Synthesis of Hollow Silica and Titania Nanospheres

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Received November 15, 2007
Revised Manuscript Received March 5, 2008

Hollow SiO_2 nanoparticles have potential applications in drug delivery, ultrasound imaging, catalysts, adsorptive filters, and photonic band gap materials.[1–7] This paper describes an advance in a simple and scalable wet chemical synthesis of monodisperse hollow silica and titania nanospheres. Colloidal template methods that have been explored include gold, silver, CdS, ZnS, and polymer beads.[8–12] Polystyrene (PS) beads are attractive nanoscale templates since they are relatively inexpensive and available in uniform sizes. They are well-suited to make hollow particles since the polystyrene template can be removed either by calcination or dissolution.[13,14] Cornelissen and co-workers[15] used polystyrene (PS) latexes with either amine functionalized or zwitterionic surfaces to template the growth of SiO_2 shells in basic aqueous solution. Many of the hollow particles obtained were observed to have large holes in the shell wall.[15] Caruso et al.[16,17] reported the fabrication of hollow SiO_2 nanoparticles using PS cores and LbL self-assembly of multilayers of prefabricated SiO_2 nanoparticles and polymers. The PS cores were 640 nm in diameter, and the prefabricated silica particles were 25 nm, leading to rather large hollow silica particles.[18] Colloidal templating[19–21] and other methods[22–25] have also been explored for preparing hollow titania nanoparticles.

Poly-L-lysine (PL) is a simple polyamino acid with a pH-dependent structure, that has been applied in biomimetic syntheses of ordered silica structures. For example, Cha et al.[26] used block copolypeptides derived from PL to produce diverse amorphous silica structures. Van Bommel et al.[27] used PL aggregates as templates to fabricate hollow silica spheres in basic aqueous solution; however, this method yields a broad size distribution (100 nm to 1.5 μm). In neutral aqueous solution the conformation of poly-L-lysine is irregular.[28] Patwardhan et al.[29–31] used poly-L-lysine as a template to form silica nanospheres and other novel silica structures. The nanospheres obtained by this process were solid with PL incorporated throughout.

Polystyrene beads with an amine functionalized surface (APS) were explored as the basic catalyst template. The growth of a durable coating was controlled by adding dilute PL in a neutral phosphate buffer. Calcination or dissolution was used to remove the polystyrene core. Hydrolyzed tetramethoxysilane (TMOS) was used as the precursor for the silica shell. The polycondensation reaction occurs on the amine functionalized surface of polystyrene beads with an adsorbed layer of PL that serves as a framework for deposition of a silica gel network. Near neutral pH conditions used in the present work also make the process interesting as a model for how silica biomaterials might form. The high synthesis yields and the use of readily available APS beads and PL make the procedure ideal for bulk fabrication of hollow porous silica nanospheres with a well-defined size.

TMOS was hydrolyzed in hydrochloric acid to give silicic acid as the precursor of silica. Figure 1 shows the mechanism of polycondensation of silicic acid. We found that by adding a low concentration of PL to the dispersion of APS beads in neutral phosphate buffer before introducing the hydrolyzed TMOS that the formation of polystyrene/silica core−shell nanospheres took place within minutes. The polycondensation reaction on the template particles was facilitated by rapid vortex mixing. Different vortex mixing times from 2 min to 1 h were applied before separating the nanoparticles by

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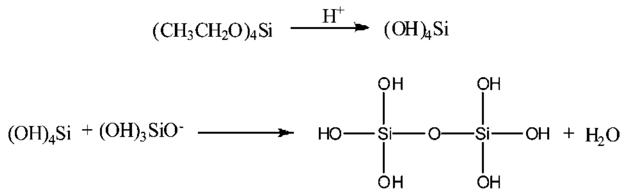
10.1021/cm703264y CCC: $40.75



$$(CH_3CH_2O)_4Si \xrightarrow{H^+} (OH)_4Si$$

$$(OH)_4Si + (OH)_3SiO^- \longrightarrow HO-\overset{OH}{\underset{OH}{Si}}-O-\overset{OH}{\underset{OH}{Si}}-OH + H_2O$$

Figure 1. Polycondensation reaction of silicic acid used to grow the silica shells.

centrifugation and washing, but the final size of the core−shell spheres was unaffected. This indicates that the formation of the silica coated nanospheres was complete within several minutes. The collected spheres could be resuspended and dispersed in water by vortex mixing and gentle sonication. Synthetic details (90% yield based on the polystyrene template) are available in the Supporting Information.

The ratio of TMOS to APS beads was varied, and it was found that increasing TMOS concentrations did not significantly increase the diameter of the core−shell spheres. At high concentrations of TMOS, amorphous silica agglomerates began to form. After calcination, SEM photographs showed that these agglomerates did not contain the APS core and consisted of nontemplated silica particles of varying size. The best ratio of TMOS and APS beads is found as 3:1 by weight for 100 nm sized beads.

In the reaction of 100 nm APS beads with silicic acid without adding PL, the surface roughness of the core−shell spheres shows that some polycondensation took place; however, the SiO_2 shell is not complete, and its diameter of 113 nm is essentially the same as the template (about 110 nm). Furthermore these nanoparticles collapsed to yield silica rubble on calcination. We postulate that a denser amine scaffold than that provided by templating with the APS surface amino groups is required to yield a silica shell with sufficient structural integrity to form isolable stable hollow particles. On addition of PL the SEM photomicrographs show that the surface of the silica shell is completely formed. After calcination of these core−shell spheres, only hollow shells were observed.

The pK_a of the primary amine groups on the PL backbone is 10.5. Therefore in neutral solution the amino groups will be positively charged and electrostatic repulsion prevents the aggregation of PL chains. It is known that the cationic nature of PL side chains leads to flat adsorption of the chains on polystyrene beads in an extended conformation. Multilayer adsorption is prevented due to charge repulsion. Figure 2 shows the relationship of the concentration of PL and the final sizes of core−shell spheres. With increasing concentration of PL the final size of the spheres rapidly increases, but then it saturates when the concentration of PL is about 0.32 mg/mL. Since adding 0.1% PL solution increases dilution somewhat at higher concentrations, the size begins to fall off at the highest concentrations. Variation of the pH between 4 and 9.5 also has little effect on the average size of the isolated nanoparticles.

Hollow silica nanospheres were prepared through calcination or by dissolution of the APS core with organic solvents. The core−shell spheres were heated at 450 °C for 4 h in order to oxidize the core organic materials. Figure 3 displays a high resolution TEM image of the hollow silica spheres obtained after the 100 nm APS template was removed by calcination. The porous silica shell appears to be about 6−10 nm thick, which is an important property for applications such as drug delivery or imaging. Organic solvents can also swell and partially dissolve or extrude the APS core and remove most (75%) of it through the porous shell under mild conditions. In general hollow intact particles were almost exclusively obtained, but the observation of a few broken shells confirmed that the spheres were hollow and the walls of the spheres were uniform. This may result from solvent swelling of the polystyrene core during the initial stages of the extraction process.

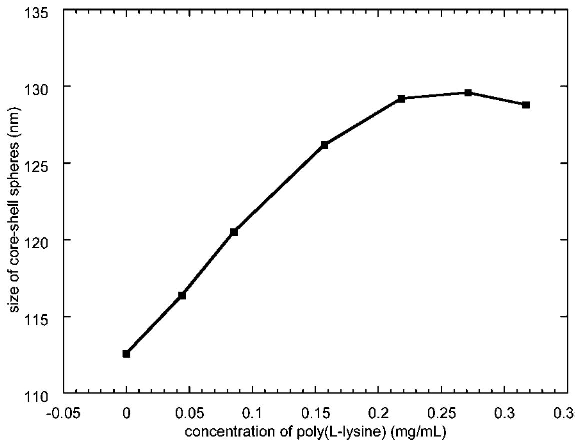


Figure 2. Size by SEM of silica coated APS spheres vs the concentration of PL using a 100 nm aminopolystyrene template.

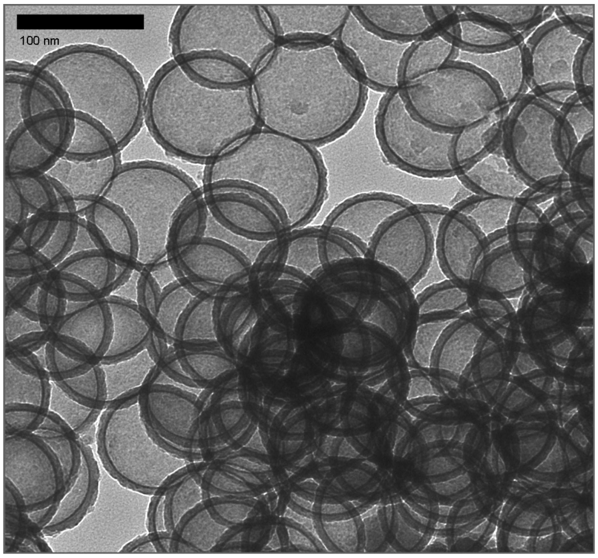


Figure 3. TEM image of hollow silica spheres obtained from 100 nm APS beads and PL (after calcination). The scale bar is 100 nm.

Hollow silica nanospheres were also prepared using 200 and 500 nm APS beads. The diameter of the larger calcined spheres decreased significantly compared with their core−shell parents. After calcination the diameters of core−shell spheres of 126, 210, and 454 nm APS beads shrunk to 102, 188, and 397 nm, respectively (Table 1). After dissolution with organic solvents, the diameter of hollow spheres prepared from 100 nm APS beads is similar to its precursor, the core−shell spheres. But a slight decrease in radius was observed for the 200 and 500 nm scale hollow spheres

Table 1. Average Diameters of Core−Shell and Hollow Spheres from SEM Photomicrographs[a]

nominal template size	100 nm	200 nm	500 nm
core sphere	126 ± 5 nm	210 ± 6 nm	454 ± 16 nm
hollow sphere solvent extracted	126 ± 7 nm	205 ± 7 nm	443 ± 21 nm
hollow sphere calcined	102 ± 8 nm	188 ± 9 nm	397 ± 15 nm

[a] Errors represent standard deviations for measurement of about 30 spheres.

obtained by core dissolution (Table 1). This may be attributed to partial dehydration of the silica hydroxyl groups on heating or extraction with anhydrous solvents. It is expected that the silica shell initially forms as a hydrated silica gel. The shrinking on dehydration appears to be isotropic, since the size distribution range before and after core removal remains uniform within 10% (Table 1).

FTIR spectroscopy was also used to monitor removal of the polystyrene core. The C−H (Ar) and $-CH_2-$ of the polystyrene stretching vibrations occur at 3030−2800 cm^{-1}. The absorption bands between 1480 and 1400 cm^{-1} are from C−H bending vibrations. These features disappear completely after calcination. When using the dissolution method to remove the APS core, the FTIR spectrum shows that about 25% of the polystyrene remained.

The amine functionalized surface APS beads can also be used directly as a template to prepare TiO_2 hollow nanospheres. Hydrolysis of titanium ethoxide, the common precursor of TiO_2, occurs too rapidly for the synthesis of monodispersed TiO_2 nanoparticles on APS beads. To slow down the hydrolysis reaction, we replaced the PBS buffer with anhydrous ethanol as the medium for the polycondensation reaction and used less reactive titanium *t*-butoxide (TBO) as the precursor. We found that even without the addition of PL, monodispersed core−shell spheres were produced, and after calcination porous, uniform-sized TiO_2 hollow spheres were obtained. Figure 4 shows the SEM images of hollow TiO_2 nanospheres templated on 200 nm amine functionalized PS beads after calcination. Addition of PL in the synthesis was ineffective and caused rapid hydrolysis of TBO—a white precipitate appeared within seconds.

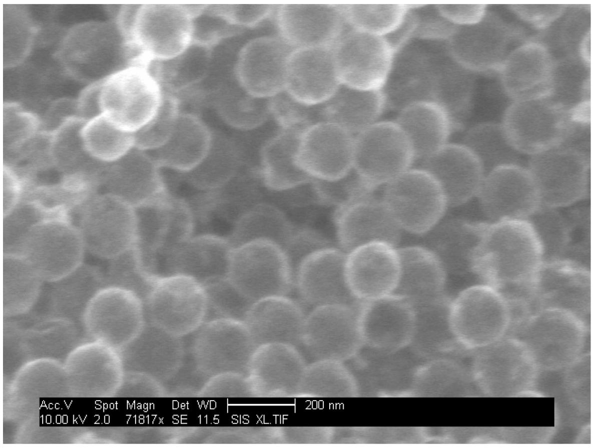


Figure 4. SEM photomicrograph of hollow titania spheres from templated hydrolysis of Ti(O-*t*-Bu)$_4$ on 200 nm aminopolystyrene beads (after calcination). The scale bar is 200 nm.

Uniform sized hollow silica nanospheres were fabricated by a new method with amine functionalized surface polystyrene beads as a template assisted by adsorbed poly-L-lysine. The positively charged PL chains in neutral buffer solution facilitate the polycondensation reaction of silicic acid yielding a silica shell, which is similar to the neutral conditions used for polyamino acid templating of biosilica in organisms, such as diatoms.[31] An isotropic shrinking of the hydrated silica shell was observed after removing the APS core by calcination or solvent dissolution. The same APS beads could also template the polycondensation of titanium *t*-butoxide in anhydrous ethanol and produced monodispersed TiO_2 hollow nanospheres after calcination. This provides a simple method to rapidly prepare monodisperse hollow silica and titania nanospheres and microspheres, which are expected to have broad applications in biomedicine, catalysis, and materials science.

Acknowledgment. This research was supported by NIH Nanotumor Grant (NIH Grant U54 CA 119335), and we thank the California Institute of Information Technology and Telecommunication for research support. The NIH National Center for Microscopy and Imaging Research at UCSD is acknowledged for assistance with obtaining the TEM images.

Supporting Information Available: Synthetic procedure for preparing hollow silica and titania nanoparticles (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

CM703264Y