Single-Step Fabrication of Monodisperse TiO_2 Hollow Spheres with Embedded Nanoparticles in Microfluidic Devices

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Hollow inorganic microspheres have attracted much attention because of their potential in diagnostics, drug delivery, bioactive materials, and optical devices. A few different methods including spray drying,[1] hard-template,[2] and emulsion methods[3] have been developed to prepare hollow inorganic spheres. Recently, uniform titania microcapsules have been fabricated successfully by the method of layer-by-layer (LBL) deposition on the polymeric templates, which requires time-consuming, multistep processes.[2,4] Compared to the template method, the conventional emulsion method is a simple and direct route for preparing titania hollow spheres.[3] However, the resulting titania shells are polydisperse and tend to form aggregates. Therefore, direct synthesis of uniform-sized hollow titania spheres in a simple and controlled manner is still a challenging issue for practical applications.

One of the potential strategies is to use high-throughput microfluidic devices which are readily scaled up. Microfluidic devices can produce highly monodisperse emulsion drops and have been used for fabricating uniform-sized spherical colloidal crystals, colloidosomes and hollow polymeric shells.[5−7] Production of inorganic materials using microfluidic devices is limited to formation of titania nanoparticles[8,9] or shells on colloidal particles[10] and formation of hierarchically structured organosilicon microcapsules.[11]

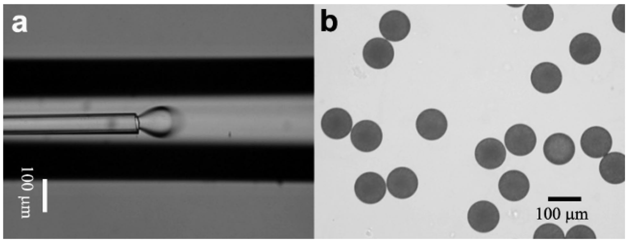

Figure 1. Optical microscope images of (a) a fluidic device fabricated with glass capillaries and (b) produced organic droplets dispersed in the continuous aqueous phase. Flow rates of oil and aqueous phases in the channels were at 5 and 100 μL/min, respectively. Oil drops contained 1 wt % titanium n-butoxides and 0.1 wt % CdS nanoparticles.

In this Communication, we report a very simple, single-step fabrication of hollow TiO_2 (titania) microspheres with embedded functional nanoparticles in a coflow microfluidic device that is composed of two coaxial microcapillaries (Figure 1a). To fabricate the microfluidic device, we heated two glass microcapillaries and pulled them to get desired geometries; a fine tip for the inside capillary and a narrow neck for the outside one. We then aligned the two capillaries manually by observing through a microscope, and mounted the tip of the inside capillary in the necking region of the outside capillary. Finally, the glass chip was assembled by connecting with the inlet and outlet tubes and sealing with optical adhesive.

The oil phase containing titanium alkoxide and functional nanoparticles was forced to flow through the inner capillary, and the aqueous phase flowing through the annulus region between two capillaries swept and broke up the oil-phase stream into highly monodisperse emulsion drops (Figure 1b). In this coflow microfluidic device, the size and production period of the emulsion drops can be precisely controlled by adjusting the tip size of the inner capillary and the flow rates of two constituting phases.[5a] The formation of emulsion drops occurred through the dripping mode of breakup. To keep the dripping mode of drop formation, the velocity of the inside stream remained at lower values. Otherwise, the emulsion drops were produced together with much smaller satellite droplets through the jet-streaming mode, which eventually deteriorated the size uniformity of the hollow particles. Also, the elongated jet stream sometimes blocked the inside capillary by chemical reaction of titania precursors in the oil phase.[12] For example, the emulsion drops in Figure 1b, which were prepared from a capillary tip of 47 μm in diameter, were 93.5 μm in average diameter with standard deviation as small as 2.4 μm. Titania shells from microfluidically generated emulsion drops are uniform in size, whereas those from conventional communition using a homogenizer are polydisperse (see Figure S1 of the Supporting Information).

Meanwhile, to employ microfluidic devices for fabricating titania microspheres, the reactivity of precursors should be controlled because sol−gel reaction of highly reactive metal

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(1) Bruinsma, P.; Kim, A.; Liu, J.; Baskaran, S. *Chem. Mater.* **1997**, *9*, 2507.

(2) Caruso, R.; Susha, A.; Caruso, F. *Chem. Mater.* **2001**, *13*, 400.

(3) Collins, A.; Spickermann, C.; Mann, S. *J. Mater. Chem.* **2003**, *13*, 1112.

(4) Wang, Y.; Angelatos, A.; Caruso, F. *Chem. Mater.* **2008**, *20*, 848.

(5) (a) Umbanhowar, P.; Prasad, V.; Weitz, D. *Langmuir* **2000**, *16*, 347. (b) Yi, G.; Thorsen, T.; Manoharan, V.; Hwang, M.; Jeon, S.; Pine, D.; Quake, S.; Yang, S. *Adv. Mater.* **2003**, *15*, 1300. (c) Subramaniam, A.; Abkarian, M.; Stone, H. *Nat. Mater.* **2005**, *4*, 553.

(6) Quevedo, E.; Steinbacher, J.; McQuade, D. *J. Am. Chem. Soc.* **2005**, *127*, 10498.

(7) Kim, J.; Utada, A.; Fernandez-Nieves, A.; Hu, Z.; Weitz, D. *Angew. Chem., Int. Ed.* **2007**, *46*, 1819.

(8) Cottam, B.; Krishnadasan, S.; deMello, A.; deMello, J.; Shaffer, M. *Lab Chip* **2007**, *7*, 167.

(9) Wang, H.; Nakamura, H.; Uehara, M.; Miyazaki, M.; Maeda, H. *Chem. Commun.* **2002**, 1462.

(10) Khan, S.; Jensen, K. *Adv. Mater.* **2007**, *19*, 2556.

(11) Steinbacher, J.; Moy, R.; Price, K.; Cummings, M.; Roychowdhury, C.; Buffy, J.; Olbricht, W.; Haaf, M.; McQuade, D. *J. Am. Chem. Soc.* **2006**, *128*, 9442.

(12) Utada, A.; Chu, L.; Fernandez-Nieves, A.; Link, D.; Holtze, C.; Weitz, D. *MRS Bull.* **2007**, *32*, 702.

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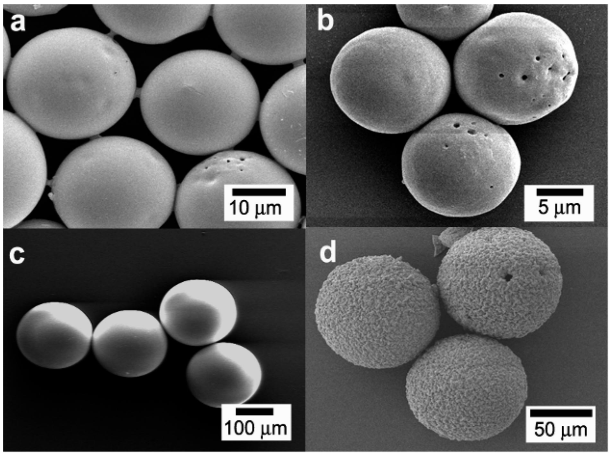

Figure 2. SEM images of microspheres prepared with (a, b) octanoic acid and (c, d) ETPTA (a, c) before and (b, d) after calcination at 500 °C for 1 h.

alkoxide precursors takes place rigorously at the emulsion interface in contact with aqueous medium. In conventional emulsion systems using titanium alkoxides, organic solvents such as formamides or ionic liquids with low water contents were used as the continuous phase to reduce the reaction rate of titanium alkoxides.[3,13] However, the organic solvents are not appropriate for the continuous phase in the microfluidic devices because of their high cost and toxicity. Also, soft materials of microfluidic devices are restricted by unfavorable effects such as deformation and swelling caused by organic solvents.[14]

Alternatively, chemical modification of metal alkoxides with glycerol, long chain acids or β-diketones reduces the rate and extent of hydrolysis by chelating parts of the coordination sites of alkoxides and thereby enables us to use water as the continuous phase instead of organic solvents.[15] In this work, long chain acid (octanoic acid) or photocurable polymer resin of ethoxylated trimethylolpropane triacrylate (ETPTA) was used as an oil phase, which contained titanium n-butoxides (TBT) as a precursor. Carboxylates in octanoic acid and acrylates in ETPTA effectively modify the reactivity of TBT, resulting in a yellow homogeneous and transparent solution. In addition, it is easy to handle octanoic acid or ETPTA because of its low toxicity.

We added a triblock copolymer Pluronic F108 in the continuous water phase at 1 wt % as an emulsion stabilizer. When the oil drops came in contact with the aqueous phase, Ti−O−Ti linkages began to form at the oil−water interface. Degree of reactions was indicated by a colormetric change from yellow to white. Formation of amorphous titania completed within 24 h for octanoic acid. The formation of Ti−O−Ti linkages was confirmed by FTIR studies, see the Supporting Information, Figure S2.

The SEM images in Figure 2 show the microspheres prepared with octanoic acid (a, b) or ETPTA (c, d) before (a, c) and after (b, d) heat treatment at 500 °C for 1 h, respectively. The organic phase in the core of titania shells prepared with octanoic acid was removed with ethanol. For ETPTA drops, UV-irradiation transformed the drops into core−shell microspheres (ETPTA @TiO_2) and calcination at 500 °C removed the ETPTA cores. The thickness of the titania shells in b is about 1.4 μm as shown in the cross-sectional TEM image in Figure S3 of the Supporting Information. It can be noted from Figure 2 that the uniformity in size and shape of the titania shells obtained after drying and calcination was not as high as the drops. This is because substantial weight loss, formation of pores, and shape deformation occurred during reaction and calcination at high temperatures. Smooth shells were formed with octanoic acid even after drying and calcination, whereas use of ETPTA led to size reduction and rough surface morphology after calcination. For experimental details of ETPTA-TBT system, see the Supporting Information, Figure S4.

In addition to its simplicity in preparing inorganic hollow spheres, our emulsion method enables us to fabricate hybrid shells of titania with embedded nanoparticles (NPs) in a single step. Quantum dots (QDs) for bioimaging and biolabling and/or magnetic particles (MPs) for biotargeting and biosensing can be used as the nanoparticles.[16,17] The advantage from the NP-TiO_2 hybrid shells is 2-fold; functionality from NPs and biocompatibility from TiO_2.[18,19] The functional NPs can be introduced without exposure into in vivo cellular environments for clinical applications because biocompatible titania prevents a direct contact between cells and NPs as a matrix for NPs.

The formation of NP-TiO_2 hybrid shells are achieved by including nanoparticles in the oil phase together with titania precusors. NPs in oil phase are captured at the drop interface on which sol−gel reactions of titanium alkoxides occurred. Previously, shells with embedded nanocrystals have been prepared by consecutive coadsorption of polyelectrolytes and nanocrystals[20,21] or solvent-controlled precipitation of nanocrystals[22] on latex spheres. These methods employ stepwise processes and the subsequent removal of the latex spheres accompanies shape deformation due to low mechanical strength of nanocrystal-embedded layers. Moreover, exchanging ligands of nanoparticles to finely disperse nanoparticles in aqueous or alcohol medium reduces quantum yield of QDs. On the other hand, the microfluidic emulsification used here provides stable NP-TiO_2 composite shells in a single step even without modification of ligands.

First, titania shells with incorporated QDs were fabricated by microfluidic emulsification of TBT-octanoic acid in aqueous medium. Oil drops contained 1 wt % TBT and 0.1 wt % CdS nanoparticles. Luminescent CdS nanocrystals embedded in titania shells were observed through confocal

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(13) Nakashima, T.; Kimizuka, N. *J. Am. Chem. Soc.* **2003**, *125*, 6386.
(14) Lee, J.; Park, C.; Whitesides, G. *Anal. Chem.* **2003**, *75*, 6544.
(15) Dunuwila, D.; Gagliardi, C.; Berglund, K. *Chem. Mater.* **1994**, *6*, 1556.
(16) Wang, D.; He, J.; Rosenzweig, N.; Rosenzweig, Z. *Nano Lett.* **2004**, *4*, 409.
(17) Tan, T.; Selvan, S.; Zhao, L.; Gao, S.; Ying, J. *Chem. Mater.* **2007**, *19*, 3112.
(18) Carbone, R.; Marangi, I.; Zanardi, A.; Giorgetti, L.; Chierici, E.; Berlanda, G.; Podesta, A.; Fiorentini, F.; Bongiorno, G.; Piseri, P.; Pelicci, P.; Milani, P. *Biomaterials* **2006**, *27*, 3221.
(19) Seo, J.; Chung, H.; Kim, M.; Lee, J.; Choi, I.; Cheon, J. *Small* **2007**, *3*, 850.
(20) Susha, A.; Caruso, F.; Rogach, A.; Sukhorukov, G.; Kornowski, A.; Mohwald, H.; Giersig, M.; Eychmuller, A.; Weller, H. *Colloids Surf., A* **2000**, *163*, 39.
(21) Wang, D.; Rogach, A.; Caruso, F. *Nano Lett.* **2002**, *2*, 857.
(22) Radtchenko, I.; Sukhorukov, G.; Gaponik, N.; Kornowski, A.; Rogach, A.; Mohwald, H. *Adv. Mater.* **2001**, *13*, 1684.

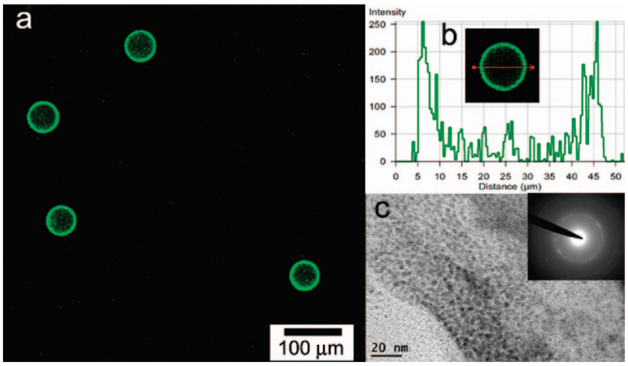

Figure 3. (a) Confocal microscopy image of titania shells with embedded luminescent CdS nanocrystals. (b) Profile of luminescence intensity in a single microsphere. (c) TEM image of quantum dots dispersed in an amorphous titania shell. Inset is the selected area diffraction pattern confirming the existence of the nanocrystals.

microscopy, as shown in Figure 3a. Fluorescence intensity profile over a cross-section of the titania shell in Figure 3b indicates the diameter of hollow spheres and the thickness of shells are about 45 and 5 μm, respectively. TEM image of Figure 3c for the fractured shells confirmed that CdS nanocrystals were dispersed uniformly in amorphous titania matrix. CdS nanocrystals used here were synthesized by reaction of Cd-oleylamine and sulfur.[23] Optical properties of CdS and supplemental fluorescence images are shown in Figure S5 and S6 of the Supporting Information.

Also, we demonstrated embedding multicomponent nanoparticles in titania shells. Octanoic acid containing TBT (1 wt %) and two different nanocrystals CdS (0.1 wt %) and Fe_2O_3 (0.1 wt %) were sonicated for 20 min to disperse the nanoparticles finely in the oil phase. Both nanocrystals have the same surface capping ligands (oleylamine). Following the same procedures, oil-in-water emulsion drops were generated in the microfluidic device. After the formation of titania shells and washing with ethanol for several times, the prepared microspheres were observed and analyzed by SEM and EDX as shown in a and b in Figure 4.

EDX analysis of the titana shells confirmed the incoporation of CdS and Fe_2O_3 nanoparticles and showed that the contents of the constituent atoms were 7.7 wt% (Cd), 26.7 wt% (S), 61.4 wt% (Ti), and 4.3 wt% (Fe). Cross-sectional TEM images of the titania shells were obtained through ultrathin section of the shells. TEM images confirmed that the binary component nanocrystals were embedded in amorphous titania matrix and assembled at the interfaces (Figure 4c). The high-resolution TEM image in Figure 4d shows coembedment of Fe_2O_3 and CdS nanoparticles at the interfaces. The assemblies of the ligand-stabilized nanoparticles at the interfaces were driven by the reduction in interfacial free energy.[24] The migration of nanoparticles toward the interface is an essential feature of the present emulsion-based method for preparing hollow spheres with embedded nanoparticles. In our system, titania shell grows as the reaction (formation of Ti−O−Ti linkages) proceeds at the liquid−liquid interface, toward which the nanoparticles migrate continuously. Therefore, nanoparticles reside in the outer edge as well as in the middle of the shell.

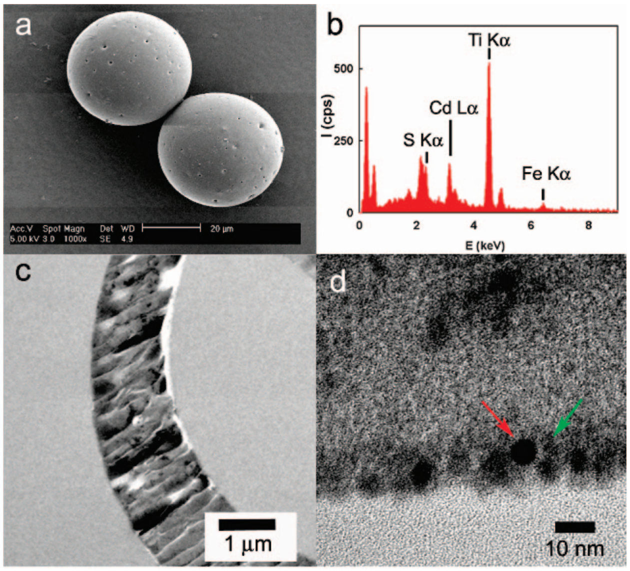

Figure 4. (a) SEM image of the prepared titana shells incoporated with CdS and Fe_2O_3 nanoparticles and (b) EDX (energy-dispersive Xray) analysis results. (c, d) TEM images at different magnifications of the titania shells embedded with CdS (2−3 nm) and Fe_2O_3 (5 nm) nanocrystals. Titania shells were cured in epoxy resin, followed by sectioning into ultrathin slices of 50−70 nm in thickness. Fe_2O_3 and CdS nanoparticles are pointed by red and green arrows in (d), respectively.

In summary, NP-TiO_2 hollow microspheres were fabricated by controlled chemical reaction of metal alkoxides and consolidation of nanoparticles at the interfaces of the emulsion drops in a coflow microfluidic device. The resulting hollow microspheres are highly monodisperse with good dispersion stability without coagulation by virtue of coflow microfluidic device. In addition, the functional nanoparticles were confined mainly in the titania shells. The proposed synthesis scheme provides a simple and controllable route for fabricating multifunctional inorganic microspheres.

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Supporting Information Available: Details in experimental procedures, FT-IR results of titania shells, absorption and emission spectra of CdS, and supplemental confocal images (PDF). This material is available free of charge via the Internet at http://pubs.acs.org

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(23) Joo, J.; Na, H.; Yu, T.; Yu, J.; Kim, Y.; Wu, F.; Zhang, J.; Hyeon, T. *J. Am. Chem. Soc.* **2003**, *125*, 11100.

(24) Lin, Y.; Skaff, H.; Emrick, T.; Dinsmore, A.; Russell, T. *Science* **2003**, *299*, 226.