Precision Synthesis of Organic/Inorganic Hybrid Nanocapsules with a Silanol-Functionalized Micelle Template**

*Kyoungmoo Koh, Kohji Ohno, Yoshinobu Tsujii, and Takeshi Fukuda**

There has been increasing interest in the encapsulation of substances into confined spaces on the molecular to micrometer scale, as they have a wide variety of applications.[1,2] The related techniques can be classified into two types: 1) molecular assemblies with an internal cavity are used such as micelles, liposomes, and hollow spheres;[1–3] 2) substances are wrapped by organic and/or inorganic gels.[4] Herein we focus on the former type of system.

Self-assemblies of amphiphilic block copolymers in selective solvents commonly result in micelles with a core of the block that is insoluble in the solvent and a shell of the block that is swollen by the solvent.[5,6] Although micelle formation is among the most popular techniques for the construction of encapsulants in polymer science, the combination of micelle formation with some other techniques may lead to a new development in encapsulation technology. In the work described herein, we have attempted to coat the surface of a block copolymer micelle with a thin silica layer. In other words, we have used the micelle as a template to prepare a hollow silica nanoparticle. Such an organic/inorganic hybrid with its stable and confined nanoscale cavity would have many potential applications.

Our strategy consists of three steps, as shown in Figure 1: First, an amphiphilic block copolymer that bears several protected silanol groups near the free end of the hydrophilic block is synthesized. Second, the amphiphile is assembled into a micelle, with the silanol groups situated at the outermost layer of the micelle. Third, the micelle is coated with a silicon dioxide layer, which grows from the reactive points of the silanol groups near the micelle surface.

The amphiphilic block copolymer of the type PMMA-*b*-PPEGMA-*b*-poly(PEGMA-*r*-MOPS) was prepared by atom-transfer radical polymerization[7] (ATRP), as described in the experimental section. Figure 2 shows the gel-permeation chromatographic (GPC) traces for the polymerization steps. The polymerization of PEGMA using the purified PMMA macroinitiator proceeded smoothly: no shoulder peak was detected at the elution position of the macroinitiator and the

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[*] Prof. Dr. T. Fukuda, K. Koh, Dr. K. Ohno, Dr. Y. Tsujii
Institute for Chemical Research, Kyoto University
Uji, Kyoto 611-0011 (Japan)
Fax: (+81) 774-38-3170
E-mail: fukuda@scl.kyoto-u.ac.jp

[**] This work was supported in part by a Grant-in-Aid for Scientific Research (Grant-in-Aid 14205131, 14750695) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

DOI: 10.1002/ange.200351398

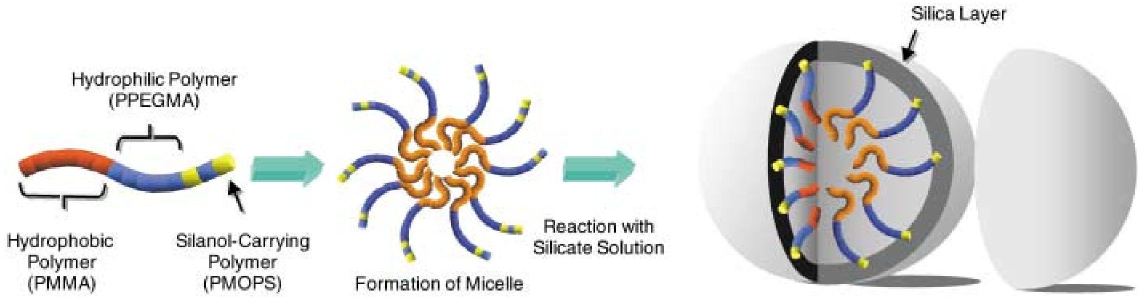

Figure 1. Strategy for the synthesis of an organic/inorganic hybrid nanocapsule.

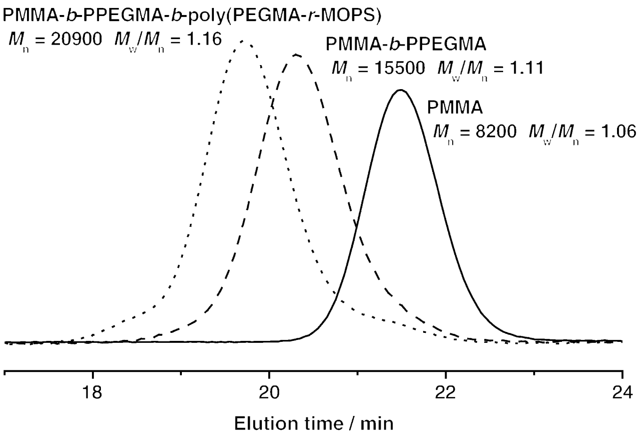

Figure 2. GPC traces for the PMMA macroinitiator, the PMMA-*b*-PPEGMA block copolymer, and the PMMA-*b*-PPEGMA-*b*-poly(PEGMA-*r*-MOPS) block copolymer.

molecular weight distribution was kept narrow. The GPC trace after the sequential addition of MOPS shows a shift of the peak position to a higher-molecular-weight region; again no shoulder peak was detected and the polydispersity index was kept low, as indicated in the figure.

Figure 3 represents the ^{1}H NMR spectrum (300 MHz) of the purified block copolymer PMMA-*b*-PPEGMA-*b*-poly(PEGMA-*r*-MOPS) with tentative assignments of the peaks. The peaks b, d, and i were assigned to the methyl protons of the polymethacrylate backbone, the methylene protons of PPEGMA, and the methylene protons of PMOPS, respectively, and were used to calculate the molar composition of the block copolymer as MMA/PEGMA/MOPS = 11.7:5.1:1. We also analyzed the composition of the random (statistical) copolymer poly(PEGMA-*r*-MOPS) independently prepared under similar conditions,[8] and estimated the molar composition of the last sequence poly(PEGMA-*r*-MOPS) in the block copolymer as PEGMA/MOPS = 1:0.84. With these molar ratios and the known number-average degrees of polymerization (DP$_n$) of the macroinitiator PMMA (DP$_n$ = 82), the DP$_n$ values of the PMMA, PPEGMA, and poly(PEGMA-*r*-MOPS) blocks were estimated to be 82, 28, and 15, respectively, and the molar composition of poly(PEGMA-*r*-MOPS) was assumed to be (1:0.84 ≈ 8:7). The $M_{n,NMR}$ of the block copolymer estimated in this way was 20700, which (accidentally, to some extent) agreed well with the PMMA-calibrated GPC value ($M_{n,GPC}$ = 20900). These results confirm the successful formation of the amphiphilic block copolymer, which bears several protected silanol groups near the free end of the hydrophilic block.

The polymeric micelle was prepared as described in the Experimental Section. The hydrodynamic diameter of the micelle was estimated to be about 30 nm by dynamic light scattering (DLS). This micelle is probably composed of a core of the hydrophobic PMMA block and a shell of the hydrophilic PPEGMA sequence, so that the MOPS moieties of the poly(PEGMA-*r*-MOPS) segment are preferentially distributed near the micelle surface. Moreover, hydrolysis of the trimethoxysilyl groups of the MOPS moieties under aqueous environment would result in silanol groups, which should be populated near the micelle surface.

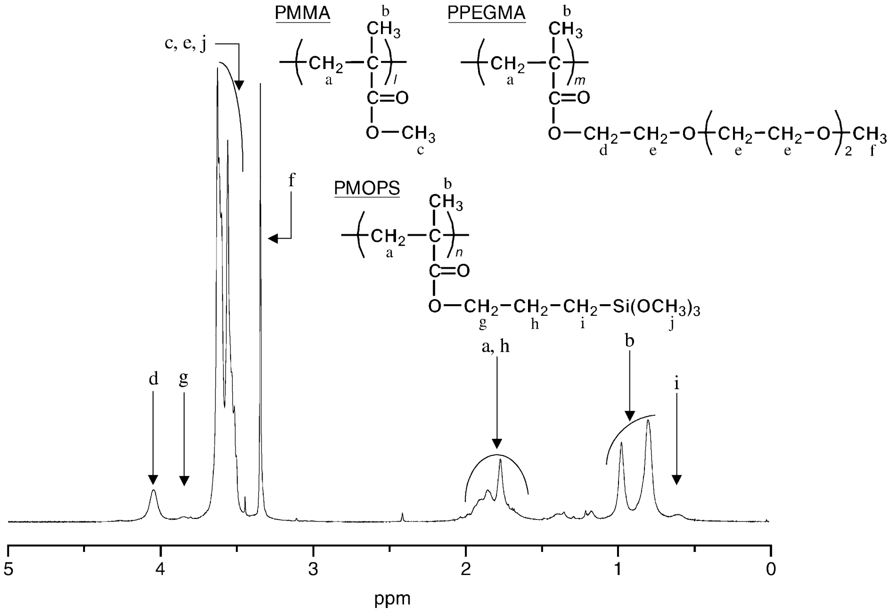

Figure 3. Typical ^{1}H NMR spectrum of the purified PMMA-*b*-PPEGMA-*b*-poly(PEGMA-*r*-MOPS) block copolymer in CDCl$_3$.

Liz-Marzán et al.[9] previously reported a method for the homogeneous silica coating of a silanol-modified gold nanoparticle by active silica to produce a fairly monodisperse particle composed of a gold core and a silica shell. We applied this method to coat the silanol-carrying micelle with a silica layer (see Experimental Section). As shown in Figure 4, the transmission electron microscopic (TEM) image of the micelle after treatment with active silica reveals black rings with a mean diameter about 25 nm, which is roughly comparable to the diameter of the original micelle estimated by DLS. No such black rings were observed for the micelle before treatment with silica or for the micelle formed from the PMMA-*b*-PPEGMA block copolymer (without silanol groups) after treatment with silica. These results show the successful formation of a silica layer growing from the anchor points of the silanol groups near the micelle surface. We also synthesized a nanocapsule with a relatively large diameter (about 42 nm) by changing the molecular weight of the block copolymer (see Supporting Information).

Figure 4. TEM image of the organic/inorganic hybrid nanocapsule.

With its unique structural features, the organic/inorganic hybrid nanocapsule obtained is potentially useful in many applications: for example, trapping substances in a micelle followed by coating with a silica layer will prove to be an efficient, yet stable form of encapsulation. (In fact, we performed a model experiment on a hydrophobic fluorescence dye, pyrene, to show that it could be contained within a nanocapsule (see Supporting Information).) Moreover, coating the micelle surface with a silica layer will offer a flexible method for further functionalization of the micelle by a variety of reactions with the silica surface.

To conclude, we precisely synthesized a silanol-functionalized amphiphilic block copolymer of the type PMMA-*b*-PPEGMA-*b*-poly(PEGMA-*r*-MOPS) by ATRP and produced the silanol-carrying micelle of the polymeric amphiphile. The micelle was mixed with a solution of active silicate to give a silica layer surrounding the micelle surface, thus producing an organic/inorganic hybrid nanocapsule. Because of the unique structural features of the nanocapsule, this chemistry will find many interesting applications. Studies on the incorporation of a reactive compound into the nanocapsule for use as a nanoscale reactor is in progress in our laboratory.

Experimental Section

Formation of the block copolymer: A solution of methyl methacrylate (MMA; 20.8 g) in diphenyl ether (19.46 g) was polymerized in the presence of *p*-toluenesulfonyl chloride (TsCl; 198 mg), copper(I) bromide (143 mg), and L-sparteine (Sp; 456 mg) at 70 °C for 4 h to obtain chlorine-terminated poly(methyl methacrylate) (PMMA; $M_n = 8200$, $M_w/M_n = 1.06$; M_n and M_w/M_n are number-average molecular weight and polydispersity index, respectively). Next, a Schlenk tube was charged with a magnetic stirrer bar and CuBr (5.2 mg), to which was quickly added a mixture of the chlorine-terminated PMMA (0.3 g) as a macroinitiator, poly(ethylene glycol) methyl ether methacrylate (PEGMA; Aldrich, $M_n \approx 300$, 2.2 g) as a hydrophilic monomer, diphenyl ether (3.8 g), and Sp (17 mg). The system was immediately degassed by three freeze–pump–thaw cycles and finally purged with argon. The polymerization was carried out in an oil bath under thermostat control at 70 °C. After 2 h, a mixture of methacryloxypropyltrimethoxysilane (MOPS; Chisso Co., Yokohama, Japan, 1.8 g), CuBr (16 mg), and Sp (51 mg), which had been degassed and charged with argon beforehand, was added into the Schlenk tube through a cannula. The polymerization was allowed to proceed at 70 °C for 2 h to obtain a block copolymer of the type PMMA-*b*-PPEGMA-*b*-poly(PEGMA-*r*-MOPS).The block copolymer was purified by passing through an activated alumina column and then by reprecipitation with *n*-hexane.

Preparation of the polymeric micelle: The block copolymer (100 mg) was dissolved in a mixture of *N,N*-dimethylacetamide (1 mL) and acetone (4 mL), to which Milli-Q-purified water (20 mL) was added dropwise at a rate of 1 mL min^{-1} with gentle stirring. The mixture was then sonicated in an ultrasound bath for 2 min to ensure complete dispersion of the amphiphile. The resultant cloudy solution was placed in a dialysis tube (Spectra/Por, molecular weight cutoff 15000) and dialyzed against Milli-Q water for 3 days. The cloudy micellar solution remaining in the tube was passed through a membrane filter (pore size 0.45 μm) and stored in clean glassware.

Coating of the micelle: An aqueous solution of sodium silicate (0.5 wt%, pH 9; 20 mL) was added to the silanol-carrying micelle solution (20 mL). The mixture was left at room temperature for 40 h and then dialyzed against distilled water to remove unreacted active silica.

Received: March 14, 2003 [Z51398]

Keywords: block copolymers · micelles · nanostructures · self-assembly · silicates

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[8] The random copolymerization of MOPS (4.48 g) and PEGMA (5.56 g) was carried out in the presence of TsCl (7 mg), CuBr (42 mg), Sp (139 mg), and diphenyl ether (9.76 g) at 70 °C under argon. At low monomer conversions below 10 %, three different aliquots of the mixture were periodically sampled. The purified copolymers were analyzed by ^{1}H NMR spectroscopy, so that the average mole ratio of PEGMA/MOPS in the copolymer was estimated to be 1:0.84.

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