A New Thermo-responsive Block Copolymer with Tunable Upper Critical Solution Temperature and Lower Critical Solution Temperature in the Alcohol/Water Mixture

Yang Su, Meihan Dan, Xin Xiao, Xiaohui Wang, Wangqing Zhang

Key Laboratory of Functional Polymer Materials of the Ministry of Education, Institute of Polymer Chemistry, Nankai University, Tianjin 300071, China Correspondence to: W. Zhang (E-mail: wqzhang@nankai.edu.cn)

Received 24 February 2013; accepted 24 June 2013; published online 19 July 2013 DOI: 10.1002/pola.26854

ABSTRACT: The multi-thermo-responsive block copolymer of poly[2-(2-methoxyethoxy)ethyl methacrylate]-*block*-poly[*N*-(4-vinylbenzyl)-*N*,*N*-diethylamine] (PMEO₂MA-*b*-PVEA) displaying phase transition at both the lower critical solution temperature (LCST) and the upper critical solution temperature (UCST) in the alcohol/water mixture is synthesized by reversible addition-fragmentation chain transfer polymerization. The poly[2-(2-methoxyethoxy)ethyl methacrylate] (PMEO₂MA) block exhibits the UCST phase transition in alcohol and the LCST phase transition in water, while the poly[*N*-(4-vinylbenzyl)-*N*,*N*-diethylamine] (PVEA) block shows the UCST phase transition in isopropanol and the LCST phase transition in the alcohol/water mixture. Both the polymer molecular weight and the co-sol-

INTRODUCTION During the past two decades, the thermoresponsive polymers have received great interest because of their various applications.^{1,2} Generally, three kinds of thermo-responsive polymers are classified. The first kind of thermo-responsive polymers are those displaying phase transition in solvent at the lower critical solution temperature (LCST).^{3–21} These LCST-type thermo-responsive polymers are molecularly soluble in solvent at temperature below LCST and become insoluble when temperature increases above LCST. Among the LCST-type thermo-responsive polymers, poly(N-isopropylacrylamide) (PNIPAM) exhibiting the LCST phase transition in water at 32 °C may be the most focused one.¹⁷⁻²¹ The second kind of thermo-responsive polymers are those displaying phase transition in solvent at the upper critical solution temperature (UCST).²²⁻²⁷ These UCST-type thermo-responsive polymers are molecularly soluble in solvent at temperature above UCST and become insoluble when temperature decreases below UCST, which is just different from those of the LCST-type thermo-responsive polymers. The UCST-type polymers are expected to be very promising for the drug delivery purposes, as the release of encapsuvent/nonsolvent exert great influence on the LCST or UCST of the block copolymer. By adjusting the solvent character including the water content and the temperature, the block copolymer undergoes multiphase transition at LCST or UCST, and various block copolymer morphologies including inverted micelles, core-corona micelles, and corona-collapsed micelles are prepared. © 2013 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2013**, *51*, 4399–4412

KEYWORDS: block copolymers; lower critical solution temperature (LCST); micelles; poly[N-(4-vinylbenzyl)-N,N-diethylamine]; stimuli-sensitive polymers; upper critical solution temperature (UCST)

lated drugs are triggered with the body temperature increasing. Up to now, only a few of UCST-type thermo-responsive polymers such as polysulfobetaines²² in water, poly(methyl methacrylate)^{23,24} in the alcohol/water mixture and PNI-PAM²⁵ in ionic liquid have been discussed. The third kind of thermo-responsive polymers are those displaying phase transition in solvent at both LCST and UCST.²⁸⁻⁴¹ These doubly thermo-responsive polymers are usually diblock copolymers,²⁸⁻³⁸ in which one block presents LCST, whereas the other block presents UCST, resulting in the double thermoresponse. For example, the schizophrenic diblock copolymers of poly(N-isopropylacrylamide)-block-poly(3-[N-(3-methacrylamidopropyl)-*N*,*N*-dimethyl] ammoniopropane sulfonate)³¹ and poly[3-dimethyl(methacryloyloxyethyl) ammonium propane sulfonate]-block-poly[2-(N-morpholino)ethyl methacrylate],³² the nonionic diblock copolymer of poly[oligo(ethylene glycol) methyl ether methacrylate]-block-poly(N-isopropylacrylamide),³³ poly(benzyl methacrylate)-block-poly(N-isopropylacrylamide),³⁴ poly(ethylene oxide)-block-poly(N-isopropylacrylaand mide),35 are demonstrated to be the doubly thermoresponsive polymers. Besides the block copolymers, some

Additional Supporting Information may be found in the online version of this article.

© 2013 Wiley Periodicals, Inc.



random copolymers based on poly(2-oxazoline)s such as poly[(2-ethyl-2-oxazoline)-*co*-(2-phenyl-2-oxazoline)]

[P(EtOx-*co*-PhOx)] and poly[(2-ethyl-2-oxazoline)-*co*-(2-nonyl-2-oxazoline)] [P(EtOx-*co*-NonOx)] are found to display phase transition in the water/ethanol mixture at both UCST and LCST.^{39,40}

To prepare suitable thermo-responsive block copolymers displaying both UCST and LCST phase transition for a given purpose, the initial selection of the suitable polymers exhibiting phase transition at LCST or UCST and the subsequent synthesis strategy such as atom transfer radical polymerization,⁴²⁻⁴⁵ nitroxide-mediated polymerization,⁴⁶ single-electron transfer living radical polymerization,^{47–49} and reversible additionfragmentation chain transfer (RAFT) polymerization^{33,36,50-53} should be involved. The family of poly[oligo(ethylene glycol) (meth)acrylate] including poly[oligo(ethylene glycol) methyl ether methacrylate] (POEGMA), poly(2-[2-(2-methoxyethoxy)ethoxy]ethyl methacrylate) (PMEO₃MA) and poly[2-(2methoxyethoxy)ethyl methacrylate] (PMEO₂MA), which are very promising biocompatible polymers, undergo phase transition either in aliphatic alcohols at UCST or in water at $\text{LCST.}^{33,54-59}$ It is found that the LCST of POEGMA in water is correlative to the number of the ethyleneoxide units, and the polymer with longer ethyleneoxide side chain usually has higher LCST.54-56 Besides, the UCST of POEGMA in isopropanol increases with the polymer molecular weight increasing.⁵⁹ Furthermore, the LCST or UCST of POEGMA is also affected by the solvent character,59 enabling a convenient tuning of LCST or UCST by an appropriate choice of solvent. Owing to the biocompatible character and the tunable phase transition temperature, the POEGMA based block copolymers have aroused much interest in polymer science.^{33,54–59}

In our recent work, a new family of thermo-responsive polymer based on poly[N-(4-vinylbenzyl)-N,N-dialkylamine] has been reported.⁶⁰ In this contribution, the multi-thermo-responsive diblock copolymer of poly[2-(2-methoxyethoxy)ethyl methacrylate]-*block*-poly[N-(4-vinylbenzyl)-N,N-diethylamine] (PMEO₂MA-*b*-PVEA) are synthesized by RAFT polymerization. The multi-thermo-responsive micellization of the PMEO₂MA-*b*-PVEA block copolymer in the isopropanol/water mixture at UCST and LCST is also demonstrated. Besides, the parameters such as the polymer molecular weight and the polymer chemical composition affecting the UCST and LCST of the thermo-responsive polymers are investigated.

EXPERIMENTAL

Materials

The monomer of 2-(2-methoxy)ethyl methacrylate (MEO₂MA, 95%, Aldrich) was purified by passing through a column of basic alumina. The chemical reagents including diethylamine (DEA, >99.5%, Tianjin Chemical Corp.), chloromethylstyrene (CMS, >97%, Alfa), K_2CO_3 (>99%, Tianjin Chemical Corp.) were used as received. 2,2'-Azobis(isobutyronitrile) (AIBN) was recrystallized from ethanol. The RAFT

agent of cumyl dithiobenzoate (CDB) was synthesized as discussed elsewhere.⁶¹ All the other chemical reagents were analytic grade and used as received. Deionized water was used in this study.

Synthesis of the *N*-(4-vinylbenzyl)-*N*,*N*-diethylamine (VEA) Monomer

Into a flask, K₂CO₃ (27.6 g, 0.20 mol), CMS (15.3 g, 0.10 mol), DEA (14.6 g, 0.20 mol), and CHCl₃ (100 mL) were added. The flask content was initially degassed by nitrogen purge and then heated at 50 °C for 24 h with magnetic stirring. The resultant mixture was filtered, washed with water (100 mL imes 3), and then the organic phase was collected. After dried over anhydrous magnesium sulfate, the solvent was removed by rotary evaporation to obtain a crude product. Finally, the crude product was purified by column chromatography using the solvent of petroleum ether and distilled under vacuum to afford a colorless or pale yellow liquid of VEA (16.0 g, 85% yield). ¹H NMR (CDCl₃): $\delta = 7.34$ (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 6.71 (dd, *J* = 11.0 and 17.7 Hz, 1H), 5.72 (dd, J = 1.0 and 16.6 Hz, 1H), 5.20 (dd, J = 1.0 and 10.0 Hz, 1H), 3.55 (s, 2H), 2.52 (q, J = 7.1 Hz, 4H), 1.04 (t, J = 7.1 Hz, 6H).

Synthesis of PVEA by RAFT Polymerization

A typical polymerization is introduced. Into a Schlenk flask, VEA (3.79 g, 20.0 mmol) and the mixture of CDB (40.8 mg, 0.15 mmol) and AIBN (8.21 mg, 0.050 mmol) dissolved in toluene (2.0 mL) were added. After removal of oxygen by three freeze-pump-thaw cycles, the polymerization was performed at 75 °C for 18 h under vigorous stirring and quenched by immersing the flask in iced water. The synthesized polymer of PVEA was precipitated into the ethanol/ water mixture (6/5 by weight) and dried at room temperature under vacuum. To detect the VEA monomer conversion, a drop of the polymerization solution (0.1 mL) was directly diluted with CDCl₃ and subjected to ¹H NMR analysis. The VEA monomer conversion was determined according to eq (1), in which $I_{2.5}$ is the integral area of the proton resonance signal at $\delta = 2.5$ ppm [PhCH₂N(CH₂CH₃)₂ in the VEA monomer and the PVEA polymer] and $I_{5.2}$ is the integral area of the proton resonance signal at $\delta = 5.2$ ppm (one of PhCH= CH_2 in the VEA monomer), respectively.

Conversion % =
$$\frac{I_{2.5} - 4I_{5.2}}{I_{2.5}} \times 100\%$$
 (1)

Synthesis of PMEO₂MA by RAFT Polymerization

Typically, into a Schlenk flask, MEO₂MA (4.52 g, 24.0 mmol) and the mixture of CDB (0.163 g, 0.60 mmol) and AIBN (16.4 mg, 0.10 mmol) dissolved in toluene (5.0 mL) were added. The flask content was degassed by three freeze-pump-thaw cycles, then the polymerization was performed at 65 °C for 8 h under vigorous stirring and quenched by immersing the flask in iced water. The synthesized polymer was precipitated in *n*-hexane and dried at room temperature under vacuum. To detect the monomer conversion, a drop of the polymerization solution was dropped into CDCl₃ and subjected to ¹H NMR analysis. The monomer conversion was



SCHEME 1 The schematic synthesis of PVEA (A), PMEO₂MA (B), and PMEO₂MA-b-PVEA (C).

calculated according to eq (2), in which $I_{4.3}$ and $I_{4.1}$ are the integral area of the proton resonance signals at $\delta = 4.3$ ppm (COOC**H**₂) in the remaining monomer and at $\delta = 4.1$ ppm in the synthesized polymer of PMEO₂MA, respectively.

Conversion % =
$$\frac{I_{4.1}}{I_{4.3} + I_{4.1}} \times 100\%$$
 (2)

Synthesis of PMEO₂MA-b-PVEA by RAFT Polymerization

The PMEO₂MA-b-PVEA block copolymer was prepared by RAFT polymerization using the synthesized PMEO₂MA as macromolecular RAFT agent (macro-RAFT agent). Typically, into a Schlenk flask, the macro-RAFT agent of $\ensuremath{\mathsf{PMEO}_2\mathsf{MA}}$ $(M_{\rm n,th} = 5.8 \text{ kg/mol}, 0.464 \text{ g}, 0.080 \text{ mmol})$, VEA (1.51 g, 8.0 mmol), and AIBN (3.28 mg, 0.020 mmol) dissolved in toluene (1.0 mL) were added. After oxygen being removed by three freeze-pump-thaw cycles, the flask content was heated at 80 °C for 8 h, and then the polymerization was quenched by immersing the flask in iced water. The monomer conversion was determined by ¹H NMR analysis as similarly as introduced in the Synthesis of PVEA by RAFT Polymerization section. The polymerization mixture was first diluted with the ethanol/water mixture (10 mL, 6/5 by weight) and then the unreacted monomer was removed by dialysis against the ethanol/water mixture (6/5 by weight) for 3 days (molecular weight cutoff: 7000 Da). After dialysis, water (100 mL) was added into the polymer solution, and the polymer was

extracted with CH_2Cl_2 (50 mL \times 3). The organic phase was collected and dried over anhydrous magnesium sulfate, and then the solvent was removed by rotary evaporation to afford the PMEO₂MA-*b*-PVEA block copolymer.

Characterization

The ¹H NMR analysis was performed on a Bruker Avance III 400 MHz NMR spectrometer using CDCl₃ as solvent. The molecular weight and its distribution or the polydispersity index (PDI, PDI = M_w/M_n) of the synthesized polymers were determined by gel permeation chromatography (GPC) equipped with a Waters 600E GPC system, where THF was used as eluent and the narrow-polydispersity polystyrene was used as calibration standard. The differential scanning calorimetry (DSC) analysis was performed on a NETZSCH DSC 204 differential scanning calorimeter under nitrogen atmosphere, in which the sample was heated to 80 $^\circ\text{C}$ at the heating rate of 10 $^{\circ}$ C/min, cooled to -80 $^{\circ}$ C in 5 min, and then heated to 80 °C at the heating rate of 10 °C/min. The LCST and UCST of the thermo-responsive polymers were determined by turbidity measurement at 500 nm on a Varian 100 ultraviolet-visible spectrophotometer equipped with a thermo-regulator (± 0.1 °C) with the heating/cooling rate at 1 °C/min. The UCST and LCST values were determined at 50% transmittance or at the half of the maximal and minimal transmittance. Dynamic light scattering (DLS) analysis was performed on a Nano-ZS90 (Malvern) laser light

Entry	Polymer	[M] ₀ :[CTA] ₀ :[I] ₀						
			Time (h)	Conv. (%) ^a	M _{n,th} ^b	$M_{ m n,GPC}{}^{ m c}$	$M_{n,NMR}^{d}$	PDI ^e
A1	PVEA ₂₀	150:3:1	11	40.3	4.1	2.3	4.5	1.10
A2	PVEA ₄₈	400:3:1	18	36.3	9.5	6.1	10.8	1.08
A3	PVEA ₇₂	800:3:1	24	27.0	14.0	9.0	14.8	1.15
B1	P(MEO ₂ MA) ₂₉	240:6:1	8	73.2	5.8	5.6	6.2	1.21
B2	P(MEO ₂ MA) ₄₇	500:6:1	8	56.0	8.9	7.9	9.7	1.23
B3	P(MEO ₂ MA) ₈₉	1000:6:1	8	53.3	17.0	13.2	17.5	1.24
C1	P(MEO ₂ MA) ₂₉ -b-PVEA ₂₆	200:4:1	8	52.1	10.7	9.5	12.3	1.29
C2	P(MEO ₂ MA) ₂₉ -b-PVEA ₄₉	400:4:1	8	48.7	15.3	11.4	16.8	1.36
C3	P(MEO ₂ MA) ₂₉ -b-PVEA ₇₂	800:4:1	8	37.9	20.1	12.8	22.5	1.38
C4	P(MEO ₂ MA) ₄₇ -b-PVEA ₄₄	400:4:1	8.5	44.4	17.2	12.3	20.1	1.36
C5	P(MEO ₂ MA) ₈₉ - <i>b</i> -PVEA ₄₂	400:4:1	10	41.4	24.9	17.2	27.0	1.37

TABLE 1 Experimental Details and Summary of the Synthesized Polymers of PVEA, PMEO₂MA, and PMEO₂MA-b-PVEA

^a The monomer conversion determined by ¹H NMR analysis.

^b Theoretical molecular weight determined by monomer conversion.

^c The molecular weight determined by GPC analysis.

scattering spectrometer with He-Ne laser at the wavelength of 633 nm at 90° angle. The transmission electron microscopy (TEM) observation was performed using a JEOL 100CX-II electron microscope at an acceleration of 100 kV, whereby a small drop of the preheated dispersion of the synthesized polymer was deposited onto a piece of preheated copper grid till the solvent was evaporated at a given temperature.

RESULTS AND DISCUSSION

Synthesis of PVEA, PMEO₂MA, and PMEO₂MA-b-PVEA

The VEA monomer was synthesized by the nucleophilic substitution reaction of CMS with DEA as discussed elsewhere,62 and its chemical structure was confirmed by ¹H NMR analysis (Supporting Information Fig. S1). The PVEA polymer was synthesized via RAFT polymerization of VEA in toluene using CDB as chain transfer agent and AIBN as initiator [Scheme 1(A)]. By varying the molar ratio of the monomer to the RAFT agent (VEA/CDB), three polymers of PVEA20, $PVEA_{48}$, and $PVEA_{72}$ with the theoretical molecular weight $(M_{\rm n\,th})$ at 4.1, 9.5, and 14.0 kg/mol and with the theoretical polymerization degree (DP) at 20, 48, and 72, in which $M_{\rm n,th}$ is calculated by the monomer conversion according to eq 3,63 were synthesized at 27%-40% monomer conversion (Entries A1-A3, Table 1). From the symmetrical and unimodal GPC traces shown in Figure 1, the molecular weight $M_{n,GPC}$ and the PDI values are obtained. The $M_{n,GPC}$ values by GPC analysis are slightly smaller than $M_{n,th}$ by the monomer conversion, and the reason is possibly due to the polystyrene standard used in the GPC analysis. The PDI value of the synthesized polymers locates at 1.08-1.15. Figure 2(A) shows the ¹H NMR spectra of the typical PVEA₄₈ polymer, in which the characteristic proton chemical shifts of the PVEA main chain and the terminal group originated from the RAFT agent of CDB are clearly observed. Based on the characteristic chemical shift at $\delta = 7.82$ ppm corresponding to the

^d The molecular weight determined by ¹H NMR analysis.

^e The PDI (M_w/M_n) value determined by GPC analysis.

terminal group and the chemical shift at $\delta = 2.5$ ppm corresponding to the polymer main chain, the molecular weight $M_{\rm n,NMR}$ of the synthesized PVEA are calculated and summarized in Table 1 (Entries A1–A3, Table 1). It shows that the $M_{\rm n,NMR}$ of PVEA is very close to the theoretical molecular weight $M_{\rm n,th}$, and it is larger than $M_{\rm n,GPC}$.

$$M_{n,th} = \frac{|\text{monomer }|_0 \times M_{\text{monomer}}}{[\text{RAFT }]_0} \times \text{conversion} + M_{\text{RAFT}} \quad (3)$$

PMEO₂MA was synthesized by the RAFT polymerization [Scheme 1(B)] as discussed elsewhere.⁶⁴ Three samples of P(MEO₂MA)₂₉, P(MEO₂MA)₄₇, and P(MEO₂MA)₈₉ with the theoretical DP at 29, 47, and 89 were synthesized (Entries B1–B3, Table 1). The synthesized polymers are characterized by GPC analysis (Supporting Information Fig. S2) and ¹H NMR analysis [Fig. 2(B)], from which $M_{n,NMR}$ is calculated based on the characteristic chemical shift at δ = 7.88 ppm corresponding to the terminal group and the chemical shift



FIGURE 1 The GPC traces of the PVEA polymers.



FIGURE 2 The ¹H NMR spectra of PVEA₄₈ (A), $P(MEO_2MA)_{29}$ (B), and $P(MEO_2MA)_{29}$ -*b*-PVEA₄₉ (C).

at $\delta = 4.1$ ppm corresponding to the main chain of PMEO₂MA, and the results are summarized in Table 1.

The PMEO₂MA-*b*-PVEA block copolymers were prepared by sequential RAFT polymerization using PMEO₂MA as macro-RAFT agent [Scheme 1(C)]. Five block copolymers of $P(MEO_2MA)_{29}$ -*b*-PVEA₂₆, $P(MEO_2MA)_{29}$ -*b*-PVEA₄₉, $P(MEO_2MA)_{29}$ -*b*-PVEA₇₆, $P(MEO_2MA)_{47}$ -*b*-PVEA₄₄, and $P(MEO_2MA)_{89}$ -*b*-PVEA₄₂ were synthesized (Entries C1–C5, Table 1). Figure 3 shows the GPC traces of the typical macro-RAFT agent of $P(MEO_2MA)_{29}$ and the synthesized block copolymers, from which the shift to less elution time with the increase in the DP of the PVEA block is observed, indicating the chain extension of the PVEA block. The slight shoulder at the high-molecular weight side (less elution time) in all the GPC traces of the block copolymers is observed and the PDI of the block copolymers (1.29–1.38) is

moderate, possibly suggesting somewhat bimolecular radical termination in the RAFT polymerization. Besides, the tailing in GPC traces is also ascribed to the column adsorption of the block copolymer and this is expected to be the main reason, since the polymer molecular weight by ¹H NMR analysis is quite close to the theoretical one as discussed subsequently. Figure 2(C) shows the typical ¹H NMR spectra of P(MEO₂MA)₂₉-b-PVEA₄₉, from which both the characteristic signals corresponding to the PMEO₂MA block and the PVEA block are discerned. Based on the area ratio of the characteristic chemical shift at $\delta = 2.5$ ppm to that at $\delta = 4.1$ ppm and the molecular weight of the PMEO₂MA macro-RAFT agent, the molecular weight $M_{n,NMR}$ of the PMEO₂MA-b-PVEA block copolymers are determined and summarized in Table 1. It shows that the $M_{n,NMR}$ values are quite close to the theoretical molecular weight $M_{\rm n,th}$ and are larger than $M_{n,GPC}$. The block copolymer is further confirmed by DSC analysis, in which the glass transition temperature (T_g) at -29.3 °C corresponding to the PMEO₂MA block and the T_g at 27.4 °C corresponding to the PVEA block are observed (Supporting Information Fig. S3).

Solubility of PMEO₂MA in Alcohol

The solubility of the synthesized PMEO₂MA in three aliphatic alcohols of methanol (MeOH), ethanol (EtOH), and isopropanol (iPrOH) is investigated and summarized in Figure 4. PMEO₂MA is soluble in methanol at temperature below the boiling point (65 °C), while it exhibits the UCST phase transition in ethanol and isopropanol. As shown in Figure 5, the UCST in either ethanol or isopropanol is positively correlated to the polymer DP or the polymer molecular weight. For example, the UCST in ethanol increases from 13.4 °C [P(MEO₂MA)₂₉] to 17.1 °C [P(MEO₂MA)₄₇] and further to 20.6 $^{\circ}\text{C}$ [P(MEO_2MA)_{89}], and the UCST in isopropanol increases from 27.8 °C [P(MEO₂MA)₂₉] to 30.5 °C $[P(MEO_2MA)_{47}]$ and further to 33.3 °C $[P(MEO_2MA)_{89}]$, when the polymer DP increases from 29 to 89. At all the UCST phase transitions, the sharp conversion at a narrow temperature range of 2 °C is observed. These results are well consistent with those of POEGMA in aliphatic alcohols reported



FIGURE 3 The GPC traces of the typical P(MEO₂MA)₂₉ macro-RAFT agent and the PMEO₂MA-*b*-PVEA block copolymers.

- <i>U</i> - F V EA ₄₉		ó	1	5	20		40 H O	. %	60	80	•	100
P(MEO ₂ MA) ₂₉	iPrOH			000	004	14	4▼	•	•	• • •	•	*
	iPrOH		0	004	14	*	*	*	*	* *	*	*
PVEA ₄₈	EtOH	0	0	οΔ4	14,	**	*	*	*	* *	*	*
	MeOH	Δ	Δ	ΔΔΔ	1 * 7	**	*	*	*	* *	*	*
	iPrOH	-	•	00	0	0	0	0	0	044	Δ	Δ
P(MEO ₂ MA) ₂₉	EtOH	•	•	00	0	0	0	0	0	044	Δ	Δ
	MeOH	0	0	00	0	0	0	0	0	Δ Δ Δ	Δ	Δ

■ UCST ○ Soluble ▲ LCST ▼ micellization ★ insoluble

FIGURE 4 Summary of the solubility of P(MEO₂MA)₂₉, PVEA₄₈, and P(MEO₂MA)₂₉-b-PVEA₄₉ in the alcohol/water mixture.

by Roth et al.,⁵⁹ and the UCST increasing with the polymer molecular weight can be ascribed to the favorable polymer-polymer interaction in the polymer with high molecular weight, in which high temperature is needed to disrupt the interaction.

Solubility of PVEA in Alcohol

The solubility of PVEA in three aliphatic alcohols of methanol, ethanol, and isopropanol is investigated. It is found that the solubility of PVEA in these three aliphatic alcohols is much different (Fig. 4). In ethanol, PVEA is molecularly soluble at temperature below the solvent boiling point and neither LCST nor UCST is detected; in methanol, the LCST phase transition is detected; in isopropanol, the UCST phase transition is found. Figure 6 shows all the phase transitions occurring at a narrow temperature range of 2 °C. Besides, both the LCST in methanol and the UCST in isopropanol are

dependent on the DP or the molecular weight of the PVEA polymer. For example, the polymer with low DP (PVEA₂₀) is molecularly soluble in methanol and no detectable LCST is observed. However, the LCST of PVEA₄₈ at 53.1 °C is detected and the LCST of PVEA₇₂ further decreases to 44.5 °C [Fig. 6(A)]. As to the UCST in isopropanol, the polymer with low DP (PVEA₂₀) is molecularly soluble at temperature below the solvent boiling temperature; and the UCST of PVEA₄₈ at 24.3 °C are detected, respectively [Fig. 6(B)].

It is generally accepted that the UCST increasing with the increasing polymer molecular weight is ascribed to the favorable polymer–polymer interaction in the polymer chains with high molecular weight.^{27,59} However, the LCST decreasing with the increasing polymer molecular weight is due to the less favorable combinatorial entropy in the binary



FIGURE 5 The transmittance versus temperature plots of $PMEO_2MA$ in the solvent of ethanol (A) and isopropanol (B). The concentration of polymer is 2.0 wt %.



FIGURE 6 The transmittance versus temperature plots of PVEA in the solvent of methanol (A) and isopropanol (B). The polymer concentration is 2.0 wt %.

mixture.²⁹ Compared with PNIPAM,^{17–21} PVEA seems interesting as its LCST can be tuned within a relatively wide range just by varying the polymer molecular weight.

Solubility of PMEO₂MA and PVEA in the Water/Alcohol Mixture

For thermo-responsive polymers, the LCST or UCST generally can be tuned by addition of co-solvent or nonsolvent.^{40,58,59,65-67} For example, the LCST of PNIPAM in water decreases from 32.5 to -7.5 °C when 35 vol % methanol is added and then increases with the further addition of methanol.⁶⁵ For POEGMA, the UCST in aliphatic alcohols increases with the chain length of the alcohol.⁵⁹ Besides, the UCST of POEGMA in isopropanol can be tuned by addition of cosolvent or nonsolvent, and it decreases from 35.6 to 23.1 °C when 1 vol % co-solvent of water is added, while it increases from 35.6 to 46.7 °C when 50 vol % nonsolvent of hexane is added.⁵⁹ The reason is generally ascribed to the variation of the solvation shell around the polymer chains by the (co)nonsolvent.^{40,42,43}

Herein, the solubility of P(MEO₂MA)₂₉ and PVEA₄₈ in the alcohol/water mixture is taken as the typical example to study the co-solvent or nonsolvent effect on their UCST or LCST. For the sake of briefness, the alcohol/water mixture with the water content at X wt % is called the X wt % alcohol/water mixture. Figure 4 summarizes the solubility of $P(MEO_2MA)_{29}$ and $PVEA_{48}$ in the alcohol/water mixture. P(MEO₂MA)₂₉ is soluble in methanol and shows UCST phase transition in ethanol or isopropanol, which is just introduced above. When the water content in the isopropanol/water mixture slightly increases from 0 to 1 wt %, the UCST of P(MEO₂MA)₂₉ decreases from 27.8 to 17.8 °C [Fig. 7(A)]. Similar co-solvent effect on the UCST of poly[oligo(ethylene glycol) (meth)acrylate] in alcohol is also reported,58,59 and the reason is possibly due to the strong hydrogen bonding between water and the P(MEO₂MA)₂₉ chains leading to the formation of a hydration shell around the polymer to increase the polymer solubility. When the water content is above 5 wt %, P(MEO₂MA)₂₉ becomes molecularly soluble in the methanol/water, ethanol/water, and isopropanol/water



FIGURE 7 The temperature dependent transmittance of $P(MEO_2MA)_{29}$ (A) and $PVEA_{48}$ (B) in the isopropanol/water mixture. The polymer concentration is 2.0 wt %.



FIGURE 8 The temperature dependent transmittance of $P(MEO_2MA)_{29}$ -*b*-PVEA₄₉ in the isopropanol/water mixture. The polymer concentration is 2.0 wt %.

mixtures and no LCST or UCST is observed. When the water content further increases, LCST in the three alcohol/water mixtures is detected, and the LCST in the isopropanol/water mixture decreases from 53.5 to 15.0 °C when the water content increases from 75 to 100 wt % [Fig. 7(A)]. The similar co-solvent effect on the solubility of $p(OEGMeA-co-OEG-PhA)^{58}$ and poly(trimethylene ether) glycol⁶⁶ in water are also reported.

Different from the co-solvent effect on LCST,^{40,58,66} the addition of the nonsolvent of octane in the poly(2-chloroethyl vinyl ether-alt-maleic anhydride) solution in *n*-butyl acetate leads to the LCST decreasing, and the reason was due to the nonsolvent disturbing the solvation shell around the polymer chains, resulting in the decreased solubility of the polymer in the solvent.⁶⁷ The similar nonsolvent effect on the solubility of PVEA is also observed. As shown in Figure 7(B), PVEA₄₈ is soluble in isopropanol at temperature above the UCST at 24.3 °C. However, the nonsolvent of water greatly changes the solubility of PVEA₄₈ in isopropanol. That is, LCST instead of UCST is detected and the LCST of PVEA₄₈ in the isopropanol/water mixture decreases from 52.8 to 7.3 °C when the water content increases from 15 to 25 wt %.

Thermo-Responsive Micellization of PMEO₂MA-*b*-PVEA in the Isopropanol/Water Mixture

With the detailed solubility of the $PMEO_2MA$ and PVEA homopolymers in the alcohol/water mixture in hand, the thermo-responsive micellization of $PMEO_2MA$ -*b*-PVEA in the typical solvent of the isopropanol/water mixture is studied. The solvent of the isopropanol/water mixture is chosen, as the variable solubility of $PMEO_2MA$ and PVEA in this solvent is demonstrated. The solubility of the typical block copolymer of $P(MEO_2MA)_{29}$ -*b*-PVEA₄₉ in the isopropanol/water mixture is checked and summarized in Figure 4. In isopropanol or the isopropanol/water mixture with water content

below 5 wt %, P(MEO₂MA)₂₉-b-PVEA₄₉ is soluble at temperature above UCST and it forms micelles at temperature below UCST. In the isopropanol/water mixture with water content at 5-20 wt %, P(MEO₂MA)₂₉-b-PVEA₄₉ is soluble and neither UCST nor LCST is detected. In the isopropanol/ water mixture with water content at 25-35 wt %, P(MEO₂MA)₂₉-b-PVEA₄₉ is soluble at temperature below LCST and it self-assembles into micelles at temperature above LCST. In the isopropanol/water mixture with water content at 40-90 wt %, the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer forms micelles. All these block copolymer micelles are stable, and no deposition is observed. In the isopropanol/water mixture with water content above 95 wt %, the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer precipitates in the solvent. Clearly, the solubility or micellization of the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer in the isopropanol/ water mixture is firmly dependent on the solubility of the PMEO₂MA and PVEA blocks except those in the isopropanol/ water mixture with 30-35 wt % water content, in which the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer is soluble below LCST whereas the reference homopolymer of $PVEA_{48}$ is insoluble. This is not surprising and the reason is due to the hydrophilic P(MEO₂MA)₂₉ block increasing the solubility of the PVEA₄₉ block and therefore the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer. In the subsequent study, the thermoresponsive micellization of the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer in the isopropanol/water mixture with water content at 0%, 25%-35%, and 40-90 wt % is discussed. The isopropanol/water mixture with water content at 5-20 wt% or above 95 wt % is not chosen, as the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer is soluble in the former solvent and precipitates in the later solvent.

As shown in Figure 8, the UCST phase transition of P(MEO₂MA)₂₉-b-PVEA₄₉ in pure isopropanol at 23.2 °C is observed. At the temperature above the UCST, P(MEO₂MA)₂₉b-PVEA₄₉ is molecularly soluble (100% transmittance), and micellization occurs when temperature decreases below UCST (0% transmittance). The UCST of the $P(MEO_2MA)_{29}-b$ -PVEA₄₉ block copolymer (23.2 °C) is slightly lower than that of the P(MEO₂MA)₂₉ homopolymer (27.8 °C) and is close to that of the reference PVEA₄₈ homopolymer (24.3 °C). This is possibly due to the soluble PVEA₄₉ block enhancing the solubility of the $P(MEO_2MA)_{29}$ block and therefore results in a lower UCST than that of the P(MEO₂MA)₂₉ homopolymer. The DLS analysis of the block copolymer dispersion/solution confirms the block copolymer micelles with the narrowdistributed apparent hydrodynamic diameter $D_{\rm h} = 151$ nm at temperature below UCST and the single polymer chains with $D_{\rm h} = 5$ nm at temperature above UCST [Fig. 9(A)]. As the UCST of the P(MEO₂MA)₂₉ reference in isopropanol is higher than that of the PVEA₄₈ reference (27.8 $^{\circ}$ C vs. 24.3 $^{\circ}$ C), the micelles are expected to contain a solvophilic PVEA₄₉ corona and a desolvated $P(MEO_2MA)_{29}$ core as those of the double hydrophilic block copolymers.^{68–73} Herein, these core-corona micelles are called inverted micelles or inverse micelles,³⁵ as the DP of PVEA₄₉ corona is larger than that of the P(MEO₂MA)₂₉ core.



FIGURE 9 The hydrodynamic diameter distribution $f(D_h)$ of P(MEO₂MA)₂₉-*b*-PVEA₄₉ in the solvent of isopropanol (A), the 30 wt % isopropanol/water mixture (B), and the 80 wt % isopropanol/water mixture (C).

In the 25-35 wt % isopropanol/water mixture, the thermoresponsive micellization of the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer occurs at temperature above LCST (Fig. 8). As the P(MEO₂MA)₂₉ reference is soluble in the 25-35 wt % isopropanol/water mixture as discussed above, the micellization should be ascribed to the LCST phase transition of the PVEA₄₉ block. It is found that the LCST of the PVEA₄₉ block is correlative to the water content in the isopropanol/water mixture. That is, the LCST of P(MEO₂MA)₂₉-b-PVEA₄₉ in the isopropanol/water mixture decreases from 34.5 °C to 21.5 $^\circ\text{C}$ and further to 8.0 $^\circ\text{C}$ when the water content increases from 25 to 30 wt % and further to 35 wt % (Fig. 8), which is as similar as the nonsolvent effect on the LCST of PVEA shown in Figure 7(B). Compared with the $PVEA_{48}$ reference, the LCST of P(MEO₂MA)₂₉-b-PVEA₄₉ is much higher (for example, 34.5 °C vs. 7.3 °C in the 25 wt % isopropanol/ water mixture), as the solvophilic P(MEO₂MA)₂₉ block increases the solubility of the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer in the isopropanol/water mixture as discussed elsewhere.⁶⁸⁻⁷³ Based on the different solubility of the P(MEO₂MA)₂₉ and the PVEA₄₉ blocks in the 25-35 wt % isopropanol/water mixture, the block copolymer micelles should contain a solvophilic P(MEO₂MA)₂₉ corona and a desolvated PVEA49 core, which is just different from the

inverted micelles formed in isopropanol. This micellization is confirmed by the DLS analysis of the P(MEO₂MA)₂₉-*b*-PVEA₄₉ block copolymer in the 30 wt % isopropanol/water mixture typically at temperature of 10 °C (below LCST) and at temperature of 30 °C (above LCST), in which $D_h = 5$ nm corresponding to the single polymer chains and apparent $D_h = 129$ nm corresponding to the core-corona micelles are indicated [Fig. 9(B)]. The TEM image shown in Figure 10(A) also confirms the formation of micelles with the average size centered at 35 nm. Clearly, the size of the micelles by TEM observation is much smaller than that by DLS analysis, and the reason is due to the TEM observation showing the dried aggregates while DLS analysis detecting the solvated micelles.

In the 40–90 wt % isopropanol/water mixture, the PVEA₄₉ block is insoluble and the P(MEO₂MA)₂₉ block is either soluble or shows the LCST phase transition (Fig. 8), and therefore the core-corona micelles containing a desolvated PVEA₄₉ core and a P(MEO₂MA)₂₉ corona are prepared in this solvent. The core-corona micelles prepared in the 40–70 wt % isopropanol/water mixture are different from those in the 75–90 wt % isopropanol/water mixture. For example, on heating the core-corona micelles prepared in the 50 wt %



FIGURE 10 The TEM images and size-distribution of the P(MEO₂MA)₂₉-*b*-PVEA₄₉ micelles in the 30 wt % isopropanol/water mixture at 30 °C (A) and in the 80 wt % isopropanol/water mixture at 20 °C (B) and 50 °C (C).

isopropanol/water mixture, the transmittance keeps almost constant; whereas for the core-corona micelles prepared in the 75-90 wt % isopropanol/water mixture, the transmittance decreases with the temperature increasing. This suggests that these core-corona micelles prepared in the 75-90 wt % isopropanol/water mixture are thermo-responsive. Based on the solubility of the PMEO₂MA and PVEA homopolymers shown in Figure 4, the thermo-response of the core-corona micelles is ascribed to the LCST phase transition of the P(MEO₂MA)₂₉ corona. This LCST phase transition of the P(MEO₂MA)₂₉ block leads to the P(MEO₂MA)₂₉ block collapsing on the PVEA₄₉ core to form the coronacollapsed micelles. This transition of the core-corona micelles to corona-collapsed micelles is confirmed by TEM observation and DLS analysis of the micelles in the 80 wt % isopropanol/water mixture at temperature below and above LCST of the P(MEO₂MA)₂₉ corona. Figure 9(C) indicates the apparent $D_{\rm h}$ decreasing from 156 nm to 128 nm when the temperature increases from 20 °C to 50 °C, suggesting the micelles shrinking on heating. The TEM images [Fig. 10(B,C)] show that the P(MEO₂MA)₂₉-b-PVEA₄₉ micelles in the 80 wt % isopropanol/water mixture at temperature of 20 °C (below LCST) and 50 °C (above LCST) have the same size at 44 nm. The difference between the DLS analysis and the TEM observation is due to the TEM observation showing the dried aggregates while DLS analysis detecting the solvated micelles, and it indicates the LCST phase transition of the $P(MEO_2MA)_{29}$ corona to corona-collapsed micelles in the 75–90 wt % isopropanol/ water mixture. As similar as the $P(MEO_2MA)_{29}$ homopolymer [Fig. 7(A)], the LCST of the $P(MEO_2MA)_{29}$ corona is also correlative to the water content in the isopropanol/ water mixture, and it generally decreases with the water content although the LCST of the $P(MEO_2MA)_{29}$ corona in the core-corona micelles is slightly lower than that of the $P(MEO_2MA)_{29}$ homopolymer.



SCHEME 2 Schematic solubility of the P(MEO₂MA)₂₉-*b*-PVEA₄₉ block copolymer in the isopropanol/water mixture.

Based on the above discussion, the thermo-responsive micellization of the $P(MEO_2MA)_{29}$ -b-PVEA_{49} block copolymer is summarized in Scheme 2. It indicates the phase transitions from soluble $P(MEO_2MA)_{29}$ -b-PVEA_{49} to inverted micelles in isopropanol at temperature below UCST, to core-corona micelles in the 30–35 wt % isopropanol/water mixture at temperature above LCST, to core-corona micelles in the 40– 70 wt % isopropanol/water mixture, to corona-collapsed micelles in the 75–90 wt % isopropanol/water mixture at temperature above LCST, and further to insoluble polymer in the isopropanol/water mixture with water content above 95 wt %.

The Effect of Block Chain Length on the Thermo-Responsive Micellization of PMEO₂MA-*b*-PVEA

Herein, the effect of the block chain length on the thermoresponsive micellization of the PMEO₂MA-*b*-PVEA block copolymer is investigated. To fulfill this investigation, five block copolymers of $P(MEO_2MA)_{29}$ -*b*-PVEA₂₆, $P(MEO_2MA)_{29}$ -*b*-PVEA₄₉, $P(MEO_2MA)_{29}$ -*b*-PVEA₇₆, $P(MEO_2MA)_{47}$ -*b*-PVEA₄₄, and $P(MEO_2MA)_{89}$ -*b*-PVEA₄₂ are synthesized. Clearly, these five block copolymers can be classified in two groups. In the first group of $P(MEO_2MA)_{29}$ -*b*-PVEA₇₆ (Group 1), the DP of the PMEO₂MA block is kept at the constant of 29 while the DP of the PVEA block increases from 26 to 76. In the second group of $P(MEO_2MA)_{29}$ -*b*-PVEA₄₉, $P(MEO_2MA)_{47}$ -*b*-PVEA₄₄, and $P(MEO_2MA)_{29}$ -*b*-PVEA₄₉, $P(MEO_2MA)_{47}$ -*b*-PVEA₄₄, and $P(MEO_2MA)_{89}$ -*b*-PVEA₄₂ (Group 2), the DP of the PVEA

block is similar with each other while the DP of the $PMEO_2MA$ block increases from 29 to 89.

As shown in Figure 11(A), there is a positive correlation between the DP of the $PMEO_2MA$ or PVEA block and the UCST of the block copolymer in isopropanol. For example, for the block copolymers in Group 1, the UCST increases from 22.6 °C to 23.2 °C and further to 27.8 °C when the DP of the PVEA block increases from 26 to 49 and further to 76; for the block copolymers in Group 2, the UCST increases from 23.2 °C to 26.7 °C and further to 30.6 °C when the DP of the PMEO₂MA block increases from 29 to 47 and further to 89. The present positive correlation between the UCST of the block copolymer and the DP of the PMEO₂MA or PVEA block is due to the strong polymer–polymer interaction in the high-molecular weight polymer as discussed above.

In the 30 wt % isopropanol/water mixture, the increasing DP of PVEA leads to the LCST of the $PMEO_2MA$ -*b*-PVEA block copolymer decreasing, whereas the increasing DP of PMEO_2MA leads to the LCST increasing [Fig. 11(B)]. For example, for the block copolymers in Group 1, the LCST decreases from 46.2 °C to 21.5 °C and further to 12.6 °C when the DP of PVEA increases from 26 to 49 and further to 76; for the block copolymers in Group 2, the LCST increases from 21.5 °C to 29.2 °C and further to 46.0 °C when the DP of PMEO_2MA increases from 29 to 47 and further to 89. These results suggest that both the increase in the DP of the solvophilic PMEO_2MA and the decrease in the DP of the



FIGURE 11 Transmittance versus temperature plots for the PMEO₂MA-*b*-PVEA block copolymers in the isopropanol/water mixture. The polymer concentration is 2.0 wt %.

thermo-responsive PVEA block increase the LCST of the PMEO₂MA-b-PVEA block copolymer in the 30 wt % isopropanol/water mixture. Similar results are also observed for the random or block copolymers of P(EtOx-co-PhOx),⁴⁰ P(MEO₂MA-*co*-OEGMA),⁵⁶ poly(ethylene oxide)-*block*-poly(*N*-isopropylacrylamide),⁷³ and poly(ethylethylene phosphate)block-poly[2-(dimethylamino)ethyl methacrylate],43 in which the hydrophilic block content increasing or the hydrophobic block content decreasing leads to the LCST increasing. As similar as the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer, the other four block copolymers self-assemble into core-corona micelles, in which the PVEA block forms the core and the PMEO₂MA block forms the corona, in the 30 wt % isopropanol/water mixture at temperature above LCST. The TEM observation confirms the formation of micelles (Supporting Information Fig. S4), and the size of the micelles of the five block copolymers is 26 nm [P(MEO₂MA)₂₉-b-PVEA₂₆], 35 nm [P(MEO₂MA)₂₉-b-PVEA₄₉], 45 nm [P(MEO₂MA)₂₉-b-PVEA₇₆], 32 nm $[P(MEO_2MA)_{47}-b-PVEA_{44}]$, and 29 nm $[P(MEO_2MA)_{89}-b-PVEA_{44}]$ b-PVEA₄₂], respectively. It indicates that the micelle size increases with the DP of the PVEA block while decreases with the DP of the PMEO₂MA block.

Finally, the DP effect on the thermo-response of the PMEO₂MA corona in the core-corona micelles prepared in the 80 wt % isopropanol/water mixture is investigated using the Group 1 block copolymers as typical example. As discussed above, core-corona micelles containing the PVEA core and the $PMEO_2MA$ corona are formed in the 80 wt % isopropanol/water mixture. The TEM images shown in Supporting Information Figure S5 confirm the formation of micelles at temperature either below or above LCST of the PMEO₂MA corona, in which the size of the micelles increases from 30 to 44 to 80 nm when the DP of the PVEA block increases from 26 to 49 and further to 76 (Note: the size of the micelles at temperature below LCST and above LCST by TEM observation is very similar). Figure 11(C) indicates that the LCST of the core-corona micelles of $P(MEO_2MA)_{29}$ -b-PVEA₄₉ and $P(MEO_2MA)_{29}$ -b-PVEA₇₆ almost the same as that of the reference P(MEO₂MA)₂₉ homopolymer. However, for the core-corona micelles of P(MEO₂MA)₂₉-b-PVEA₂₆ containing a short PVEA block, its LCST is lower than that of the P(MEO₂MA)₂₉ reference (32.4 °C vs. 38.6 °C). The reason of the different LCST of the $P(MEO_2MA)_{29}$ corona in the core-corona micelles is not very clear, and it is expected that the interaction between the PMEO₂MA block and the PVEA block should be involved. Besides, the phase transition of the $P(MEO_2MA)_{29}$ corona in the core-corona micelles is not as sharp as that of the reference P(MEO₂MA)₂₉ homopolymer, and the reason is possibly due to the steric repulsion between the tethered P(MEO₂MA)₂₉ chains in the core-shell particles as discussed elsewhere.74

CONCLUSIONS

The thermo-responsive homopolymers of $PMEO_2MA$ and PVEA and the $PMEO_2MA$ -*b*-PVEA block copolymer are

prepared by RAFT polymerization. The solubility of PMEO₂MA, PVEA, and PMEO₂MA-b-PVEA in aliphatic alcohols and in the isopropanol/water mixture is investigated. PMEO₂MA is soluble in methanol, shows UCST phase transition in ethanol and isopropanol, and shows LCST phase transition in the alcohol/water mixture. The UCST of PMEO₂MA is firmly dependent on the polymer DP, and it increases with the DP increase. The LCST of PMEO₂MA in the alcohol/water mixture is dependent on the water content, and it decreases with the water content increase. PVEA exhibits LCST phase transition in methanol, is soluble in ethanol, shows UCST phase transition in isopropanol, and shows LCST phase transition in the isopropanol/water mixture, respectively. The polymer molecular weight and the co-solvent/nonsolvent exert great influence on the LCST or UCST of PVEA. By combining the thermo-responsive PMEO₂MA and PVEA through RAFT polymerization, the multi-thermo-responsive PMEO2MA-b-PVEA block copolymer is prepared. The PMEO₂MA-*b*-PVEA block copolymer undergoes phase transition from soluble polymer to inverted micelles in isopropanol at temperature below UCST, to corecorona micelles in the 30-35 wt % isopropanol/water mixture at temperature above LCST, to core-corona micelles in the 40-70 wt % isopropanol/water mixture, to coronacollapsed micelles in the 75-90 wt % isopropanol/water mixture at temperature above LCST, and further to insoluble polymer in the isopropanol/water mixture with water content above 95 wt % just by changing the water content in the solvent mixture or by adjusting the solvent temperature. The multi-thermo-responsive micellization of the P(MEO₂MA)₂₉-b-PVEA₄₉ block copolymer is checked by DLS analysis and TEM observation and the tunable thermoresponse at LCST or UCST is demonstrated.

ACKNOWLEDGMENTS

The financial support by National Science Foundation of China (Nos. 20974051 and 21074059) and PCSIRT (IRT1257) is gratefully acknowledged.

REFERENCES

1 C. Weber, R. Hoogenboom, U. S. Schubert, *Prog. Polym. Sci.* 2012, *37*, 686–714.

2 V. Aseyev, H. Tenhu, F. M. Winnik, *Adv. Polym. Sci.* 2011, 242, 29–89.

3 L. Gu, Y. Gao, Y. Qin, X. Chen, X. Wang, F. Wang, *J. Polym. Sci. Part A: Polym. Chem.* **2013**, *51*, 282–289.

4 J. W. Robinson, C. Secker, S. Weidner, H. Schlaad, *Macromolecules* 2013, 46, 580–587.

5 N. Zhang, S. Salzinger, B. Rieger, *Macromolecules* **2012**, *45*, 9751–9758.

6 S. Monge, S. Antoniacomi, V. Lapinte, V. Darcos, J.-J. Robin, *Polym. Chem.* **2012**, *3*, 2502–2507.

7 Y. Zou, D. E. Brooks, J. N. Kizhakkedathu, *Macromolecules* 2008, *41*, 5393–5405.

8 H. Mori, H. Iwaya, A. Nagai, T. Endo, *Chem. Commun.* 2005, 4872–4874.

JOURNAL OF POLYMER SCIENCE Chemistry

9 D. J. Phillips, M. I. Gibson, *Chem. Commun.* **2012**, *48*, 1054–1056.

10 P. J. Roth, F. D. Jochum, F. R. Forst, R. Zentel, P. Theato, *Macromolecules* **2010**, *43*, 4638–4645.

11 A. Miasnikova, A. Laschewsky, *J. Polym. Sci. Part A: Polym. Chem.* **2012**, *50*, 3313–3323.

12 S.-H. Jung, H.-Y. Song, Y. Lee, H. M. Jeong, H.-I. Lee, *Macromolecules* 2011, *44*, 1628–1634.

13 N. S. leong, M. Hasan, D. J. Phillips, Y. Saaka, R. K. O'Reilly, M. I. Gibson, *Polym. Chem.* **2012**, *3*, 794–799.

14 G. B. H. Chua, P. J. Roth, H. T. T. Duong, T. P. Davis, A. B. Lowe, *Macromolecules* **2012**, *45*, 1362–1374.

15 K. Rahimian-Bajgiran, N. Chan, Q. Zhang, S. M. Noh, H.-I. Lee, J. K. Oh, *Chem. Commun.* **2013**, *49*, 807–809.

16 X. Jiang, M. R. Smith, G. L. Baker, *Macromolecules* 2008, 41, 318–324.

17 R. Plummer, D. J. T. Hill, A. K. Whittaker, *Macromolecules* 2006, *39*, 8379–8388.

18 J. Xu, J. Ye, S. Liu, *Macromolecules* **2007**, *40*, 9103–9110.

19 C.-T. Lai, R.-H. Chien, S.-W. Kuo, J.-L. Hong, *Macromole-cules* **2011**, *44*, 6546–6556.

20 C. K. Chee, B. J. Hunt, S. Rimmer, I. Soutar, L. Swanson, *Soft Matter* 2011, *7*, 1176–1184.

21 M. E. Alf, T. A. Hatton, K. K. Gleason, *Polymer* **2011**, *52*, 4429–4434.

22 V. M. M. Soto, J. C. Galin, Polymer 1984, 25, 254-262.

23 C. Pietsch, R. Hoogenboom, U. S. Schubert, *Polym. Chem.* 2010, *1*, 1005–1008.

24 O. Zhang, P. Schattling, P. Theato, R. Hoogenboom, *Polym. Chem.* **2012**, *3*, 1418–1426.

25 T. Ueki, Y. Nakamura, A. Yamaguchi, K. Niitsuma, T. P. Lodge, M. Watanabe, *Macromolecules* **2011**, *44*, 6908–6914.

26 G. V. Assche, B. V. Mele, T. Li, E. Nies, *Macromolecules* 2011, 44, 993–998.

27 S. Glatzel, A. Laschewsky, J.-F. Lutz, *Macromolecules* **2011**, *44*, 413–415.

28 Y. Maeda, H. Mochiduki, I. Ikeda, *Macromol. Rapid Commun.* 2004, *25*, 1330–1334.

29 H.-Y. Tian, J.-J. Yan, D. Wang, C. Gu, Y.-Z. You, X.-S. Chen, *Macromol. Rapid Commun.* 2011, *32*, 660–664.

30 Y.-J. Shih, Y. Chang, A. Deratani, D. Quemener, *Biomacro-molecules* 2012, *13*, 2849–2858.

31 M. Arotçaréna, B. Heise, S. Ishaya, A. Laschewsky, *J. Am. Chem. Soc.* **2002**, *124*, 3787–3793.

32 J. V. M. Weaver, S. P. Armes, V. Bütün, *Chem. Commun.* 2002, *18*, 2122–2123.

33 P. J. Roth, T. P. Davis, A. B. Lowe, *Macromolecules* **2012**, 45, 3221–3230.

34 T. Ueki, M. Watanabe, T. P. Lodge, *Macromolecules* **2009**, *42*, 1315–1320.

35 H.-N. Lee, Z. Bai, N. Newell, T. P. Lodge, *Macromolecules* 2010, *43*, 9522–9528.

36 F. D. Jochum, P. J. Roth, D. Kessler, P. Theato, *Biomacro-molecules* **2010**, *11*, 2432–2439.

37 H. Mori, I. Kato, S. Saito, T. Endo, *Macromolecules* **2010**, *43*, 1289–1298.

38 J. Weiss, C. Böttcher, A. Laschewsky, *Soft Matter* **2011**, *7*, 483–492.

39 G. Wu, S.-C. Chen, Q. Zhan, Y.-Z. Wang, *Macromolecules* **2011**, *44*, 999–1008.

40 R. Hoogenboom, H. M. L. Thijs, D. Wouters, S. Hoeppener, U. S. Schubert, *Soft Matter* 2008, *4*, 103–107.

41 H. M. L. Lambermont-Thijs, R. Hoogenboom, C.-A. Fustin, C. Bomal-D'Haese, J.-F. Gohy, U. S. Schubert, *J. Polym. Sci. Part A: Polym. Chem.* **2009**, *47*, 515–522.

42 Y.-Y. Liu, Y.-B. Zhong, J.-K. Nan, W. Tian, *Macromolecules* **2010**, *43*, 10221–10230.

43 X. Liu, P. Ni, J. He, M. Zhang, *Macromolecules* **2010**, *43*, 4771–4781.

44 X. J. Loh, Z.-X. Zhang, Y.-L. Wu, T. S. Lee, J. Li, *Macromolecules* **2009**, *42*, 194–202.

45 S. Medel, J. M. García, L. Garrido, I. Quijada-Garrido, R. París, *J. Polym. Sci. Part A: Polym. Chem.* **2010**, *48*, 690–700.

46 Lessard, B. H.; Ling, E. J. Y.; Marić, *M. Macromolecules* 2012, *45*, 1879–1891.

47 O. Zhang, P. Wilson, Z. Li, R. McHale, J. Godfrey, A. Anastasaki, C. Waldron, D. M. Haddleton, *J. Am. Chem. Soc.* **2013**, *135*, 7355–7363.

48 N. H. Nguyen, J. Kulis, H.-J. Sun, Z. Jia, B. van Beusekom, M. E. Levere, D. A. Wilson, M. J. Monteiro, V. Percec, *Polym. Chem.* **2013**, *4*, 144–155.

49 B. M. Rosen, V. Percec, *Chem. Rev.* **2009**, *109*, 5069–5119.

50 Y. Li, B. S. Lokitz, C. L. McCormick, *Macromolecules* **2006**, *39*, 81–89.

51 C. Pietsch, U. Mansfeld, C. Guerrero-Sanchez, S. Hoeppener, A. Vollrath, M. Wagner, R. Hoogenboom, S. Saubern, S. H. Thang, C. R. Becer, J. Chiefari, U. S. Schubert, *Macromolecules* **2012**, *45*, 9292–9302.

52 X. Xu, J. D. Flores, C. L. McCormick, *Macromolecules* 2011, 44, 1327–1334.

53 C. Zhou, M. A. Hillmyer, T. P. Lodge, *Macromolecules* 2011, 44, 1635–1641.

54 J.-F. Lutz, J. Polym. Sci. Part A: Polym. Chem. 2008, 46, 3459–3470.

55 S. Han, M. Hagiwara, T. Ishizone, *Macromolecules* 2003, *36*, 8312–8319.

56 J.-F. Lutz, A. Hoth, *Macromolecules* 2006, *39*, 893–896.

57 T. Terashima, M. Ouchi, T. Ando, M. Kamigaito, M. Sawamoto, *Macromolecules* 2007, *40*, 3581–3588.

58 P. J. Roth, M. Collin, C. Boyer, *Soft Matter* 2013, *9*, 1825–1834.

59 P. J. Roth, F. D. Jochum, P. Theato, *Soft Matter* **2011**, *7*, 2484–2492.

60 M. Dan, Y. Su, X. Xiao, S. Li, W. Zhang, *Macromolecules* 2013, *46*, 3137–3146.

61 S. Perrier, C. Barner-Kowollik, J. F. Quinn, P. Vana, T. P. Davis, *Macromolecules* **2002**, *35*, 8300–8306.

62 J. Xu, X. Xiao, Y. Zhang, W. Zhang, P. Sun, *J. Polym. Sci.* Part A: Polym. Chem. 2013, 51, 1147–1161.

63 H. de Brouwer, M. A. J. Schellekens, B. Klumperman, M. J. Monteiro, A. L. German, *J. Polym. Sci. Part A: Polym. Chem.* 2000, *38*, 3596–3603.

64 G. Chen, S. Amajjahe, M. H. Stenzel, *Chem. Commun.* 2009, 10, 1198–1200.

65 H. G. Schild, M. Muthukumar, D. A. Tirell, *Macromolecules* **1991**, *24*, 948–952.

66 H.-N. Lee, B. M. Rosen, G. Fenyvesi, H. B. Sunkara, J. Polym. Sci. Part A: Polym. Chem. 2012, 50, 4311–4315.

67 Z. Liu, Y. Guo, K. Inomata, Polym. J. 2011, 43, 676–682.

68 C. M. Schilli, M. Zhang, E. Rizzardo, S. H. Thang, Y. K. Chong, K. Edwards, G. Karlsson, A. H. E. Müller, *Macromolecules* **2004**, *37*, 7861–7866.

69 J. Zhao, G. Zhang, S. Pispas, *J. Polym. Sci. Part A: Polym. Chem.* **2009**, *47*, 4099–4110.

70 W. Agut, A. Brûlet, C. Schatz, D. Taton, S. Lecommandoux, *Langmuir* 2010, *26*, 10546–10554.

71 R.-S. Lee, W.-H. Chen, Y.-T. Huang, *Polymer* 2010, *51*, 5942–5951.

72 W. Zhang, L. Shi, K. Wu, Y. An, *Macromolecules* 2005, *38*, 5743–5747.

73 S. Qin, Y. Geng, D. E. Discher, S. Yang, *Adv. Mater.* 2006, 18, 2905–2909.

74 C. Yang, J. N. Kizhakkedathu, D. E. Brooks, F. Jin, C. Wu, *J. Phys. Chem. B* **2004**, *108*, 18479–18484.