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A Facile and Continuous Fabrication of Polyimide Hollow Nanoparticles Using a Microfluidic System

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A facile and continuous synthesis method of polyimide hollow nanoparticles has been developed by microemulsion reprecipitation method using a microfluidic system within a short reaction time (10 s). The mean particle size and the coefficient of variation were 314 nm and 0.22, respectively. We also successfully demonstrated that the polyimide hollow nanoparticles can be used as a nanocontainer as well as nanoreactor by retracting a chemical dye such as Rhodamine 6G.

In recent years, fabrication of hollow spheres has attracted much attention because of their many potential applications such as adsorbents, low dielectric fillers, nanocontainers as drug delivery carriers, and nanoreactors.[1] Polyimide (PI) hollow nanoparticles (NPs) are promising next generation materials and might have potential to act as nanoreactors with high stability and specific reaction selectivity due to their molecular sieve function. PIs have excellent physical properties like high thermal stability, high mechanical durability, exceptional chemical resistance, and high elasticity, which could be employed extensively as a representative high-performance polymer in microelectronics, photonics, optics, and aerospace industries.[2]

Different template methods are generally used for the synthesis of polymer hollow particles.[3] For example, core template such as polymer or silica particles is dispersed into water, followed by coating with polymer as shells via surface polymerization processes or layer-by-layer (LbL) adsorption using electrostatic attraction, and finally removal of template results in hollow particles. Although template methods with stepwise operations can fabricate hollow particles simply, these methods are done in aqueous medium, often require strictly controlled synthetic conditions, and are very expensive and time-consuming. Commonly, PI NPs are fabricated by dehydration of precursor of PI, poly(amic acid) (PAA) under nonaqueous conditions.[4] Thus, there are many shortcomings when the above-mentioned template method is applied to prepare PI hollow NPs, and to the best of our knowledge, there is no existing method for continuous synthesis of PI hollow NPs.

Recently, chemical microprocessing has been applied for the preparation of NPs.[5] Chemical microprocessing is generally defined as continuous flow through regular domains with characteristic dimensions of internal fluid channels, typically in the sub-millimeter range, thereby, microfluidic systems can achieve the control of rapid heating and mixing of streams with good heat and mass-transfer properties.[6]

Previously, we developed a new continuous method of PI nonhollow NPs and proposed a new strategy of emulsion reprecipitation method for the synthesis of NPs and controlling the particle sizes.[7] The described method can produce PI nonhollow NPs continuously at the rate of 0.24 g min^{-1} for laboratory scale. Therefore, in this report, we applied the microfluidic system to synthesize the PI hollow NPs, demonstrated a continuous process with simple and easy operations, and show their potential as a nanocontainer by retracting Rhodamine 6G.

To prepare the PI hollow NPs, we used a solution of PAA of PMDA–ODA synthesized from pyromellitic dianhydride (PMDA) and 4,4′-oxydianiline (ODA) in *N*-methyl-2-pyrrolidone (NMP) and *n*-hexane as a poor solvent of PAA. To cyclodehydrate the PAA particles, pyridine with acetic anhydride was used as a catalyst and a dehydrating agent. For the formation of hollow particles, poly(methyl methacrylate) (PMMA, M_W: 15000) and poly(vinylpyrrolidone) (PVP, M_W: 29000) were used as porogens and added in PAA solution. All the chemicals used were reagent grade, purchased from Sigma-Aldrich Chemical Co. and used without further purification. Dynamic light-scattering (DLS) spectroscopy (DLS-7000, Otsuka Electronics Co., Ltd.) was used to determine particle size and size distribution of PI hollow NPs. External appearance of particles was observed by scanning electron microscopy (SEM, JSM-6700F, JEOL Ltd.) operated at an acceleration voltage of 1 kV and emission current of 10 µA. Observation of inner structure of PI hollow NPs was performed using transmission electron microscopy (TEM, TECNAI G2; FEI Co.). A laser scanning confocal microscope (FV300, OLYMPUS Co.) was used to collect light-scattering and luminescence images of PI hollow NPs introducing Rhodamine 6G solution. He-Ne (632 nm) and Ar$^+$ (488 nm) lasers were used as incident beams for scattering and luminescence images, respectively.

Figure 1 shows the schematic fabrication method of the dispersion liquid containing PI hollow NPs. Fabrication of PI hollow NPs was similar to that reported previously.[7] We used a Y-type micromixer (channel width: 500 µm) followed with a micro heat exchanger (channel width: 2000 µm) made of stainless steel (KeyChem-L, YMC Co., Ltd., Japan). NMP solution of PAA (1 wt %) with porogen (0.4 wt %) and *n*-hexane were introduced into the first micromixer by pumps (JASCO PU-2086). The streams of the NMP solution of PAA (0.5, 1, and 2 mL min^{-1}, respectively) were struck against an *n*-hexane

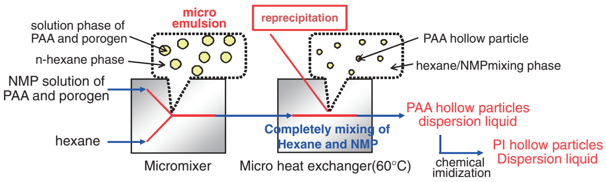

Figure 1. Schematic representation of the emulsion reprecipitation method for PI hollow nanoparticles using microfluidic system.

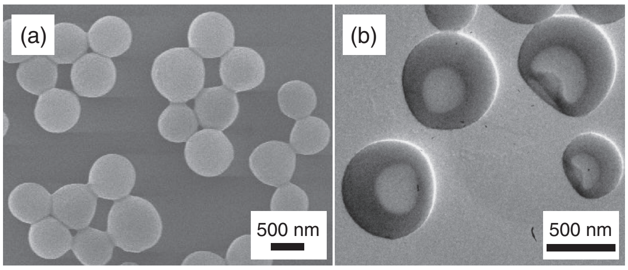

Figure 2. (a) SEM and (b) TEM images of typical PI hollow nanoparticles. Nanoparticles were fabricated by using PAA (1 wt %)–PMMA (0.4 wt %) solution.

stream (10 mL min^{-1}) at ambient temperature followed by the introduction to micro heat exchanger at 60 °C ± 0.1 °C through a Teflon tube (i.d.: 500 µm, length: 15 cm). The dispersion liquid of PAA hollow NPs was collected by glass vessel heated at 60 °C; the total residence time from the mixing point to the end was 63 ms.

When the NMP was introduced into the *n*-hexane stream, we can see that the NMP is immiscible in the first micromixer and then changes to miscible in hexane rapidly after heating in the heat exchanger. After forming a uniform liquid (Figure 1S in a Supporting Information; SI),[8] PAA hollow particles were reprecipitated. Pyridine and acetic anhydride were added to the vessel to cyclodehydrate PAA hollow particles, and then yellow PI hollow particles dispersed in a liquid were formed after stirring for 1 h at 60 °C. After cooling to room temperature, phase separation of *n*-hexane and NMP occurred in the static condition, and then the clear upper phase of *n*-hexane was removed. Finally, PI hollow NPs were separated simply by filtration of NMP phase with a membrane filter (pore size: 0.45 µm), washed with methanol three times, and dried in vacuo. At this stage, the porogen still remains in the as-prepared particles and will be removed by thermal decomposition without deformation of the particle morphology.[1b]

Figure 2 shows a SEM image (a) and corresponding TEM image (b) of PI hollow NPs when we used a composite solution of PAA (1 wt %) and PMMA (0.4 wt %). The SEM confirms the spherical morphology of particles without any pores on the surface as shown in Figure 2a, and Figure 2b suggests the hollow spherical morphology with the presence of one or several low-density domains in the center of particles. The concave shape supports the presence of a pore inside. When we also used another porogen, PVP, instead of PMMA, similar hollow NPs as shown in Figure 2S in SI were obtained.[8] On the other hand, without addition of porogen (Figure 3S in SI),[8] nonhollow NPs were formed without any low-density domains.

According to the results, we propose the formation mechanism of PI hollow NPs as follows.[1b] When the two streams of NMP solution of PAA/PMMA composite and *n*-hexane were mixed in the micromixer at 25 °C, droplets of the NMP solution were formed in *n*-hexane medium. NMP and *n*-hexane were completely dissolved and formed a single phase over 50 °C; therefore, after heating to 60 °C by micro heat exchanger, NMP was transferred into *n*-hexane phase from the droplets of NMP solution. With transferring NMP into *n*-hexane medium from the PAA/PMMA composite droplets, the phase of PMMA-rich solution was separated inside the PAA/PMMA composite droplets. By further transfer of NMP from the droplets phase-separated, the outside of droplets became solidified as PAA solid phase due to the reprecipitation effect. As a result, the PMMA-rich phase fixed inside PAA particle. Finally, by the chemical imidization of PAA hollow particles, these particles converted to PI hollow particles.

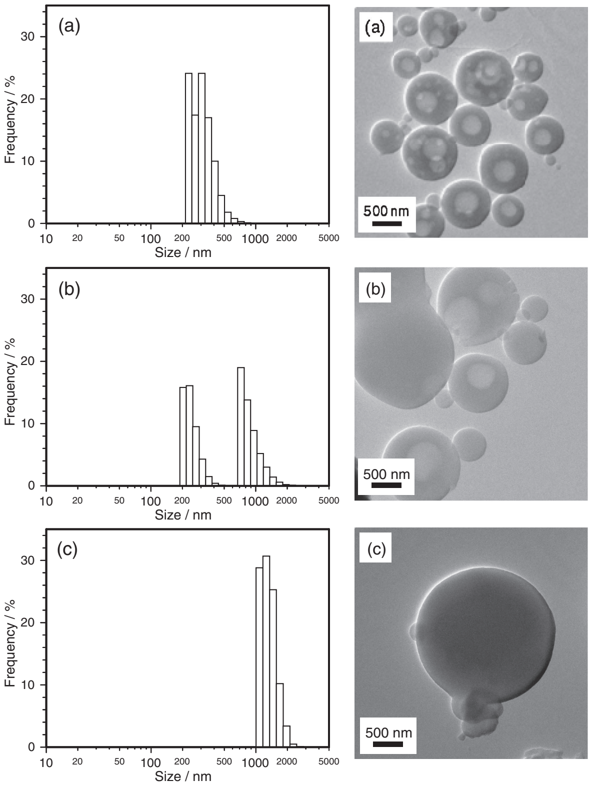

Figure 3. Size distribution of PI particles fabricated by various flow rates of PAA–porogen solution (left hand), and TEM images of corresponding the particles (right hand). (a) 0.5, (b) 1, and (c) 2 mL min^{-1}.

To check the influence of flow rate of polymer composite solution on a structure of PI NPs, synthesis of PI hollow NPs with the different flow rates of 0.5, 1.0, and 2.0 mL min^{-1} with fixed *n*-hexane flow rate (10 mL min^{-1}) was investigated. The results were shown in Figure 3 with the size-distributions (left) and TEM images (right) of PI hollow NPs. At a flow rate of 1.0 mL min^{-1} of PAA/PMMA composite solution (Figure 3b), we successfully obtained PI hollow NPs having a single pore in each particle. However, when a slower flow rate of 0.5 mL min^{-1} (Figure 3a) was used, some PI hollow NPs with multi inner pores were formed with a single particle size distribution of mean particle size 314 nm and variation coefficient of 0.22.

When the flow rate was faster, i.e., 2 mL min^{-1} (Figure 3c), nonporous particles with larger particle size of 1333 nm were formed. This indicates that the phase separation in the PAA/PMMA composite droplets did not occur, because of the absence of transferring NMP to *n*-hexane. Subsequently PMMA-rich phase was not separated in the droplets of PAA/PMMA solution phase. Finally, PAA was dehydrated and a PI nonhollow NP generated inside a droplet with PMMA. To confirm these phenomena, we checked the solubility of NMP with PMMA into

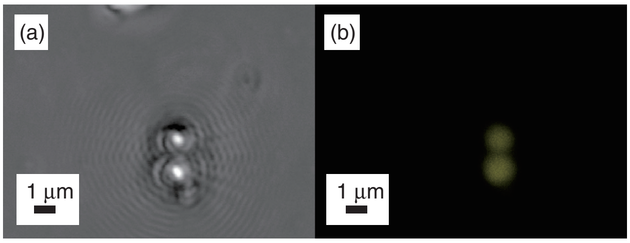

Figure 4. Confocal microscopy images of PI hollow microparticles after immersion treatment into Rhodamine 6G solution. (a) Light-scattering image, (b) luminsecsence image.

n-hexane at the same volume ratio of 2 to 10, and interestingly, NMP with PMMA did not dissolve completely and maintained two liquid phases even at 60 °C,[9] but a single liquid phase was formed at 60 °C when the ratio was 0.5 or 1.0 to 10. Therefore, even after the formation of NMP emulsion with PAA/PMMA composite, the third component of PMMA prevents the formation of a single phase between NMP and *n*-hexane.

Generally, polymers possess many voids, in which small molecules can be absorbed and percolated easily. Therefore, some molecules can penetrate through the shell of nano- and microcapsules easily and reach an inner pore. To utilize the inner pore of PI hollow NPs as nanostorages and nanoreactors, Rhodamine 6G was introduced into PI hollow NPs by simple impregnation. The PI NPs (3 mg) and Rhodamine 6G (5 mg) were simply put into NMP (2.5 g), and the mixture was irradiated with ultrasound for 30 min at room temperature to form a slurry. After ultrasonic treating, the slurry was centrifuged at 12000 rpm for 5 min, and a red solution with orange sedimentation was obtained. After the red clear solution was removed, orange sedimentation was redispersed into NMP by ultrasonic irradiation for washing excess Rhodamine 6G. Centrifuging and washing operation were repeated until the red color of the supernatant disappeared. Finally, the particles were redispersed into acetone and cast on a glass slide for observation by a laser scanning confocal microscope as shown in Figure 4.

Figure 4 shows light-scattering (a) and luminescence images (b) of PI hollow particles after immersion treatment with Rhodamine 6G. With naked-eye observation, we clearly observed a characteristic strong yellow luminescence, which derives from Rhodamine 6G, and luminescence was mainly seen from the core of the particles (Figure 4b). This indicates that Rhodamine 6G can percolate through the shell of PI NPs and can be collected at an inner pore, because in the absence of core, doughnut-like images must be observed.[10] From luminescence measurement, the specific peak at 572 nm attributed to the luminescence from Rhodamine 6G was observed (Figure 4S in SI).[8] It is well-known that in a bulk state, Rhodamine 6G shows no luminescence because excitation is annihilated by a intermolecular interaction. Therefore, Figure 4b indicates that Rhodamine 6G exists as a monomer in solvent inside the inner pore of PI hollow NPs and/or in the shell matrix and that these NPs can act as nanocontainers. We also tested to absorb Au NPs prepared by a microreactor into this PI hollow NPs.[11] However, when the smallest Au NPs were used, Au NPs could not be percolated into the inner pore but just absorbed on the surface of PI hollow NPs.

In summary, we developed a facile and continuous synthetic method of PI hollow NPs by using microemulsion reprecipitation method with a microfluidic system within the short residence time of 10 s. The described method can be applied to prepare a variety of PI hollow NPs by changing the starting PAA. We also demonstrated that this PI hollow NP has the potential to be used as a nanocontainer and nanoreactor by permeation of Rhodamine 6G.

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