Adsorption (2010) 16: 577–586
DOI 10.1007/s10450-010-9252-z

Synthesis of chiral mesoporous silica and its potential application to asymmetric separation

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Abstract Chiral mesoporous silica (CMS) has been successfully synthesized in the presence of basic amino acids; the use of basic amino acids in combination with the chiral anionic surfactant is advantageous for the formation of CMS in terms of uniformity in the twisted morphology. We first demonstrate that thus obtained chiral mesoporous silicas can be used for the enantioselective separation of racemic compounds; the helical rod-shaped CMS is found to be capable of asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-Ala-OEt). The left handedness-rich CMS shows asymmetric preferential adsorption of the L isomer and vice versa.

Keywords AMS · Chiral mesoporous silica · Basic amino acid · Handedness · Asymmetric separation

1 Introduction

Mesoporous materials with well-ordered and tunable mesopores have attracted a great deal of attention because of their controllable structures and compositions, which make them suitable for a wide range of applications in catalysis, adsorption, separation and chromatography. (These efforts have been excellently summarized in recent reviews, e.g., Ying et al. 1999; Stein et al. 2000; He and Antonelli 2002; Trong et al. 2003; Hoffmann et al. 2006.) In general, the formation of these unique mesostructures has been promoted through a micelle-templating method including electrostatic charge-matching and electrically neutral pathways using surfactants as structure-directing agents (SDA) (Huo et al. 1994; Firouzi et al. 1997). Up to now, a variety of cationic, nonionic and anionic surfactants has been applied to the synthesis of well-ordered mesostructured materials.

Recently, synthesis of anionic surfactant templated mesoporous silicas (AMS) series have been developed (Yokoi et al. 2003; Che et al. 2003; Garcia-Bennett et al. 2004). AMS-*n* series ($n = 1$–10) of novel structures have been synthesized, based on the self-assembly between anionic surfactants and silica precursors by using aminosilane or quaternized aminosilane as a co-structure-directing agent (CSDA). We employed 3-aminopropyltrimethoxysilane (APS) or 3-trimethylammoniopropyltrimethoxysilane (TMAPS) chloride as CSDA. The methoxysilane moiety of CSDA is co-condensed with the silica precursor, $Si(OC_2H_5)_4$ (TEOS), to form the silica framework. Note that anionic surfactants derived from diverse amino acids can be used for the synthesis of AMS (Che et al. 2003; Garcia-Bennett et al. 2004).

In particular, the use of chiral anionic surfactants, *N*-miristoyl derivatives of L- and D-alanines (C_{14}-L-AlaA and C_{14}-D-AlaA), provides chiral mesoporous silica (CMS) with helical mesopores about 2.2 nm in diameter (Che et al. 2004; Ohsuna et al. 2005; Jin et al. 2006). CMS has a twisted hexagonal rod-like morphology with hexagonally well-ordered mesopores. The left-/right-handed ratios for the helical particles synthesized with L- and D-isomers have proved to be 75/25 and 25/75, respectively, indicating that the predominant handedness of helices is directed by the handedness of the surfactants. These discoveries could lead to new uses of mesoporous silica and other chiral pore materials for catalysis and separation media, where enantiomeric

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space could be applied to the manufacturing of enantiomerically pure chemicals and pharmaceuticals.

Although the CMS materials are structurally unique, there are still problems in its production by the original method as mentioned below (Yokoi et al. 2007). First, the macroscopic morphology as well as the mesostructure of the chiral mesoporous silica is extremely sensitive to the synthetic conditions. Their reproducibility for the synthesis of CMS is not high. The morphology of the product is drastically affected by small changes in synthesis conditions. According to the original method, the composition of the reactants was 0.94 TEOS: 0.06 TMAPS: 0.135 surfactant: 0.120 NaOH: 0.010 HCl: 233 H_2O (Che et al. 2004). The addition of NaOH and HCl to the solution containing C_{14}-L-AlaA controls the equilibrium between –COOH and –COONa. We found that the molar fraction of free COOH of the surfactant ([–COOH]/[–COOH + –COO$^-$]) in the synthesis system is a critical parameter in the formation of CMS with a rod-like 2d-hexagonal structure. The optimum molar fraction was in the range of 0.19–0.26 (Yokoi et al. 2007). When synthesis conditions such as temperature, the stirring rate and purity of chemicals were slightly changed, spherical and irregular particles were obtained in addition to the desired helical rod. Therefore, facile method for controlling the morphology as well as improving the uniformity in the morphology are required for applications of CMS. The modification of the synthesis method will be thus indispensable for obtaining CMS with a high quality.

Synthesis of enantiomerically pure compounds is of great importance in diverse fields including pharmaceuticals, agrochemicals, foods and feed additives and perfumes because enantiomers often show different physiological activities depending on their absolute configurations (Maier et al. 2001; Diéguez et al. 2004; Gübitz and Schmid 2006). One of the methods for asymmetric separation in their production is high-performance liquid chromatography (HPLC) using polymer and metal oxides as a stationary phase (SP).

Silica-based SP has attracted attention because of its high thermal stability, and in particular surfactant-templated "mesoporous silica" is expected to be an efficient SP because of its high specific surface area and high pore volume (Grün et al. 1996; Raimondo et al. 1997). Micrometer-sized spherical particles of organically functionalized mesoporous silica spheres have been used as SP to separate large biomolecules such as proteins (Boissiere et al. 2001; Nassivera et al. 2002; Zhao et al. 2002; Ma et al. 2003; Zhu et al. 2006; Guo and Ding 2007; Yang et al. 2008). For asymmetric separation, SP must be modified with chiral ligands. Jacobs et al. reported the preparation of MCM-41 and MCM-48 materials functionalized with chiral selector (*R*)-naphthylethylamine as supports in chiral HPLC (Thoelen et al. 1999, 2000). Jasra et al. also reported the syntheses of other chiral porous materials, MCM-41 and SBA-15 modified with chiral ligands, and the potential application to chiral SP (Mayani et al. 2006, 2008). Recently, Mastai et al. reported the preparation of templating mesoporous silica with chiral block copolymers and its application for enantioselective separation (Gabashvili et al. 2007). Unfortunately, in SP materials containing chiral ligand, the chemical and thermal stabilities of the chiral moiety are severely affected. Over 30 years ago, Kavasmaneck and Bonner reported the first example of enantiomeric adsorption of chiral amino acid derivatives by d- and l-quartz and their potential application as chiral SP (Kavasmaneck and Bonner 1977). Since this pioneering report, however, only little attention has been paid to the development of purely inorganic silica without any modifications as SP for asymmetric separation. Its success will be a breakthrough achievement in the field of asymmetric science and technology.

Here, we report that the use of basic amino acids with the chiral anionic surfactant is advantageous for the formation of CMS in terms of uniformity in the twisted morphology. The difference in the method for preparing CMS between the original and current methods is the use of basic amino acids such as arginine and lysine in place of a combination of NaOH and HCl. We also first demonstrate that CMS can be applied to the enantioselective separation of racemic solutions; the helical rod-shaped CMS is found to be capable of asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-Ala-OEt).

2 Experimental

2.1 Synthesis of chiral anionic surfactant

A chiral anionic surfactant, *N*-myristoyl-L-alanine (C_{14}-L-AlaA), was synthesized by acylation of L-alanine with myristoyl chloride ($C_{13}H_{27}COCl$). The antipode, *N*-myristoyl-D-alanine (C_{14}-D-AlaA) was also synthesized from D-alanine by the same method. Detailed procedures were described in our previous paper (Yokoi et al. 2007).

2.2 Synthesis of chiral mesoporous silica

L-Arginine was used as basic amino acid. In a typical synthesis procedure, a mixture of TEOS and TMAPS was added to a solution of C_{14}-L-AlaA, L-arginine and deionized water with stirring at 30°C. The gel composition was 0.94 TEOS: 0.06 TMAPS: 0.130 surfactant: 0.120 arginine: 233 H_2O (pH 7.4). The mixture was allowed to react under stirring conditions at 30°C for 7 min and static conditions at 30°C for 2 h. Then, the product was cured at 80°C for 15 h. The products were collected by centrifugal separation and dried at 100°C. The as-synthesized sample was calcined at 600°C for 8 h to remove both the anionic surfactant and the organics of the CSDA used. The CMS samples were synthesized with enantiomerism of the surfactant and/or arginine varied. For example, when C_{14}-L-AlaA and L-arginine were used as surfactant and basic amino acid, respectively, the product was designated as L-C_{14}/L-Arg-CMS. Here, L-C_{14}/L-Arg-CMS, L-C_{14}/D-Arg-CMS, D-C_{14}/D-Arg-CMS and D-C_{14}/L-Arg-CMS samples were synthesized. When L-lysine (Lys) and L-histidine (His) were used as a basic amino acid, the products were designated as L-C_{14}/L-Lys-CMS and L-C_{14}/L-His-CMS, respectively.

2.3 Immobilization of chiral ligand onto SBA-15

As a control, typical rod-shaped SBA-15 modified with the chiral ligand was prepared. First, a purely inorganic SBA-15 was synthesized according to the standard procedure (Zhao et al. 1998). The as-synthesized SBA-15 was calcined at 823 K in air for 5 h to remove the surfactant. 2.0 g of dehydrated SBA-15 was stirred vigorously in 50 ml of a dry toluene containing 2.8 mmol of (*S*)-*N*-1-phenylethyl-*N*′-triethoxysilylpropylurea ((*S*)-PEPU). This solution was refluxed for 2.5 h. The powder was collected by filtration, washed with toluene and dried at 373 K. The obtained functionalized SBA-15 sample with the (*S*)-PEPU was designated as (*S*)-PEPU-SBA-15. The (*R*)-PEPU-SBA-15 sample was also prepared by using (*R*)-PEPU.

2.4 Characterizations of the mesoporous silicas

The structures of the synthesized CMS samples were characterized by X-ray diffraction (XRD). XRD patterns were recorded on a Mac Science M3X Model 1030 instrument equipped with a CuKα X-ray source (40 kV and 20 mA). Nitrogen adsorption–desorption measurements were conducted to obtain information on the mesoporosity. The measurements were conducted at 77 K on a Belsorp mini, Bel Japan. The BET (Brunauer-Emmett-Teller) specific surface area was calculated from the adsorption data in the relative pressure ranging from 0.04 to 0.1. The pore size distribution was calculated from adsorption branch of isotherms according to the BJH formula. Scanning electron microscope (SEM) images of the silica product were obtained on a Hitachi S-5200 field emission scanning electron microscope. The samples were observed without any metal coating. Solid-state ^{1}H-^{13}C CP/MAS NMR spectra were recorded on a JEOL-ECA400 spectrometer at 100.6 and a sample spinning frequency of 4 kHz. The immobilization of the chiral ligand onto SBA-15 was confirmed by a FT-IR (Spectrum one, Perkin Elmer) and TG-DTA (DTG-60H, Shimadzu) analyses.

2.5 Asymmetric separation

Slurry of the silica samples in *n*-hexane (n-C_6H_{14}) and ethyl acetate (AcOEt) was packed in a 160 mm ×6 mm glass column under vacuum using an aspirator. Asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-DL-Ala-OEt) was conducted at room temperature. A portion of the adsorbate solution in n-C_6H_{14} and AcOEt (volume ratio 20:1) was pipetted into a thus prepared packed glass column. The eluate was appropriately fractionized and collected. Each fraction was concentrated under vacuum and then dissolved in chloroform. The resultant sample was analyzed by gas chromatography (GC-2014, Shimadu) equipped with a chiral capillary column (RT-GAMMA-DEXsa, GL science) to estimate enantiomeric excess (ee) %. Schematic diagram of the asymmetric separation used in this study is shown in Fig. 1.

3 Results and discussion

3.1 Synthesis of CMS

3.1.1 Structural properties of CMS with basic amino acids

Figures 2(a) and 2(b) show XRD patterns of the L-C_{14}/L-Arg-CMS and L-C_{14}/D-Arg-CMS samples after the calcination, respectively, indicating that the uses of either L-arginine or D-arginine with C_{14}-L-AlaA led to the formation of well-ordered mesoporous silicas with a 2d hexagonal structure.

The nitrogen adsorption-desorption isotherms of the both samples exhibit the type IV pattern, indicating the presence of uniform mesopores. The BET surface areas of L-C_{14}/L-Arg-CMS and L-C_{14}/D-Arg-CMS samples were found to be 603 and 735 m^2g^{-1}, respectively, and both of their average pore sizes calculated by the BJH method using the adsorption branches were found to be 2.2 nm.

Figures 3(a) and 3(b) show representative SEM images of the L-C_{14}/L-Arg-CMS and L-C_{14}/D-Arg-CMS samples, respectively. Representative SEM images indicate that the both particles have a twisted hexagonal rod-like morphology (Fig. 3), about 200 nm in outer diameter and about 2 μm in average length. From the six distinct surfaces, the helical pitch along the rod axis was estimated to be about 0.5 μm. The detailed characterization of the L-C_{14}/L-Arg-CMS sample by high-resolution transmission electron microscope (HRTEM) was representatively performed (Fig. 4). Considering the previous works on CMS (Che et al. 2004), it is inferred that thus obtained silicas have chiral channels. Handedness of the porous materials was estimated based on 500 randomly chosen particles in the SEM images, and

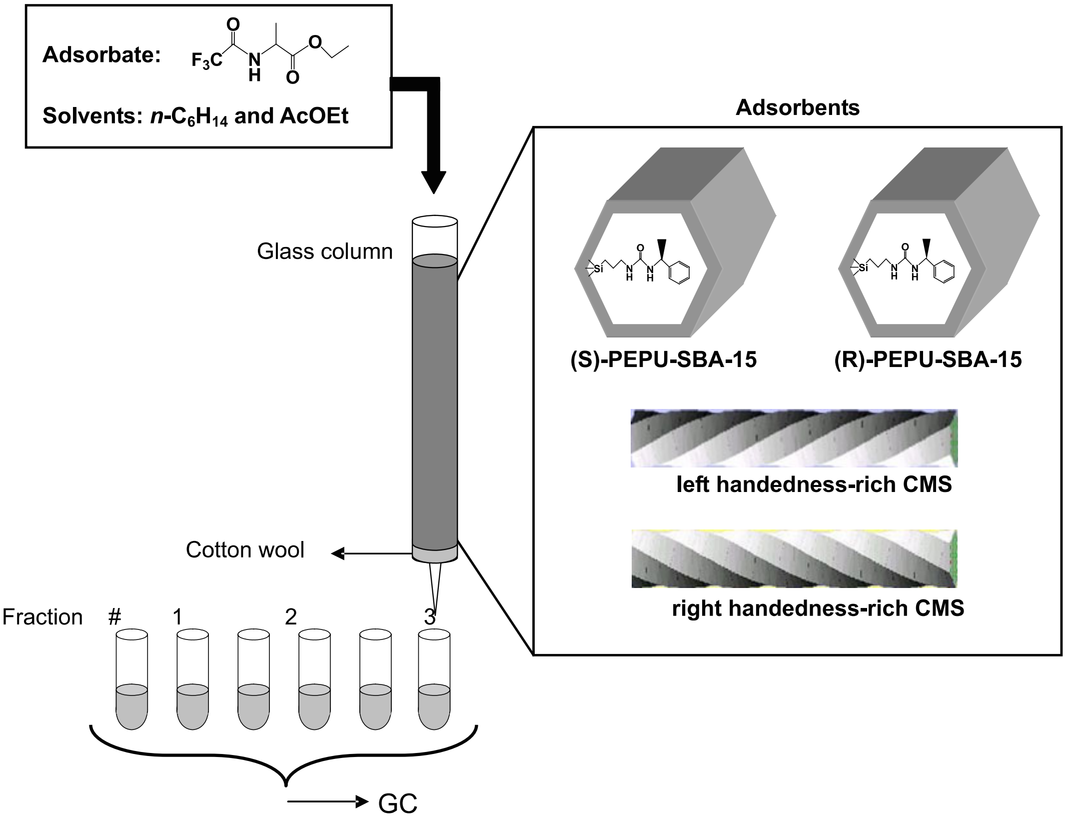

Fig. 1 Schematic diagram of the asymmetric separation

left-/right-handed ratios for the L-C_{14}/L-Arg-CMS and L-C_{14}/D-Arg-CMS samples proved to be 77/23 and 77/23, respectively. It is concluded that CMS materials rich in left-handedness were synthesized with the combination of C_{14}-L-AlaA with either L-arginine or D-arginine. Note that the handedness of chiral helices in CMS was essentially governed by the stereoisomerism of the surfactant, not that of arginine.

The CMS samples were also synthesized by using C_{14}-D-AlaA as a surfactant with L- or D-arginine (D-C_{14}/D-Arg-CMS and D-C_{14}/L-Arg-CMS). The XRD patterns of the both samples after the calcination exhibit the formation of well-ordered mesoporous silicas with a 2d hexagonal structure (not shown here). The representative SEM images of the D-C_{14}/D-Arg-CMS and D-C_{14}/L-Arg-CMS samples are shown in Figs. 5(a) and 5(b), respectively. The left-/right-handed ratios for the D-C_{14}/D-Arg-CMS and D-C_{14}/L-Arg-CMS samples proved to be 23/77 and 23/77, respectively. The handedness of chiral helices in right-handed rich CMS was also not governed by the stereoisomerism of arginine.

3.1.2 *Role of basic amino acids*

The chemical state of arginine in the synthesis system is important and dependent on pH (McKee and McKee 2003) because of its potential capability to interact with arginine itself and other molecules during the synthesis. The guanidine group ($H_2NC(=NH)NH–$) of arginine can naturally interact with free –COOH group of the anionic surfactant, forming $–COO^-$ groups. Although the surfactant (C_{14}-L/D-AlaA) is a fatty acid (R–COOH) and insoluble in water, $R–COO^-$ species are soluble in the synthesis system. The presence of

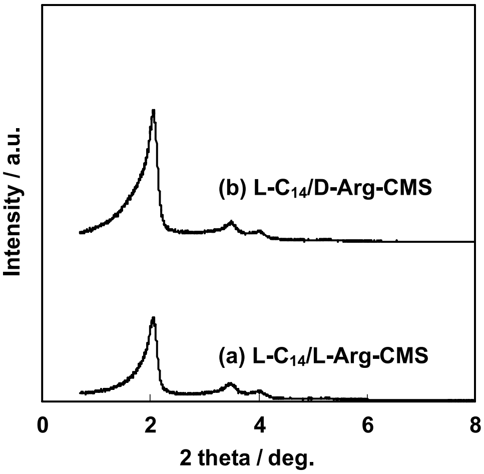

Fig. 2 XRD patterns of (**a**) L-C_{14}/L-Arg-CMS and (**b**) L-C_{14}/D-Arg-CMS

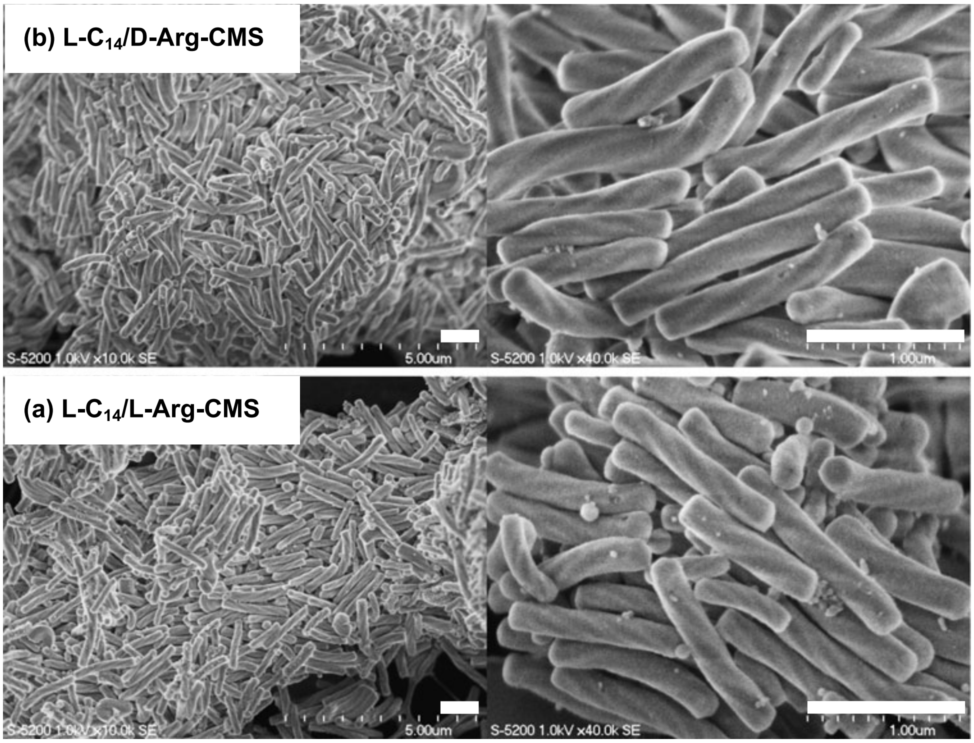

Fig. 3 Typical SEM images of (**a**) L-C_{14}/L-Arg-CMS and (**b**) L-C_{14}/D-Arg-CMS (scale bar: 1 μm)

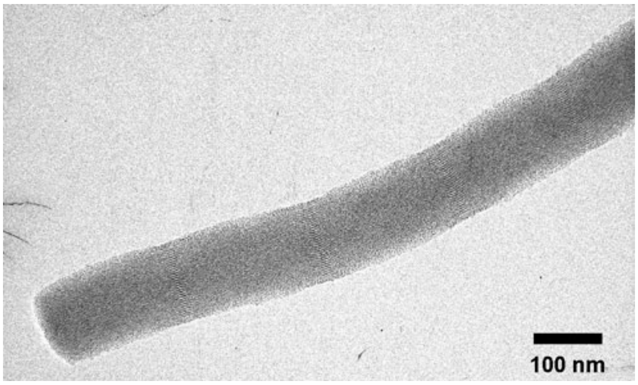

Fig. 4 Typical HRTEM image of L-C_{14}/L-Arg-CMS

the –COOH and –COO^- species with the optimum proportion enhances the formation of CMS (Yokoi et al. 2007).

Considering the pH in the synthesis system (about 7.4), isoelectric point (10.8) and pK_a (2.2, 9.0, 12.5) of arginine, a part of the guanidine group is protonated, while silicate species derived from TEOS and TMAPS are negatively charged ($\equiv SiO^-$) under the synthesis condition. Therefore, electrostatic interaction between positively charged arginine molecules and negatively charged silicate species would be possible.

The ^1H-^{13}C CP/MAS NMR spectrum of the as-synthesized L-C_{14}/L-Arg-CMS sample is shown in Fig. 6(a). As a reference, C_{14}-L-AlaA and a reagent grade arginine (Aldrich, 98%) used were measured. Perusal of these spectra indicates that the C_{14}-L-AlaA molecules were present in the as-synthesized sample. Note that, in addition to the peak at 180 ppm attributed to the –COOH group, two peaks at around 158 and 54 ppm were observed in the spectrum of the as-synthesized sample. These peaks are attributed to C atoms in the guanidine group ($H_2NC(=NH)NH$–) and to the carbon adjacent to the amino group (–$C(NH_2)(COOH)$) of arginine, indicating that arginine was present in the as-synthesized sample. The arginine molecule would be present at the interface between the surfactant micelle and silica wall and/or at the external surface of the CMS particle. The stereoisomerism of arginine as well as the surfactant would enhance the formation helical rod.

Both arginine, which is a weak base, and C_{14}-L-AlaA, which is a derivative of alanine and a weak acid, show a buffering action to control the pH. Therefore, the pH of the synthesis system ranged from 7 to 8 throughout the synthesis reaction. Such synthesis conditions would result in the optimum proportion of the –COOH to the –COO^- species, leading to the formation of CMS with a high quality.

3.1.3 *Control experiments*

In addition to arginine, lysine and histidine are also basic amino acids. The use of lysine led to the formation of well-ordered CMS similar to that prepared by using arginine. Unfortunately, the use of histidine under the same conditions was unsuccessful in synthesizing the CMS. This is possibly due to the relatively low basicity of histidine. When the molar composition of histidine in the synthesis was increased to

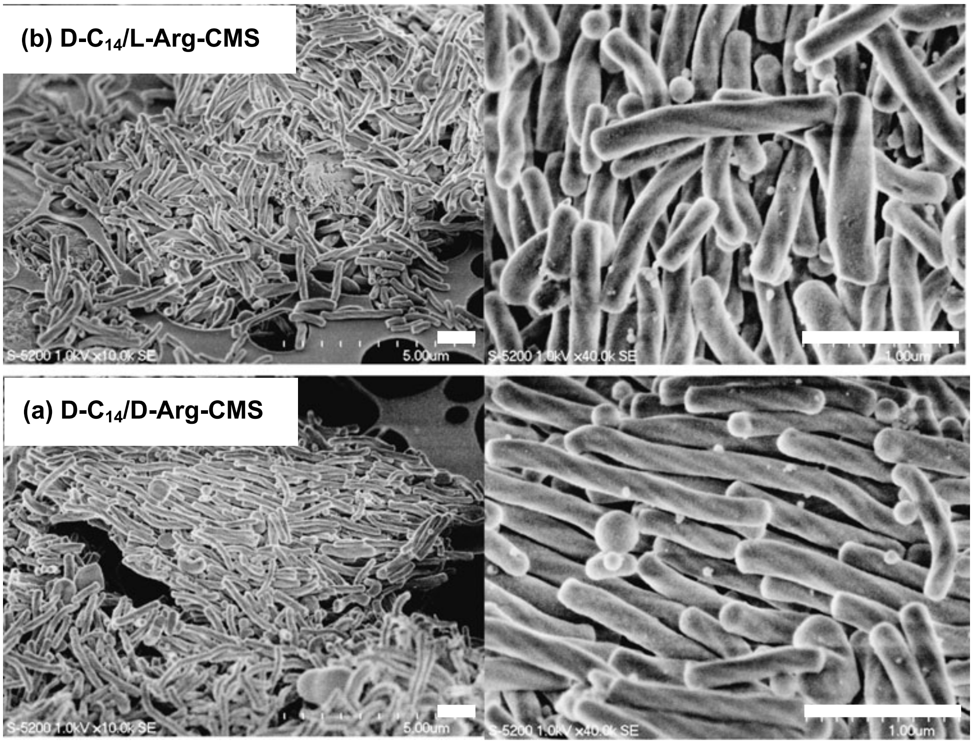

Fig. 5 Typical SEM images of (**a**) D-C_{14}/D-Arg-CMS and (**b**) D-C_{14}/L-Arg-CMS (scale bar: 1 μm)

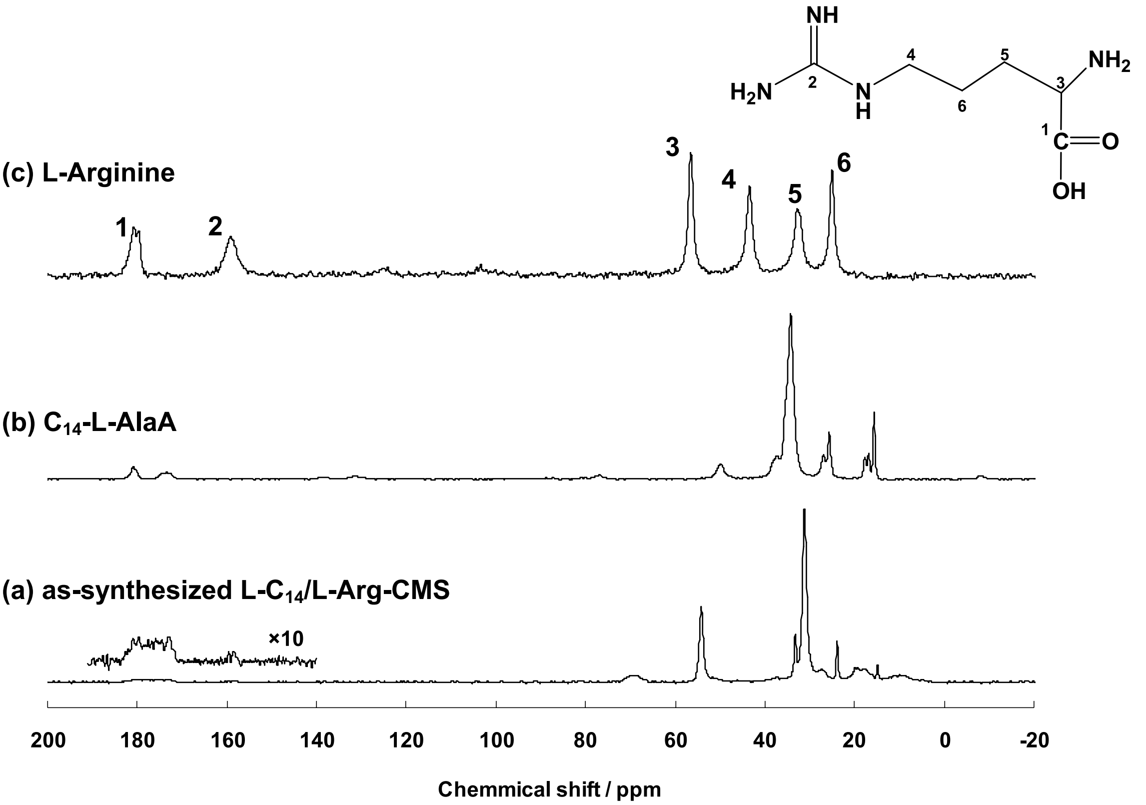

Fig. 6 ^{1}H-^{13}C CP/MAS NMR spectra of (**a**) as-synthesized L-C_{14}/L-Arg-CMS sample, (**b**) chiral surfactant (C_{14}-L-AlaA) and (**c**) reagent grade arginine

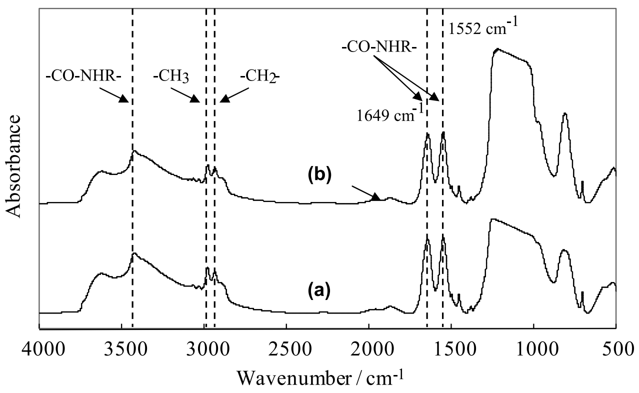

Fig. 7 FT-IR spectra of (**a**) (*S*)-PEPU- and (**b**) (*R*)-PEPU-SBA-15 samples

0.75, the well-ordered CMS with a twisted hexagonal rod-like morphology were obtained.

In order to obtain further information about the role of the basic amino acids, the use of neutral amino acids such as alanine and leucine instead of basic amino acids were examined. In these cases, ammonia was used as a base catalyst under otherwise identical conditions. It was confirmed by XRD patterns and SEM images that products were mostly mesoporous silica with an irregular morphology. Weakly basic conditions derived from the basic amino acids are advantageous for the formation of CMS with a high quality.

We found that morphology of CMS can be tuned by changing the molar composition of arginine and the pH of the synthesis system. The precise control of the morphology is currently being studied and will be reported elsewhere.

3.2 Immobilization of chiral ligand onto SBA-15

The (*S*)- and (*R*)-PEPU-SBA-15 samples were characterized by XRD and nitrogen adsorption-desorption measurements. Both the samples retained the original 2d-hexagonal mesostructure after the immobilization of the chiral ligand. The specific surface areas and pores size of the (*S*) and (*R*)-PEPU-SBA-15 samples were estimated at 481 m^2/g and 7.0 nm, and 465 m^2/g and 7.0 nm, respectively. The FT-IR spectra of the (*S*)- and (*R*)-PEPU-SBA-15 samples showed the bands (1552 and 1649 cm^{-1}) attributed to urea group (–NH–CO–NH–), implying that the chiral organic silanes were immobilized onto the SBA-15 (Fig. 7). By the TG-DTA analyses, the loading amounts of the chiral ligand in the (*S*)-PEPU-SBA-15 and (*R*)-PEPU-SBA-15 were found to be 0.94 and 0.96 mmol/g, respectively.

3.3 Asymmetric separation

3.3.1 SBA-15 functionalized with chiral ligand

As a preliminary experiment, asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-DL-Ala-OEt) was conducted by using the column packed with

Table 1 Asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-DL-Ala-OEt) over (*S*)-PEPU-SBA-15

Fraction #	Volume[a] (ml)	Recovered adsorbate		ee[b] (%)
		Weight (mg)	Recovery (%)	
1	2	0.1	0.2	–
2	2	0.1	0.2	–
3	2	1.0	2.4	4.54-D
4	2	10.7	25.4	1.96-D
5	2	2.7	6.4	0.34-L
6	2	5.5	13.1	2.48-L
7	2	1.4	3.3	4.78-L
8	2	5.1	12.1	2.46-L
9	2	1.2	2.9	3.20-L
10	2	1.5	3.6	1.44-L
11	2	0.2	0.5	2.54-L
12	2	0.9	2.1	–
13	15	0.0	0.0	–

Adsorbent: (*S*)-PEPU-SBA-15, 1.0 g. Adsorbate: CF_3CO-DL-Ala-OEt, 42.1 mg

[a] Eluent: n-C_6H_{14}/AcOEt = 20:1 (vol%)

[b] Enantiomeric excess

the (*S*)- and (*R*)-PEPU-SBA-15 samples. Table 1 summarizes the results of the asymmetric separation of racemic CF_3CO-DL-Ala-OEt over (*S*)-PEPU-SBA-15. Eventually, 72 wt% of the adsorbate was recovered in the eluate throughout the separations. CF_3CO-D-Ala-OEt (D-isomer) was excessively present in the eluates up to fraction #4. However, the D-isomer became excess later from fraction #5 to #11. Finally, 2.5 % of the maximum ee was finally achieved.

In the case of (*R*)-PEPU-SBA-15, the column packed with 2.0 g of the silica was employed (Table 2). Unfortunately, the material balance of the adsorbate was decreased to 48 wt% because about half of adsorbate loaded was left in the column. The opposite trend in the asymmetric separation was observed when (*R*)-PEPU-SBA-15 was used; excess enantiomer was the L-isomer at the early stage of the fractionation (up to fraction #6), then the D-isomer became excess later. These results imply that SBA-15 functionalized with the chiral ligands has a potential as a chiral SP; (*S*)-PEPU-SBA-15 can preferentially interact with the L-isomer rather than the D-isomer and vice versa.

3.3.2 CMS

The left handedness-rich CMS (L-C_{14}/L-Arg-CMS) and right handedness-rich CMS (D-C_{14}/D-Arg-CMS) samples were packed in the glass column. Table 3 summarizes the results of the asymmetric separation of 20.2 mg of racemic CF_3CO-DL-Ala-OEt over the column packed with 1.5 g of

Table 2 Asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-DL-Ala-OEt) over (*R*)-PEPU-SBA-15

Fraction #	Volume[a] (ml)	Recovered adsorbate		ee[b] (%)
		Weight (mg)	Recovery (%)	
1	5	0.3	0.7	–
2	5	0.1	0.2	–
3	2	3.7	8.8	0.22-L
4	2	2.7	6.4	0.14-D
5	2	1.3	3.1	0.54-L
6	2	3.1	7.4	0.32-L
7	2	1.2	2.9	–
8	2	3.0	7.2	0.16-D
9	2	1.6	3.8	0.26-D
10	2	1.0	2.4	0.66-D
11	2	0.3	0.7	1.12-D
12	2	0.9	2.1	0.46-D
13	2	0.0	0.0	–
14	2	0.0	0.0	–
15	2	0.0	0.0	–
16	2	0.0	0.0	–
17	10	0.0	0.0	–

Adsorbent: (*R*)-PEPU-SBA-15, 2.0 g. Adsorbate: CF_3CO-DL-Ala-OEt, 41.9 mg

[a] Eluent: *n*-C_6H_{14}/AcOEt = 20:1 (vol%)

[b] Enantiomeric excess

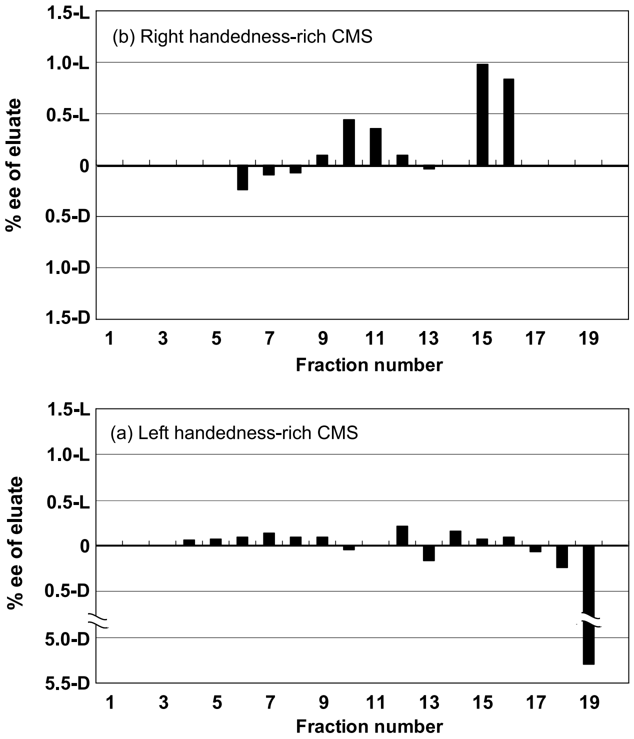

Fig. 8 Asymmetric separations of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-DL-Ala-OEt) over (**a**) light handedness-rich and (**b**) right handedness-rich CMS samples, corresponding to Tables 3 and 5, respectively

the left handedness-rich CMS. The excess enantiomer in the fractions #2–#16 was L-isomer. Then 40 ml of AcOEt was loaded into the column to extrude the adsorbate from the silica at fraction #19, and eventually a total of 77 wt% of the adsorbate was recovered in the eluate throughout the separations. It should be noted that the excess enantiomer in the eluates was changed from the L-isomer to the D-isomer during the separation (Fig. 8(a)) and fractions #17–#19 excessively contained D-isomers (max. 5.12 %ee).

When the amount of the adsorbate loaded was decreased, the higher enantiomeric excess was expected. Therefore, 10.1 g of the CMS adsorbent was employed (Table 4), wherein excess enantiomer was changed from the L-isomer to the D-isomer throughout the separation and a total of 70 wt% of the adsorbate was recovered. These results suggest that left handedness-rich CMS preferentially adsorbed the D-isomer rather than the L-isomer.

Table 5 summarizes the results of the asymmetric separation of 20.0 mg of racemic CF_3CO-DL-Ala-OEt over the column packed with 1.5 g of the right handedness-rich CMS. Up to fraction # 16, 40 ml of AcOEt was loaded into the column and a total of 84 wt% of the adsorbate was recovered in the eluate. Excess enantiomer was changed from the D-isomer to the L-isomer during the separation (Fig. 8(b)). These results indicate that the L-isomer was adsorbed more strongly than the D-isomer on the right handedness-rich CMS.

It was confirmed that purely inorganic SBA-15 as a control, which has a hexagonal rod-like morphology, did not show any asymmetric preferential adsorption property. The fact that purely inorganic CMS shows the unique ability to separate enantiomers, although slightly but reproducibly, is highly significant. Consideration is described below.

The adsorbate molecules approach into the chiral mesopores because external surface area of CMS is quite low as compared with the internal one. The silanol (≡Si–OH) groups are present on the surface of chiral mesopores (about 1–2 groups/nm^2) and their distribution on the surface must be chiral with the same scale as the morphology. Admitting that the size of adsorbate is extremely small compared to the size of the mesopore (2.2 nm), the ≡Si–OH groups would work together as adsorption sites for the adsorbate, leading to the asymmetric preferential adsorption property. Considering the pioneering asymmetric separation using the *d*- and *l*-quartz (Kavasmaneck and Bonner 1977), the contribution of the external surface of the twisted particle is not negligible. Further experiments are indispensable for clarifying the asymmetric separation mechanism, and currently being studied.

Table 3 Asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-DL-Ala-OEt) over the left handedness-rich CMS

Fraction #	Volume[a] (ml)	Recovered adsorbate		ee[b] (%)
		Weight (mg)	Recovery (%)	
1–3	12	0.0	0.0	–
4	4	0.6	3.0	0.06-L
5	4	1.5	7.4	0.08-L
6	4	1.2	5.9	0.10-L
7	4	1.4	6.9	0.14-L
8	4	1.6	7.9	0.10-L
9	4	1.0	5.0	0.10-L
10	4	0.5	2.5	0.04-D
11	4	0.4	2.0	–
12	4	0.7	3.5	0.22-L
13	4	1.0	5.0	0.16-D
14	4	0.6	3.0	0.16-L
15	4	0.4	2.0	0.08-L
16	4	0.8	4.0	0.10-L
17	35	2.0	9.9	0.06-D
18	20	1.1	5.4	0.24-D
19	40[c]	0.7	3.5	5.12-D

Adsorbent: left handedness-rich CMS, 1.5 g. Adsorbate: CF_3CO-DL-Ala-OEt, 20.2 mg

[a] Eluent: n-C_6H_{14}/AcOEt = 20:1 (vol%)

[b] Enantiomeric excess

[c] 40 ml of AcOEt was loaded into the column to extrude adsorbate from the silica

Table 4 Asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-DL-Ala-OEt) over the left handedness-rich CMS

Fraction #	Volume[a] (ml)	Recovered adsorbate		ee[b] (%)
		Weight (mg)	Recovery (%)	
1–4	16	0.1	1.0	–
5–8	16	0.1	1.0	–
9–10	8	0.0	0.0	9.02-L
11	4	1.4	13.9	0.06-L
12	4	2.0	19.8	0.14-L
13	4	2.3	22.8	0.10-L
14	4	0.8	7.9	0.20-L
15	4	0.2	2.0	1.18-D
16	20	0.2	2.0	0.48-D
17	16	0.0	0.0	–
18	40[c]	0.0	0.0	–

Adsorbent: left handedness-rich CMS, 1.5 g. Adsorbate: CF_3CO-DL-Ala-OEt, 20.2 mg

[a] Solvent: n-C_6H_{14}/AcOEt = 20:1 (vol%)

[b] Enantiomeric excess

[c] 40 ml of AcOEt was loaded into the column to extrude adsorbate from the silica

Table 5 Asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-DL-Ala-OEt) over the right handedness-rich CMS

Fraction #	Volume[a] (ml)	Recovered adsorbate		ee[b] (%)
		Weight (mg)	Recovery (%)	
1–5	20	1.1	5.5	–
6	4	1.3	6.5	0.24-D
7	4	3.8	19.0	0.10-D
8	4	3.8	19.0	0.08-D
9	4	1.0	5.0	0.10-L
10	4	1.6	8.0	0.44-L
11	4	0.2	1.0	0.36-L
12	4	0.0	1.0	0.10-L
13	4	0.0	0.0	0.04-D
14	40	0.6	3.0	–
15	12	0.0	0.0	0.98-L
16	40[c]	3.5	17.5	0.84-L

Adsorbent: right handedness-rich CMS, 1.5 g. Adsorbate: CF_3CO-DL-Ala-OEt, 20.2 mg

[a] Solvent: n-C_6H_{14}/AcOEt = 20:1 (vol%)

[b] Enantiomeric excess

[c] 40 ml of AcOEt was loaded into the column to extrude adsorbate from the silica

4 Conclusions

Chiral mesoporous silica (CMS) with a uniform twisted rod-like morphology was successfully synthesized with TEOS, TMAPS and the chiral anionic surfactant in the presence of basic amino acids. The handedness of chiral helices in CMS was essentially governed by the stereoisomerism of the surfactant, not that of arginine. Weakly basic conditions derived from the basic amino acids are advantageous for the formation of CMS with a high quality. Thus obtained chiral mesoporous silica can be used for the enantioselective separation of racemic compounds; the helical rod-shaped CMS is found to be capable of asymmetric separation of racemic *N*-trifluoroacetylalanine ethyl ester (CF_3CO-Ala-OEt). The left handedness-rich CMS shows asymmetric preferential adsorption of the L-isomer and vice versa. Although adsorption differential is small, we believe that this is the first valid demonstration of the ability of helical mesoporous silica to produce optically active substrates with an asymmetric bias.

Acknowledgements This work was supported by Grant-in-Aid for Scientific Research on Priority Areas (No. 20037023, "Chemistry of Concerto Catalysis") from Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan. This work was also partly supported by Grant-in-Aid for Scientific Research (*S*) (No. 19106015) of MEXT, and Project of Development of Microspace and Nanospace Reaction Environment Technology for Functional Materials (NEDO).

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