Polymer Nanostructures

DOI: 10.1002/ange.200602116

Fabrication of Hollow Capsules Composed of Poly(methyl methacrylate) Stereocomplex Films**

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Considerable effort has been devoted to the development of nanostructured particles constructed by the self-assembly of polymeric systems.[1] In particular, polymeric hollow capsules have attracted much attention in the biomedical and pharmaceutical fields,[2] since they can be utilized as drug carriers and containers in which sensitive biomolecules can be preserved. The construction of hollow capsules of uniform size and controlled film thickness has been efficiently carried out by the deposition of polymer films onto the surface of colloidal core templates through the layer-by-layer (LbL) technique and the subsequent removal of the template cores.[3] However, this method has been limited to the preparation of hollow capsules composed of polyelectrolyte multilayers based on electrostatic interactions,[4] except for a few cases reported by Zhang et al.[5] and Sukhishvili et al.[6] where hollow capsules were prepared using the hydrogen-bonding interactions between the uncharged polymers.[7] Much less attention has been paid to hollow capsules composed of nonionic multilayers constructed through their van der Waals interactions, possibly because these hollow capsules were believed to be easily ruptured after the removal of the template core on account of the much weaker van der Waals interactions. Hollow capsules composed of nonionic multilayers can be expected to possess a shell permeability and morphology unlike those of conventional hollow capsules composed of polyelectrolyte multilayers.

Poly(methyl methacrylate) (PMMA) has found many applications in the biomedical field as a result of its excellent biocompatibility. The stereoregular PMMA stereocomplex, which is a double-stranded helical assembly formed with van der Waals interactions between isotactic (it) and syndiotactic

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[**] The authors appreciate the technical support for the living anionic polymerization by Prof. Tatsuki Kitayama (Osaka University) and the TEM observations by Prof. Akio Takaoka and Toshiaki Hasegawa (Research Center for Ultrahigh-Voltage Electron Microscopy, Osaka University). This work was financially supported by a Grant-in-Aid for Scientific Research (No. 15655041) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

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

(st) PMMA units,[8] has been used as a component of hollow-fiber membranes for artificial dialysis.[9] Recently, our research group prepared stable, ultrathin films of double-stranded PMMA stereocomplex by the alternate LbL assembly of it- and st-PMMA on a solid substrate.[10] The application of these it-/st-PMMA stereocomplex films to the hollow capsule shell allows the construction of novel hollow capsules of nonionic multilayers based on their van der Waals interactions. Herein, we report the preparation of hollow capsules composed of PMMA stereocomplex multilayer shells by a combination of the alternate LbL assembly of it- and st-PMMA and the silica template method.

The fabrication of hollow capsules of it-/st-PMMA stereocomplex was carried out according to the process shown in Figure 1. We chose silica particles as the template core, as

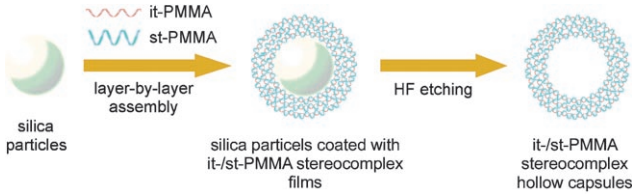

Figure 1. Fabrication process of it-/st-PMMA stereocomplex hollow capsules.

silica can be readily removed from the particles coated with polymer films by treatment with aqueous HF.[5,11] Acetonitrile/water (9:1) was chosen as the immersion solvent, since this solvent should make it possible to deposit a relatively large amount of the LbL assembly composed of PMMA stereocomplex onto the silica particles, in accordance with previous results on the alternate LbL assembly of it- and st-PMMA onto a Au plate.[10] Silica nanoparticles with a diameter of 330 nm were alternately immersed in acetonitrile/water (9:1) solutions (25 mL) of it-PMMA ($M_n = 20400$, $M_w/M_n = 1.21$; isotactic (mm)/heterotactic (mr)/syndiotactic (rr) triads = 99:1:0) and st-PMMA ($M_n = 73200$, $M_w/M_n = 1.20$; mm/mr/rr = 1:9:90). The immersion process was continued for ten cycles to afford ten double layers of it- and st-PMMA. The resulting particles were then treated with 2.3 % aqueous HF to remove the silica cores. Inductively coupled plasma (ICP) emission analysis of the obtained particles indicated that more than 99.8 % of the Si atoms were removed from the film-coated silica particles by HF etching.

Figure 2b and c shows the transmission electron microscopic (TEM) images of silica particles coated with PMMA film and PMMA hollow capsules, respectively. These images clearly indicate that the PMMA films were constructed on the surface of the silica particles, and PMMA hollow capsules were successfully fabricated by the removal of the silica core from the core–shell particles without any damage to the shell. The PMMA hollow capsules have a spherical shape with an average diameter of 510 nm, and their shell thickness is approximately 90 nm. The scanning electron microscope (SEM) images of silica particles coated with PMMA film and PMMA hollow capsules are shown in the Supporting Information. Self-assembled multilayer films of it- or st-

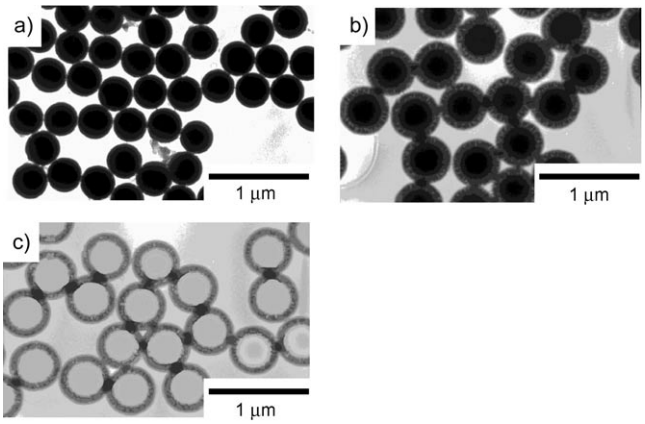

Figure 2. TEM images of a) bare silica particles, b) PMMA film-coated silica particles, and c) PMMA hollow capsules obtained after HF etching.

PMMA alone were not formed on the silica particles, in accordance with the previous result on the LbL assembly of it- or st-PMMA onto a Au plate.[10] This finding shows that the formation of a stereocomplex between it- and st-PMMA is a crucial driving force for the construction of the PMMA multilayered film on a silica particle.

X-ray diffraction (XRD) analysis and infrared (IR) spectroscopy are effective methods for evaluating the formation of a stereocomplex between stereoregular PMMAs. The XRD patterns of the particles before (Figure 3b) and after the HF etching of PMMA film-coated silica particles (Figure 3a) showed two peaks characteristic of the PMMA stereocomplex ($2\theta = 11$ and 15°),[12] whose peaks were significantly different from those of it- and st-PMMA. This result clearly indicates that films of PMMA stereocomplex were formed on the silica surface by the LbL assembly of it- and st-PMMA. This stereocomplex structure was maintained even after the removal of the silica template. In the FTIR/

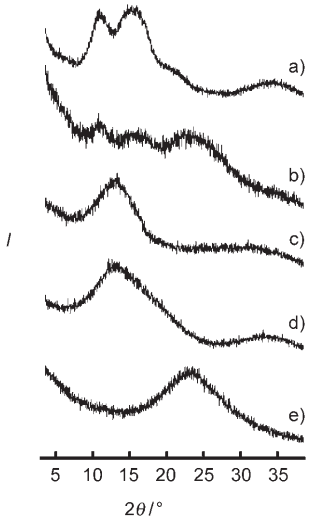

Figure 3. XRD patterns of a) PMMA hollow capsules obtained after HF etching, b) PMMA film-coated silica particles, c) it-PMMA, d) st-PMMA, and e) bare silica particles.

attenuated total reflection (ATR) spectra of the PMMA hollow capsules obtained after removal of the silica core (Figure 4a), absorption peaks corresponding to the C=O stretching vibrations and the main-chain CH_2 rocking vibrations of the PMMA stereocomplex were observed at around 1750 and 860 cm^{-1}, respectively,[8,10,13] thus strongly supporting the formation of hollow capsules of the PMMA stereocomplex.

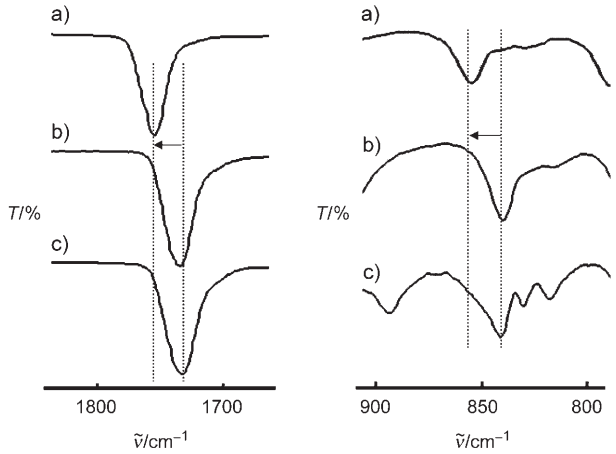

Figure 4. FTIR/ATR spectra of a) PMMA hollow capsules, b) it-PMMA, and c) st-PMMA.

In conclusion, we have demonstrated that hollow capsules of PMMA stereocomplex were successfully fabricated by a combination of LbL assembly of the stereocomplex and the silica template method. To the best of our knowledge, this is the first example of hollow capsules composed of nonionic multilayers constructed through van der Waals interactions. We believe that these PMMA stereocomplex hollow capsules are potentially applicable as drug carriers and containers. Replacement of the st-PMMA with st-poly(methacrylic acid) (st-PMAA) in the stereocomplex shell will allow construction of pH-responsive hollow capsules, as the st-PMAA is readily and selectively extracted from the it-PMMA/st-PMAA stereocomplex shell by an alkaline aqueous solution.[14]

Experimental Section

it-PMMA ($M_n = 20400$, $M_w/M_n = 1.21$; mm/mr/rr = 99:1:0) and st-PMMA ($M_n = 73200$, $M_w/M_n = 1.20$; mm/mr/rr = 1:9:90) were synthesized by conventional anionic polymerization using MMA monomers and the appropriate initiators (t-C_4H_9MgBr and t-$C_4H_9Li/(C_2H_5)_3Al$ for it- and st-PMMA, respectively).[15] Silica nanoparticles with a diameter of 330 nm (180 mg) were alternately immersed in acetonitrile/water (9:1) solutions (25 mL) of it- and st-PMMA (both concentrations were 1.7 mg mL^{-1}) for 15 min at 25 °C under gentle shaking. After each immersion, the silica nanoparticles were rinsed with acetonitrile/water (9:1). The immersion process was continued for ten cycles to afford ten double layers of it- and st-PMMA. The resulting particles were then treated with 2.3 % aqueous HF for 12 h at 25 °C to remove the silica cores.

Received: May 27, 2006
Revised: July 29, 2006
Published online: October 20, 2006

Keywords: multilayers · nanostructures · polymers · template synthesis · thin films

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