

PREPARATION OF SINGLE-HOLE HOLLOW POLYMER NANOSPHERES BY RASPBERRY-LIKE TEMPLATE METHOD*

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Abstract Single-hole hollow polymer nanospheres were fabricated by raspberry-like template method using “graft-from” strategy through atom transfer radical polymerization (ATRP). Nanometer-sized silica spheres were covalently attached onto the surfaces of micrometer-sized silica spheres. Crosslinked polymer shells on the nano-sized spheres outside the attached area were formed by “graft-from” strategy through ATRP. After removal of the silica cores, single-hole hollow crosslinked polymer nanospheres were obtained. In this strategy, most of ATRP monomers may be used and thus many functional groups can be easily incorporated into the single-hole hollow crosslinked polymer nanospheres.

Keywords: Single-hole; Hollow polymeric nanoparticles; ATRP.

INTRODUCTION

Functional hollow nanospheres are of particular interest because of their potential applications such as controlled release of drugs, protection of biologically active species, removal of pollutants and as catalytic carriers and microreactors^[1–7]. The characteristics of hollow nanospheres such as high surface-to-volume ratio, low density and low coefficients of thermal expansion facilitate the manipulation of the surface properties of microspheres to control interactions with various species. However, in the encapsulation or release of the entities of interest, especially large entities such as proteins and DNA, their diffusion into or out the hollow nanospheres through the closed shell is usually a slow or even impossible process. To solve this problem, creating transverse holes or pores in the shell is required to facilitate mass transportation.

Recently, single-hole hollow polymer nanospheres have stimulated significant interests because of their higher effective diffusivity^[8–15]. Up to now, several representative strategies have been developed to fabricate the polymer materials with such structures, such as phase-separation method^[8], self-assembling of phase-separated polymer (SaPSeP) method^[9], interface-initiated emulsion polymerization method^[10, 11] and coaxial electrohydrodynamic atomization (CEHDA) method^[12]. The phase-separation process was also observed in most of the methods, and the hole in the surface of hollow polymer nanospheres was attributed to the evaporation efflux of the solvent or the concomitant microphase separation and symmetrical volume shrinkage. In the fabrication strategies in which phase-separation process was included, linear polymers such as polystyrene must be used. The application of the resulting single-hole hollow polymer nanospheres in good solvents of the polymer would not be possible because the polymer shell can be dissolved in such solvents. Guan *et al.*^[13]

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fabricated shell-crosslinked single-hole hollow polymer nanospheres by precipitation polymerization of acrylamide and ethylene glycol dimethacrylate that were adsorbed onto the surfaces of carboxyl-capped polystyrene beads due to the formation of hydrogen-bonds, followed by dissolving the polystyrene core. The formation of the hole was attributed to the shrinkage of the polymer shell during polymerization. However, the range of monomers usable in this strategy is limited. Another method, CEHDA method, required highly specialized equipment and/or processing environments^[12]. Notwithstanding these ingenious strategies, the design and preparation of single-hole hollow polymer nanospheres with well-controlled size and shape was still a significant challenge.

Raspberry-like composite particles have been prepared by heterocoagulation, templating, layer-by-layer assembly, emulsion polymerization, and chemical bonding^[16–20]. These composite particles have been successful in the construction of superhydrophobic/superhydrophilic surfaces because of their rough surface morphology. Hollow spheres and janus nanoparticles were also fabricated from such composite particles^[21, 22]. Here, we report a novel strategy for fabricating single-hole hollow polymer nanospheres by raspberry-like template method using surface-initiated ATRP polymerization. To the best of our knowledge, this study gives the first example of fabricating single-hole hollow polymer nanospheres by raspberry-like template method. In this strategy, most of the ATRP monomers may be used and thus many functional groups can be easily incorporated into the single-hole hollow crosslinked polymer nanospheres by using the corresponding monomers.

EXPERIMENTAL

Materials

Tetraethyl orthosilicate (TEOS), ammonium hydroxide (25%), acetic acid, succinic anhydride and hydrofluoric acid (HF, containing 40% of HF) were purchased from Tianjin Jinhuaoyongsheng Co. Ltd. Aminopropyltrimethoxysilane (APTMS) and 1-nonylamine were purchased from Alfa-Aesar. *N,N,N',N',N'*-pentamethyldiethyltrimine (PMDETA) and bromoisobutyl bromide (BIBB) were purchased from Acros. Cyclohexanone, triethylamine, (*N,N*-diethylamino)ethyl methacrylate (DEAEMA) and ethyleneglycol dimethacrylate (EGDMA) were distilled over CaH₂ under reduced pressure before use. All other chemicals were purchased commercially and used without purification.

Preparation of Amino-capped Silica Nanospheres

Amino-capped silica nanospheres were prepared following a recipe^[23, 24] in literature. Briefly, a mixture of TEOS (0.1 mL), ammonium hydroxide (0.38 mL), deionized water (0.46 mL) and ethanol (9 mL) were stirred at 50°C for 12 h. To this mixture was added ethanol (80 mL), ammonium hydroxide (3.8 mL) and deionized water (4.6 mL) in succession, followed by addition of 1 mL of TEOS every 5 h for four times. To this new resulting mixture (10 mL) was added ethanol (80 mL), ammonium hydroxide (3.8 mL) and deionized water (4.6 mL) in succession, followed by addition of 1 mL of TEOS every 5 h for four times. To this was added APTMS (4 mL) and the resulting mixture was vigorously stirred at 40°C for 12 h. The resulting amino-capped silica nanospheres were collected by centrifugation and then redispersed in ethanol. This procedure was repeated three times. Finally, the amino-capped silica nanospheres were dried in a vacuum oven at 40°C overnight. The diameter of the nanospheres obtained was 340 nm according to the SEM images.

Preparation of Carboxyl-capped Silica Microspheres

Silica microspheres were prepared according to a literature method^[25]. Briefly, TEOS (77.6 mL) was added to a mixture of deionized water (25 mL) and acetic acid (79.4 mL) under stirring at 25°C. After becoming cloudy, the suspension was further stirred for 30 min. The particles were collected by filtration and successively washed with ethanol and acetone. The resulting microspheres were dried at 60°C for 10 h.

To obtain amino-capped silica microspheres, the above-prepared silica microspheres (10 g) were dispersed in a mixture of ammonium hydroxide (3.8 mL), deionized water (4.6 mL) and ethanol (90 mL). To this was added APTMS (5 mL). The mixture was stirred magnetically at 40°C for 24 h. The microspheres were filtered, washed with ethanol and acetone, and dried in a vacuum oven at 60°C for 10 h.

Carboxyl-capped silica microspheres were prepared by the following procedure^[26]. Succinic anhydride (10 g) was added to a suspension of the amino-capped silica microspheres (10 g) in THF (90 mL) under stirring. The mixture was heated to reflux for 40 h. The microspheres were filtered, washed with THF, ethanol and acetone, and dried in a vacuum oven at 60°C for 10 h.

Preparation of the Raspberry-like Templates

The amino-capped silica nanospheres (30 mg) were suspended in ethanol (5 mL). The suspension was sonicated for 20 min and then was added dropwise to a suspension of the carboxyl-capped silica microspheres (3 g) in ethanol (10 mL) under stirring. The mixture was stirred for 5 h at room temperature. The resulting raspberry-like templates were collected by filtration, washed with acetone and dried in a vacuum oven at 40°C overnight.

To convert the ionic bonds to amide bonds between the nanospheres and microspheres, the above-prepared raspberry-like templates were gradually heated to 150°C and kept at the temperature for 3 h under a constant flow of nitrogen.

Capping Residual Carboxyl Groups on the Silica Microspheres of the Raspberry-like Templates

To a mixture of the raspberry-like templates (3 g) and ethanol (10 mL) was added 1-nonylamine (0.2 mL). The mixture was stirred for 5 h at room temperature. The raspberry-like templates were collected by filtration, washed by acetone and dried in a vacuum oven at 40°C overnight.

The raspberry-like templates were gradually heated to 150°C and kept at the temperature for 3 h under a constant flow of nitrogen.

Immobilization of ATRP Initiator on the Raspberry-like Templates

ATRP initiators were immobilized on the raspberry-like template according to a literature method^[27]. The raspberry-like templates (3 g) were suspended in a solution of triethylamine (0.3 mL) in dichloromethane (50 mL). To this was added dropwise a solution of BIBB (0.2 mL) in dichloromethane (10 mL) in an ice bath. The reaction was allowed to proceed at room temperature for 24 h. The resulting raspberry-like templates were filtered, washed with dichloromethane, ethanol, water and acetone, and dried in a vacuum oven at room temperature overnight.

ATRP Polymerization of EGDMA

The above-prepared raspberry-like templates (3 g), EGDMA (20 μ L) and CuBr (14 mg) were added to a Schlenk flask equipped with a stir bar. After sealing with a rubber septum, the flask was evacuated and purged with nitrogen (3 cycles). Deoxygenated cyclohexanone (4 mL) was added to the flask, and the mixture was stirred for 90 min. Deoxygenated PMDETA (21.5 μ L) was added to the flask, and the mixture was stirred for 10 min. The flask was immersed into a water bath preheated to 70°C. The polymerization was allowed to proceed for 12 h under stirring. The resulting particles were filtered and washed with cyclohexanone, ethanol, water and acetone. Yield: 2.9 g, 96%.

Preparation of Single-hole Hollow Polymer Nanospheres

The above-prepared particles (3 g) were immersed in the aqueous HF solution (40%) for 3 h. The resulting mixture was dialyzed against deionized water till neutral. The resulting single-hole hollow nanospheres suspension was freeze-dried. The mass of resulting single-hole hollow nanospheres was 17 mg.

ATRP Copolymerization of EGDMA and DEAEMA

The above-prepared raspberry-like templates (3 g) and CuBr (14 mg) were added to a Schlenk flask equipped with a stir bar. After sealing with a rubber septum, the flask was evacuated and purged with nitrogen (3 cycles). Deoxygenated cyclohexanone (4 mL) was added to the flask, and the mixture was stirred for 90 min. Deoxygenated PMDETA (21.5 μ L) was added to the flask, and the mixture was stirred for 10 min. A deoxygenated mixture of DEAEMA (10 μ L) and EGDMA (10 μ L) was added to the flask, and the mixture was stirred for 10 min. The flask was immersed into a water bath preheated to 70°C. The polymerization was allowed to proceed for 12 h under stirring. The resulting particles were filtered and washed with cyclohexanone, ethanol,

water and acetone. Yield: 2.85 g, 95%. And the mass of resulting single-hole hollow nanospheres of DEAEMA and EGDMA was 16 mg.

RESULTS AND DISCUSSION

Figure 1 shows the schematic illustration of the raspberry-like template strategy. Nanometer-sized amino-capped silica spheres were first covalently attached to micrometer-sized carboxyl-capped silica spheres (raspberry-like templates) by forming amide bonds between the amino and carboxyl groups. ATRP initiators were coupled onto the surfaces of the nanospheres outside the attached areas by treating with bromoisobutyryl bromide (BIBB). Polymer coating on the nanospheres were fabricated by surface-initiated ATRP polymerization. After removal of the silica cores by immersing the raspberry-like templates into hydrofluoric acid, hollow polymer nanospheres with a single hole in the shell of each hollow nanospheres were obtained. When the monomers contain a divinyl monomer, single-hole hollow crosslinked polymer nanospheres were fabricated.

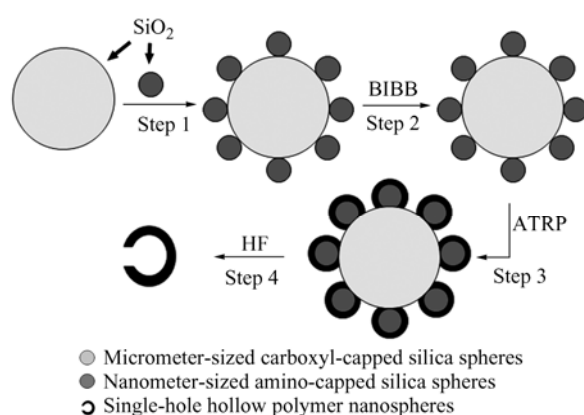


Fig. 1 Illustrative fabrication of single-hole hollow polymer nanospheres by raspberry-like template method

Preparation of Amino-capped Silica Nanospheres and Carboxyl-capped Silica Microspheres

Nanometer-sized amino-capped silica spheres were prepared by hydrolysis of tetraethyl orthosilicate (TEOS) with aqueous ammonia in ethanol, followed by treating with aminopropyltrimethoxysilane (APTMS) to incorporate amino groups on the surface^[23, 24]. As shown in Fig. 2(a), amino-capped silica nanospheres of 340 nm in diameter have smooth surfaces. The presence of amino groups on the nanospheres was confirmed calorimetrically by ninhydrin test.

Micrometer-sized carboxyl-capped silica spheres were prepared by hydrolyzing TEOS with acetic acid in water, followed by treating with APTMS and then with succinic anhydride^[25, 26]. The diameter of the resulting microspheres was about 30 μm in average. The amino-capped silica microspheres showed a positive ninhydrin test. After treating with succinic anhydride, the ninhydrin test gave a negative result, indicating a successful modification with succinic anhydride.

Preparation of the Raspberry-like Templates

In order to obtain the raspberry-like templates, the nanospheres were attached onto the surfaces of the microspheres by mixing them in ethanol due to the formation of ionic bonds (salts) between the amino and carboxyl groups. The ionic bonds were then converted to stable covalent amide bonds by heating the raspberry-like templates at 150°C for 3 h. The formation of amides from carboxylic acid and amines at high temperature (150°C) was reported previously^[28]. The formation of amide bonds between the nanospheres and microspheres was confirmed by SEM images (Fig. 2b) of the templates after treating with diluted hydrogen chloride and then repeatedly washing with water. The nanospheres were still attached on the microspheres (Fig. 2b) after such

treating, while the nanospheres were completely removed from the surface of the microspheres without the annealing after such treating (data not shown). We initially tried to convert the ionic bonds to amide bonds by using coupling reagents such as *N,N'*-diisopropylcarbodiimide or *N,N'*-dicyclohexylcarbodiimide, but failed.

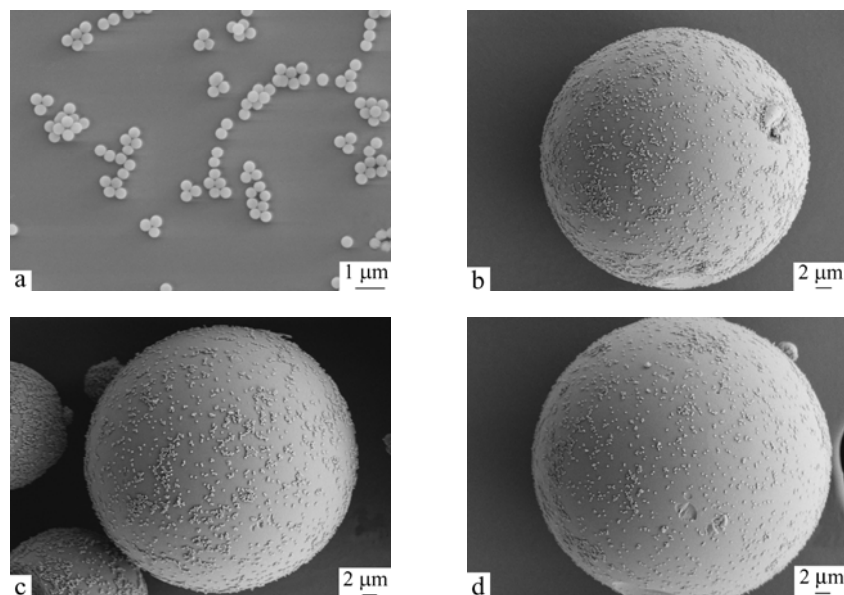


Fig. 2 SEM images of (a) nanometer-sized amino-capped silica spheres, (b) raspberry-like composite microspheres after forming amide bonds, (c) raspberry-like composite microspheres after BIBB modification and (d) raspberry-like composite microspheres after ATRP polymerization of EGDMA

Research into asymmetric particles has boomed since deGennes coined the term “Janus grains” in 1991. Masking method appears to be particularly attractive as it makes preparation simple. In general, janus-like nanoparticles can be achieved by masking portions of nanoparticle surfaces so that they are not available for chemical modification while leaving the exposed surface open for desired functionalization. The method in this paper was mainly based on this. The formation of isolated nanospheres on the microsphere surfaces is the key to forming single-hole hollow polymer nanospheres. So the adsorption degree of nanospheres on microspheres must be controlled by the mass ratio of the nanospheres to microspheres. It should be neither too high, following a result that hollow nanospheres may not be separated from each other, nor too low, resulting in a low yield of the single-hole hollow polymer nanospheres. The ideal mass ratio of the nanospheres to microspheres can be predicted according to the following formula:

$$\frac{m}{M} = \pi \left(\frac{r}{R} \right)^3 \left(\frac{R+r}{r+d+k} \right)^2$$

where m is the mass of the nanospheres, M is the mass of the microspheres, r is the radius of the nanospheres, R is the radius of the microspheres, d is the thickness of the shell, k is the interspace between the nanospheres, usually k is half the radius of the nanospheres. We changed the mass ratio of the nanospheres to microspheres to adjust the adsorption degree of the nanospheres on the microspheres. Figure 2(b) shows that the adsorption degree was appropriate, when the mass ratio of the nanospheres to microspheres was 1:100 ($m:M$), which was in accordance with the value calculated according to the above formula.

The residual carboxyl groups on the carboxyl-capped silica microsphere surfaces may hinder ATRP polymerization. We protected the residual carboxyl groups by treating the templates with 1-nonylamine at the same condition to that in the formation of amide bonds between the nanospheres and microspheres. After the

formation of ionic bonds between the 1-nonylamine and the residual carboxyl groups on the microspheres, ionic bonds were converted to covalent amide bonds by treating the templates at 150°C for 3 h.

After capping the residual carboxyl groups on the carboxyl-capped silica microsphere surfaces, the residual reactive amino groups on the amino-capped silica nanospheres surfaces were acylated with BIBB to anchor alkyl bromide groups to serve as the ATRP initiators for further surface-initiated ATRP polymerization. After BIBB modification, the morphology of the templates changed little (Fig. 2c). The ninhydrin test gave a negative result, indicating that the amino groups on the nanosphere surfaces were totally acylated. The energy disperse spectroscopy (EDS) analysis of the acylated templates indicated the existence of Br element on the nanospheres (Fig. 3).

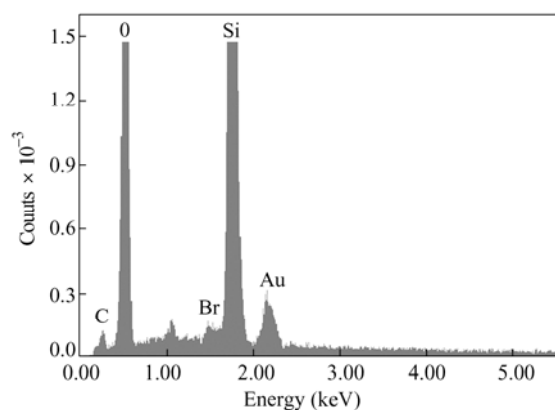


Fig. 3 EDS spectrum of nanospheres on raspberry-like composite microspheres after BIBB modification

Single-hole Hollow Polymer Nanospheres of EGDMA

The crosslinked polymer layers on the nanospheres were fabricated using “graft-from” strategy through ATRP polymerization of ethyleneglycol dimethacrylate (EGDMA). The SEM image of the resulting raspberry-like composite spheres is shown in Fig. 2(d). The average diameter of nanospheres on the microspheres was about 400 nm, indicating that the thickness of the resulting single-hole hollow polymer nanospheres was about 30 nm.

Figure 4 shows the SEM image of the single-hole hollow PEGDMA nanospheres prepared after removal of the silica cores by immersing the PEGDMA-coated raspberry-like composite spheres into hydrofluoric acid. Clearly, the expected single-hole hollow polymer nanospheres were obtained.

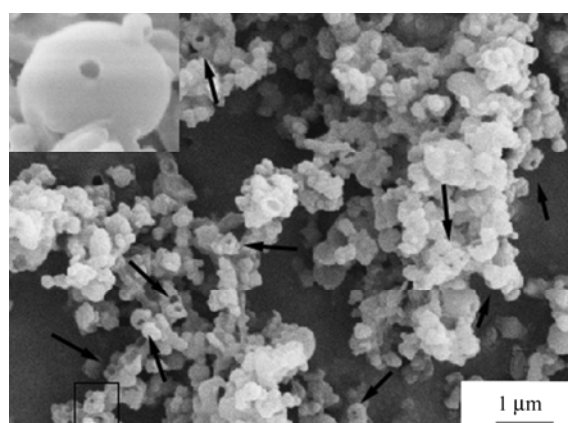


Fig. 4 SEM images of single-hole hollow crosslinked polymer nanospheres of poly(EGDMA)

Single-hole Hollow Polymer Nanospheres of EGDMA and DEAEMA

Copolymerization of various monomers and different sizes of the nanospheres may be used to prepare single-hole hollow polymer nanospheres using this strategy. We used the nanospheres of 180 nm in diameter to prepare the raspberry-like templates. Initiation of copolymerization of EGDMA and (*N,N*-diethylamino)ethyl methacrylate (DEAEMA) by the raspberry-like templates was performed. After removal of the silica cores by treating with hydrofluoric acid, amine group-containing single-hole hollow crosslinked polymer nanospheres were obtained.

Figure 5 shows the SEM images of the single-hole hollow polymer nanospheres. The hollow crosslinked polymer nanospheres had a zeta potential of +5.30 mV as measured at pH of 3.0, indicating the amine groups were successfully incorporated into the single-hole hollow polymer nanospheres. Theoretically, many other monomers may be used in ATRP polymerization to incorporate different functional groups into the single-hole hollow polymer nanospheres. The diameter of the hollow polymer nanospheres and the composition, thickness of the shell may be controlled.

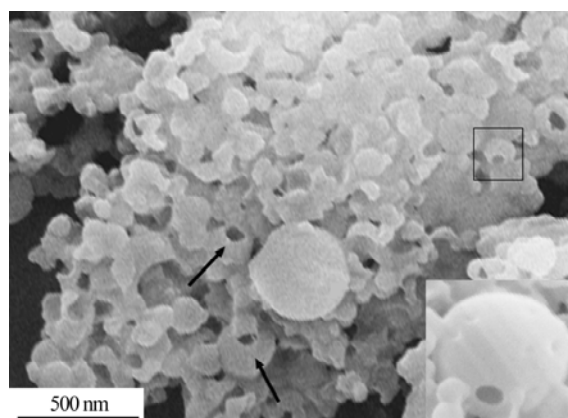


Fig. 5 SEM images of single-hole hollow crosslinked polymer nanospheres of poly(EGDMA-DEAEMA)

CONCLUSIONS

Hollow PEGDMA nanospheres with a single hole in the shell were successfully prepared by ATRP polymerization using the raspberry-like template method. DEAEMA monomers can be copolymerized into the single-hole hollow nanospheres to incorporate the functional groups, which may enlarge the potential applications of the single-hole hollow nanospheres.

REFERENCES

- 1 Deng, Z., Chen, M., Zhou, S., You, B. and Wu, L., *Langmuir*, 2006, 22: 6403
- 2 Duan, L., He, Q., Wang, K., Yan, X., Cui, Y., Mohwald, H. and Li, J., *Angew. Chem. Int. Ed.*, 2007, 46: 6996
- 3 Zhu, Y., Shi, J., Shen, W., Dong, X., Feng, J., Ruan, M. and Li, Y., *Angew. Chem. Int. Ed.*, 2005, 44: 5083
- 4 Shchukin, D.G. and Sukhorukov, G.B., *Adv. Mater.*, 2004, 16: 671
- 5 Peyratout, C.S. and Dahne, L., *Angew. Chem. Int. Ed.*, 2004, 43: 3762
- 6 Huang, B., Bai, F., Yang, X.L. and Huang, W.Q., *Chinese J. Polym. Sci.*, 2010, 28(2): 277
- 7 Wang, W., Yang, J.X., He, B. and Gu, Z.W., *Chinese J. Polym. Sci.*, 2007, 25(5): 431
- 8 IM, S.H., Jeong, U. and Xia, Y., *Nat. Mater.*, 2005, 4: 671
- 9 Minami, H., Kobayashi, H. and Okubo, M., *Langmuir*, 2005, 21: 5655p
- 10 Chen, Y., Qian, Z. and Zhang, Z.C., *Chem. Lett.*, 2007, 36: 944

- 11 Han, J., Song, G. and Guo, R., *Chem. Mater.*, 2007, 19: 973
- 12 Chang, M.W., Stride, E. and Edirisinghe, M., *Langmuir*, 2010, 26: 5115
- 13 Guan, G.J., Zhang, Z.P., Wang, Z.Y., Liu, B.H., Gao, D.M. and Xie, C.G., *Adv. Mater.*, 2007, 19: 2370
- 14 Lim, Y.T., Kim, J.K., Noh, Y.W., Cho, M.Y. and Chung, B.H., *Small*, 2009, 5:324
- 15 Luo, S.C., Jiang, J., Liour, S.S., Gao, S.J., Ying, J.Y. and Yu, H.H., *Chem. Commun.*, 2009, 2664
- 16 Reculosa, S., Poncet-Legrand, C., Ravaine, S., Mingotaud, C., Duguet, E. and Bourgeat-Lami, E., *Chem. Mater.*, 2002, 14: 2354
- 17 Cho, Y.S., Yi, G.R., Kim, S.H., Jeon, S.J., Elsesser, M.T., Yu, H.K., Yang, S.M. and Pine, D.J., *Chem. Mater.*, 2007, 19: 3183
- 18 Fleming, M.S., Mandal, T.K. and Walt, D.R., *Chem. Mater.*, 2001, 13: 2210
- 19 Barthet, C., Hickey, A.J., Cairns, D.B. and Armes, S.P., *Adv. Mater.*, 1999, 11: 408
- 20 Ming, W., Wu, D., van Benthem, R. and de With, G., *Nano Lett.*, 2005, 5: 2298
- 21 Qian, Z., Zhang, Z.C., Song, L.Y. and Liu, H.R., *J. Mater. Chem.*, 2009, 19: 1297
- 22 Frederik, W. and Andreas, F.M. Kilbinger, *Angew. Chem. Int. Ed.*, 2009, 48: 8412
- 23 Wu, Z., Xiang, H., Kim, T., Chun, M.S. and Lee, K., *J. Colloid Interface Sci.*, 2006, 304: 119
- 24 Qi, Y., Chen, M., Liang, S., Yang, W. and Zhao, J., *Appl. Surf. Sci.*, 2008, 254: 1684
- 25 Chen, F.H., Gao, Q. and Ni, J.Z., *Nanotechnology*, 2008, 19: 165103
- 26 Calvo, A., Joselevich, M., Soler-Illia, G.J.A.A. and Williams, F.J., *Microporous Mesoporous Mater.*, 2009, 121: 67
- 27 Ayres, N., Haddleton, D.M., Shooter, A.J. and Pears, D.A., *Macromolecules*, 2002, 35: 3849
- 28 Perreux, L., Loupy, A. and Volatron, F., *Tetrahedron*, 2002, 58: 2155