Asymmetric reactions on chiral catalysts entrapped within a mesoporous cage†

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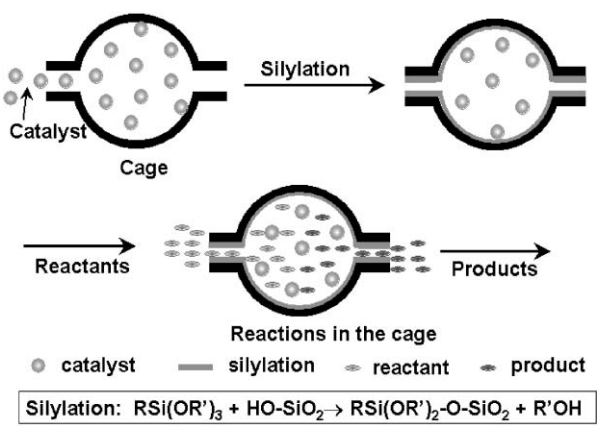
The encapsulation of homogeneous chiral catalysts, *e.g.* Co(Salen) and Ru-TsDPEN, in the mesoporous cage of SBA-16 is demonstrated; the encapsulated catalysts show performance as good as that of the homogeneous catalysts, and can be recycled for more than 10 times without significant loss of catalytic performance.

Heterogenization of homogeneous catalysts, especially chiral homogeneous catalysts, is of both scientific and industrial interest,[1–10] because it could be helpful for the recovery of homogeneous catalyst and the product purification that are usually obstacles to practical applications of homogeneous catalysts. However, in most cases, the immobilized catalysts exhibit lower activity and enantioselectivity, except for a few examples, which show better performance when the catalysts are in a nanopore.[11] The development of an efficient method for the heterogenization of homogeneous catalysts still remains a challenging objective.

The entrapment of homogeneous catalysts within the porous matrix, compared with other immobilization methods such as covalent-bonding and electronic interaction, is highly desirable because the properties of the trapped homogeneous catalyst in principle could be kept as those of its free form. Mesoporous silicas with an ordered pore arrangement, a high surface area and a rigid framework are ideal porous materials to trap catalysts. Balkus and co-workers attempted to encapsulate an enzyme within the channel of MCM-41.[12] Compared with enzymes, most homogeneous catalysts are much smaller in size, therefore, it is more difficult to trap the homogeneous catalyst within the mesoporous silicas while still keeping the catalyst as free as in homogeneous medium. As far as we know, a successful entrapment of a small metal complex, especially a chiral metal complex, within mesoporous silicas has been rarely reported so far.

Herein, we present the preparation of heterogeneous asymmetric catalysts through entrapment of a metal complex within the cage of mesoporous silicas, as illustrated in Scheme 1. A preformed homogeneous catalyst is first introduced into the cage-like pore of a mesoporous material (*e.g.* SBA-16 with tunable small pore entrance and large cage size[13,14]) by impregnation or adsorption. The pore entrance size is finely tailored by a silylation method, according to the molecular size of the catalyst, reactants and products. Thereby the metal complexes can be confined in the mesoporous cages. Reactants and products (usually smaller than the size of the pore entrance) are allowed to freely diffuse through the entrance to the mesoporous cage, in which the entrapped catalysts can catalyze the reaction with high activity in a similar way to that in the actual homogeneous catalysis process. The advantages of the present strategy over other immobilization methods are that the identity of a homogeneous catalyst can be largely kept because the trapped catalyst is almost intact. A typical synthetic procedure is as follows: 1.0 g of SBA-16 (evacuated at 398 K for 6 h) was dispersed in 6 mL of dichloromethane (DCM) (containing 0.12 g of Co(Salen)(II)). After stirring the mixture at refluxing temperature for 24 h under Ar atmosphere, DCM was removed by evaporation. The resulting solid was added to a solution containing 0.9 mL of dried toluene, 1.25 mL of anhydrous pyridine and 5 mmol of octyltrimethoxysilane. After refluxing for 24 h under Ar atmosphere, the resulting solid was isolated by filtration and washed thoroughly with toluene, DCM and THF. The prepared catalyst was denoted as Co(Salen)/SBA-16-C8 (Co: 0.310 wt%, ICP analysis). The synthesis of Ru-TsDPEN/SBA-16-2Ph, for asymmetric transfer hydrogenation, is similar to that of Co(Salen)/SBA-16-C8 except that diphenyldichlorosilane is used as the silylation agent (see ESI).

The pore entrance size of SBA-16 was tailored by alkoxysilanes with different molecular sizes, such as methyltrimethoxysilane (C1), propyltrimethoxysilane (C3), phenyltrimethoxysilane (Bz), octyltrimethoxysilane (C8) and dodecyltrimethoxysilane (C12). The modified SBA-16 was denoted as SBA-16-X according to the type of the alkoxysilane. The N_2 sorption isotherms of SBA-16-X (X = C1, C3, Bz, C8) exhibit typical type IV isotherm patterns with



Scheme 1 Schematic description of entrapping homogeneous catalyst within the cage of mesoporous silicas.

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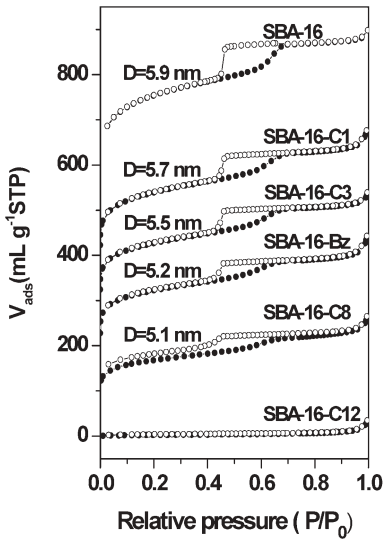


Fig. 1 N_2 sorption isotherms of SBA-16 before and after the modification with trimethoxyalkylsilane. D is the cage size of mesoporous material. SBA-16, offset vertically by 500; SBA-16-C1 (blocked with methyltrimethoxysilane), by 400; SBA-16-C3 (blocked with propyltrimethoxysilane), by 300; SBA-16-Bz (blocked with phenyltrimethoxysilane), by 200; SBA-16-C8 (blocked with octyltrimethoxysilane), by 100; SBA-16-C12 (blocked with dodecyltrimethoxysilane).

H2 hysteresis loop, similar to the parent SBA-16 with cage-like pore structure (Fig. 1). The hysteresis loop shifts to lower relative pressure for the modified SBA-16 compared with the parent SBA-16, owing to the decreased pore diameter resulting from the silylation. When the carbon chain is increased to 12 (C12), the pore entrance of SBA-16 is completely blocked, as evidenced by nearly no adsorption of N_2.[15] The BET surface area and pore volume of the modified SBA-16-X are decreased with increasing molecular size of the alkoxysilane (see ESI).

The pore entrance size of modified SBA-16-X was further estimated using Co(Salen)(II) as a probe molecule through the absorption of Co(Salen)(II) in SBA-16-X. When Co(Salen)(II) in DCM is absorbed into the cage of SBA-16-X, the concentration of Co(Salen)(II) in the filtrate should be decreased. The concentration of Co(Salen)(II) in the filtrate was analyzed by UV–vis spectroscopy because the probe molecule exhibits characteristic bands at 360 nm and 420 nm (Fig. S1 in ESI). When SBA-16, SBA-16-C1, SBA-16-C3, and SBA-16-Bz were used as adsorbents, the intensity of the characteristic bands of the filtrate decreased sharply compared with that of the parent solution, showing that most of Co(Salen)(II) can be absorbed in the above mentioned mesoporous silicas (Table 1). This means that the pore entrance size of SBA-16 before and after the modification with C1, C3 and Bz is still large enough to allow the free diffusion of Co(Salen)(II) into the cage of SBA-16. When SBA-16-C8 was used as adsorbent, the intensity of the characteristic bands in the filtrate hardly changed, indicating that the probe molecule cannot get into the cage of SBA-16-C8. The absorption experiments clearly tell us that the pore entrance size of SBA-16 tailored using C8 is able to block the Co(Salen) from diffusion through the pore entrance.

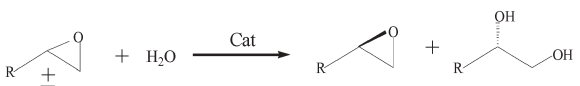
The catalyst, Co(Salen)/SBA-16-C8, was prepared by the encapsulaton of Co(Salen) in SBA-16 with silylation. For comparison, the catalyst Co(Salen)/SBA-16 (without silylation) was also prepared. Table 2 summarizes the catalytic results of asymmetric ring-opening of epoxides.[16,17] Co(Salen)/SBA-16 is nearly inactive for asymmetric ring-opening of epoxides, indicating that most of the adsorbed Co(Salen) was washed away from SBA-16 during the catalyst preparation because of its large pore entrance size. The fresh Co(Salen)/SBA-16-C8 gives comparable diol yield and ee (43% yield and 91% ee) with its homogeneous counterpart. The catalyst can be conveniently recovered by a simple centrifugation or filtration. The diol yield and ee value are almost kept even after the fifth use (entry 4, Table 2). The Co(Salen)/SBA-16-C8 can even be run for twelve times (33% yield and 88% ee). During the catalyst recycle process, a longer reaction time was needed to complete the reaction compared with the fresh catalyst. This is partly due to the

Table 1 UV–vis absorbance intensity of the parent solution and after absorption with SBA-16-X[a]

	UV–vis absorbance intensity[b]	
Samples	Before absorption	After absorption
SBA-16	3.84	0.79
SBA-16-C1	3.84	1.06
SBA-16-C3	3.84	1.48
SBA-16-Bz	3.84	1.50
SBA-16-C8	3.84	3.80
SBA-16-C12	3.84	3.82

[a] UV–vis spectra of Co(Salen)(II) in dichloromethane before and after the absorption with SBA-16-X samples (0.08 g of SBA-16-X was dispersed in 3.8 mL of CH_2Cl_2 containing 1.33×10^{-6} mol (*R*,*R*)-Co(Salen)(II). The mixture was stirred in a sealed tube for 5 h. After centrifugation, the solution was measured with UV–vis spectroscopy). [b] The absorbance intensity of the band at 420 nm before and after the absorption with SBA-16-X.

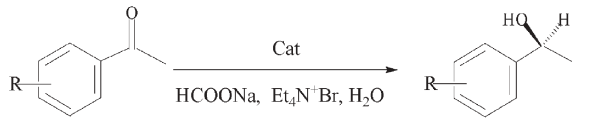
Table 2 Asymmetric ring-opening of epoxides on Co(Salen), Co(Salen)/SBA-16 (A) and Co(Salen)/SBA-16-C8 (B)[a]



Entry	R	Catalysts	t^b	Yield %[c]	Ee %[d]
1[e]	CH_2Cl	Co(Salen)	12–14	40	95 (*R*)
2	CH_2Cl	A[f]	16	trace	
3	CH_2Cl	B (1st)[g]	16	43	91 (*R*)/99[h]
4	CH_2Cl	B (5th)	20	39	91 (*R*)/84[h]
5	CH_2Cl	B (10th)	26	37	87 (*R*)
6	CH_2Cl	B (12th)	28	33	88 (*R*)
7[i]	CH_3	Co(Salen)	12–14	45	99 (*R*)
8	CH_3	A[f]	20	trace	
9	CH_3	B (1st)	20	51	95 (*R*)
10	CH_3	B (4th)	22	50	93 (*R*)
11	CH_3	B (6th)	24	47	96 (*R*)
12	CH_3	B (13th)	28	46	97 (*R*)

[a] For R = CH_2Cl, 0.5 mol% equiv (epoxide) of catalyst, 0.2 g of THF as solvent, 2 mmol of epichlorohydrin, 0.65 mol equiv of H_2O, 298 K; for R = CH_3, 0.25 mol% equiv of catalyst, 0.75 mol equiv of H_2O, 283 K. [b] Reaction time (hour). [c] Diol yield, derived with dimethoxypropane in presence of *p*-toluenesulfonic acid, GC analysis (HP-Chiral19091G-B213 capillary column) using nonane as internal standard. [d] Ee value of diol. [e] Data from [Ref. 16], 0.5 mol% equiv of catalyst, 0.45 equiv of H_2O, room temperature. [f] A is Co(Salen)/SBA-16 prepared without a silylation step; the weight of added catalyst is the same as B. [g] The catalyst is run for the first time. [h] Ee % of epoxide. [i] Data from [Ref. 16], 0.2 mol% catalyst, 0.45 mol equiv of H_2O.

Table 3 Asymmetric transfer hydrogenation of ketones on Ru-TsDPEN and Ru-TsDPEN/SBA-16-2Ph (C)[a]



Entry	R	Catalysts	S/C[b]	Conv. % (h)[c]	Ee %
1	H	Ru-TsDPEN	100	>99 (1.5)	93 (*S*)
2	H	C (1st)[d]	100	>99 (5)	93 (*S*)
3	H	C (2nd)		>99 (6)	92 (*S*)
4	H	C (3rd)		92 (6)	92 (*S*)
5	H	C (6th)		99 (19)	92 (*S*)
6	*p*-F	C	200	>99 (8)	87 (*S*)
7	*p*-Cl	C	200	>99 (8)	88 (*S*)
8	*o*-Cl	C	200	>99 (8)	88 (*S*)
9	*o*-MeO	C	200	94 (7.5)	90 (*S*)

[a] The reaction was carried out with 0.2 mmol of ketones, 0.016 mmol of $Et_4N^+Br^-$, 1.5 mmol of HCOONa in 0.3 g of water at 313 K, catalyst C is Ru-TsDPEN/SBA-16-2Ph (the pore entrance blocked with diphenyldichlorosilane). Conversion and ee value were obtained from GC analysis (HP-Chiral19091G-B213 capillary column). [b] The molar ratio of substrate/Ru. [c] The data in parentheses are the reaction time (hour). [d] The catalyst is run for the first time.

loss of solid catalysts during the course of recovery (for the 12th run, the catalyst weight is *ca.* 65% of the original one). The filtrate does not show any activity for the ring-opening reaction. This confirms that the conversion is contributed by the catalyst trapped in the cage of the mesoporous materials. Catalyst Co(Salen)/SBA-16-C8 was also used to catalyze the asymmetric ring-opening of propylene oxide (entries 9–12, Table 2). No obvious loss of activity and ee was observed even when Co(Salen)/SBA-16-C8 was run for the thirteenth time (entry 12, Table 2). After the thirteen cycles of reaction, the Co content in Co(Salen)/SBA-16-C8 was 87% of that in the fresh one.

TsDPEN is among the most efficient catalysts for the asymmetric transfer hydrogenation of prochiral ketones.[18,19] The heterogeneous catalyst Ru-TsDPEN/SBA-16-2Ph was prepared by the encapsulation of Ru-TsDPEN in the mesoporous cage of SBA-16 using diphenyldichlorosilane as silylation agent. The UV–vis absorption measurements show that the pore entrance size of SBA-16 modified by diphenyldichlorosilane can effectively confine Ru-TsDPEN within the mesoporous cage (Fig. S6 in ESI). Table 3 summarizes the results of the asymmetric transfer hydrogenation of different ketones in the HCOONa–H_2O system. The heterogeneous catalyst Ru-TsDPEN/SBA-16-2Ph exhibits comparable enantioselectivity with the homogeneous counterpart. The recycle reaction test shows that similar conversion and ee value are obtained for the first three runs. When the catalyst was run for the sixth time, the reaction could still reach 99% conversion. A longer reaction time was needed to complete the reaction, partly due to the loss of solid catalysts during the course of recovery. The activity is relatively lower than that of the homogeneous catalyst because of the diffusion limitation. Moreover, Ru-TsDPEN/SBA-16 can catalyze different kinds of ketones to corresponding chiral alcohols with high activity and enantioselectivity.

In conclusion, the chiral metal complex catalysts can be trapped in the cage of mesoporous materials like SBA-16 by modifying the entrance pore size of the cage using silylation. The entrapped chiral catalyst can be easily recycled without significant loss of catalytic performance and can show catalytic performance comparable to that in a homogeneous catalysis process. This strategy could be generally applicable for various chemical transformations and nano-reactor design.

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