Mechanism of a self-templating synthesis of monodispersed hollow silica nanospheres with tunable size and shell thickness†

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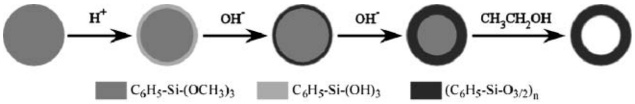
This study clarifies the mechanism of the hollow structure formation in the simple self-templating preparation of monodispersed hollow silica structures; the role of the polarity of washing solvent in creating the hollow structure is emphasized.

Hollow sphere nanostructures are important due to their wide range of potential applications in drug delivery and bioimaging.[1] Different strategies have been developed to prepare hollow structures of various materials.[2–15] Among these, template-free methods[10–15] are attracting much attention due to their simplicity. Recently, Hah *et al.*[10] reported a novel strategy to prepare monodispersed hollow silica particles *via* a two-step sol–gel process using phenyltrimethoxysilane (PTMS) as the precursor. This method is simple and reproducible. However, the underlying reaction mechanism is still ambiguous and remained as a proposal. In brief, it was proposed that:[10] first, the PTMS formed oil-in-water emulsions when dispersed in an aqueous solution; second, the hydrolyzed PTMS became more soluble into the solution; third, condensation in the next step happened on the surface of the oil droplets; fourth, the unhydrolyzed PTMS was released from the droplet, which was then used for the growth of the particle onto the outer surface. Since inner material migrated outwards, a hollow structure was finally formed. In this communication, we designed a series of experiments to clarify the mechanism of this method. Our observations led to a revised mechanism which is illustrated in Scheme 1 and supported by the results described below.

The revised mechanism can be summarized as the following reaction steps: first, when PTMS is dispersed in an acidic solution under stirring, it forms an oil-in-water emulsion and the hydrolysis reaction initially happens only on the surface of the PTMS droplets; second, in a basic solution, the hydrolyzed PTMS molecules on the outer surface of the droplet condense to yield a porous silica shell. With progressing time, the growth of the shell proceeds from the outer surface to the inner part of the droplet as more hydrolyzed PTMS molecules condense onto the inner side of the shell (the reaction frontline is on the inner side of the shell). Finally, the resultant particles are subject to washing with a solvent to dissolve the inner part of the particle that is not completely condensed, generating the inside hollow. Based on this mechanism, it can be predicted that the outer diameter of the hollow structure is determined by the shearing force provided in formation of the emulsion at the beginning, and the inner diameter of the hollow structure can be tuned by varying the reaction time, the concentration of the reagents, and importantly, the solvent used for washing the product after the reactions.



Scheme 1 The reaction scheme of preparing a hollow silica nanostructure from PTMS.

In a typical reaction, under mechanical stirring, 930 μL of PTMS (1 g) was added into 100 mL of water containing 6.6 mM HNO_3 that is kept in an isothermal water bath (60 °C). At the initial acidic pH condition (within 1 min), the hydrolysis quickly occurs at the proximity of the PTMS/water interface. The acid-catalyzed hydrolysis reaction is brief because it is desirable that only a thin layer of hydrolyzed PTMS is prepared for the condensation reaction in the next step. The condensation reaction was initiated by adding 10 mL of NH_4OH solution (28–30%). The transparent mixture solution became a milky solution immediately. This is due to the fact that the hydrolyzed molecules at the interface region of the PTMS droplet, once in contact with the basic solution, start to condense, forming a network of silica (modified with a phenyl group on each Si atom). After a certain time of condensation, the resultant particles were precipitated out by centrifugation, washed with a different solvent and dried. The size and morphology of the particles from different wash and drying routines were determined using transmission electron microscopy (TEM, JEOL 2010F) and scanning electron microscopy (SEM, FEI XL30).

We first used ethanol as the washing solvent, and varied the condensation time from 30 min to 180 min. All products show a hollow structure (Fig. 1). The outer diameters of the hollow spheres are very uniform in each preparation, with the average diameters in the narrow range of 450–500 nm, while the shell thicknesses of the hollow structures increase continuously, from 75 nm to 165 nm (measured over 100 particles from several TEM micrographs). This result is expected from our mechanism that with shorter condensation time, the condensation reaction is less complete. After the reaction is stopped, in the washing step, ethanol can diffuse through the porous shell, which can dissolve the unreacted PTMS or linear uncondensed PTMS oligomers.

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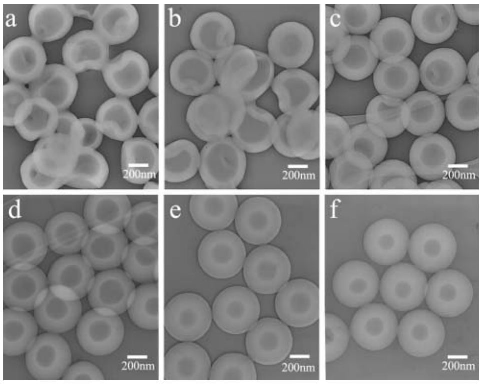

Fig. 1 TEM images show that the thickness of the shell or the inner diameter of the hollow spheres can be tuned by changing the condensation time. The samples are washed with 100% ethanol for 30 min. The condensation times are: (a) 30 min, (b) 45 min, (c) 60 min, (d) 90 min, (e) 120 min, (f) 180 min. The outer diameters of the hollow structure all show narrow size distribution averaging 450–500 nm. The shell thicknesses are 75 ± 3 nm, 83 ± 5 nm, 103 ± 6 nm, 125 ± 4 nm, 150 ± 4 nm, and 165 ± 3 nm from a to f, respectively.

With centrifugation, ethanol extracts the incompletely reacted core part, leaving the hole in the center.

Surprisingly, the washing solvent plays a key role in determining if the hollow structure can be obtained or not. By changing the solvent from ethanol to water, the silica particles change from hollow shells to solid balls (Fig. 2). When the as-prepared silica particles (hydrolysis time 1 min and condensation time 60 min, same as below) were washed with water or water–ethanol mixtures up to a ratio of water to ethanol = 1 : 8.5, (89% of ethanol by volume), the particles were solid showing no visible pores. The hollow structures appeared only at ratios of water to ethanol below 1 : 9 (v/v), and the pore size increased with the increase in ethanol content in the washing solution. This effect can not be expected from the proposed mechanism by Hah *et al.*[10] Methanol acts the same as ethanol does and leads to similar hollow structures (Fig. S1†). However, lower polarity solvents, such as acetone, chloroform and hexanes *etc.*, can completely dissolve the polymeric hollow structures.

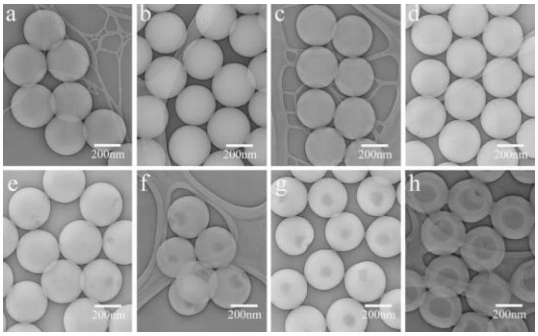

Fig. 2 TEM images of the as-prepared silica nanoparticles washed with solvents of different compositions: (a) water; (b) water–ethanol = 5 : 5 (v/v); (c) water–ethanol = 2 : 8; (d) water–ethanol = 1 : 8.5; (e) water–ethanol = 1 : 9; (f) water–ethanol = 1 : 19; (g) water–ethanol = 1 : 39; (h) 100% ethanol. The washing time in each solvent was 30 min, and the samples were collected by centrifugation.

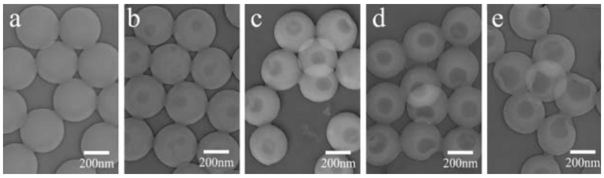

Fig. 3 TEM images of (a) the as-prepared silica particles (with no washing) do not show any pores. With the increase in the dissolving time in 100% ethanol, the pore size increases from (b) 10 min to (c) 35 min, and stabilizes after that; (d) 15 hours, and (e) 14 days. The outer diameters did not show significant changes with up to 14 days soaking in ethanol.

To manifest the dynamic dissolving process, we investigated the effect of dissolving time on the hollow structure. After collecting the as-synthesized silica particles by centrifugation, the silica particles were re-dispersed in 100% ethanol solution. After different times, an aliquot of the silica particles was taken out and observed using TEM. Images in Fig. 3 show that with the increase in the dissolving time the pore size increases and stabilizes after about a half hour. From 35 min to 14 days soaking in ethanol, the outer diameter also showed no significant change.

The TEM images shown in Fig. 2 and 3 indicate that the as-prepared samples do not show any pore structure without further treatment, and no pores can be generated by washing with water or a mixture of water–ethanol that has ethanol content less than 90%. These are surprising results that cannot be predicted from the original proposal of Hah *et al.*[10] Here, we demonstrate that the hollow structures can only be generated by ethanol extraction with at least 90% ethanol content, and ethanol only dissolves the center part of the particle that contains monomeric or oligomeric units of PTMS, but not the polymeric shell.

In another set of experiments, we further changed the solvent order to check the roles of different solvents in the hollow structure formation. When the silica spheres were first washed with water, and then with ethanol, there are only small pores formed in the silica particles (Fig. 4a). Washing with ethanol first then followed with water, larger pores formed inside the silica spheres (Fig. 4b). There is no obvious difference between the silica spheres washed with ethanol then water (Fig. 4b) and ethanol only (Fig. 4c).

The dynamic dissolving process with different time and different solvents was also monitored using UV-Vis spectroscopy (Fig. 5). Shown in Fig. 5, we clearly observed that water cannot dissolve PTMS out of the silica particle but ethanol is very effective to extract out the unreacted PTMS or PTMS oligomers. When ethanol was used followed with water, PTMS can be partially dissolved from the inner part of the silica particle. This observation further confirms our proposed mechanism.

In addition to the results described above, we also investigated the effects of other experimental parameters (see ESI†) on the size and morphology of the hollow structures. We found that:

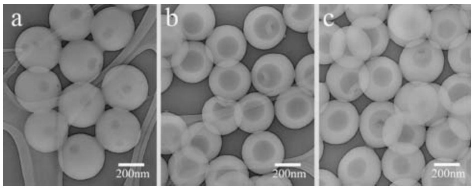

Fig. 4 TEM images of the as-prepared silica spheres washed with different solvent orders. (a) Water followed with ethanol; (b) ethanol followed with water; (c) ethanol only.

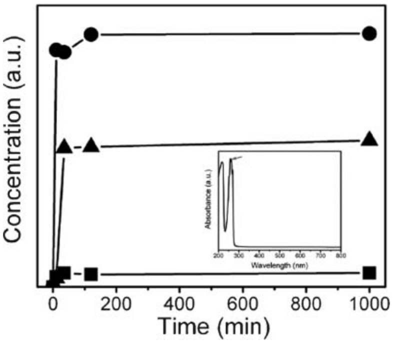

Fig. 5 PTMS concentration changes in different washing solvents (■: water; ▲: water followed with ethanol; ●: ethanol) with increasing time. The inset curve is from the absorbance of PTMS solution. The PTMS concentration in different washing solvents is calculated from the PTMS absorption peak at 258.5 nm as marked by the arrow in the inset.

increasing the stirring speed in the reaction caused a decrease in the outer diameter of the hollow structure (Fig. S2†); increasing the concentration of PTMS in the reaction led to larger particles with similar shell thicknesses (Fig. S3†); lowering the reaction temperature to 40 °C led to no well-defined structures and increasing the reaction temperature to 70 °C generated solid balls (Fig. S4†); the concentration of HNO_3 in the hydrolysis step has little effect on the particle and pore sizes generated (Fig. S5†); increasing the concentration of NH_4OH caused no change in the outer diameters of the particles but a decrease in the cavity sizes (Fig. S6†).

Based on our mechanism, we can explain all the above observations. When PTMS is added to the acidic solution, droplets of PTMS are formed in the aqueous solution under mechanical stirring because of its immiscibility with water. With a constant stirring speed, a narrow size distribution in the emulsion will be achieved. The average size of the oil droplets will decrease upon increasing the stirring speed. In the initial acid condition, PTMS is promptly hydrolyzed at the water/PTMS droplet interface. The hydrolysis step is brief to make sure only a thin layer on the oil droplet surface is hydrolyzed. When NH_4OH is added, the condensation reaction commences immediately, and a condensed layer of $(C_6H_5SiO_{3/2})_n$ is formed on the outside of the PTMS droplet. This step will fix the outer diameter of the final structure obtained, which solely depends on the initial diameter of the oil droplet, but not the acid and base concentrations or the reaction time. The thin condensed layer is porous, containing pores or channels in the size range of ~2–5 nm.[16] These nanopores allow water molecules and small ions from the outside aqueous solution to diffuse through the shell to gain access to the unreacted PTMS entrapped inside, so that the hydrolysis and condensation reaction can continue. However, the unreacted PTMS or oligomers of PTMS do not diffuse out to the water phase because of their low solubility in the aqueous phase. Therefore the reaction always happens at a solid–liquid interface. The observations indicate that the reaction frontline is not at the outer solid/water interface, but at the inner solid/oil interface. With prolonged reaction time, the PTMS inside the shell is subjected to hydrolysis and condensation slowly, from the inner surface of the shell toward the interior of the droplet. However, due to the increasing thickness of the silica layer, the diffusion of water and ions into the PTMS droplet becomes more and more limited. Therefore, the hydrolysis–condensation process may not be complete when it is stopped at a certain time. This can explain why the shell thickness increases with longer condensation time and higher temperature (40–60 °C). When the product is first washed with water using high speed centrifugation, water molecules can be forced deeper into the core part of the ball through the pores within the shell. Thus, the unreacted PTMS and oligomers can further hydrolyze and condense to get more filled silica particles. After water washing, even with a later ethanol washing, only tiny pores (~30–50 nm) can be formed. However, when the product is washed first with ethanol, the unreacted PTMS or PTMS oligomers inside the particles can be extracted out and hollow structures with larger cavities are obtained.

In summary, this study clarifies the mechanism of the hollow structure formation in the simple template-free preparation of monodispersed hollow silica structures. The role of the polarity of washing solvent in creating the hollow structure is emphasized. Since this is a self-templating reaction, the outer diameter of the hollow structure is determined by the diameter of the oil droplets in the oil-in-water emulsion initially prepared by stirring, thus it can be controlled by varying the stirring speed. The shell thickness can be controlled by the reaction time and concentration of the base in the condensation step. The insights obtained from this new mechanism will allow us to gain better controls for the synthesis of monodispersed hollow structures with tunable sizes and shell thicknesses.

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