Temperature- and pH-Responsive Dense Copolymer Brushes Prepared by ATRP

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ABSTRACT: Dual responsive molecular brushes consisting of statistical copolymers of di(ethylene glycol) methyl ether methacrylate (MEO_2MA) and either methacrylic acid (MAA) or *N,N*-dimethylaminoethyl methacrylate (DMAEMA) were synthesized by grafting from poly(2-(2-bromoisobutyroyloxy)ethyl methacrylate (PBIEM) macroinitiators using atom transfer radical polymerization (ATRP). Copolymer brushes with controlled composition and molecular weights ranging from M_n = 600 000 to 1 400 000 with polydispersity indexes (M_w/M_n) between 1.18 and 1.45 were obtained. The lower critical solution temperature (LCST) of MEO_2MA-*stat*-MAA decreased with the increasing molar fraction of MAA in the copolymer in deionized water but increased in buffer solution at pH 7. At pH 9, the hydrophilicity of polymer increased with ionization of carboxylic acid to further raise the LCST. On the other hand, the LCST of MEO_2MA-*stat*-DMAEMA copolymers increased with increasing DMAEMA content at pH 4, 7, and 9. A bottle-brush terpolymer prepared from all three comonomers exhibited LCST at pH 4 and 7 but not at pH 9, which can be attributed to the stronger ionization of MAA. The responsive nature of the copolymer is enhanced by the densely graft structure of a brush copolymer.

Introduction

Stimuli-responsive polymers have been extensively investigated for the development of smart materials for various applications.[1−6] Thermoresponsive, water-soluble polymers exhibiting a lower critical solution temperature (LCST) in aqueous media have been increasingly investigated for nanotechnology and biotechnology applications.[7−9] Poly(*N*-isopropylacrylamide) (PNIPAM) has been the most studied thermoresponsive polymer targeting biological applications.[10,11] In addition, polymers consisting of poly(ethylene glycol) (PEG), which is an uncharged, water-soluble, nontoxic polymer, are being developed as new thermoresponsive water-soluble polymers.[12−14] Such thermoresponsive polymers containing oligo(ethylene oxide) side chains were prepared by controlled/living cationic, anionic, and radical polymerizations.[15−23] "Smart" polymers with stimuli based on acid−base reactions or on changes in pH are attractive materials for biological applications.[24,25] Typical examples are polymers with amines or carboxylic acids as substituents, which become charged species by protonation or deprotonation and thus undergo a pronounced change in their hydrophilicity.[26] Another approach employs zwitterionic block copolymers, possessing schizophrenic micellization behavior dependent on pH.[27−29]

Even more interesting are systems responsive to two different stimuli.[30] For example, a linear block copolymer, poly(*N*-isopropylacrylamide)-*block*-poly(acrylic acid), was reported to be responsive to both thermal and pH stimuli.[31,32] Poly(*N,N*-dimethylaminoethyl methacrylate), PDMAEMA, is responsive to changes in pH as well as temperature, and the thermal behavior changes significantly with pH.[33−35] In a similar way, the LCST properties of copolymers of DMAEMA and poly(ethylene glycol) methyl ether methacrylate ($M_n \sim 300$) varied with pH.[36]

Recently, we reported the synthesis of thermoresponsive copolymer brushes containing DMAEMA units in the side chains by atom transfer radical polymerization (ATRP).[37] We also reported the synthesis of the brush molecules having side chains with either a statistical distribution or blocks of di(ethylene glycol) methyl ether methacrylate (MEO_2MA) and tri(ethylene glycol) methyl ether methacrylate (MEO_3MA) units. The thermal properties of an aqueous solution of the brush copolymers are strongly dependent on the composition and architecture of the copolymer side chains.[21,22] Molecular brushes, with a dual response to light and temperature, were prepared by copolymerizing *trans*-4-methacryloyloxyazobenzene and DMAEMA units into the side chains by ATRP.[38]

ATRP is one of the most efficient techniques for synthesis of polymers with precisely controlled molecular architecture,[39−42] hybrid materials,[43−47] and bioconjugates.[48−51] The conformational behavior of molecular brush copolymers can be influenced by external factors such as solvent, light, pH, and temperature to exhibit unique material properties.[52−55] In this article we report the synthesis and characterization of statistical copolymer brushes of MEO_2MA, methacrylic acid (MAA), and DMAEMA prepared by ATRP using a copper-based catalyst and how the cloud point of aqueous solutions of these brush molecules depends on the composition of the copolymer side chains and pH.

Experimental Section

Materials. Ethyl 2-bromoisobutyrate (EBiB), 4,4′-dinonyl-2,2′-bipyridine (dNbpy), *N,N,N′N″,N‴,N‴*-hexamethyltriethylenetetraamine (HMTETA), copper(II) bromide, trifluoroacetic acid (TFA), and solvents were purchased from Aldrich at the highest purity available and used as received without further purification. Di(ethylene glycol) methyl ether methacrylate (MEO_2MA), *tert*-butyl methacrylate (*t*BMA), and *N,N*-dimethylaminoethyl methacrylate (DMAEMA) were purified by vacuum distillation before use. Copper(I) bromide (Aldrich, 98+%) was purified by stirring with glacial acetic acid, followed by filtration and washing the solids with ethanol (3 times) and diethyl ether (2 times).

Analysis. The apparent molecular weights and molecular weight distributions were measured by GPC (Waters Microstyragel columns (guard, 10^2, 10^3, and 10^5 Å), using THF or DMF as the eluent at 35 °C, and a flow rate of 1.00 mL/min). Apparent molecular weights were determined with a calibration based on poly(methyl

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Scheme 1

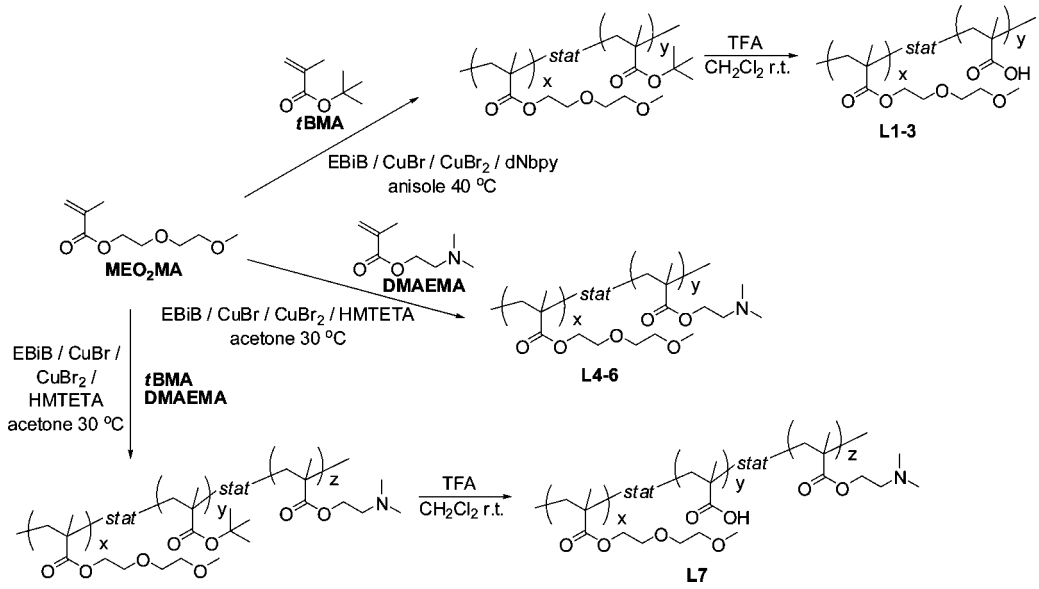

Table 1. Conversion and Molecular Weight Data of Copolymerization of MEO_2MA with *t*BMA and DMAEMA

entry	$[EBiB]_0/[MEO_2MA]_0/[tBMA]_0/[DMAEMA]_0$	time (h)	conv	M_n^{theo}	M_n^{GPC}	M_w/M_n	contents[c] $MEO_2MA/tBMA/DMAEMA$
L0[a]	1/200/0/0	2.5	0.50	19 000	20 400	1.08	100/0/0
L1[a]	1/150/50/0	3	0.62	22 200	19 100	1.14	72/28/0
L2[a]	1/180/20/0	3	0.69	25 600	22 700	1.14	88/11/0
L3[a]	1/190/10/0	2	0.60	22 600	21 500	1.13	93/7/0
L4[b]	1/375/0/125	12	0.50	45 300	38 700	1.31	74/0/26
L5[b]	1/180/0/20	7	0.49	18 300	16 200	1.23	89/0/11
L6[b]	1/190/0/10	7	0.48	18 100	17 600	1.19	94/0/4
L7[b]	1/190/10/10	6	0.52	19 300	18 400	1.19	89/6/5

[a] Conditions: $[EBiB]_0/[CuBr]_0/[CuBr_2]_0/[dNbpy]_0 = 1/0.9/0.1/2$ in anisole (40 vol %) at 40 °C. [b] Conditions: $[EBiB]_0/[CuBr]_0/[CuBr_2]_0/[HMTETA]_0 = 1/0.85/0.15/1$ in acetone (40 vol %) at 30 °C. [c] Estimated by ^1H NMR.

methacrylate) (PMMA) standards using GPCWin software from Polymer Standards Service. Conversions were determined by gas chromatography (GC) using a Shimadzu GC-14A gas chromatograph equipped with a FID detector and ValcoBond 30 m VB WAX Megabore column. ^1H NMR spectra of copolymers were examined in $CDCl_3$ at 30 °C using a Bruker Advance 300 MHz spectrometer. UV−vis spectra were recorded using a Varian Cary 7 Bio UV−vis spectrophotometer equipped with a digital temperature controller. The wavelength of 600 nm was used for the determination of the LCST. The temperature range was from 10 to 80 °C, and heating and cooling rates were 1 °C/min.

Synthesis. Poly(2-(2-bromoisobutyryloxy)ethyl methacrylate) (PBIEM) was prepared as previously reported ($M_n = 68\,000$, $M_w/M_n = 1.10$).[52]

General Procedure for Copolymerization of Di(ethylene glycol) Methyl Ether Methacrylate with *tert*-Butyl Methacrylate (P(MEO_2MA-*stat*-*t*BMA)) (L2). 0.061 g (0.15 mmol) of dNbpy, 1.67 mg (7.5 μmol) of $CuBr_2$, 11.5 μL (75 μmol) of EBiB, 2.5 mL (13.5 mmol) of MEO_2MA, 0.25 mL (1.5 mmol) of *t*BMA, and 3 mL of anisole were added to a 25 mL Schlenk flask, and oxygen was removed by subjecting the contents of the flask to three freeze−pump−thaw cycles. Next, 10.5 mg (67.5 μmol) of CuBr was added under nitrogen flow. The stirred flask was placed in an oil bath controlled at 40 °C; samples were withdrawn periodically to monitor monomer conversion (GC) and molecular weight (GPC). The polymerization was stopped by opening the flask and exposing the contents to air. The reaction mixture was diluted with THF and passed through an alumina column to remove the catalyst. The polymer was precipitated by adding the solution to hexane, filtered, and dried under high vacuum, yielding a polymer with $M_n = 22\,700$ and $M_w/M_n = 1.14$ (THF eluent). Other P(MEO_2MA-*stat*-*t*BMA)s (**L1** and **L3**) were also prepared using the same procedure.

General Procedure for Copolymerization of Di(ethylene glycol) Methyl Ether Methacrylate with *N,N*-Dimethylaminoethyl Methacrylate (P(MEO_2MA-*stat*-DMAEMA)) (L5). 20 μL (75 μmol) of HMTETA, 2.5 mg (11 μmol) of $CuBr_2$, 11.5 μL (75 μmol) of EBiB, 2.5 mL (13.5 mmol) of MEO_2MA, 0.25 mL (1.5 mmol) of DMAEMA, and 3 mL of acetone were added to a 25 mL Schlenk

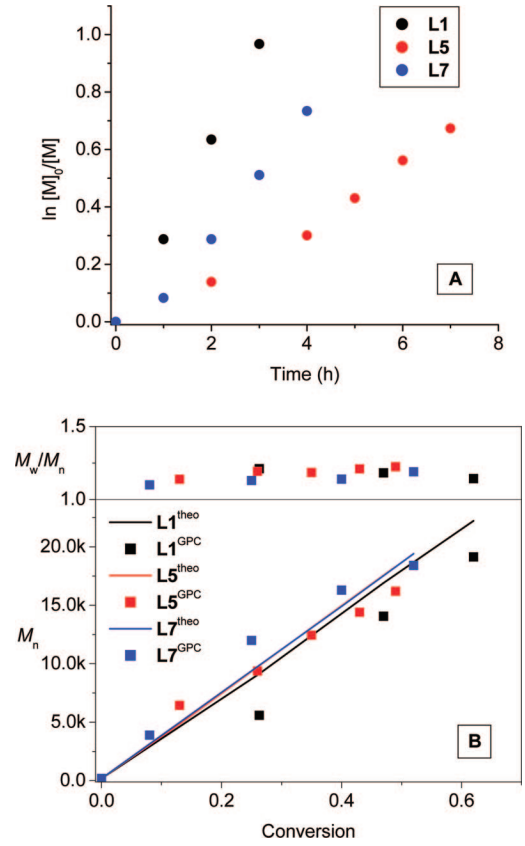

Figure 1. (A) First-order kinetic plots. (B) Evolution of molecular weights with conversion for ATRP of MEO_2MA with *t*BMA and DMAEMA (**L1**, **L5**, and **L7**).

Scheme 2

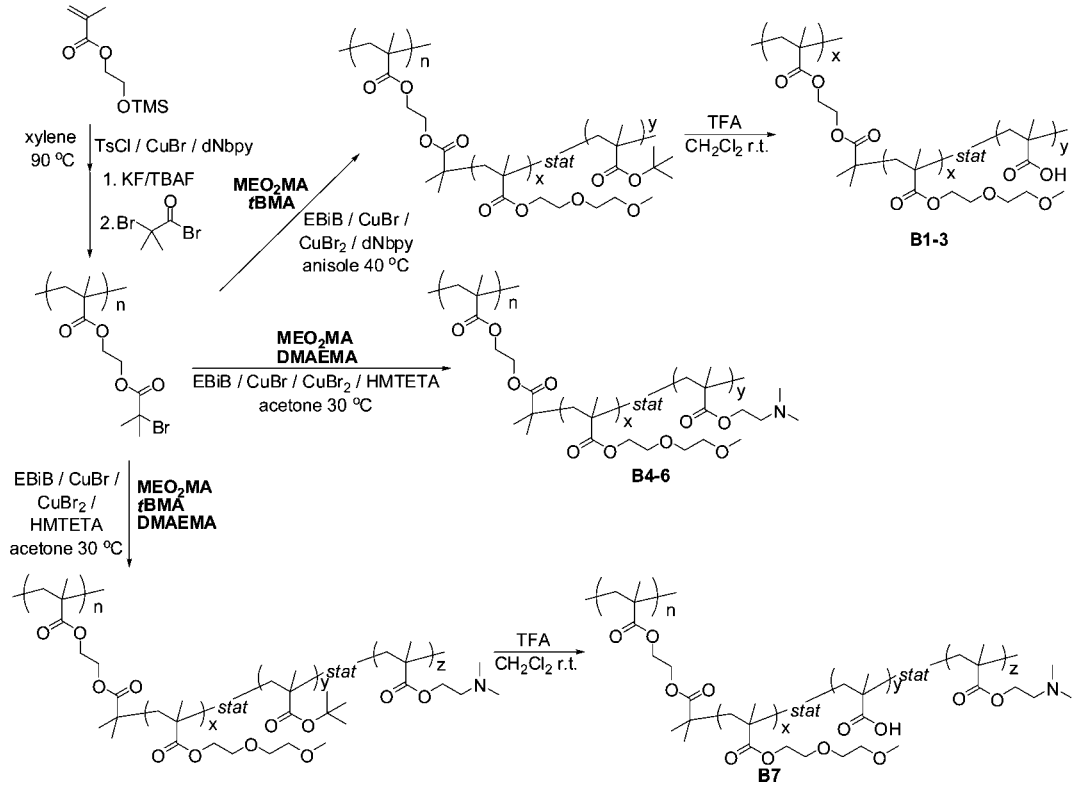

Table 2. Conversion and Molecular Weight Data of Graft Copolymerization of MEO_2MA with *t*BMA and DMAEMA

entry	$[Br]_0/[MEO_2MA]_0/[tBMA]_0/[DMAEMA]_0$	time (h)	DP	M_n^{theo}	M_n^{GPC}	M_w/M_n	contents[c] $MEO_2MA/tBMA/DMAEMA$
B1[a]	1/375/125/0	10	94	3 860 000	746 000	1.18	72/28/0
B2[a]	1/450/50/0	7	104	4 423 000	852 000	1.24	88/12/0
B3[a]	1/475/25/0	7	100	4 268 000	829 000	1.19	93/7/0
B4[b]	1/375/0/125	3	76	3 230 000	1 534 000	1.27	76/0/24
B5[b]	1/450/0/50	3	67	2 785 000	1 456 000	1.25	91/0/9
B6[b]	1/475/0/25	3	61	2 597 000	1 418 000	1.21	95/0/5
B7[b]	1/450/25/25	4	75	3 226 000	966 000	1.31	89/6/5

[a] Conditions: $[Br]_0/[CuBr]_0/[CuBr_2]_0/[dNbpy]_0 = 1/0.9/0.1/2$ in anisole (40 vol %) at 40 °C. [b] Conditions: $[Br]_0/[CuBr]_0/[CuBr_2]_0/[HMTETA]_0 = 1/0.85/0.15/1$ in acetone (40 vol %) at 30 °C. [c] Estimated by ^1H NMR.

flask, and oxygen was removed by subjecting the contents of the flask to three freeze−pump−thaw cycles. Next, 9.1 mg (63.8 μmol) of CuBr was added under nitrogen flow. The stirred flask was placed in an oil bath controlled at 30 °C; samples were withdrawn periodically to monitor monomer conversion (GC) and molecular weight (GPC). The polymerization was stopped by opening the flask and exposing the contents to air. The reaction mixture was diluted with acetone and passed through an alumina column to remove the catalyst. The polymer was precipitated by adding the solution to hexane, filtered, and dried under high vacuum, yielding a polymer with M_n = 16 200 and M_w/M_n = 1.23 (DMF eluent). Other P(MEO_2MA-*stat*-DMAEMA)s (**L4** and **L6**) were also prepared using the same procedure.

Copolymerization of Di(ethylene glycol) Methyl Ether Methacrylate with *tert*-Butyl Methacrylate and *N,N*-Dimethylaminoethyl Methacrylate (P(MEO_2MA-*stat*-*t*BMA-*stat*-DMAEMA)) (L7). The copolymerization carried out under the same conditions used for preparation of P(MEO_2MA-*stat*-DMAEMA), yielding a polymer with M_n = 18 400 and M_w/M_n = 1.19 (DMF eluent).

General Procedure for the Preparation of Poly[(2-bromoisobutyryloxy)ethyl methacrylate)-*graft*-(di(ethylene glycol) methyl ether methacrylate-*stat*-*tert*-butyl methacrylate)] (PBIEM-*g*-P(MEO_2MA-*stat*-*t*BMA)) (B2). 0.025 g (0.06 mmol) of dNbpy, 0.67 mg (0.003 mmol) of $CuBr_2$, 7.60 mg (0.03 mmol −Br) of PBIEM (M_n = 68 000, M_w/M_n = 1.10), 2.5 mL (13.5 mmol) of MEO_2MA, 0.25 mL (1.5 mmol) of *t*BMA, and 2.4 mL of anisole were added to a 25 mL Schlenk flask, and oxygen was removed by subjecting the contents of the flask to three freeze−pump−thaw cycles. Next, 3.86 mg (27 μmol) of CuBr was added under nitrogen flow. The stirred flask was placed in an oil bath controlled at 40 °C. Samples were withdrawn periodically to monitor monomer conversion (GC) and evolution of molecular weight (GPC). The polymerization was stopped by opening the flask and exposing the contents to air. The reaction mixture was diluted with THF and passed through an alumina column to remove the catalyst. The polymer was precipitated by adding the solution to hexane, filtering, and drying under high vacuum, yielding a polymer with M_n = 852 000 and M_w/M_n = 1.24 (THF eluent). Other PBIEM-*g*-P(MEO_2MA-*stat*-*t*BMA)s (**B1** and **B3**) were also prepared using the same procedure.

General Procedure for the Preparation of Poly[(2-bromoisobutyryloxy)ethyl methacrylate)-*graft*-(di(ethylene glycol) methyl ether methacrylate-*stat*-*N,N*-dimethylaminoethyl methacrylate)] (PBIEM-*g*-P(MEO_2MA-*stat*-DMAEMA)) (B5). 8 μL (0.03 mmol) of HMTETA, 1.00 mg (0.0045 mmol) of $CuBr_2$, 7.60 mg (0.03 mmol −Br) of PBIEM (M_n = 68 000, M_w/M_n = 1.10), 2.5 mL (13.5 mmol) of MEO_2MA, 0.25 mL (1.5 mmol) of DMAEMA, and 3 mL of acetone were added to a 25 mL Schlenk flask, and oxygen was removed by subjecting the contents of the flask to three freeze−pump−thaw cycles. Next, 3.65 mg (0.026 mmol) of CuBr was added under nitrogen flow. The stirred flask was placed in an oil bath controlled at 30 °C. Samples were withdrawn periodically to monitor monomer conversion (GC) and evolution of molecular weight (GPC). The

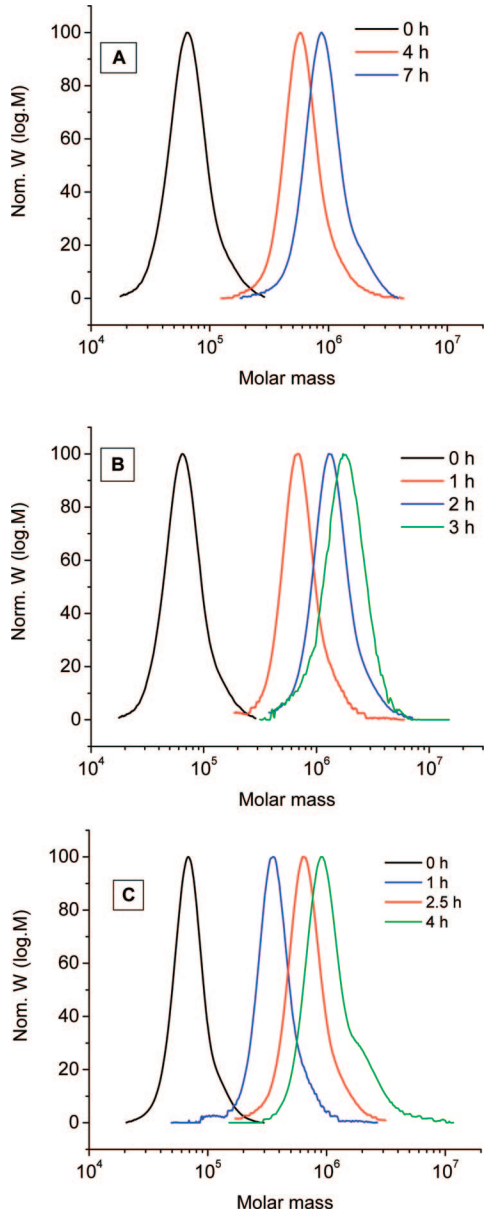

Figure 2. GPC traces for graft polymerization from PBIEM: (A) PBIEM-*g*-P(MEO$_2$MA-*stat*-*t*BMA) (**B1**), (B) PBIEM-*g*-P(MEO$_2$MA-*stat*-DMAEMA) (**B4**), and (C) PBIEM-*g*-P(MEO$_2$MA-*stat*-*t*BMA-*stat*-DMAEMA) (**B7**).

Table 3. Conversion and Molecular Weight Data of Cleavage of *tert*-Butyl Group[a]

	before		after	
entry	$M_{n,GPC}$	M_w/M_n	$M_{n,GPC}$	M_w/M_n
L1	19 100	1.14	17 200	1.20
L2	22 700	1.14	19 700	1.18
L3	22 600	1.13	17 900	1.21
B1	746 000	1.18	603 000	1.33
B2	852 000	1.24	622 000	1.45
B3	829 000	1.19	640 000	1.38
L7	18 400	1.19	20 100	1.16
B7	966 000	1.31	801 000	1.33

[a] Conditions: 10 equiv of TFA in CH_2Cl_2 at rt for 6 h.

polymerization was stopped by opening the flask and exposing the contents to air. The reaction mixture was diluted with THF and passed through an alumina column to remove the catalyst. The polymer was precipitated by adding the solution to hexane, filtering, and drying under high vacuum, yielding a polymer with M_n = 1 456 000 and M_w/M_n = 1.25 (DMF eluent). Other PBIEM-*g*-P(MEO$_2$MA-*stat*-DMAEMA)s (**B4** and **B6**) were also prepared using the same procedure.

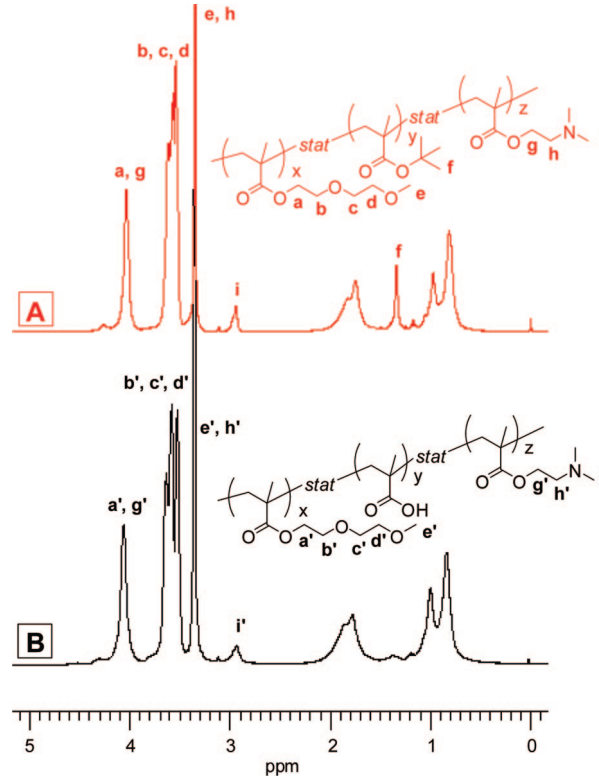

Figure 3. ^{1}H NMR spectra of **L7**: (A) before cleavage of *tert*-butyl group; (B) after cleavage.

Preparation of Poly[(2-bromoisobutyryloxy)ethyl methacrylate)-*graft*-poly(di(ethylene glycol) methyl ether methacrylate-*stat*-*tert*-butyl methacrylate-*stat*-*N,N*-dimethylaminoethyl methacrylate)] (PBIEM-*g*-P(MEO$_2$MA-*stat*-*t*BMA-*stat*-DMAEMA)) (B7). The copolymerization carried out under the same conditions used for the preparation of (PBIEM-*g*-P(MEO$_2$MA-*stat*-DMAEMA), yielding a polymer with M_n = 966 000 and M_w/M_n = 1.31 (DMF eluent).

Hydrolysis of PBIEM-*g*-P(MEO$_2$MA-*stat*-*t*BMA). 0.24 g (0.34 mmol *t*-Bu group) of P(MEO$_2$MA-*stat*-*t*BMA) (**L1**), 1.0 mL (1.36 mmol) of TFA, and 30 mL of CH_2Cl_2 were added to a 50 mL round-bottom flask and stirred at room temperature for 6 h. The product was precipitated by adding the solution to hexane, filtering, and drying under high vacuum, yielding a polymer with M_n = 17 200 and M_w/M_n = 1.20. Other polymers containing *t*BMA (**L2**, **L3**, **L7**, **B1**−**3**, and **B7**) were also treated using the same procedure.

Results and Discussion

Synthesis of Linear Copolymers. A series of linear statistical copolymer of MEO$_2$MA with *t*BMA and/or DMAEMA were prepared by ATRP. The reaction procedures are shown in Scheme 1.

The statistical copolymerization of MEO$_2$MA with *t*BMA was carried out at 40 °C in anisole in the presence of EBiB as initiator, CuBr/dNbpy as catalyst, and 10 mol % of $CuBr_2$ as added deactivator to provide instantaneous control over the polymerization. HMTETA and acetone were used as ligand and solvent for the copolymerization of DMAEMA. These results are listed in Table 1. In every case, the polymerization was well controlled, providing a polymer with low PDI. The composition of the copolymers, estimated by ^{1}H NMR, were very close to the feed ratios of the comonomers. Kinetic plots and evolution of molecular weights with conversion are shown in Figure 1. The reaction proceeded with first-order kinetics and a linear increase in molecular weight vs conversion. The molecular weight estimated by GPC fit the theoretical values. Synthesis

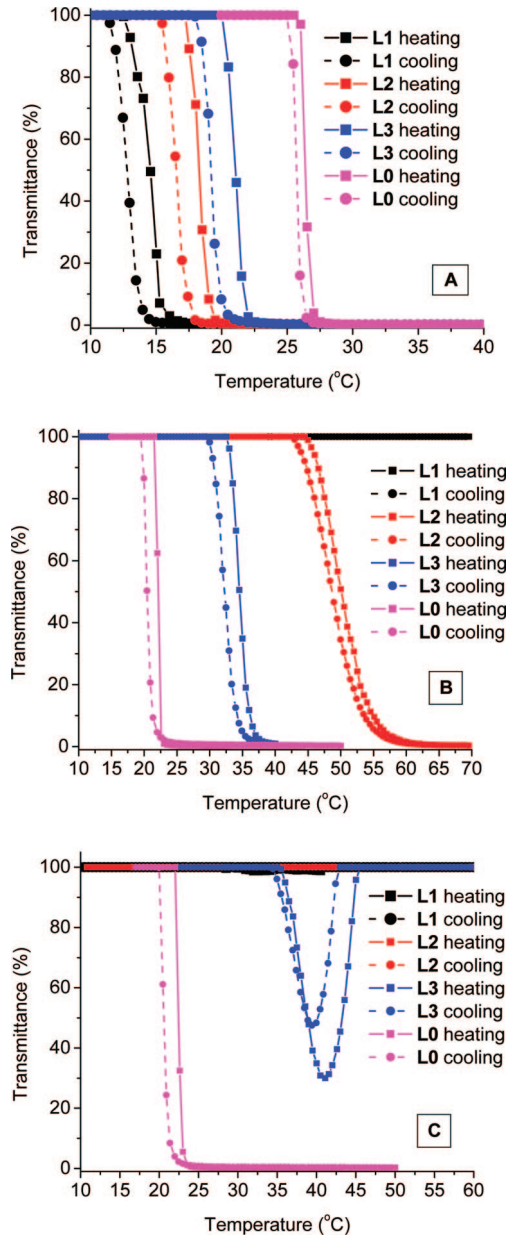

Figure 4. Temperature dependence of transmittance change for 0.3 wt % aqueous solution of P(MEO_2MA-*stat*-MAA): (A) deionized water (pH 7); (B) phosphate buffer (pH 7); (C) at pH 9.

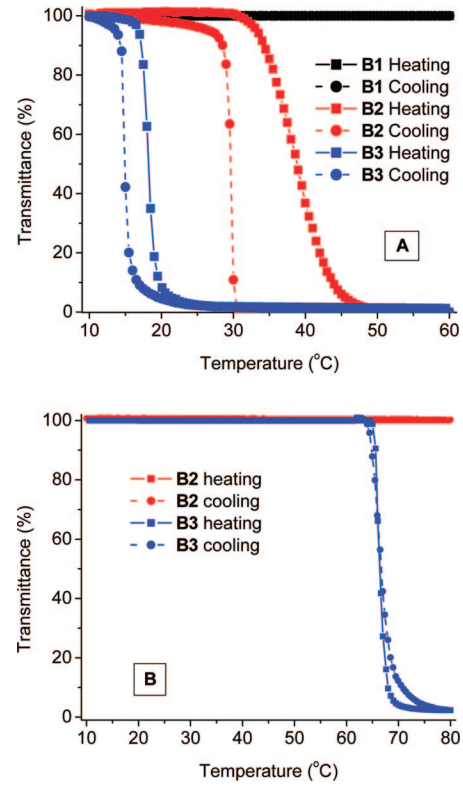

Figure 5. Temperature dependence of transmittance change for 0.3 wt % aqueous solution of PBEIM-*g*-P(MEO_2MA-*stat*-MAA): (A) at pH 7 (phosphate buffer); (B) at pH 9.

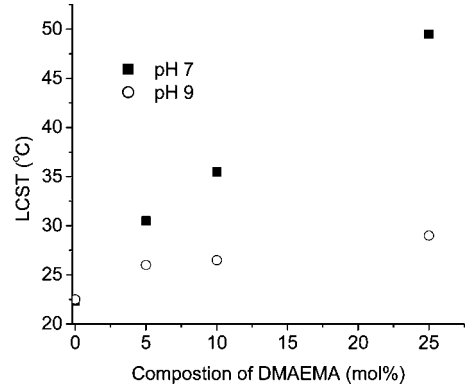

Figure 6. Effect of pH on temperature dependence of optical transmittance changes at 600 nm for 0.3 wt % aqueous solution of P(MEO_2MA-*stat*-DMAEMA).

of a low PDI terpolymer of MEO_2MA, *t*BMA, and DMAEMA (**L7**) was also conducted with CuBr/HMTETA catalyst in acetone solution.

Synthesis of Brush Copolymers. Molecular brushes comprising statistical copolymers of MEO_2MA, MAA, and DMAEMA as side chains were synthesized by "grafting from" ATRP from the PBIEM macroinitiator. The reaction conditions used for the synthesis of side chains prepared by the copolymerization of MEO_2MA, *t*BMA, and DMAEMA are shown in Scheme 2.

The results are summarized in Table 2. The graft copolymerization reactions went smoothly, resulting in synthesis of the corresponding brushes having low PDI. The final composition of the copolymers was very close to the feed ratio of the comonomers. The reaction proceeded with first-order kinetics and displayed a linear increase in molecular weight vs conversion. The apparent molecular weight, estimated by GPC, was significantly lower than the theoretical value estimated from conversion. GPC traces are shown in Figure 2. GPC traces shifted cleanly to the higher molecular region with monomer conversion while retaining narrow molecular weight distribution. This observation is consistent with brush copolymers containing ethylene oxide units.[21]

Cleavage of *t*Bu Groups. Several ratios of TFA were examined for the cleavage of *tert*-butyl group from *t*BMA contained copolymers in dichloromethane solution. The use of 10 equiv was the most effective at providing P(MEO_2MA-*stat*-MAA) copolymers while retaining low PDI. The molecular weights and PDI of the resulting methacrylic acid containing copolymers are summarized in Table 3. Successful transformation was confirmed by ^1H NMR spectroscopy (Figure 3). The characteristic peak at 1.4 ppm assignable to methyl proton in *t*Bu (f) disappeared after the reaction. The other peaks assigned to MEO_2MA and DMAEMA did not shift after cleavage, suggesting that MEO_2MA and DMAEMA unit were not affected by TFA under these conditions.

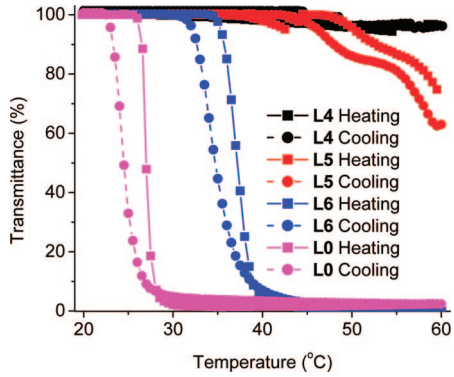

Figure 7. Temperature dependence of optical transmittance changes at 600 nm for 0.3 wt % aqueous solution of P(MEO_2MA-*stat*-DMAEMA) at pH 4.

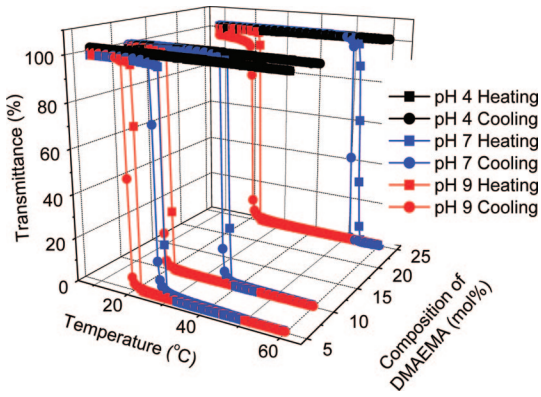

Figure 8. Effect of pH on temperature dependence of optical transmittance changes at 600 nm for 0.3 wt % aqueous solution of PBIEM-*g*-P(MEO_2MA-*stat*-DMAEMA).

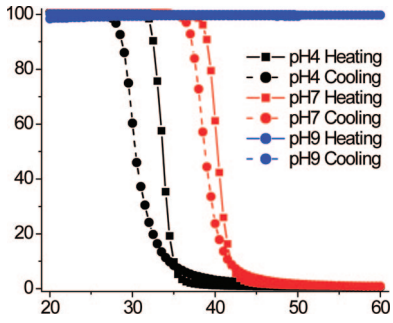

Figure 9. Effect of pH on temperature dependence of optical transmittance changes at 600 nm for 0.3 wt % aqueous solution of P(MEO_2MA89-*stat*-DMAEMA5-*stat*-MAA6) (**L7**).

Thermal Properties of P(MEO_2MA−MAA) Copolymers. In order to determine the dependence of the thermal properties on temperature, the transmittance of light through aqueous solutions of the polymer was measured using a UV spectrometer. The transmittance of 0.3 wt % aqueous solution of the polymer was monitored at 600 nm at a heating or cooling rate of 1.0 °C min^{-1}. The results are illustrated in Figure 4. In deionized water, all solutions exhibited a LCST, and their thermoresponsive behaviors were consistently reversible. The cloud point was lowered with increasing levels of MAA units in the copolymer, suggesting that the balance between hydrophilicity and hydrophobicity of copolymer was shifted toward hydrophobicity with higher MAA content due to the decreasing number of hydrogen bonds between water and the copolymers (Figure 4A). In a phosphate buffer solution, sample **L1**, which displayed a LCST of 15 °C in deionized water, did not show a LCST. Furthermore,

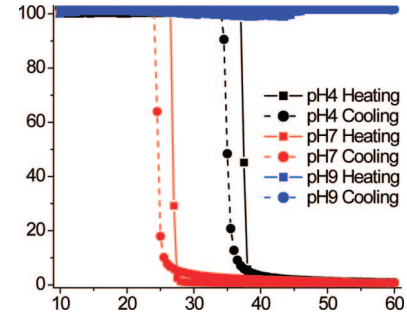

Figure 10. Effect of pH on temperature dependence of optical transmittance changes at 600 nm for 0.3 wt % aqueous solution of PBIEM-*g*-P(MEO_2MA89-*stat*-DMAEMA5-*stat*-MAA6) (**B7**).

the LCST of **L2** and **L3** shifted to 50 and 35 °C, respectively (Figure 4B). In a previous report, discussing the LCST of PNIPAM methacrylic acid copolymers, the presence of the carboxylic acid groups in the copolymer led to additional polymer−polymer interactions with hydrogen bonds in deionized water leading to phase separation at lower temperature. In a pH 7 buffer solution, a fraction of the MAA units are ionized by the buffer effect, increasing the hydrophilicity of copolymer.[56,57] Therefore, the sharpness of aggregation was reduced by incorporation of MAA into the copolymer. Furthermore, the change of transmittance was also investigated at pH 9 (Figure 4C). The LCST of **L2** also disappeared, and the transmittance of **L3** started to drop around 35 °C but increased from 41 °C to return to 100% at 45 °C. Meanwhile, the LCST of homo-PMEO_2MA, **L0**, shifted to ∼22 °C in both buffer solutions because of salting out.

The change of transmittance of solutions the brush copolymers is shown in Figure 5. Similar to the linear polymer, in pH 7 buffer, sample **B1** containing 25% MAA did not display any thermal response, and samples **B2** and **B3** exhibited LCSTs which increased with increasing content of MAA. Furthermore, sample **B3** showed a large hysteresis. At pH 9 the cloud point of **B2** disappeared and **B3** shifted to around 65 °C, which is higher than the corresponding linear polymer. Additionally, transmittance completely dropped to 0%, although it returned to 100% in the case of the linear copolymer. In the molecular brushes, the concentrations of both the thermoresponsive ethylene oxide units and the pH-responsive carboxylic acid units are very high, due to the nature of the densely grafted side chains. Thus, aggregation of MEO_2MA is efficient and the copolymer precipitates at even lower temperatures at pH 7. At pH 9, the aggregation of ionized carboxylic acid group retains the hydrophilicity of the brush and shifts the LCST toward higher temperature. However, the hydrophobicity of the particle increases when the aggregation starts. Consequently, the brush copolymer is insoluble even with additional heating. The large hysteresis of **B2** could also be attributed to this behavior, resulting in a shift of the transmittance change region in the cooling cycle toward lower temperature.

Thermal Properties of P(MEO_2MA−DMAEMA) Copolymers. The effect of pH on the thermal properties of P(MEO_2MA-*stat*-DMAEMA) copolymers was investigated. All of the copolymers showed a sharp decrease in transmittance around their LCST in neutral and basic conditions. The changes, which are summarized in Figure 6, were consistently reversible. At pH 7, in the presence of a phosphate buffer, the LCST of the copolymers increased as the fraction of DMAEMA in the copolymer increased. The LCST also increased at pH 9, but the results are not as pronounced as at pH 7. At pH 9, every polymer displayed a lower LCST than at pH 7, suggesting deprotonation of DMAEMA under basic conditions, which was previously reported for a copolymer of PEGMA (M_n = 300)

with DMAEMA.[36] Furthermore, the LCST of **B1** at pH 7 was 51 °C, which was higher than the intrinsic LCST of homo-PDMAEMA, so that DMAEMA units behave as hydrophilic groups rather than thermoresponsive units. The change in light transmittance of aqueous solutions of the copolymers at pH 4, using citrate buffer, was also measured (Figure 7). The LCST of **L4**, containing 5% DMAEMA, shifted to 38 °C because of the protonation of DMAEMA. The decrease in the transmittance of **L5**, 10% DMAEMA, stopped around 60% even at 60 °C, and **L6** (25% DMAEMA) did not display any LCST. Additionally, the LCST of solutions of sample **L0** were very close to each other at every pH, verifying MEO_2MA units are inert to changes in pH. These results demonstrate that the introduction of a small amount of DMAEMA into $PMEO_2MA$ generates temperature- and pH-responsive polymers.

Figure 8 shows how the changes in transmittance through solutions of P(MEO_2MA-*stat*-DMAEMA) brush copolymers depend on temperature under several pH conditions. At pH 9, the solution clouded around 22 °C, which was almost the same as the pure $PMEO_2MA$, irrespective of composition. It appears that at pH 7 LCSTs increased with DMAEMA content. This behavior is consistent with that of the corresponding linear polymers, **L4**−**L6**. The hysteresis between heating and cooling cycles at pH 7 was smaller than that of P(MEO_2MA-*stat*-MAA), indicating DMAEMA units display their own individual thermoresponsive behavior. They independently assemble to support efficient aggregation of the entire polymer brush. However, under acidic conditions (pH 4), protons coordinate to the amino group in DMAEMA and no LCST was detected in any of the brush copolymers. This suggests that the protonated DMAEMA groups in the dense side chain localize along polymer backbone and maintain the solubility of the brush copolymer in water above the intrinsic cloud point of corresponding linear polymer.

Thermal Properties of P(MEO_2MA−MAA−DMAEMA) Copolymers. The thermal properties of the linear polymer, **L7**, are shown in Figure 9. The LCST at pH 4 (34 °C) was lower than that observed at pH 7 (40 °C), but there was no LCST at pH 9. These results indicate that the LCST varies with the degree of protonation of the DMAEMA and MAA units. At pH 9, carboxylic acid groups behave as hydrophilic groups due to the dissociation of the acidic proton, and they prevent aggregation of DMAEMA and MEO_2MA. At pH 4, although DMAEMA loses its thermally responsive behavior by protonation of amino group, the association of the MAA groups with protons dominates and results in the aggregation of MEO_2MA units. In the case of the brush copolymer, no LCST was detected in pH 9, which is similar to the linear copolymer (Figure 10). However, in a solution buffered at pH 7 LCST (26 °C) was lower than in a solution buffered at pH 4 (38 °C). The LCST was slightly higher than that measured for the homo-$PMEO_2MA$ brush (22 °C), but the difference was smaller than that for the linear polymer (from 26 to 40 °C). The LCST of the linear and brush copolymers were slightly closer (35 and 40 °C) at pH 4. These results indicate that there could be an additional association between side chains due to the high graft density in molecular brushes. This can facilitate the aggregation of side chains. Consequently, the LCST of the brush is less sensitive to the polymer composition.

Conclusions

Well-defined doubly responsive, thermo- and pH-responsive, linear and brush copolymers of MEO_2MA with MAA and/or DMAEMA were prepared by ATRP. The copolymers with well-defined molecular weights and low polydispersities were formed. The thermal properties of aqueous solutions of the polymers were studied by UV−vis spectrometry. The thermal properties of the copolymers and terpolymers varied with pH. The MAA group has hydrophobic character and forms strong hydrogen bonds at low pH. The presence of a buffer affects the ionization of the carboxylic acid even under neutral conditions. An excess of ionized units, around 25%, inhibits the LCST. On the other hand, the presence of DMAEMA units increases the hydrophilicity of the copolymer, especially at lower pH. At pH 7, it raises the LCST to higher temperatures than the intrinsic LCST of either $PMEO_2MA$ or PDMAEMA. In a linear terpolymer of MEO_2MA, MAA, and DMAEMA, the final thermal properties rely on the amount of MAA present in the terpolymer. The ambivalent character of DMAEMA is amplified with densely grafted structure in a brush copolymer. Consequently, LCST of brush copolymers increased at pH 4 but decreased at pH 7. Stability of MEO_2MA units was not affected by pH under studied conditions.

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