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Tetrahedron
Tetrahedron 62 (2006) 6640–6649

Asymmetric epoxidation of 6-cyano-2,2-dimethylchromene on Mn(salen) catalyst immobilized in mesoporous materials

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Received 2 November 2005; revised 6 January 2006; accepted 25 January 2006
Available online 30 May 2006

Abstract—This article reports our recent work on the heterogeneous asymmetric epoxidation catalyzed by chiral Mn(salen) catalyst axially immobilized via phenoxyl groups and organic sulfonic groups. The asymmetric epoxidation of 6-cyano-2,2-dimethylchromene was especially presented in detail. The factors that affected the asymmetric induction, such as the nanopores and the external surface, the linkage length, and the modification of nanopores with methyl groups were discussed. It was found that the enantioselectivities increased with decreasing the nanopore sizes or increasing the linkage length in nanopore, and the Mn(salen) catalyst immobilized into nanopores generally gave higher ee values than those on the external surface. The heterogeneous Mn(salen) catalysts with modified nanopores gave a TOF of 14.8 h^{-1} and an ee value of 90.6% for the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene, which were higher than the results (TOF 10.8 h^{-1}, ee 80.1%) obtained for the homogeneous catalyst.

1. Introduction

Chiral building blocks are widely used in the synthesis of fine chemicals, pharmaceuticals, vitamins, agrochemicals, flavors, fragrances, and functional materials.[1] How to prepare the chiral compounds via asymmetric catalysis has received great attention. Catalytic enantioselective epoxidation is one of the most important processes for the synthesis of chiral epoxides, which can be further converted into many important chiral building blocks via stereoselective ring-opening or functional group transformations. Chiral Mn(salen) complexes are excellent catalysts for the asymmetric epoxidation of unfunctionalized conjugated *cis*-olefins.[2] However, the homogeneous asymmetric epoxidation always suffers some difficulties in practical applications, such as the separation of catalysts and purification of products. The heterogeneous Mn(salen) catalysts have received much attention in recent years due to their potential advantages of easy separation, recycling catalysts, purification of products, and better handling properties.[3]

In the last two decades, many kinds of mesoporous materials with new structures and well-ordered pore arrays have been synthesized, which offer large surface area, uniform pore size distribution, and tunable pore diameters.[4] Among the mesoporous materials, MCM-41 and SBA-15 are the most promising supports for the immobilization of homogeneous catalysts for chiral synthesis. First, MCM-41 and SBA-15 have narrow and tunable nanopore size distributions in the range 2–20 nm, which is suitable for the synthesis of fine chemicals and pharmaceuticals. Second, the hydrothermal stability of the materials is good enough for the chiral synthesis under mild reaction conditions. Finally, their nanopores can be chemically modified. Therefore, the nanopores of the mesoporous materials could be employed as ideal nanoreactors for the chiral synthesis.[3e]

The earlier examples of the heterogeneous chiral Mn(salen) catalysts were the chiral Mn(salen) embedded into mesoporous silicates[5] or encapsulated within the cages of zeolite Y (a microporous material).[6] Chiral Mn(salen) catalyst attached with soluble or insoluble polymers for the heterogeneous asymmetric epoxidation was also reported.[7] In the last several years, various strategies have been reported to immobilize Mn(salen) complexes, including covalent grafting of Mn(salen) on mesoporous materials[8] or carbon materials,[9] ion-exchange of Mn(salen) into clay materials[10] or Al–MCM-41,[11] encapsulation of Mn(salen) in zeolites,[12] and co-condensation of VO(salen) into periodic mesoporous materials.[13] It was reported that the Mn(salen)Cl complexes were prone to form the inactive dimers in homogeneous catalytic systems.[14] The immobilization of Mn(salen) catalysts onto the supports could isolate the active sites of Mn(salen), which might greatly reduce the formation of the dimers and increase the catalytic stability.

It is generally believed that tuning the steric and electronic properties of chiral ligands can alter the enantioselectivity for the asymmetric catalysis. Notably, the nanopores of

Keywords: Heterogeneous chiral catalysis; Asymmetric epoxidation; Mn(salen); Confinement effect; Nanopore; Enantioselective.
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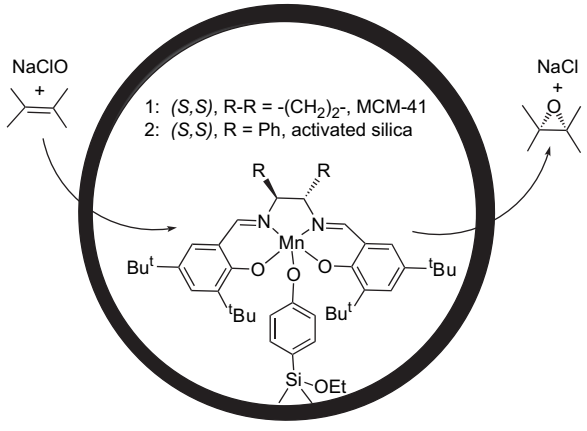
doi:10.1016/j.tet.2006.01.117

mesoporous supports might influence the chiral induction for the asymmetric epoxidation when the chiral Mn(salen) catalysts immobilize into the nanopores of mesoporous supports.[3d,e] A few heterogeneous Mn(salen) catalysts have been reported to give higher ee values than those of the homogeneous ones for the asymmetric epoxidation and this was attributed to the confinement effect of supports.[8a–d,f–h,10b] It was proposed by Thomas et al. that the confinement effect originating from the nanopores enhances the chiral induction for the heterogeneous asymmetric hydrogenation.[15] Hutchings et al. also proposed that confinement effect of the supports improves the enantioselectivities for the heterogeneous asymmetric aziridination of styrene and hydrogenation of carbonyl- and imino-ene.[16] Herein, the factors that could affect the chiral induction in a confined environment for the asymmetric epoxidation of unfunctionalized olefins were studied to understand the nature of the confinement effect. Accordingly, the effects of the different grafting modes, the linkage length, the types of supports, the nanopores or the external surface of supports, and the modification of the nanopore surface on the heterogeneous asymmetric epoxidation have been systematically investigated.

2. Background of the research

2.1. Immobilization via phenoxyl groups

Mn(salen) catalysts were grafted onto mesoporous materials generally via the salen ligands. However, the axial immobilization of Mn(salen) catalysts from Mn atom has seldom been reported.[3] Our group has shown the first example of the chiral Mn(salen) complex axially immobilized into the nanopores of MCM-41 via the phenoxyl groups.[8d] The heterogeneous Mn(salen) catalyst (**1**, Scheme 1) showed an ee value of 72% for the asymmetric epoxidation of α-methylstyrene, higher than 56% ee obtained for the homogeneous catalyst. And the immobilized catalysts were quite stable and could be recycled several times with constant ee values for the asymmetric epoxidation.

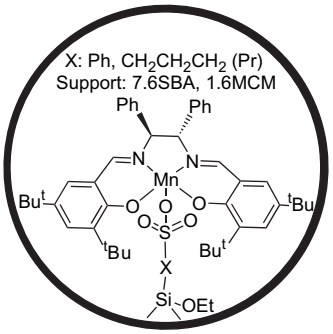


Scheme 1. The chiral Mn(salen) complex immobilized into the nanopores of mesoporous materials via phenoxyl groups.[8d,g]

Then we tried to find out the reasons for the increase in the enantioselectivities for the heterogeneous asymmetric epoxidation in the nanopores. Firstly, the preparation of the heterogeneous Mn(salen) catalyst was improved by the direct oxidation of the phenyl groups on supports to phenoxyl groups.[8g] And the heterogeneous Mn(salen) catalyst grafted via the phenoxyl group (**2**, Scheme 1) gave 79.9% ee for the asymmetric epoxidation of α-methylstyrene, much higher than 26.4% ee for the homogeneous catalyst. The cis/trans ratio of epoxides was also increased from 0.46 for homogeneous catalyst to 21 for the catalyst **2** for the asymmetric epoxidation of *cis*-β-methylstyrene. The supports used in this work included MCM-41 (nanopore sizes 1.6 and 2.7 nm), SBA-15 (nanopore sizes 6.2 and 7.6 nm), and activated silica (nanopore size 9.7 nm), which are, respectively, marked as 1.6MCM, 2.7MCM, 6.2SBA, 7.6SBA, and 9.7AS. Supports with different nanopore sizes obviously affected the enantioselectivity for the heterogeneous asymmetric epoxidation. The free Mn(salen)OPh catalyst gave similar reaction results to those of the Mn(salen)Cl catalyst under the same conditions.[8g] Therefore, the increase in ee values and change in cis/trans ratio are mainly attributed to the axial grafting mode and the support effect of the heterogeneous catalysts.

2.2. Immobilization via organic sulfonic groups

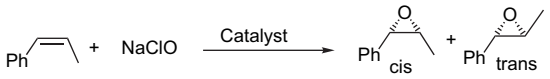
We have axially immobilized the chiral Mn(salen) complexes onto inorganic mesoporous materials via phenyl sulfonic groups (Scheme 2, X=Ph).[8f] The recyclable heterogeneous catalyst 7.6SBA–$PhSO_3$Mn(salen) offered 92.6% ee (*cis*-epoxide) for the asymmetric epoxidation of *cis*-β-methylstyrene, higher than 25.3% ee obtained for the homogeneous catalyst (entries 1 and 2, Table 1). The ratio of cis/trans of epoxides was also increased from 0.46 for the homogeneous Mn(salen)Cl to 7.71 for the heterogeneous Mn(salen) catalyst under the same conditions.



Scheme 2. The chiral Mn(salen) catalyst axially immobilized via organic sulfonic groups.[8f,17]

In order to study the effect of the grafting modes on the catalytic reaction, the chiral Mn(salen) was immobilized into the nanopores or onto external surface of supports via rigid phenyl sulfonic groups or flexible propyl sulfonic groups (Scheme 2, X=Ph or Pr).[17] Table 1 shows that the Mn(salen) catalyst immobilized via phenyl sulfonic groups gave higher ee value (for *cis*-epoxide) and cis/trans ratio than those of the catalyst grafted via propyl sulfonic groups for the asymmetric epoxidation of *cis*-β-methylstyrene (entries 2 and 3). The molecular sizes of Mn(salen) complex was larger than that of the nanopores of 1.6MCM, and the results of N_2 adsorption also proved that the Mn(salen)

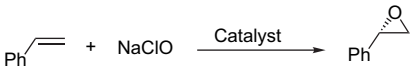
Table 1. Asymmetric epoxidation of *cis*-β-methylstyrene[8f,17,19]



Entry	Catalyst	cis		trans		cis/trans ratio
		Yield (%)	ee (%)[a]	Yield (%)	ee (%)[b]	
1	Mn(salen)Cl	25.3	25.3	55.0	93.3	0.46
2	7.6SBA–$PhSO_3$Mn(salen)	34.7	92.6	4.5	81.4	7.71
3	7.6SBA–$PrSO_3$Mn(salen)	21.0	71.7	24.3	87.0	0.87
4	PS–$PhSO_3$Mn(salen)	43.3	68.8	42.5	89.2	1.02

[a] (*S*,*R*)-Configuration.
[b] (*S*,*S*)-Configuration.

Table 2. Asymmetric epoxidation of styrene[17]



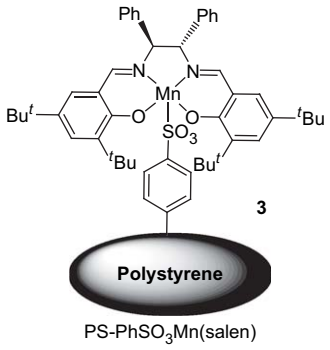
Entry	Catalyst	*T* (h)	Conv. (%)	Sel. (%)[a]	ee (%)[b]
1	Mn(salen)Cl	6	100	100	58.0
2	7.6SBA–$PhSO_3$Mn(salen)	24	44.5	78.4	50.6
3	7.6SBA–$PrSO_3$Mn(salen)	24	75.5	94.5	60.0
4	1.6MCM–$PrSO_3$Mn(salen)	24	91.5	87.6	52.5

[a] Benzaldehyde and acetophenone as by-products.
[b] (*S*)-Configuration.

complex was anchored on the external surface of 1.6MCM and in the nanopores of 7.6SBA. Table 2 shows that Mn(salen) catalyst immobilized into the nanopores via propyl sulfonic groups presented higher chemical selectivity and ee value than those of the same catalyst anchored onto the external surface via phenyl sulfonic groups for the asymmetric epoxidation of styrene. Therefore, the axially rigid and flexible grafting modes and the nanopores or external surface of supports significantly affected the heterogeneous asymmetric epoxidation.

2.3. Polymers as supports

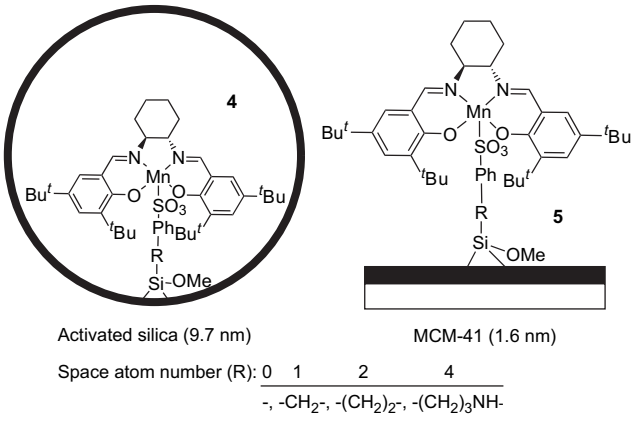
Besides the grafting modes, the types of supports might also affect the heterogeneous asymmetric epoxidation. Polymers have been used as supports to immobilize chiral Mn(salen) catalysts,[3b,18] which generally gave comparable or lower ee values than the homogeneous counterparts for the asymmetric epoxidation due to the less effective steric restriction in the polymer microenvironment.[14b] The chiral Mn(salen) complexes were grafted onto insoluble polystyrene resins (PS) via phenoxy groups or phenyl sulfonic groups through axial coordination (Scheme 3).[19] These heterogeneous Mn(salen) catalysts showed comparable or even higher enantioselectivities than those of the homogeneous catalysts for the asymmetric epoxidation of unfunctionalized olefins. For example, PS–$PhSO_3$Mn(salen) (**3**, Scheme 3) gave higher ee value than that of the homogeneous catalyst (68.8% vs 25.3% for *cis*-epoxide) for the asymmetric epoxidation of *cis*-β-methylstyrene (entries 1 and 4, Table 1). Notably, the catalyst **3** presented lower ee values (for *cis*-epoxide) and cis/trans ratio than those of the same Mn(salen) catalyst immobilized on inorganic material 7.6SBA (entries 2 and 4, Table 1). Therefore, the different types of supports obviously affected the reaction performance for the heterogeneous asymmetric epoxidation.



Scheme 3. The chiral Mn(salen) catalyst axially immobilized onto the insoluble polystyrene resins via phenyl sulfonic groups.[19]

2.4. Grafting using different linkage lengths

The effect of the axial linkage length between the Mn(salen) catalysts and the surface of supports on the heterogeneous asymmetric epoxidation has seldom been investigated.[3d,e] We have immobilized the chiral Mn(salen) into nanopores of 9.7AS and onto the external surface of 1.6MCM via phenyl sulfonic groups with different linkage lengths (Scheme 4).[20] One of the representative examples was the heterogeneous asymmetric epoxidation of 1-phenylcyclohexene (see the results shown in Fig. 1). The ee values obtained for the reactions catalyzed by **4** increased from 14% to 65% when the number of the space atoms increased from 0 to 4. In contrast, the ee values obtained for the reactions catalyzed by **5** were nearly unaffected by the linkage lengths and remained almost constant at about 45%.



Scheme 4. The Mn(salen) catalyst immobilized into the nanopores of 9.7AS (**4**) and on the external surface of 1.6MCM (**5**).[20]

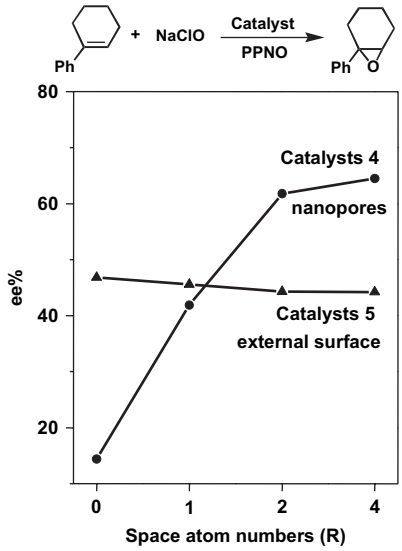
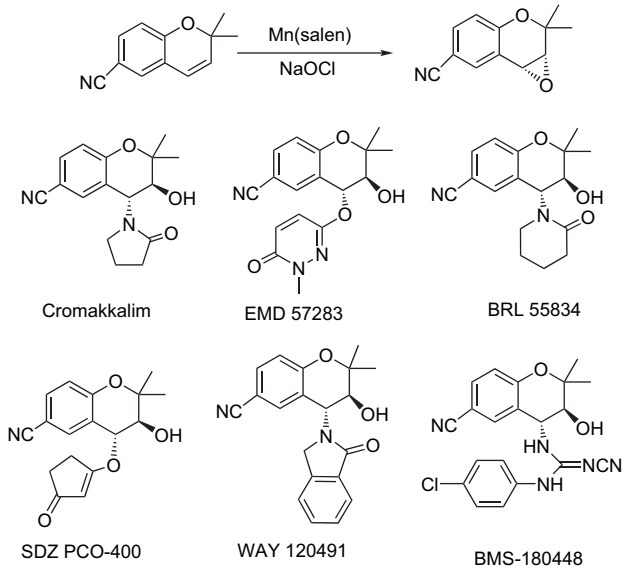


Figure 1. The ee values obtained for the heterogeneous asymmetric epoxidation of 1-phenylcyclohexene catalyzed by catalysts **4** and **5**.[20]

The effect of PPNO on the heterogeneous asymmetric epoxidation of 1-phenylcyclohexene was also studied. The use of catalyst **5** (R=0, Scheme 4) improved the ee values from 13% to 47% after the addition of PPNO (4-phenylpyridine *N*-oxide), whereas the catalyst **4** (R=0) gave almost unchanged ee values (14% vs 14%) with or without the axial additive PPNO. This implied that the Mn(salen) catalyst axially immobilized on the open surface of 1.6MCM (**5**) had the interaction with PPNO, but the same catalyst on the concave surface of nanopores of 9.7AS (**4**) had no such interaction. The catalysts **4** and **5** (R=1) gave similar ee values due to the enhanced interaction between Mn(salen) and PPNO with increasing linkage length. When the number of the space atoms became 2 or 4 (Fig. 1), the catalyst **4** gave higher ee values than those of the catalyst **5**, which could be due to the fact that the confinement effect originating from the nanopores enhanced the asymmetric induction for the asymmetric epoxidation.

3. Results and discussion

Based on our recent work,[8f,g,17,20] we conclude that the confinement effect not only alters the cis/trans ratios of epoxides, but also improves the chemical selectivities and enantioselectivities for the asymmetric epoxidation using the catalysts immobilized in mesoporous materials. Among all the factors that contributed to the confinement effect, the nanopores and linkage lengths were found to be the most significant ones for the heterogeneous asymmetric epoxidation. In this work, the chiral Mn(salen) was immobilized on supports with different nanopore sizes via phenoxyl groups or phenyl sulfonic groups with different linkage lengths. To test the catalytic performance of these heterogeneous Mn(salen) catalysts, 6-cyano-2,2-dimethylchromene[21] was selected as a representative substrate because its corresponding epoxide was an important, biologically active compound.[22] Scheme 5 shows a variety of compounds that can be produced from the epoxidation of 6-cyano-2,2-dimethylchromene and these compounds generally exhibit potential antihypertensive activity by controlling the ATP-sensitive K^+ channels in the cell membrane.[23] In this work, we demonstrated that the optimized heterogeneous Mn(salen) catalysts could give even higher TOF and ee values than their homogeneous counterparts for the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene under the same conditions.

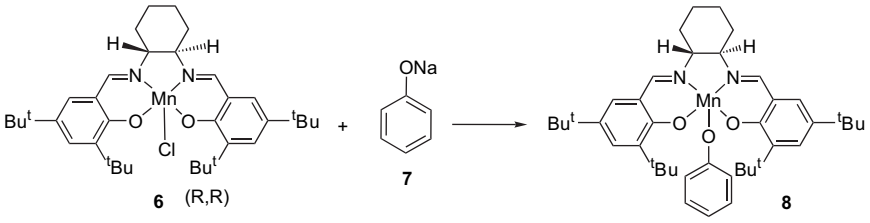


Scheme 5. Benzopyran-based ATP-sensitive potassium channel openers.

3.1. Synthesis and characterization of Mn(salen) catalysts

(*R*,*R*)-Mn(salen)Cl (**6**) was synthesized and characterized according to the literature.[24] Mn(salen)OPh catalyst (**8**) was prepared by ion-exchange of Mn(salen)Cl with PhONa in refluxing ethanol (Scheme 6).[8g,19] The BET measurement of activated silica showed that the activated silica used in this work has a nanopore size of 9.7 nm with a narrow pore distribution (Fig. 2). The phenyl groups anchored on supports were oxidized to phenoxyl groups with H_2O_2 in the presence of $FeCl_3$ and H_2SO_4, and then the phenoxyl groups were transformed into their sodium salts (Scheme 7).[8g,19] The supports modified with sulfonic groups were prepared by a sulfonation of substituted phenyl groups with fuming sulfuric acid and subsequent conversion into their sodium salts (Scheme 7).[8f,20] Then the chiral Mn(salen) complex was immobilized onto supports according to the methods reported previously (Scheme 8).[8f,g]

These heterogeneous Mn(salen) catalysts were characterized by FTIR, UV–vis, TEM, and XRD.[8g,20] The FTIR spectra of the heterogeneous Mn(salen) catalysts confirmed the presence of the phenyl groups (1490 cm^{-1}), alkyl linkage groups (1431 and 1454 cm^{-1}), methyl groups (2979, 2952, and 2850 cm^{-1}), and the Mn(salen) complex (characteristic band at 1535 cm^{-1}) on the supports. Mn(salen)Cl and Mn(salen)OPh complexes gave similar peaks at 331 and 446 nm in their UV–vis spectra. After grafting Mn(salen) complex onto the modified supports, the characteristic bands of Mn(salen) complex appeared again in their spectra, but the bands shifted from 331 and 446 nm, respectively, to 430 and 327 nm for 7.6SBA–PhOMn(salen)[8g] and to 432 and 329 nm for 9.7AS–2-$PhSO_3$Mn(salen),[20] indicating the presence of



Scheme 6. Preparation of homogeneous Mn(salen)OPh catalyst (**8**).

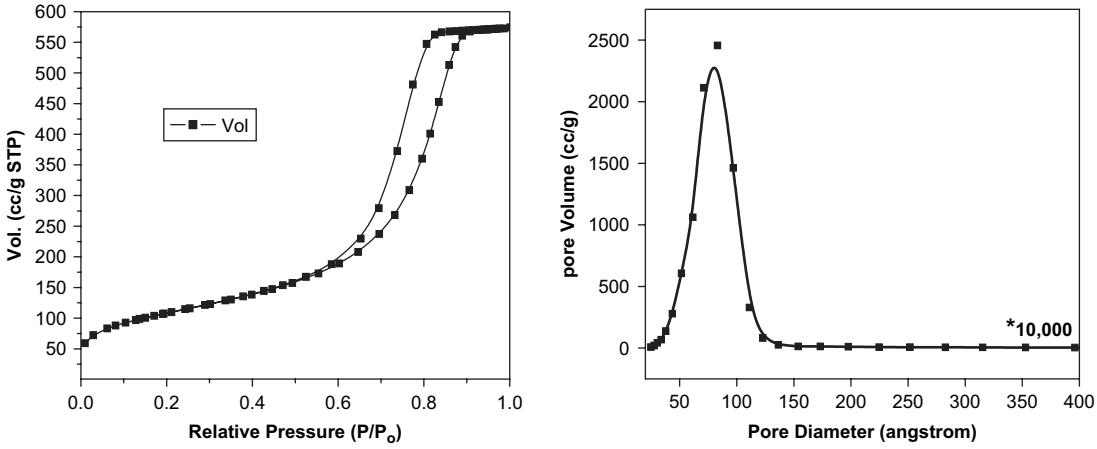
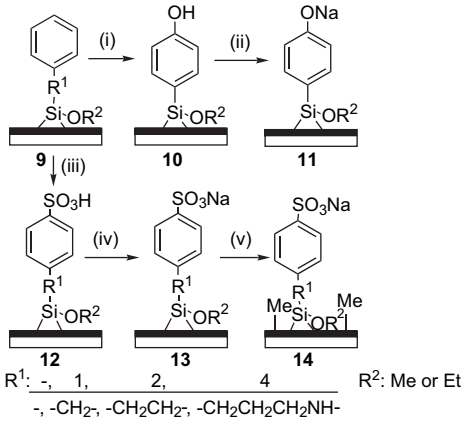


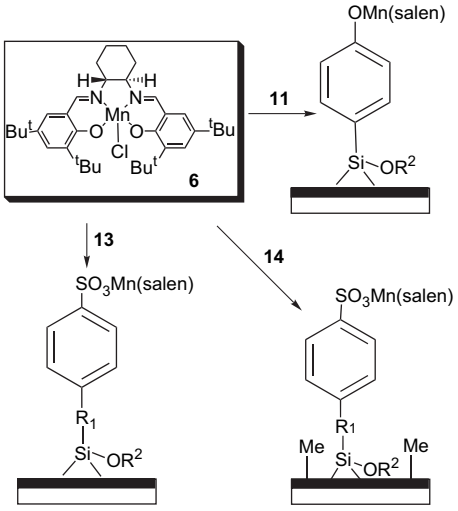
Figure 2. The nitrogen adsorption–desorption isotherms of activated silica (9.7AS) (the left) and pore size distribution curve of 9.7AS calculated from the desorption branch (the right).[20]

interaction between the immobilized Mn(salen) and the supports. The TEM images and the XRD patterns of the heterogeneous Mn(salen) catalysts showed that the mesoporous supports in the heterogeneous Mn(salen) catalysts still kept good periodic structure after the immobilization of Mn(salen) catalyst onto supports. The amount of Mn(salen) complex immobilized in the heterogeneous catalysts was in the range of 0.01–0.055 mmol/g based on the Mn element analyzed by ICP–AES.

The size of solvated Mn(salen)Cl complex was estimated to be 2.05 nm×1.61 nm by MM2 based on the minimized energy.[8g,17,20] The results of nitrogen sorption of the heterogeneous catalysts showed that when the Mn(salen) complex was immobilized on the supports of 2.7MCM, 6.2SBA, 7.6SBA, and 9.7AS, the nanopore sizes, surface areas, and pore volumes all decreased compared to those of the supports before the immobilization.[17,20] For example, the nanopore size decreased from 7.0 to 6.7 nm, the surface area decreased



Scheme 7. Preparation of the supports modified with phenoxyl groups (**11**) and phenyl sulfonic groups with different linkage lengths (**13**, **14**). Mesoporous supports: 9.7AS, 7.6SBA, 6.2SBA, 2.7MCM, and 1.6MCM. Reagents and conditions: (i) H_2O_2, H_2SO_4, $FeCl_3 \cdot 6H_2O$, 50 °C, 5 h; (ii) NaOH, rt, 3 h; (iii) 10% fuming sulfuric acid, 40 °C, 2 h; (iv) $NaHCO_3$, rt, 3 h; (v) $MeSi(OMe)_3$, toluene, reflux.



Scheme 8. The grafting of Mn(salen) catalyst onto various modified supports. Mesoporous supports: 9.7AS, 7.6SBA, 6.2SBA, 2.7MCM, and 1.6MCM.

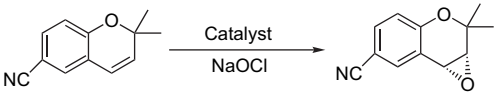
from 455 to 331 m^2/g, and the pore volume decreased from 0.52 to 0.37 cm^3/g after the immobilization of Mn(salen) on 7.6SBA–$PhSO_3Na$. These results clearly suggested that Mn(salen) complex immobilized mainly into the nanopores of supports.[8h] However, the solvated Mn(salen)Cl complex is too big to be accommodated into the nanopores of 1.6MCM. The results of nitrogen sorption showed that the nanopore sizes (from 1.4 to 1.4 nm), surface areas (from 431 to 403 m^2/g), and pore volumes (from 0.26 to 0.27 cm^3/g) were almost unchanged after the immobilization of Mn(salen) onto 1.6MCM–$PhSO_3Na$.[17,20] Thus Mn(salen) complex was mainly immobilized onto the external surface of 1.6MCM.

3.2. The Mn(salen) catalyst immobilized on mesoporous materials

The results of the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene are compared in Table 3. Homogeneous Mn(salen)Cl catalyst showed almost stoichiometric conversion and 80.1% ee value (entry 1). When the chlorine ion was displayed by phenoxyl group, the Mn(salen)OPh catalyst also showed the similar results, indicating that the electronic effect originating from the phenoxyl groups did not obviously affect the reaction performance (entry 2). The Mn(salen) catalyst grafted onto the external surface of 1.6MCM gave 49.0% ee for the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene (entry 3). The differences in the catalytic performance between 1.6MCM–PhOMn(salen) and Mn(salen)OPh could be attributed to the axial grafting mode and the influence of support surface, which resulted in the decreased enantioselectivity.

The chiral Mn(salen) catalyst was then immobilized into the nanopores of supports with different nanopore sizes (from 2.7 nm for 2.7MCM to 9.7 nm for 9.7AS). These heterogeneous catalysts had the effect of the axial grafting mode, the effect of support surface, and the confinement effect originating from the nanopores. The reaction results in Table 3 show that the ee values increased from 26.4% for 2.7MCM–PhOMn(salen) to 84.9% for 6.2SBA–PhOMn(salen) under the same reaction conditions (entries 4 and 5). Considering the sizes of Mn(salen), substrate, and the nanopore of 2.7MCM, the poor activity and enantioselectivity for 2.7MCM–PhOMn(salen) should be mainly attributed to the spatially overcrowded catalytic microenvironment in the nanopores of 2.7MCM. When the nanopore sizes were increased, the configuration of Mn(salen) in nanopore became free and optimal to adapt the reaction. The ee value of 84.9% obtained for 6.2SBA–PhOMn(salen) was higher than 49.0% for 1.6MCM–PhOMn(salen), which might be mainly due to the confinement effect of the nanopores of 6.2SBA. Although the axial grafting mode and the surface influence decreased the ee values for the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene, the catalyst 6.2SBA–PhOMn(salen) gave 84.9% ee, comparable to the 80.1% ee for the homogeneous catalyst, as a result of the positive confinement effect.

Table 3. Asymmetric epoxidation catalyzed by homogeneous Mn(salen) catalyst and Mn(salen) catalyst immobilized via phenoxyl groups[a]



Entry	Catalyst	Pore size (nm)	Time (h)	Conv. (%)	ee (%)[b]
1	Mn(salen)Cl	—	6	97.0	80.1
2	Mn(salen)OPh	—	6	100	84.6
3	1.6MCM–PhOMn(salen)	1.6	24	76.9	49.0
4	2.7MCM–PhOMn(salen)	2.7	24	31.9	26.4
5	6.2SBA–PhOMn(salen)	6.2	24	100	84.9
6	7.6SBA–PhOMn(salen)	7.6	24	72.6	76.9
7	9.7AS–PhOMn(salen)	9.7	24	84.1	68.8

[a] Reactions were performed in CH_2Cl_2 (3 ml) with olefin (1.0 mmol), *n*-nonane (1.0 mmol), homogeneous or heterogeneous Mn(salen) catalyst (0.015 mmol, 1.5 mol %), PPNO (0.38 mmol), and NaClO aqueous solution (pH=11.5, 0.55 M, 3.64 ml) at 20 °C.

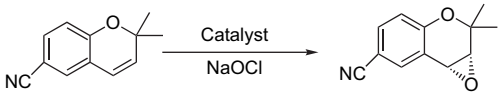
[b] (*R*,*R*)-Configuration.

The further increase in nanopore sizes from 6.2 to 7.6 and 9.7 nm resulted in the ee values to decrease slightly from 84.9% to 76.9% and 68.8% (entries 4–7), which were still higher than that for 1.6MCM–PhOMn(salen). It was reported that the chiral restriction did indeed boost the ee values for the asymmetric hydrogenation on the heterogeneous Rh(COD)DED catalyst, in which the influence of spatial constraint was declined in proceeding from the 3.8 nm to the 6.0 nm and then to the 25 nm pore diameter silica.[15c] For our study on the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene, the confinement effect[15a] originating from the nanopores improved the asymmetric induction for the heterogeneous asymmetric epoxidation and resulted in higher ee values for the epoxide in nanopores than that on the external surface. And when the nanopore sizes were increased further above 7.6 nm, the confinement effect was weakened, leading to the decrease in ee values.

3.3. The Mn(salen) catalyst immobilized via various linkage lengths

The asymmetric epoxidation of 6-cyano-2,2-dimethylchromene was investigated for the Mn(salen) catalysts immobilized into the nanopores of 9.7AS via phenyl sulfonic groups with different linkage lengths. The linkage lengths between the surface and the phenyl group varied from a single-bond long to five-bonds long (R=0, 1, 2, and 4, Scheme 7). The results of the asymmetric epoxidation are summarized in Table 4. Mn(salen) catalyst immobilized into the nanopores of 9.7AS directly via phenyl sulfonic groups gave a relatively low enantioselectivity, 44.9% ee (entry 2). The enantioselectivities increased with increasing the linkage length between the Mn(salen) catalyst and the pore wall (entries 3–5). The highest ee value of 82.6% could be obtained for the heterogeneous catalyst 9.7AS–4-$PhSO_3$Mn(salen) with the linkage of five-bonds long (R^1= 4, Scheme 7), which was comparable to that of the homogeneous catalyst under the same reaction conditions (entries 1 and 5). The tendency was similar to that of the heterogeneous asymmetric epoxidation of 1-phenylcyclohexene catalyzed by Mn(salen) immobilized into the nanopores of 9.7AS with different linkage lengths (Scheme 4, Fig. 1). When the chiral Mn(salen) catalyst was immobilized into the nanopores of 7.6SBA, the heterogeneous catalysts also showed that the ee values increased with increasing the linkage length for the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene (entries 6 and 7, Table 4). The TOF

Table 4. Asymmetric epoxidation catalyzed by homogeneous Mn(salen) catalyst and Mn(salen) catalyst immobilized via substituted phenyl sulfonic groups[a]



Entry	Catalyst	Time (h)	Conv. (%)	ee (%)[b]	TOF (h^{-1})
1	Mn(salen)Cl	6	97.0	80.1	10.8
2	9.7AS–$PhSO_3$Mn(salen)	24	26.3	44.9	0.73
3	9.7AS–1-$PhSO_3$Mn(salen)	24	54.0	60.4	1.5
4	9.7AS–2-$PhSO_3$Mn(salen)	24	88.8	78.7	2.47
5	9.7AS–4-$PhSO_3$Mn(salen)	24	87.3	82.6	2.43
6	7.6SBA–2-$PhSO_3$Mn(salen)	24	88.5	84.6	2.46
7	7.6SBA–4-$PhSO_3$Mn(salen)	24	91.0	89.4	2.53
8	1.6MCM–4-$PhSO_3$Mn(salen)	24	76.8	71.1	2.14
9	9.7AS(Me)–2-$PhSO_3$Mn(salen)	6	98.3	86.5	10.9
10	9.7AS(Me)–4-$PhSO_3$Mn(salen)	4.5	100	90.6	14.8

[a] Reactions were performed in CH_2Cl_2 (3 ml) with olefin (1.0 mmol), *n*-nonane (1.0 mmol), homogeneous or heterogeneous Mn(salen) catalyst (0.015 mmol, 1.5 mol %), PPNO (0.38 mmol), and NaClO aqueous solution (pH=11.5, 0.55 M, 3.64 ml) at 20 °C.
[b] (*R*,*R*)-Epoxide.

of these heterogeneous catalysts also improved with increasing the linkage length. These results obviously suggested that the longer linkage length could improve the catalytic performance for the epoxidation of 6-cyano-2,2-dimethylchromene.

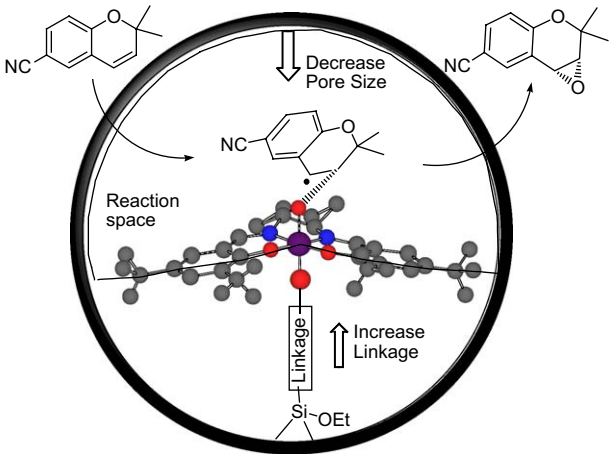
Mn(salen) catalyst immobilized into the nanopores of 7.6SBA gave higher ee values than that of the same catalyst immobilized into the nanopores of 9.7AS (entries 6 and 7, Table 4). For example, 7.6SBA–4-$PhSO_3$Mn(salen) gave 89.4% ee, higher than 82.6% ee obtained for 9.7AS–4-$PhSO_3$Mn(salen) (entries 5 and 7). But 1.6MCM–4-$PhSO_3$Mn(salen) gave 71.1% ee (entry 8, Table 4), lower than that obtained for the catalysts in the nanopores of 7.6SBA and 9.7AS (entries 7 and 5). This further proved that the confinement effect originating from the nanopores improved the asymmetric induction for the epoxidation.[20]

3.4. Mn(salen) catalyst immobilized into the nanopores modified with methyl groups

In order to increase the reaction efficiency, particularly the diffusion of reactants and products in the nanopores, the nanopore of the heterogeneous Mn(salen) catalysts was modified with methyl groups. The results of the asymmetric epoxidation on the methyl-modified catalysts are listed in Table 4 (entries 9 and 10). Similarly, the ee values increased from 86.5% to 90.6% when the linkage lengths were increased from three-bonds long to five-bonds long. And the modified catalysts showed higher ee values than those of the same catalysts without modification (entries 9, 10 and 4, 5).[17] For example, the ee values increased from 82.6% to 90.6% for the catalyst 9.7AS–4-$PhSO_3$Mn(salen) after the modification of its nanopores with methyl groups (entries 5 and 10), which was also higher than the ee value of 80.1% for the corresponding homogeneous catalyst.

The modification of the nanopores of 9.7AS with methyl groups not only increased the ee values but also greatly improved the reaction conversion. The catalyst 9.7AS(Me)–2-$PhSO_3$Mn(salen) could completely convert the substrate into its epoxide within 6 h, with a TOF of 10.9 h^{-1}. The catalyst 9.7AS(Me)–4-$PhSO_3$Mn(salen) with longer linkage length could completely epoxidize the olefin within 4.5 h with a TOF of 14.8 h^{-1} (entries 9 and 10), which was higher than the TOF of 10.8 h^{-1} (entries 1 and 10) obtained for the homogeneous catalyst, as a result of the modified catalytic microenvironment in the nanopore reactors. However, the heterogeneous Mn(salen) catalysts generally gave a lower conversion (or TOF) than that for the homogeneous one due to the lower activity of the immobilized catalysts and/or the difficulty in the diffusion of reactants and products in nanopores.[3,8f,g,17,20]

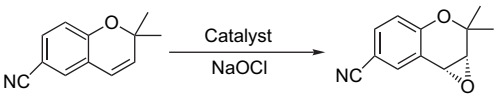
The asymmetric epoxidation of 6-cyano-2,2-dimethylchromene was actually performed in the space between the salen plane and the upper wall of nanopores (Scheme 9). When the chiral Mn(salen) catalyst was immobilized in various nanopores of mesoporous materials via phenoxyl groups or sulfonic groups, ee values increased with decreasing the nanopore sizes of supports for the heterogeneous asymmetric epoxidation (except for 2.7MCM). When the Mn(salen) catalyst was immobilized into the nanopores of 9.7AS or 7.6SBA via substituted phenyl sulfonic groups, the asymmetric induction enhanced with increasing the linkage length. Both modes led to the same result that the reaction space in nanopores between the salen plan and the upper pore wall was gradually optimized, and accordingly the confinement effect improved the enantioselectivities for the asymmetric epoxidation in the nanopores. Mn(salen) catalysts immobilized into the nanopores of mesoporous supports always gave higher ee values than those obtained on the external surface of 1.6MCM. These results confirmed that the confinement effect originating from nanopores enhanced the asymmetric induction for the heterogeneous asymmetric epoxidation of 6-cyano-2,2-dimethylchromene.



Scheme 9. A schematic description of the heterogeneous asymmetric epoxidation in nanopores of mesoporous supports with decrease in pore sizes and increase in linkage lengths.

Table 5 shows the results of the recycling heterogeneous Mn(salen) catalysts for the asymmetric epoxidation of 6-cyano-2,2-dimethylchromene. The heterogeneous catalysts could be recycled at least three times for the asymmetric

Table 5. The recycles of the heterogeneous Mn(salen) catalysts for the asymmetric epoxidation[a]



Catalyst	Run	Time (h)	Conv. (%)	ee (%)[b]
9.7AS–PhOMn(salen)	1st	24	84.1	68.8
	2nd	24	80.1	67.2
	3rd	24	71.3	65.7
9.7AS(Me)–4-PhSO$_3$Mn(salen)	1st	4.5	100	90.6
	2nd	4.5	95.0	87.3
	3rd	6	77.3	83.2

[a] Reactions were performed in CH_2Cl_2 (6 ml) with olefin (2.0 mmol), *n*-nonane (2.0 mmol), heterogeneous Mn(salen) catalyst (0.030 mmol, 1.5 mol %), PPNO (0.72 mmol), and NaClO aqueous solution (pH= 11.5, 0.55 M, 7.3 ml) at 20 °C.
[b] (*R*,*R*)-Configuration.

epoxidation of 6-cyano-2,2-dimethylchromene without showing dramatic deterioration of the performance.

4. Conclusion

This paper summarized the asymmetric epoxidation of unfunctionalized olefins on Mn(salen) catalysts axially immobilized on inorganic supports or polymers via phenoxyl groups and substituted phenyl sulfonic groups. These heterogeneous catalysts usually gave higher ee values and cis/trans ratios than those of the homogeneous ones for the asymmetric epoxidation of *cis*-β-methylstyrene. Mn(salen) catalysts immobilized into the nanopores via flexible propyl sulfonic groups generally presented higher ee values and chemical selectivities than those obtained for the catalysts anchored on the external surface via rigid phenyl sulfonic groups for the asymmetric epoxidation of styrene and 1,2-dihydronaphthalene. It was also observed that the ee values increased with increasing the linkage length of Mn(salen) catalysts immobilized into the nanopores for the asymmetric epoxidation. The nanopores and the linkage length were found to be the two most significant factors that influenced the enantioselectivity for the heterogeneous asymmetric epoxidation.

The asymmetric epoxidation of 6-cyano-2,2-dimethylchromene on the Mn(salen) catalysts immobilized into the various nanopores via different linkage lengths was reported for the first time. The Mn(salen) catalyst grafted via phenoxyl groups gave the highest ee value of 84.9% when the nanopore sizes of supports were tuned to 6.2 nm, which was also higher than 49.0% ee obtained for the catalyst anchored on the external surface. When the linkage lengths were increased from one single-bond long to five-bonds long, the ee values increased from 44.9% to 82.6% for the Mn(salen) catalyst grafted into the nanopores of 9.7AS via substituted phenyl sulfonic groups. The decrease in nanopores or increase in linkage length strengthened the confinement effect and subsequently enhanced the enantioselectivities for the heterogeneous asymmetric epoxidation. It was also observed that the Mn(salen) catalyst immobilized into the nanopores modified with methyl groups gave higher ee value (90.6% vs 80.1%) and TOF (14.8 h^{-1} vs 10.8 h^{-1}) than those of the homogeneous catalyst.

5. Experimental

5.1. General

Activated silica (pore size of 9.7 nm with sharp pore distribution, Fig. 2), SBA-15 (pore sizes of 7.6 and 6.2 nm), and MCM-41 (pore sizes 2.7 and 1.6 nm) were used as supports and marked as 9.7AS, 7.6SBA, 6.2SBA, 2.7MCM, and 1.6MCM, respectively. The racemic epoxides were prepared by epoxidation of the olefin with *m*-CPBA in $CHCl_3$ at 0 °C[8g] and confirmed by GC–MS (GC6890–MS5973N). Epoxide was analyzed by GC–MS, and the conversions (with *n*-nonane as internal standard) and the ee values were determined by gas chromatography (6890N, Agilent Co.) using a chiral column (HP19091G-B213, Agilent Co.). All FTIR spectra were collected on a Fourier transform infrared spectrometer (Nicolet Nexus 470) with a resolution of 4 cm^{-1} and 64 scans. IR spectra of the free complexes and the supported complexes were recorded, respectively, by making samples into KBr pellets and self-supporting wafers. NMR spectra were accumulated on a Bruker DRX-400 spectrometer. The UV–vis spectra were recorded on a JASCO V-550 spectrometer. The free Mn(salen) complexes were dissolved in CH_2Cl_2 for UV–vis adsorption with CH_2Cl_2 as reference. Diffuse reflectance UV–vis spectra of the solid samples were recorded in the spectrophotometer with an integrating sphere using $BaSO_4$ as reference. XRD patterns were recorded on a Rigaku D/Max 3400 powder diffraction system using Cu Kα radiation over the range $0.5 \leq 2\theta < 10°$. The nitrogen sorption experiments were performed at 77 K on ASAP 2000 system in static measurement mode. The samples were degassed at 100 °C for 5 h before the measurement. The pore size distribution curve was obtained from desorption isotherm with BJH method.

5.2. Synthesis of homogeneous Mn(salen)OPh catalysts (8)

Homogeneous Mn(salen)Cl (**6**) was synthesized according to literature[24] and their structures were well confirmed by ^{13}C NMR, ^{1}H NMR, FTIR, rotational analysis, and element analysis. Salen: ^{13}C NMR ($CDCl_3$, 400 MHz): δ(ppm)=165.9, 158.1, 139.9, 136.4, 126.7, 126.0, 118.0, 72.4, 35.0, 34.0, 33.2, 31.4, 29.5, 24.3; IR (KBr, cm^{-1}): ν=2952, 1629, 1468, 1434, 1360, 830; $[\alpha]_D^{20}$ +300 (*c* 0.1, CH_2Cl_2); elemental analysis calcd (%) for $C_{36}H_{54}N_2O_2$: C 79.12, H 9.89, N 5.13; found: C 78.85, H 9.90, N 5.23. Mn(salen)Cl (**6**): IR (KBr, cm^{-1}): ν=2952, 2864, 1609, 1535, 1253, 837; elemental analysis calcd (%) for $C_{36}H_{52}ClMnN_2O_2$: C 68.13, H 8.20, N 4.41; found: C 70.13, H 8.70, N 4.27.

Phenol (25 g, 0.265 mol) was dissolved in a solution of NaOH (9.54 g, 0.238 mol) in distilled water (10 ml). After stirring for 30 min at room temperature (rt), the mixture was filtrated and washed thoroughly with toluene until no residual phenol could be detected by $FeCl_3$, then was washed with 3×30 ml of ethanol. The white power PhONa (**7**) was obtained after being dried for 8 h at 80 °C under high vacuum (20.71 g, 75%) and was stored under argon.

Mn(salen)Cl complex (**6**, 0.256 mmol) and PhONa (**7**, 35.9 mg, 0.309 mmol, 1.2 equiv) were added to ethanol (60 ml), and the mixture was refluxed for 3 h at 80 °C

(Scheme 6).[8g,19] Then ethanol was removed after the mixture was cooled to rt. To this dark solid was added 30 ml of CH_2Cl_2, and the organic phase was washed with 15 ml of distilled water. Samples of the aqueous layer were checked by the HNO_3–$AgNO_3$ solution until no characteristic white floc was observed (needed about three times). Then the CH_2Cl_2 solution was washed with 10 ml of saturated NaCl solution, dried over anhydrous Na_2SO_4, and concentrated to give the brown-dark solid Mn(salen)OPh (**8**). IR (KBr, cm^{-1}): ν=2955, 1612, 1535, 1477, 1312, 1253, 1175, 837; elemental analysis calcd (%) for $C_{42}H_{57}MnN_2O_3$: C 73.26, H 8.28, N 1.16; found: C 74.09, H 8.37, N 1.04.

5.3. Synthesis of modified supports 11, 13, and 14[8f,g,20]

Pure siliceous support (activated silica, SBA-15 or MCM-41, 9 g) was dehydrated at 125 °C under 0.01 torr for 4 h before the addition of the fresh $PhSi(OEt)_3$, $PhCH_2Si(OEt)_3$, $PhCH_2CH_2Si(OMe)_3$ or $PhNHCH_2CH_2CH_2Si(OMe)_3$ (21 ml) and dry toluene (450 ml). The resulting mixture was stirred for 1 h at rt, and then refluxed for 18 h at 120 °C under Ar, in which the phenyl groups were grafted on the supports.[25] After being cooled, filtrated, and washed with toluene, the solid was dried at 60 °C under reduced pressure overnight to obtain support-R^1-Ph (**9**) as a white powder (Scheme 7).

The supports modified with phenoxyl sodium (**11**) were prepared as follows. Support-Ph (5 g) was added to distilled water (90 ml) containing concentrated sulfuric acid (1.3 g) and catalyst $FeCl_3\cdot 6H_2O$ (50 mg), and this suspension was stirred at 50 °C for 30 min (Scheme 7).[26] Then H_2O_2 (4 ml) was added and the mixture was stirred for an additional 5 h. The solid was filtrated and washed by distilled water till the pH equaled 7 to give support-PhOH (**10**) as a white solid. A solution of NaOH (160 mg, 4 mmol) in distilled water (200 ml) was added to support-PhOH (4 g) and this mixture was stirred for 3 h at rt. The solid was filtrated and washed with distilled water till pH equaled 7 to produce **11** as a white powder (Scheme 7).

The supports modified with sulfonic groups (**13**) were prepared as follows. The support-R^1-Ph (**9**, 3 g) was dehydrated at 125 °C under 0.01 torr for 4 h, then was cooled to 40 °C under Ar atmosphere. Fuming sulfuric acid (10%, 10 ml) was added to the solid and the resulting mixture was stirred for 2 h at 40 °C, in which the phenyl groups were sulfonated to phenyl sulfonic groups (Scheme 7).[27] The solid was filtrated under reduced pressure, washed with distilled water till pH near 7, and then washed with 1,4-dioxane for three times, ethanol for three times, and distilled water to obtain support-R^1-$PhSO_3H$ (**12**). To this wet solid **12**, a solution of $NaHCO_3$ (0.33 g, 3.9 mmol) in distilled water (20 ml) was added to neutralize the $PhSO_3H$ groups and this mixture was stirred for 3 h at rt. The solid was filtrated and washed to neutrality to produce support-R^1-$PhSO_3Na$ as a white powder (**13**).

The 9.7AS–R^1-$PhSO_3Na$ (**13**, 3 g) were dehydrated at 125 °C under 0.01 torr for 4 h and then combined with fresh $MeSi(OMe)_3$ (3 ml) in dry toluene (50 ml) (Scheme 7). The resulting mixture was stirred for 1 h at rt, and then refluxed for 18 h at 120 °C under Ar, in which the methyl groups were grafted onto the supports. After being cooled, filtrated, and washed thoroughly with toluene, the solid was dried at 60 °C under reduced pressure overnight to obtain 9.7AS(Me)–R^1-$PhSO_3Na$ (**14**) as a white powder.

5.4. Synthesis of heterogeneous Mn(salen) catalysts

The grafting of Mn(salen) complexes on the supports was performed by refluxing the mixture of Mn(salen)Cl (**6**, 1.0 mmol) and **11**, **13** or **14** (1.0 g) in ethanol (60 ml) for 5 h (Scheme 8).[8d,g] Then the solid was filtrated and washed thoroughly with ethanol, and then with CH_2Cl_2 in order to eliminate all the Mn(salen) complexes adsorbed on the supports. The CH_2Cl_2 filtrates were detected by UV–vis spectra until no characteristic peaks of Mn(salen) could be detected (CH_2Cl_2 as reference). After being dried, the three kinds of heterogeneous Mn(salen) catalysts were obtained as brown powder: support-PhOMn(salen), support-R^1-$PhSO_3Mn$(salen), and 9.7AS(Me)–R^1-$PhSO_3Mn$(salen) (Scheme 8).

5.5. Asymmetric epoxidation of 6-cyano-2,2-dimethylchromene[8d,g]

In order to quantitatively compare the catalytic performance, the amount of heterogeneous catalysts was normalized based on the same amount of Mn(salen) active center. Dichloromethane was used as the optimal solvent. *n*-Nonane was used as internal standard due to its stability, inertia, and easy handling (bp 151 °C). A typical epoxidation[8g] was processed in a stirred solution of olefin (1 mmol) in CH_2Cl_2 (3 ml) containing *n*-nonane (1.0 mmol), PPNO as axial additive (0.38 mmol), homogeneous or heterogeneous Mn(salen) catalyst (0.015 mmol, 1.5 mol%, based on Mn element), and NaClO aqueous solution (pH=11.5, 0.55 M, 3.64 ml, 2 equiv) at 20 °C. After the reaction, the organic layer was concentrated and purified by flash chromatography for the homogeneous systems or filtered to remove catalysts for the heterogeneous systems. The recycling experiments were carried out following the same procedure but the amounts of all the components were doubled. After a reaction, the solid catalysts were filtrated and washed thoroughly with distilled water, ethanol, and dichloromethane for the next cycle.

Acknowledgements

The financial support from the National Natural Science Foundation of China (NSFC, Grant No. 20321303) is gratefully acknowledged. We would like to thank Dr. Jianliang Xiao at the University of Liverpool, UK, for helpful discussion.

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