties, modify the microenvironment of the pore, and hence influence their catalytic performance. The chiral moieties were incorporated in the pores of mesoporous organosilicas with -CH_2CH_2- bridging in the pore walls by cocondensation of *N*-[(triethoxysilyl)propyl]-(−)-(1*R*,2*R*)-diaminocyclohexane (compound **1** in Scheme 8) with $(MeO)_3SiCH_2CH_2Si(OMe)_3$ (BTME) in basic medium.[28] For comparison, a mesoporous silica counterpart with a chiral ligand in the mesopore was also synthesized under similar conditions except that BTME was replaced by TEOS. After complexing with [{Rh(cod)Cl}$_2$], the material with a -CH_2CH_2- group in the pore wall exhibited 96% conversion with 23% *ee* in the ATH of acetophenone using *i*PrOH as a hydrogen source. The material with a pure silica pore wall composition showed 48% conversion with 14% *ee* under identical conditions. The enhanced catalytic activity of the mesoporous organosilicas is mainly caused by the specific adsorption and physical properties of the mesoporous network bridged with ethane groups, particularly the hydrophobic properties.

Recently, large-pore mesoporous ethane silicas functionalized with (1*R*,2*R*)-diaminocyclohexane were synthesized by cocondensation of BTME and *N*-[(triethoxysilyl)benzyl]-(−)-(1*R*,2*R*)-diaminocyclohexane (compound **11** in Scheme 8) in acidic medium using P123 as the template.[50] The pore diameter of the material can be as large as 7.5 nm. (1*R*,2*R*)-Diaminocyclohexane protruding in the mesopore was further modified through treatment with *p*-toluenesulfonyl chloride (Scheme 10). After complexing with [{RhCp*Cl$_2$}$_2$], the modified catalyst exhibited 53% conversion with 68% *ee* in the ATH of acetophenone in a HCOONa–H_2O system, which was much higher than that of the unmodified material (18% conversion with 38% *ee*) under similar conditions. Moreover, a number of different



Scheme 10. Postsynthetic modification of mesoporous organosilica with (1*R*,2*R*)-diaminocyclohexane in the pore by treatment with *p*-toluenesulfonyl chloride, and after modification the catalytic performance in the asymmetric transfer hydrogenation of acetophenone is improved.[50]

aromatic ketones can be converted into the corresponding chiral alcohols on the modified material. For 2-acetylnaphthalene substrate, the highest enantioselectivity of 81% was observed. The above results show that the direct synthesis associated with postmodification is a facile method to synthesize mesoporous materials with chiral functional groups.

The incorporation of chiral catalysts in the pores of PMOs provides another alternative for the synthesis of chiral solids. Our studies show that the surface hydrophilicity/hydrophobicity has a great influence on the catalytic activity of chiral solid catalysts. Owing to the limited numbers of chiral silane precursors, the cocondensation method associated with the postmodification is one of the efficient ways for the synthesis of mesoporous materials containing new functionalities. Adjusting the organic groups in the framework can change the surface properties of the mesoporous materials at the molecular level. Through finely adjusting the microenvironment of the chiral catalyst, the catalytic activity and even the enantioselectivity could be greatly improved. The mesoporous materials with different organic groups in the framework and chiral ligands in the mesopores are a new class of promising materials for developing heterogeneous chiral catalysts.

4. Encapsulation of Chiral Metal Complexes in Nanoreactors

The encapsulation method by enclosing metal complexes in the rigid pore space has overwhelming advantages over other immobilization methods. The metal complex does not require any modification with extra functional groups for the immobilization as with covalent linkages. The structure and properties of the catalyst, on which the catalytic performance depends, consequently remain intact after immobilization. Under the reaction conditions, the metal complex catalyst encapsulated in a void space could, in principle, remain as free as the catalyst in solution since there is not a strong interaction between the catalyst and solid matrix, and the inherent catalytic performance of the metal complex could thus be maintained.

4.1. Encapsulation of Chiral Metal Complexes in the Nanoreactors

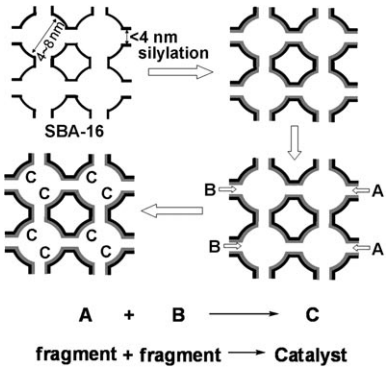
Since the 1970s, the "ship in a bottle" synthesis has become an efficient method for encapsulating metal complexes within a solid matrix, particularly in microporous materials like zeolites.[51] However, the synthesis of constructed chiral complexes in zeolites through "ship in a bottle" methods was not reported until 1997 when Corma and Bein reported that a chiral catalyst in the zeolite matrix exhibited moderate enantioselectivity in asymmetric epoxidations.[52,53] The "ship in a bottle" synthesis in zeolites was recently reviewed by Corma.[54] Here, we mainly summarize the recent advances which use mesoporous silica as a host material.

Compared with microporous zeolites, ordered mesoporous silicas have a larger pore size and pore volume, which provides huge possibilities for the encapsulation of larger molecules. The Algarra and Tanamura groups reported the synthesis of copper phthalocyanine and porphyrin in MCM-41 through the "ship in a bottle" method.[55,56] However, the cylinderlike pores of MCM-41 could not prevent the metal complex from leaching. Compared with MCM-41 and SBA-15 with cyclinder channels, mesoporous silicas with cagelike structures, such as SBA-1 (cubic, *Pm3n*),[57] SBA-16 (cubic, *Im3m*),[58,59] FDU-12 (cubic, *Fm3m*),[60] and FDU-1 (cubic, *Fm3m*),[61] are more suitable as host materials for the encapsulation. These mesoporous cagelike silicas have tunable cage sizes (4–8 nm for SBA-16; 10–22 nm for FDU-12) and their cages are interconnected three dimensionally by tunable pore entrances. Additionally, the existence of plentiful hydroxyl groups in the mesoporous silicas provides the possibility of tailoring the pore entrance size by a simple silylation method.

We constructed chiral [Co(salen)] complexes (salen = (*R*,*R*)-*N*,*N*′-bis(3,5-di-tertbutylsalicylidene)-1,2-cyclohexanediamine) in the nanopores of SBA-16 through a "ship in a bottle" synthesis followed by tailoring the pore enterance size by using a silylation method (Scheme 11).[62] Chiral [Co(salen)] encapsulated inside SBA-16 shows enantioselectivity (up to 96% *ee*) as high as that of the homogeneous counterpart for the hydrolytic kinetic resolution (HKR) of terminal epoxides. The catalysts can be recycled for at least 10 times, indicating that the metal complex is confined stably in the nanocages of SBA-16.

The "ship in a bottle" synthesis in mesoporous cagelike materials combined with tailoring the pore entrance size provides a promising method for encapsulating metal complexes with large molecular size. However, the "ship in a bottle" synthesis may have problems such as formation of undesired species in the solid matrix, which probably causes

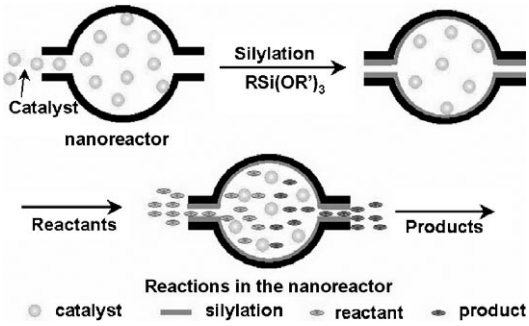
CHEMISTRY
AN ASIAN JOURNAL



Scheme 11. The general process for encapsulation of chiral [Co(salen)] in the cages of phenyl-modified SBA-16 through the "ship in a bottle" synthesis.[62]

the undesired reactions. Moreover, this method is suitable for only a few metal complexes which can be constructed through one or two steps under mild reaction conditions. Most chiral metal complexes are generally synthesized through multiple steps and sometimes even under very harsh conditions, which are not possible in nanoreactors. To solve this problem, our group has developed a new strategy for the encapsulation of various chiral metal complexes in the nanoreactor through postmodification of the pore entrance.[63]

A preformed metal complex catalyst is first introduced into the cagelike pore of a mesoporous material SBA-16 by impregnation or adsorption (Scheme 12). The pore entrance



Scheme 12. General process for encapsulation of a chiral catalyst within the nanoreactor cage of mesoporous silica followed by tailoring the pore entrance size through silylation, which prevents the catalyst from leaching, while allowing the reactants and products to diffuse through the pore entrance freely.[63]

size is then finely tailored by a silylation method according to the molecular size of the catalyst, reactants, and products.[64,65] Thereby the metal complexes can be encapsulated in the mesoporous cages while the reactants and products can still diffuse freely through the pore entrance. For example, chiral catalysts [Co(salen)] and [Ru(tsdpen)] were encapsulated in the mesoporous cage of SBA-16 by this strategy. The encapsulated [Co(salen)] and [Ru(tsdpen)] catalysts show enantioslectivity and activity that are as good as the homogeneous analogues in the HKR of epoxides and asymmetric transfer hydrogenation of ketones, respectively. The encapsulated catalysts can be recycled for more than 10 times without significant loss of catalytic performance. The chiral reactions in the nanoreactor just mimic those that occur in the homogeneous process because chiral metal complexes encapsulated in the nanoreactor have very weak interactions with the host material. Thus they can move and change their configuration freely during the catalytic process.

Through the encapsulation method, the chiral metal complex catalysts can be trapped in the cage of mesoporous materials like SBA-16 by modifying the pore entrance size of the cage using a silylation reaction. The as-prepared heterogeneous catalyst can be easily recycled without significant loss of catalytic performance and shows catalytic performance comparable to the homogeneous catalyst. This strategy could be generally applicable for various chemical transformations and nanoreactor design.

4.2. Cooperative Activation Effects in Nanoreactors

It has been recognized that the cooperative activation by two or more catalytic centers with proper proximity could greatly increase the activity and enantioselectivity of homogeneous chiral catalysts through a specific control of the transition state, like in enzymatic catalysis.[66] If the cooperative activation is realized in heterogeneous asymmetric catalysis, it can provide new possibilities for developing high-performance heterogeneous catalysts, especially solid chiral catalysts. However, the generation of such a cooperative activation in a solid catalyst is difficult, because of the inability to elaborately control the proper proximity and the relative conformation of the active centers. Previously, it was reported that the enantioselectivity and diastereoselectivity of photochemical reactions were significantly increased by performing the reactions in the supracages of zeolites.[67–69] This is because the confined space of the supercage could enforce an appropriate proximity and an interaction between the reactant and chiral inductor in a constrained space.[67] The encapsulation of chiral metal complexes in the nanocages of mesoporous silica provides new possibilities for the generation of cooperative activation because the chiral transition-metal complexes are confined but allowed to move freely in the isolated nanospace of porous solids, and the proper proximity and the relative conformation of the catalysts required for the cooperative activation could be realized through precisely adjusting the loadings and types of transition-metal complexes in the confined space.

In our recent work, two or more than two chiral [Co(salen)] catalyst molecules could be confined in a single nanocage of SBA-16.[70] The [Co(salen)]/SBA-16 catalysts with two or more than two [Co(salen)] complexes in each cage show a significantly enhanced cooperative activation effect and exhibit much higher activity than the homogeneous [Co(salen)] catalyst for the hydrolytic kinetic resolution (HKR) of epoxides (Figure 4a). The catalytic activity gradu-

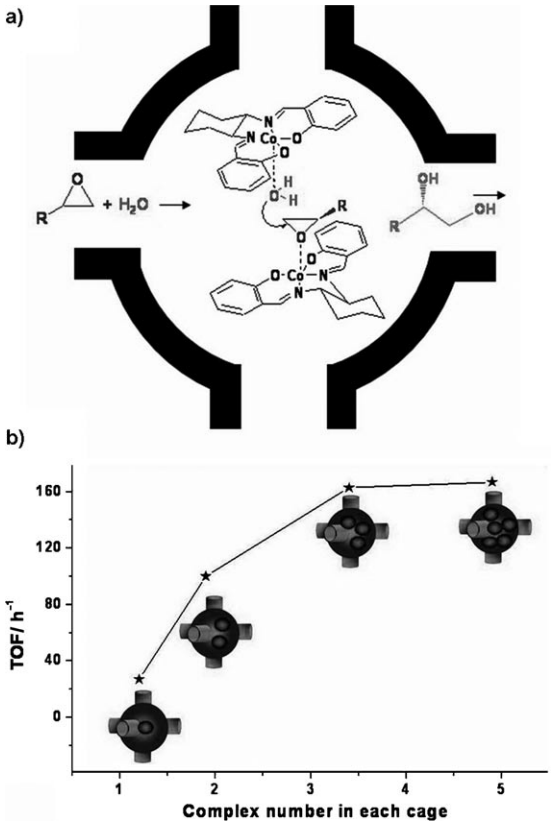


Figure 4. a) Hydrolytic kinetic resolution of epoxides on [Co(salen)] complexes confined in the nanocages of SBA-16. For clarity, the four *tert*-butyl groups on the 3,5,3′,5′-postions of the salen ligand, the CH_3COO group of [Co(salen)], and the propyl groups on the surface of SBA-16 are omitted; b) The catalytic activity of [Co(salen)]/SBA-16 as a function of [Co(salen)] number in each cage.[70]

ally increases as the number of [Co(salen)] units in each cage increases, and then reaches a plateau when the number of [Co(salen)] molecules reaches five (Figure 4b). The increase in the activity and enantioselectivity with an increase in the number of [Co(salen)] complexes per cage obviously indicates that the cooperative activation effect of [Co(salen)] complexes in the nanocages can be strengthed owing to the crowded situation of the cobalt complexes in the nanocages. The appropriate proximity and the free movement of [Co(salen)] in the confined space offer the possibility that H_2O activated by one [Co(salen)] complex can attack the epoxide activated by another [Co(salen)] complex, and then facially produce the diol with high activity. This reasoning is corroborated by DFT calculations.

To further understand the enhanced cooperative activation effect in the nanocage, we compared the catalytic performances of the homogeneous [Co(salen)] and [Co(salen)]/SBA-16 (with a Co content of 0.157 wt%) for the HKR of propylene epoxide at high substrate/catalyst (S/C) ratio (the molar ratio of racemic epoxide to [Co(salen)]; Figure 5). Homogeneous [Co(salen)] affords 34% conversion at a S/C ratio of 4000:1. Under the similar conditions, [Co(salen)]/SBA-16 gives 49% conversion. The catalytic activity of [Co-

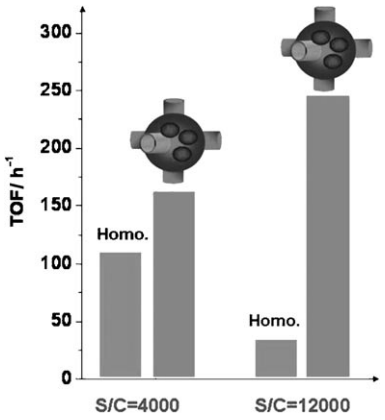


Figure 5. Hydrolytic kinetic resolution of racemic propylene oxide on homogeneous [Co(salen)] catalyst and heterogeneous [Co(salen)]/SBA-16 catalyst.[70]

(salen)]/SBA-16 is higher than that of the homogeneous catalyst (TOF: 163 h^{-1} versus 113 h^{-1}). When the S/C ratio is increased from 4000:1 to 12000:1, the conversion for the homogeneous catalyst sharply decreases from 34% to 7% even though the reaction time is prolonged to 24 h, and the TOF decreases from 113 h^{-1} to 35 h^{-1}. The enantioselectivity simultaneously decreases from 98% *ee* to 89% *ee*. In contrast, under similar conditions, [Co(salen)]/SBA-16 can still afford 50% conversion with 98% *ee* of the diol at an S/C ratio of 12000:1 (the average TOF increases because the reaction undergoes an induction period for the solid catalyst). Thus, [Co(salen)] confined in the nanocage displays a much higher activity and enantioselectivity in the HKR of propylene epoxide than the homogeneous counterpart, especially at high S/C ratios.

We have demonstrated that the cooperative activation effect can be enhanced in the nanocages of mesoporous materials. By accommodating [Co(salen)] complexes in the nanocages of SBA-16, an efficient solid chiral catalyst for the hydrolytic kinetic resolution of epoxides was developed. The solid catalyst exhibits significantly higher activity and enantioselectivity than the homogeneous [Co(salen)] complex in the HKR of epoxides at high S/C ratios. The solid catalyst can be easily recycled by filtration without apparent loss of catalytic activity and enantioselectivity. The nanocages of mesoporous materials can be used as nanoreactors to confine metal complexes with a high local concentration and thus lead to a crowded microenvironment of the complexes, which enhances the cooperative activation. This work provides a new opportunity for the design of efficient solid catalysts for asymmetric reactions as well as many other reactions which involve cooperative activation by separate catalytic centers or second-order kinetic dependence on the local concentration of the catalysts.

The encapsulation of enzymes in nanoreactors for organic synthesis is an exciting and rapidly growing area. Recently, we reported the immobilization of lipases in the nanopores of magnetic siliceous mesocellular foam for the kinetic resolution of secondary alcohols. The heterogenized biocatalyst

CHEMISTRY
AN ASIAN JOURNAL

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 catalytic performance.[71] The enhanced activity of enzymes encapsulated in the nanoreactor is most possibly due to the cooperative activation effect, but this effect for enzyme catalysts is not well understood at present.

5. Conclusions and Perspectives

This Focus Review summarizes the recent advances in chiral catalysis in nanoreactors of mesoporous materials and organosilicas with an emphasis on the confinement and cooperation effect induced in the nanoreactor. The chiral catalysts can be introduced into the nanopores by various methods, including chemical grafting, ion exchange, and some novel methods, such as "ship in a bottle" synthesis, encapsulation of the chiral catalysts in the nanocage of mesoporous silicas, and cocondensation of chiral catalysts into the framework of PMOs. Some examples clearly suggest that the confinement effect of nanopores can improve the chiral induction for asymmetric catalysis. It is noteworthy to mention that [Co(salen)] encapsulated in the nanocage of SBA-16 exhibits an even higher catalytic activity than the homogeneous counterpart in the HKR of propylene oxide through cooperative activation despite the diffusion barriers of the reactants and products in the heterogeneous process. This result indicates that the confined space of the nanopore can enhance the cooperative activation for asymmetric catalysis.

When a homogeneous chiral catalyst is immobilized into pores of mesoporous materials, the enantioselectivity can be remarkably increased or decreased compared with the homogeneous counterpart. It can be reasonably explained by the kinetics of the chiral reactions. As we mentioned in the introduction, weak interactions such as van der Waals forces, hydrogen bonding, and physical adsorption are possibly involved in the reactions inside the pores, which have a similar energy magnitude to the small difference (usually less than 15 kJ mol^{-1}) between the chiral transition states *R* and *S*, are able to affect the energy difference between the two transition states accordingly to change the enantioselectivity or even to reverse the chiral selectivity. The small energy difference between the two transition states is very sensitive to the pore environment of the immobilized metal complex catalysts. From the viewpoint of kinetics, it could be possible to explain the remarkable increase or decrease of the enantioselectivity for a homogeneous catalyst confined in pore materials.

The steric constraints of porous supports can not only form restricted chiral environments to confine the stereoconfiguration of the products, but also affect the dynamic diffusion of the substrates or the products along the reaction coordinate. When the pore size is decreased to the nano or sub-nano scale, electronic interactions in nanopores could become a dominant factor, the so-called nano effect. In addition to the steric effect of the pore, the microenvironment of the pore may also have a big influence on the performance of a chiral catalyst confined in the nanopore. For asymmetric reactions, the role solvents play in liquid reactions is of pivotal importance in determining the enantioselectivity. Solvent effects are closely related to the intermolecular interactions between solvent, chiral catalyst, and reactant(s) that constitute a solvation microsphere. The static influence of solvents on the enantioselectivity could be understood in terms of transition-state theory. According to this theory, solvents can modify the Gibbs energy of two different stereoisomers by different solvation of the reactants and the activated chiral catalyst, thus exerting stereospecific solvation control over enantioselectivity. The dynamic influence of the solvent on enantioselectivity is related to the polarity and molecular structure of the molecules that determine solvent dynamics such as solvent relaxation and reorientation. For asymmetric reactions in a nanoreactor, the solvent microsphere, solvent dynamics, and intermolecular interactions may be quite different from those of the conventional homogeneous reaction owing to the influences from the rigid pore wall, the hydrophilicity/hydrophobicity of the surface, and the confined space of nanoreactor. It is reasonable to expect that novel solvent effects in nanoreactors will provide a new opportunity to improve the enantioselectivity for heterogeneous asymmetric reactions.

Many efforts have been made toward designing new chiral metal complexes through finely adjusting the microenvironment of the active site. When a chiral metal complex is in the nanoreactor, additional parameters, such as the surface properties (hydrophilicity/hydrophobicity), the size of the nanoreactor, the interactions of chiral metal complexes with the nanoreactor, the amounts and types of chiral metal complexes in the nanoreactor, and the rigid environment of the nanoreactor, can also greatly influence the catalytic performance, especially the enantioselectivity. As we observed for the HRK reaction, the confinement and cooperative activation effects of the nanoreactor results in higher enantioselectivity and catalytic activity for the asymmetric catalysis. The above-mentioned factors provide versatile possibilities to improve the chiral inductivity for asymmetric catalysis in nanoreactors.

Asymmetric catalysis in nanoreactors has both scientific significance and potential applications. However, research in this direction is still in an early stage and there is plenty of room for further development: 1) The cooperative effect in nanoreactors should be investigated in detail and the asymmetric reactions in nanoreactors should be extended to many different types of reactions which involve cooperative activation by separating catalytic centers or second-order kinetic dependence on the local concentration of the catalysts; 2) The dynamics and kinetics of the asymmetric reactions in the nanoreactor might be very different from those in macroscale reactions and are needed for a detailed investigation; 3) The nature of the confinement effect on the catalytic performance of the chiral catalyst is a very interesting

issue to be extensively investigated; 4) The chiral catalysts to be trapped in the nanoreactor are not limited to chiral transition-metal complexes, and various other types of chiral catalysts, such as organocatalysts, Lewis acid catalysts, and even biocatalysts could also be immobilized in the nanoreactor; 5) The development of new strategies for the immobilization of chiral catalysts in nanoreactors of new porous materials and the synthesis of porous materials with suitable nanocages are also important for preparing chiral solid catalysts for chiral synthesis in nanoreactors.

Acknowledgements

The authors thank Lei Zhang, Jian Liu, and Jinsuo Gao for their kind help in preparing the manuscript, and Huidong Zhang and Dongmei Jiang for their contributions to the related research work. This work was financially supported by the National Science Foundation of China (NSFC 20621063, 20423004, 20773123) and the Program for Strategic Scientific Alliances between China and The Netherlands (grant no. 2004CB720607, NSFC 20520130214).

[1] a) R. Noyori, *Angew. Chem.* **2002**, *114*, 2108–2123; *Angew. Chem. Int. Ed.* **2002**, *41*, 2008–2022; b) B. M. Trost, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5348–5355.

[2] a) W. S. Knowles, M. J. Sabacky, B. D. Vineyard, *Chem. Commun. (London)* **1968**, 1445–1446; b) W. S. Knowles, R. Noyori, *Acc. Chem. Res.* **2007**, *40*, 1238–1239.

[3] a) T. Ohkuma, D. Ishii, H. Takeno, R. Noyori, *J. Am. Chem. Soc.* **2000**, *122*, 6510–6511; b) Y. J. Yan, X. M. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 7198–7202; c) W. C. Zhang, X. M. Zhang, *Angew. Chem.* **2006**, *118*, 5641–5644; *Angew. Chem. Int. Ed.* **2006**, *45*, 5515–5518; d) C. A. Sandoval, T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, R. Noyori, *Chem. Asian J.* **2006**, *1*, 102–110; e) C. A. Sandoval, T. Ohkuma, K. Muniz, R. Noyori, *J. Am. Chem. Soc.* **2003**, *125*, 13490–13503; f) W. B. Wang, S. M. Lu, P. Y. Yang, X. W. Han, Y. G. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 10536–10537; for reviews, see: g) *Comprehensive Asymmetric Catalysis*, *Vol. 1* (Eds: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**; h) *Asymmetric Catalysis in Organic Synthesis* (Ed.: R. Noyori), Wiley, New York, **1994**; i) *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), Wiley, New York, **1999**.

[4] a) R. Mariz, X. Luan, M. Garri, A. Linden, R. Dorta, *J. Am. Chem. Soc.* **2008**, *130*, 2172–2173; b) T. Ohkuma, K. Tsutsumi, N. Utsumi, N. Arai, R. Noyori. K. Murata, *Org. Lett.* **2007**, *9*, 255–257; c) T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, C. Sandova, R. Noyori, *J. Am. Chem. Soc.* **2006**, *128*, 8724–8725; d) E. P. Balskus, E. N. Jacobsen, *Science* **2007**, *317*, 1736–1740; e) M. Wiesner, J. D. Revell, H. Wennemers, *Angew. Chem.* **2008**, *120*, 1897–1900; *Angew. Chem. Int. Ed.* **2008**, *47*,1871–1874; f) T. Yamaguchi, K. Matsumoto, B. Satio, T. Katsuki, *Angew. Chem.* **2007**, *119*, 4813–4815; *Angew. Chem. Int. Ed.* **2007**, *46*, 4729–4731.

[5] *Asymmetric Catalysis on Industrial Scale* (Eds.: H. U. Blaser, E. Schmidt), Wiley-VCH, Weinheim **2004**.

[6] a) L. Zhong, Q. Gao, J. S. Gao, J. L. Xiao, C. Li, *J. Catal.* **2007**, *250*, 360–364; b) K. Burgemeister, G. Franciò, V. H. Gego, L. Greiner, H. Hugl, W. Leitner, *Chem. Eur. J.* **2007**,*13*, 2798–2804.

[7] a) K. L. Ding, Z. Wang, L. Shi, *Pure. Appl. Chem.* **2007**, *79*, 1531–1540; b) Y. X. Liang, Z. Wang, K. L. Ding, *Adv. Synth. Catal.* **2006**, *348*, 1533–1538; <*lit* c> K. L. Ding, Z. Wang, X. W. Wang, Y. X. Liang, X. S. Wang, *Chem. Eur. J.* **2006**, *12*, 5188–5197.

[8] a) M. E. Orglmeister, A. Baiker, Mallat, E. Orglmeister, A. Baiker, *Chem. Rev.* **2007**, *107*, 4863–4890; b) M. Heitbaum, F. Glorius, I. Escher, *Angew. Chem.* **2006**, *118*, 4850–4881; *Angew. Chem. Int. Ed.* **2006**, *45*, 4732–4762; c) G. J. Hutchings, *Annu. Rev. Mater. Sci.* **2005**, *35*, 143–166.

[9] a) M. Tada, T. Taniike, L. M. Kantam, Y. Iwasawa, *Chem. Commun.* **2004**, 2542–2543; b) M. Tada, N. Kojima, Y. Izumi, T. Taniike, Y. Iwasawa, *J. Phys. Chem. B* **2005**, *109*, 9905–9916; c) M. Tada, S. Tanaka, Y. Iwasawa, *Chem. Lett.* **2005**, 1362–1363; d) M. Tada, Y. Iwasawa, *Chem. Commun.* **2006**, 2833–2844.

[10] a) J. L. Margitfalvi, E. Talas, E. Tfirst, *Top. Catal.* **2006**, *39*, 77–87; <*lit* b> N. J. Coulston, R. P. K. Wells, P. B. Wells, G. J. Hutchings, *Catal. Today* **2006**, *114*, 353–356.

[11] A. Cornejo, J. M. Fraile, J. I. Garcia, M. J. Gil, C. I. Herrerias, G. Legarreta, V. Martinez-Merino, J. A. Mayoral, *J. Mol. Catal. A: Chem.* **2003**, *196*, 101–108.

[12] a) S. Taylor, J. Gullick, P. McMorn, D. Bethell, P. C. B. Page, F. E. Hancock, F. King, G. J. Hutchings, *Top. Catal.* **2003**, *24*, 43–50; b) C. K. W. Kwong, R. Huang, M. Zhang, M. Shi, P. H. Toy, *Chem. Eur. J.* **2007**, *13*, 2369–2376; c) A. Corma, M. Iglesias, C. Del Pino, F. Sanchez, *J. Chem. Soc. Chem. Commun.* **1991**, *18*, 1253–1255.

[13] L. Xing, F. Du, J. J. Liang, Y. S. Chen, Q. L. Zhou, *J. Mol. Catal. A: Chem.* **2007**, *276*, 191–196.

[14] C. E. Song, D. H. Kim, D. S. Choi, *Eur. J. Inorg. Chem.* **2006**, 2927–2935.

[15] a) G. H. Liu, M. Yao, F. Zhang, Y. Gao, H. X. Li, *Chem. Commun.* **2008**, 347–349; b) M. W. C. Robinson, D. A. Timms, S. M. Williams, A. E. Graham, *Tetrahedron Lett.* **2007**, *48*, 6249–6251; <*lit* c> A. Corma, H. García, *Adv. Synth. Catal.* **2006**, *348*, 1391–1412; <*lit* d> S. Xiang, Y. L. Zhang, Q. Xin, C. Li, *Angew. Chem.* **2002**, *114*, 849–852; *Angew. Chem. Int. Ed.* **2002**, *41*, 821–824; e) S. S. Lee, J. Y. Ying, *J. Mol. Catal. A: Chem.* **2006**, *256*, 219–224.

[16] a) R. Nishio, M. Sugiura, S. Kobayashi, *Chem. Asian J.* **2007**, *2*, 983–995; <*lit* b> H. S. He, J. J. Yan, R. X. Shen, S. J. Zhuo, P. H. Toy, *Synlett* **2006**, 563–566.

[17] a) C. Li, *Catal. Rev. - Sci. Eng.* **2004**, *46*, 419–492; b) C. Li, H. Zhang, D. Jiang, Q. Yang, *Chem. Commun.* **2007**, 547–558; c) C. E. Song, D. H. Kim, D. S. Choi, *Eur. J. Inorg. Chem.* **2006**, 2927–2935.

[18] B. F. G. Johnson, S. A. Raynor, D. S. Shephard, T. Mashmeyer, J. M. Thomas, G. Sankar, S. Bromley, R. Oldroyd, L. Gladden, M. D. Mantle, *Chem. Commun.* **1999**, 1167–1168.

[19] a) F. Hoffmann, M. Cornelius, J. Morell, M. Fröba, *Angew. Chem.* **2006**, *118*, 3290–3328; *Angew. Chem. Int. Ed.* **2006**, *45*, 3216–3251; b) A. Stein, B. J. Melde, R. C. Schroden, *Adv. Mater.* **2000**, *12*, 1403–1419; c) A. P. Wight, M. E. Davis, *Chem. Rev.* **2002**, *102*, 3589–3614.

[20] S. Inagaki, S. Guan, Y. Fukushima, T. Ohsuna, O. Terasaki, *J. Am. Chem. Soc.* **1999**, *121*, 9611–9614.

[21] B. J. Melde, B. T. Holland, C. F. Blanford, A. Stein, *Chem. Mater.* **1999**, *11*, 3302–3308.

[22] T. Asefa, M. J. MacLachlan, N. Coombs, G. A. Ozin, *Nature* **1999**, *402*, 867–871.

[23] M. C. Burleigh, M. A. Markowitz, S. Jayasundera, M. S. Spector, C. W. Thomas, B. P. Gaber, *J. Phys. Chem. B* **2003**, *107*, 12628–12634.

[24] S. Shylesh, R. K. Jha, A. P. Singh, *Microporous Mesoporous Mater.* **2006**, *94*, 364–370.

[25] E.-B. Cho, K.-W. Kwon, K. Char, *Chem. Mater.* **2001**, *13*, 3837–3839.

[26] J. Liu, J. Yang, Q. H. Yang, G. Wang, Y. Li, *Adv. Funct. Mater.* **2005**, *15*, 1297–1302.

[27] J. Liu, Q. H. Yang, M. P. Kapoor, N. Setoyama, S. Inagaki, J. Yang, L. Zhang, *J. Phys. Chem. B* **2005**, *109*, 12250–12256.

[28] D. M. Jiang, Q. H. Yang, J. Yang, L. Zhang, G. R. Zhu, W. G. Su, C. Li, *Chem. Mater.* **2005**, *17*, 6154–6160.

[29] a) M. Tada, Y. Iwasawa, *Coord. Chem. Rev.* **2007**, *251*, 2702–1216; b) G. Simonneaux, P. L. Maux, Y. Ferrand, J. Rault-Berthelot, *Coord. Chem. Rev.* **2006**, *250*, 2212–2221; c) D. Yu, P. Makl-Arvela, E. Toukonlity, T. Salmi, *Catal. Rev. Sci. Eng.* **2005**, *47*, 175–256; d) M. Heitbaum, F. Glorius, I. Escher, *Angew. Chem.* **2006**, *118*, 4850–4881; *Angew. Chem. Int. Ed.* **2006**, *45*, 4732–4762; e) R. Abdallah, B. Fumey, V. Meille, C. De Bellefon, *Catal. Today* **2007**, *125*, 34–39.

[30] a) S. Sahoo, P. Kumar, F. Lefebvre , S. B. Halligudi, *J. Mol. Catal. A: Chem.* **2007**, *273*, 102–108; b) L. Lou, K. Yu, F. Ding, X. Peng, M. Dong, C. Zhang, S. Liu, *J. Catal.* **2007**, *249*, 102–110; c) Y. Perez, D. P. Quintanilla, M. Fajardo, I. Sierra, I. del Hierro, *J. Mol. Catal. A: Chem.* **2007**, *271*, 227–237; d) A. Crosman, W. F. Hoelderich, *Catal. Today* **2007**, *121*, 130–139; e) K. Pathak, A. P. Bhatt, S. H. R. Abdi, R. I. Kureshy, N. H. Khan, I. Ahmad, Raksh V. Jasra, *Tetrahedron: Asymmetry* **2006**, *17*, 1506–1513; f) A. P. Bhatt, K. Pathak, Raksh V. Jasra, R. I. Kureshy, N. H. Khan, S. H. R. Abdi, *J. Mol. Catal. A: Chem.* **2006**, *244*, 110–117; g) W. P. Hems, P. McMorn, S. Riddel, S. Watson, F. E. Hancock, G. J. Hutchings, *Org. Biomol. Chem.* **2005**, *3*, 1547–1550.

[31] a) H. Zhang, S. Xiang, C. Li, *Chem. Commun.* **2005**, 1209–1211; b) H. Zhang, S. Xiang, J. Xiao, C. Li, *J. Mol. Catal. A: Chem.* **2005**, *238*, 175–184; c) H. Zhang, Y. Zhang, C. Li, *Tetrehedron: Asymmetric* **2005**, *16*, 2417–2423; d) H. Zhang, Y. Zhang, C. Li, *J. Catal.* **2006**, *238*, 369–381.

[32] C. Baleizao, B. Gigante, H. García, A. Corma, *Tetrahedron* **2004**, *60*, 10461–10468.

[33] H. Zhang, C. Li, *Tetrahedron* **2006**, *62*, 6640–6649.

[34] a) K. Malek, A. P. J. Jansen, C. Li, R. A. van Santen, *J. Catal.* **2007**, *246*, 127–135; b) K. Malek, C. Li, R. A. van Santen, *J. Mol. Catal. A: Chem.* **2007**, *271*, 98–104.

[35] a) R. I. Kureshy, I. Ahmad, N. H. Khan, S. H. R. Abdi, K. Pathak, R. V. Jasra, *J. Catal.* **2006**, *238*, 134–141; b) R. I. Kureshy, I. Ahmad, N. H. Khan, S. H. R. Abdi, K. Pathak, R. V. Jasra, *Tetrahedron: Asymmetry* **2005**, *16*, 3562–3569; c) R. I. Kureshy, I. Ahmad, N. H. Khan, S. H. R. Abdi, S. Singh, P. H. Pandia, R. V. Jasram, *J. Catal.* **2005**, *235*, 28–34.

[36] K. Yu, Z. Gu, R. Ji, L. Lou, F. Ding, C. Zhang, S. Liu, *J. Catal.* **2007**, *252*, 312–320.

[37] S. Bhattacharjee, J. A. Anderson, *Adv. Synth. Catal.* **2006**, *348*, 151–158.

[38] a) S. A. Raynor, J. M. Thomas, R. Raja, B. F. G. Johnson, R. G. Bell, M. D. Mantle, *Chem. Commun.* **2000**, 1925–1926; b) R. Raja, J. M. Thomas, M. D. Jones, B. F. G. Johnson, D. E. W. Vaughan, *J. Am. Chem. Soc.* **2003**, *125*, 14982–14983; c) M. D. Jones, R. Raja, J. M. Thomas, B. F. G. Johnson, D. W. Lewis, J. Rouzaud, K. D. M. Harris, *Angew. Chem.* **2003**, *115*, 4462–4467; *Angew. Chem. Int. Ed.* **2003**, *42*, 4326–4331.

[39] A. Crosman, W. F. Hoelderich, *Catal. Today* **2007**, *121*, 130–139.

[40] V. Caps, I. Paraskevas, S. C. Tsang, *Chem. Commun.* **2005**, 1781–1783.

[41] a) N. A. Caplan, F. E. Hancock, P. P. C. Bulman, G. J. Hutchings, *Angew. Chem.* **2004**, *116*, 1717–1720; *Angew. Chem. Int. Ed.* **2004**, *43*, 1685–1688; b) S. Taylor, J. Gullick, P. McMorn, D. Bethell, P. C. Bulman, F. E. Hancock, F. King, G. J. Hutchings, *J. Chem. Soc. Perkin Trans. 2* **2001**, 1714–1723.

[42] a) S. Chang, N. H. Lee, E. N. Jacobsen, *J. Org. Chem.* **1993**, *58*, 6939–6941; b) M. Palucki, P. J. Pospisil, W. Zhang, E. N. Jacobsen, *J. Am. Chem. Soc.* **1994**, *116*, 9333–9334; c) S. Chang, J. M. Galvin, E. N. Jacobsen, *J. Am. Chem. Soc.* **1994**, *116*, 6937–6938; d) K. Srinivasan, P. Michaud, J. K. Kochi, *J. Am. Chem. Soc.* **1986**, *108*, 2309–2310; e) B. B. De, B. B. Lohray, S. Sivaram, P. K. Dhal, *Tetrahedron: Asymmetry* **1995**, *6*, 2105–2108.

[43] X. Meng, T. Yokoi, D. Lu, T. Tatsumi, *Angew. Chem.* **2007**, *119*, 7942–7944; *Angew. Chem. Int. Ed.* **2007**, *46*, 7796–7799.

[44] a) M. Alvaro, M. Benitez, D. Das, B. Ferrer, H. García, *Chem. Mater.* **2004**, *16*, 2222–2228; b) M; Benitez, G. Bringmann, M. Dreyer, H. García, H. Ihmels, M. Waidelich, K. Wissel, *J. Org. Chem.* **2005**, *70*, 2315–2321.

[45] C. Baleizão, B. Gigante, De. Das, M. Alvaro, H. García, A. Corma, *Chem. Commun.* **2003**, 1860–1861.

[46] D. M. Jiang, Q. H. Yang, H. Wang, G. R. Zhu, J. Yang, C. Li, *J. Catal.* **2006**, *239*, 65–73.

[47] S. Polarz, A. Kuschel, *Adv. Mater.* **2006**, *18*, 1206–1209.

[48] A. Ide, R. Voss, G. Scholz, G. A. Ozin, M. Antonietti, A. Thomas, *Chem. Mater.* **2007**, *19*, 2649–2657.

[49] S. Inagaki, S. Guan, Q. H. Yang, M. P. Kapoor, T. Shimada, *Chem. Commun. Chem. Commum.* **2008**, 202–204.

[50] D. M. Jiang, J. S. Gao, Q. H. Yang, J. Yang, C. Li, *Chem. Mater.* **2006**, *18*, 6012–6018.

[51] N. Herron, *Inorg. Chem.* **1986**, *25*, 4714–4717.

[52] S. B. Ogunwumi, T. Bein, *Chem. Commun.* **1997**, 901–903.

[53] M. Sabater, A. Corma, A. Domenech, V. Fornés, H. García, *Chem. Commun.* **1997**, 1285–1286.

[54] A. Corma, H. García, *Eur. J. Inorg. Chem.* **2004**, *6*, 1143–1164.

[55] F. Algarra, M. A. Esteves, V. Fornés, H. García, J. Primo, *New J. Chem.* **1998**, *22*, 333–338.

[56] Y. Tanamura, T. Uchida, N. Teramae, M. Kikuchi, K. Kusaba, Y. Onodera, *Nano Lett.* **2001**, *1*, 387–390.

[57] M. J. Kim, R. Ryoo, *Chem. Mater.* **1999**, *11*, 487–491.

[58] T. W. Kim, R. Ryoo, M. Kruk, K. P. Gierszal, M. Jaroniec, S. Kamiya, O. Terasaki, *J. Phys. Chem. B* **2004**, *108*, 11480–11489.

[59] J. M. Kim, Y. Sakamoto, Y. K. Hwang, Y. U. Kwon, O. Terasaki, S. E. Park, G. D. Stucky, *J. Phys. Chem. B* **2002**, *106*, 2552–2558.

[60] J. Fan, C. Z. Yu, J. Lei, Q. Zhang, T. C. Li, B. Tu, W. Z. Zhou, D. Y. Zhao, *J. Am. Chem. Soc.* **2005**, *127*, 10794–10795.

[61] C. Yu, Y. Yu, D. Y. Zhao, *Chem. Commun.* **2000**, 575–576.

[62] H. Q. Yang, L. Zhang, W. G. Su, Q. H. Yang, C. Li, *J. Catal.* **2007**, *248*, 204–212.

[63] H. Q. Yang, J. Li, J. Yang, Z. M. Liu, Q. H. Yang, C. Li, *Chem. Commun.* **2007**, 1086–1088.

[64] H. Q. Yang, G. Y. Zhang , X. l. Hong , Y. Y. Zhu, *Microporous Mesoporous Mater.* **2004**, *68*, 119–125.

[65] M. Kruk, V. Antochshuk, J. R. Matos, L. P. Mercuri, M. Jaroniec, *J. Am. Chem. Soc.* **2002**, *124*, 768–769.

[66] a) J. A. Ma, D. Cahard, *Angew. Chem.* **2004**, *116*, 4666–4683; *Angew. Chem. Int. Ed.* **2004**, *43*, 4566–4583; b) G. M. Sammis, H. Danjo, E. N. Jacobsen, *J. Am. Chem. Soc.* **2004**, *126*, 9928–9929.

[67] A. Joy, V. Ramamurthy, *Chem. Eur. J.* **2000**, *6*, 1287–1293.

[68] A. Joy, S. Uppili, M. R. Netherton, J. R. Scheffer, V. Ramamurthy, *J. Am. Chem. Soc.* **2000**, *122*, 728–729.

[69] T. Poon, N. J. Turro, J. Chapman, P. Lakshminarasimhan, X. Lei, W. Adam, S. G. Bosio, *Org. Lett.* **2003**, *5*, 2025–2028.

[70] H. Q. Yang, L. Zhang, L. Zhong, Q. H. Yang, C. Li, *Angew. Chem.* **2007**, *119*, 6985–6989; *Angew. Chem. Int. Ed.* **2007**, *46*, 6861–6865.

[71] Y. M. Zhang, J. Li, D. F. Han, H. D. Zhang, P. Liu, C. Li, *Biochem. Biophys. Res. Commun.* **2008**, *365*, 609–61.

Received: March 17, 2008
Revised: May 24, 2008
Published online: August 4, 2008

