doi:10.1246/cl.2010.70

Published on the web December 12, 2009

Tighter Packing Leads to Higher Enantiopurity: Effect of Basicity on the Enantiopurity of *N*-Acylamino Acid-templated Chiral Mesoporous Silica

Huibin Qiu and Shunai Che*

School of Chemistry and Chemical Engineering, State Key Laboratory of Metal Matrix Composites, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, P. R. China

(Received October 19, 2009; CL-090938; E-mail: chesa@sjtu.edu.cn)

Tighter packing of aromatic group-substituted *N*-acylamino acids in micelles at lower basicity significantly enhances intermolecular steric hindrance between adjacent amphiphiles and helps the formation of chiral mesoporous silica with higher enantiopurtiy.

Controlling the chirality (handedness) of helical supramolecular architectures is of prime interest in the fields of materials science, chemical sensing, and asymmetric catalysis. Normally, the given chirality of the molecules that form the chiral arrays has a decisive effect on the resulting supramolecular structure and hence leads invariably to a single chiral sense upon stacking. Nevertheless, many exceptions from this simple belief that relates the molecular chirality with the supramolecular chirality have also been observed.[1,2] The molecular chirality is not the only driving force but some other factors governing the formation of chiral structure should exist to cancel the inherent molecular chirality.

It is well known that mesoporous inorganic materials can be templated by various amphiphiles.[3] We have achieved the first synthesis of chiral mesoporous silica (CMS) with external twisted hexagonal rod-like morphology through the self-assembly of chiral amphiphiles.[4,5] It was found that the enantiomeric excess (ee) of the CMSs formed with the chiral *N*-acylamino acids was a critical function of both the substituent's steric bulk and the reaction temperature.[6] Conformational change induced diastereomeric rotamers of the chiral amphiphiles were supposed to survive in the stacked micelle to form the antipodal helical structures independently. The intermolecular steric hindrance, which dominates the conformational change and the proportion of the rotamers, is critical for the enantiopurity of the CMS.

Herein, the effect of such intermolecular steric hindrance on the CMS's enantiopurity was further evaluated by precise control of the distance between the adjacent amphiphiles, which was experimentally performed by changing the basicity of the reaction solution since the current chiral *N*-acylamino acids are weak acids.[7] The ee–basicity dependence of the CMSs was analyzed in relation to the substitutents and the intermolecular steric hindrance restricted comformational change of the *N*-acylamino acids.

N-Palmitoyl-L-Ala (C_{16}-L-Ala), *N*-palmitoyl-L-Val (C_{16}-L-Val), *N*-palmitoyl-L-Ile (C_{16}-L-Ile), and *N*-palmitoyl-L-Phe (C_{16}-L-Phe) were employed in this work. The synthesis of the CMS samples was performed by adding the silica precursors to a 1% aqueous *N*-acylamino acid solution with varying NaOH/amphiphile molar ratio. Typically, 0.404 g of C_{16}-L-Phe (1 mmol) and 11.6 g of NaOH aqueous solution (0.1 mmol L^{-1}) were added to 20 g of deionized water with stirring at 288 K. After the amphiphile was dissolved, 0.258 g of *N*-trimethoxysilylpropyl-*N,N,N*-trimethylammonium chloride (TMAPS, 50% in methanol, 0.5 mmol) and 1.2 g of tetraethoxysilane (5.8 mmol) was added to the solution with stirring in 10 min. Then, the mixture was allowed to react at 288 K for 3 days. The products were collected by centrifugal separation and dried in air at 313 K.

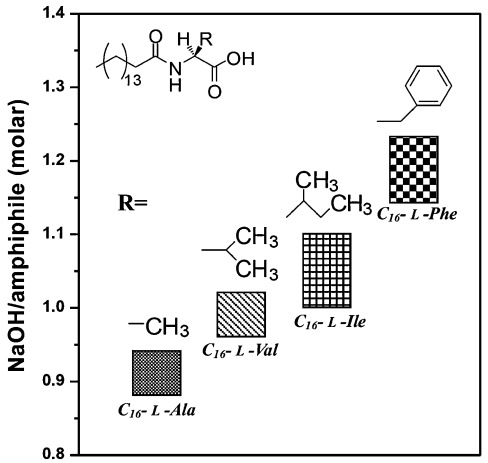


Figure 1. Optimized basicity regions for the formation of the CMSs templated by different *N*-acylamino acids.

As shown in Figure 1, the optimized basicity region for the formation of the CMSs varied with the substituent attached to the chiral center of the *N*-acylamino acids. The *N*-acylamino acids with bulkier substituent require higher NaOH/amphiphile molar ratio to form the CMSs. This could be explained in terms of (i) the ionization equilibrium constant decreases with increasing steric bulk and (ii) the chiral amphiphiles with larger head group require higher ionization degree to create more packing space to form the chiral micelles in the CMS formation.

Figure 2 shows the SEM images of the CMSs formed with C_{16}-L-Phe under different basicities at 288 and 313 K, which all exhibited homogeneous morphology and well-defined twisted rod-like shape with a hexagonal cross-section. The crystals formed at 288 K were longer (1–2 μm) than those formed at 313 K (0.5–1 μm), indicating a more anisotropic growth of the CMS crystal at lower temperature. It can be seen that the contents of the left-handed rods (denoted by the blue circles) increased obviously with decreasing NaOH/amphiphile molar ratio. The sample synthesized with NaOH/amphiphile molar ratio of 1.14 at 288 K was composed of almost exclusively left-handed rods. All of the samples were confirmed to have hexagonally ordered channels twisted from 2D-hexagonal *p6mm* by the HRTEM images and XRD patterns (see Supporting Information,[8] Figures S1 and S2).

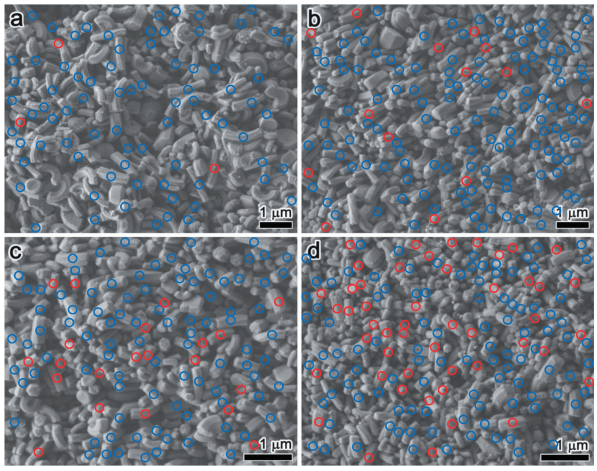


Figure 2. SEM images of the CMSs formed with C_{16}-L-Phe at (a) 288 K, NaOH/C_{16}-L-Phe = 1.14, (b) 288 K, NaOH/C_{16}-L-Phe = 1.23, (c) 313 K, NaOH/C_{16}-L-Phe = 1.14, and (d) 313 K, NaOH/C_{16}-L-Phe = 1.23.

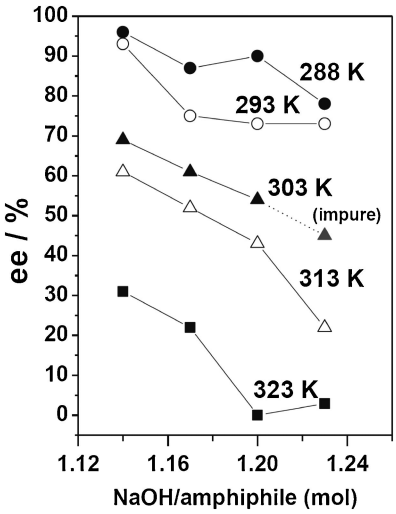
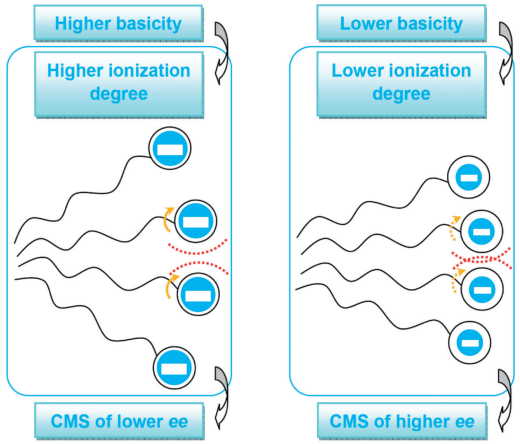


Figure 3. Basicity dependence of the ee of the CMSs formed with C_{16}-L-Phe at different temperatures.

Figure 3 shows the basicity dependence of the ee of the CMSs templated by C_{16}-L-Phe. The ee increased almost linearly with decreasing NaOH/C_{16}-L-Phe molar ratio at different temperatures. At higher temperatures, the ee increased rapidly from zero to the maximum with decreasing basicity. While at lower temperatures, the ee remained at a higher level and increased slightly with decreasing basicity. The CMS of about 95% ee was obtained under NaOH/C_{16}-L-Phe molar ratio of 1.14 at 288 K. On the contrary, the ee of the CMSs formed with C_{16}-L-Ala, C_{16}-L-Val, and C_{16}-L-Ile are not so sensitive to the basicity and only fluctuations can be observed.

The chiral *N*-acylamino acids employed in this work are carboxylic acid-based weak acids and their ionization degree decreases with decreasing the base content in the solution. Low ionization degree of the amphiphile at lower basicity contributes to a partial reduction of the electrostatic repulsion between the charged amphiphile head groups and a decrease in the distance



Scheme 1. Effect of basicity on the enantiopurity of the CMSs via controlling the conformational change of the chiral amphiphiles.

between the adjacent amphiphiles in the micelles,[7] which subsequently enhance the intermolecular steric hindrance between the adjacent amphiphiles to resist the conformational change of the chiral amphiphiles,[6] leading to the CMSs of higher ee (Scheme 1). However, as mentioned above, only the ee of the CMS formed with C_{16}-L-Phe is depended on the basicity. It is likely that the intermolecular steric hindrance of the aromatic group ($-CH_2C_6H_5$) is more sensitive to the intermolecular distance than that of the alkyl groups [$-CH_3$, $-CH(CH_3)_2$, and $-CH(CH_3)CH_2CH_3$], which may be attributed to the size and rigidness of the substituted groups.

In conclusion, the ee of the CMSs formed with C_{16}-L-Phe dramatically increased with decreasing basicity of the reaction solution. Tighter packing of the aromatic group substituted C_{16}-L-Phe molecules in the micelles at lower basicity significantly enhances the intermolecular steric hindrance between the adjacent amphiphiles which helps the formation of the CMSs with higher enantiopurity. We believe that the present study promotes our in-depth understanding of the CMS formation mechanism at the molecular level and stimulates similar endeavors in related systems.

This work was supported by the National Natural Science Foundation of China (Grant Nos. 20890121 and 20821140537) and 973 project (No. 2009CB930403) of China.

References and Notes

1 T. Tachibana, S. Kitazawa, H. Takeno, *Bull. Chem. Soc. Jpn.* **1970**, *43*, 2418.
2 B. N. Thomas, C. M. Lindemann, R. C. Corcoran, C. L. Cotant, J. E. Kirsch, P. J. Persichini, *J. Am. Chem. Soc.* **2002**, *124*, 1227.
3 C. T. Kresge, M. E. Leonowicz, W. J. Roth, J. C. Vartuli, J. S. Beck, *Nature* **1992**, *359*, 710.
4 S. Che, Z. Liu, T. Ohsuna, K. Sakamoto, O. Terasaki, T. Tatsumi, *Nature* **2004**, *429*, 281.
5 T. Ohsuna, Z. Liu, S. Che, O. Terasaki, *Small* **2005**, *1*, 233.
6 H. Qiu, S. Wang, W. Zhang, K. Sakamoto, O. Terasaki, Y. Inoue, S. Che, *J. Phys. Chem. C* **2008**, *112*, 1871.
7 C. Gao, H. Qiu, W. Zeng, Y. Sakamoto, O. Terasaki, K. Sakamoto, Q. Chen, S. Che, *Chem. Mater.* **2006**, *18*, 3904.
8 Supporting Information is available electronically on the CSJ-Journal Website, http://www.csj.jp/journals/chem-lett/index.html.

