

Chiral enhancement in diethyl malonate addition by morphosynthesized L-proline mesoporous silica†

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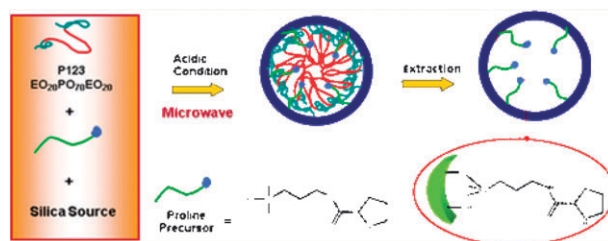
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L-Proline was immobilized onto mesoporous silica through direct synthesis method *via* morphosynthesis possessing short channels and plugs in the pore structure which provided chiral enhancement in the diethyl malonate addition reaction.

Since its discovery 15 years ago, mesoporous silica materials have attracted great interest for their widely potential applications in catalysis, separation, drug delivery, *etc.*¹ Among them, utilization of mesoporous silica as catalyst support for asymmetric catalytic reactions is a promising one.² Although many research groups have tried to functionalize the mesoporous silica,³ to obtain functionalized mesoporous silica with simple preparation, controllable morphology and high catalytic activity especially in asymmetric catalysis is still challenging. In addition, to the best of our knowledge, there has been no study of direct immobilization of amino acid based chiral organo-catalyst to mesoporous silica.

We have overcome this challenge by direct synthesis of chiral organo functionalized materials with well controlled morphology. Here, we report direct synthesis of L-proline functionalized mesoporous silica by using microwave and illustrate its catalytic activity in the asymmetric diethyl malonate addition. L-Proline has been favoured due to several advantages such as high catalytic activity, no toxicity, inexpensiveness, availability in both enantiomers, stability in air, and can be used in wet solvents.⁴ Further, the malonate addition reaction is valuable example for the asymmetric conjugate addition of carbon nucleophiles to electron-deficient alkenes due to their facile direct decarboxylation.⁵

The synthetic procedure of L-proline functionalized mesoporous silica is illustrated in Scheme 1. L-Proline functionalized mesoporous silica was synthesized under acidic condition using a poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer template (EO₂₀PO₇₀EO₂₀, Pluronic P-123, BASF). (*S*)-*N*-(3-(triethoxysilyl)propyl)pyrrolidine-2-carboxamide was used as proline precursor. L-Proline precursor to SiO₂ molar ratios in the initial synthesis mixture were 2.5% (2.5%-PMS), 5.0% (5.0%-PMS) and 7.5% (7.5%-PMS). Throughout the hydrothermal aging treatment, microwave irradiation was applied as a heating source in order to achieve the potential advantages of microwave synthesis such as rapid



Scheme 1 The synthesis route used in preparation of L-proline functionalized mesoporous silica (see experimental section in ESI†).

and homogeneous heating, homogeneous nucleation and fast crystallization, phase selectivity, and facile particle size and morphological control.⁶ The obtained samples showed that the addition of proline precursor can change the morphology systematically. The addition of 2.5% molar ratio gave fibrous type mesoporous silica. However, addition of more proline precursor can reduce the length to submicron range gradually and change the shape to hexagonal type uniformly.

Fig. 1 shows the low angle XRD powder patterns and N₂ adsorption-desorption isotherms of proline functionalized mesoporous silica. The XRD patterns showed well-resolved peaks with very intense diffraction peaks at 2 θ = 0.8–0.9 and two or more peaks at higher degrees, which were indexed to the 100, 110, and 200 planes characteristic of the long range order and excellent textural uniformity of mesoporous material with a mesostructure of hexagonal space group symmetry *P6mm*. Compared with 2.5%-PMS, in cases of 5.0%-PMS and 7.5%-

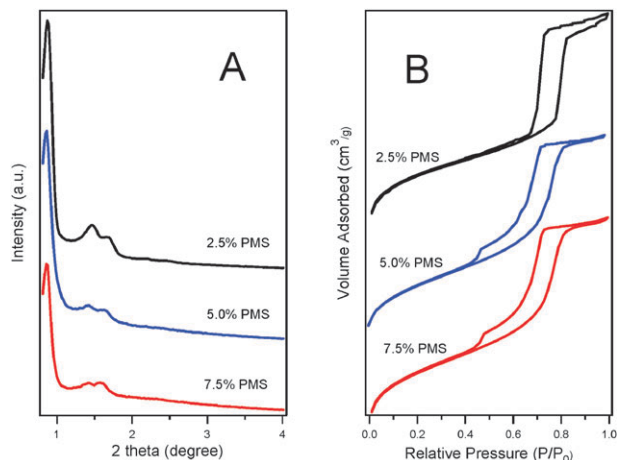


Fig. 1 Powder XRD patterns (A) and N₂ adsorption-desorption (B) of samples 2.5% PMS, 5.0% PMS and 7.5% PMS.

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Table 1 BET surface area (SBET), Pore Diameter (d), Pore Volume (V_p) and Micropore Volume (V_m) of the proline functionalized mesoporous silica

Catalysts	SBET (cm ² /g)	Pore volume	Pore size
2.5% PMS	715 m ² /g	0.78 cm ³ /g	6.5 nm
5.0% PMS	707 m ² /g	0.75 cm ³ /g	5.7 nm
7.5% PMS	727 m ² /g	0.77 cm ³ /g	5.6 nm

PMS, the intensities of all peaks diminished. From the N₂ adsorption–desorption isotherms, the samples had the “hysteresis loop” resembling the type IV isotherm with H1-type which was characteristic for highly ordered two-dimensional hexagonal mesostructured with uniform cylindrical channels. Furthermore, we could observe interesting phenomena. With increasing loading of L-proline, a two step desorption branch appeared indicating the pore plugging effect and the formation of micropores. Van Der Voort *et al.* reported that plugging effect could increase the stability of mesoporous silica.⁷ For practically catalytic application, plugs could provide confinement effect. Table 1 lists the physico-chemical properties of the samples. BET surface area, pore size and pore volume of each sample is almost similar even usually by those parameters will be decreased when by increasing the amounts of grafted material. In here, the key factor is the evolution of the morphology and not the amounts of grafted organo molecules. With the pore size were about 5.6–6.5 nm, most of all reaction substrates could pass easily. It will be important for reaction with bulky molecules.

The SEM images of L-proline functionalized mesoporous silica are shown in Fig. 2. The SEM images revealed that the addition of a small amount of proline precursor (2.5%) to the initial reaction mixture resulted in a fibrous-like morphology with connected rod-like particles as in the case of ordered SBA-15. With increasing proline precursor loading, directly synthesized proline mesoporous silica under microwave irradiation gave uniform particle sizes with hexagonal prism and platelet morphologies. Therefore, the amounts of L-proline precursor in the initial synthesis mixtures were definitely controlling the morphologies of the proline functionalized mesoporous silica.

TEM images (Fig. 3) show that the samples have ordered 1D mesopore structure with 2D hexagonal arrangement. By carefully comparing the TEM images of 5%-PMS and 7.5%-PMS, it can be clearly seen that the channel direction are parallel to the thickness of the plate. The length of 7.5%-PMS

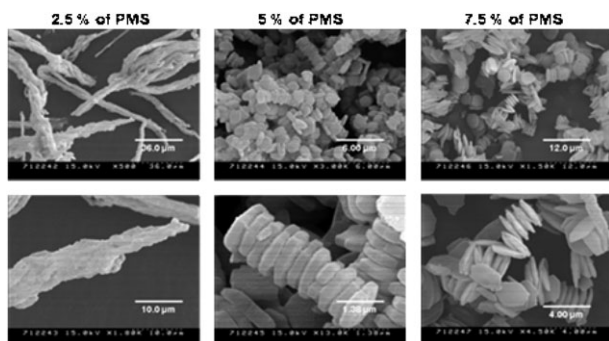


Fig. 2 SEM images of L-proline functionalized mesoporous silicas with different molar ratio.

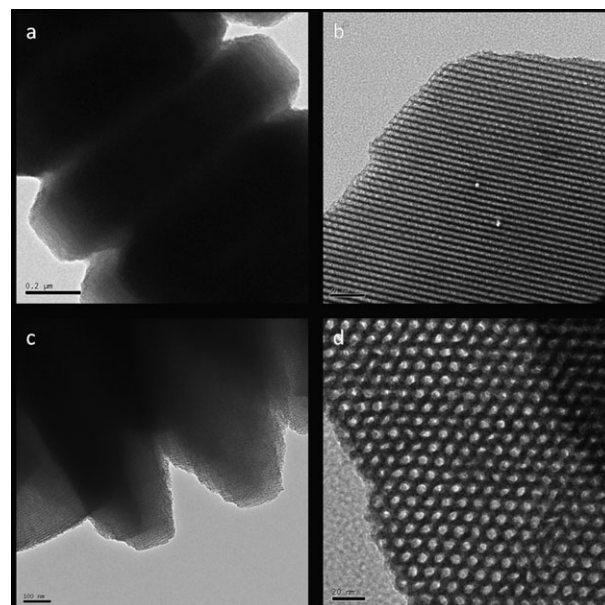


Fig. 3 TEM images of 5.0% (a, b) and 7.5% (c, d) L-proline functionalized mesoporous silica.

channel was around 150–200 nm. On the other hand, 5.0%-PMS had channel length around 300–400 nm.

The successful direct incorporation of L-proline onto mesoporous silica was traced with FTIR (Fig. 4) and Raman spectroscopy (Fig. 5). The intensities of the bands near 3000 cm⁻¹, which were due to C–H stretching of alkyl chain, increased with the increasing of tethered proline. IR band at around 1860 cm⁻¹ could be assigned to C=O double bond in amide moiety. Moreover, Raman spectra confirmed by clearly show the presence of N–H of pyrrolidine ring and C–H of alkyl chain that were not observed on the base SBA-15. The amounts of tethered proline were characterized by TGA measurement (ESI[†]). The amounts of L-proline groups were 0.82, 0.98 and 1.23 mole per gram, respectively (Table 2).

The catalytic activity of L-proline functionalized mesoporous silica was observed through asymmetric diethyl malonate addition

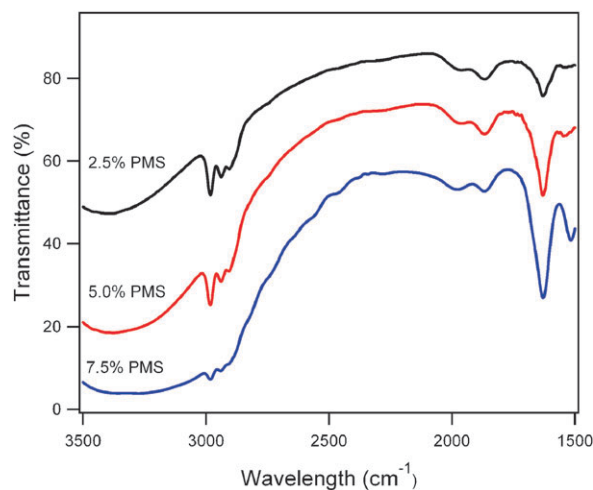


Fig. 4 FTIR spectra of 2.5%, 5.0% and 7.5% L-proline functionalized mesoporous silica.

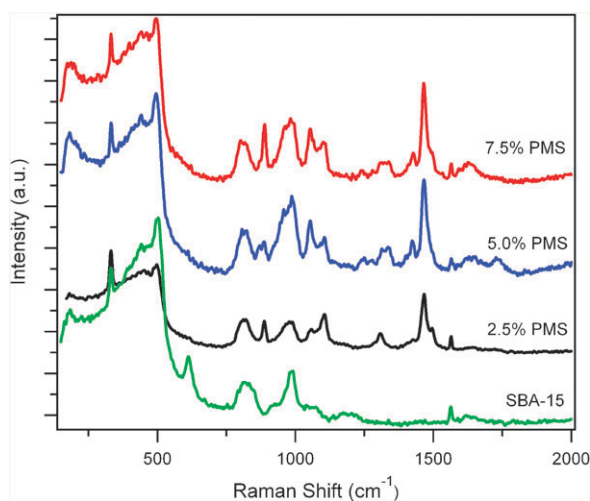


Fig. 5 Raman spectra of L-proline functionalized mesoporous silicas exciting at 325 nm.

reaction. We employed cyclohexenone and diethyl malonate as reactants, and obtained the corresponding enone. CH_2Cl_2 and piperidine were used as solvent and a base, respectively. 2.5%-PMS gave 32% conversion and 72% enantiomeric excess. To evaluate our catalyst system against the parent homogeneous catalyst, L-proline was used as catalyst and gave 67% conversion in only 39% ee even though we used more than 7 times the amount of catalyst. Furthermore, the highest activity was reached in the case of 7.5% L-proline functionalized mesoporous silica. Concerning the enantioselectivity, 7.5% L-proline functionalized mesoporous silica also gave highest result. Increasing conversion also could be achieved by increasing temperature of the reaction, but it followed by decreasing of ee. In fact, there were two factors playing a role in this catalyst; (i) amount of loaded proline and (ii) length of the pore channels. The increasing activity of the catalysts was supposed due to the difference

Table 2 Catalytic investigation of L-proline functionalized mesoporous silica^a

Catalyst	Temperature (K)	Conversion ^b (%)	ee ^c (%)
L-Proline homogeneous ^d	298	67	39
SBA-15	298	0	—
2.5%-PMS	298	32	72
2.5%-PMS	313	49	64[64] ^e
5.0%-PMS	298	39	76
5.0%-PMS	313	57	68[67] ^e
7.5%-PMS	298	43	78
7.5%-PMS	313	61	70[69] ^e

^a Reactants (0.2 mmol), catalyst (2 mol%), base (0.2 mmol), solvent 3 mL. ^b Estimated by GC. ^c Determined by chiral HPLC. ^d Catalyst (15 mol%). Absolute configuration determined from ref. 8. ^e After second run.

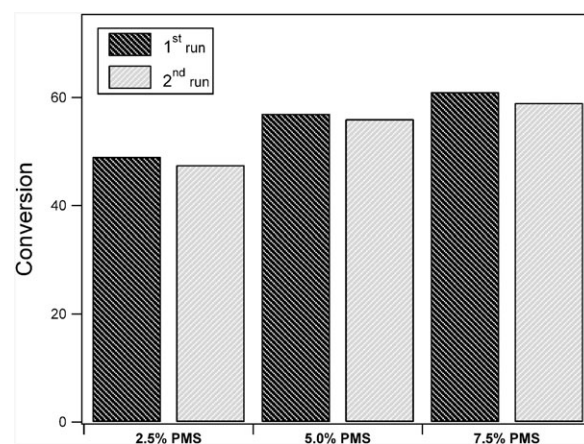
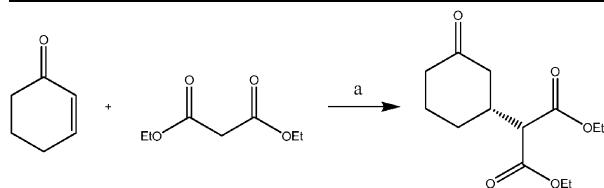


Fig. 6 Catalytic recyclability of proline functionalized mesoporous silica for diethyl malonate addition reaction. Reaction condition was reactants (0.2 mmol), catalyst (2 mol%), base (0.2 mmol), solvent 3 mL, 313 K.

amount of active site and overcoming diffusion limitation.⁹ Furthermore the formation of plugs in the pore structure could enhance the stereoselectivity by providing confinement effect. Overall, the catalyst showed good catalytic activity with high enantiomeric excess. Interestingly, the L-proline functionalized mesoporous silica could be reused without losing significant stereoselectivity, but with a slight reduction of the conversion, probably due to a loss of catalytic material (Fig. 6).

In conclusion, L-proline functionalized mesoporous silica has been successfully synthesized through simple one pot reaction method assisted by microwave heating and the morphology could be controlled by L-proline precursor amounts during synthesis time. The catalysts having short channel with plugs in the pore structure showed remarkable catalytic activity as well as chirality enhancement in the diethyl malonate addition reaction.

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Notes and references

- C. T. Kresge, M. E. Leonowicz, W. J. Roth, J. C. Vartuli and J. S. Beck, *Nature*, 1992, **359**, 710; J. S. Beck, J. C. Vartuli, W. J. Roth, M. E. Leonowicz, C. T. Kresge, K. D. Schmitt, C. T.-W. Chu, D. H. Olson, E. W. Sheppard, S. B. McCullen, J. B. Higgins and J. L. Schlenker, *J. Am. Chem. Soc.*, 1992, **114**, 10834.
- E. G. Doyagües, F. Calderón, F. Sánchez and A. Fernández-Mayoralas, *J. Org. Chem.*, 2007, **72**, 9353.
- E. R. Jarvo and S. J. Miller, *Tetrahedron*, 2002, **58**, 2481–2495.
- C. Thomassigny, D. Prim and C. Greck, *Tetrahedron Lett.*, 2006, **47**, 1117–1119.
- K. R. Knudsen, C. E. T. Mitchell and S. V. Ley, *Chem. Commun.*, 2006, 66–68; A. P. Krapcho, *Synthesis*, 1982, 805.
- Y. K. Hwang, J.-C. Chang, S.-E. Park, D. S. Kim, Y.-U. Kwon, S. H. Jung, J.-S. Hwang and M. S. Park, *Angew. Chem., Int. Ed.*, 2005, **117**, 562; Y. K. Hwang, J.-S. Chang, Y.-U. Kwon and S.-E. Park, *Microporous Mesoporous Mater.*, 2004, **68**, 21.
- P. Van Der Voort, P. I. Ravikovitch, K. P. De Jong, A. V. Neimarkb, A. H. Janssen, M. Benjelloun, E. Van Bavel, P. Cool, B. M. Weckhuysen and E. F. Vansant, *Chem. Commun.*, 2002, 1010.
- H. Sasai, T. Arai, Y. Satow, K. N. Houk and M. Shibasaki, *J. Am. Chem. Soc.*, 1995, **117**, 6194.
- Sujandi, S.-E. Park, D.-S. Han, S.-C. Han, M.-J. Ji and T. Ohsuna, *Chem. Commun.*, 2006, **39**, 4131–4133.