

PREPARATION OF SILICA/POLY(METHACRYLIC ACID)/POLY(DIVINYLBENZENE-*CO*-METHACRYLIC ACID) TRI-LAYER MICROSPHERES AND THE CORRESPONDING HOLLOW POLYMER MICROSPHERES WITH MOVABLE SILICA CORE*

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Abstract Hollow poly(divinylbenzene-*co*-methacrylic acid) (P(DVB-*co*-MAA)) microspheres were prepared by the selective dissolution of the non-crosslinked poly(methacrylic acid) (PMAA) mid-layer in ethanol from the corresponding silica/PMAA/P(DVB-*co*-MAA) tri-layer hybrid microspheres, which were afforded by a three-stage reaction. Silica/PMAA core-shell hybrid microspheres were prepared by the second-stage distillation polymerization of methacrylic acid (MAA) *via* the capture of the oligomers and monomers with the aid of the vinyl groups on the surface of 3-(methacryloxy)propyl trimethoxysilane (MPS)-modified silica core, which was prepared by the Stöber hydrolysis as the first stage reaction. The tri-layer hybrid microspheres were synthesized by the third-stage distillation precipitation copolymerization of functional MAA monomer and divinylbenzene (DVB) crosslinker in presence of silica/PMAA particles as seeds, in which the efficient hydrogen-bonding interaction between the carboxylic acid groups played as a driving force for the construction of monodisperse hybrid microspheres with tri-layer structure. The morphology and the structure of silica core, silica/PMAA core-shell particles, the tri-layer hybrid microspheres and the corresponding hollow polymer microspheres with movable silica cores were characterized by transmission electron microscopy (TEM), Fourier transform infrared spectroscopy and X-ray photoelectron spectroscopy (XPS).

Keywords: Tri-layer hybrid microspheres; Hollow polymer microspheres with movable core; Distillation precipitation polymerization.

INTRODUCTION

The development of composite micro- and nano-particles consisting of either organic or inorganic cores coated with shells of different chemical composition has been a fundamental focus of chemical research. The organic-inorganic core-shell composite hybrid materials, which combine the properties of inorganic and organic building components within a single material, have attracted increasing attention from material scientists due to the combination of the thermally stable and robust inorganic blocks and flexible organic blocks with various functional groups^[1,2]. These composite hybrid materials exhibit novel and excellent properties (*e.g.* mechanical, chemical, electrical, rheological, magnetic, optical and catalytic) by varying the composition, dimension, and structure of the components, which have found diverse applications including as drug delivery system (DDS), diagnostics, coatings and protecting sensitive agents, such as enzymes and proteins^[2–8].

Silica/polymer composite hybrid particles with diverse interesting morphologies, such as organic core/silica shell^[9], silica core/organic shell^[6], silica/polymer/silica tri-layer structure^[10], raspberry-like^[11], multipod-like^[12],

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snowman-like^[13] and rabinun-like^[14], have been prepared by different techniques. The preparation of silica/polymer composite/hybrid materials can be generally classified into two categories: the assembly of the resultant silica and polymer particles *via* physical or physicochemical interaction^[15, 16], and direct polymerization of monomers on the surface of silica particles^[17, 18].

Hollow micro- and nano-spheres have attracted much attention for their broad applications in catalysis, paints, controlled drug delivery and as electronics materials^[19–21]. Various physical and chemical techniques, such as layer-by-layer (LbL) assembly^[22], colloidal crystal templating^[23] and surface-initiated atom transfer radical polymerization (ATRP)^[24], have been utilized for the preparation of functional hollow particles with different materials, including carbons, polymers, metals and inorganic materials. The physical and chemical properties of the hollow microspheres were more uniform in the case of narrow-size distribution, which made it easier to formulate a more sophisticated drug delivery system (DDS)^[25]. Further, the interaction of the hollow particles with biological cells was dependent on the particle size and size distribution^[26]. Hollow particles with complex structures and unique morphology have been prepared^[27, 28]. For instance, hollow polymer microspheres with movable guest cores have been developed, in which the gold nano-particles^[29, 30], hematite cores^[31, 32], tin^[33], silver^[34], silica^[35] and iron oxide^[36] have been incorporated by various methods. An important concern of hollow microspheres is to accommodate guest nano-particles in their cavity, which results in an interesting structure as hollow microspheres with movable cores and novel properties different from those of the host hollow microspheres and the guest nano-particles. In this context, the synthesis of hollow microspheres with movable silica nano-particles and narrow size distribution warrants further exploration, which will be of scientific and technical interest.

In our previous work, distillation precipitation polymerization has been developed as a facile and powerful technique for the synthesis of monodisperse polymer microspheres with different functional groups free of any additive^[37–42], the functional core-shell polymer microspheres^[43, 44] and the further development of hollow polymer microspheres with gold nanoparticles on the interior surfaces^[45]. More recently, polydivinylbenzene (PDVB) hollow microspheres with pyridyl groups located on the interior surface were prepared by a facile two-stage distillation precipitation polymerization with the aid of the vinyl group on the surface of PMAA core incorporated through the hydrogen-bonding interaction between the carboxylic acid group and pyridyl group of 4-vinylpyridine (VPy)^[46]. More recently, monodisperse silica/poly(*N,N'*-methylenebisacryamide) (SiO₂/PMBAAm) core-shell composite microspheres^[47], silica/polydivinylbenzene (SiO₂/PDVB) and silica/poly(ethyleneglycol dimethacrylate) (SiO₂/PEGDMA)^[48] core-shell hybrid microspheres, tri-layer Au/silica/PMBAAm^[30], hematite/silica/PDVB^[32], and poly(divinylbenzene-*co*-acrylic acid)/poly(acrylic acid)/poly(divinylbenzene-*co*-acrylic acid) (P(DVB-*co*-AA)/PAA/P(DVB-*co*-AA))^[49] microspheres were prepared by distillation precipitation polymerization and the further development of the functional hollow polymer microspheres were described. Herein, we introduce the distillation precipitation polymerization as a facile method for the synthesis of monodisperse tri-layer silica/poly(methacrylic acid)/poly(divinylbenzene-*co*-methacrylic acid) (SiO₂/PMAA/P(DVB-*co*-MAA)) microspheres containing silica core and functional polymer shell, in which the non-crosslinked PMAA mid-layer could be selectively removed in ethanol to afford the corresponding hollow polymer microspheres with movable silica cores. The present method offers an alternative approach to the preparation of monodisperse inorganic/polymer tri-layer microspheres and the further development of functional hollow polymer microspheres with movable nano-particle cores.

EXPERIMENTAL

Chemicals

Divinylbenzene (DVB, 80% divinylbenzene isomers) was supplied as technical grade by Shengli Technical Factory, Shandong, China, which was washed by 5% aqueous sodium hydroxide and water, then dried over anhydrous magnesium sulfate prior to use. Methacrylic acid (MAA) was purchased from Tianjin Chemical Reagent II Co. and purified by vacuum distillation. 3-(Methacryloxy)propyl trimethoxysilane (MPS) was bought from Aldrich and distilled under vacuum. Tetraethylorthosilicate (Si(OEt)₄, TEOS) was obtained from Aldrich

and used without further purification. Ammonia (25%, aqueous solution) was purchased from Tianjin Dongsheng Fine Chemical Reagent Factory, China. 2,2'-Azobisisobutyronitrile (AIBN) was provided by Chemical Factory of Nankai University and recrystallized from methanol. Acetonitrile (analytical grade, Tianjin Chemical Reagent II Co.) was dried over calcium hydride and purified by distillation before utilization. All the other reagents were analytical grade and used without any further purification.

Preparation of SiO₂/PMAA Core-Shell Hybrid Microspheres

Silica nanospheres were prepared according to the classical Stöber method^[50]: 4 mL of TEOS was added to the reaction mixture of 150 mL ethanol and 12 mL aqueous solution of 25% ammonium with vigorous stirring at room temperature, and the reaction was continued further for 24 h with stirring. The MPS-modified silica microspheres were afforded by coupling silica alcosol particles according to the literature^[51, 52]: excess MPS (2.0 g, 8.0 mmol) was introduced into 120 mL of the silica mixture under stirring in a 250 mL round-bottom flask. Coating of silica nanospheres with MPS was achieved by stirring the mixture of alcosol silica particles and MPS for 48 h at room temperature. The resultant MPS-modified silica particles were purified by three cycles of centrifugation, decantation and resuspension in ethanol with ultrasonic-bathing. The MPS-modified silica particles were dried in a vacuum oven at 50°C till constant weight.

The synthesis of MPS-modified silica nano-spheres was referred as the first-stage reaction in the present work.

The MPS-modified silica core particles were prepared as described above for the second-stage distillation precipitation polymerization to afford silica/polymer core-shell hybrid microspheres. A typical procedure for the polymerization of MAA in presence of MPS-modified silica particles as seeds was as following: 0.10 g of MPS-modified silica nanospheres were suspended in 40 mL of acetonitrile as a white suspension in a 100 mL two-necked flask under ultrasonic bathing. Then MAA (0.40 mL, as 1.0 vol% of the reaction system) together with AIBN initiator (0.008 g, 2 wt% relative to the MAA monomer) were dissolved in the suspension. The two-necked flask attaching with a fractionating column, Liebig condenser and receiver was then submerged in a heating mantle. The reaction mixture was heated from ambient temperature till the boiling state within 15 min, and the reaction mixture was kept under refluxing state for further 10 min. The white color was deepened during the heating process and the solvent was then distilled off the reaction system. The reaction was ended after 20 mL of acetonitrile was distilled from the reaction system within 70 min. After the polymerization, the resultant silica/PMAA core-shell hybrid microspheres were purified by repeated centrifugation, decantation and resuspension in acetonitrile with ultrasonic bathing for three times. The hybrid core-shell particles were finally dried in a vacuum oven at 50°C till constant weight.

Preparation of SiO₂/PMAA/P(DVB-co-MAA) Tri-layer Microspheres

A typical procedure for the distillation precipitation copolymerization of DVB as crosslinker and MAA in the presence of SiO₂/PMAA core-shell nanospheres as seeds to synthesize SiO₂/PMAA/P(DVB-co-MAA) tri-layer microspheres: In a dried 100 mL two-necked flask, 0.10 g of SiO₂/PMAA seeds were suspended in 40 mL of acetonitrile as a white suspension. Then DVB (0.20 mL, as 0.5 vol% of the whole reaction system), MAA (0.20 mL, as 0.50 vol% of the total reaction system) and AIBN (0.008 g, 2 wt% relative to the comonomers) were dissolved in the suspension. The two-necked flask attaching with a fractionating column, Liebig condenser and receiver was submerged in a heating mantle. The reaction system was heated from the ambient temperature till the boiling state within 10 min and kept under refluxing state for further 10 min. Then the polymerization was performed with distilling the solvent out of the reaction system and the reaction was ended after 20 mL of acetonitrile was distilled off the reaction mixture within 70 min. After the polymerization, the resultant SiO₂/PMAA/P(DVB-co-MAA) tri-layer microspheres were purified by repeating centrifugation, decantation and resuspension in acetonitrile for three times. Then the tri-layer microspheres were dried in a vacuum oven at 50°C till constant weight.

Preparation of Hollow P(DVB-co-MAA) Microspheres with Movable Silica Cores

Monodisperse SiO₂/PMAA/P(DVB-co-MAA) tri-layer microspheres were dispersed in ethanol solution with

ultrasonic bathing. Hollow P(DVB-co-MAA) microspheres with movable silica cores were subsequently redispersed in ethanol, followed by washing with ethanol and centrifugation for three times to remove the residual PMAA on the surface of the hollow microspheres. The resultant hollow polymer microspheres with movable silica cores were dried at room temperature in a vacuum oven till constant weight.

Characterization

The size and morphology of the polymer microspheres and hollow polymer microspheres with movable silica cores were characterized by transmission electron microscopy (TEM, Tecnai G2 20-S-TWIN) and scanning electron microscopy (SEM, Philips-XL-30). All the size and size distribution reflect the average of about 100 particles, which are calculated according to the following formula:

$$U = D_w / D_n \quad D_n = \sum_{i=1}^k n_i D_i / \sum_{i=1}^k n_i \quad D_w = \sum_{i=1}^k n_i D_i^4 / \sum_{i=1}^k n_i D_i^3$$

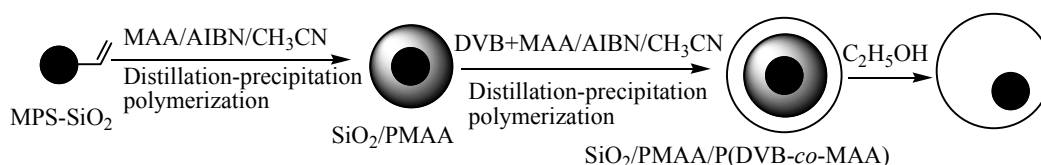
where U is the polydispersity index, D_n is the number-average diameter, D_w is the weight-average diameter, D_i is the particle diameter of the determined microparticles. The thickness of the outer shell-layer for the core-shell particles was calculated as half of the difference between the diameter of the core and that of core-shell particles.

Fourier transform infrared spectra were determined on a Bio-Rad FTS 135 FT-IR spectrometer over potassium bromide pellet and the diffuse reflectance spectra were scanned over the range of 4000–400 cm^{-1} .

X-ray photoelectron spectroscopy (XPS) analysis was carried out with a PHI 5300 XPS surface analysis system (Physical Electronics, Eden Prairie, MN, US) using a Mg $K\alpha$ X-ray source operating at 250 W and 13 kV ($h\nu = 1253.6$ eV). The electron binding energy of C_{1s} (284.6 eV) was used as the internal standard.

RESULTS AND DISCUSSION

Scheme 1 illustrated the synthesis of SiO_2 /PMAA/P(DVB-co-MAA) tri-layer microspheres *via* a three-stage reaction and the further development of the corresponding hollow P(DVB-co-MAA) microspheres with movable silica cores after the selective removal of the non-crosslinked PMAA mid-layer in ethanol.



Scheme 1 Preparation of silica/PMAA/polymer tri-layer hybrid particles and hollow polymer microspheres with movable silica core

Monodisperse MPS-modified silica nanospheres were prepared by the hydrolysis of siloxane TEOS *via* a sol-gel process having the active hydroxyl groups with the successive coating of MPS to incorporate the reactive vinyl groups on the surface^[51, 52]. The TEM micrographs of the MPS-modified silica nanospheres as shown in Fig. 1(a) indicated that the particles had spherical shape and smooth surface with an average diameter of 93 nm and monodispersity index (U) of 1.016. The MPS-modified silica nanospheres with the reactive vinyl groups on the surface would permit the growth of the particles by radical capture of the newly formed oligomers and monomers during the further-stage distillation precipitation polymerization of MAA to result in silica/PMAA core-shell hybrid microspheres.

Preparation of SiO_2 /PMAA Core-Shell Hybrid Microspheres

It is difficult to directly perform the polymerization of MAA on the surface of silica nanospheres for the preparation of silica/PMAA core-shell particles, as the hydrogen-bonding interaction between the active hydroxyl group on the surface of silica nanospheres and the carboxylic acid group of PMAA species was too weak to capture the newly formed MAA oligomers and monomers during the polymerization of MAA in

presence of silica nanospheres as seeds. To overcome such a problem, the reactive vinyl groups were incorporated onto the surface *via* the modification of silica nanospheres by further hydrolysis of MPS, which was confirmed by FT-IR spectra shown in Fig. 2 with the bands at 1632 and 1699 cm^{-1} corresponding to the stretching vibration of the vinyl groups and carbonyl groups of MPS component, respectively. Furthermore, the XPS spectrum in Fig. 3(b) for MPS-modified silica particles had an enhancing C_{1s} signal with simultaneous decrease of surface Si concentration from 41% in Fig. 3(a) before modification to 27% as shown in Fig. 3(b). In the present work, the MPS-modified silica nanospheres with reactive vinyl groups on the surface were used as seeds during the further-stage distillation precipitation polymerization for the growth of PMAA shell-layer to afford monodisperse silica/PMAA hybrid core-shell microspheres as shown in Scheme 1. The TEM micrograph of SiO_2 /PMAA core-shell microspheres by distillation precipitation polymerization of MAA in presence of MPS-modified silica nanospheres as seeds was shown in Fig. 1(b), in which a typical core-shell structure was clearly observed with a deep contrast of silica core and a light contrast of PMAA shell-layer. The results indicated that the SiO_2 /PMAA core-shell hybrid microspheres had spherical shape with uniform size distribution in absence of any secondary-initiated particles during the distillation precipitation polymerization of MAA, which implied that all the PMAA species were exclusively encapsulated over the MPS-modified silica nanosphere cores. Here, the encapsulation of the PMAA shell-layer onto the MPS-modified silica core was performed by the capture of the newly formed MAA oligomers and monomers during the polymerization *via* the reactive vinyl groups on the surface of the MPS-modified silica particles, which were consistent with the essential role of the residual vinyl groups located on the surface of PDVB microspheres for the formation of monodisperse polymer particles in precipitation polymerization^[53] and distillation precipitation polymerization^[37].

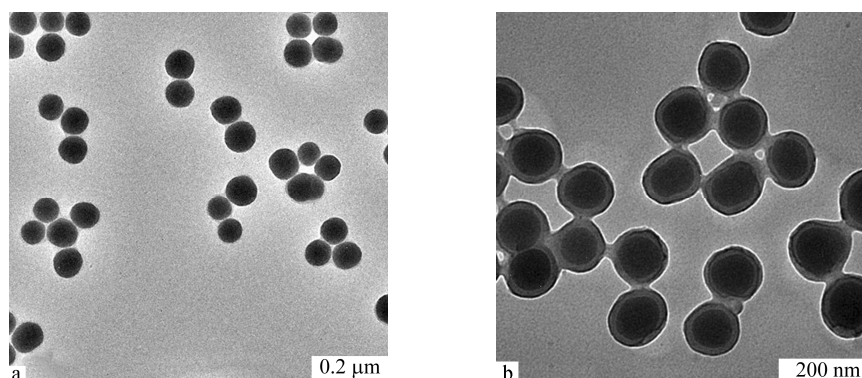


Fig. 1 TEM micrographs: (a) MPS modified silica nanoparticles and (b) silica/PMAA core-shell microspheres

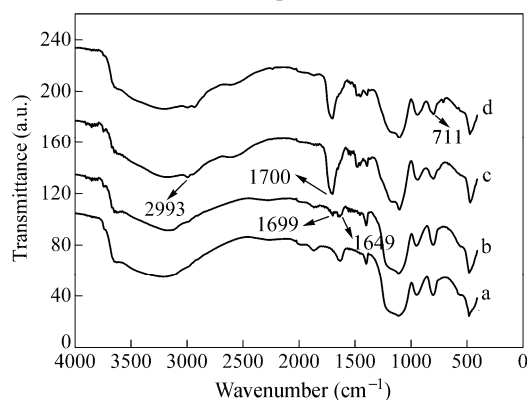


Fig. 2 FT-IR spectra: (a) silica nanoparticles, (b) MPS modified silica nanoparticles, (c) silica/PMAA core-shell microspheres and (d) silica/PMAA/P(DVB-co-MAA) tri-layer hybrids microspheres

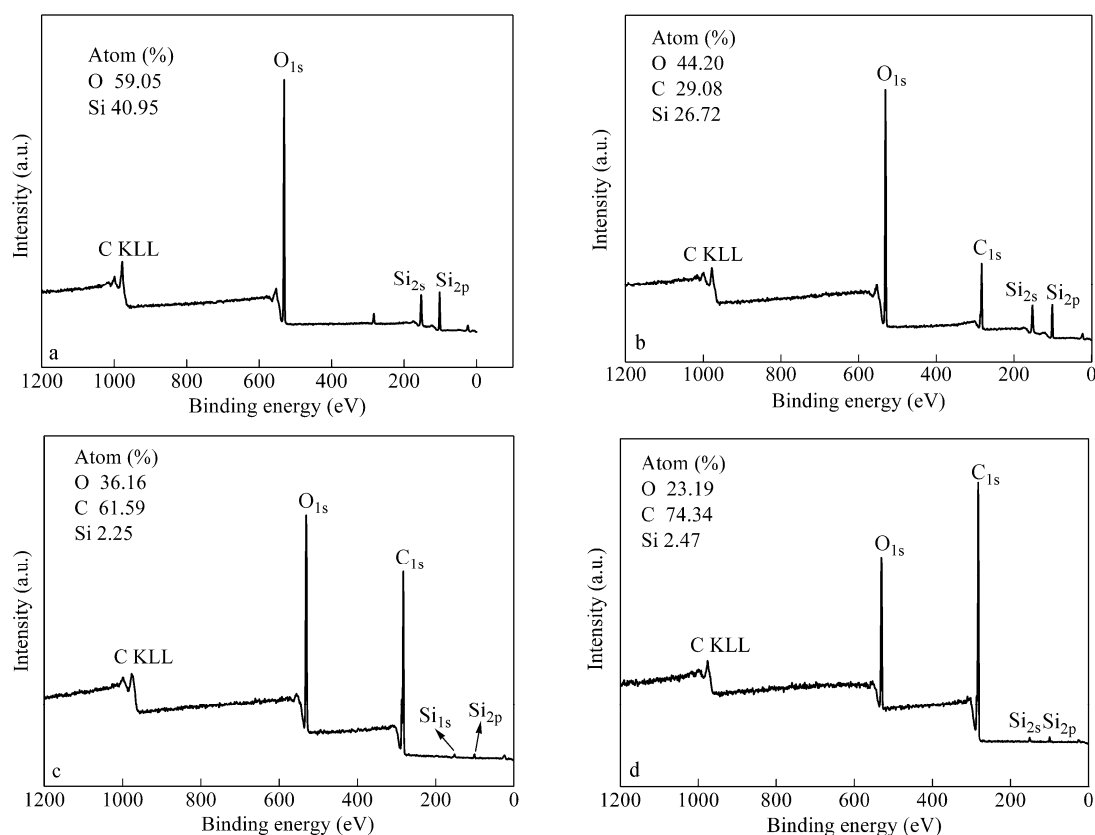


Fig. 3 XPS wide-scan spectra: (a) silica nanoparticles, (b) MPS modified silica nanoparticles, (c) silica/PMAA core-shell microspheres and (d) silica/PMAA/P(DVB-co-MAA) tri-layer hybrids microspheres

The particle size of the SiO_2 /PMAA core-shell hybrid microspheres was significantly increased from 93 nm of MPS-modified silica core to 122 nm with a monodispersity index (U) of 1.019 as summarized in Table 1 and the encapsulation yield of the PMAA shell-layer was 67%. This was much different from the results in the literature for both dispersion polymerization^[51, 52] and emulsion polymerization^[54], in which the morphology and the size distribution of the resultant hybrid microspheres were difficult to control and the encapsulation efficiency was low. The results meant that the thickness of the PMAA shell-layer was about 15 nm *via* coating of the MPS-modified silica cores during the further-stage distillation precipitation polymerization of MAA in the presence of MPS-modified silica nanospheres as the seeds in the present work.

The successful encapsulation of PMAA shell-layer onto the silica cores was confirmed further by FT-IR spectra and the XPS spectra in Fig. 2 and Fig. 3, respectively. The FT-IR spectra of SiO_2 /PMAA core-shell hybrid microspheres in Fig. 2 displayed the bands at 1700 cm^{-1} assigning to the stretching vibration of the carboxylic acid groups from PMAA component. Furthermore, the XPS spectrum of MPS-modified silica cores in Fig. 3(b) had the strong peaks at 531.4, 288.0, 150.0, and 102.1 eV corresponding to the binding energy of O_{1s} , C_{1s} , Si_{2s} , and Si_{2p} , respectively. While for the XPS spectrum of SiO_2 /PMAA core-shell hybrid microspheres in Fig. 3(c), the peaks at 531.4 and 288.0 eV were clearly observed ascribing to the binding energy of O_{1s} and C_{1s} from PMAA outer shell-layer and the peaks at 150.0 and 102.1 eV for the electronic binding energy for Si_{2s} and Si_{2p} were almost disappeared with simultaneous decrease of surface Si concentration from 27% of MPS-modified silica seeds to only 2% of SiO_2 /PMAA core-shell hybrid microspheres. All these results demonstrated that the PMAA shell-layer with thickness of 15 nm was successfully encapsulated onto the silica core microspheres *via* the further-stage distillation precipitation polymerization of MAA.

An important concern for the synthesis of such SiO₂/PMAA core-shell hybrid microspheres was to retain the particle monodispersity and prevented the secondary-initiated particle with the aid of surface vinyl groups of MPS-modified silica cores. A key requirement to obtain monodisperse core-shell microspheres by the present distillation precipitation polymerization was that the hydrogen-bonding interaction between the carboxylic acid groups as a driving force can grow the hybrid microspheres further during the polymerization. As a result, the transient gel layers on the particle surface were highly swollen and collapsed during the polymerization, while the newly formed MAA oligomers were captured with the aid of efficient hydrogen-bonding interaction between the carboxylic acid groups. In such a way, the particles grew to larger diameter in a uniform fashion to get monodisperse SiO₂/PMAA core-shell as illustrated in Scheme 1 *via* the polymerization in the case of suitable MAA loading as summarized in Table 1 in the present work. The preparation of monodisperse poly(methacrylic acid) (PMAA) microspheres by distillation precipitation polymerization in acetonitrile was reported in our previous paper, in which the growth mechanism of PMAA microspheres was investigated in detail^[55]. The highly swollen ability of the PMAA shell-layer indicated that the carboxylic acid groups on the shell-layer of SiO₂/PMAA core-shell hybrid microspheres were highly accessible, which permitted the further growth of the third-layer through the efficient hydrogen-bonding interaction between the carboxylic acid groups during the third-stage distillation precipitation polymerization to result in inorganic/polymer/polymer tri-layer structure microspheres.

Table 1. Reaction conditions, sizes, polymer shell-thicknesses, yields and parameters of the silica nanoparticles, silica/PMAA core-shell microspheres and silica/PMAA/P(DVB-co-MAA) tri-layer particles

Entry	D_n (nm)	D_w (nm)	U	Shell thickness (nm)	Yield (%)
SiO ₂	93	95	1.016	—	—
SiO ₂ /PMAA	122	124	1.019	15	67 ^a
SiO ₂ /PMAA/P(DVB-co-MAA)	170	172	1.014	24	7 ^b

^a Yield = $(M_{\text{SiO}_2/\text{PMAA}} - M_{\text{SiO}_2}) / M_{\text{MAA}} \times 100\%$;

^b Yield = $(M_{\text{SiO}_2/\text{PMAA/P(DVB-co-MAA)}} - M_{\text{SiO}_2/\text{PMAA}}) / M_{\text{(DVB-co-MAA)}} \times 100\%$

Preparation of SiO₂/PMAA/P(DVB-co-MAA) Tri-layer Microspheres

In our previous work, P(DVB-co-AA)/PMAA/P(DVB-co-AA) tri-layer structure microspheres were prepared by a three-stage distillation precipitation polymerization in neat acetonitrile with AIBN as initiator^[49], in which the hydrogen-bonding interaction between the carboxylic acid groups played an essential role in the formation of monodisperse tri-layer polymer microspheres. Here, SiO₂/PMAA core-shell hybrid microspheres contained many accessible carboxylic acid groups on the surface, which would capture the MAA monomer and soluble oligomers with carboxylic acid groups with the aid of the hydrogen-bonding interaction as illustrated in Scheme 1 to allow the further growth of the microspheres during the third-stage distillation precipitation copolymerizations of MAA and the crosslinker DVB resulting in tri-layer structure microspheres. The typical TEM and SEM micrographs of SiO₂/PMAA/P(DVB-co-MAA) tri-layer microspheres were shown in Fig. 4(a) and Fig. 4(b), respectively, which indicated that the tri-layer particles had spherical shape with lightly rough surface in Fig. 4(a). This may be attributed to the rigidity of the PDVB network. The absence of any secondary-initiated irregular particles for these tri-layer microspheres as shown in Figs. 4(a) and 4(b) demonstrated that the efficient hydrogen-bonding interaction between the carboxylic acid groups on the surface of SiO₂/PMAA seeds and PMAA component in the reaction system favored the efficient capture of the residual oligomers and comonomers from the solution to grow the tri-layer particles further during the third-stage distillation precipitation copolymerization. The average diameter of the particle size of SiO₂/PMAA/P(DVB-co-MAA) tri-layer particles was considerably enhanced to 170 nm as summarized in Table 1. These results implied that P(DVB-co-MAA) shell-layer with thickness of 24 nm were encapsulated onto the SiO₂/PMAA seeds through the third-stage polymerization. The tri-layer microspheres SiO₂/PMAA/P(DVB-co-MAA) retained monodispersion with U of 1.014, which indicated that the polymer outer shell-layers were uniformly coated onto the surface of the SiO₂/PMAA seeds during the third-stage polymerization. The yield of SiO₂/PMAA/P(DVB-

co-MAA) tri-layer microspheres was 7% as tabulated in Table 1. These results were consistent with those of the distillation precipitation polymerization of DVB^[37, 47] in our previous papers.

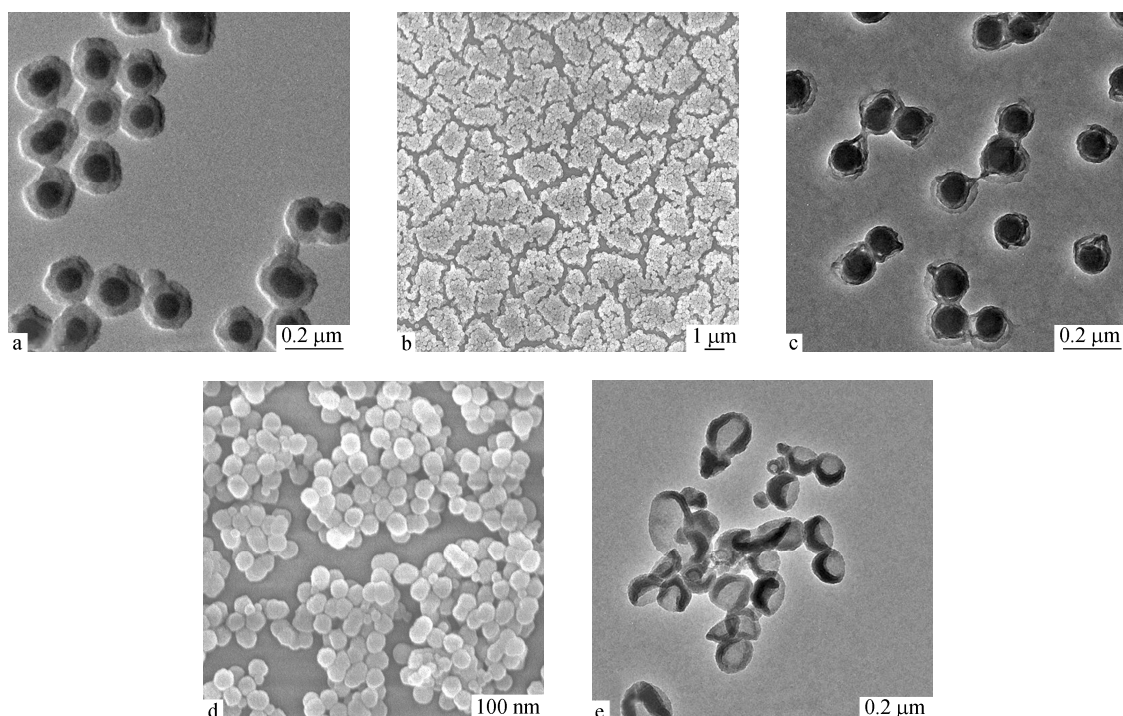


Fig. 4 Micrographs: (a) TEM of silica/PMAA/P(DVB-*co*-MAA) tri-layer hybrids microspheres (DVB 0.2 mL, MAA 0.2 mL), (b) SEM of SiO₂/PMAA/P(DVB-*co*-MAA) tri-layer hybrids microspheres (DVB 0.2 mL, MAA 0.2 mL), (c) TEM of hollow silica/PMAA/P(DVB-*co*-MAA) tri-layer hybrids microspheres (after dissolution of PMAA core for 6 h in ethanol), (d) SEM of hollow silica/PMAA/P(DVB-*co*-MAA) tri-layer hybrids microspheres (after dissolution of PMAA core for 6 h in ethanol) and (e) silica/PMAA/P(DVB-*co*-MAA) tri-layer hybrids microspheres (after dissolution of PMAA core for 6 h in ethanol)

To further prove the tri-layer structure of SiO₂/PMAA/P(DVB-*co*-MAA) microspheres, the surface components of SiO₂/PMAA seeds and tri-layer particles were determined by XPS spectra as shown in Figs. 3(c) and 3(d), respectively. The XPS spectrum of SiO₂/PMAA/P(DVB-*co*-MAA) tri-layer microspheres in Fig. 3(d) had an increasing C_{1s} signal from 62% to 74% with simultaneous decrease of surface O concentration from 36% to 23% comparing those of SiO₂/PMAA seeds. The new peak at 711 cm⁻¹ for the FT-IR spectrum of SiO₂/PMAA/P(DVB-*co*-MAA) tri-layer microspheres in Fig. 2 was attributed to the typical stretching vibration of the phenyl groups of PDVB component after the third-stage distillation precipitation polymerization, which also implied that P(DVB-*co*-MAA) outer shell-layer was successfully encapsulated onto SiO₂/PMAA seeds as the tri-layer structure. All these results confirmed the successful construction of the SiO₂/PMAA/P(DVB-*co*-MAA) tri-layer microspheres *via* the present three-stage reaction. Furthermore, outer shell-layer of the SiO₂/PMAA/P(DVB-*co*-MAA) tri-layer microspheres could be under a highly swollen-state, which permitted the subsequent removal of the non-crosslinked PMAA mid-layer to afford hollow polymer microspheres with movable silica cores.

Preparation of Hollow P(DVB-*co*-MAA) Microspheres with Movable Silica Cores

The non-crosslinked PMAA mid-layers of the resultant SiO₂/PMAA/P(DVB-*co*-MAA) tri-layer microspheres were selectively removed through the tiny pores of the outer polymer shell-layer in ethanol to get hollow P(DVB-*co*-MAA) microspheres with movable silica cores as illustrated in Scheme 1. The driving force for such

selective removal was the solubility of the non-crosslinked PMAA mid-layer in ethanol as solvent. The successful removal of the non-crosslinked PMAA mid-layer results in hollow P(DVB-*co*-MAA) microspheres with movable silica cores shown by typical TEM micrograph in Fig. 4(c) and SEM micrograph in Fig. 4(d) after the dissolution of PMAA core in ethanol for 6 h, respectively. The convincing hollow polymer microspheres were observed with the presence of circular rings of sectional spheres with an inner movable silica core and an interior cavity in the mid-layer in Fig. 4(c), while the hollow polymer particles were observed with good shape without deformation and broken shell-layers in Fig. 4(d). It was believed that the functional silica cores were free to move in the hollow P(DVB-*co*-MAA) spheres filled with solvent, as the silica cores were not located in the center of the hollow P(EGDMA-*co*-MAA) microspheres as shown in Fig. 4(c). More interestingly, as shown in Fig. 4(e), it was found that the silica seeds could be released out of the hollow polymer spheres by slightly destroying the polymer shell-layer of the resultant hollow P(DVB-*co*-MAA) structure *via* mechanical force during the dissolution of PMAA core, such as ultrasonication and centrifugation, which indicated that the functional silica cores were released out of the hollow spheres successfully. The release mechanism of the movable core from the hollow polymer microspheres may be due to the rigidity of the DVB network and the thin polymer shell layer. The development of hollow polymer microspheres was performed *via* the facile dissolution of the non-crosslinked mid-layer PMAA, which was different from the preparation of hollow TiO₂ nanospheres with movable silica nanoparticles *via* the calcination under high temperature to remove the polymer mid-layer in the literature^[35]. One of the most desirable characteristics of the oral delivery of peptides and proteins is the ability to protect the drugs from photolytic attack during their transit through the gastrointestinal (GI) tract. The release process in the present work may provide some effective guidance in drug protection and delivery and in mimic biological process. Furthermore, the study on the scope of this technique, including the extension to the synthesis of the other multi-layer and the corresponding hollow polymer microspheres with movable functional cores, and the applications of such functional hollow polymer microspheres, is in progress in our group.

CONCLUSIONS

Tri-layer SiO₂/PMAA/P(DVB-*co*-MAA) microspheres were synthesized by a facile route with a three-stage reaction, which included the modified Stöber technique for the synthesis of silica core with the subsequent two-stage distillation precipitation polymerization. Silica/PMAA core-shell hybrid microspheres with 15 nm of PMAA shell-layer were prepared by the second-stage distillation precipitation polymerization of MAA in the presence of MPS-modified silica nanospheres as seeds *via* the capture of the newly formed oligomers with the aid of the reactive vinyl groups on the surface of inorganic core and the efficient hydrogen-bonding interaction between the carboxylic acid groups for the growth of PMAA shell-layer. SiO₂/PMAA/P(DVB-*co*-MAA) tri-layer microspheres were synthesized by the third-stage distillation precipitation copolymerizations of MAA comonomer together with DVB crosslinker in the presence of silica/PMAA particles as seeds, in which the hydrogen-bonding interaction between the carboxylic acid groups acted as the driving force for the formation of monodisperse tri-layer polymer microspheres. Further, hollow P(DVB-*co*-MAA) spheres with shell-layer thickness of 24 nm and movable silica cores were developed *via* the selective removal of the non-crosslinked PMAA mid-layer in ethanol from the corresponding SiO₂/PMAA/P(DVB-*co*-MAA) tri-layer microspheres. The concept of hydrogen-bonding interaction to construct the tri-layer spheres and the further development of the corresponding hollow polymer spheres with movable functional cores are expected to be useful in the design of micro-reactors in catalysis, adsorption and drug delivery system (DDS).

REFERENCES

- 1 Zhang, Y.D., Lee, S.H., Yonnessi, M., Liang, K.W. and Pittman, C.U., *Polymer*, 2006, 47: 2984
- 2 Strachotova, B., Strachota, A., Ulchman, M., Slouf, M., Brus, J., Plestil, J. and Matejka, L., *Polymer*, 2007, 48: 1472
- 3 Giersig, M., Ung, T., Liz-Marzan, L.M. and Malvancym, P., *Adv. Mater.*, 1997, 9: 570
- 4 Zhou, J., Zhang, S.W., Qiao, X.G., Li, X.Q. and Wu, L.M., *J. Polym. Sci. Part A: Polym. Chem.*, 2006, 44: 3202
- 5 Fleming, M.S., Mandal, T.K. and Walt, D.R., *Chem. Mater.*, 2001, 13: 2210
- 6 Zhang, K., Chen, H.T., Chen, X., Chen, Z.M., Cui, Z.C. and Yang, B., *Macromol. Mater. Eng.*, 2003, 288: 380
- 7 Cho, J.D., Ju, H.T. and Hong, J.W., *J. Polym. Sci. Part A: Polym. Chem.*, 2005, 43: 658
- 8 Caruso, F., Spasova, M., Susha, A., Giersig, H. and Caruso, R.A., *Chem. Mater.*, 2001, 13: 109
- 9 Bourgeat-Lami, E., Tissot, I., Movat, C. and Lefebvre, F., *Macromolecules*, 2002, 35: 6185
- 10 Li, G.L., Liu, G., Kang, E.T., Neoh, K.G. and Yang, X.L., *Langmuir*, 2008, 24: 9050
- 11 Reculosa, S., Ponet-Legrand, C., Ravaine, S., Mongostaud, S., Ouguet, E. and Bourgeat-Lami, E., *Chem. Mater.*, 2002, 14: 2354
- 12 Reculosa, S., Mingotaud, C., Bourgeat-Lami, E., Duguet, E. and Ravaine, R., *Nano Lett.*, 2004, 4: 1677
- 13 Perro, A., Reculosa, S., Bourgeat-Lami, E., Duguet, E. and Ravaine, S., *Colloid Surf. A*, 2006, 284/285: 78
- 14 Barthet, C., Hickey, A.J., Carins, D.B. and Armes, S.P., *Adv. Mater.*, 1999, 11: 408
- 15 Kulbaba, K., Cheng, A., Bartole, A., Safa-Senat, A., Combs, N., Safa-Sefat, A., Greedan, J.E., Stöver, H.D.H., Ozin, G.A. and Manners, I., *J. Am. Chem. Soc.*, 2002, 124: 12522
- 16 Caruso, R.A., Susha, A. and Caruso, F., *Chem. Mater.*, 2001, 13: 400
- 17 Corcos, F., Lidenfeld, H., Giesig, M. and Möhwald, H., *J. Am. Chem. Soc.*, 1998, 120: 8523
- 18 von Werne, T. and Patten, T.E., *J. Am. Chem. Soc.*, 2001, 123: 7497
- 19 Shchukin, D.G., Sukhorukov, G.B. and Möhwald, H., *Angew. Chem. Int. Ed.*, 2003, 41: 4472
- 20 McDonald, C.J., Bouck, C.J., Chaupt, A.B. and Stevens, C.J., *Macromolecules*, 2000, 33, 1593
- 21 Li, G.L., Yang, X.Y., Wang, B., Wang, J.Y. and Yang, X.L., *Polymer*, 2008, 49: 3436
- 22 Park, M.K., Onishi, K., Locklin, J., Caruso, F. and Advincula, R.C., *Langmuir*, 2003, 19: 8550
- 23 Chen, Z., Zhan, P., Wang, Z.L., Zhang, J.H., Zhang, W.Y., Ming, N.B., Chan, C.T. and Sheng, P., *Adv. Mater.*, 2004, 16: 417
- 24 Mandal, T.K., Fleming, M.S. and Walt, D.R., *Chem. Mater.*, 2000, 12: 3481
- 25 Chattopadhyay, P., Shekunov, B.Y., Yim, D., Cipolla, D., Boyd, B. and Farro, S., *Adv. Drug Delivery Rev.*, 2007, 59: 444
- 26 Shiga, K., Muramatsu, N. and Kondo, T., *J. Pharm. Pharmacol.*, 1996, 48: 891
- 27 Dai, Z.F., Möhwald, H., Tiersch, B. and Dähne, L., *Langmuir*, 2002, 18: 9533
- 28 Yang, M., Ma, J., Zhang, C.L., Yang, Z.Z. and Lu, Y.F., *Angew. Chem. Int. Ed.*, 2005, 44: 6727
- 29 Kumata, K., Lu, Y. and Xia, Y.N., *J. Am. Chem. Soc.*, 2003, 125: 2384
- 30 Liu, G.Y., Ji, H.F., Yang, X.L. and Wang, Y.M., *Langmuir*, 2008, 24: 1019
- 31 Hao, L.Y., Zhu, C.L., Jiang, W.Q., Chen, C.N., Hu, Y. and Chen, Z.Y., *J. Mater. Chem.*, 2004, 14: 2929
- 32 Liu, G.Y., Yang, X.L. and Wang, Y.M., *Langmuir*, 2008, 24: 5485
- 33 Lee, K.T., Jung, Y.S. and Oh, S.M., *J. Am. Chem. Soc.*, 2003, 125: 1452
- 34 Cheng, D.M., Zhou, X.D., Xia, H.B. and Chan, H.S.O., *Chem. Mater.*, 2005, 17: 3578
- 35 Zhang, K., Zhang, X., Chen, H., Chen, X., Zhang, L., Zhang, J. and Yang, B., *Langmuir*, 2004, 20: 11312
- 36 Zheng, T., Pang, J.B., Tan, G., He, J., McPherson, G.L., Lu, Y., John, V.T. and Zhan, J., *Langmuir*, 2007, 23: 5143
- 37 Bai, F., Yang, X.L. and Huang, W.Q., *Macromolecules*, 2004, 37: 9746
- 38 Bai, F., Yang, X.L., Li, R., Huang, B. and Huang, W.Q., *Polymer*, 2006, 47: 5775
- 39 Lu, X.Y., Huang, D., Yang, X.L. and Huang, W.Q., *Acta Polymerica Sinica(in Chinese)*, 2007, (2): 103
- 40 Li, S.F., Yang, X.L. and Huang, W.Q., *Chinese J. Polym. Sci.*, 2005, 23(2): 197
- 41 Dai, Z., Yang, X.L. and Huang, W.Q., *Chinese J. Polym. Sci.*, 2007, 25(3): 303
- 42 Li, S.N., Yang, X.L. and Huang, W.Q., *Chinese J. Polym. Sci.*, 2007, 25(6): 555

- 43 Qi, D.L., Bai, F., Yang, X.L. and Huang, W.Q., *Eur. Polym. J.*, 2005, 41: 2320
- 44 Qi, D. L., Yang, X.L. and Huang W.Q., *Polym. Int.*, 2007, 56: 208
- 45 Liu, W., Yang, X.L. and Huang, W.Q., *Chinese J. Polym. Sci.*, 2009, 27(2): 275
- 46 Li, G.L., Yang, X.L. and Bai, F., *Polymer*, 2007, 48:3074
- 47 Liu, G.Y., Yang, X.L. and Wang, Y.M., *Polymer*, 2007, 48: 4385
- 48 Liu, G.Y., Zhang, H., Yang, X.L. and Wang, Y.M., *Polymer*, 2007, 48: 5896
- 49 Li, G.L. and Yang, X.L., *J. Phys. Chem. B.*, 2007, 111: 12781
- 50 Stöber, W. and Fink, A., *J. Colloid Interface Sci.*, 1968, 26: 62
- 51 Bourgeat-Lami, E. and Lang, J., *J. Colloid Interface Sci.*, 1999, 210: 281
- 52 Bourgeat-Lami, E. and Lang, J., *J. Colloid Interface Sci.*, 1998, 197: 293
- 53 Korprinarov, I., Hitchcock, A.P., Li, W.H, Yang, Y.M. and Stöver, H.D.H., *Macromolecules*, 2001, 34: 4424
- 54 Luna-Xavier, J.L., Guyot, A. and Bourgeat-Lami, E., *J. Colloid Interface Sci.*, 2002, 250: 82
- 55 Bai, F., Huang, B., Yang, X.L. and Huang, W.Q., *Eur. Polym. J.*, 2007, 43: 3923