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Mesoporous SBA-15 with Short Mesochannels Immobilized Natural Quinine for Asymmetric Michael Addition of Chalcones

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Abstract A heterogeneous catalyst of natural quinine supported on the mesoporous SBA-15 of short mesochannels was originally synthesized through a simple co-condensation approach for asymmetric organocatalysed Michael addition of malononitrile to chalcones. The catalytic activity was greatly enhanced, compared with the conventional analogue. Furthermore, the enantioselectivity could also be significantly improved for all substrates.

Keywords Asymmetric catalysis · Michael reaction · Immobilization · Quinine · Short-mesochannel SBA-15

1 Introduction

The asymmetric Michael addition of carbanion nucleophiles to α,β-unsaturated systems is one of the most important carbon–carbon bond forming reactions [1–5]. It is worthwhile to note that malononitrile is an attractive nucleophile to obtain 1,3-dicarbonyl derivatives or amines [6, 7]. Among various catalysts, the cinchona alkaloid derivatives such as 9-amino-9-deoxyepi-quinidine/cinchonine and thiourea-substituted cinchona alkaloid, have been widely employed in the asymmetric Michael addition of malononitrile to α,β-unsaturated systems [8–10]. However, the preparation of those cinchona alkaloid derivatives is often a very complex process. Recently, the natural cinchona alkaloids, quinine, has emerged as an efficient catalyst for the conjugate addition of α,β-enones [11, 12].

However, the high cost and the difficulties in separation and recycling of the catalyst restrict its use in industry. These problems resulting from homogeneous process can be overcome by the immobilization of chiral catalysts on organic polymers and inorganic supports [13–16]. Among these supports mentioned above, the siliceous mesoporous material SBA-15 with well-ordered pore arrays, large pore volume and pore size has been of great interest. Variety of chiral cinchona alkaloid catalysts were successfully immobilized on SBA-15 [17–19]. However, the rather long mesochannel of SBA-15 in micrometer scale was often unfavorable for the mass transfer and molecular diffusion [20].

The mesoporous SBA-15 with short mesochannels has fascinated researchers owing to facilitated mass transfer and less possibility of pore blockage in the adsorption or catalysis processes, especially when bulky molecules are involved as adsorbates and reactants. Up to now, several works were successful in providing the evidence for the effect [21–23]. However, it is essential to point out that the majority of the reports about applications of the mesoporous SBA-15 with short mesochannels dealt with adsorption or base catalysis, while the efforts toward the development of asymmetric catalysis were scarce. The commercial availability of quinine and advantage of the mesoporous SBA-15 with short mesochannels as supports encouraged us to investigate the heterogeneous catalysts' utility in asymmetric Michael addition. Excitingly, the incorporation of chiral quinine onto the mesoporous SBA-15 materials with short mesochannels was still rare.

Herein, we firstly reported a heterogeneous catalyst of natural quinine immobilized on the mesoporous SBA-15 with short mesochannels by the co-condensation approach for Michael addition of malononitrile to α,β-unsaturated

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carbonyl compounds. In comparison to the conventional SBA-15, not only the higher chemical activity but also enhanced enantioselectivity was obtained.

2 Experimental

2.1 Preparation of Catalyst

The route to synthesize the catalyst is shown in Scheme 1. The mesoporous SBA-15 with short mesochannels and conventional SBA-15 functionalized with mercapto groups were prepared by a co-condensation process described in references [22, 24] and denoted as SH-ST-SBA-15 and SH-SBA-15, respectively. The template was removed by ethanol extraction at 351 K. The thiol-functionalized mesoporous materials (1 g), quinine (0.4 g), and AIBN (0.1 g) as radical initiator were added into 25 mL of chloroform in a round-bottomed bottle. Then the mixture was refluxed for 24 h [18]. The sample was filtered, washed with chloroform, Soxhlet extracted and dried under vacuum for 24 h. The quinine-functionalized mesoporous SBA-15 with short mesochannels and conventional SBA-15 were denoted as QN-ST-SBA-15 (1.47 wt% of N) and QN-SBA-15 (1.51 wt% of N), respectively.

2.2 Characterization

Powder XRD patterns of the samples were conducted with R/max-2500 diffractometer with Cu Kα source and a step size of 0.02°. FT-IR spectra were performed on a Bruker Vector 22 spectrometer using self-supporting wafers. Elemental analysis was obtained by using a Perkin-Elmer 240C analyzer. N_2 adsorption–desorption analysis was carried out at 77 K on a Micromeritics TriStar 3000 apparatus. The experimental data were further processed by the BET equation for surface areas and by the BJH model for pore size distributions. The scanning electron microscopy (SEM) photographs were taken using a Shimadu SS-550 Scanning Electron Microscope operating at 15 kV. The transmission electron microscopy (TEM) experiments were performed on a Philips Tecnai G^{2}F20 Transmission Electron Microscope operating with a voltage of 120 kV. Enantiomeric excess (ee) values were determined by HPLC with a chiral AS-H column, using an Agilent-1200 chromatograph equipped with a VWD detector.

2.3 Typical Procedure for the Asymmetric Michael Addition

A general process was as follows: the catalyst QN-ST-SBA-15 or QN-SBA-15 (0.02 mmol) and chalcones substrate (0.2 mmol) were added to 2 mL of dry toluene and stirred at room temperature for 4 h. Then malononitrile (0.4 mmol) was added and the reaction was conducted at room temperature for 5 days. The catalyst was filtered and the reaction products were analyzed by HPLC. The homogeneous reaction was carried out with quinine (0.02 mmol), malononitrile (0.4 mmol) and substrates (0.2 mmol) in 2 mL of dry toluene, at room temperature for 5 days.

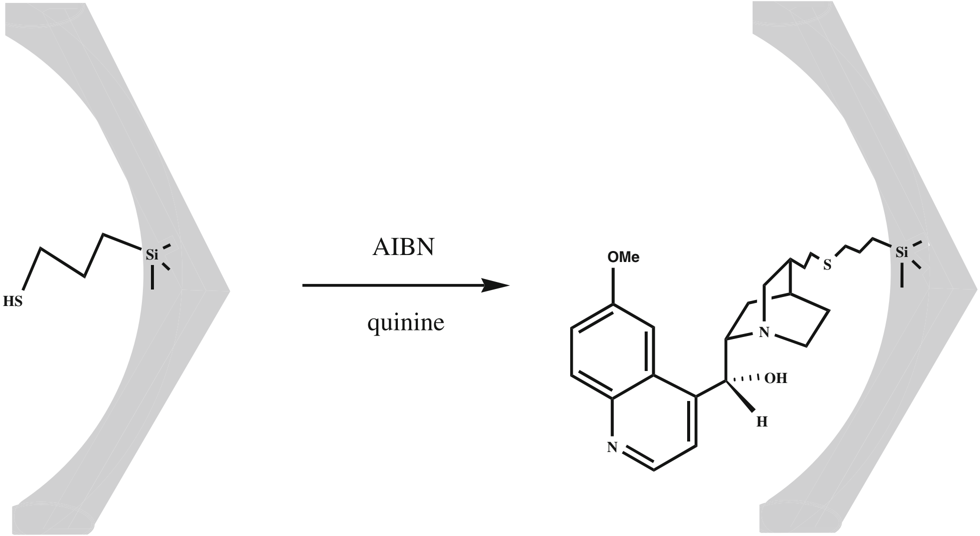
The catalyst was reused for asymmetric addition of malononitrile to chalcone. When a reaction was over, the catalyst was filtered, washed thoroughly with toluene (20 mL), acetone (20 mL) and dried before the next run.

3 Results and Discussion

3.1 Characterization of the Catalyst

The FT-IR spectrum of QN-ST-SBA-15 (Fig. 1a) showed an absorption band at 1594 cm^{-1} assigned to the –C=N– stretching of the quinoline ring. The bands observed

Scheme 1 Depiction of the immobilization of quinine onto mesoporous supports



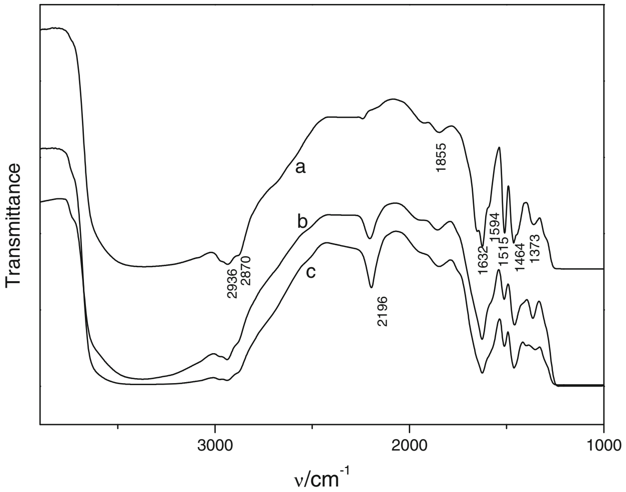


Fig. 1 FT-IR spectra of (*a*) QN-ST-SBA-15, (*b*) used QN-ST-SBA-15 after Soxhlet extraction with acetone, and (*c*) QN-ST-SBA-15 after three runs

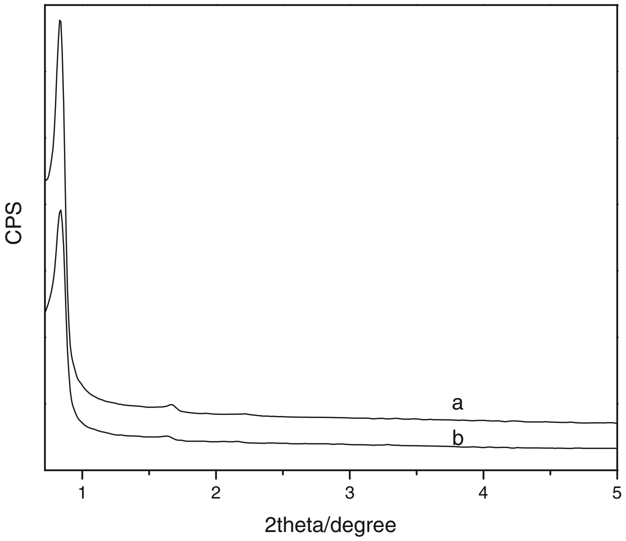


Fig. 2 Powder XRD patterns of (*a*) SH-ST-SBA-15 and (*b*) QN-ST-SBA-15

between 2936 and 2870 cm^{-1} were assigned to –C–H stretching vibrations, bands at 1632 and 1515 cm^{-1} which are presented in the spectrum of quinine can also be observed. All of these peaks indicated the successful incorporation of quinine onto SBA-15. The elemental analysis of QN-ST-SBA-15 showed that the loading of quinine was about 0.52 mmol/g. Figure 2 shows the powder XRD patterns of SH-ST-SBA-15 and QN-ST-SBA-15. All of the diffractograms showed the well-resolved reflections at (100) (intense and sharp), (110) and (200) (weak and broad), suggesting the less ordered pore array after introduction of 3-mercaptopropyltrimethoxysilane by the co-condensation approach [22, 25, 26]. Moreover, the decrease of peak intensity suggested that the incorporation of quinine moiety onto SH-ST-SBA-15 might disturb the ordered mesostructure by a certain degree [27]. The N_2 adsorption–desorption isotherms and pore size distributions of QN-SBA-15 and QN-ST-SBA-15 are shown in Fig. 3. Both of the catalysts exhibited typical IV type isotherms with a steep increase in adsorption at $P/P_0 = 0.45$–0.75. All the materials possess a narrow pore size distribution, characteristic of well-ordered mesoporous materials. The corresponding structural parameters calculated by N_2 adsorption–desorption isotherms are listed in Table 1. It was found that incorporation of quinine resulted in a remarkably decrease in BET surface area, pore volume and pore size, which suggested that quinine was successfully immobilized on SBA-15. The pore size of QN-ST-SBA-15 is slightly larger than the typical one, which may be attributed to the so-called salting out effect in the presence of Zr(IV) ion [22]. Figure 4 shows the EM photographs of QN-ST-SBA-15. The catalyst possesses a platelet morphology and short mesochannels which are quite different from typical SBA-15 with fiberlike morphology and long mesochannels in micrometer scale. The well-ordered pore arrays could be easily observed and the pore size of QN-ST-SBA-15 may be directly measured to be about 6 nm, in good accordance with the N_2 sorption results.

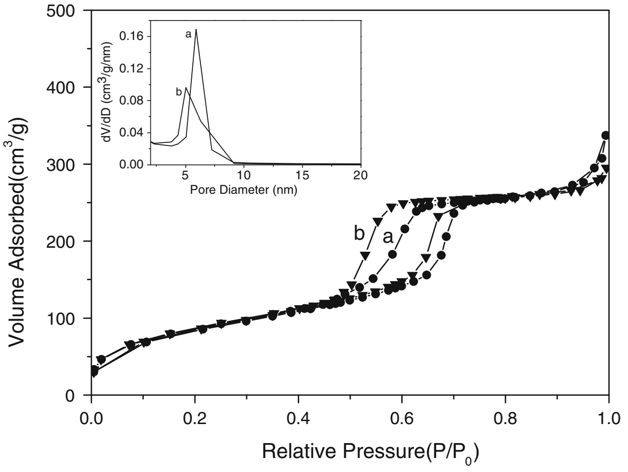


Fig. 3 N_2 adsorption–desorption isotherms and pore size distributions of (*a*) QN-ST-SBA-15 and (*b*) QN-SBA-15

Table 1 Pore structural parameters of various materials

Sample	Mesopore volume (cm^3/g)	Surface area (m^2/g)	Pore diameter (nm)
SH-ST-SBA-15	1.0	880	6.3
SH-SBA-15	0.60	519	6.1
QN-ST-SBA-15	0.46	315	5.9
QN-SBA-15	0.39	317	5.0

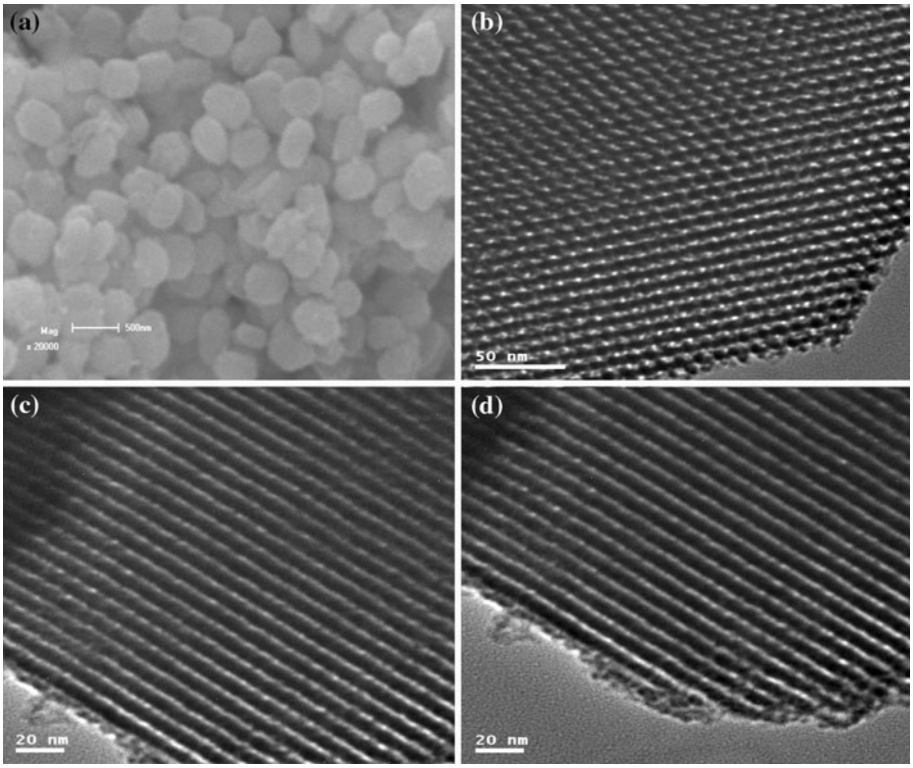
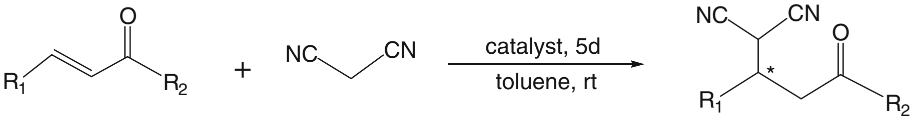


Fig. 4 EM micrographs of QN-ST-SBA-15: **a** SEM image, **b**, **c**, **d** TEM images

Table 2 Asymmetric Michael addition of malononitrile to chalcones[a]



Entry	Catalyst	R_1	R_2	Yield (%)[b]	ee (%)[c]
1[d]	QN-ST-SBA-15	Ph	Ph	52	48
2	QN-ST-SBA-15	Ph	Ph	72	62
3[e]	QN-ST-SBA-15	Ph	Ph	76	39
4[f]	QN-ST-SBA-15	Ph	Ph	74	49
5	QN-SBA-15	Ph	Ph	38	44
6	Quinine	Ph	Ph	78	88
7	QN-ST-SBA-15	4-$CH_3OC_6H_4$	Ph	44	49
8	QN-SBA-15	4-$CH_3OC_6H_4$	Ph	27	35
9	Quinine	4-$CH_3OC_6H_4$	Ph	68	71
10	QN-ST-SBA-15	4-FC_6H_4	Ph	57	50
11	QN-SBA-15	4-FC_6H_4	Ph	32	46
12	Quinine	4-FC_6H_4	Ph	92	86
13[g]	QN-ST-SBA-15	Ph	Ph	52	44

[a] Reactions were performed with catalyst (0.02 mmol), chalcones substrate (0.2 mmol) and malononitrile (0.4 mmol) in solvent (2 mL) at room temperature for 5 days

[b] Isolated yield

[c] Ee% were determined by HPLC with a chiral AS-H column. The absolute configuration was *S*

[d] Reaction was performed for 3 days

[e] Reaction was performed using 20 mol% catalyst

[f] Reaction was performed at 323 K

[g] The catalyst was filtered after 3 days, and the reaction was performed for another 2 days

Table 3 Recycle studies of the heterogeneous catalyst in the asymmetric Michael addition of malononitrile to chalcone[a]

Run	Yield (%)	ee (%)	N content (%)
1	72	62	1.47
2	58	20	1.84
3	46	11	1.91
4[b]	48	27	1.76

[a] Reactions were performed in toluene at room temperature for 5 days

[b] The catalyst was Soxhlet extracted with acetone and dried under vacuum for 12 h

3.2 Catalytic Studies

The synthesized heterogeneous catalyst was evaluated in the conjugate addition of malononitrile to chalcones. The reaction results are summarized in Table 2. The QN-ST-SBA-15 shows 52% yield and 48% ee for chalcone in 3 days with a loading of 10 mol% (Table 2, entry 1). When the reaction time was prolonged to 5 days, 72% yield and 62% ee were obtained (Table 2, entry 2). As the amount of catalyst was increased to 20 mol%, the catalytic activity increased from 72 to 76% for yield (Table 2, entry 3) but the enantioselectivity was significantly decreased. The similar phenomenon was observed when the reaction was carried out at 323 K (Table 2, entry 4). On the basis of these results, a range of chalcones were examined as substrates. In general, the QN-ST-SBA-15 was found to afford both higher yield and ee value than QN-SBA-15 for all of the substrates (Table 2, entry 2 vs. 5, entry 7 vs. 8, entry 10 vs. 11). This may be possibly attributed to the faster mass transfer and specific morphology of the mesoporous SBA-15 with short mesochannels. Furthermore, it is noteworthy that substituted chalcone was less effective than chalcone under similar conditions (Table 2, entry 2 vs. 7 and 10, entry 5 vs. 8 and 11). The electron-withdrawing substituent, gave the product in higher yields and ee values compared with the electron donating substituent (Table 2, entry 7 vs. 10, entry 8 vs. 11). To make sure the catalysis is indeed heterogeneous, the catalyst was filtered after 3 days and the filtrate was allowed to react for another 2 days [28]. Finally, it was found that no further reaction was observed (Table 2, entry 1 vs. 13).

The catalyst was reused for asymmetric addition of malononitrile to chalcone. When the reaction was over, the catalyst was filtered, washed thoroughly with toluene, acetone and dried before the next run. It is shown that this kind of heterogeneous catalyst could be used three times with acceptable loss of activity (Table 3, entries 1–3), but a significant decrease was observed in enantioselectivity. Therefore, the catalyst was Soxhlet extracted with acetone. Surprisingly, not only enantioselectivity but aslo chemical activity was improved (Table 3, entry 4). To make clear what is responsible for the drop in the activity, the catalyst after three runs was characterized by FT-IR (Fig. 1c). The characteristic peaks remain mostly the same but a drop in the intensity after the reaction, which shows that there were no character changes of the quinine moiety in the whole process. A new and strong absorption peak at 2196 cm^{-1} could be observed which was assigned to the characteristic $-\mathrm{C}\equiv\mathrm{N}$ stretching vibrations of malononitrile. The used catalyst after Soxhlet extraction was also characterized by FT-IR (Fig. 1b). Compared with the catalyst before Soxhlet extraction, the intensity of the absorption peak at 2196 cm^{-1} decreased while the intensities of the other absorption peaks were enhanced. It indicates that the active sites being covered by the adsorbed reactants might be the main reason for the decrease of activity and enantioselectivity. The results provided by elemental analysis have also verified our assumptions. The N content of the catalyst in the four runs was 1.47, 1.84, 1.91 and 1.76%, respectively (Table 3).

4 Conclusion

In summary, for the first time, chiral quinine was successfully immobilized on the mesoporous SBA-15 with short mesochannels, and the prepared heterogeneous catalyst exhibited both higher catalytic activity and enantioselectivity than those of conventional counterpart for asymmetric Michael addition of malononitrile to chalcones.

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