Novel Amphiphilic Centipede-Like Copolymer Bearing Polyacrylate Backbone and Poly(ethylene glycol) and Polystyrene Side Chains

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Received September 8, 2006; Revised Manuscript Received April 12, 2007

ABSTRACT: A series of well-defined asymmetric centipede-like copolymers, containing polyacrylate backbone, hydrophilic poly(ethylene glycol), and hydrophobic polystyrene side chains, was synthesized by successive atom transfer radical polymerization. The grafting-through strategy was first employed for the preparation of poly-[poly(ethylene glycol) methyl ether acrylate] comb copolymer. The grafting-from route was used following for the synthesis of the final amphiphilic centipede-like copolymer, poly[poly(ethylene glycol) methyl ether acrylate]-*g*-polystyrene. At each grafting point, two different chains are connected and the spacing between the grafting points is constant. Polystyrene side chains were connected to the polyacrylate backbone through stable C−C bonds instead of ester connections. The molecular weights of both the backbone and the side chains were controllable. The molecular weight distributions were in the range of 1.24−1.38. The critical micelle concentrations of these amphiphilic centipede-like graft copolymers in water were determined by fluorescence probe technique. The morphologies of the micelles formed from these centipede-like graft copolymers were preliminarily explored by TEM and were found to be spheres.

Introduction

Self-assembly of amphiphilic copolymers have attracted much attention during the past decade.[1−5] This interest is sustained due to the potential applications in the fields including the solubilizer,[6] drug delivery,[7−10] catalysis,[11,12] and microelectronics.[13] Studies of self-assembly behaviors of block copolymers in water have showed that the critical micelle concentration (cmc), micelle radius (R_h), and micelle aggregation number (N_{agg}) as well as the micellar shape are influenced by many factors such as pH value of the solution, the ionic strength of the solution, micelle's preparation conditions, the concentration of copolymer, the molecular weight of copolymer and the composition of copolymer.[14−16] As most of the research focused on the self-assembly behavior of amphiphilic "block" copolymers, only few researches touched on the self-assembly of amphiphilic "graft" copolymers.[17] Recently, it was found that the architecture of copolymer also played an important role in determining the properties of micelle.[18−20] Graft copolymers possess the additional complexity in the solution-state
assembly due to its complicated and confined structure. More information about the controlling of micellar morphologies and the design of new nanomaterials can be obtained through the studies of the self-assembly behavior of graft copolymer.

However, the studies of the self-assembly behavior of graft copolymers were restrained due to the synthetic difficulties of well-defined graft copolymers with controlled molecular weights and narrow molecular weight distributions.

Generally, three strategies including grafting-through, grafting-onto, and grafting-from were used for the synthesis of graft copolymer.[21] The grafting-through strategy is to get graft copolymer via the polymerization of macromonomers, the resulting graft copolymer via conventional radical polymerization of macromonomers possessed a broad chain-length distribution;[22] also the living polymerization of macromonomers yielded well-defined graft copolymer with low molecular weight.[23] The grafting-onto technique is the grafting of side chains onto the backbone by a coupling reaction, normally with an insufficient grafting efficiency.[24] The grafting-from method appeared recently; it utilizes the pendant initiation groups on the backbone to initiate the polymerization of another monomer to form side chains.[25] The development of atom transfer radical polymerization (ATRP)[26−29] and modified ATRP[30−33] has enabled the preparation of versatile comb copolymers with well-defined molecular architectures from grafting-through[34−36] and grafting-from strategies.[37] In particular, those side chains can be formed in a well-defined way via ATRP initiated by the pendant initiating groups on the backbone through grafting-from strategy, the living characteristic of ATRP enabled it to control both the molecular weights and molecular weight distributions of side chains.

Recently, researches started to focus on the synthesis of graft copolymers with complex architectures due to their key roles in understanding the correlation of structure and properties and exploring new materials.[38,39] In particular, the synthesis of novel symmetric graft copolymers with two identical branches at each grafting point, named centipede-like polymer, have been reported. This family of polymers possesses the following characteristics: at each grafting point, two different chains are connected and the spacing between the grafting points is constant. Mays and Hadjichristidis synthesized polystyrene- (PS-) based homocentipedes (PS-*g*-PS_2) and co-centipedes containing PS and polyisoprene (PI) segments (PI-*g*-PS_2) by step-growth polymerization of $(PS)_2SiCl_2$ with difunctional PS or PI.[38] Hirao and his co-workers employed grafting-onto strategy to synthesize well-defined centipede-like copolymers via styrene and isoprene.[39] All these centipede-like copolymers were homo- or AB_2-type copolymers with two identical and symmetric "centipede feet" connected to each grafting point. Their centipede feet were enantiomorphous.

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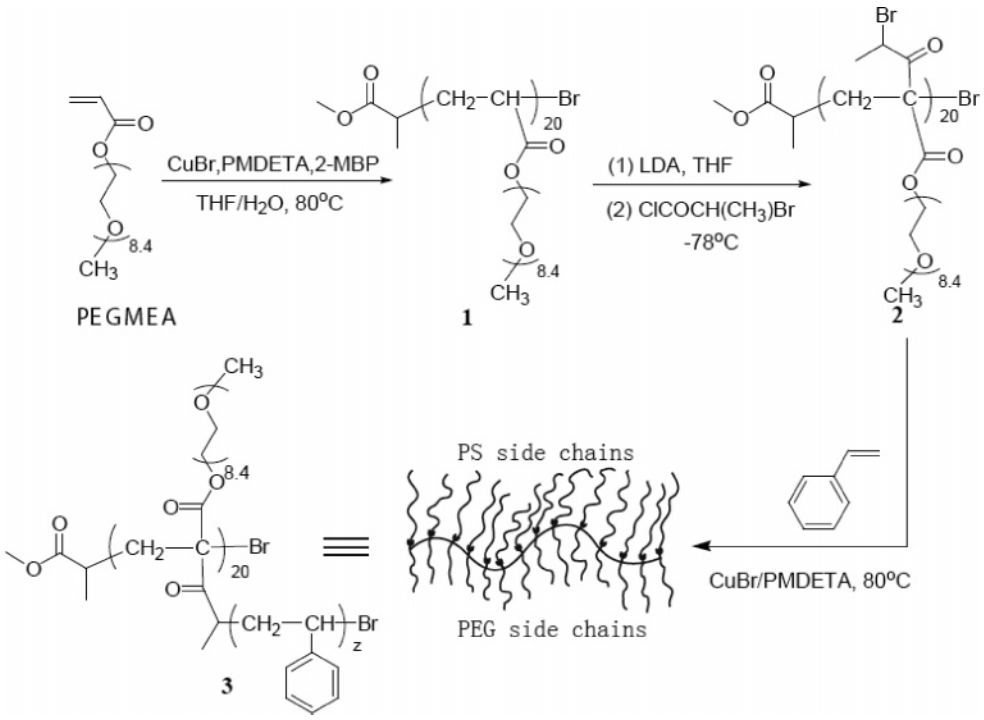
10.1021/ma062083v CCC: $37.00
Published on Web 05/23/2007

Scheme 1. Synthesis of Asymmetric Centipede-Like Graft Copolymer PPEGMEA-*g*-PS



In this work, a new approach (Scheme 1) to prepare "asymmetric" centipede-like graft copolymer via "grafting-from" strategy will be presented. Poly[poly(ethylene glycol) methyl ether acrylate]-*g*-polystyrene (PPEGMEA-*g*-PS) with a well-defined centipede structure was synthesized via successive ATRP of poly(ethylene glycol) methyl ether acrylate and styrene. The critical micelle concentrations (cmc) of these amphiphilic centipede-like graft copolymers in water were determined by fluorescence probe technique. Moreover, the morphologies of the micelles formed from these asymmetric centipede-like graft copolymers were preliminarily explored by transmission electron microscopy (TEM).

Experimental Section

Materials. Styrene (Aldrich, 99%) was washed with 5% aqueous NaOH solution and water, dried over CaH_2 and distilled under reduced pressure before use. Copper(I) bromide (CuBr, Aldrich, 98%) was purified by stirring overnight over CH_3CO_2H at room temperature, followed by washing the solid with ethanol, diethyl ether, and acetone prior to drying at 40 °C under vacuum for 1 day. Diisopropylamine (Aldrich, 99.5%) was dried over KOH for several days and distilled from CaH_2 under N_2 atmosphere before use. Tetrahydrofuran (THF) was dried over CaH_2 for 7 days and distilled from sodium and benzophenone under N_2 atmosphere just before use. Methyl 2-bromopropionate (2-MBP, Acros, 99%), *n*-butyllithium (*n*-BuLi, Aldrich, 1.6 M in hexane), poly(ethylene glycol) methyl ether acrylate (PEGMEA, M_n = 454, Aldrich), *N*,*N*,*N*′,*N*′,*N*″-pentamethyldiethylenetriamine (PMDETA, Aldrich, 99%) and α-bromopropionyl chloride (Acros, 99%) were used as received.

Measurements. FT-IR spectra were recorded on a Nicolet AVATAR-360 FT-IR spectrophotometer with 4 cm^{-1} resolution. All ^1H NMR and ^{13}C NMR analyses were performed on a Varian Mercury 300 spectrometer (300 MHz) in $CDCl_3$ and THF-d_8, TMS (^1H NMR), and $CDCl_3$ (^{13}C NMR) were used as internal standards. Conversion of styrene was determined by gas chromatography (GC) using a HP 6890 system with an SE-54 column. Relative molecular weights and molecular weight distributions were measured by conventional gel permeation chromatography (GPC) system equipped with a Waters 1515 Isocratic HPLC pump, a Waters 2414 refractive index detector, and a set of Waters Styragel columns (HR3, HR4 and HR5, 7.8 × 300 mm). GPC measurements were carried out at 35 °C using THF as the eluent with a flow rate of 1.0 mL/min. The system was calibrated with polystyrene standards. The absolute molecular weights of the centipede-like copolymers were determined by GPC equipped with a multiangle light scattering detector (GPC/MALS). THF was used as the eluent with a flow rate of 1.0 mL/min. detectors: Wyatt Optilab rEX refractive index detector and Wyatt DAWN HELEOS 18-angle light scattering detector with a 50 mW solid-state laser operating at 658 nm. Steady-state fluorescent spectra were recorded on a HITACHI FL-4500 spectrofluorometer with the bandwidth of 2.5 nm for excitation and emission. The emission spectra were recorded with a λ_{ex} = 339 nm. TEM images were obtained using a Philips CM120 instrument operated at 80 kV.

Homopolymerization of PEGMEA by ATRP. ATRP of PEGMEA was carried out in H_2O/THF (v:v = 10:1) under N_2 atmosphere. To a 25 mL Schlenk flask (flame-dried under vacuum just before use) sealed with a rubber septum, CuBr (0.0287 g, 0.2 mmol) was first added for degassing and kept under N_2. Next, PEGMEA (M_n = 454, 1.67 mL, 4 mmol) and PMDETA (0.042 mL, 0.2 mmol) which were stored under N_2, were introduced via a gastight syringe, and the mixture was stirred for several minutes. Then, the mixed solvent, H_2O/THF (v:v = 10:1, 1.67 mL) which was purged with N_2 for 10 min and mixed under N_2, was added via a gastight syringe. The mixture was light green and homogeneous. Finally, the initiator, 2-MBP (0.037 mL, 0.2 mmol) stored under N_2, was charged via a gastight syringe. The solution was degassed by three cycles of freeze−pump−thaw followed by immersing the flask into an oil bath thermostated at 80 °C to start the polymerization. The polymerization was terminated by immersing the flask into liquid nitrogen after 5 h. THF was added to the flask for dilution and the solution was filtered through a short Al_2O_3 column to remove the copper catalyst. The resulting solution was concentrated and precipitated into hexane. After repeated purification by dissolving in THF and precipitating in hexane for three times, 0.9556 g poly[poly(ethylene glycol) methyl ether acrylate] (PPEGMEA **1**) was obtained with a yield of 51.8%. GPC: M_n = 2200, M_w/M_n = 1.05. FI−IR (film): ν (cm^{-1}): 2869, 1728 (C═O), 1455, 1109 (C−O−C), 952. ^1H NMR: δ (ppm): 0.86 (3H, CH_3CH), 1.26, 1.65 (2H, CH_2CH), 2.18 (1H, COCH(CH_3)CH_2),

2.22−2.53 (1H, CH_2CH), 3.39 (3H, OCH_3), 3.68 (4H, OCH_2CH_2O), 3.88 (3H, $COOCH_3$), 4.18 (2H, $COOCH_2CH_2O$), 4.33 (1H, CHBr). ^{13}C NMR: δ (ppm): 26.0, 29.7 (CH_2CH), 35.2, 38.9 (CH_2CH), 55.1 (CH_2OCH_3), 59.4−72.6 (OCH_2CH_2O), 174.0 ($COOCH_2$).

The conversion of PEGMEA was determined by ^1H NMR according to previous literature.[40] The procedure was same with the above-mentioned polymerization except that the mixed solvent was changed to D_2O/THF (v:v = 10:1). Conversion of PEGMEA: 99.0%. GPC: M_n = 2100, M_w/M_n = 1.06.

Synthesis of PPEGMEA—Br Macroinitiator 2. In a 100 mL sealed three-neck flask, dried THF (10 mL) and diisopropylamine (0.281 mL, 2 mmol) were added under N_2. The solution was cooled to −78 °C and *n*-BuLi (1.6 M in hexane, 1.25 mL, 2 mmol) was added slowly. After 1 h, the mixture was treated with PPEGMEA (**1**, 0.9080 g, M_n = 2,200, M_w/M_n = 1.05) in 40 mL of dried THF under −78 °C. The reaction lasted for 3 h. Next, α-bromopropionyl chloride (0.2 mL, 2 mmol) in 10 mL THF was introduced. After 3 h, the reaction was terminated by water. The organic phase was washed with water and brine and dried over $MgSO_4$ overnight. After filtration, the solution was concentrated, and precipitated into hexane. The product was dried under vacuum to give 0.4970 g of macroinitiator (PPEGMEA−Br, **2**). GPC: M_n = 1800, M_w/M_n = 1.03. FT-IR (film): ν (cm^{-1}): 2871, 1734, 1453, 1351, 1105, 951, 855. ^1H NMR: δ (ppm): 0.86 (3H, CH_3CH), 1.26, 1.71 (2H, CH_2−CH), 1.90 (3H, $CH(CH_3)Br$), 2.28 (1H, $COCH(CH_3)CH_2$), 3.38 (3H, -OCH_3), 3.67 (4H, OCH_2CH_2O), 3.89 (3H, $COOCH_3$), 4.19 (2H, $COOCH_2CH_2O$), 4.33 (1H, CHBr). ^{13}C NMR ($CDCl_3$): δ (ppm): 18.7−21.0 ($CH(CH_3)Br$), 26.2−34.0 (CH_2 on PPEGMEA backbone), 41.0, 42.3 (CH on PPEGMEA backbone), 47.1 ($CH(CH_3)Br$), 52.2 (*tert-C* on PPEGMEA backbone), 54.7 (CH_2OCH_3), 58.6−72.4 (OCH_2CH_2O), 169.7−174.0 (O−C=O), 211.1 (C=O).

Synthesis of Centipede-like Graft Copolymer PPEGMEA-*g*-PS, 3. In a typical procedure, a 25 mL dried Schlenk flask was charged with CuBr (0.0143 g, 0.10 mmol). The flask was degassed and CuBr was kept under N_2. Next, PMDETA (0.021 mL, 0.10 mmol) and styrene (5.7 mL, 50 mmol) which were stored under N_2, were introduced via a gastight syringe. Finally, PPEGMEA-Br (**2**, 0.0590 g, M_n = 1,800, M_w/M_n = 1.03) in 2 mL of toluene stored under N_2, was introduced via a gastight syringe. The flask was degassed by three cycles of freezing−pumping−thawing followed by immersing the flask into an oil bath thermostated at 90 °C. After 24 h, the polymerization was terminated by putting the flask into liquid nitrogen. The reaction mixture was diluted by THF and filtered through an alumina column to remove the catalyst. The solution was concentrated and precipitated into methanol. The final product, 0.7303 g of poly[poly(ethylene glycol) methyl ether acrylate]-*g*-polystyrene (PPEGMEA-*g*-PS **3c**), was obtained after drying. GPC: M_n = 36 700, M_w/M_n = 1.24. FT-IR (film): ν (cm^{-1}): 3025, 2955, 2923, 2851, 1739, 1601, 1493, 1452, 1377, 1180, 1150, 1025, 907, 757, 698. ^1H NMR: δ (ppm): 0.89 (3H, CH_3), 1.25, 1.43, 1.59, 1.68−2.11 (2H, CH_2 and 1H, CH), 3.39 (3H, OCH_3), 3.65 (4H, OCH_2CH_2O), 6.54, 7.06 (5H, C_6H_5).

Determination of Critical Micelle Concentration. Pyrene was used as fluorescence probe to measure the cmc of the micelle solution formed from those asymmetric centipede graft copolymers. The acetone solution of pyrene (0.252 mg/mL) was added to a large amount of water until the concentration of pyrene reached 6×10^{-7} mol/L. Different amounts of THF solutions of PEGMEA-*g*-PS (**3**) graft copolymer (1 mg/mL) were added to water containing pyrene ([pyrene] = 6×10^{-7} mol/L). All fluorescence spectra were recorded at 25 °C.

TEM Measurements. To prepare micelles, THF solution of PPEGMEA-*g*-PS **3** graft copolymer (1 mg/mL) was added dropwise to water with vigorous stirring until the concentration of PPEGMEA-*g*-PS **3** graft copolymer was 0.01 mg/mL. The solution was stirred for another several hours for the evaporation of THF. For TEM studies, a drop of micellar solution was deposited on an electron microscopy copper grid coated with carbon film and the water evaporated at room temperature.

Results and Discussion

Synthesis of PPEGMEA (1) by the Grafting-through Technique. The comb copolymer PPEGMEA (**1**) was prepared by grafting-through strategy via ATRP using 2-MBP as the initiator, CuBr as the catalyst and PMDETA as the ligand. The polymerization was run in the mixed solvent of water and THF (v:v = 10:1) at 80 °C since, in recent reports, ATRP of poly(ethylene glycol) methyl acrylate or acrylate macromonomer were successfully carried out in aqueous solution.[40,41]

It was found that the feeding sequence was important to determine whether PEGMEA could be polymerized. In our experiment, PEGMEA and PMDETA were added before the addition of H_2O/THF. After the adding of mixed solvent, the mixture was light green and homogeneous and no dark precipitation of Cu metal was observed. PPEGMEA (**1**) with narrow molecular weight distribution (M_w/M_n = 1.05) was obtained. The polymerization of PEGMEA was also performed in D_2O/THF to measure the conversion of PEGMEA by ^1H NMR.[40] The conversion was 99.0%. This confirmed the successful ATRP of PEGMEA in aqueous using CuBr/PMDETA system when PEGMEA was added before the addition of the solvent. A comparative experiment was carried out with changing of feeding sequence: the mixed solvent of D_2O/THF was added before the addition of PEGMEA instead of after. Under this case, the solution turned into dark blue rapidly and the brown precipitation of Cu metal was observed due to the disproportionation.[42] The color of the solution lightened after PEGMEA was added, but the precipitation remained in the solution. After the initiator was introduced, the mixture was kept at 80 °C for 5 h and the conversion of PEGMEA was measured to be almost zero. It thus can be concluded, for our current polymerization case, that PEGMEA could stabilize the system of CuBr/PMDETA in aqueous when the monomer was added before the addition of the solvent.

The ^1H NMR spectrum of PPEGMEA (**1**) is shown in Figure 1A. The signals of the double bond protons disappeared and the peaks of polyacrylate backbone appeared at δ = 1.26−2.53 ppm, which meant the macromonomer has been polymerized. The peaks at 0.86 and 4.33 ppm were attributed to 3 protons of CH_3CH of the initiator at one end of polyacrylate backbone and 1 proton of CHBr (peak "e") at the other end of polyacrylate backbone, respectively.

The successful ATRP can be evidenced from the unimodal and symmetrical GPC curve with narrow molecular weight distribution (M_w/M_n = 1.05).[26] The feed ratio of the macromonomer to the initiator was 20:1, but the result of GPC measurement showed M_n of PPEGMEA (**1**) was just 2200, which was much lower than the theoretical value. It is well-known that the molecular weight of branched polymer is usually underestimated by GPC due to the lower hydrodynamic radius.[43,44] The theoretical molecular weight of PPEGMEA (**1**) can be calculated from the data of the conversion (99.0%) of PEGMEA according to eq 1 (20 is the feed ratio and 454 is the molecular weight of repeating unit).

$$M_{n,theo} = \text{conversion} \times 20 \times 454 \quad (1)$$

The theoretical molecular weight was calculated to be 9000. The accurate molecular weight of PPEGMEA (**1**) was calculated by ^1H NMR. The peaks "a" (3.39 ppm) and "c" (3.88 ppm) belong to three protons of terminal $-OCH_3$ of PEG side chains and three protons of $-COOCH_3$ of the initiation group of polyacrylate backbone, respectively. So the accurate molecular weight of PPEGMEA (**1**) can be obtained from ^1H NMR

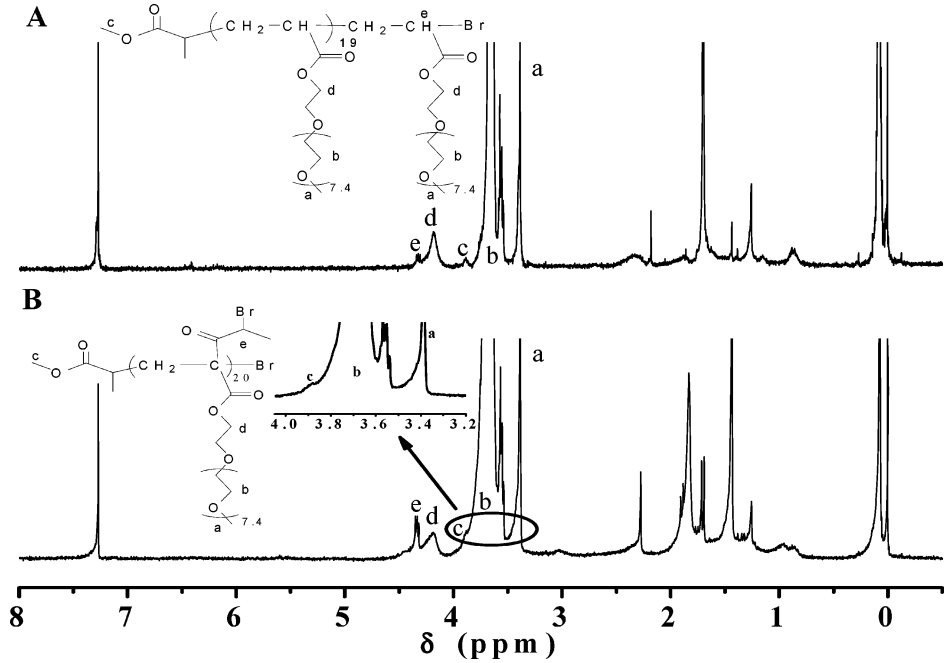


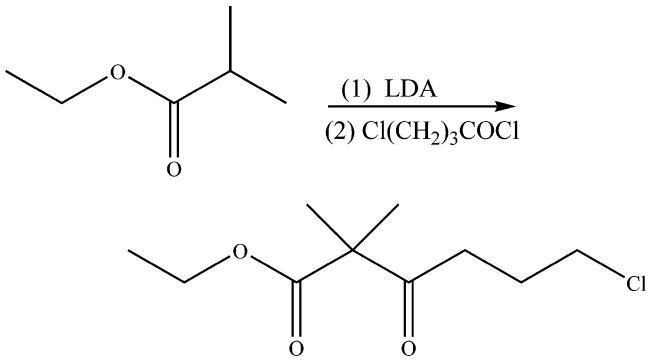
Figure 1. ^{1}H NMR spectra of PPEGMEA (**1**) (A) and PPEGMEA−Br (**2**) (B).

according to eq 2 (S is the peak area and 454 is the molecular weight of repeating unit).

$$M_{n(abs)} = [S_a/S_c] \times 454 \quad (2)$$

The value of S_a/S_c was 20 and the molecular weight was calculated to be 9100, which was in accordance with the theoretical molecular weight calculated from the conversion of PEGMEA. It can be concluded that every PPEGMEA (**1**) chain possesses 20 poly(ethylene glycol) side chains.

Synthesis of Macroinitiator 2. Generally, graft copolymers prepared by ATRP had a hydrophobic backbone and hydrophilic side chains because the ester groups of the backbone were easy to be converted to the halogen-containing ATRP initiation groups.[21,45] Here, the ester groups of polyacrylate backbone have been used to connect poly(ethylene glycol) side chains. An alternative method was used to connect ATRP initiation groups to the α-carbon of the ester groups of polyacrylate backbone using lithium diisopropylamide (LDA) and α-bromopropionyl chloride as shown in Scheme 1. CHBr groups of ATRP initiation groups, ester groups and CHBr end groups of PPEGMEA (**1**) were supposed to be not affected during the reaction, as evidenced from the previous literature and was as shown below.[46]



By this approach, PPEGMEA (**1**) comb copolymer was successfully transformed into the macroinitiator and all the ATRP initiation groups were connected to polyacrylate backbone through stable C−C bonds instead of ester connections.

The ^{1}H NMR spectrum of PPEGMEA−Br (**2**) is shown in Figure 1B. It was found that a new peak, which was attributed to 3 protons of newly introduced −CH(CH_3)Br group, appeared at 1.90 ppm. But this peak was overlapped with the signals of polyacrylate backbone. Also, the integration area ratio of peak "e" to peak "d" (S_e/S_d) was found to be much higher than that of PPEGMEA (**1**). Since the peak "d" belonged to two protons of −COOCH_2CH_2O of PEG side chains and this group was not involved in the reaction of synthesizing the macroinitiator, the integration area of peak "d" should not change after the reaction. The increasing of the ratio was thus caused by the increasing of the integration area of peak "e" , which was attributed to one proton of the newly introduced −CH(CH_3)Br group. No signal of alkene was found in the region between 4.5 and 7.0 ppm, which meant that the possible elimination reaction of CHBr end group did not occur during the chemical modification with LDA and α-bromopropionyl chloride. Moreover, a new peak at 211.1 ppm, which belonged to the ketone carbon of −COCH(CH$_3$)Br, was found in ^{13}C NMR spectrum of PPEGMEA−Br (**2**). All of these points affirmed the successful introduction of ATRP initiation groups.

The approximate grafted ATRP initiation group density can be calculated from ^{1}H NMR according to eq 3 since peak "d" represented 40 protons of 20 poly(ethylene glycol) side chains (N_{In} is the number of ATRP initiation groups per PPEGMEA chain).

$$N_{In} = [S_e/S_d] \times 40 \quad (3)$$

The value of N_{In} was 19.80, and the approximate grafted ATRP initiation group density was calculated to be 19.80/20 = 0.99, which meant ATRP initiation groups were introduced to every repeating unit of the polyacrylate backbone.

As we can see from Figure 2, only a unimodal peak was found in GPC curve after the reaction with LDA and α-bromopropionyl chloride. The molecular weight distribution kept narrow (M_w/M_n = 1.03), which meant the architecture of polymer chain was not altered during the reaction. The M_n of

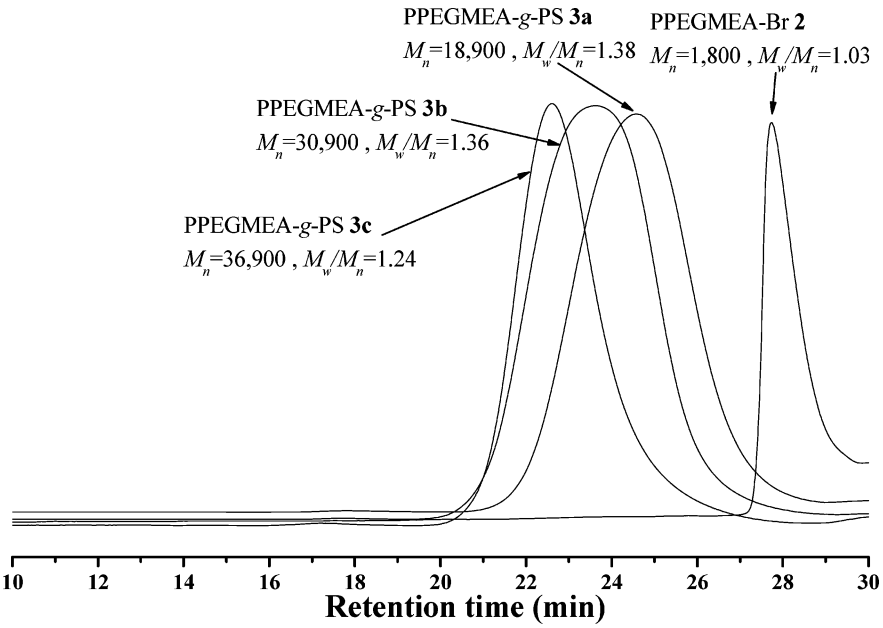


Figure 2. GPC traces of PPEGMEA−Br (**2**), PPEGMEA-*g*-PS (**3a**, **3b**, and **3c**) in THF.

Table 1. Syntheses of PPEGMEA-*g*-PS Centipede-like Graft Copolymers[a]

	time (h)	M_n[b] (g/mol)	M_w/M_n[b]	N_{St}/N_{EG}[c]	$M_{n,NMR}$[d] (g/mol)	$n_{st,NMR}$[e]	convn[f] (%)	cmc[g] (g/mL)
3a	12	18 900	1.38	9.53	176 000	79.8	7.0	6.99×10^{-7}
3b	18	30 900	1.36	10.8	198 000	90.7	9.9	5.88×10^{-7}
3c	24	36 700	1.24	11.9	217 000	100	13.5	4.53×10^{-7}

[a] Initiated by PPEGMEA **2** macroinitiator (M_n = 1800, M_w/M_n = 1.03, grafted ATRP initiation group density: 0.99/1), [St]:[Br group]:[CuBr]:[PMDETA] = 500:1:1:1. [b] Measured by GPC in THF. [c] The ratio of the total number of St unit to EG unit obtained by ^{1}H NMR, solvent: $CDCl_3$. [d] Obtained by ^{1}H NMR. [e] The number of St repeating unit per PS side chain. [f] Conversion of styrene measured by GC. [g] Critical micelle concentration determined by fluorescence spectroscopy.

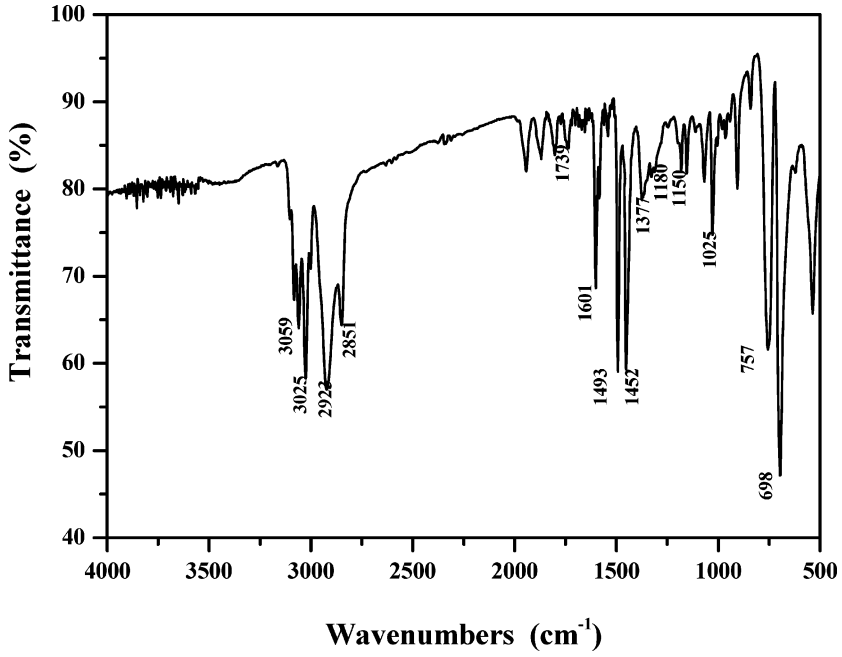


Figure 3. FT-IR spectrum of centipede-like PPEGMEA-*g*-PS (**3**).

PPEGMEA−Br (**2**) macroinitiator (M_n = 1800) was slightly smaller than that of PPEGMEA (**1**) (M_n = 2200) which is similar to our previous report,[44] we could attribute this to the newly branched ATRP initiation groups.

Graft Copolymerization of Styrene. ATRP of styrene was initiated by PPEGMEA−Br (**2**) macroinitiator and the results are listed in Table 1. All graft copolymers' molecular weights were much higher than that of the macroinitiator, which meant St was initiated for polymerization. The molecular weights of graft copolymers increased with the extending of polymerization time, which is the characteristic of ATRP. GPC curves of PPEGMEA-*g*-PS with different polymerization time are shown in Figure 2. All graft copolymers showed unimodal and symmetrical GPC curves with narrow molecular weight distri-

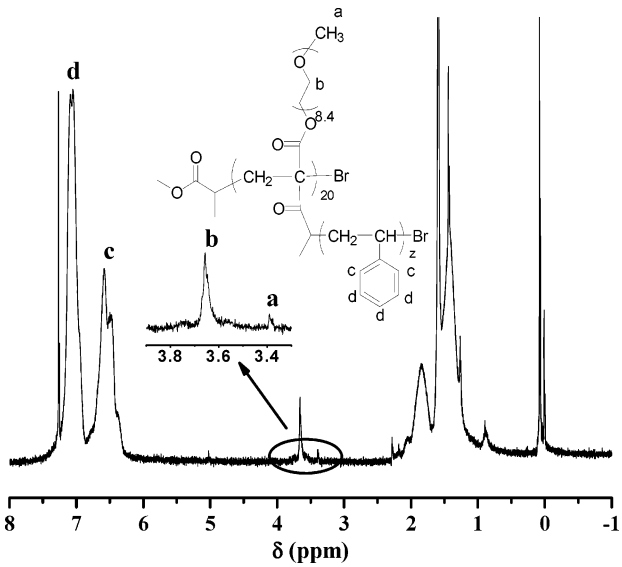


Figure 4. ^{1}H NMR spectrum of centipede-like PPEGMEA-*g*-PS (**3**).

butions ($M_w/M_n \leq 1.38$), which are characteristic of ATRP,[26] and also indicated that intermolecular coupling reactions could be neglected.[45] In the synthesis of linear graft copolymer,[21,45,47−50] a high feed ratio of monomer to initiator and a low conversion of monomer were necessary to suppress the intermolecular coupling reactions, which was the same in the present study.

The structure of centipede-like PPEGMEA-*g*-PS was characterized by FT-IR and ^{1}H NMR, respectively. The FT-IR spectrum of PPEGMEA-*g*-PS is shown in Figure 3. The typical signals of polystyrene segment were found to appear at 3025, 1601, 1493, and 1452 cm^{-1}. Also, the sharp bands at 757 and 698 cm^{-1} confirmed the monosubstituted benzene ring of polystyrene segment. The peaks at 1739, 1180, 1150, and 1025 cm^{-1} can be attributed to polyacrylate and poly(ethylene glycol) segments.

The signals of the corresponding protons of polyacrylate backbone and PEG and PS side chains were found in ^{1}H NMR spectrum as shown in Figure 4. Generally, ^{1}H NMR was used to determine the composition of the copolymer. In our studies, the ratio of total number of St unit to EG unit (N_{St}/N_{EG}) was calculated from ^{1}H NMR according to eq 4 as listed in Table 1 (S_{St} is the integration area of five protons of phenyl of PS side chains at 6.54 and 7.06 ppm, S_{EG} is the integration area of three protons of terminal $-OCH_3$ of the PEG side chains at 3.39 ppm):

$$N_{St}/N_{EG} = [S_{St}/8.4S_{EG}] \times 0.6 \quad (4)$$

From the values of N_{St}/N_{EG} and the molecular weight of PPEGMEA (**1**) (M_n = 9100), the molecular weights of graft copolymers ($M_{n,NMR}$) were also obtained according to eq 5 as listed in Table 1 (8.4 is the number of EG repeating unit per PEG side chain and 104 is the molecular weight of St repeating unit), which were higher than those determined by GPC.[43,44]

$$M_{n,NMR} = 9100 + [N_{St}/N_{EG}] \times (8.4 \times 20) \times 104 \quad (5)$$

Moreover, the numbers of St repeating unit per PS side chain ($n_{St,NMR}$) were also calculated according to eq 6 as listed in Table 1:

$$n_{St,NMR} = [N_{St}/N_{EG}] \times 8.4 \quad (6)$$

Table 2. Different Compositions of PPEGMEA-*g*-PS 3c Determined by ^{1}H NMR

	$CDCl_3$		THF-d_8	
concn (mg/mL)	N_{St}/N_{EG}	$n_{st,NMR}$	N_{St}/N_{EG}	$n_{st,NMR}$
2.5	8.78	73.7	6.54	54.94
5.0	12.49	105.0	9.68	81.34
10.0	15.47	130.0	15.55	130.58
20.0	17.88	150.2	19.21	161.36

Table 3. Compositions of PPEGMEA-*g*-PS Determined by Light Scattering

sample	$M_{n,GPC/MALS}$[a] (g/mol)	N_{St}/N_{EG}	$n_{st,MALS}$
3a	31 300	1.27	10.66
3b	46 100	2.11	17.76
3c	58 700	2.84	23.82

[a] Obtained by GPC equipped with a multiangle light scattering detector (GPC/MALS) in THF with a flow rate of 1.0 mL/min.

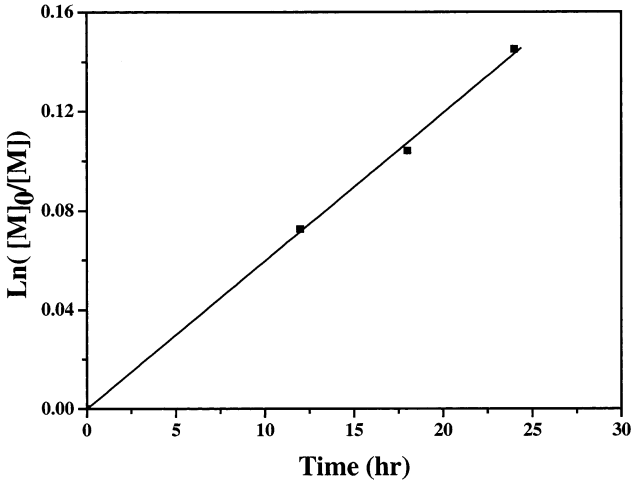


Figure 5. Kinetic plot for solution ATRP of styrene initiated by PPEGMEA−Br (**2**).

It has been reported that ^{1}H NMR spectrum of amphiphilic copolymer was affected by the conditions of the measurement.[45,51−53] ^{1}H NMR measurements of PPEGMEA-*g*-PS (**3c**) were carried out in different solvents ($CDCl_3$ and THF-d_8) with different concentrations. The values of N_{St}/N_{EG} and $n_{st,NMR}$ were calculated according to eq 4 and 6, respectively, and listed in Table 2. The values of N_{St}/N_{EG} and $n_{st,NMR}$ are different when ^{1}H NMR measurements were run in different solvents ($CDCl_3$ and THF-d_8) with the same concentration. Also, the values of N_{St}/N_{EG} and $n_{st,NMR}$ varied when ^{1}H NMR measurements were run in the same solvent with different concentrations. These results demonstrated that the values of N_{St}/N_{EG} and $n_{st,NMR}$ of these three amphiphilic centipede-like graft copolymers obtained from ^{1}H NMR spectra were dependent on the conditions of the measurement, the values varied when the solvent or the concentration was changed. This phenomenon could be due to the selectivity of the solvents on the complicated composition (including hydrophobic polyacrylate backbone, hydrophilic PEG and hydrophobic PS side chains) and the complex architecture of PPEGMEA-*g*-PS. Further study to understand the solution behavior is in progress.

Since it was difficult for us to determine the "actual" compositions of amphiphilic PPEGMEA-*g*-PS from the results of ^{1}H NMR due to a large uncertainty, the absolute molecular weights of amphiphilic PPEGMEA-*g*-PS were measured by light scattering in THF instead.

From the molecular weight of PPEGMEA (**1**) (M_n = 9100) and the absolute molecular weights of amphiphilic PPEGMEA-

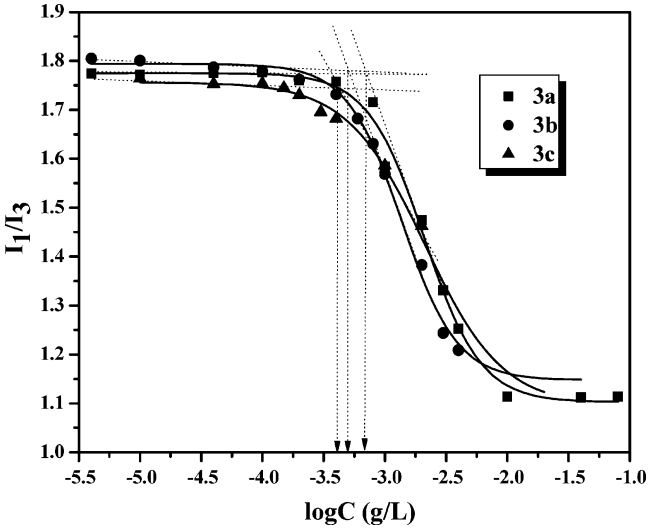


Figure 6. Dependence of fluorescence intensity ratios of pyrene emission bands on the concentration of PPEGMEA-*g*-PS (**3**).

g-PS determined by light scattering, the "actual" compositions of PPEGMEA-*g*-PS were obtained. The values of N_{St}/N_{EG} were calculated according to eq 7 as listed in Table 3:

$$N_{St}/N_{EG} = (M_{n,GPC/MALS} - 9100)/(8.4 \times 20 \times 104) \quad (7)$$

Also, the values of $n_{St,\ MALS}$ were also calculated according to eq 8 as listed in Table 3:

$$n_{St,MALS} = [N_{St}/N_{EG}] \times 8.4 \quad (8)$$

From the data of conversions of styrene listed in Table 1, the semilogarithmic plot of $\ln([M]_0/[M])$ vs time was drawn in Figure 5. It can be concluded that the apparent polymerization rate is first order with respect to the concentration of styrene. This phenomenon accorded with the characteristic of ATRP.

So the polymerizations of backbone and side chains were both controllable and centipede-like copolymer PPEGMEA-*g*-PS (**3**) is well-defined, with a polyacrylate backbone possessing 20 repeating units and short PEG (8.4 repeating units per chain) and long PS (10−25 repeating units per chain) side chains at each grafting point.

Properties of Micelle. The critical micelle concentrations of PPEGMEA-*g*-PS (**3**) in aqueous solution were determined by fluorescence technique using pyrene as probe.[54,55] Fluorescence spectrum of pyrene is sensitively affected by the environment and the polarity of its surrounding.[54,55] In the presence of micelles, pyrene is solubilized within the interior of the hydrophobic part. As a result, the values of I_1/I_3 of the emission spectrum changed sharply. The intensity ratios (I_1/I_3) against the logarithm of polymer concentrations were plotted to determine cmc as the onset of micellization (Figure 6).

As shown in Table 1, the values of cmc are around 10^{-7} g/mL, which were very low compared with those of traditional surfactants or block copolymers.[56] The cmc values of PPEGMEA-*g*-PS (**3**) decreased when the molecular weights increased due to the increasing of the content of hydrophobic PS side chains. These low cmc values are related with the branched structure of graft copolymers and the asymmetric compositions since the percentage of hydrophobic PS side chains is very high. With such low cmc values, amphiphilic centipede-like copolymers can form highly stable micellar aggregates with low rates of dissociation in vivo.[57]

Finally, the micelle structures were preliminarily explored by TEM. The typical TEM images of the micelles of PPEGMEA-*g*-PS (**3**) in freshly aqueous solution are shown in Figure 7. The micelles formed by PPEGMEA-*g*-PS (**3**) in pure water with different molecular weights were all spheres (ca. 150−300 nm).

Conclusion

A new approach was developed to synthesize the well-defined centipede-like amphiphilic copolymers with two different side chains by ATRP and grafting-from technique. At each grafting point, two different chains (PS and PEG) are connected and the spacing between the grafting points is constant. Hydrophobic polystyrene side chains were connected to polyacrylate backbone through stable C−C bonds instead of ester connections. The molecular weights of both the backbone and the side chains were controllable. The molecular weight distributions were in the range of 1.24−1.38. The critical micelle concentrations of

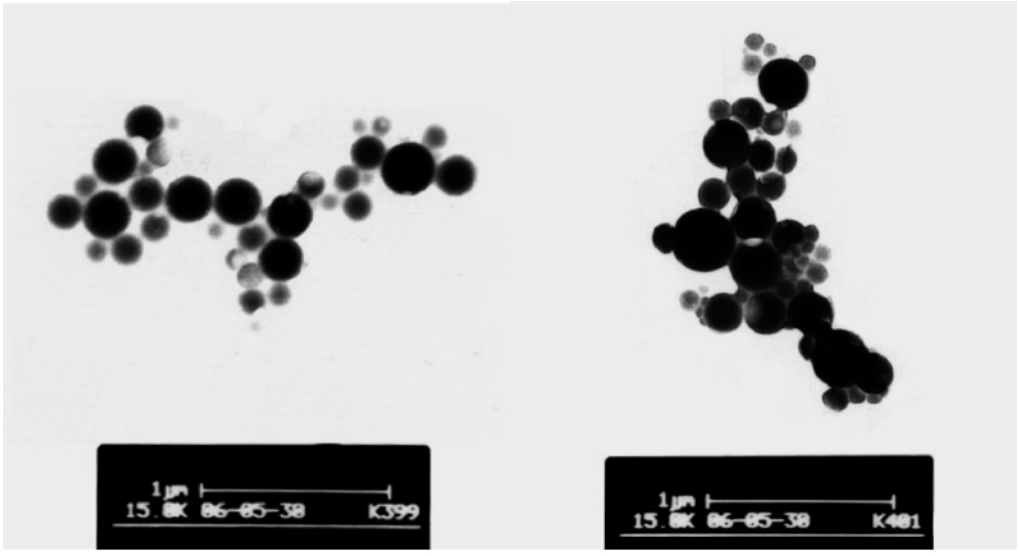


Figure 7. TEM images of micelles formed from centipede-like PPEGMEA-*g*-PS (**3a**, A; **3c**, B) in pure water.

these amphiphilic centipede-like graft copolymers in water were determined by fluorescence probe technique. The morphologies of the micelles formed from these centipede-like graft copolymers were preliminarily explored by TEM and were found to be spheres.

This approach can be used to obtain centipede-like graft copolymers simply by replacing monomers. This will bring more development to synthesize complex graft copolymers. Further works, including changing monomers to alter the amphiphilicity of graft copolymers and controlling the length of each "foot" of the "centipede" to see their effects on the morphology, are in progress.

Acknowledgment. The authors express thanks for the financial support from the National Natural Science Foundation of China (Grant No. 20404017).

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MA062083V