# Synthesis, Characterization, and Stimuli-Sensitive Properties of Triblock Copolymer Poly(ethylene oxide)-*b*-poly(2-(diethylamino)ethyl methacrylate)-*b*-poly(*N*-isopropylacrylamide)

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**ABSTRACT:** Well-defined triblock copolymer poly(ethylene oxide)-*b*-poly(2-(diethylamino)ethyl methacrylate)-*b*-poly(*N*-isopropyl-acrylamide) (PEO-*b*-PDMAEMA-*b*-PNIPAAm) was synthesized via sequential reversible addition-fragmentation chain transfer polymerization (RAFT) of 2-(dimethylamino)ethyl methacrylate (DMAEMA) and *N*-isopropylacrylamide (NIPAAm) using α-methoxy-ω-S-1-dodecyl-S-α-(α,α′-dimethyl-α″-acetate) poly(ethylene oxide) (mPEO-DDAT) as macro-RAFT agent, AIBN as initiator in dioxane at 80°C. The polymerization data indicated that the both RAFT processes were well controlled. The molecular weights of macro-RAFT agents showed the influence on the RAFT polymerization process. The final PEO-*b*-PDMAEMA-*b*-PNIPAAm triblock copolymer can form uniform micelles in aqueous media above the lower critical solution temperature (LCST) due to containing temperature-sensitive PNIPAAm block. The micelle size and $D_h$ were dependent on the composition of triblock copolymer and the pH value of the solution. The PEO-*b*-PDMAEMA-*b*-PNIPAAm triblock copolymer showed dual temperature- and pH-sensitive property in aqueous media. © 2008 Wiley Periodicals, Inc. J Appl Polym Sci 108: 2180–2188, 2008

**Key words:** block copolymer; RAFT; stimuli-sensitive polymer; poly(ethylene oxide); poly(dimetylaminoethyl methacrylate); poly(*N*-isopropyl acrylamide)

## INTRODUCTION

Polymers with unique structures, such as block, star, gradient, and graft structures, have been widely used in tissue engineering, drug delivery, micelle formation, and so on.[1–5] Recent progress in controlled living radical polymerization, especially in reversible addition-fragmentation transfer polymerization (RAFT), has provided a powerful tool for preparing polymers with well-defined structure[6–9] because of its versatility and simplicity, and the obtained polymer is free from the contamination of metal catalysts. Most importantly, it also offers all advantages of a conventional free radical polymerization, nearly the same polymerization conditions as temperatures, the used monomers and initiators, and solvents could be applied.

Recently, the polymer systems that undergo phase transitions in response to environmental stimuli such as pH and temperature have been widely investi-gated for drug delivery, separations, and diagnostics applications.[10] Poly(2-(diethylamino)ethyl methacrylate) (PDMAEMA) is a kind of pH-sensitive polymer which has a pKa of 7.0–7.3 in water,[11–13] which is widely used to prepare pH-sensitive materials.[14]

Poly(*N*-Isopropyl acrylamide) (PNIPAAm) is a well-known thermosensitive polymer and exhibits a coil-to-globule transition at lower critical solution temperature (LCST) of about 32°C in an aqueous medium. This thermoresponsive property of PNIPAAm can be used to prepare thermoreversible separator, thermoresponsive soft actuator, automatic gel valve,[15] and smart, reusable catalysts.[16] Thus, block copolymers containing PDMAEMA block and PNIPAAm segment which possesses both pH- and temperature-sensitive properties allows a flexible control over the polymer phase behavior, resulting in multifunctional smart materials. These copolymers can be potentially useful for applications in many biomedical areas, such as in tissue engineering and in controlled drug delivery and release.[17,18] Herein, we reported consecutive RAFT polymerization of DMAEMA and NIPAAm using PEO-*b*ased macro-RAFT agent. The resulting triblock copolymers showed the double pH- and thermosensitive properties in aqueous media.

## EXPERIMENTAL

### Materials

DMAEMA obtained from Aldrich was passed through an activated basic alumina column and distilled under reduced pressure from $CaH_2$, then stored at $-20°C$ prior to use. NIPAAm (Aldrich) and 2,2-azobisisobutyronitrile (AIBN) were purified by recrystallization twice in *n*-hexane and methanol, respectively. mPEO-OHs ($M_n = 4120$ g/mol, $M_w/M_n = 1.06$; $M_n = 7780$ g/mol, $M_w/M_n = 1.07$, respectively) were prepared by anionic polymerization of ethylene oxide using potassium 2-(2-methoxyethoxy) ethoxide as initiator according to the previous report.[19] The RAFT agent, S-1-dodecyl-S'-(α,α'-dimethyl-α''-acetic acid) trithiocarbonate (DDAT) was prepared as described in the Ref. 20 in 80% yield, and further purified by recrystallization from *n*-hexane [its ^{1}H NMR spectrum was shown in Fig. 2(B)] (Scheme 1).

### Preparation of macro-CTA mPEO-DDAT

In a 150-mL one-neck round-*b*ottom flask equipped with a magnetic stirring bar, mPEO-OH ($M_n = 4120$ g/mol, $M_w/M_n=1.06$) (4.12 g, 1.0 mmol) was dissolved in 50 mL of toluene. After azeotropic distillation to remove traces of water, DDAT (0.73 g, 2.0 mmol), DMAP (0.12 g, 1.0 mmol), and methylene chloride (50 mL) were added. After the solution was homogenized by stirring, the flask was put into an ice bath. Then, DCC (0.41 g, 2.0 mmol) was added in portions. After 12 h of stirring at 0°C, the reaction mixture was raised to room temperature and kept stirring for another 2 days. The solid dicyclohexyl-

urea was filtered off, then the filtrate was precipitated into excess of diethyl ether three times, and dried under vacuum at 35°C for 24 h. The product with yellow color was stored in a sealed bottle in a cool and dark place. The other sample of mPEO-DDAT with the molecular weight 7780 g/mol was prepared using the same method. The DDAT contents of mPEO-DDATs could be calculated by ^{1}H NMR and UV spectra.

### Preparation of trithioester-terminated mPEO-*b*-PDMAEMA-DDAT

An ampoule charged with AIBN (0.0084 mmol, 1.375 mg), mPEO-DDAT ($M_n = 4470$, 0.084 mmol, 0.375 g), DMAEMA (6.35 mmol, 1.0 g), and dioxane (5 mL) was freeze-thawed three times to remove oxygen, sealed, and placed in a constant temperature oil bath at 80°C. After a predetermined polymerization time (Table I, series 1 (1a–1d)), the ampoule was rapidly put in an ice bath and cooled half an hour. The polymerization product was precipitated in petroleum ether (30–60°C) and purified by dissolution/precipitation with $CH_2Cl_2$/petroleum ether (30–60°C) twice, and the further purification was carried out by ultrafiltration membrane separator. The cut-off molecular weight of the poly(ether sulfone) film was 20 kDa(calibrated by a global protein), and then it was dried to constant weight under vacuum at 35°C.

### Preparation of triblock PEO-*b*-PDMAEMA-*b*-PNIPAAm

An ampoule charged with mPEO-*b*-PDMAEMA-DDAT (sample 1b, $M_n = 8100$ g/mol, 0.0123 mmol,
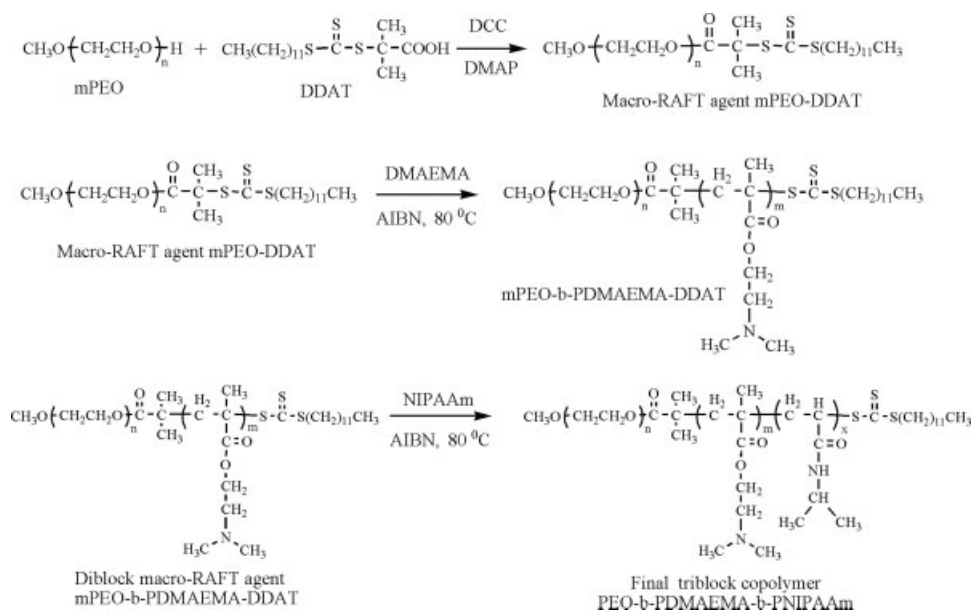


**Scheme 1** RAFT polymerization process of triblock copolymer.

## TABLE I
### RAFT Polymerization of DMAEMA[a]

| Diblock copolymer[b] | Time (h) | $M_{n,\text{GPC}}$[c] | $M_w/M_n$[d] | Conv (%)[e] | $M_{n,\text{CONV}}$[f] | $M_{n,\text{NMR}}$[g] |
|---|---|---|---|---|---|---|
| 1a | 1 | 3900 | 1.11 | 17.6 | 6600 | 6800 |
| 1b | 2 | 4200 | 1.08 | 28.6 | 7900 | 8100 |
| 1c | 3 | 4900 | 1.12 | 37.0 | 8900 | 9000 |
| 1d | 6 | 5900 | 1.11 | 52.4 | 10,700 | 11,900 |
| 2a | 1 | 4200 | 1.13 | 9.50 | 9300 | 9600 |
| 2b | 2 | 4600 | 1.11 | 20.2 | 10,600 | 10,400 |
| 2c | 3 | 5500 | 1.09 | 27.6 | 11,400 | 11,900 |
| 2d | 7.5 | 6100 | 1.14 | 44.8 | 13,500 | 14,100 |
| 2e | 10 | 6400 | 1.14 | 58.2 | 15,100 | 14,900 |

[a] Polymerization condition: [mPEO-DDAT] = $1.34 \times 10^{-2}$ mol/L; [mPEO-DDAT] : [AIBN] = 10 : 1; [DMAEMA] = 1.02 mol/L; temperature: 80°C; solvent: dioxane.
[b] mPEO-PDMAEMA-DDAT 1a–1d: using mPEO-DDAT ($M_n$: 4470 g/mol; $M_w/M_n$ = 1.06) as RAFT agent; 2a–2e: using mPEO-DDAT ($M_n$: 8150 g/mol; $M_w/M_n$ = 1.07) as RAFT agent.
[c] Number-average molecular weight measured by GPC.
[d] Molecular weight distribution measured by GPC.
[e] Conversion of monomer obtained from gravimetry.
[f] Theoretical molecular weight calculated by monomer conversion.
[g] Number-average molecular weight derived from ${}^1$H NMR data.

0.10 g), AIBN (0.00123 mmol, 0.20 mg), NIPAAm (1.46 mmol, 0.165 g), and dioxane (1.45 mL) was vacuumed three freeze-thaw cycles at liquid nitrogen temperature, then sealed and placed in a constant temperature oil bath at 80°C. After a predetermined polymerization time (showed in Table II), the ampoule was rapidly put in an ice bath and cooled half an hour. The polymerization product was precipitated in diethyl ether, purified by dissolution/precipitation with tetrahydrofuran (THF)/diethyl ether twice, and the further purification was carried out by ultrafiltration membrane separator. The cut-off molecular weight of the poly(ether sulfone) film was 20 kDa(calibrated by a global protein), and then it was dried to constant weight under vacuum at 35°C.

### Measurements

The monomer conversion was measured gravimetrically. The molecular weight and the molecular weight distribution ($M_w/M_n$) were determined by gel permeation chromatography (GPC) (HP1100) assembled by an Agilent1100 with a G1310A pump, a G1362A refractive index detector, and a G1314A variable wavelength detector using THF as eluant at 35°C with an elution rate of 1.0 mL/min, one 5-μm PL gel column (500 Å, molecular range 500–502 $\times$ $10^4$ g/mol), and two 5-μm PL gel mixed bed columns (molecular range 200–203 $\times$ $10^6$ g/mol) were calibrated by the monodistributed polystyrene standard samples. For mPEO-OH, GPC was performed in

## TABLE II
### RAFT Polymerization of NIPAAm[a]

| Triblock copolymer[b] | Time (h) | $M_{n,\text{GPC}}$[c] | $M_w/M_n$[d] | Conv (%) | $M_{n,\text{CONV}}$[e] | $M_{n,\text{NMR}}$[f] |
|---|---|---|---|---|---|---|
| 1b1 | 0.33 | 5800 | 1.25 | 15.6 | 10,200 | 10,900 |
| 1b2 | 0.66 | 6400 | 1.31 | 32.8 | 12,500 | 14,600 |
| 1b3 | 1 | 6900 | 1.24 | 43.6 | 14,000 | 15,600 |
| 1b4 | 1.5 | 7500 | 1.24 | 57.8 | 15,900 | 17,100 |
| 1b5 | 2 | 8500 | 1.33 | 71.3 | 17,700 | 21,200 |

[a] Polymerization condition: Using mPEO-b-PDMAEMA-DDAT (1b) as macro-RAFT agent. [mPEO-b-PDMAEMA-DDAT] = $7.27 \times 10^{-3}$ mol/L; [mPEO-b-PDMAEMA-DDAT] : [AIBN] = 10 : 1; [NIPAAm] = 0.86 mol/L; temperature: 80°C; solvent: dioxane.
[b] mPEO-PDMAEMA-PNIPAAm-DDAT.
[c] Number-average molecular weight measured by GPC.
[d] Molecular weight distribution obtained from GPC data.
[e] Theoretical molecular weight calculated by monomer conversion.
[f] Number-average molecular weight derived from ${}^1$H NMR data.

distilled water at 40°C with an elution rate of 0.5 mL/min, three TSK-gel PW columns were in series (bead size: 6, 13, 13 μm; pore size: 200 Å, greater than 1000 Å, less than 100–1000 Å; molecular range: 0–5 × 10⁴, 5 × 10⁴ to 8 × 10⁶, (5–8) × 10⁶ g/mol, respectively) were calibrated by PEO standard samples, the injection volume was 20 μL with the concentration 5 mg/mL. UV spectra were taken on a 756 MC ultraviolet-visible light spectrophotometer (Shanghai Third Analytical Instrument Factory, China) and methanol was used as solvent. ¹H NMR measurement was carried out on a Bruker (500 MHz) spectrometer with tetramethylsilane as the internal standard, CDCl₃ and D₂O as the solvents. Dynamic light scattering (DLS) measurement was performed at 30°C on a Malvern Autosizer 4700 Dynamic Light Scattering Instrument. The ultrafiltration membrane separator was purchased form the Shanghai Institution of Nuclear Research, Chinese Academy of Science. The cut-off molecular weight of the poly(ether sulfone) film was 20 kDa (calibrated by a global protein).

## RESULTS AND DISCUSSION

### Characterization of the macro-RAFT agent mPEO-DDAT

The macro-RAFT agent mPEO-DDAT was prepared via the reaction of mono-hydroxyl mPEO-OH with DDAT in the presence of DCC using DMAP as catalyst. To make sure that the subsequent polymerization of DMAEMA and NIPAAm was successfully carried out, the DDAT end group content in the macro-RAFT agent mPEO-DDAT should be exactly determined. Here, UV and NMR methods were used to measure it. Figure 1 showed the UV absorption spectrum of mPEO-DDAT in methanol with the concentration of 4.0 × 10⁻⁵ mol/L. The maximal absorb-
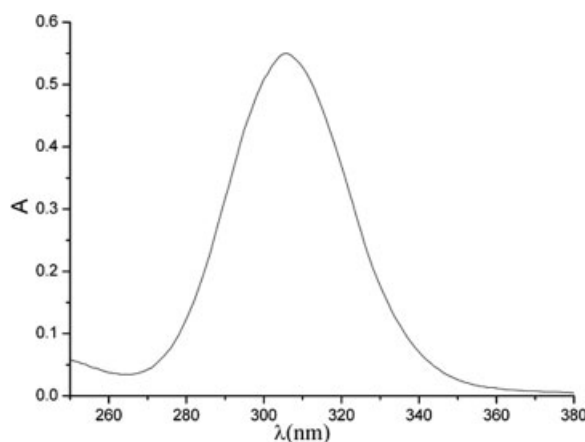


**Figure 1** UV absorbance spectrum of macro-RAFT agent mPEO-DDAT ($M_n$ = 4470, concentration: 4 × 10⁻⁵ mol/L, methanol as solvent).

ance of small molecule DDAT was at 307 nm, and the mole extinction coefficient was 1.383 × 10⁴ L Mol⁻¹ cm⁻¹, from which the contents of DDAT end groups in mPEO-DDAT (reaction efficiency) could be derived. The mPEO-DDAT was purified by washing several times using diethyl ether. When there was no UV absorption at 307 nm in the collected washing filtrate, it meant the unreacted DDAT was completely removed. Thus, the absorbance at 307 nm could be attributed to the DDAT end groups of mPEO-DDAT. The reaction efficiency (RAFT agent content) could be calculated by the following equation:

$$\text{Efficiency} = \frac{A_{\text{meas}}}{A_{\text{theo}}} \times 100\% \tag{1}$$

$$A_{\text{theo}} = \varepsilon C l \tag{2}$$

where $A_{\text{meas}}$ was the absorbance of mPEO-DDAT at 307 nm measured by UV spectrum, $A_{\text{theo}}$ was the absorbance obtained from the eq. (2), $C$ was the concentration of the mPEO-DDAT, $\varepsilon$ was mole extinction coefficient, and $l$ was the length of sample cell. The obtained value was ∼ 100% which indicated that nearly all the hydroxyl groups of mPEO-OH were reacted with the carboxyl groups of DDAT.

Figure 2 showed the ¹H NMR spectra of mPEO-OH (A), DDAT (B), and mPEO-DDAT (C). Comparing the ¹H NMR spectrum of mPEO-OH (A) with that of mPEO-DDAT (C), the peak (i) at 2.68 ppm attributed to the protons of hydroxyl groups of mPEO-OH completely disappeared after condensation with carboxyl groups of DDAT, which indicated that the reaction efficiency was much high. It should also be noted that the peak attributed to the protons of methene neared to the end hydroxyl of mPEO-OH was overlapped with other protons [Fig. 2(A)], but shifted from 3.64 to 4.25 ppm (f) [Fig. 2(C)] after esterification, so the exact value could be calculated by the following formula:

$$\text{Efficiency} = \frac{A_f/2}{A_h/3} \times 100\% \tag{3}$$

where $A_f$ and $A_h$ were the integral areas of the methylene protons at 4.25 ppm and the methyl group of mPEO-OH at 3.38 ppm, respectively. The calculated efficiency was ∼ 98%, which was consistent with that derived from the UV method. Thus it could be reliably concluded that all the hydroxyl groups of mPEO-OH were reacted with DDAT in the presence of DCC and DMAP. So the molecular weights of macro-RAFT agents mPEO-DDAT could be calculated from the number-average molecular weight of mPEO-OH derived by GPC plus molecular weight of DDAT, they are 4470 and 8150 g/mol, respectively.
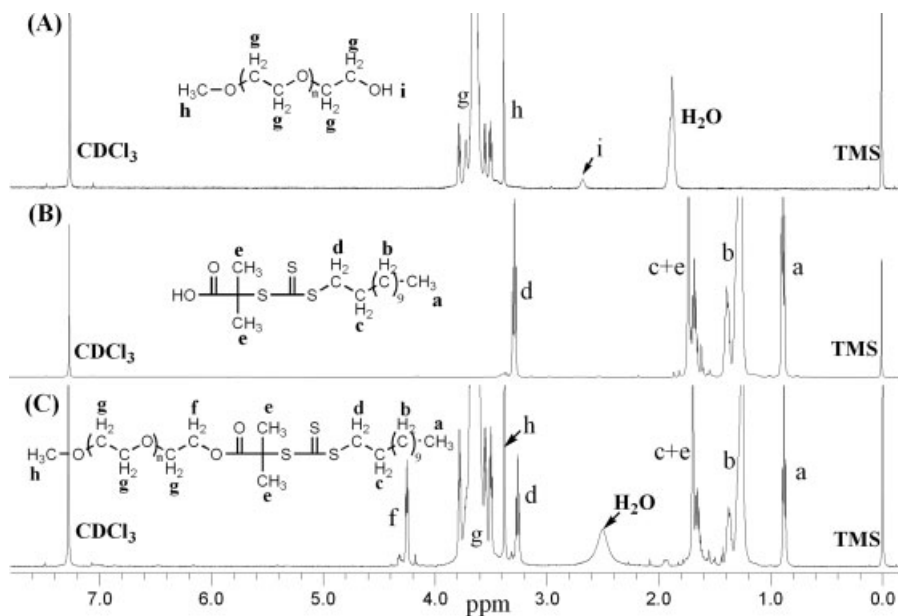
**Figure 2** ^{1}H NMR spectra of mPEO-OH ($M_n$ = 4120) (A), DDAT (B), and macro-RAFT agent mPEO-DDAT (C) (CDCl$_3$ as solvent).

## Preparation of trithioester-terminated diblock copolymer mPEO-*b*-PDMAEMA-DDAT

The trithioester-terminated diblock copolymer mPEO-*b*-PDMAEMA-DDAT was obtained by RAFT polymerization of DMAEMA with AIBN as initiator and mPEO-DDAT as macro-RAFT agent. According to the report of Lai et al.,[20] DDAT showed extremely high chain-transfer efficiency and the ability to control the RAFT polymerization. Thus, the macro-RAFT agent containing DDAT end group was selected to control the polymerization of DMAEMA and NIPAAm.

Figure 3 showed the ^{1}H NMR spectrum of mPEO-*b*-PDMAEMA-DDAT (Table I, 1b) on which all the signals were marked. Comparing with Figures 2(C) and 1(B), all peaks attributed to trithioester as (a) at 0.88 (t, 3H, —CH$_3$), (b) at 1.25–1.47 (m, 18H, —(CH$_2$)$_9$—), and (e) at 1.62–1.81(m, 8H —C(CH$_3$)$_2$ overlapped with methelene (c) were still observed in Figure 3, which confirmed that the trithiocarbonate groups still existed in the ends of diblock copolymers. In addition, the characteristic peaks at 4.08 ppm (c) (the protons connected to the ester bond), 2.64 ppm (d) (the protons connected to dimethyl amino), and 2.24 ppm (k) (the protons of dimethylamino) for DMAEMA units were assigned according to previous report appeared.[21] The molecular weight of PDMAEMA block could be readily obtained from the ratio of area of peak (c) and peak (g) based on the known molecular weight of mPEO segment. Thus, the molecular weight of diblock copolymer mPEO-*b*-PDMAEMA-DDAT could be calculated by the sum of molecular weight of mPEO segment and

PDMAEMA block. On other hand, for comparison, the molecular weights of trithioester-terminated diblock copolymer mPEO-*b*-PDMAEMA-DDATs were also measured by GPC and evaluated from conversion. All the data were listed in Table I, from which it was found that the molecular weights of mPEO-*b*-PDMAEMA-DDAT derived from ^{1}H NMR data were very close to that obtained from conversion. However, obvious discrepancies between the molecular weight measured by GPC and that came from ^{1}H NMR were observed which might be attributed to the sharp difference in hydrodynamic volume between diblock copolymer mPEO-*b*-PDMAEMA-DDAT and polystyrene
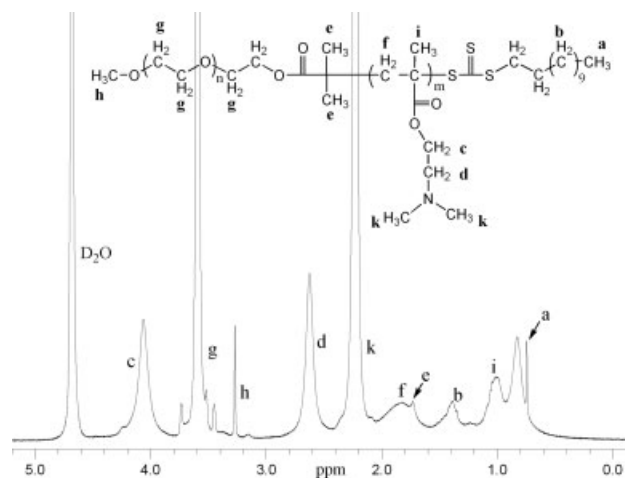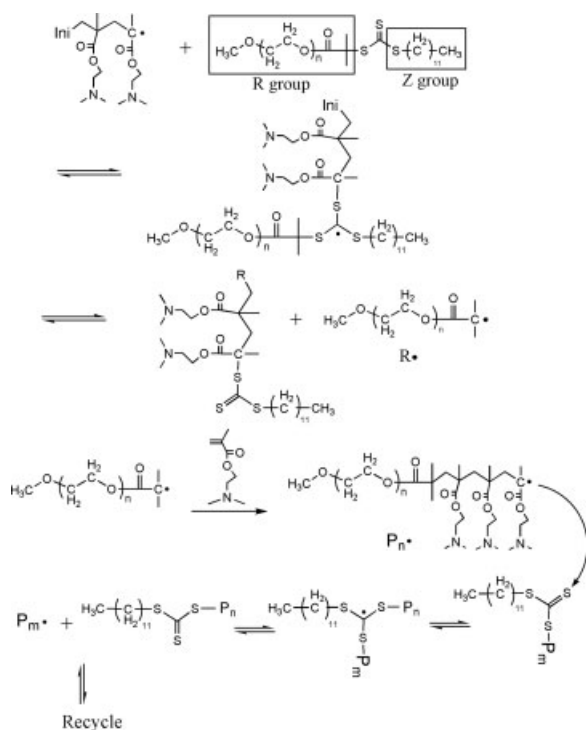


**Figure 3** ^{1}H NMR spectrum of trithioester-terminated diblock copolymer mPEO-*b*-PDMAEMA-DDAT 1b. (D$_2$O as solvent).

**Scheme 2** Mechanism of RAFT polymerization of DMAEMA with mPEO-DDAT as macromolecular chain transfer agent.



**Figure 4** GPC traces of the macro-RAFT agent mPEO-DDAT ($M_n$ = 4470) and trithioester-terminated diblock mPEO-*b*-PDMAEMA-DDAT 1a, 1b, 1c, and 1d with THF as eluant.

standards in THF. Similar phenomenon has been discussed in the previous report.[22]

To investigate the influence of molecular weights of mPEO-DDAT on the polymerization of DMAEMA, mPEO-DDAT of $M_n$ = 4470 and 8150 g/mol were used for RAFT polymerization, respectively. As showed in Table I, at the same polymerization time, the conversion of monomer was higher when the mPEO-DDAT with lower molecular weight was used. This phenomenon might be attributed to effect of diffusion. The formation mechanism of diblock copolymer via RAFT process was depicted in Scheme 2. The transfer of a propagating radical to the thiocarbonylthio group of mPEO-DDAT generated an intermediate adduct radical, which was split into a polymeric trithiocarbonate compound and a new radical R•. The radical R• could reinitiate polymerization of DMAEMA to give a new propagating radical $P_n$•. Subsequent addition-fragmentation steps built equilibrium between the propagating radicals $P_n$•, $P_m$•, and the dormant polymeric trithiocarbonate compounds. In our RAFT process, the leaving group (R group) of DDAT was connected with mPEO via ester linkage, so the R• with lower molecular weight of mPEO had lower viscosity, and therefore moved and diffused easily, which resulted in faster polymerization of monomer and higher conversion under the same polymerization time.
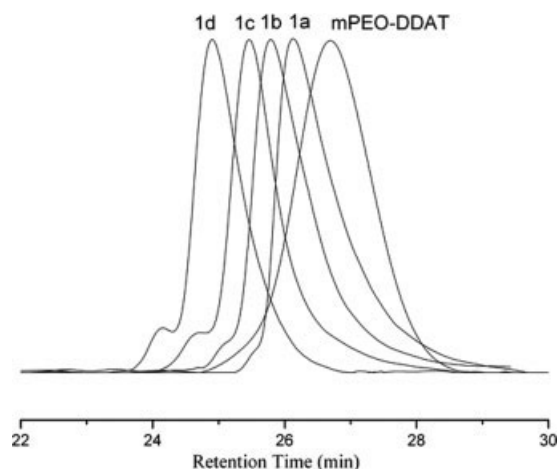
GPC traces of trithioester-terminated diblock copolymers (1a, 1b, 1c, and 1d, Table I) were illustrated in Figure 4. It was worth to point out that obvious shoulder peak was present at low retention time. The number-average molecular weight of shoulder peak was almost twice of that of main peak, and the weight fraction of the former increased from ∼ 1% (1a), 2% (1b), 4% (1c) to 6% (1d) with the increasing of polymerization time. It meant that the probability of coupling termination[23] (showed in Scheme 3) in RAFT process was increased with increasing of conversion of monomer. The evolution of number-average molecular weight of mPEO-*b*-PDMAEMA-DDAT (the values derived from ^{1}H NMR data, listed in Table I) versus conversion of DMAEMA was plotted in Figure 5, in which no matter what kind of mPEO-DDAT was used, the molecular weight increased proportionally with conversion, confirming the controlled behavior of polymerization in the presence of macro-RAFT agent mPEO-DDAT.
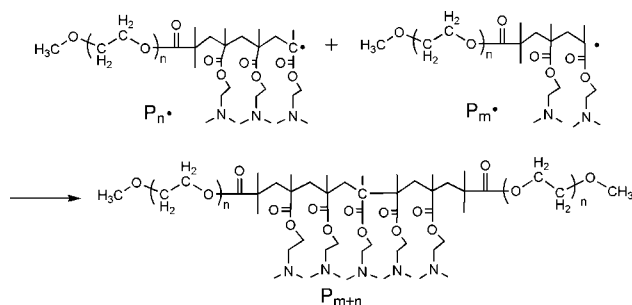


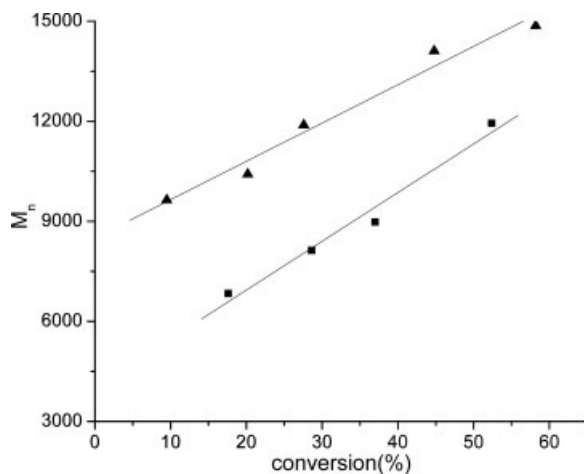**Scheme 3** Bimolecular termination of free macroradicals to form "dead" polymeric product.

**Figure 5** Dependence of $M_n$ of mPEO-b-PDMAEMA-DDAT on the conversion of DMAEMA. (■: $M_n$ (mPEO-DDAT): 8200 g/mol; ▲: $M_n$ (mPEO-DDAT): 4470 g/mol).

### Preparation of triblock copolymer PEO-b-PDMAEMA-b-PNIPAAm

The object triblock copolymer PEO-b-PDMAEMA-b-PNIPAAm (poly(ethylene oxide)-b-poly(2-(diethyl-amino)ethyl methacrylate)-b-poly(N-isopropyl-acryl-amide)) was obtained via RAFT process using trithioester-terminated mPEO-b-PDMAEMA-DDAT as macrochain transfer agent. The ^{1}H NMR spectrum of one sample (1b5) was illustrated in Figure 6 from which the chemical shift at 3.79 ppm attributed to protons of methine of NIPAAm units (j) was clearly observed. The molecular weight of PNIPAAm segment was easily calculated from the ratio of area of peak g at 3.44–3.70 ppm for the protons of PEO chains and peak j. Thus the number-average molecular weight of the triblock copolymer PEO-b-PDMAEMA-b-PNIPAAm could be obtained by the
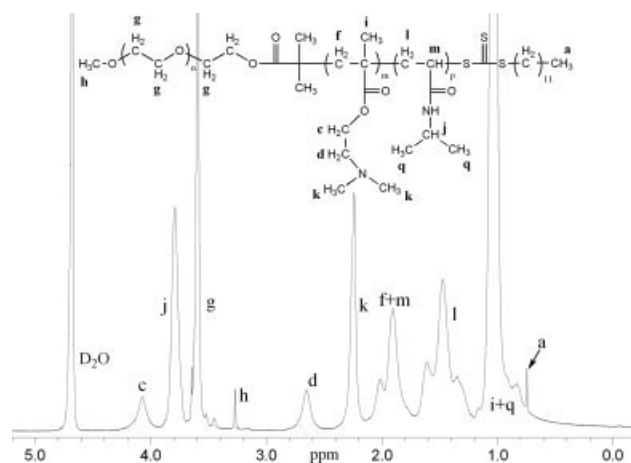
sum of molecular weights of PNIPAAm segment and macro-RAFT agent mPEO-b-PDMAEMA-DDAT. The values were similar to those calculated from conversion but significant different with the data derived from GPC. All these data were listed in Table II. The linear relationship between number-average molecular weight (obtained from ^{1}H NMR data) and conversion showed that the chain extension of PNIPAAm from macro-RAFT agent mPEO-b-PDMAEMA-DDAT was well controlled (Figure 7).

### Stimuli-sensitive properties of triblock Copolymer PEO-b-PDMAEMA-b-PNIPAAm in aqueous media

As it is well known, the hydrophilicity of PNIPAAm could be varied with the temperature, when the temperature is lower than LCST (~ 32°C, dependent on the molecular weigh of PNIPAAm), PNIPAAm chains are hydrophilic and soluble in water; However, when the temperature is higher than LCST, PNIPAAm turns to hydrophobic. In our case, at low temperature (less than LCST of PNIAAm), the triblock copolymer PEO-b-PDMAEMA-b-PNIPAAm was dissolved in the aqueous solution as mono-molecule. As raising the temperature over LCST, the PNIPAAm block turned to hydrophobic which caused formation of the global micelle composed of PNIPAAm core, PDMAEMA shell and PEO coronal. Figure 8 showed that the variation of hydrodynamic diameter ($D_h$) of global micelle depended on the solution temperature. When the temperature was lower than the LCST, the $D_h$ of all copolymers was about 10 nm, which meant the copolymer existed as mono-molecule in solution. As the solution temperature was raised to 32°C, the copolymer 1b4 with high molecular weight of PNIPAAm segment started to form the micelle, the diameter is about 70 nm;
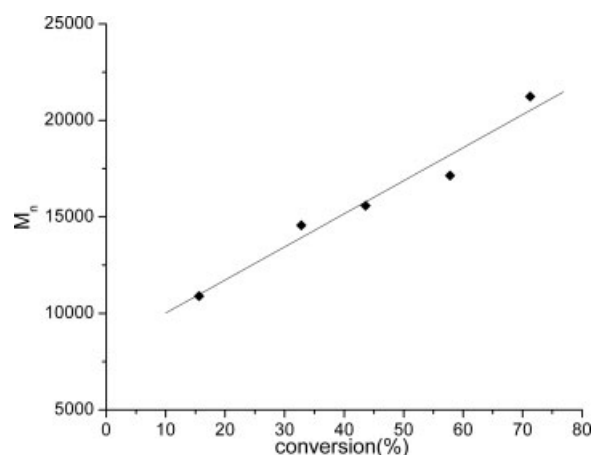


**Figure 6** ^{1}H NMR spectrum of final triblock copolymer PEO-b-PDMAEMA-b-PNIPAAm 1b5. (D₂O as solvent).



**Figure 7** Dependence of $M_n$ of mPEO-b-PDMAEMA-PNIPAAm on the conversion of PNIPAAm.

The sample 1b2 started to form the micelles with $D_h$ about 40 nm at 35°C while the sample 1b1 containing low molecular weight of PNIPAAm block formed the micelles with $D_h$ about 30 nm at 37°C. Those DLS data showed that the LCST and the size of formed micelle of triblock copolymers were dependent on the molecular weights of PNIPAAm segments: the higher the molecular weight of PNIPAAm, the lower the LCST, and the larger micelle was formed. It was also worth to note that an obvious decrease in size was found with increasing temperature above the LCST. Yusa et al. pointed that this decrease in size was attributed to either a decrease in the aggregation number of the aggregates or further dehydration of the PNIPAAm blocks.[24]

The triblock copolymer PEO-*b*-PDMAEMA-*b*-PNIPAAm displayed pH-sensitive in aqueous media since it contained the pH-sensitive PDMAEMA middle block.[24] Figure 9 showed the dependence of $D_h$ of the micelles (formed by triblock copolymer 1b2) on the solution pH at 37°C. Because of the existing of permanent hydrophilic PEO and the short PDMAEMA block ($M_n$ = 3900 g/mol, calculated from ^{1}H NMR data), the $D_h$ did not change significantly with the variation of solution pH (45 nm at pH 10.6 compared with 40 nm at pH 8.9). The existence of hydrophilic PEO in the triblock copolymer is stabilizing the formed three-layer micelles. At high temperature (above LCST of PNIPAAm), the PNIPAAm block was turned to hydrophobic; hence, the triblock copolymer starts to form micelles with PNIPAAm core, PDMAEMA shell, and PEO coronal. If there is no PEO block in the triblock copolymer, at high temperature (PNIPAAm block turns to hydrophobic) and high pH (PDMAEMA turns to hydro-
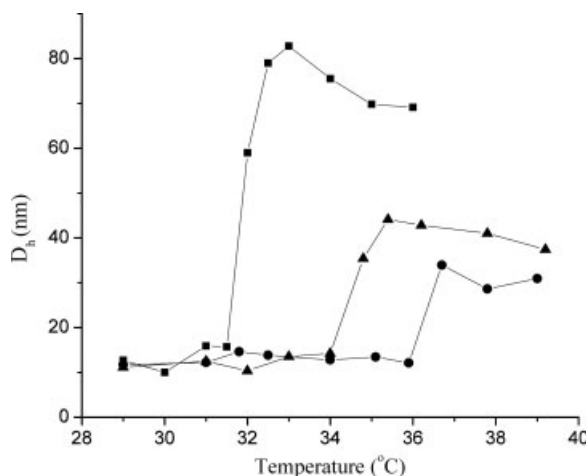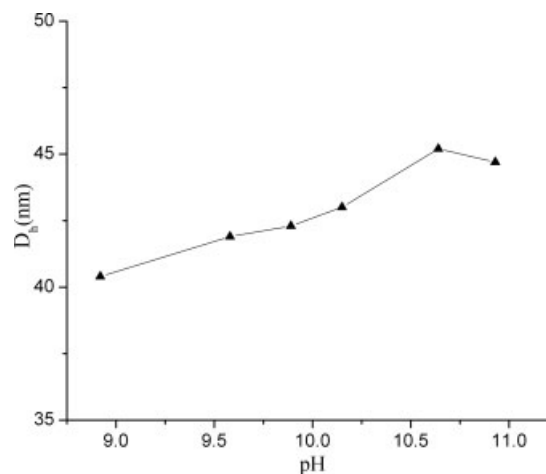


**Figure 9** Hydrodynamic diameter versus pH for the triblock copolymers 1b2 in aqueous solution at 37°C (concentration: 0.5 wt %).

phobic), the copolymer will precipitate, no micelle was formed.

## CONCLUSIONS

Macro-RAFT agent mPEO-DDAT could be used to mediate the polymerization of DMAEMA and subsequent NIPAAm to generate the triblock copolymer PEO-*b*-PDMAEMA-*b*-PNIPAAm with narrow molecular weight distribution. The polymerization data showed both of the RAFT processes were controllable. The resultant copolymers can form the uniform micelles as the temperature was higher than the LCST of PNIPAAm blocks. The formed micelles also displayed pH-sensitive property due to the existence of PDMAEMA middle block.



**Figure 8** Relationship between hydrodynamic diameter ($D_h$) and temperature for the three triblock copolymers in aqueous solution (concentration: 0.5 wt %). (●: 1b1; ▲, 1b2; ■: 1b4).

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