ABSTRACT: A series of well-defined double hydrophilic graft copolymers containing poly(poly(ethylene glycol) methyl ether acrylate) (PPEGMEA) backbone and poly(poly(ethylene glycol) ethyl ether methacrylate) (PPEGEEMA) side chains were synthesized by the combination of single electron transfer-living radical polymerization (SET-LRP) and atom transfer radical polymerization (ATRP). The backbone was first prepared by SET-LRP of poly(ethylene glycol) methyl ether acrylate macromonomer using CuBr/tris(2-(dimethylamino)ethyl)amine as catalytic system. The obtained comb copolymer was treated with lithium diisopropylamide and 2-bromoisobutyryl bromide to give PPEGMEA-Br macroinitiator. Finally, PPEGMEA-g-PPEGEEMA graft copolymers were synthesized by ATRP of poly(ethylene glycol) ethyl ether acrylate macromonomer using PPEGMEA-Br macroinitiator via the grafting-from route. The molecular weights of both the backbone and the side chains were controllable and the molecular weight distributions kept narrow ($M_w/M_n < 1.20$). This kind of double hydrophilic copolymer was found to be stimuli-responsive to both temperature and ion (0.3 M Cl$^-$ and SO$_4^{2-}$).

INTRODUCTION Stimuli-responsive polymers exhibit characteristics structural and property changes in response to an external signal, such as the electric potential, magnetic field, temperature, light and pH. Therefore, they have attracted considerable interest for applications including the actuation, surface engineering, stimuli-gated filtration, affinity control, drug delivery, and so forth. Poly(ethylene glycol) (PEG) is a thermoresponsive, water-soluble, uncharged, and nontoxic polymer. PEG has a lower critical solution temperature (LCST) in aqueous media; thus, it has been extensively investigated for nano- and biotechnology applications. To the best of our knowledge, most researchers focused on the thermoresponsive linear copolymers, only few reports were concerned with the graft thermoresponsive copolymers; however, it should be noted that these reported thermoresponsive graft copolymers were not well defined or double hydrophilic, since that the synthesis of well-defined double hydrophilic graft copolymers is more difficult compared with that of linear block copolymers.

As well known as molecular bottle brushes, densely grafted copolymers have received great attentions because of their unusual architecture and properties. A molecular bottle brush is composed of a flexible backbone with a high density of side chains separated by a distance much smaller than their unperturbed dimensions, which leads to significant congestion and entropically unfavorable extension of the backbone and side chains so that the polymers are prevented from adopting a random coil conformation. Moreover, the thermal properties of an aqueous solution containing the brush copolymers reckon strongly on the composition and architecture of the side chains. In general, the synthesis of graft copolymers can be accomplished by three different routes: grafting-through, grafting-onto, and grafting-from strategies. The grafting-through strategy is to prepare graft copolymer via the polymerization of the macromonomers, the resulting graft copolymers via the conventional free radical polymerization of the macromonomers possess a broad chain-length distribution; also, the living polymerization of the macromonomers yielded well-defined graft copolymers with low molecular weights. The grafting-onto technique is to graft the side chains onto the backbone by a coupling reaction, normally with an
insufficient grafting efficiency. The grafting-from strategy is usually used to prepare well-defined graft copolymers by introducing side chains via controlled/living free radical polymerization, including atom transfer radical polymerization (ATRP), single electron transfer-living radical polymerization (SET-LRP), and reversible addition-fragmentation chain transfer (RAFT), polymerization, initiated by the pendant initiation groups. Specifically, the side chains can be formed in a well-defined way via ATRP initiated by the pendant initiating groups on the backbone through the grafting-from strategy, the living characteristic of ATRP enabled it to control both the molecular weights and molecular weight distributions of side chains.

In this work, we report the synthesis of well-defined densely grafted double hydrophilic copolymers via the grafting-from strategy. Poly[poly(ethylene glycol) methyl ether acrylate]-g-poly[poly(ethylene glycol) ethyl methacrylate] (PPEGMEA-g-PPEGEMA) double hydrophilic densely grafted copolymers were synthesized via sequential SET-LRP and ATRP. Temperature response and ion-sensitive isothermal response of the graft copolymers were also investigated.

**EXPERIMENTAL**

**Materials**

Poly(ethylene glycol) methyl ether acrylate (PEGMEA, $M_n = 454$, Aldrich, 99%) was passed through a column filled with basic alumina. Poly(ethylene glycol) ethyl ether methacrylate (PEGEEA, $M_n = 246$, Aldrich, 99%) was distilled in vacuo before use. Diisopropylamine (DIPA, Aldrich, 99.5%) was dried over KOH for several days and distilled from CaH$_2$ under N$_2$ before use. Copper (I) bromide (CuBr, Aldrich, 98%) and copper (II) bromide (CuBr$_2$, Aldrich, 98%) were purified by stirring overnight with acetic acid at room temperature followed by washing the solid with ethanol, diethyl ether, and acetone before drying at 40 °C in vacuo for 1 day. Tetrahydrofuran (THF) was dried over CaH$_2$ for 7 days and distilled from sodium and benzophenone under N$_2$ before use. Acetone was dried over CaSO$_4$ for several days and distilled before use. Methyl 2-bromopropionate (2-MBP, Acros, 99%), 2-bromoisobutyryl bromide (Alfa Aesar, 97%), n-butyllithium (n-BuLi, Aldrich, 1.6 M in hexane), and tris(aminoethyl)amine (TREN, Aldrich, 96%) were used as received. Tris(2-di-methylamino)ethylamine (Me$_6$TREN) and 4,4'-diheptyl-2,2'-dipyridine (dHbpyp) were synthesized according to previous literatures.

**Measurements**

All $^1$H NMR (500 MHz) and $^{13}$C NMR (125 MHz) analyses were performed on a Bruker Avance 500 spectrometer in CDCl$_3$ and D$_2$O, TMS ($^1$H NMR) and CDCl$_3$ ($^{13}$C NMR) were used as internal standards. Elemental analysis was carried out on a Carlo Erba 1106 system. 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 mm × 300 mm). The system was calibrated with linear polystyrene standards. GPC measurements were carried out at 35 °C using THF as eluent with a flow rate of 1.0 mL/min. The phase transition temperatures of the graft copolymers were measured by UV-vis using a Varian Cary 300 spectrophotometer over a temperature range between 8 and 45 °C; the temperature was controlled and measured using a DC-1006 variable temperature cryostat with an ascending rate of 2 °C/min; the value of LCST was determined from the onset of the sharp decrease of the transmittance. Hydrodynamic diameter ($D_h$) was measured by dynamic light scattering (DLS) with a Malvern Nano-ZS90 Zetasizer.

**SET-LRP Homopolymerization of PEGMEA**

SET-LRP homopolymerization of PEGMEA macromonomer was carried out in H$_2$O/THF under N$_2$ using 2-MBP as initiator and CuBr/Me$_6$TREN as catalytic system. CuBr (0.2304 g, 1.6 mmol) was first added to a 25-mL Schlenk flask (flame-dried under vacuum before use) sealed with a rubber septum for degassing and kept under N$_2$. Next, PEGMEA ($M_n = 454$, 13.36 mL, 32 mmol), Me$_6$TREN (0.44 mL, 1.6 mmol), dried THF (1.2 mL), and redistilled H$_2$O (12.0 mL) were introduced in turn via a gastight syringe. The solution was degassed by three cycles of freezing-pumping-thawing. Finally, 2-MBP (0.178 mL, 1.6 mmol) was charged via a gastight syringe followed by immersing the flask into an oil bath preset at 40 °C to start the polymerization. The flask was cooled by liquid N$_2$ to terminate the polymerization after 5 h. The mixture was diluted with THF and the residual copper catalyst was removed by filtering the solution through a short Al$_2$O$_3$ column. The resulting solution was concentrated and precipitated into n-hexane. After repeated purification by dissolving in THF and precipitating in n-hexane for three times, 8.3643 g of PPEGMEA 1 was obtained with a yield of 57.6%. GPC: $M_n = 2900$, $M_w/M_n = 1.03$.

$^1$H NMR: δ (ppm): 1.26, 1.65 (2H, CH$_2$CH), 2.15 (1H, CH$_2$CH), 3.38 (3H, OCH$_3$), 3.65 (4H, OCH$_2$CH$_2$O), 3.88 (3H, COOCH$_3$), 4.18 (2H, COOCH$_2$CH$_2$O). $^{13}$C NMR: δ (ppm): 26.1, 29.8 (CH$_2$CH), 35.0, 39.0 (CH$_2$CH), 55.0 (CH$_2$OCH$_3$), 59.6–72.5 (OCH$_2$CH$_2$O), 174.1 (COOCH$_3$).

The conversion of PEGMEA was determined by $^1$H NMR according to previous literature. The procedure was same as the above polymerization except that the mixed solvent was changed to D$_2$O/THF (v:v = 10:1). The conversion of PEGMEA was 71.6%.

**Preparation of PPEGMEA-Br Macrominitiator**

Lithium diisopropylamide (LDA) and 2-bromoisobutyryl bromide were used to transform PPEGMEA 1 comb homopolymer into the macrominitiator. Dried THF (350 mL) and diisopropylamine (1.68 mL, 12 mmol) were first added to a sealed 1000-mL three-neck flask (flame-dried under vacuum before use) under N$_2$. The solution was cooled to −78 °C, and n-BuLi (7.5 mL, 12 mmol) was added slowly. After 1 h, the mixture was treated with PPEGMEA 1 (8.364 g, $M_n = 2900$, $M_w/M_n = 1.03$) in 100 mL of dried THF under −78 °C. The reaction lasted for 3 h. Next, 2-bromoisobutyryl bromide (1.2 mL, 12 mmol) was introduced via a gastight syringe. After another 3 h, water was added to quench the reaction. The solution was concentrated and dialyzed in
water for 3 days. The aqueous solution was extracted by CHCl3 and dried against MgSO4 overnight. After the filtration, the solution was concentrated and precipitated into n-hexane. The product was dried in vacuo to give 5.3385 g of PPEGMEA-Br 2 macroinitiator. GPC: \( M_n = 2500, M_w/M_n = 1.07 \).

\[ 1^1H\text{ NMR: } \delta (ppm): 1.26, 1.68 \ (2H, CH_2CH), 1.94 \ (3H, CH(CH_3)_2Br), 2.17 \ (1H, CH_2CH), 3.38 \ (3H, OCH_3), 3.64 \ (4H, OCH_2CH_2O), 3.87 \ (3H, COOCH_3), 4.17 \ (2H, COOCH_2CH_2O). \]

\[ 1^3C\text{ NMR: } \delta (ppm): 18.9-21.1 \ (CH(CH_3)Br), 26.6-33.8 \ (CH_2 on PPEGMEA backbone), 41.2 \ (CH on PPEGMEA backbone), 47.0 \ (CH(CH_3)Br), 52.1 \ (\text{tert-C on PPEGMEA backbone}), 54.5 \ (CH_2OCH_3), 59.0-72.1 \ (OCH_2CH_2O), 169.5-174.2 \ (O-C=0), 211.0 \ (C=O). \]

Elemental analysis: C\% = 53.40%.

**APTR Graft Copolymerization of PEGEEMA**

PPEGMEA-g-PEGEEMA double hydrophilic double-grafted copolymer was synthesized by ATRP of PPEGEMA macromonomer initiated by PPEGMEA-Br 2 macroinitiator using CuBr/dHbpy catalytic system. CuBr and dHbpy in dried THF were added to a 100 mL Schlenk flask (flame-dried before use) sealed with a rubber septum under N\textsubscript{2}. After three cycles of evacuating and purging with N\textsubscript{2}, PPEGMEA-Br 2 macroinitiator (\( M_n = 2500, M_w/M_n = 1.07 \)) in dried acetone and PEGEEMA macromonomer were charged via a gas-tight syringe. The flask was degassed by three cycles of freezing-pumping-thawing followed by immersing the flask into an oil bath preset at 40 °C. The polymerization was terminated by putting the flask into liquid N\textsubscript{2} after certain time. The reaction mixture was diluted by THF and passed through an Al\textsubscript{2}O\textsubscript{3} column to remove the residual copper catalyst. The solution was concentrated and precipitated into n-hexane. After repeated purification by dissolving in THF and precipitating in n-hexane for three times, the white viscous solid was dried in vacuo overnight to obtain the final product, PPEGMEA-g-PEGEEMA 3 graft copolymer.

\[ 1^1H\text{ NMR: } \delta (ppm): 0.88, 1.03 \ (3H, CH_3 on PPEGEMA side chains), 1.25, 1.77, 1.85 \ (2H, CH_2CH), 2.17 \ (1H, CH_2CH), 3.38 \ (3H, OCH_3), 3.65 \ (4H, OCH_2CH_2O), 4.09 \ (2H, COOCH_2CH_2O). \]

**RESULTS AND DISCUSSION**

**Synthesis of PPEGMEA Comb Homopolymer**

PPEGMEA 1 comb homopolymer was prepared by the grafting-through strategy via SET-LRP of PEGMEA macromonomer at 40 °C in THF/H\textsubscript{2}O using 2-MBP as initiator and CuBr/Me\textsubscript{6}TREN as catalytic system. The unimodal and symmetrical GPC curve with a narrow molecular weight distribution (\( M_w/M_n = 1.03 \)) demonstrated the successful SET-LRP of PPEGMA macromonomer. The theoretical molecular weight of PPEGMEA 1 can be estimated from the data of the conversion (71.6%) of PEGMEA macromonomer according to eq 1 (20 is the feed ratio of PEGMEA macromonomer to 2-MBP and 454 is the molecular weight of PEGMEA repeating unit). The theoretical molecular weight was calculated to be 6500. The accurate molecular weight of PPEGMEA 1 was determined by \(^1H\) NMR according to our previous report.\textsuperscript{18} The result was 6400, which was very close to the theoretical value. Thus, we can conclude that every PPEGMEA 1 chain possesses 14 side chains.

\[ M_n,\text{theo} = \text{Conversion} \times 20 \times 454. \]

**SET-LRP Mechanism of PEGMEA Homopolymerization in H\textsubscript{2}O/THF**

We have reported ATRP homopolymerization of PEGMEA macromonomer at 80 °C in H\textsubscript{2}O/THF (v:v = 10:1) using CuBr/PMDETA as catalytic system,\textsuperscript{48} in which the result of the homopolymerization was very sensitive to the feeding sequence. The previous example needed a high temperature (80 °C) and a relatively complicated procedure. To make the homopolymerization more facile and simplify the operation process, the homopolymerization of PEGMEA macromonomer was carried out at a relatively low temperature (40 °C) in current case using CuBr/Me\textsubscript{6}TREN as catalytic system in place of CuBr/PMDETA. However, the condition of this polymerization was much closer to that of SET-LRP according to previous literatures\textsuperscript{42,49-54} due to the rapid disproportionation of CuBr in water in the presence of Me\textsubscript{6}TREN. A control experiment was performed to clarify the mechanism of this polymerization. A mixture of THF (0.15 mL) and H\textsubscript{2}O (1.5 mL) was added to a Schlenk flask containing CuBr (28.8 mg) and Me\textsubscript{6}TREN (0.055 mL), and another mixture of THF (0.15 mL) and H\textsubscript{2}O (1.5 mL) was added to a Schlenk flask containing 44.8 mg of CuBr\textsubscript{2} and 0.050 mL of Me\textsubscript{6}TREN. Both solutions were degassed by three cycles of freezing-pumping-thawing. Next, both solutions were stirred at room temperature and clear Cu(0) black sedimentation appeared at the bottom of the flask containing CuBr/Me\textsubscript{6}TREN (inset A of Fig. 1) because that Cu(0) was formed by the disproportionation of Cu(I) in THF/H\textsubscript{2}O in the existence of Me\textsubscript{6}TREN, whereas the solution containing CuBr\textsubscript{2}/Me\textsubscript{6}TREN remained homogeneous (inset B of Fig. 1). The maximum absorption wavelength of the solution containing CuBr/Me\textsubscript{6}TREN located at 861 nm (red line in Fig. 1) resulting from the absorption of Cu(II) complex (blue line in Fig. 1), which

**FIGURE 1** UV–vis spectra of THF/H\textsubscript{2}O solutions containing CuBr/Me\textsubscript{6}TREN, CuBr\textsubscript{2}/Me\textsubscript{6}TREN, and CuBr/Me\textsubscript{6}TREN/2-MBP.
further evidenced the disproportionation of Cu(I). Cu(I) is shown to hardly remain in the mixture of THF/H$_2$O since that a high equilibrium constant (about $10^7$) of the disproportionation of Cu(I) in H$_2$O in the presence of Me$_6$TREN has already been reported. $^{42,51,53,54}$ The black Cu(0) sedimentation almost disappeared in 5 min and the solution became homogeneous after 2-MBP was added. Moreover, the solution turned blue (inset C of Fig. 1), the same color as that of the solution containing CuBr$_2$/Me$_6$TREN (inset B of Fig. 1). Previous studies have demonstrated that the mechanism of SET-LRP involves the reversible activation of dormant polymer chains via a Cu(0)-mediated outer-sphere electron transfer process involving the heterolytic C-X cleavage. $^{49,56,57}$ Therefore, it can be concluded that the mechanism of the homopolymerization of PEGMEA should be that of SET-LRP via the above results.

This mechanism shows that the disproportionation of Cu(I)X generates Cu(0) activator and Cu(II)X$_2$ deactivator in situ, and the extent of Cu(I)X disproportionation is mainly dependent on the selection of ligand and solvent. $^{51-63}$ In this study, the disproportionation of Cu(I)X into Cu(0) and Cu(II)X$_2$ was assured by using Me$_6$TREN as ligand and THF/H$_2$O as solvent. Cu(0) and Cu(II) changed into soluble Cu(I) through the reversible activation and deactivation steps when 2-MBP was added; on the other side, Cu(0) generated in situ was disproportionated into Cu(0) and Cu(II) again. In view of that in situ generated Cu(0) was consumed in the activation step at the rate that rived that of the agglomeration, the "visible" agglomeration of Cu(0) disappeared and turned into "atomic" Cu(0) or "invisible" Cu(0) colloids. $^{49,56,57}$ Therefore, it can be concluded that the mechanism of the homopolymerization of PEGMEA should be that of SET-LRP via the above results.

Characterization of PPEGMEA-Br Macroinitiator

In this case, the ester groups of the backbone have been used to link PEG side chains. An alternative approach is to connect ATRP initiation groups to the $\alpha$-carbon of the ester groups of the backbone using LDA and 2-bromoisobutyryl bromide as shown in Scheme 1. $^{36,64-67}$ C-Br groups of ATRP initiation groups, ester groups and CHBr end groups of PPEGMEA 1 have not been influenced during the reaction according to the previous reports. $^{36,64-67}$ By this newly developed method, all the ATRP initiation groups are linked to the backbone through the stable C-C bonds instead of the environment-sensitive ester connections.

The chemical structure of PPEGMEA-Br 2 was examined by $^1$H and $^{13}$C NMR. A new peak attributed to six protons of newly introduced C(CH$_3$)$_2$Br group appeared at 1.94 ppm in $^1$H NMR spectrum after the reaction, which is overlapped with the signals of the backbone. The absence of the signal of alkene in the region between 4.5 and 7.0 ppm showed that the possible elimination reaction of CHBr end group did not occur during the chemical modification with LDA and 2-bromoisobutyryl bromide. Furthermore, a new peak appeared at 211.0 ppm in $^{13}$C NMR spectrum after the reaction, which belonged to the ketone carbon of $\text{COC(CH$_3$)$_2$Br}$. All the aforementioned evidences confirmed the successful introduction of ATRP initiation groups. Only a unimodal and symmetric peak was found in the GPC curve of PPEGMEA-Br 2 and the molecular weight distribution kept narrow
chains can be found in the spectrum. The characteristic signals of three protons of CH$_3$ of PPEGEEMA side chains appeared at 0.88 and 1.03 ppm (peak “a”), respectively, and the peak “b” at 4.09 ppm is attributed to two protons of COOC$_2$H$_2$ of both PPEGMEA and PPEGEEMA segments, which assured us of the structure of PPEGMEA-g-PPEGEEMA graft copolymer.

The molecular weight of the graft copolymer measured by GPC has been reported to be much lower than the “real” value, therefore, the lengths of PPEGEEMA side chains were determined by $^1$H NMR instead of GPC. In our studies, the number of PEGEEMA repeating unit per side chain ($n_{\text{PEGEEMA}}$) was calculated according to eq 3 (S is the peak area and $D_{\text{init}}$ is the grafting density of ATRP initiation group) as summarized in Table 1. Moreover, the molecular weights of the graft copolymers ($M_{\text{NMR}}$) were obtained according to eq 4 (7000 and 246 are the molecular weights of PPEGMEA-Br$_2$ macroinitiator and PEGEEMA, respectively). From the data in Table 1, we can find that the molecular weights of the graft copolymers increased with the extending of polymerization time, which is the characteristic of ATRP. Thus, it can be concluded that the polymerizations of the backbone and the side chains were both controllable.

The obtained graft copolymers have the well-defined structures (Scheme 1): a polyacrylate backbone (14 repeating units) with two different side chains, one is shorter PPEGMEA chain (8.4 repeating units per chain) at each grafting site and the other is much longer PPEGEEMA chain (33–94 repeating units per chain) at a quarter grafting sites.

$$n_{\text{PEGEEMA}} = 2S_a/(3S_b - 2S_a) \times D_{\text{init}}$$  \hspace{1cm} (3)

$$M_{\text{NMR}} = 7000 + 3.8 \times 246 \times n_{\text{PEGEEMA}}$$  \hspace{1cm} (4)

Thermoresponsive Phase Transition Behavior of PPEGMEA-g-PPEGEEMA

The aqueous PEG solutions have been found to exhibit unique phase behaviors where the solubility decreases with the ascending of the temperature, and the LCST behavior of PEG is attributed to a balance between hydrophilic and hydrophobic interactions and the resulting hydrogen-bonding interactions between water molecules and the polymer chain. The phase transition temperatures of PPEGMEA-g-PPEGEEMA graft copolymers could be determined from the temperature dependence of UV–vis transmittance as listed in Table 1. Figure 3 shows UV–vis transmittance of

<table>
<thead>
<tr>
<th>Sample</th>
<th>Time (h)</th>
<th>$M_w/M_n$</th>
<th>$n_{\text{PEGEEMA}}$</th>
<th>$M_{\text{NMR}}$ (g/mol)</th>
<th>LCST ($^\circ$C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>1.5</td>
<td>1.19</td>
<td>33</td>
<td>37,800</td>
<td>23</td>
</tr>
<tr>
<td>3b</td>
<td>2</td>
<td>1.16</td>
<td>53</td>
<td>46,500</td>
<td>25</td>
</tr>
<tr>
<td>3c</td>
<td>4</td>
<td>1.15</td>
<td>66</td>
<td>68,700</td>
<td>25</td>
</tr>
<tr>
<td>3d</td>
<td>6</td>
<td>1.20</td>
<td>84</td>
<td>85,500</td>
<td>24</td>
</tr>
<tr>
<td>3e</td>
<td>8</td>
<td>1.19</td>
<td>94</td>
<td>94,900</td>
<td>23</td>
</tr>
</tbody>
</table>

* Initiated by PPEGMEA-Br$_2$ macroinitiator ($M_n = 2500$, $M_w/M_n = 1.07$, grafted ATRP initiation group density: 0.273/1), [PEGMEA]:[Br group]:[CuBr]:[dHbpy] = 500:1:1:2.

* Measured by GPC in THF.

* The number of PEGEEMA repeating unit per side chain obtained by $^1$H NMR in CDCl$_3$.

* Obtained by $^1$H NMR.

* Lower critical solution temperature determined by UV–vis in the heating process.
double-distilled water solution of PPEGMEA-g-PPEGEEMA 3a as a function of temperature in a heating process. It is apparent that this graft copolymer displays an abrupt change in transmittance from 23 °C during the course of heating; therefore, 23 °C is determined to be LCST of PPEGMEA-g-PPEGEEMA 3a. Temperature-dependent 1H NMR (Fig. 4) was also used to investigate the phase behavior of PPEGMEA-g-PPEGEEMA 3a. 1H NMR spectra at 10 and 20 °C show all the signals of the corresponding protons of both PPEGMEA and PPEGEEMA segments, indicating the complete dissolution of both side chains. However, the characteristic signals of three protons of \( \text{CH}_3 \) of PPEGEEMA side chains at 0.75 and 0.93 ppm weakened when temperature was increased to 30 °C and entirely disappeared at 40 °C. The peak at 4.03 ppm attributed to two protons of COO\( \text{CH}_2 \) of both PPEGMEA and PPEGEEMA segments became almost invisible at 40 °C, which also illustrated that PPEGEEMA side chains were “frozen” by the micellar shell (PPEGMEA segments) at that temperature. These result confirmed the formation of micelles containing PPEGEEMA core and PPEGMEA shell.

The thermoresponsive behavior of PPEGMEA-g-PPEGEEMA 3a was also analyzed by DLS. The hydrodynamic diameter \( D_h \) of PPEGMEA-g-PPEGEEMA 3a is apparently influenced by the temperature as shown in Figures 5 and 6. When the temperature was just 21 °C, PPEGMEA-g-PPEGEEMA 3a dissolved molecularly in aqueous media with a low \( D_h \) around 5 nm (Fig. 5). However, \( D_h \) of PPEGMEA-g-PPEGEEMA 3a increased sharply from 23 °C (Fig. 6) upon the increasing of the temperature, indicating the occurrence of the micellization. \( D_h \) of PPEGMEA-g-PPEGEEMA 3a increased to 138 nm at 25 °C (Fig. 5) and it was 1902 nm while the temperature was 35 °C. This result is in good accordance with those of UV-vis and 1H NMR.
TABLE 2 LCST of PPEGMEA-g-PPEGEEMA 3 in Different Salt Solutions

<table>
<thead>
<tr>
<th>Sample</th>
<th>( n_{\text{PEGMEA}} )</th>
<th>DDW</th>
<th>NaCl</th>
<th>Na2SO4</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>33</td>
<td>23</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td>3b</td>
<td>53</td>
<td>25</td>
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<td>19</td>
</tr>
<tr>
<td>3c</td>
<td>66</td>
<td>25</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>3d</td>
<td>84</td>
<td>24</td>
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<td>16</td>
</tr>
<tr>
<td>3e</td>
<td>94</td>
<td>23</td>
<td>22</td>
<td>16</td>
</tr>
</tbody>
</table>

* The number of PEGEEMA repeating unit per side chain obtained by \(^1\)H NMR in CDC\(_3\).

** Measured by UV-vis in the heating process.

d [Na2SO4] = 0.3 mol/L.

d [NaCl] = 0.3 mol/L.

Effect of Ionic Strength on LCST of PPEGMEA-g-PPEGGEEMA

Ion effect on the cloud point of thermoresponsive polymer is found to be related with the Hofmeister series, which arranges the ions in a specific order (SO\(_4^{2-}\) > HPO\(_4^{2-}\) > F\(^-\) > Cl\(^-\) > Br\(^-\) > I\(^-\) > NO\(_3^{-}\) > ClO\(_4^{-}\)), where the ions on the right side can salting-in the solutes more effectively.\(^{26,71-74}\)

To investigate the effect of salinity on thermoresponsive behavior of PPEGMEA-g-PPEGGEEMA 3a, three different representative salts of NaSCN (a strong chaotropic, water "structure breaker"), NaCl, and Na2SO4 (a strong kosmotrope, water "structure maker") are selected from the Hofmeister series. It can be seen from Figure 7 that the remarkable changes in LCST of PPEGMEA-g-PPEGGEEMA 3a took place following the mixture of 0.3 M Na2SO4 (salting-out salt) and 0.3 M NaCl solutions, and the LCSTs were shifted to the lower temperature compared with that without any ion. The degree of moving is different, LCST of PPEGMEA-g-PPEGGEEMA 3a just decreased to 22 °C in the aqueous solution containing 0.3 M NaCl, whereas it acutely declined to 18 °C in the aqueous solution containing 0.3 M Na2SO4. This result accorded with the specific order of Hofmeister series. When NaSCN was added to the aqueous solution of the graft copolymer, the decreasing scale of UV-vis transmittance was too modest so that the phase transition temperature could not be observed due to SCN\(^-\), a strong chaotropic anion.

Table 2 shows the influence of ionic strength on LCSTs of all PPEGMEA-g-PPEGGEEMA 3 graft copolymers with different lengths of PPEGGEEMA side chains. Their LCSTs were all shifted to the lower temperature while adding NaCl and Na2SO4, indicating that the thermoresponsive phase behavior of PPEGMEA-g-PPEGGEEMA 3 graft copolymer can be regulated by salt additions. Furthermore, Na2SO4 was found to have an more strong effect on decreasing the LCST compared with NaCl.

CONCLUSIONS

In summary, a series of well-defined graft copolymers comprising two different hydrophilic side chains were synthesized via the combination of SET-LRP, ATRP, and the grafting-from strategy. The molecular weights of the backbone and the side chains were both controllable, and the molecular weight distributions were in the range of between 1.15 and 1.20. All these graft copolymers respond sharply to the temperature and this unique thermoresponsive phase behavior can be modified by salt additions. This kind of thermoresponsive brush-like copolymer should be a promising biomaterial with systematically controlled ion responsiveness.

The authors thank the financial support from National Natural Science Foundation of China (20974117, 20904065, and 50873029), Shanghai Nano-Technology Program (0952nm05800), and Shanghai Scientific and Technological Innovation Project (08431902300).

REFERENCES AND NOTES


