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Catalysis of a Peptidic Micellar Assembly Covalently Immobilized within Mesoporous Silica Channels: Importance of Amphiphilic Spatial Design

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Abstract: A mesostructured silica/organic composite **1-MS**, constructed from a rodlike micelle of amino acid amphiphile **1** that has a condensable head group and that can be used as a template, was found to be able to catalyze the acetalization of cyclohexanone, in ethanol at 25 °C (50 % in 12 h), whereas no reaction took place with unfunctionalized mesoporous silica. In sharp contrast, hydrolytic removal of the C_{16} alkyl tail of immobilized **1** resulted in the complete disappearance of the catalytic activity, which suggests the importance of a hydrophobic inner domain for the admission of cyclohexanone. Unsupported peptide amphiphile **2**, under identical conditions to those above, was inefficient for acetalization regardless of the absence (2 % in 24 h) or presence of mesoporous silica (7 % in 24 h). Reference composite **2-MS**, which is a noncovalently immobilized peptidic micelle, was virtually inactive (1 % in 24 h). These observations indicate the importance of covalent immobilization of the peptidic rod micelle for catalysis. Mesostructured silicate **3-MS** hybridized with a nonpeptidic, ammonium ion amphiphile (**3**) showed a certain catalytic activity, but the yield (12 % in 24 h) of the acetal was much lower than that achieved by using **1-MS** as the catalyst. Amorphous silica with immobilized **1** on its surface was much less active than **1-MS** for acetalization (5 % in 24 h).

Keywords: acetalization · heterogeneous catalysis · mesoporous materials · micelles · peptides

Introduction

Catalysis of micellar assemblies has attracted much attention not only for promoting organic transformations in aqueous media but also as models of enzymatic reactions.[1,2] Similarly to enzymes, micelles can trap and concentrate organic substrates in their hydrophobic interior. In some cases, synergetic effects of multiple functional groups, assembled on the surface or in the interior of micelles, can be expected for the activation of substrates. Noncovalent architectures of micelles allow easy incorporation of different catalytic functionalities. However, despite these major advantages, there exist some essential drawbacks arising from the dynamic nature of micelles. The stability of micelles from nonpolymeric amphiphiles is highly dependent on environmental factors such as polarity, ionic strength, and temperature. Furthermore, ordinary amphiphiles rarely form micelles in organic media. In relation to these essential problems, amphiphilic polymers or polymerizable amphiphiles have been considered potential precursors for "frozen" micelles.[3]

Here we propose a new strategy by using mesoporous silica as a support for potential micellar catalysts. Mesoporous silicates are prepared by hydrothermal condensation of alkoxysilanes by using rodlike micelles as templates, followed by calcination of the resulting silica/organic nanocomposites.[4] In 2001, we[5a] and another group[5b] reported the first functional silica/organic nanocomposites templated by rod micelles of engineered amphiphiles.[5,6] More recently, we have also reported the use of a peptide amphiphile (**1**, Scheme 1) with a condensable alkoxysilane head group for the hydrothermal synthesis of a nanocomposite (**1-MS**), in

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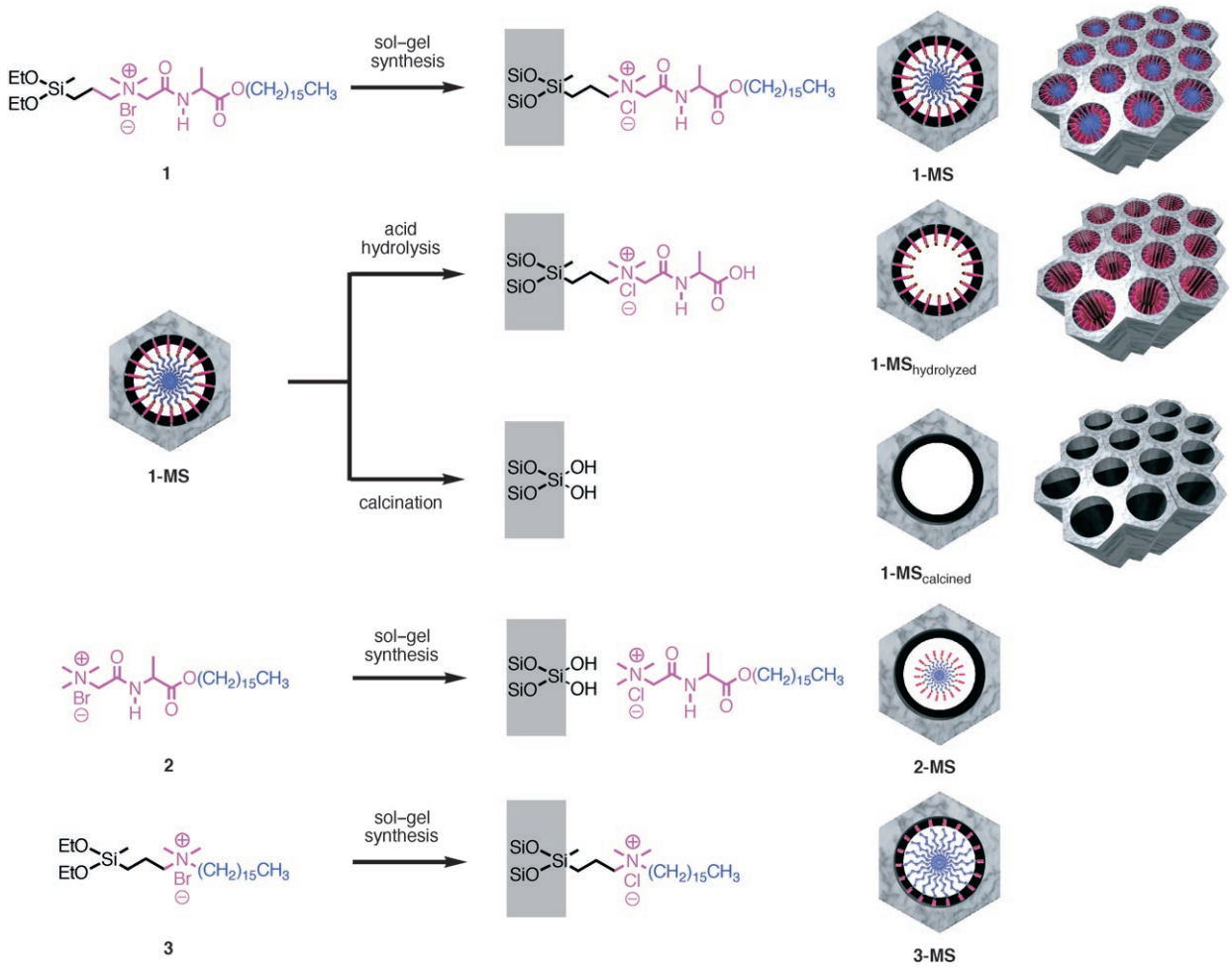
Supporting information (powder X-ray diffraction analyses and IR spectra of **2-MS** and **3-MS**) for this article is available on the WWW under http://www.chemeurj.org/ or from the author.



Scheme 1. Schematic representation of the synthesis of mesostructured silica composites **1-MS**–**3-MS** with amphiphiles **1**–**3**.

which a peptidic rod micelle consisting of **1** is covalently immobilized within the silica channel.[7] In the present work, we took notice of the potential catalytic activities of peptides, and found that **1-MS** catalyzes acetalization of a ketone, such as cyclohexanone, in ethanol (EtOH) under mild conditions.

Results and Discussion

Preparation and structural characteristics of 1-MS: Mesoporous silica-immobilized peptidic micelle **1-MS** was prepared by using a method analogous to that reported in our previous paper.[7] Thus, a mixture of tetraethyl orthosilicate (TEOS), H_2O, EtOH, and HCl at a molar ratio of 1:4:3:0.01, respectively, was heated for 2 h at 70 °C for the partial condensation of TEOS. Compound **1** (0.041 g), H_2O (0.82 g), and concentrated hydrochloric acid (0.43 g) were successively added to an aliquot of the reaction mixture (0.20 g), and the mixture was stirred at room temperature for 4 h. Filtration of the reaction mixture allowed isolation of **1-MS** as a white powder. X-ray diffraction (XRD) analysis of **1-MS** showed a *d* spacing for the (100) diffraction of 4.4 nm, which can be indexed as the interpore distance of a hexagonal structure. Differential scanning calorimetry/thermogravimetry (DSC-TG) analysis under an N_2 atmosphere showed that an initial minor weight loss due to dehydration occurs, followed by a major weight loss at 180–440 °C, from which the total organic content in **1-MS** was estimated to be 46 wt %. As reported previously,[7] an IR spectrum of **1-MS** showed a C=O stretching vibration at $\tilde{\nu} = 1685\ cm^{-1}$, which suggests that the amide group of **1** is free from hydrogen-bonding interactions.

Scheme 1 shows a schematic structure of the cross section of a silica channel of **1-MS**. The incorporated rod micelle, which consists of a hydrophobic inner domain (blue) and a hydrophilic outer shell with onium-ion functionalities (pink) and is covalently attached to the surface of the silica wall (gray), has a coaxial structure. The peptide functionalities are likely located at the core–shell interface. We expected that the hydrophobic inner domain would be suitable for the incorporation of cyclohexanone, while the hydrophilic outer shell might promote admission of EtOH. In fact, we confirmed that **1-MS** can trap a hydrophobic dye molecule in its inner domain. A UV-visible spectrum of a suspension of **1-MS** in EtOH in the presence of erythrosine B (Fig-

ure 1a) showed an absorption band centered at $\lambda = 552$ nm, which is redshifted by 7 nm from that of only erythrosine B in EtOH (Figure 1c). The redshift of the absorption band of erythrosine B observed in the presence of **1-MS** indicates

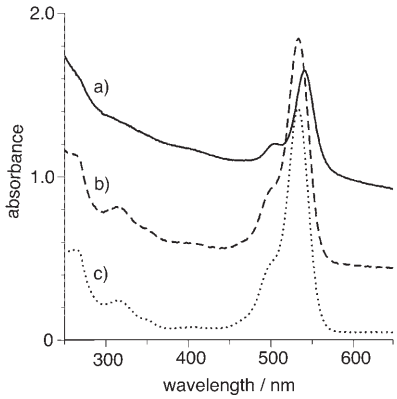
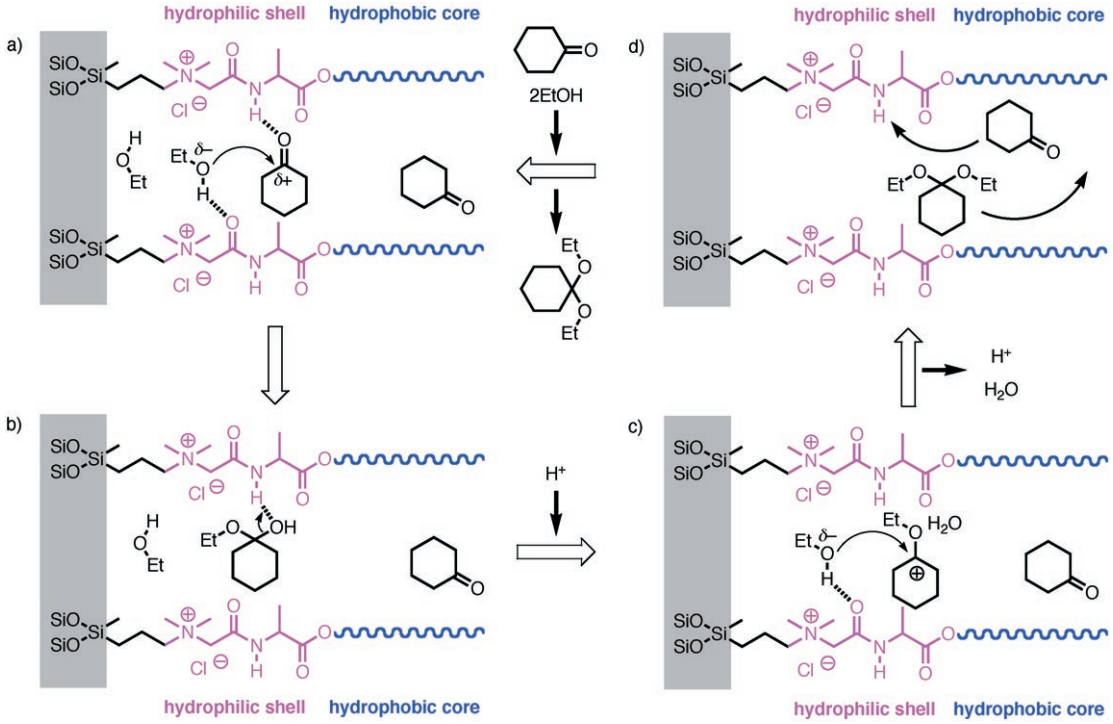


Figure 1. Absorption spectra of erythrosine B in EtOH at 25 °C in the presence of a) **1-MS**, b) SBA-3, and c) absence of these additives.

that this dye molecule is incorporated into the hydrophobic domain inside the silica channels.[8] In contrast, such a redshift was not observed for erythrosine B in EtOH containing mesoporous silica SBA-3 with hollow channels[9] (Figure 1b). Because the peptide functionalities in **1-MS**, located at the core–shell interface (Scheme 1), are free from hydrogen-bonding interactions,[7] one would expect that cyclohexanone and EtOH, incorporated into the silica channels, can be activated by forming hydrogen bonds with the amide NH and carbonyl groups of the peptide functionalities, respectively (Scheme 2).

Acetalization of cyclohexanone in EtOH: Acetalization of cyclohexanone in EtOH was investigated at 25 °C. Typically, **1-MS** (30 mg) was added to EtOH (5 mL), and the resulting suspension was stirred (500 rpm) at 25 °C for 12 h under an N_2 atmosphere. Cyclohexanone (2.0 mmol) and octane (0.2 mL; internal reference for GC) were then successively added to the suspension, and aliquots of the reaction mixture were periodically removed and subjected to GC analysis on a cross-linked methyl silicon gum capillary column (Shimadzu CBP1-M25-025). As a reference, mesoporous silica **1-MS**$_{calcined}$ (Scheme 1) was prepared by calcination of **1-MS** at 560 °C in air, and its catalytic activity was investigated together with conventional mesoporous silica SBA-3, which was synthesized under acidic conditions analogous to those for the synthesis of **1-MS**.[9] A noncovalently immobilized reference, **2-MS** (Scheme 1), was prepared by using peptide amphiphile **2**, which has no condensable alkoxysilane head group, as the template for the hydrothermal silica synthesis. In addition to these three reference samples, we also prepared **1-MS**$_{hydrolyzed}$ with no hydrophobic inner domain (Scheme 1) by refluxing **1-MS** in a solution of THF and HCl. As reported previously,[7] this post-treatment allowed hydrolysis of the ester functionality of **1**, so that the hydrophobic inner domain was selectively cleaved to leave a hydrophilic channel with densely packed amino acid functionalities on the surface.

We found that **1-MS** catalyzes acetalization of cyclohexanone (Figure 2). For the acetalization of cyclohexanone in



Scheme 2. A plausible mechanism (a–d) for acetalization of cyclohexanone with EtOH in a silicate channel of **1-MS**.

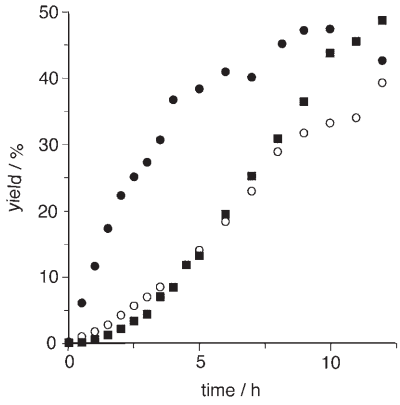


Figure 2. Time profiles for the acetalization of cyclohexanone with EtOH in the presence of **1-MS**, used after immersion for 12 h in EtOH (●) and cyclohexanone (○), and without immersion (■).

the presence of **1-MS** (used after immersion for 12 h in EtOH), the GC yield of the corresponding acetal increased gradually to 22 and 40% in 2 and 7 h, respectively, and reached a plateau after 12 h at around 50%, as a result of the acetalization–hydrolysis equilibrium (Table 1, entry 1). For confirmation, a suspension of **1-MS** in EtOH, after **1-MS** had been immersed for 24 h at 25°C, was filtered off from an insoluble fraction, and cyclohexanone was added to the resulting filtrate. However, no acetalization took place. We also found that the acetalization rarely takes place with amphiphile **2** alone, which was used as an unsupported reference sample of **1-MS** (2% in 24 h, entry 4). Furthermore, neither unfunctionalized mesoporous silicate **1-MS**$_{calcined}$ nor SBA-3 brought about acetalization of cyclohexanone (entries 3 and 9).[10] On the other hand, when a mixture of **2** and **1-MS**$_{calcined}$ was used as the catalyst, the acetalization did take place, but only sluggishly (7% in 24 h, entry 5). In relation to this observation, noncovalently immobilized reference **2-MS** also exhibited a negligibly small catalytic activity (1% in 24 h, entry 6) just like unsupported **2** (entry 4). This result is reasonable, as noncovalently immobilized template amphiphiles are known to be readily rinsed off by alcohols from silicate channels. Therefore, covalent immobilization of the micellar assembly of **1** in the silicate channels is quite essential for the observed catalytic activity of **1-MS** (entry 1).

We conducted further control experiments by using **1-MS**$_{hydrolyzed}$ and **3-MS** as reference catalysts. **1-MS**$_{hydrolyzed}$, prepared by acidolysis of the ester functionalities of **1-MS**, is devoid of any hydrophobic inner domain, whereas **3-MS**, prepared with condensable amphiphile **3** as a template for the hydrothermal silica synthesis, does not contain peptidic functionalities in the silica channels. When **1-MS**$_{hydrolyzed}$ was used as the catalyst, no acetalization of cyclohexanone took place (entry 2). On the other hand, **3-MS** brought about the acetalization, but the yield of the product (12% in 24 h, entry 7) was much lower than that with peptidic **1-MS**. The catalytic activity of **3-MS** could be a result of a possible contribution of the ammonium salt functionalities, because certain ionic species are known to accelerate acetalization of ketones.[11] Taking into account all of the above observations, we propose that the catalysis of engineered solid catalyst **1-MS** in the acetalization of cyclohexanone should proceed according to the sequence of events illustrated in Scheme 2. Namely, cyclohexanone and EtOH are simultaneously incorporated into the silica channels at the hydrophobic inner domain and hydrophilic (ionic) outer shell, respectively, and then activated through hydrogen-bonding interactions with the amide NH and carbonyl groups of the peptide functionalities, located at the core–shell interface (Scheme 2a and c). The acetalization should transiently involve carbocationic intermediates (Scheme 2c), which are favorably generated in a highly polar environment containing concentrated onium salt functionalities.

Of further interest is the fact that the reaction clearly shows a sigmoidal time-conversion profile when dry **1-MS**, without prior immersion in EtOH, is employed (Figure 2). Because the reaction profile with **1-MS** pre-immersed in cyclohexanone was not much different from that with non-immersed **1-MS**, EtOH must play some role in modification of the catalytic site of **1-MS**.[12] In the dry state, the ionic outer shell of the immobilized micelle must be shrunken owing to a possible interionic interaction. However, when **1-MS** is exposed to EtOH, the ionic outer shell might become gradually swollen by the admission of EtOH. Consequently, the reaction could be self-promoted. We also confirmed a possible importance of the honeycomb structure of the silica support for **1-MS**. For this purpose, amorphous silica **1-AS**, which bears covalently immobilized peptide amphiphile **1**

Table 1. Acetalization of cyclohexanone in EtOH. Structural elements and catalytic activities of mesostructured silica composites, calcined mesoporous silica, and amphiphile **2**.[a]

Entry	Additive	Structural elements of additive			Yield [%]
		micellar component	peptide functionality	hydrophobic domain	
1	**1-MS**	covalently immobilized	+	+	50
2	**1-MS**$_{hydrolyzed}$	covalently immobilized	+	–	0
3	**1-MS**$_{calcined}$	–	–	–	0
4	**2**[b]	–	+	–	2
5	**2**+**1-MS**$_{calcined}$[c]	–	+	–	7
6	**2-MS**	noncovalently immobilized	+	not guaranteed (deciduous)	1
7	**3-MS**	covalently immobilized	–	+	12
8	**1-AS**	covalently immobilized	+	not guaranteed	5
9	**SBA-3**	–	–	–	0

[a] Reagents and conditions: cyclohexanone (2.0 mmol); EtOH (5.0 mL); additive (30 mg); reaction temperature, 25°C; reaction time, 24 h. [b] 0.024 mmol of **2** used. [c] 0.024 mmol of **2** and 16 mg of **1-MS**$_{calcined}$ used. MS and AS represent mesostructured and amorphous silica, respectively. SBA-3 denotes hexagonal mesoporous silica prepared under acidic conditions.[9]

on its surface, was prepared. Although the total organic content in **1-AS** (26 wt%) was not as high as that in **1-MS** (46 wt%), **1-AS** displayed a marked drop of the catalytic activity and resulted in the formation of the acetal in only 5% yield in 24 h (Table 1, entry 8). It is clear that a large surface area of the silica support for **1** in **1-MS** can contribute to high accessibility of the reactants to the catalytic sites. In addition to this, the above contrasting observations may also indicate again the importance of the amphiphilic, coaxial structure of the micellar assembly of **1**, maintained by the hexagonal silicate channels, for the simultaneous admission of hydrophilic and hydrophobic reactants into the catalytically active channels.

Conclusion

We have developed novel engineered solid catalyst **1-MS**, which is composed of a coaxial peptidic rod micelle covalently immobilized in the regularly aligned hexagonal channels of mesoporous silica. As a result of the amphiphilic core–shell architecture of the immobilized rod micelle, hydrophobic and hydrophilic reactants can be incorporated simultaneously into the silica channels and activated through hydrogen-bonding interactions with the peptidic functionalities located at the core–shell interface. Mesoporous silica has caught particular attention as a catalyst support due to a high accessibility of substrates to the interior channels, along with their practical advantages in separation and recycling. Hence, immobilization of metal complexes and enzymes by post-treatment of mesoporous silica has so far been reported.[13] However, in contrast to these previous examples, our design strategy made use of templated hydrothermal synthesis of mesostructured silica with engineered amphiphiles, which allowed three-dimensional design of catalytic and substrate-binding sites—essential elements for enzymes—in the silica channels. Therefore, the present work provides a novel and general strategy for rational molecular design of bioinspired solid catalysts.

Experimental Section

Materials: All reagents for synthesis were used as received from Peptide Institute, Tokyo Kasei, Wako Pure Chemical Industries, Nacalai Tesque, Shin-etsu Chemical Industries, and Kanto Kagaku. Cyclohexanone and octane were dried over Na_2SO_4 and then distilled. Anhydrous grade ethanol, commercially available from Kanto Kagaku, was used without further dehydration treatment. Cyclohexanone diethyl acetal was identified by comparison of their NMR spectra and GC profiles with those of the authentic sample, prepared according to a literature method.[14] Amphiphiles **1**–**3** and corresponding composites **1-MS**–**3-MS** were prepared by using methods analogous to those reported previously.[7]

Measurements: Electronic absorption spectra were recorded on a JASCO U-best V-570 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL GSX-270 spectrometer. MALDI-TOF-MS spectra were recorded by using dithranol as a matrix on an Applied Biosystems BioSpectrometry Workstation Voyager-DE STR spectrometer. High-resolution mass spectroscopy (HRMS) was carried out by using 3-nitrobenzyl alcohol as a matrix on a JEOL JMS-AX505H spectrometer. Infrared spectra of KBr pellet samples were recorded on a JASCO FT/IR-600 Fourier transform infrared spectrophotometer. XRD analysis was carried out on a Rigaku model RINT 2400 X-ray diffractometer. DSC-TG profiles were recorded on a Shimadzu model TGA 50 thermogravimetric analyzer. Gas chromatography was carried out on a Shimadzu GC-14 A. Calcination of composite silica was carried out at 560°C for 6 h with an ADVANTEC model KM-160 electric muffle furnace.

Synthesis of 2: *N*-Bromoacetyl-L-alanine hexadecyl ester was synthesized by using the method reported previously.[7] A 28% aqueous solution of trimethylamine (0.62 g, 2.94 mmol) was added to an EtOH/CH_2Cl_2 (50 mL/50 mL) solution of the ester (1.28 g, 2.95 mmol), and the mixture was stirred at room temperature for 2 d and then evaporated to dryness. The residue was subjected to chromatography on silica gel with $CHCl_3$/EtOH (75:25 v/v) as an eluent to allow isolation of **2** (72%, 1.05 g). ^{1}H NMR (270 MHz, [D$_6$]DMSO, 20°C): $\delta = 9.01$ (d, J = 6.5 Hz, 1H), 4.32–4.27 (m, 1H), 4.10 (s, 2H), 4.06–4.04 (d, 2H), 3.20 (s, 9H), 1.55 (br, 2H), 1.31 (d, $J = 7.3$ Hz, 3H), 1.22 (m, 26H), 0.84 ppm (t, $J = 6.8$ Hz, 3H); IR (KBr): $\tilde{\nu} = 3230$ m, 3072 m, 2917 s, 2850 s, 1751 m, 1736 m, 1685 m, 1468 w, 1209 w, 1169 w cm^{-1}; MALDI-TOF-MS (dithranol): *m*/*z*: calcd for $C_{24}H_{49}N_2O_3$: 413.37; found: 413.40 $[M-Br^-]^+$; elemental analysis calcd (%) for $C_{24}H_{49}BrN_2O_3 \cdot {}^1/_2H_2O$: C 57.36, H 10.03, N 5.57; found: C 57.23, H 10.09, N 5.39.

Synthesis of 3: Hexadecyl bromide (7.20 g, 23.5 mmol) was dissolved in a mixture of EtOH (50 mL) and CH_2Cl_2 (50 mL) containing 3-dimethylaminopropyl-diethoxymethylsilane (1.29 g, 5.90 mmol), and the resulting solution was stirred at room temperature for 7 d and then evaporated to dryness. The residue was subjected to chromatography on silica gel with acetone/EtOH (50:50 v/v) as an eluent to allow isolation of **3** (50%, 1.57 g). ^{1}H NMR (270 MHz, [D$_6$]DMSO, 20°C): $\delta = 3.72$ (q, 4H), 3.20 (br, 4H), 2.98 (s, 6H), 1.63 (br, 4H), 1.22 (m, 26H), 1.16 (t, 6H), 0.84 (t, 3H), 0.52–0.47 (m, 2H), 0.10 ppm (s, 3H); ^{13}C NMR (67.5 MHz, [D$_6$]DMSO, 20°C): $\delta = 68.4$, 65.0, 62.9, 49.9, 31.2, 29.0, 28.6, 25.8, 21.8, 18.3, 15.9, 13.9, 11.6, −2.8 ppm; IR (KBr) $\tilde{\nu} = 2954$ s, 2914 s, 2858 s, 1633 w, 1467 m, 1259 m, 1078 m, 950 w, 806 w cm^{-1}; MALDI-TOF-MS (dithranol): *m*/*z*: calcd for $C_{26}H_{58}NO_2Si$: 444.42; found: 444.35 $[M-Br^-]^+$; HRMS (3-nitrobenzylalcohol): *m*/*z*: calcd for $C_{26}H_{58}NO_2Si$: 444.4231; found: 444.4225 $[M-Br^-]^+$.

Amorphous silica with immobilized peptide amphiphile 1 (1-AS): **1-AS** was prepared by using a method analogous to that reported previously.[15] Under an Ar atmosphere, a solution of **1** (250 mg) in toluene (10 mL) was added to silica gel (500 mg; Wakogel C-300HG, 0.040–0.060 mm in diameter), which had been dried under reduced pressure (1 mmHg) at 200°C for 12 h. The mixture was shaken overnight and then left at reflux for 3 h. After half of the volume of the solvent was distilled off from the reaction mixture, toluene (5 mL) was added to the residue, and then 5 mL of a volatile fraction was distilled off again. The resulting mixture was filtered to isolate an insoluble fraction, which was washed subsequently with hot toluene (30 mL) and hot EtOH (50 mL), and then dried overnight under vacuum. Thermogravimetric analysis indicated that **1-AS** has a total organic content of 26 wt%.

[1] a) E. H. Cordes, R. B. Dunlap, *Acc. Chem. Res.* **1969**, *2*, 329–337; b) T. Kunitake, S. Shinkai, *Prog. Polym. Sci.* **1982**, *8*, 435–487.

[2] J. H. Fendler, E. J. Fendler, *Catalysis in Micellar and Macromolecular Systems*, Academic Press, London, **1975**.

[3] J. H. Fendler, P. Tundo, *Acc. Chem. Res.* **1984**, *17*, 3–8.

[4] a) C. T. Kresge, M. E. Leonowicz, W. J. Roth, J. C. Vartuli, J. S. Beck, *Nature* **1992**, *359*, 710–712; b) 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, J. L. Schlenker, *J. Am. Chem. Soc.* **1992**, *114*, 10834–10843.

[5] a) T. Aida, K. Tajima, *Angew. Chem.* **2001**, *113*, 3919–3922; *Angew. Chem. Int. Ed.* **2001**, *40*, 3803–3806; b) Y. Lu, Y. Yang, A. Sellinger, M. Lu, J. Huang, H. Fan, R. Haddad, G. Lopez, A. R. Burns, D. Y. Sasaki, J. Shelnutt, C. J. Brinker, *Nature* **2001**, *410*, 913–917.

[6] a) A. Okabe, M. Niki, T. Fukushima, T. Aida, *Chem. Commun.* **2004**, 2572–2573; b) A. Okabe, T. Fukushima, K. Ariga, M. Niki, T. Aida, *J. Am. Chem. Soc.* **2004**, *126*, 9013–9016; c) M. Ikegame, K. Tajima, T. Aida, *Angew. Chem.* **2003**, *115*, 2204–2207; *Angew. Chem. Int. Ed.* **2003**, *42*, 2154–2157; d) A. Okabe, T. Fukushima, K. Ariga, T. Aida, *Angew. Chem.* **2002**, *114*, 3564–3567; *Angew. Chem. Int. Ed.* **2002**, *41*, 3414–3417.
[7] Q. Zhang, K. Ariga, A. Okabe, T. Aida, *J. Am. Chem. Soc.* **2004**, *126*, 988–989.
[8] a) M. L. Corrin, W. D. Harkins, *J. Am. Chem. Soc.* **1947**, *69*, 679–683; b) T. Nakagawa, K. Tori, K. Kuniyama, *Nippon Kagaku Zasshi* **1956**, *77*, 1684–1689.
[9] Q. Huo, D. I. Margolese, G. D. Stucky, *Chem. Mater.* **1996**, *8*, 1147–1160.
[10] Mesoporous silica prepared under basic conditions has been reported to serve as an acidic catalyst, see: a) M. Iwamoto, Y. Tanaka, N. Sawamura, S. Namba, *J. Am. Chem. Soc.* **2003**, *125*, 13032–13033; b) Y. Tanaka, N. Sawamura, M. Iwamoto, *Tetrahedron Lett.* **1998**, *39*, 9457–9460.
[11] T. S. Davis, G. A. Gettys, D. G. Kubler, *J. Org. Chem.* **1976**, *41*, 2349–2350.
[12] The reactions reached a plateau in 24 h to furnish 54 and 50% conversions using **1-MS** pre-immersed in cyclohexanone and non-immersed, respectively.
[13] a) A. Corma, *Chem. Rev.* **1997**, *97*, 2373–2419; b) M. Hartmann, *Chem. Mater.* **2005**, *17*, 4577–4593.
[14] R. Gopinath, S. J. Haque, B. K. Patel, *J. Org. Chem.* **2002**, *67*, 5842–5845.
[15] E. Paetzold, I. Jovel, G. Oehme, *J. Mol. Catal. A* **2004**, *214*, 241–247.

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