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Synthesis of Highly Monodisperse Surface-Functional Microspheres by Photoinitiated RAFT Dispersion Polymerization Using Macro-RAFT Agents

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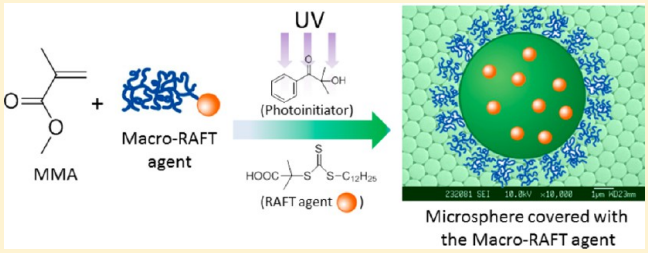
Supporting Information

ABSTRACT: Highly monodisperse PMMA microspheres have been synthesized by photoinitiated RAFT dispersion polymerization in the presence of a Macro-RAFT agent and a small molecular RAFT agent. A particle yield of over 90% was achieved within 3 h under UV irradiation at room temperature. The Macro-RAFT agent acts as a stabilizer and stabilizes the particles via formation of block copolymers in situ, and XPS analysis shows that about 29.9% of the particle surface was covered by the stabilizer. Various surface functional microspheres were prepared by using four kinds of Macro-RAFT agents, including poly(methoxy poly(ethylene glycol) acrylate)-based trithiocarbonate (P(mPEGA)-TTC), poly(methoxy poly(ethylene glycol) acrylate-*co*-acrylic acid)-based trithiocarbonate (P(mPEGA-*co*-AA)-TTC), poly(acrylic acid)-based trithiocarbonate (PAA-TTC), and poly(methoxy poly(ethylene glycol) acrylate-*co*-4-vinylpyridine)-based trithiocarbonate (P(mPEGA-*co*-4VP)-TTC). Ag/PMMA nanocomposite spheres were prepared using the P(mPEGA-*co*-AA)-TTC stabilized microspheres. The PAA-TTC stabilized microspheres showed pH sensitivity. The colloidal stability of the particles prepared by this photoinitiated RAFT dispersion polymerization was also investigated.



INTRODUCTION

Surface-functional polymeric microspheres with reactive groups or environment-sensitive groups on the particle surface have attracted much attention due to their broad applications in drug delivery, protein purification, and bioassays.[1−4] As a facile and single-step strategy, dispersion polymerization is in principle a very attractive method to synthesize monodisperse polymeric microspheres in the range of 1−15 μm. Functional polymeric microspheres can be obtained by dispersion polymerization via the addition of functional comonomers to the reaction. When these functional microspheres are used in biotechnological fields, however, the attachment of monoclonal antibodies or bioaffinity agents to the surface of the microspheres will be restricted by the stabilizer corona formed on the polymeric microsphere surface.[1] In addition, most of the functional monomers will polymerize inside the particles or remain in the reaction medium, while only a small portion of functional groups stay on the particle surface.[1,5−7]

Many efforts have been devoted to overcome the disadvantages of dispersion copolymerization. Yang et al. developed a two-stage dispersion polymerization by using a charged monomer as the stabilizer.[8] In their method, polystyrene particles with a certain amount of benzophenone groups on the surface were prepared. These photoreactive microspheres can be used as the precursor for the synthesis of various core−shell microspheres by using different functional monomers. The use of macromonomers or block copolymers as the stabilizer in dispersion polymerization is another useful strategy to functionalize polymeric microspheres.[9−13] Baines et al.[9] used a functional block copolymer as the stabilizer to synthesize surface-functional polystyrene microspheres in an alcoholic medium by dispersion polymerization. The particles obtained by this method were not uniform in size. Thompson et al.[10] synthesized a range of well-defined methacrylic macromonomers based on glycerol monomethacrylate by atom transfer radical polymerization (ATRP) in alcoholic media. They used these macromonomers as stabilizers for the synthesis of polymeric particles by using alcoholic or aqueous dispersion polymerization. McKee et al.[11] successfully synthesized thermoresponsive polystyrene microspheres based on alcoholic dispersion polymerization by using a series of well-defined poly(*N*-isopropylacrylamide) (PNIPAM) macromonomers as the stabilizers. Yang et al.[12] synthesized a series of polyacid macromonomers based on atom transfer radical polymerization via a two-step route, and near monodisperse polyacid-stabilized latexes were obtained by emulsion and alcoholic dispersion polymerization. Li et al.[13] used poly(ethylene oxide) macromonomers as reactive stabilizers in two-

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stage ATRP dispersion polymerization and investigated the influence of various reaction conditions on the particles. On the basis of these methods, one can synthesize various surface-functional polymeric microspheres by using different kinds of functional macromonomers or block copolymers. However, the size uniformity of the particles obtained is limited in most cases, and a complicated process is normally required to obtain monodisperse surface-functional microspheres.

Reversible addition−fragmentation chain transfer (RAFT) polymerization has been a powerful technique for the synthesis of well-defined polymers with low polydispersities, functionalized end groups, and polymers with complex architectures.[14−16] Furthermore, the "living" property of RAFT polymerization provides us with a new strategy to synthesize functional microspheres by using a Macro-RAFT agent as the stabilizer. In recent years, there has been a focus on the RAFT-mediated dispersion polymerization to synthesize nanomaterials with various morphologies by using Macro-RAFT agents as the RAFT agent and the stabilizer.[17−28] However, the synthesis of polymeric microspheres by RAFT dispersion polymerization with a Macro-RAFT agent is rare due to the poor control of particle size distribution;[11,29] the presence of the RAFT agent in dispersion polymerization will disturb the nucleation stage, leading to a broad particle size distribution. Two-stage dispersion polymerization proposed by Winnik et al.,[30,31] in which the RAFT agent or other functional reagent is added after the nucleation stage, is a useful method to solve the problem, and monodisperse "living" particles can be obtained.[1,2,5,6] However, this two-stage procedure is not suitable for the case of using the Macro-RAFT agent as a stabilizer because the Macro-RAFT agent must be added at the beginning to stabilize the nuclei. Recently, we have developed a one-stage strategy, photoinitiated RAFT dispersion polymerization,[32] that overcomes the problems arising from the high sensitivity of the nucleation stage and allows for the addition of functional reagents, such as the RAFT agent, cross-linking agents, and functional comonomers, to the system at the beginning. This one-stage character is very suitable for the procedure using a Macro-RAFT agent as the stabilizer.

In this paper, we report the synthesis of surface-functional PMMA microspheres by photoinitiated RAFT dispersion polymerization using poly(methoxypoly(ethylene glycol) acrylate)-based trithiocarbonate (P(mPEGA)-TTC) Macro-RAFT agent as the hydrophilic steric stabilizer. Highly monodisperse microspheres were obtained in a single step at room temperature, and several kinds of surface-functional PMMA microspheres were synthesized by this strategy.

EXPERIMENTAL SECTION

Materials. Methyl methacrylate (MMA, Tianjin Kermel Chemical Reagents Development Center) was purified by distillation under reduced pressure and stored in a refrigerator prior to use. 4,4′-Azobis(4-cyanovaleric acid) (ACVA, Aladdin), methoxypoly(ethylene glycol) (350) acrylate (mPEGA, Sartomer), dipropylene glycol diacrylate (DPGDA, Sartomer), $AgNO_3$ (Aladdin), 4-vinylpyridine (4VP, Aladdin), acrylic acid (AA, Tianjin Kermel Chemical Reagents Development Center), and 2,2-dimethyl-2-phenylacetophenone (Darocur 1173, Ciba) were used as received. The RAFT agent *S*-1-dodecyl-*S*′-(*α*,*α*′-dimethyl-*α*″-acetic acid) trithiocarbonate (DDMAT) was synthesized using the published procedure.[33]

Synthesis of Macro-RAFT Agents. In a typical experiment, DDMAT (0.6464 g, 1.8 mmol), ACVA (0.068 g, 0.24 mmol), mPEGA monomer (30 g, 70 mmol), and ethanol (30 g) were weighed into a 100 mL three-neck round-bottomed flask and purged with N_2 for 30 min. The sealed flask was immersed into an oil bath set at 70 °C for 24 h and quenched in ice water. The product was precipitated by excess ether, washed several times, and dried in a vacuum oven for 24 h. The weight-average molecular weight and distribution of the product tested by GPC are 23 000 g mol^{-1} and 1.34, respectively. Other Macro-RAFT agents were synthesized by the same procedure using the monomer(s) listed in Table 1. Figure 1 shows the structures of DDMAT and the Macro-RAFT agents synthesized.

Table 1. Monomer Feeding for the Synthesis of Macro-RAFT Agents

Macro-RAFT agent	mPEGA (g)	AA (g)	4VP (g)
P(mPEGA)-TTC	30		
P(mPEGA$_{0.5}$-*co*-AA$_{0.5}$)-TTC	30	5	
PAA-TTC		20	
P(mPEGA$_{0.75}$-*co*-4VP$_{0.25}$)-TTC	30		2.47
P(mPEGA$_{0.5}$-*co*-4VP$_{0.5}$)-TTC	30		7.41

Photoinitiated RAFT Dispersion Polymerization of MMA in the Presence of Macro-RAFT Agents. In a typical experiment, an ethanol/water (7.2 g/10.8 g) mixture with a weight ratio of 40/60 was introduced into the reactor as the reaction medium, and 10 wt % of the monomer (MMA, 2 g) relative to the system, 15 wt % of the stabilizer (P(mPEGA)-TTC or other Macro-RAFT agents listed in Table 1, 0.30 g) relative to MMA, 0.25 wt % of the RAFT agent (DDMAT, 0.005 g) relative to MMA, and 3 wt % of the photoinitiator (Darocur 1173, 0.06 g) relative to MMA were dissolved into the reaction medium. The mixture was purged with N_2 for 15 min, sealed, and then irradiated by a 3 W 365 nm LED lamp (light intensity 0.8 mW/cm^2) from the top of the reaction cell for 3 h. The reaction mixture became turbid after 2 min of UV irradiation. The product was separated by centrifugation, rinsed with the ethanol/water mixture (40/60, w/w), and centrifuged repeatedly. The washed product was dried in a vacuum oven for 24 h to give a fine powder and then weighed for calculating the conversion. Other microspheres were synthesized by this strategy using different Macro-RAFT agents as the stabilizers.

Synthesis of Ag/PMMA Nanocomposite. The PMMA microspheres were synthesized by the photoinitiated RAFT dispersion polymerization as described above with 15 wt % P(mPEGA$_{0.5}$-*co*-AA$_{0.5}$)-TTC or 15 wt % P(mPEGA)-TTC as the stabilizer. PMMA microspheres (0.02 g) were dispersed in the Ag^+ solution formed by dissolving $AgNO_3$ (0.2 g) in water (0.5 g). The mixture was then immersed in an oil bath at 50 °C, and 1.0 g PVP solution (0.2 g of PVP dissolved in 0.8 g of water) was added slowly to the reaction over 1 h. The reaction was maintained at 50 °C for 13 h in the dark. The product was separated by centrifugation, rinsed with the ethanol/water mixture, centrifuged repeatedly, and dried in a vacuum oven for 24 h.

Characterization. Morphology analysis was carried out on a JSM-6330F field emission scanning electron microscope (FE-SEM) at 10 kV. Samples were dispersed in water, and a drop of the solution was placed on a clean glass film. The samples were gold-coated prior to taking the SEM measurement. Image-Pro Plus 5.1 (Media Cybernetics) was used to analyze the SEM micrographs to determine the microsphere diameters and size distributions. Transmission electron microscope (TEM) observations were carried out on a JEM-2010HR instrument operated at 120 kV.

X-ray photoelectron spectroscopy (XPS) analysis was performed on a Thermo Electron Corporation Escalab 250 spectrometer operated at 20 eV pass energy. An Al K*α* X-ray source was used.

The molecular weight and polydispersity were determined by a Waters 1515 GPC instrument with THF as the mobile phase. The flow rate of tetrahydrofuran was 1 mL/min. Narrow distribution linear polystyrenes were used as the standard to calibrate the apparatus, and the molecular weights of the samples were measured using universal calibration.

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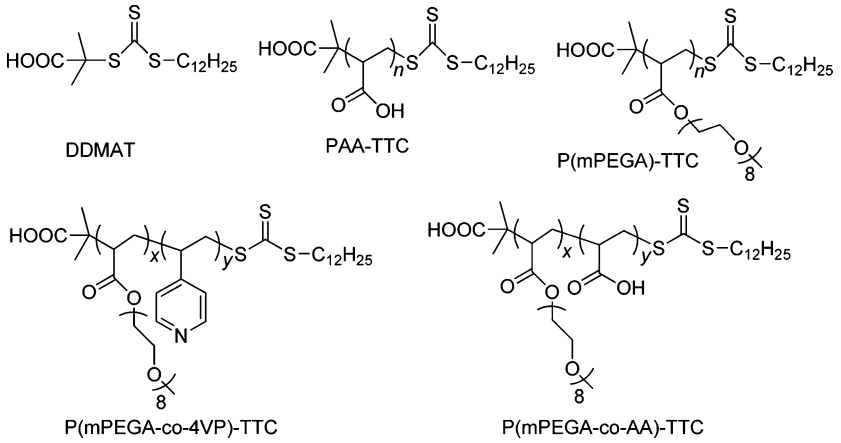

Figure 1. Structures of DDMAT and the Macro-RAFT agents.

RESULTS AND DISCUSSION

Photoinitiated RAFT Dispersion Polymerization with a Macro-RAFT Agent. In dispersion polymerization, the stabilizer plays an important role in keeping the system stable and obtaining monodisperse polymeric microspheres. After the polymerization, a certain amount of stabilizers will be attached to the particle surface, which provides a convenient platform to functionalize the polymeric particles. In the present work, photoinitiated dispersion polymerization was carried out with a Macro-RAFT agent as the stabilizer in order to obtain polymeric microspheres with a tailored functional surface.

P(mPEGA)-TTC, a comb-like Macro-RAFT agent with poly(ethylene glycol) side chains, was selected as the hydrophilic steric stabilizer, since poly(ethylene glycol) is an attractive hydrophilic polymer with biocompatible, antifouling, and thermoresponsive properties and is widely used in various areas.[34−41] We carried out the photoinitiated dispersion polymerization of MMA with P(mPEGA)-TTC concentration ranging from 5 to 20 wt % and without the addition of any small molecular RAFT agent. Figure 2 shows that PMMA microspheres were obtained; however, the particle size distribution was relatively broad in all cases. These results are similar to what has been observed for conventional photoinitiated dispersion polymerization.[42] Because of rapid decomposition of the photoinitiator, the nucleation occurs so fast that the stabilizer cannot be absorbed by the nuclei immediately, resulting in limited size uniformity of the obtained particles. In our recent work,[32] highly monodisperse polymeric microspheres were prepared by photoinitiated RAFT dispersion polymerization, in which a RAFT agent was added at the beginning of the reaction, and the nucleation stage was controlled by the RAFT process. In the present case, although there are reactive groups at the end of P(mPEGA)-TTC polymer chains, the amount of RAFT groups is too low to control the nucleation stage effectively. Monodisperse microspheres could be obtained (Figure S3c) by decreasing the chain length of the Macro-RAFT agent, since there would be an increase in the relative amount of the RAFT groups at the same weight percentage of Macro-RAFT agent; however, the universality of this method would be greatly depressed with the strict condition.

To address this problem, we further added 0.25 wt % DDMAT to the reaction as the compensation for the RAFT agent to ensure the effective control of the procedure. As shown in Figure 3b−d, highly monodisperse PMMA micro-

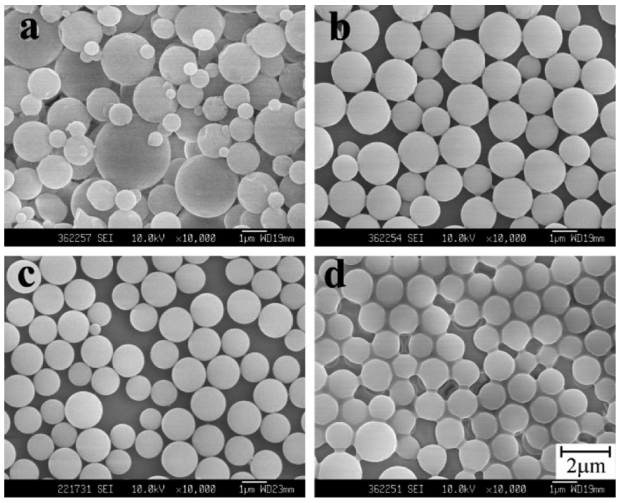

Figure 2. SEM images of PMMA microspheres prepared by photoinitiated dispersion polymerization of MMA with P(mPEGA)-TTC concentration of (a) 5, (b) 10, (c) 15, and (d) 20 wt %.

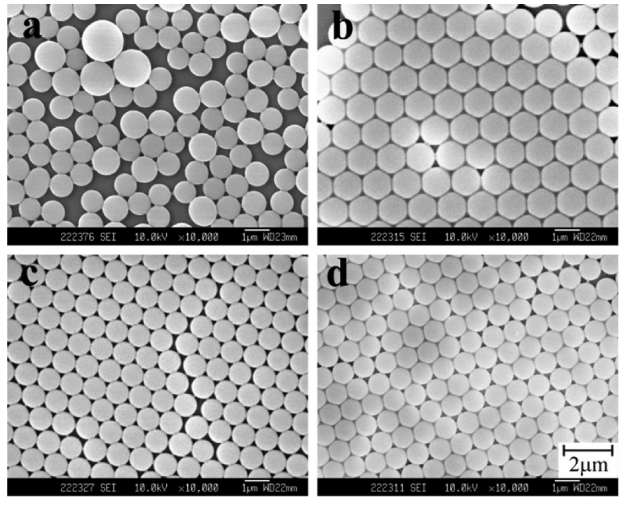

Figure 3. SEM images of PMMA microspheres prepared by photoinitiated dispersion polymerization of MMA in the presence of 0.25 wt % DDMAT with P(mPEGA)-TTC concentrations of (a) 5, (b) 10, (c) 15, and (d) 20 wt %.

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spheres were obtained with P(mPEGA)-TTC concentration ranging from 10 to 20 wt %, suggesting that the Macro-RAFT agent is an effective stabilizer in photoinitiated RAFT dispersion polymerization. The diameter of the microspheres decreased from 1.21 to 0.89 μm with increasing the concentration of P(mPEGA)-TTC, which is similar in trend to traditional dispersion polymerization. Higher stabilizer concentration induces faster adsorption of the stabilizer, which reduces aggregation of the nuclei, and thus gives final microspheres of smaller size. The procedure with 5 wt % P(mPEGA)-TTC only gave microspheres with a broad size distribution (Figure 3a). In this case, the stabilizer concentration is too low to stabilize the particles, and thus the particles are more likely to aggregate together, resulting in the broad particle size distribution.

Formation and Growth of Particles. Figure 4 shows the plots of conversion versus time for photoinitiated RAFT dispersion polymerization of MMA in the presence of 15 wt % P(mPEGA)-TTC and 0.25 wt % DDMAT. The conversion reaches 90% at 180 min, indicating a fast process in comparison with the traditional dispersion polymerization. Figure 5 presents the morphology of the products formed at different reaction times. Small particles with some extremely large spheres were produced at the beginning of reaction. The large spheres then gradually reduced in size as the reaction progressed and disappeared at 120 min. This phenomenon was also observed in photoinitiated RAFT dispersion polymerization with PVP as the stabilizer.[32] The large spheres are primarily composed of polymer chains with a shorter chain length and are derived from "pseudo-nuclei" formed during the initial stages via the precipitation of the uncontrolled polymer chains.[32] These large spheres act as a short-chain reservoir at the nucleation stage, providing a buffering effect to the nucleation process. Combining the results of the conversion curve and the SEM images, we can deduce that the nucleation stage finished at around 90 min. At the growth stage, the polymerization site was primarily in the monomer swollen particles, and thus the reaction rate increased. The conversion increased from 37.5% to 81.5% within 30 min (time point 90 to 120 min), and the particles became uniform.

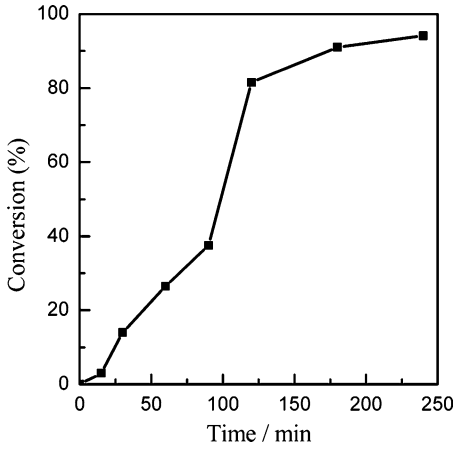

Figure 4. Plots of conversion versus time for photoinitiated RAFT dispersion polymerization of MMA in the presence of 15 wt % P(mPEGA)-TTC and 0.25 wt % DDMAT.

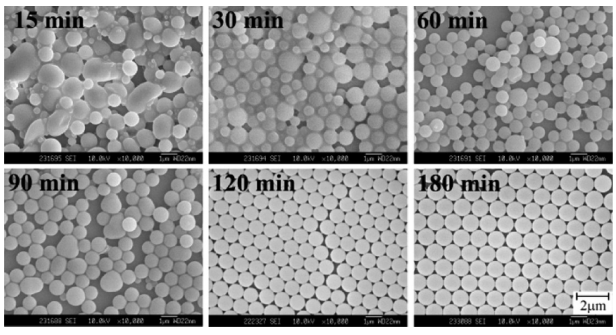

Figure 5. SEM images of PMMA particles prepared by photoinitiated RAFT dispersion polymerization of MMA with 15 wt % P(mPEGA)-TTC and 0.25 wt % DDMAT at irradiation time marked on the images.

The GPC results of the PMMA microspheres obtained at different UV irradiation times are shown in Figure 6. The GPC peak at irradiation time of 15 min can be attributed to the homo-PMMA chains rather than the block copolymer chains since its molecular weight is slightly lower than that of P(mPEGA)-TTC. At the early stage, the length of the PMMA segment in P(mPEGA)-*b*-PMMA is short. In this case, the block copolymers have a higher medium affinity and poorer anchoring ability on the particles and thus can be washed out easily from the particles during the separation and purification processes. Therefore, no GPC signal for the block copolymer is found in this period, and the GPC curve is unimodal. During the particle growth stage, the length of the PMMA segment in P(mPEGA)-*b*-PMMA becomes longer, and the block copolymers can be adsorbed more effectively by the particles. The PMMA homopolymers and the P(mPEGA)-*b*-PMMA block copolymers propagate synchronously in the particles, causing the GPC curves to shift to higher molecular weight and exhibit the bimodal shape. The left and right peaks of the GPC trace may be assigned to the block copolymer and homopolymer, respectively, in view of the fact the molecular weight of P(mPEGA)-*b*-PMMA would be higher than that of the PMMA.

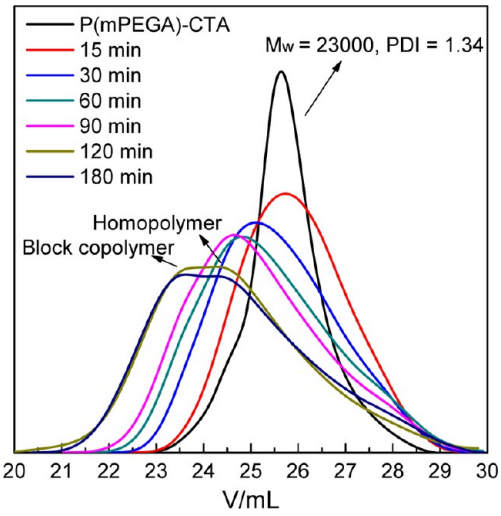

Figure 6. GPC traces for photoinitiated RAFT dispersion polymerization of MMA in the presence of 15 wt % P(mPEGA)-TTC and 0.25 wt % DDMAT.

Scheme 1 shows the formation and growth processes of the particles in the procedure. Under UV irradiation, PMMA homopolymers and P(mPEGA)-*b*-PMMA block copolymers

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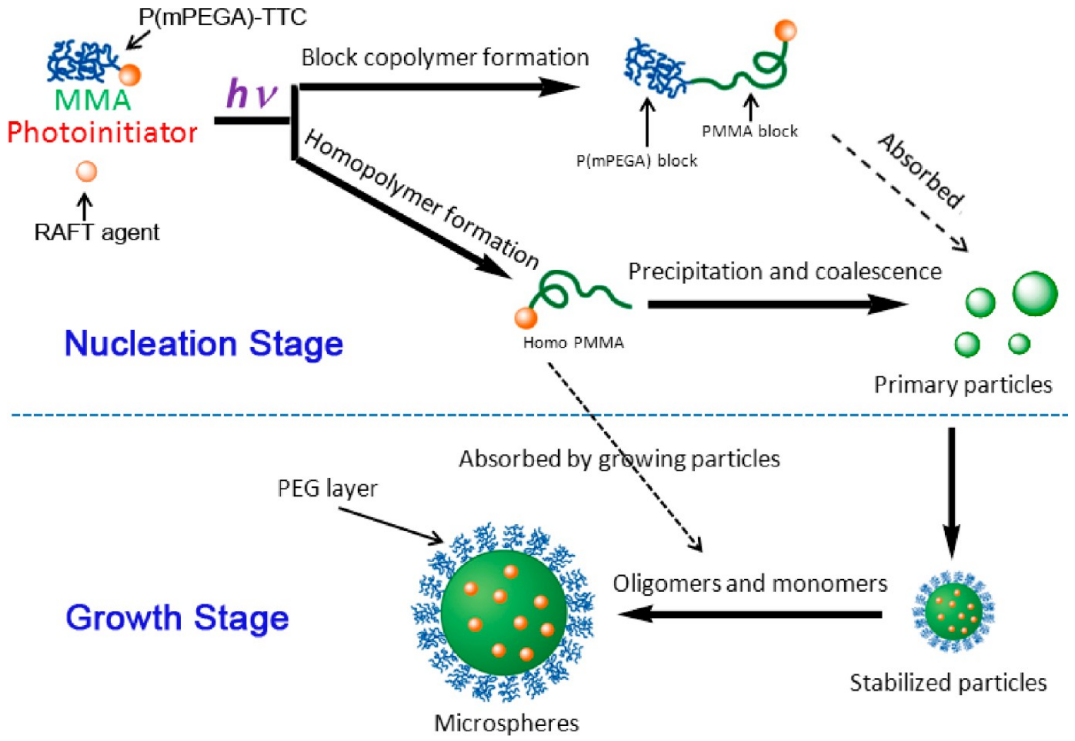
Scheme 1. Formation of the Surface-Functional PMMA Microspheres in Photoinitiated RAFT Dispersion Polymerization with the Macro-RAFT Agent as a Stabilizer



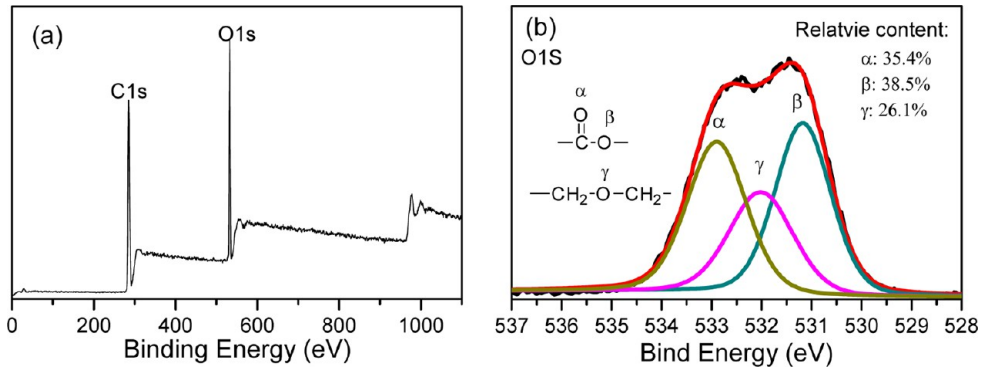


Figure 7. (a) XPS survey spectra of PMMA microspheres. (b) XPS (O 1s) spectra of PMMA microspheres. The microspheres were prepared by photoinitiated RAFT dispersion polymerization with 15 wt % P(mPEGA)-TTC as the stabilizer.

will form simultaneously. Nucleation occurs as the PMMA chains propagate to the critical chain length, at which point the formation of polymeric microspheres begins. The block copolymers formed *in situ* act as the stabilizers and are adsorbed by the particles via the PMMA blocks, with the P(mPEGA) blocks stretching into the medium to stabilize the particles. As a result, the surface of the microspheres is covered with the P(mPEGA) chains.

The surface of the P(mPEGA) stabilized PMMA microspheres was analyzed by means of X-ray photoelectron spectra (XPS). Strong signals of carbon (C 1s, around 285 eV) and oxygen (O 1s, around 532 eV) were found in the wide survey XPS (Figure 7a). The O 1s signal is composed of three peaks, which are attributed to three types of oxygen (tagged as α, β, and γ, Figure 7b). From the relative content of different types of oxygen, it can be calculated that the P(mPEGA) content on the surface of the microspheres is around 29.9%. This result suggests that a large amount of the stabilizer is attached to the particle surface.

Synthesis of Cross-Linked and Functional Polymeric Microspheres. Cross-linked polymeric microspheres are insoluble but can be swollen in the solvent, which is a desirable character for some applications. In some cases, functional groups embedded in the microspheres are also required. In dispersion polymerization, however, adding functional reagents (e.g., cross-linkers, dyes, or comonomers) at the beginning of the reaction will disturb the nucleation stage, resulting in particles with poor monodispersity.[5,30,31] Thus, it is difficult to synthesize highly monodisperse, cross-linked, and functional polymeric microspheres by dispersion polymerization in a single batch mode. In our previous research, this problem was solved by a one-stage photoinitiated RAFT dispersion polymerization, in which the nucleation stage is insensitive to the cross-linker or comonomer.[32] Poly(*N*-vinylpyrrolidone) (PVP) was used as the stabilizer therein. In the present work, the same

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procedure has been carried out with P(mPEGA)-TTC as the stabilizer. As shown in Figure 8, highly monodisperse PMMA

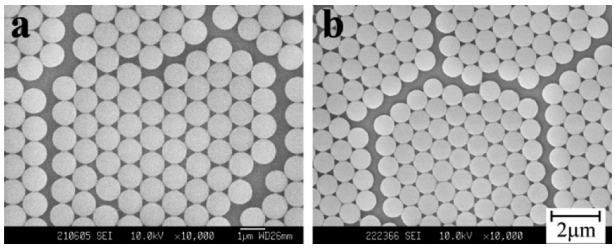

Figure 8. SEM images of PMMA microspheres prepared by photoinitiated RAFT dispersion polymerization in the presence of 15 wt % P(mPEGA)-TTC and 0.25 wt % DDMAT with (a) 2 wt % AA and (b) 1 wt % DPGDA.

microspheres were obtained in the presence of 1 wt % DPGDA cross-linker or 2 wt % AA comonomer. These results suggest that the photoinitiated RAFT dispersion polymerization with a Macro-RAFT agent as the stabilizer is also an effective method to synthesize monodisperse functional polymeric microspheres with the addition of the functional reagent at the beginning of the reaction.

Pyridyl-Functionalized Microspheres. Based on photoinitiated RAFT dispersion polymerization with a Macro-RAFT agent as the stabilizer, monodisperse surface-functional microspheres can be easily synthesized by using different Macro-RAFT agents. The pyridyl group is one of the most commonly used pH-responsive groups and can be used as the reaction site for the synthesis of inorganic/organic nanocomposites.[43−45] We have tried to synthesize pyridyl-functionalized polymeric microspheres by using a pyridyl-containing Macro-RAFT agent as the stabilizer. As shown in Figure 9, highly monodisperse

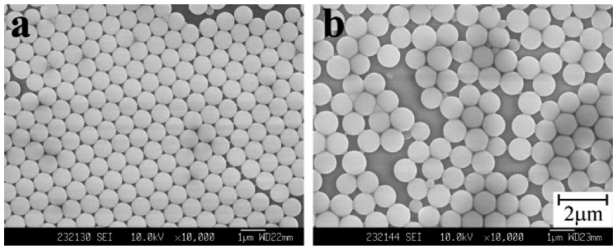

Figure 9. SEM images of PMMA microspheres prepared by photoinitiated RAFT dispersion polymerization in the presence of 0.25 wt % DDMAT with (a) 15 wt % P(mPEGA$_{0.75}$-*co*-4VP$_{0.25}$)-TTC and (b) 15 wt % P(mPEGA$_{0.5}$-*co*-4VP$_{0.5}$)-TTC.

microspheres were obtained by photoinitiated RAFT dispersion polymerization with P(mPEGA$_{0.75}$-*co*-4VP$_{0.25}$)-TTC as the stabilizer. When P(mPEGA$_{0.5}$-*co*-4VP$_{0.5}$)-TTC was used as the stabilizer, the particle size distribution of the microspheres obtained became broader (Figure 9b). This may be ascribed to the weak solvent affinity of Macro-RAFT agents with a high ratio of 4VP in ethanol/water mixtures, leading to poor stabilized particles under these conditions. The result reveals that the surface functionality of the microspheres is limited by the solvent affinity of the functional comonomer.

Carboxyl-Functionalized Microspheres. The carboxyl group is one of the most important reactive functional groups for polymeric microspheres intended for biomedical or biodiagnostics applications,[1,46−48] and carboxyl-functionalized polymeric microspheres are common precursors for the preparation of silver or gold nanocomposites.[49−51] Carboxyl groups can be introduced to the surface of the microspheres by using a carboxyl-containing Macro-RAFT agent as the stabilizer in photoinitiated RAFT dispersion polymerization. Figure 10a

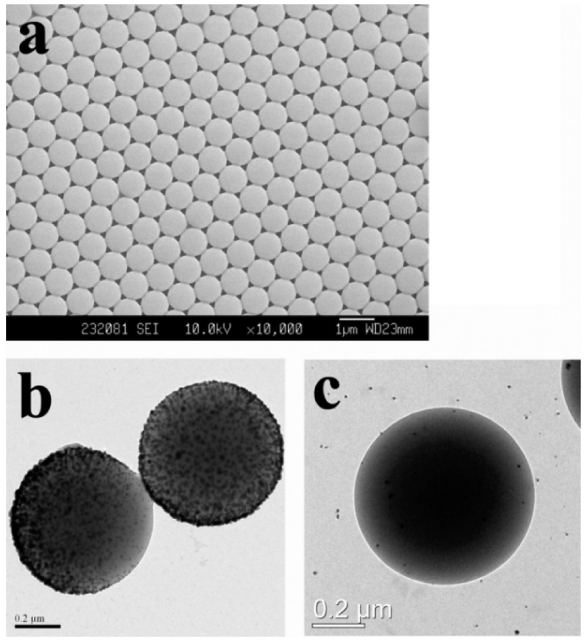

Figure 10. (a) SEM image of PMMA microspheres prepared by photoinitiated RAFT dispersion polymerization with 15 wt % P(mPEGA$_{0.5}$-*co*-AA$_{0.5}$)-TTC and 0.25 wt % DDMAT. (b) TEM image of Ag/PMMA nanocomposite spheres with P(mPEGA$_{0.5}$-*co*-AA$_{0.5}$) functional PMMA microspheres as the precursor. (c) TEM image of Ag/PMMA nanocomposite spheres with P(mPEGA) functional PMMA microspheres as the precursor.

shows that highly monodisperse PMMA microspheres were obtained when P(mPEGA$_{0.5}$-*co*-AA$_{0.5}$)-TTC was used as the stabilizer in the procedure. We have used these microspheres as the precursor to synthesize Ag/PMMA nanocomposite spheres. As shown in Figure 10b, a large number of silver nanoparticles were attached to the PMMA microspheres. As a comparison, we have also tried to use the P(mPEGA)-stabilized PMMA microspheres as precursors for the synthesis of Ag/PMMA nanocomposite spheres (Figure 10c). The result indicates that the silver nanoparticles could not be attached to the microspheres, which can be attributed to the lack of carboxyl groups on the surface of the P(mPEGA)-stabilized PMMA microspheres.

pH-Sensitive Microspheres Based on PAA-TTC. The carboxyl group has a high affinity for ethanol/water mixtures, the dispersion medium. Therefore, the carboxyl functionality of the Macro-RAFT agent can be adjusted easily without disturbing the monodispersity of the microspheres synthesized. We have used a fully carboxylated Macro-RAFT agent, PAA-TTC, as the stabilizer to synthesize PMMA microspheres by photoinitiated RAFT dispersion polymerization, and highly monodisperse PMMA microspheres were obtained (Figure 11a). This result is more attractive because it is expected that a high carboxyl content on the surface of the microspheres may result in pH-responsive properties. As shown in Figure 11b, the PAA-stabilized particles precipitated at acidic condition due to the weak solubility of the protonated PAA chains on the

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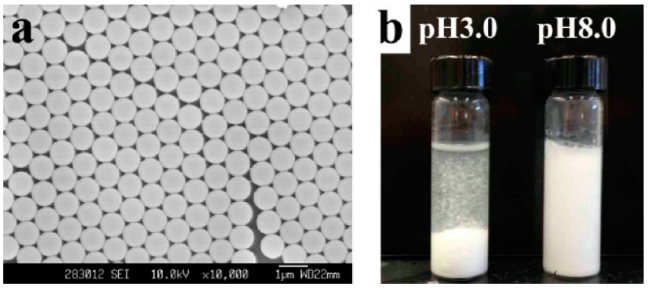

Figure 11. (a) SEM image of PMMA microspheres prepared by photoinitiated RAFT dispersion polymerization with 15 wt % PAA-TTC and 0.25 wt % DDMAT. (b) pH-responsive behavior of the PAA-stabilized PMMA microspheres. Vial on the left corresponds to the aqueous particle dispersion (5 wt %) at pH 3.0; vial on the right corresponds to the aqueous particle dispersion (5 wt %) at pH 8.0.

particle surface but can be redispersed with gentle sonication by increasing the pH value of the solution. This characteristic is useful for some applications, since the microspheres can be easily separated and redispersed by adjusting the pH value of the medium.

Colloidal Stability of the Particles Prepared by Photoinitiated RAFT Dispersion Polymerization. Colloidal stability is very important for the application of microspheres in biomedical analysis, as microspheres should remain stable during the bioconjugation procedure in different buffer solutions. Moreover, high colloidal stability is also crucial for long-term storage. Table 2 shows the colloidal stability in water

Table 2. Summary of the Colloid Stabilities of Selected PMMA Particles Stabilized by Different Macro-RAFT Agents

		pH		$CaCl_2$ concn (M)			
stabilizer	freeze–thaw[a]	3.0	8.0	0.05	0.1	0.2	0.5
P(mPEGA)-TTC	√	√	√	√	√	√	√
P(mPEGA$_{0.5}$-*co*-AA$_{0.5}$)-TTC	√	√	√	√	√	√	√
P(mPEGA0.75-*co*-4VP0.25)-TTC	√	√	√	√	√	√	√
PAA-TTC	√	*	√	*	*	*	*

[a]Freeze–thaw cycle proceeded at −20 °C; √ indicates no particle aggregation; * indicates particle aggregation.

of the selected particles prepared by photoinitiated RAFT dispersion polymerization under different conditions. All the particles were stable after a freeze thaw cycle, which proceeded at −20 °C. It also clearly shows that the particles prepared with PEG-functionalized stabilizers remained stable at different pH values (acidic or basic), and upon the addition of 0.5 M $CaCl_2$, indicating that PEG chains can provide highly stability to the particles, which is very important for further applications. In contrast, the PAA-stabilized particles flocculated substantially upon the addition of just 0.05 M $CaCl_2$. The presence of electrolytes may disturb the electrosteric stabilization mechanism of PAA-stabilized PMMA particles.

CONCLUSION

Photoinitiated RAFT dispersion polymerization of methyl methacrylate has been carried out in the presence of a Macro-RAFT agent under UV irradiation at room temperature. The Macro-RAFT agent primarily acts as a stabilizer and partially as a control reagent. A small molecular RAFT agent is required to ensure the effective control of the procedure and for obtaining monodisperse microspheres. XPS revealed that the surface of the microspheres was covered with the stabilizers. By changing the chain structure of the Macro-RAFT agent, various monodisperse microspheres with tailored surfaces have been synthesized, of which the PAA stabilized PMMA microspheres exhibited pH-responsive properties. The colloidal stability experiments showed that microspheres prepared with PEG-functionalized Macro-RAFT agents displayed excellent resistance to both freeze–thaw cycles and electrolyte-induced flocculation up to 0.5 M $CaCl_2$. The PAA-stabilized microspheres, on the other hand, also exhibited excellent resistance to freeze–thaw cycles but aggregated in a salt solution containing only 0.05 M $CaCl_2$.

ASSOCIATED CONTENT

Supporting Information

Schematic diagram of the equipment for photoinitiated dispersion polymerization, additional research results, recipes and particle size data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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