Organic–Inorganic Hybrid Nanoparticles with a Complex Hollow Structure**

Jianzhong Du and Yongming Chen

Block copolymers spontaneously self-organize into nano-meter-scale structures and are therefore of great interest for emerging nanomaterials and nanotechnologies.[1] Well-defined polymer aggregates, such as spheres, vesicles, rods, tubules, and lamellae, form in selective solvents.[1–11] Vesicles, which contain a cavity, are particularly interesting owing to their potential applications in encapsulation, drug release, and catalyst supports.[2, 3b,c, 4, 7] However, copolymer-derived nanoparticles with complex internal structure are less common. Eisenberg and co-workers discovered so-called large-compound vesicles (LCVs) in their family of crew-cut aggregates formed by self-assembly of asymmetric polystyr-ene-*b*-poly(acrylic acid) and polystyrene-*b*-poly(ethylene oxide) block copolymers in solution.[8] LCVs, which were supposed to be the fusion of many vesicles, consist of many small compartments separated by a copolymer matrix. Furthermore, meso-sized crystallike aggregates with internal hexagonally packed hollow hoops (HHHs) in the matrix have been reported.[9] These are the only examples of polymer aggregates with complex hollow structures as far as we know.[10] Moreover, if one segment of block copolymers bears reactive groups, the resulting aggregates can be fixed by chemical crosslinking. Such nanoparticles are shape-persis-tent, even with changes in the environment. Thus far, a few successful crosslinking reactions within the vesicle wall have been reported, such as photodimerization and polymeriza-tion.[3b,c, 4, 11]

Herein, we report a simple approach to prepare novel organic–inorganic hybrid nanoparticles with a complex hollow structure. The method is based on the self-assembly of a reactive amphiphilic block copolymer, poly(ethylene

[*] Dr. J. Du, Prof. Dr. Y. Chen
State Key Laboratory of Polymer Physics and Chemistry
Joint Laboratory of Polymer Sciences and Materials
Institute of Chemistry, The Chinese Academy of Sciences
Beiyijie No. 2, Zhongguancun, Haidian, Beijing 100080 (People's
Republic of China)
Fax: (+86) 10-62559373
E-mail: ymchen@iccas.ac.cn

Dr. J. Du
Graduate School of The Chinese Academy of Sciences
Yuquanlu No. 19 (Jin). Shijingshan, Beijing 100039 (People's
Republic of China)

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oxide)-*block*-poly[3-(trimethoxysilyl)propyl methacrylate] (PEO-*b*-PTMSPMA, Scheme 1) in *N,N'*-dimethylformamide (DMF)/water solution, followed by a sol–gel process cata-
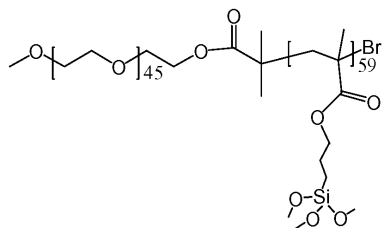
Scheme 1. The structure of poly(ethylene oxide)-*block*-poly[3-(trimeth-oxysilyl)propyl methacrylate] (PEO-*b*-PTMSPMA).

lyzed by triethylamine (TEA).[11] Owing to the crosslinking in preformed polymer aggregates, the particles are very stable and shape-persistent. PEO_{45}-*b*-$PTMSPMA_{59}$ diblock copolymer was first dissolved in DMF, and then water, a selective solvent for PEO, was added dropwise.[12] A pale, blue solution formed spontaneously, indicating micelle formation.[12] Finally, a small amount of TEA (1.5 wt%) was added to fix the morphology by hydrolysis and polycondensation of the -$Si(OCH_3)_3$ groups. Several days later, a drop of this solution was spread on a carbon-coated copper grid for transmission electron microscopy (TEM) analysis.

A TEM image of the gelated mesoporous particles obtained at an initial polymer concentration (c_i) of 0.1 mg mL^{-1} is shown in Figure 1 A. The majority of the material consists of particles with a well-defined and uniform internal structure. Since the polysilsesquioxane absorbs more of the electron beam relative to PEO, the white area corresponds to the cavities, which are separated by the crosslinked walls. The size of these interior compartments ranges from 5 to 20 nm, and the compartment wall thickness is around 15 nm. In addition, a few simple vesicles were also found. Exclusive complex particles with many small cavities were found as the c_i was increased to 1.0, 2.0, 6.0, and 8.0 mg mL^{-1}.[12] A typical TEM image ($c_i = 2.0$ mg mL^{-1}) is shown in Figure 1 B. The size of the particles increased, and the amount of the cavities increased while the cavity size remains essentially constant. The morphology is quite similar to that of the LCVs[8] reported in the literature, but the particle size is much smaller and shows low polydispersity (see Supporting Information). Such hollow particles were produced at $c_i = 2.0$ mg mL^{-1}, and the proportion of water ranged from 40 to 94 wt%. A typical TEM image for a sample prepared in 94 wt% water is shown in Figure 1 C.

In particular, flowerlike particles appeared when c_i was increased to 10 or 20 mg mL^{-1}. The corresponding TEM images are shown in Figure 1 D and in the Supporting Information. A scanning electron microscopy (SEM) image of the flower (Figure 1 E) shows a clear three-dimensional morphology consistent with a robust particle that does not collapse when the water is removed.[13] Interestingly, there are some vesiclelike mastoids protruding from the multicavity core. The core of the flowers did not collapse in the dry state,
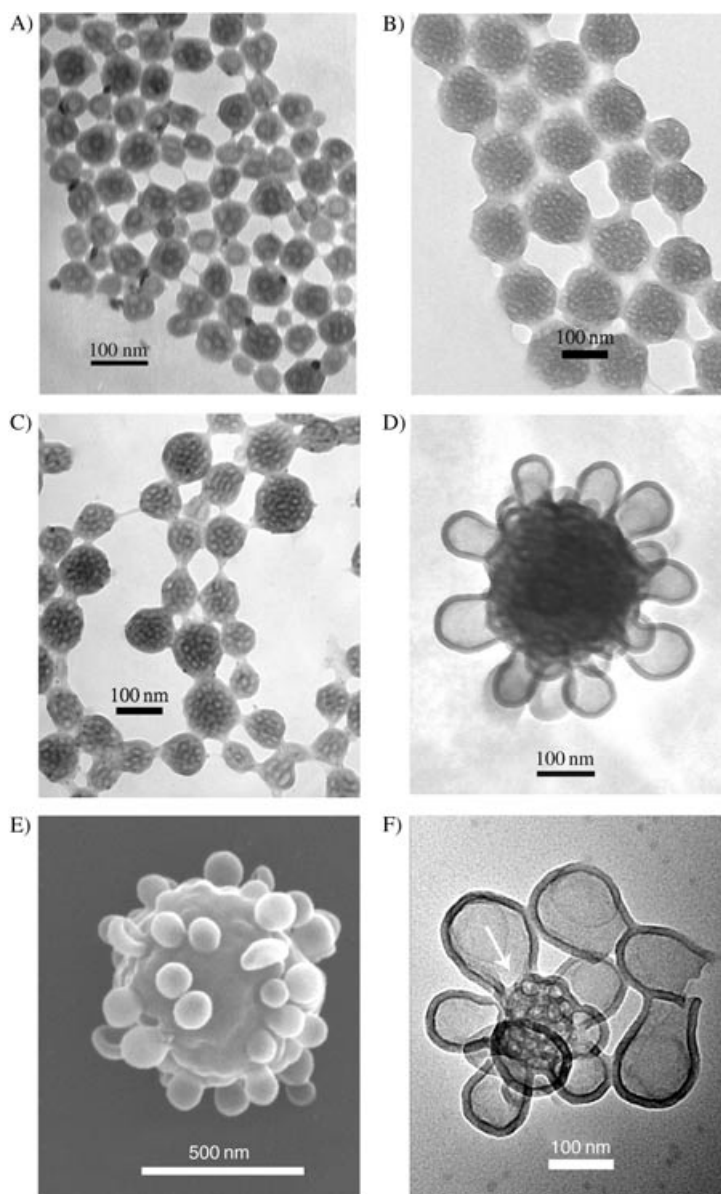
Figure 1. Typical TEM (A, B, C, D, and F) and (E) SEM images of complex hollow particles. The initial polymer concentration in DMF (c_i) is 0.1 (A), 2.0 (B, C), and 20.0 mg mL^{-1} (D, E, F). Water content is 51.4 wt%, except for C (94 wt%). F: TEM image of a smaller flower and fallen petals.

although the diameter reached 500 nm.[14] Thus, an internal polymer skeleton must be present to support the particle. The "wavy skin" between the petals reflects the complicated inner structure beneath the skin. From the smaller particles in Figure 1 F (see also Supporting Information) which contain fewer cavities, we observe that the cavities are separated by uniform walls whose thickness (≈ 15 nm) is the same as that of the petals. There are few individual vesicles with an opening like that in Figure 1 F. Accordingly, some holes are observed from the surface of some flower cores (see Supporting Information). The holes result from stripping the petals, possibly during stirring or sample preparation.

To confirm further the multihollow structure, a powder sample was embedded in epoxy resin, and sections ≈ 50–

80 nm thick were obtained by microtoming. As indicated by the white spots in Figure 2 A, the particles formed at lower c_i have a multicavity hollow structure with polydispersed cavity sizes. This observation agrees with the TEM results in Figure 1 B. More cavities form with increasing particle size, as a result of increasing c_i. The size of the honeycomblike cavities ranges from 19 to 26 nm, which is more uniform than that of particles prepared at lower c_i (Figure 2 B.
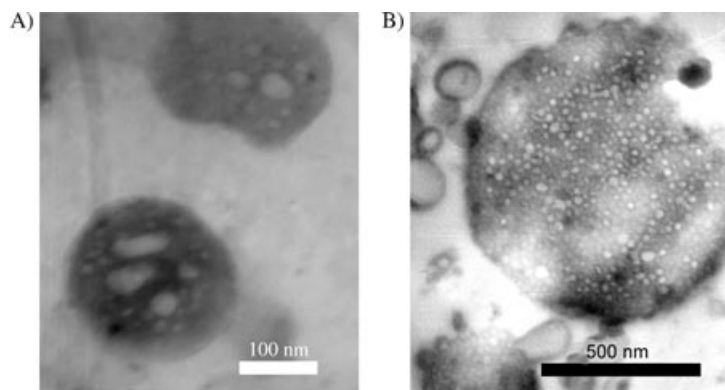

Figure 2. TEM images of particles embedded in epoxy resin showing the internal morphology of the hollow particles. In this case, A and B correspond to the samples of Figure 1 B and D, respectively.

The novel particles with the complex hollow structure described herein are striking. However, it is still difficult to know the actual morphology before gelation, as the particles are too soft to retain their fine inner structure in the dry state. After addition of the TEA catalyst, however, we believe that the gelation fixes the aggregates without altering the hollow structure. This conclusion works with simple vesicle formation.[11] This is because the hydrolysis reaction catalyzed by the base is slower than polycondensation. Once partial hydrolysis occurs in the PTMSPMA domain, the polycondensation proceeds simultaneously. As a result, the morphology is retained. Furthermore, the wall thickness of the hollow particles is very uniform and is consistent with a bilayer structure[15] that results from the self-assembly of a block copolymer in solution. In addition, similar hollow structures were also found with the self-assembly of other block copolymers.[8,9]

The diblock copolymer PEO-*b*-PTMSPMA self-assembles into LCVs, which are possibly fused vesicles, in DMF/water. This result is very different from the simple vesicles in the methanol/water mixture described in our previous work.[11] Actually, the bilayer which consists of PTMSPMA aggregated phase and PEO corona at two sides, is still the basic structure of LCVs, just like the simple vesicles. The morphological difference is related to the nature of common solvents. The vesicles in methanol/water solution are stabilized by the repulsive interaction of the PEO corona. However, such interactions are not strong enough to stabilize the individual vesicles in the DMF/water system owing to the high interfacial potential. The vesicles tend to undergo adhesion and fusion to decrease the interfacial potential,

thus leading to the formation of LCVs. Therefore, the thickness of the wall of the outermost particle and that of the membrane between the cavities inside the core are uniform, that is, a bilayer structure. At low c_i, the amount of vesicles in solution is lower, and therefore correspondingly fewer vesicles are fused to produce smaller LCVs with fewer cavities (Figure 1 A). As c_i increases, the number of vesicles increases, and more vesicles are fused to give larger particles with more cavities (Figure 1 B). Therefore, like simple vesicles, the hydrophilic PEO corona covers the two sides of a bilayer; but many solvent pools are encapsulated by the copolymer matrix inside one particle (Scheme 2). When the gelation catalyst was introduced, the crosslinking reaction occurred immediately, and the morphologies were fixed (Scheme 2). However, the formation of flowerlike particles at high c_i is still puzzling. We speculate that different sizes of simple vesicles were formed at high c_i. The interfacial potential is high for smaller particles and relatively low for larger particles. Therefore, adhesion and fusion occur preferentially with smaller rather than with larger vesicles. After the smaller vesicles are consumed, the larger vesicles adhere to the surface of the compound vesicles and fuse with them.

In conclusion, organic–inorganic hybrid particles with complex hollow structures were prepared very simply by the gelation of trimethoxylsilyl groups in the preformed self-assembly of PEO-*b*-PTMSPMA in DMF/water solution.
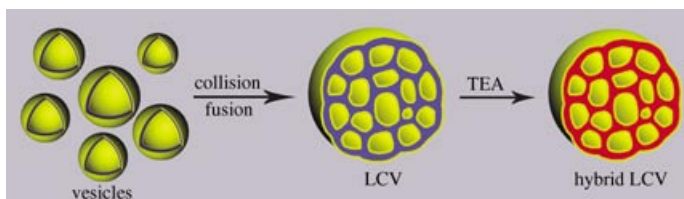
Scheme 2. Possible mechanism for the formation of hybrid large-compound vesicles (LCVs): Simple vesicles collide each other and then fuse into LCVs. The triethylamine (TEA) catalyzes the hydrolysis and polycondensation reactions. Yellow: PEO, blue: PTMSPMA, red: polyorganosiloxane from the sol–gel processes of PTMSPMA.

Inside the resulting particle, there are many cavities insulated by crosslinked hybrid bilayers of uniform thickness. Owing to gelation, the morphology of particles is stable against drastic changes in conditions.[16] The potential application of such novel nanomaterials in encapsulation is very promising. For example, as there are many cavities inside the particles, it may be possible to encapsulate functional species into different cavities of a particle for stepwise-release.

Experimental Section

The block copolymer, PEO$_{45}$-*b*-PTMSPMA$_{59}$ (composition determined from ^{1}H NMR spectrum (CDCl$_3$), $M_w/M_n = 1.34$ by SEC calibrated by PS standard), which was synthesized by atom-transfer radical polymerization.[11a,17] To prepare micelles, copolymer (0.1–20 mg) was dissolved in DMF (1.0 mL), and water was then added dropwise over 10 min by syringe with vigorous stirring. A pale blue

solution forms spontaneously, indicating the formation of polymeric micelles. After five hours, TEA (20 μL) was added to induce the hydrolysis and crosslinking of micelles. TEM images were obtained on a JEM 100 instrument. To prepare TEM samples, 5 μL of micelle solution was dropped on a carbon-coated copper grid and dried at ambient temperature for 2 or more days. For the observation of internal morphologies of the particles, a powder sample was embedded in a mixture of epoxy resin and diethylenetriamine (100:11, w/w), and then placed in an oven at 60°C for 12 h. Sections (50–80 nm) were obtained by microtoming. To obtain an SEM image, a drop of solution was spread on a silica wafer and left to dry. Samples were coated with platinum and viewed on an Hitachi S-4300 electron microscope operated at 15 kV. The images were recorded with a digital camera. Particle size and size distribution were determined from the TEM image.

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[12] The initial concentration (c_i) of the block copolymer was 0.1, 1.0, 2.0, 6.0, 8.0, 10, 20 mg mL^{-1}. The proportion of water was 51.4 wt%. If c_i is higher than 10 mg mL^{-1}, the solution becomes turbid, but no precipitation occurs for several months. The corresponding final particle diameter is 63 ± 10, 125 ± 24, 100 ± 12, 148 ± 23, 172 ± 19, 278 ± 60, 530 ± 113 nm, respectively.

[13] A low-magnification view of the flowers is shown in the Supporting Information.

[14] Simple vesicles larger than 100 nm obtained from a methanol/water mixture may collapse upon dryness for analysis; unpublished results.

[15] The wall thickness by TEM is ~ 15 nm, and the contour length of PTMSPMA$_{59}$ is 14.8 nm.

[16] The shape of the flowers did not change when the particle solution was sonicated for 30 min, and no clear change was found when the sample was calcined at 450°C for 7 h.

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