Synthesis of Well-Defined Y-Shaped Zwitterionic Block Copolymers via Atom-Transfer Radical Polymerization

Yuanli Cai[†,‡] and Steven P. Armes[*,†]

Department of Chemistry, University of Sheffield, Brook Hill, Sheffield, South Yorkshire, S3 7HF, U.K. and Institute of Polymer Science, College of Chemistry, Xiangtan University, Xiangtan, Hunan, 411105, P. R. China

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ABSTRACT: A series of well-defined Y-shaped (AB_2-type) zwitterionic block copolymers were synthesized by atom-transfer radical polymerization (ATRP). First, a bishydroxy-functional ATRP initiator was synthesized by esterification of 2-hydroxyethyl acrylate with 2-bromoisobutyryl bromide, followed by Michael addition using excess diethanolamine. 2-(Diethylamino)ethyl methacrylate (DEA) was polymerized via ATRP using this bishydroxy-functional initiator. The bromine end groups of PDEA were then quantitatively removed by radical chain transfer using excess *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA). Esterification of the ω-bishydroxyl end groups using excess 2-bromoisobutyryl bromide afforded a PDEA-based ω-bifunctional macroinitiator [PDEA-$(Br)_2$]. A series of Y-shaped zwitterionic PDEA-$(PSEMA)_2$ [PSEMA poly(succinyloxyethyl methacrylate)] block copolymers were synthesized via ATRP of 2-hydroxyethyl methacrylate (HEMA) using this PDEA-$(Br)_2$ macroinitiator, followed by reacting the HEMA hydroxyl groups with succinic anhydride. The ‘schizophrenic’ micellization character of these Y-shaped zwitterionic block copolymers in aqueous solution was confirmed by ^{1}H NMR spectroscopy, aqueous electrophoresis, and dynamic light-scattering studies.

Introduction

Zwitterionic diblock copolymers possess both positive and negative charges that are spatially separated along the copolymer backbone. Unlike zwitterionic statistical copolymers, block architectures usually lead to macroscopic precipitation at the isoelectric point.[1] Such copolymers have been claimed to be ‘ubiquitous’ pigment dispersants[2,3] and also evaluated for protein isolation and purification.[4] Recently, we reported a new type of zwitterionic AB diblock copolymer[5−9] that could undergo spontaneous self-assembly in aqueous solution at ambient temperature to form both A-core and B-core micelles, simply by adjusting the solution pH. These pH-responsive copolymers and related thermoresponsive examples[10,11] are described as having ‘schizophrenic’ character.[12] Recent research has revealed that the precise nature of the block copolymer architectures play an important role in determining their aqueous solution properties. For example, nonlinear asymmetric (AB_2 or AB_3 type) block copolymers exhibit fundamentally different micellization behavior compared to the corresponding linear AB diblocks.[13−16] Of particular relevance to the present study are the AB_2-type[13−16] or Y-shaped block copolymers. However, to the best of our knowledge, zwitterionic block copolymers with well-defined *nonlinear* architectures have not yet been reported, presumably due to the technical difficulties involved in their synthesis.

Y-Shaped block copolymers have been typically synthesized via living anionic[13,14,17−19] or cationic[15] polymerization. For example, Gnanou and co-workers[19] synthesized styrene-functionalized polystyrene-*block*-[poly(ethylene oxide)]$_2$ [PS-$(PEO)_2$] macromonomers using anionic polymerization in combination with protecting-group chemistry. These copolymers were used as reactive surfactants in emulsion polymerization[19] and also as steric stabilizers for dispersion polymerization.[20] Recently, the same group synthesized polystyrene-*block*-[poly(*tert*-butyl acrylate)]$_2$ [PS-$(PtBA)_2$] Y-shaped block copolymers by atom-transfer radical polymerization (ATRP) using a multistep route involving protecting-group chemistry.[21] Hydrolysis of the *tert*-butyl groups led to the formation of amphiphilic PS-$(PAA)_2$ Y-shaped block copolymers. In a recent review Haddleton et al. briefly described the synthesis of an ABA_2-type block copolymer, again using ATRP in combination with protecting-group chemistry.[22] More recently, Zhao et al.[23] reported the synthesis of ABC miktoarm star terpolymers by combining ring-opening polymerization (ROP), ATRP, and nitroxide-mediated radical polymerization (NMRP) using a new trifunctional initiator bearing a hydroxyl group, an ATRP initiator, and an NMRP initiator. These miktoarm star terpolymers were synthesized by three sequential polymerizations. First, ROP of ϵ-caprolactone (CL) was carried out, followed by ATRP of methyl methacrylate (MMA). Finally, after removal of the bromine end groups using tributyl tin hydride, the NMRP of styrene gave the target PCL-PMMA-PS miktoarm star copolymers.

In a recent communication[24] we reported the first examples of Y-shaped stimulus-responsive block copolymers synthesized from two commercially available monoamine-capped poly(alkylene oxide)s. ω-Bisfunctional macroinitiators were prepared by Michael addition of the amine end groups of these poly(alkylene oxide)s using 2-hydroxyethyl acrylate, followed by esterification of the bishydroxy end groups with excess 2-bromoisobutyryl bromide. Methanolic ATRP of a series of hydrophilic methacrylic monomers with these ω-bis-

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[*] To whom correspondence should be addressed. E-mail: S.P.Armes@sheffield.ac.uk.

[†] University of Sheffield.

[‡] Xiangtan University.

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functional macroinitiators at room temperature afforded a wide range of well-defined, Y-shaped hydrophilic block copolymers. Some of these copolymers exhibit pH- or thermoresponsive micellization character in aqueous solution.

Herein, we describe the first synthesis of well-defined Y-shaped zwitterionic block copolymers, namely, poly-[2-(diethylamino)ethyl methacrylate]-*block*-[poly(succinyloxyethyl methacrylate)]$_2$ [PDEA-(PSEMA)$_2$]. The pH-modulated 'schizophrenic' micellization behavior of these copolymers in aqueous solution was confirmed by ^{1}H NMR spectroscopy, aqueous electrophoresis, and dynamic light-scattering (DLS) studies.

Experimental Section

Materials. 2-Hydroxyethyl methacrylate (HEMA, 99%) and 2-hydroxyethyl acrylate (HEA, 99%) were kindly donated by Cognis Performance Chemicals (Hythe, U.K.). 2-(Diethylamino)ethyl methacrylate (DEA, 99%), 2-bromoisobutyryl bromide (98%), triethylamine (TEA, 99%), diethanolamine (99%), copper(I) bromide [CuBr, 99.999%], 2,2′-bipyridine (bpy, ≥99%), anhydrous methanol (≥99.9%), 2-propanol (IPA, ≥99%), succinic anhydride (SA, ≥99%), and *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA, 98%) were all purchased from Aldrich. The silica gel (column chromatography grade silica gel 60) used for removal of the inhibitors and also the spent ATRP catalyst was purchased from E. Merck (Darmstadt, Germany). Each monomer was passed through a silica column to remove its inhibitor and stored in a refrigerator before use. All other chemicals were used as received.

Synthesis of Acryloyloxyethyl 2-Bromoisobutyrate. 2-Hydroxyethyl acrylate (10.00 g, 86.2 mmol), anhydrous dichloromethane (100 mL), and triethylamine (9.60 g, 94.8 mmol) were added to a dry 250 mL round-bottomed flask. The flask was immersed in an ice bath under stirring. 2-Bromoisobutyryl bromide (21.81 g, 94.8 mmol) was added dropwise to the flask via syringe over 30 min. The mixture was stirred at 0 °C for 1 h and then at 20 °C for 4 h. The resulting reaction solution was filtered to remove the insoluble amine hydrobromide salt and washed three times with 4% sodium carbonate aqueous solution. The combined organic solution was dried over anhydrous magnesium sulfate and passed through a silica column using dichloromethane as an eluent. This solvent was removed under vacuum to afford a light yellow liquid. Yield: 19.2 g, 84%. ^{1}H NMR (CDCl$_3$): δ 6.4−5.8 (3H, $CH_2{=}CHCOO$), 4.4 (4H, $COOCH_2CH_2OCO$), 1.9 (6H, $C(CH_3)Br$). The purified product was stored in a refrigerator at −20 °C prior to use.

Synthesis of 2-(Diethanolamino)acetyloxyethyl 2-Bromoisobutyrate [Br-Init-(OH)$_2$]. Acryloyloxyethyl 2-bromoisobutyrate (15.00 g, 56.6 mmol) and diethanolamine (7.13 g, 67.9 mmol) were added to a 50 mL flask and stirred at 20 °C for 24 h. The resulting reaction mixture was extracted using toluene and *n*-hexane, followed by passing through a silica column using toluene as an eluent to remove residual reactants. Solvents were removed under vacuum to afford a light yellow liquid. Yield: 18.3 g, 87%. ^{1}H NMR (CDCl$_3$): δ 4.3 (4H, $COOCH_2CH_2OCO$), 3.5 (4H, CH_2OH), 3.2 (2H, OH), 2.8 (2H, $OOCCH_2$), 2.6 (4H, $CH_2N(CH_2)_2$), 2.4 (2H, $CH_2N(CH_2)_2$), 1.8 (6H, $C(CH_3)_2Br$).

Synthesis of ω-Bishydroxy-Functionalized PDEA [Br-PDEA-(OH)$_2$]. A typical protocol for the ATRP of DEA monomer using the Br-Init-(OH)$_2$ initiator was as follows. The Br-Init-(OH)$_2$ initiator (0.80 g, 2.2 mmol), DEA monomer (20.00 g, 108 mmol, target DP$_n$ = 50), and methanol (20 mL) were added to a 100 mL flask and purged with nitrogen gas for 30 min. CuBr (0.31 g, 2.2 mmol) and bpy (0.67 g, 4.3 mmol) were added to this stirred solution under nitrogen. The reaction mixture immediately became dark brown and progressively more viscous, indicating the onset of polymerization. Aliquots were taken regularly for ^{1}H NMR and GPC analyses to assess the extent of polymerization. DEA conversions were assessed by comparing the NMR signals at δ 5.5−6.5, which correspond to the two vinylic protons [$CH_2C(CH_3)COO$], to those peaks found at δ 0.5−1.5 due to the methyl group [$CH_2C(CH_3)COO$] of DEA monomer and the methyl and methylene groups [$CH_2C(CH_3)COO$] of the PDEA backbone. The DEA had almost completely polymerized after 6 h (98% conversion). The reaction solution was exposed to air and diluted with methanol, followed by silica treatment to remove the spent ATRP catalyst. This polymer solution was concentrated under vacuum and precipitated into excess water. The resulting Br-PDEA-(OH)$_2$ was isolated by centrifugation, redissolved in toluene, and dried over anhydrous magnesium sulfate. Solvent was removed under vacuum to give 17.1 g of a light yellow solid (87% yield). No vinyl double bonds at δ 5.5−6.5 could be detected by ^{1}H NMR, indicating that the residual DEA monomer was completely removed.

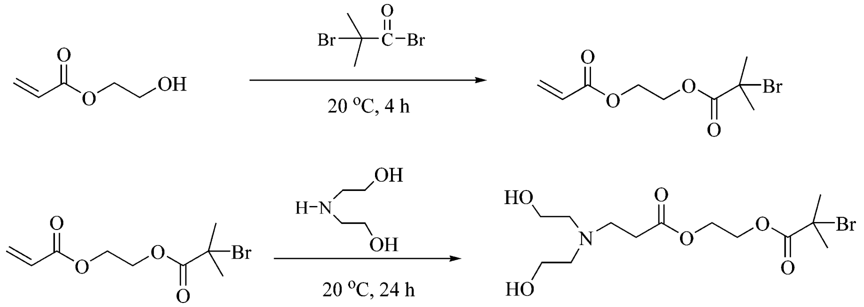
Removal of Bromine End Groups To Obtain Halogen-Free PDEA-(OH)$_2$. A typical protocol for the removal of bromine end groups from Br-PDEA-(OH)$_2$ was as follows. Br-DEA$_{50}$-(OH)$_2$ (M_n = 11 900 and M_w/M_n = 1.20; 8.0 g, 0.8 mmol) was dissolved in a mixture of triethylamine (8 mL) and 2-propanol (8 mL) in a 50 mL flask and purged with nitrogen gas for 2 h. CuBr (60 mg, 0.4 mmol) and PMDETA (732 mg, 4.2 mmol) were added to this stirred solution under nitrogen. The mixture was stirred at 50 °C under nitrogen for 3 days. The resulting reaction mixture was exposed to air and diluted with 2-propanol, followed by passing through a silica column to remove the spent catalyst. After rotary evaporation to remove most of the 2-propanol and triethylamine, the crude halogen-free PDEA polymer was precipitated into excess water and isolated by centrifugation to remove residual PMDETA and solvents. The purified polymer was dissolved into toluene and dried over anhydrous magnesium sulfate. Solvent was removed under vacuum to produce a yellow solid. Yield: 6.5 g, 82%.

Confirmation of Removal of Bromine End Groups. The efficiency of the removal of the bromine end groups was assessed by the attempted ATRP of DEA using the halogen-free PDEA-(OH)$_2$ as a macroinitiator. No chain extension should occur if the terminal Br atoms are no longer present. A typical protocol was as follows. PDEA$_{50}$-(OH)$_2$ (0.50 g, 0.05 mmol), DEA monomer (1.93 g, 104 mmol), methanol (2 mL), and doubly distilled water (0.2 mL) were added to a 25 mL flask. After purging with nitrogen for 30 min, CuBr (16 mg, 0.1 mmol) and bpy (33 mg, 0.2 mmol) were introduced into this flask under nitrogen. After stirring at 20 °C for 5 h, the reaction mixture was exposed to air. The resulting PDEA polymer was characterized by THF GPC measurement.

Synthesis of the PDEA-Based ω-Bisfunctional Macroinitiator [PDEA-(Br)$_2$]. A typical protocol for the synthesis of the PDEA-based ω-bisfunctional macroinitiator (PDEA-Br$_2$) was as follows. PDEA$_{50}$-(OH)$_2$ (M_n = 12 700; M_w/M_n = 1.19; 6.00 g, 1.3 mmol hydroxyl groups) was dissolved in anhydrous toluene (100 mL) in a dry 250 mL round-bottomed flask. After azeotropic distillation of 40−50 mL of toluene at reduced pressure to remove trace amounts of water, triethylamine (0.38 g, 3.8 mmol) was added to the flask. The flask was immersed in an ice bath. 2-Bromoisobutyryl bromide (0.88 g, 3.8 mmol) was added dropwise into the flask via syringe over 30 min. After initial stirring at 0 °C for 2 h, this solution was further stirred at 20 °C for 3 days. The resulting reaction solution was filtered to remove insoluble amine hydrobromide salt and washed three times with 4% sodium carbonate aqueous solution. The combined organic solution was dried over anhydrous magnesium sulfate and passed through a silica column using toluene as an eluent. The toluene was removed under vacuum to afford 5.13 g of the PDEA-(Br)$_2$ as an off-white solid (83% yield). ^{1}H NMR analysis indicated that the functionalization of this macroinitiator was essentially complete. THF GPC: M_n = 13 100, M_w/M_n = 1.18 (vs PMMA standards).

Synthesis of Y-Shaped PDEA-(PHEMA)$_2$ Block Copolymer Precursors. A typical protocol for the ATRP of HEMA monomer using the PDEA-(Br)$_2$ macroinitiator was as follows. PDEA$_{50}$-(Br)$_2$ macroinitiator (M_n = 13 100; M_w/M_n = 1.18; 1.2 g, 0.24 mmol Br) was dissolved in HEMA monomer (1.56 g, 12.0 mmol, target DP$_n$ = 25 per PHEMA chain) and

Scheme 1. Synthesis Route for the Bishydroxy-Functional Atom-Transfer Radical Polymerization (ATRP) Initiator, 2-(Diethanolamino)acetyloxyethyl 2-Bromoisobutyrate [Br-Init-$(OH)_2$]



methanol (4 mL) in a 50 mL flask. After purging with nitrogen gas for 30 min, CuBr (35 mg, 0.24 mmol) and bpy (75 mg, 0.48 mmol) were introduced into the flask to start the polymerization. HEMA conversions were assessed by comparing the signals at δ 5.5−6.5 due to the vinyl groups [$CH_2C(CH_3)COO$] to those at δ 0.5−1.5 due to the methyl group [$CH_2C(CH_3)$-COO] of HEMA monomer and the methyl and methylene groups [$CH_2C(CH_3)COO$] on the PDEA and PHEMA backbones. After 4 h ^{1}H NMR studies indicated a HEMA conversion of 85%; the reaction mixture was exposed to air and diluted with methanol. Termination occurred rapidly, as indicated by the color change from brown to blue. The solution was passed through a silica column to remove the spent catalyst. Most of the methanol was removed under vacuum. The Y-shaped PDEA-$(PHEMA)_2$ block copolymer was precipitated into excess *n*-hexane to remove residual HEMA monomer and then dried under vacuum overnight to afford a dark yellow solid. Yield: 2.1 g, 81%. The block copolymer compositions were calculated by comparing the signal at δ 3.8 due to the CH_2OH of the HEMA residues and the signal at δ 0.8 due to the two methyl groups $N(CH_2CH_3)$ on the DEA residues.

Synthesis of Y-Shaped Zwitterionic PDEA-$(PSEMA)_2$ Block Copolymers. A typical protocol for the synthesis of Y-shaped zwitterionic block copolymers was as follows. The DEA_{50}-$(HEMA_{24})_2$ block copolymer precursor (1.0 g, 3.0 mmol HEMA units) was dissolved in anhydrous pyridine (5 mL) in a dry 25 mL round-bottomed flask. SA (0.6 g, 6.0 mmol) was added to the flask, and the mixture was stirred at 20 °C for 24 h. ^{1}H NMR studies indicated that essentially complete esterification was achieved under these conditions. Methanol (0.5 mL) was added to the flask to consume unreacted SA, followed by copolymer precipitation into excess 2:1 diethyl ether/*n*-hexane to remove small molecule impurities. The solvent was removed under vacuum overnight to produce 1.1 g of a light brown solid (84% yield).

Polymer Characterization. ^{1}H NMR spectra were recorded using a Bruker Avance DPX 300 MHz spectrometer. The molecular weights and polydispersities of the PDEA-based macroinitiators and their precursors were assessed by a GPC setup consisting of a Perkin-Elmer LC pump and an Agilent 1100 Series refractive index detector and either a PLgel 3 μm 300 × 7.5 mm Mixed 'E' or a 5 μm 300 × 7.5 mm Mixed 'D' column (Polymer Labs). The GPC eluent was HPLC-grade BHT-stabilized THF and 2.0 vol % TEA at 20 °C and a flow rate of 1.0 mL min^{-1}. The molecular weights and polydispersities of the PDEA-$(PHEMA)_2$ and PDEA-$(PSEMA)_2$ copolymers were assessed using a DMF GPC setup comprising a Polymer Laboratories PLgel 5 μm Mixed 'B' column and a refractive index detector. The GPC eluent was HPLC-grade DMF-stabilized with 0.01 M LiBr. A flow rate of 1.0 mL/min was used, and the column temperature was set at 70 °C. A series of near-monodisperse poly(methyl methacrylate) calibration standards (Polymer Labs) was used for both types of GPC measurements.

Aqueous Solution Characterization. The solution pH was monitored using a HI 8424 microcomputer pH meter comprised of a HI 1230B combination, double junction, gel pH electrode and a HI 7669AW temperature probe. Calibration was carried out using pH 4, 7, and 10 buffer solutions.

DLS studies were performed using a Brookhaven Instrument Corp. BI-200SM goniometer equipped with a BI-9000AT digital correlator and a solid-state laser (125 mV, $\lambda = 532$ nm) at a fixed scattering angle of 90° at 20 °C. The intensity-average hydrodynamic diameter, $<D_h>$, and polydispersity index, μ_2/Γ^2, of the micelles were assessed by cumulants analysis.

A PC-controlled Perkin-Elmer Lambda 2S UV/VIS spectrometer was used for turbidimetry studies of the copolymer aqueous solutions at different solution pH. The transmittance (at $\lambda = 500$ nm) of the solutions was recorded at 20 °C.

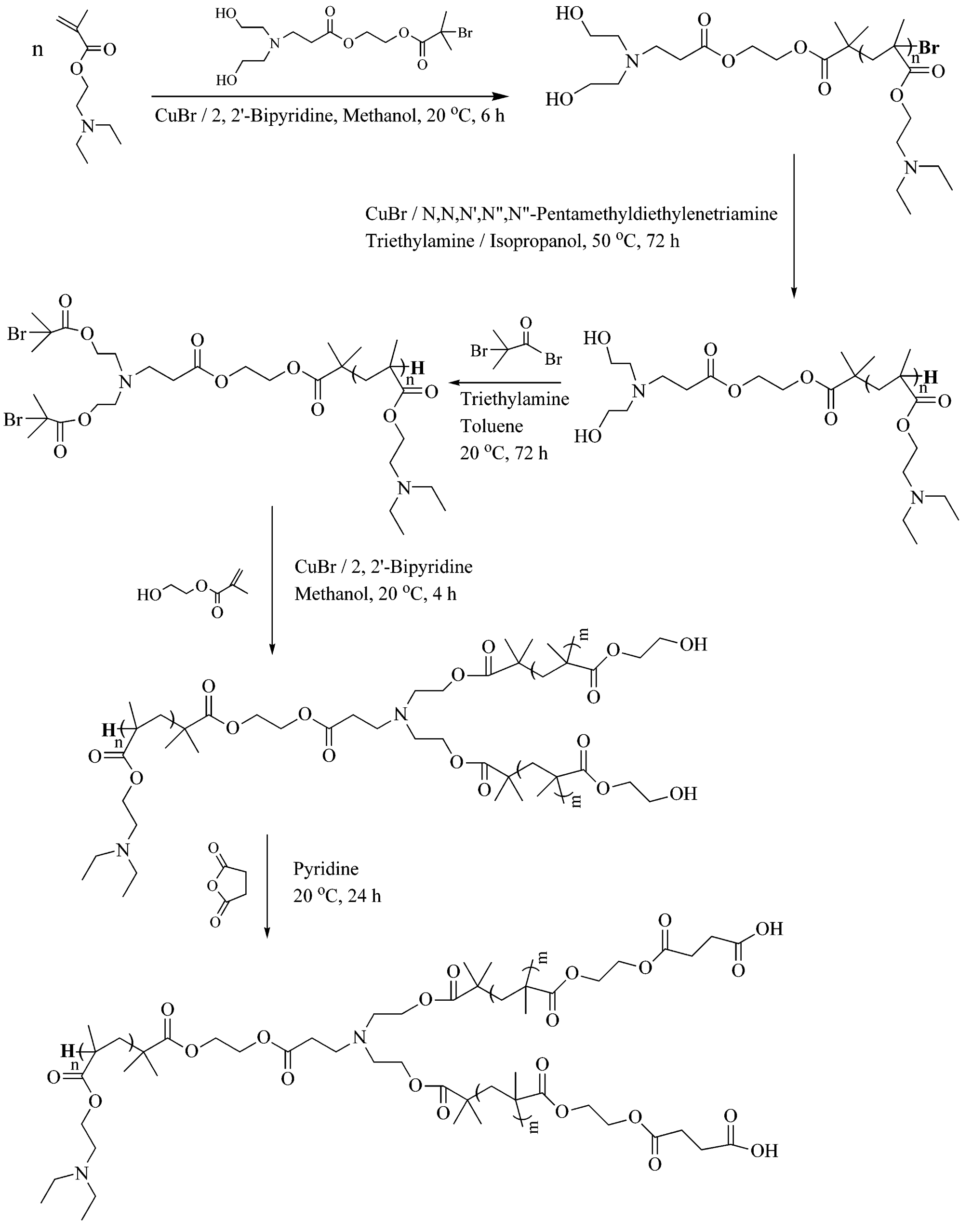
Aqueous electrophoresis measurements of the Y-shaped zwitterionic block copolymer micelles were carried out using a Malvern ZetaMasterS instrument. Zeta potentials were calculated from mobilities using the Henry equation and determined as a function of solution pH, which was adjusted using either HCl or NaOH. All measurements were carried out at 20 °C on diluted (0.2 g L^{-1}) copolymer solutions.

Results and Discussion

The synthetic route to these zwitterionic Y-shaped block copolymers is summarized in Schemes 1 and 2. First, the bishydroxy-functionalized ATRP initiator Br-Init-$(OH)_2$ was prepared by esterification of 2-hydroxyethyl acrylate using excess 2-bromoisobutyryl bromide, followed by Michael addition using excess diethanolamine (see Scheme 1). PDEA-based ω-bisfunctional macroinitiators [PDEA-$(Br)_2$] were obtained by ATRP of DEA monomer using this Br-Init-$(OH)_2$ initiator in methanol at 20 °C, followed by removal of the bromine end groups via the radical chain transfer reaction shown in Scheme 2. Finally, the ω-bishydroxy end groups were esterified using excess 2-bromoisobutyryl bromide. Well-defined Y-shaped zwitterionic PDEA-$(PSEMA)_2$ block copolymers were prepared by methanolic ATRP of HEMA monomer using this PDEA-$(Br)_2$ macroinitiator at 20 °C, followed by esterification of the HEMA hydroxyl groups using succinic anhydride (see Scheme 2).

Synthesis of the Bishydroxy-Functional ATRP Initiator [Br-Init-$(OH)_2$]. First, ^{1}H NMR studies indicated that the esterification of 2-hydroxyethyl acrylate using excess 2-bromoisobutyryl bromide was essentially complete after 4 h at 20 °C, since HEA signals at δ 3.8 (CH_2OH) could no longer be detected. The single peak at δ 1.9 (the upper ^{1}H NMR spectrum in Figure 1) indicated that the unreacted 2-bromoisobutyryl bromide was completely removed. Peak integrals (see Experimental Section) were consistent with the target compound, acryloyloxyethyl 2-bromoisobutyrate. The bishydroxy-functional ATRP initiator [denoted Br-Init-$(OH)_2$] was obtained by Michael addition of acryloyloxyethyl 2-bromoisobutyrate to a 20% excess of diethanolamine at 20 °C. No residual acryloyl signals were observed at δ 5.7−6.5 after stirring for 24 h. ^{1}H NMR

Scheme 2. Synthesis Route for the Y-Shaped Zwitterionic PDEA-(PSEMA)$_2$ Block Copolymers



studies indicated that the desired Br-Init-(OH)$_2$ initiator was isolated after purification (see the lower ^{1}H NMR spectrum in Figure 1 and the Experimental Section).

Synthesis of ω-Bishydroxy-Functional PDEA Homopolymers [Br-PDEA-(OH)$_2$]. On the basis of the GPC results and the conversions calculated from concomitant ^{1}H NMR studies, the kinetics of ATRP of DEA using the Br-Init-(OH)$_2$ initiator in methanol and 9:1 methanol/water mixtures were investigated. Figure 2a depicts the kinetic data for the ATRP of DEA monomer: 93% conversion was achieved within 4 h in 50% anhydrous methanol solution at 20 °C. The linear increase in ln([M$_0$]/[M]) vs time (see Figure 2a) indicated that this reaction was first order with respect to DEA monomer and hence implies that the concentration of active species (polymer radicals) remained essentially constant throughout the polymerization.[25] The GPC data (see Figure 2b) indicated that the number-average molecular weight increased linearly with conversion. The theoretical evolution of molecular weight with conversion was calculated according to eq 1

$$M_{\text{cal}} = M_{i\text{nitiator}} + M_{\text{DEA}} \times DP_{n,\text{target}} \times \text{Conversion} \quad (1)$$

where M_{cal} is the theoretical molecular weight at a specific conversion, $M_{\text{initiator}}$ is the molecular weight of the Br-Init-(OH)$_2$ initiator (370 g mol^{-1}), M_{DEA} is the molecular weight of the DEA monomer, and DP$_{n,\text{ target}}$ is the target degree of polymerization. The theoretical molecular weight vs conversion line lies parallel to the experimental data but is offset due to either GPC calibration errors incurred using the poly(methyl methacrylate) standards or an imperfect initiator efficiency. The relatively narrow molecular weight distribution (final $M_w/M_n = 1.26$) confirmed that the polymerization was well controlled. A small amount of added water (see Figure 2a) can accelerate the polymerization:[26,27] 97% conversion was achieved within around 3 h in a 9:1 methanol/water mixture. First-order kinetics and rela-

Table 1. Summary of the Synthesis Parameters and Molecular Weight Data for the Atom-Transfer Radical Polymerization of 2-(Diethylamino)ethyl Methacrylate Monomer Using 2-(Diethanolamino)acetyloxyethyl 2-Bromoisobutyrate [Br-Init-(OH)$_2$] as an Initiator at 20 °C

entry	target DP$_n$ ^{a}	solvent	time (h)	conversion^b (%)	$M_{n,cal.}$^{c} (g/mol)	$M_{n,GPC}$^{d} (g/mol)	M_w/M_n^{d}	macroinitiator ID^e
1	25	CH_3OH	4.0	99	5000	6400	1.27	PDEA$_{25}$-(Br)$_2$
2	50	CH_3OH	6.0	98	9400	13 000	1.24	PDEA$_{50}$-(Br)$_2$
3	100	CH_3OH	14.5	95	17 900	28 500	1.21	PDEA$_{100}$-(Br)$_2$
4	50	CH_3OH/H_2O	3.0	96	9300	11 900	1.20	
5	100	CH_3OH/H_2O	4.5	93	17 600	22 000	1.24	
6	25	IPA/H_2O	5.0	96	4800	7700	1.37	
7	100	IPA/H_2O	6.0	91	17 200	22 100	1.38	

^{a} Target DP$_n$ = [DEA]/[Br-Init-(OH)$_2$]; [Br-Init-(OH)$_2$]/[CuBr]/[bpy] = 1:1:2. ^{b} Conversions of polymerization of DEA, determined by ^{1}H NMR analysis, see Experimental section. ^{c} The theoretical molecular weights are calculated as: $M_{n,\mathrm{cal}} = M_{\mathrm{initiator}} + M_{\mathrm{DEA}} \times DP_{n,\mathrm{target}} \times$ conversion. ^{d} Determined by THF GPC (vs PMMA standards). ^{e} PDEA-based ω-bisfunctional macroinitiator achieved by esterification of the ω-bishydroxy end groups of PDEA-(OH)$_2$ with 2-bromoisobutyryl bromide.

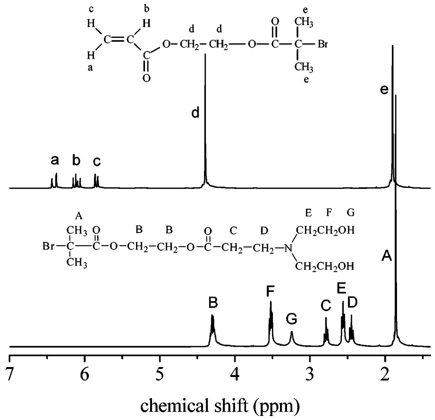


Figure 1. ^{1}H NMR spectra recorded for the bishydroxy-functional atom-transfer radical polymerization (ATRP) initiator, 2-(diethanolamino)acetyloxyethyl 2-bromoisobutyrate [Br-Init-(OH)$_2$], and its precursor, acryloyloxyethyl 2-bromoisobutyrate.

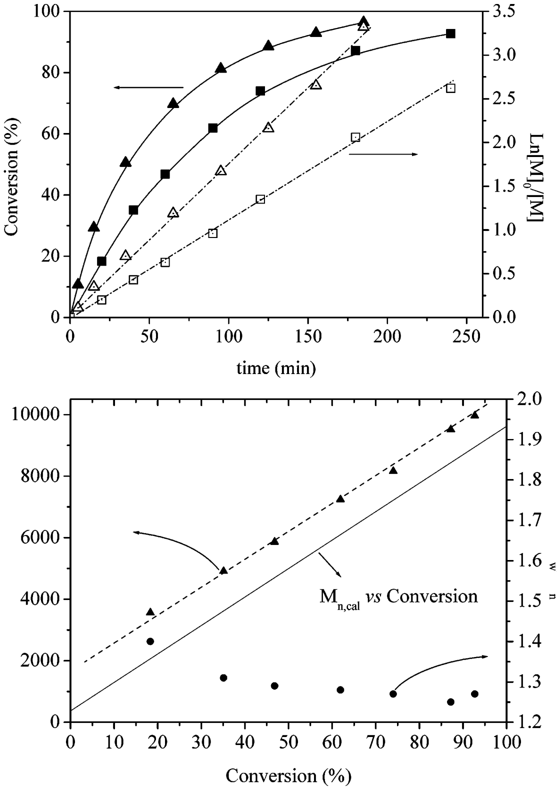


Figure 2. (a) Kinetics of atom-transfer radical polymerization (ATRP) of 2-(diethylamino)ethyl methacrylate (DEA) monomer using the Br-Init-(OH)$_2$ initiator at a [DEA]$_0$:[Br-Init-(OH)$_2$]$_0$:[CuBr]$_0$:[bpy]$_0$ relative molar ratio of 50:1:1:2 in (■) 50% anhydrous methanol or (▲) 50% 9:1 methanol/water at 20 °C. (b) Evolution of number-average molecular weight and polydispersity as a function of conversion for atom-transfer radical polymerization (ATRP) of 2-(diethylamino)ethyl methacrylate (DEA) monomer using the Br-Init-(OH)$_2$ initiator at a [DEA]$_0$:[Br-Init-(OH)$_2$]$_0$:[CuBr]$_0$:[bpy]$_0$ relative molar ratio of 50:1:1:2 in 50% anhydrous methanol at 20 °C.

tively narrow polydispersities (see Table 1) were also observed under these conditions. However, the polymerization was much less controlled in 9:1 IPA/water mixtures. In summary, the ATRP of DEA can be well controlled when using the Br-Init-(OH)$_2$ initiator in anhydrous methanol or 9:1 methanol/water mixtures at 20 °C.

Removal of Terminal Bromine Atoms from Br-PDEA-(OH)$_2$. In principle, the terminal bromine atoms can be replaced by hydrogen atoms via reduction with tributyltin hydride.[23,28,29] However, studies by Müller's group[30] suggest that the hydroxy groups of an OH-functionalized polymer react with tributyltin hydride to form an alcoholate, making purification of the product somewhat problematic. An alternative approach to replace the bromine termini with hydrogen atoms was reported by Bednarek et al.,[31] who employed excess PMDETA during ATRP, since this ligand can act as a radical chain transfer agent under monomer-starved conditions. This reaction has been successfully employed for the synthesis of halogen-free macromonomers.[30,32] In the present study, a 10-fold molar excess of PMDETA ligand relative to CuBr was employed to replace the terminal bromine atoms of Br-PDEA-(OH)$_2$ with hydrogen atoms. Since a relatively high free-radical concentration unavoidably leads to combination of the polymer radicals, a relatively small amount of CuBr (molar ratio of CuBr/PDEA = 0.30) was used in all cases. Moreover, a 1:1 triethylamine/IPA mixture was employed as a solvent so as to minimize the possibility of the tertiary amine groups on the PDEA chains from undergoing chain transfer. GPC studies (see Figure 3) indicated that no high molecular weight shoulder was detected, suggesting that little or no combination occurred under these conditions. The slightly higher molecular weight and narrower polydispersity of the bromine-free PDEA polymer (compared to its bromine-terminated precursor) is attributed to partial fractionation during precipitation into the methanol/water solution.

Quantitative removal of bromine end groups from the Br-PDEA-(OH)$_2$ polymers is essential to obtain well-defined AB$_2$-typed Y-shaped block copolymers. Otherwise, ABA$_2$-type copolymers are inevitably generated during the subsequent ATRP of HEMA monomer.[22] The

Table 2. Summary of the Synthesis Parameters and Molecular Weight Data for the Atom-Transfer Radical Polymerization of 2-Hydroxyethyl Methacrylate Monomer Using Three ω-Bisfunctional PDEA-(Br)$_2$ Macroinitiators in 50% Anhydrous Methanol at 20 °C and the Resulting Y-Shaped Zwitterionic PDEA-(PSEMA)$_2$ Block Copolymers

entry	initiator	target DP$_n$^{a}	conversion^b (%)	$M_{n,cal}$^{c} (g/mol)	X_{DEA}^{d} (%)	$M_{n,NMR}$^{e} (g/mol)	$M_{n,GPC}$^{f} (g/mol)	M_w/M_n^{f}	$M_{n,GPC}$^{g} (g/mol)	M_w/M_n^{g}	block composition
1	PDEA$_{25}$-Br$_2$	12	81	7500	52	8000	13 400	1.18	76 110	1.07	PDEA$_{25}$-(PSEMA$_{11}$)$_2$
2	PDEA$_{25}$-Br$_2$	25	82	10 300	34	11 300	18 400	1.22	126 800	1.10	PDEA$_{25}$-(PSEMA$_{17}$)$_2$
3	PDEA$_{50}$-Br$_2$	25	75	14 500	54	15 200	32 500	1.24	116 100	1.18	PDEA$_{50}$-(PSEMA$_{24}$)$_2$
4	PDEA$_{50}$-Br$_2$	50	92	21 600	35	21 700	45 500	1.30	152 700	1.25	PDEA$_{50}$-(PSEMA$_{47}$)$_2$
5	PDEA$_{50}$-Br$_2$	100	72	28 300	25	29 100	63 800	1.24	235 400	1.22	PDEA$_{50}$-(PSEMA$_{75}$)$_2$
6	PDEA$_{100}$-Br$_2$	50	89	30 400	51	31 400	54 700	1.25	119 500	1.21	PDEA$_{100}$-(PSEMA$_{50}$)$_2$

[a] The target degree of polymerization of each PHEMA branch, target DP$_n$ = [HEMA]/[Br], where initiator species concentration [Br] is twice [PDEA-(Br)$_2$], [Br]/[CuBr]/[bpy] = 1:1:2. [b] Conversions as determined by ^{1}H NMR analysis, see Experimental section. [c] M_n of the PDEA-(PHEMA)$_2$ Y-shaped block copolymer precursors as calculated based on conversions assuming living character. [d] Molar fraction of DEA units in the copolymers as determined by ^{1}H NMR analysis, see Experimental section. [e] M_n of copolymers as determined by ^{1}H NMR studies. [f] M_n and M_w/M_n of the Y-shaped PDEA-(PHEMA)$_2$ block copolymer precursors as determined by DMF GPC (vs PMMA standards). [g] M_n and M_w/M_n of the Y-shaped zwitterionic PDEA-(PSEMA)$_2$ block copolymers as determined by DMF GPC (vs PMMA standards).

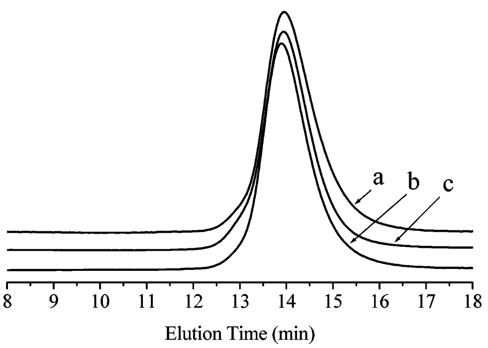


Figure 3. THF GPC traces of (a) Br-PDEA$_{50}$-(OH)$_2$ homopolymer before removal of bromine ends, M_n = 11 900, M_w/M_n = 1.20; (b) PDEA$_{50}$-(OH)$_2$ homopolymer after removal of bromine ends, M_n = 12 700, M_w/M_n = 1.19, and (c) PDEA$_{50}$-(OH)$_2$ homopolymer after attempted chain extension via ATRP of DEA monomer using the halogen-free PDEA$_{50}$-(OH)$_2$ as a macroinitiator at a [DEA]:[PDEA-(OH)$_2$]:[CuBr]:[bpy] relative molar ratio of 200:1:2:4 and 50% DEA monomer in 4:1 methanol/water at 20 °C for 5 h, M_n = 12 500, M_w/M_n = 1.18 (vs PMMA standards).

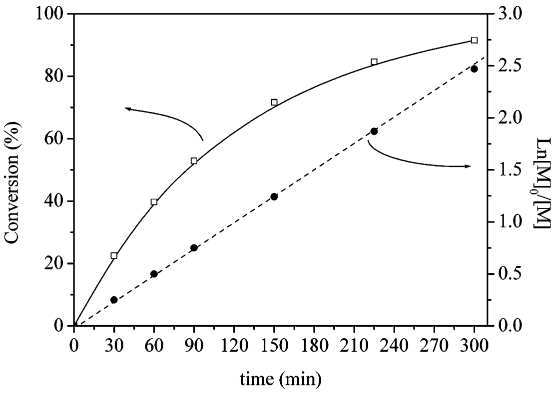


Figure 4. Kinetics of atom-transfer radical polymerization (ATRP) of 2-hydroxyethyl methacrylate (HEMA) monomer using the ω-bisfunctional PDEA$_{50}$-(Br)$_2$ macroinitiator in 50% anhydrous methanol at 20 °C. The relative molar ratio of [HEMA]:[Br]:[CuBr]:[bpy] is 25:1:1:2, where [Br] is the molar concentration of initiating species.

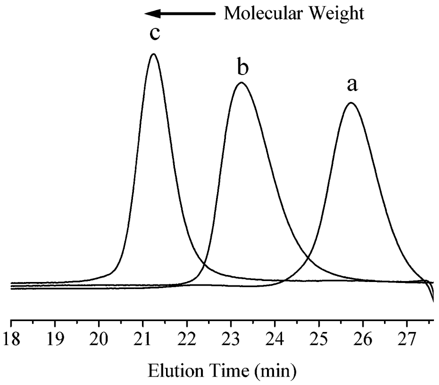


Figure 5. DMF GPC traces of (a) the ω-bisfunctional PDEA$_{50}$-(Br)$_2$ macroinitiator (M_n = 4240, M_w/M_n = 1.20), (b) the corresponding Y-shaped PDEA$_{50}$-(PHEMA$_{24}$)$_2$ block copolymer precursor (M_n = 32 500, M_w/M_n = 1.24), and (c) the final Y-shaped zwitterionic PDEA$_{50}$-(PSEMA$_{24}$)$_2$ block copolymer (M_n = 116 100, M_w/M_n = 1.18). All GPC data were obtained relative to PMMA standards.

efficiency of the removal of bromine end groups was assessed by attempted ATRP of DEA monomer using the halogen-free PDEA-(OH)$_2$ as a macroinitiator. A [DEA]/[PDEA]/[CuBr]/[bpy] relative molar ratio of 200/1/2/4 was employed at 50% DEA in 4:1 methanol/water at 20 °C. After stirring for 5 h under a nitrogen atmosphere, the reaction solution was assessed by THF GPC. As shown in Figure 3, no chain extension was detected, indicating that the PDEA-(OH)$_2$ did not act as a macroinitiator. This control experiment confirmed the efficient removal of the terminal Br atoms from the Br-PDEA-(OH)$_2$ precursor.

Synthesis of PDEA-Based ω-Bifunctional Macroinitiators [PDEA-(Br)$_2$]. After quantitative removal of the bromine end groups from the Br-PDEA-(OH)$_2$ precursor, the terminal hydroxy groups were esterified by adding a 3-fold molar excess of 2-bromoisobutyryl bromide and triethylamine and stirring at 20 °C for 3 days. ^{1}H NMR studies confirmed that the degree of functionalization of these PDEA-(Br)$_2$ macroinitiators was at least 95%.

Synthesis of Y-Shaped PDEA-(PHEMA)$_2$ Block Copolymers. Y-Shaped PDEA-(PHEMA)$_2$ block copolymers were synthesized by the ATRP of HEMA monomer using the PDEA-(Br)$_2$ macroinitiators. Figure 4 depicts the kinetic data obtained using the PDEA$_{50}$-(Br)$_2$ macroinitiator in 50% anhydrous methanol at 20 °C. This polymerization is approximately first order with respect to HEMA monomer up to around 90 % conversion. Copolymers with reasonably low polydispersities were obtained, as shown in Table 2. Figure 5 shows the GPC traces obtained for the PDEA$_{50}$-(Br)$_2$ macroinitiator and the PDEA$_{50}$-(PHEMA$_{24}$)$_2$ Y-shaped block copolymer. Clearly there is a shift to higher molecular weight, indicating chain extension of the PDEA$_{50}$-(Br)$_2$ macroinitiator by the HEMA monomer. Moreover, there is almost no residual peak due to the macroinitiator,

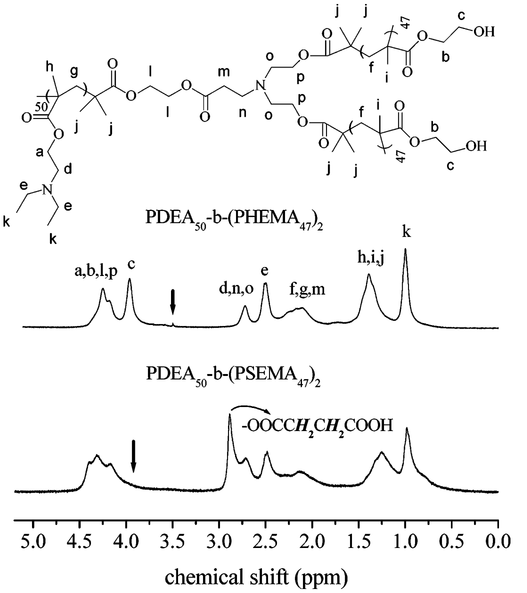


Figure 6. ^{1}H NMR spectra (d_5-pyridine) of the Y-shaped PDEA$_{50}$-(PHEMA$_{47}$)$_2$ block copolymer precursor and the final Y-shaped zwitterionic PDEA$_{50}$-(PSEMA$_{47}$)$_2$ block copolymer.

indicating relatively high initiator efficiency. Thus, the ATRP of HEMA using PDEA-(Br)$_2$ macroinitiators under these conditions appears to have good living character.

All polymerizations were deliberately terminated below 90% conversion so as to minimize the unwanted termination by combination that can occur under monomer-starved conditions, since this might otherwise lead to ill-defined copolymer architectures. The monomodal GPC traces and reasonably narrow polydispersities of the final copolymers (see Figure 5 and Table 2) indicated that combination was negligible under these conditions. Thus, the final Y-shaped block copolymers each had well-defined Y-shaped architectures.

Previously, we reported the unexpected propensity for tertiary amine methacrylates to undergo transesterification under mild conditions in methanol, leading to undesired statistical copolymers of the tertiary amine methacrylate and methyl methacrylate (MMA).[33] Fortunately this side reaction was much slower than the methanolic ATRP of DEA monomer under the conditions used in the present studies. As shown in Figure 6 (upper spectrum, marked with an arrow), only a very small peak can be detected at δ 3.5 in the ^{1}H NMR spectrum, which is attributed to the methyl ester protons of polymerized MMA generated by in situ transesterification. Peak integration indicated that less than 5% DEA was converted into MMA. This low level of MMA incorporation was considered to have a negligible effect on the aqueous solution properties of the final Y-shaped zwitterionic block copolymers (see below).

Synthesis of Y-Shaped Zwitterionic PDEA-(PSEMA)$_2$ Block Copolymers. The Y-shaped zwitterionic PDEA-(PSEMA)$_2$ block copolymers were obtained by esterification of the hydroxy groups of PDEA-(PHEMA)$_2$ copolymers using a 2-fold molar excess of succinic anhydride (relative to the HEMA residues) in anhydrous pyridine.[34,35] As shown in Figure 6 (lower spectrum, marked with an arrow), the signal assigned to the HEMA residues at δ 3.9 (CH_2OH) disappeared and a new signal assigned to the succinyloxyethyl methacrylate (SEMA) residues at δ 2.8 ($OOCCH_2CH_2COO$) was observed. Peak integration indicated that very high degrees of esterification were achieved (typically more than 95%). DMF GPC data (see Table 2 and Figure 5) indicated much higher molecular weight and narrower polydispersities of these zwitterionic Y-shaped block copolymers than expected. This is attributed to the aggregation of these zwitterionic copolymers in DMF, which was supported by the observation of significantly higher light-scattering intensities for these solutions than for those of the PDEA-(PHEMA)$_2$ precursors. However, given the mild reaction conditions employed for this esterification, it is reasonable to assume that the relatively narrow molecular weight distributions of the Y-shaped block copolymer precursors are retained in the final zwitterionic Y-shaped block copolymers.[35]

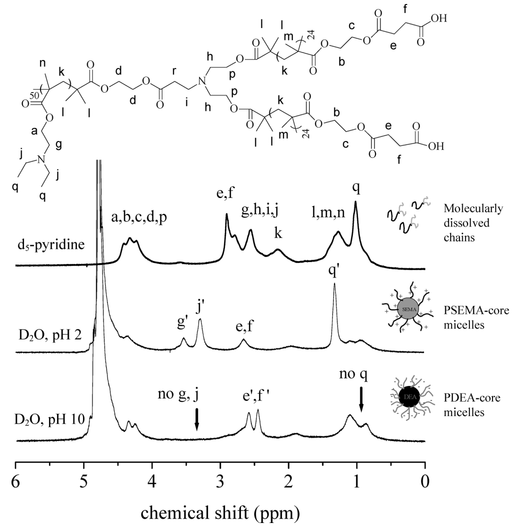


Figure 7. ^{1}H NMR spectra of the Y-shaped zwitterionic PDEA$_{50}$-(PSEMA$_{24}$)$_2$ block copolymer recorded in d_5-pyridine, D_2O/DCl (at pH 2), and D_2O/NaOD (at pH 10).

Aqueous Solution Properties of Y-Shaped Zwitterionic Block Copolymers. PDEA homopolymer is molecularly soluble as a weak cationic polyelectrolyte in acidic media and precipitates at neutral or alkaline pH. In contrast, PSEMA homopolymer is molecularly soluble as a weak anionic polyelectrolyte in basic media and precipitates in acidic solution.[35] Thus, it was anticipated[9] that the Y-shaped PDEA-(PSEMA)$_2$ block copolymer would form PSEMA-core micelles with cationic PDEA coronas at low pH and PDEA-core micelles with anionic PSEMA coronas at high pH.

Figure 7 shows the ^{1}H NMR spectra recorded for the Y-shaped PDEA$_{50}$-(PSEMA$_{24}$)$_2$ block copolymer in d_5-pyridine and D_2O (at pH 2 and 10), respectively. Both blocks are fully solvated in d_5-pyridine; thus, all the signals expected for each block are visible, and the DEA/SEMA molar ratios of the zwitterionic copolymers were calculated from these spectra. In DCl/D_2O solution at pH 2, the PSEMA signal at δ 2.7 can be detected but this is somewhat attenuated (middle spectrum in Figure 7); peak integral analysis indicated that approximately 27% PSEMA residues are hydrated under these conditions. The downfield shift of the PDEA signals confirmed that this block is protonated in acidic solution; thus, these aggregates should have cationic coronas. Adjusting the solution pH to 10 leads to the disappearance of the PDEA signals at δ 3.5−3.0 and 1.0 (lower spectrum in Figure 7), indicating that the PDEA blocks formed the micelle cores. The PSEMA signal ($OOCCH_2CH_2$-$COOH$ at δ 2.7) in basic solution shifted to δ 2.6−2.4 and splits into two peaks due to ionization of the

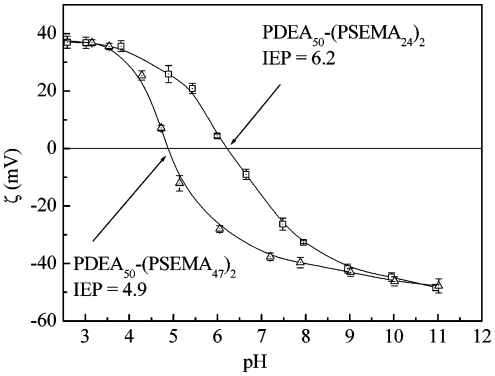


Figure 8. Variation of zeta potential with solution pH for 0.2 g L^{-1} aqueous solutions of the Y-shaped zwitterionic PDEA$_{50}$-(PSEMA$_{47}$)$_2$ and PDEA$_{50}$-(PSEMA$_{24}$)$_2$ block copolymers at 20 °C.

carboxylic acid groups (OOCCH_2CH_2COONa), suggesting the formation of anionic PSEMA coronas.

Figure 8 shows the variation of zeta potential with pH for a 0.2 g L^{-1} aqueous solution of the Y-shaped PDEA$_{50}$-(PSEMA$_{47}$)$_2$ and PDEA$_{50}$-(PSEMA$_{24}$)$_2$ zwitterionic block copolymers at 20 °C. The net charge on these copolymers is zero at pH 6.2 for the PDEA$_{50}$-(PSEMA$_{24}$)$_2$ copolymer and pH 4.9 for the PDEA$_{50}$-(PSEMA$_{47}$)$_2$ copolymer. These pH values can be regarded as the isoelectric points (IEP) of these copolymers and are in close agreement with those obtained by DLS and turbidimetric studies, within experimental error (data not shown).[36] At low pH the copolymer micelles have positive zeta potentials due to the cationic PDEA coronas, whereas at high pH negative zeta potentials due to the anionic PSEMA coronas are observed.

Figure 9 shows the variation of average hydrodynamic diameter ($\langle D_h \rangle$) with solution pH at 20 °C for 2.0 g L^{-1} aqueous solutions of the Y-shaped PDEA$_{50}$-(PSEMA$_{47}$)$_2$ and PDEA$_{50}$-(PSEMA$_{24}$)$_2$ copolymers. For the aqueous PDEA$_{50}$-(PSEMA$_{47}$)$_2$ copolymer solution at pH 2 (see Figure 9a), large aggregates are formed with a $\langle D_h \rangle$ of 83 nm and a relatively high μ_2/Γ^2 of 0.28. Given the contour length of this copolymer, these aggregates are too large to be well-defined core–shell micelles.

Increasing the solution pH leads to a concomitant decrease in the degree of protonation of the PDEA block and an increasing degree of ionization of the PSEMA block. This interplay results in interpolyelectrolyte complexation between the cationic PDEA blocks and anionic PSEMA blocks. Both the $\langle D_h \rangle$ and polydispersity increased monotonically (see Figure 9a).

Above pH 3 the solution became cloudy. Further increase in the solution pH led to macroscopic precipitation of the copolymer from aqueous solution. At around pH 7 the copolymer redissolved and colloidal aggregates were detected by DLS ($\langle D_h \rangle$ was around 130 nm, and the corresponding polydispersity was 0.38). Above pH 7 the transmittance of the solution increases dramatically and the size and polydispersity of the micelles gradually decreased (see Figure 9a). Above pH 9 well-defined PDEA-core micelles with a constant $\langle D_h \rangle$ of 38 nm and a μ_2/Γ^2 of 0.09–0.17 were observed.

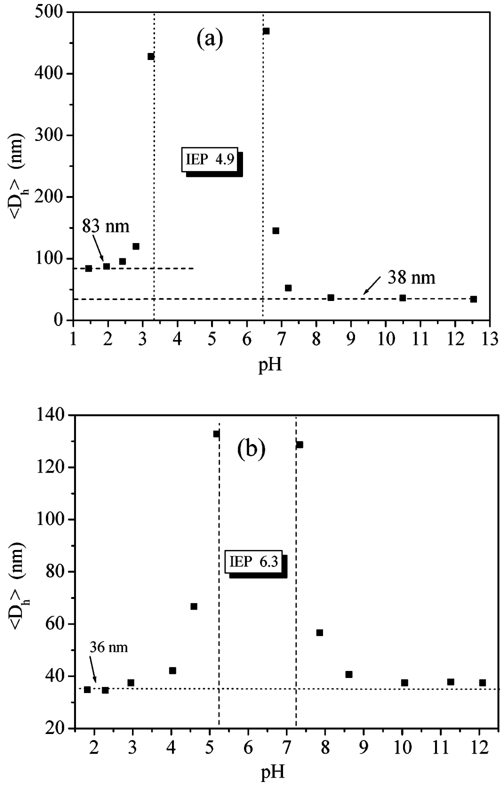


Figure 9. Variation of hydrodynamic diameter (<D_h>) with solution pH for 2.0 g L^{-1} aqueous solutions of (a) PDEA$_{50}$-(PSEMA$_{47}$)$_2$ and (b) PDEA$_{50}$-(PSEMA$_{24}$)$_2$ zwitterionic Y-shaped block copolymers at 20 °C.

The Y-shaped PDEA$_{50}$-(PSEMA$_{24}$)$_2$ zwitterionic block copolymer shows similar aggregation behavior to the PDEA$_{50}$-(PSEMA$_{47}$)$_2$ copolymer (see Figure 9b). However, much smaller micelles with a $\langle D_h \rangle$ of 36 nm and a μ_2/Γ^2 of 0.22 were formed at pH 2. Precipitation occurred between approximately pH 5.3 and pH 7.3, which is a narrower range than that of the PDEA$_{50}$-(PSEMA$_{47}$)$_2$ copolymer (pH 3.3–6.4). This was confirmed by turbidimetry studies of the Y-shaped PDEA$_{50}$-(PSEMA$_{47}$)$_2$ and PDEA$_{50}$-(PSEMA$_{24}$)$_2$ zwitterionic block copolymers, which agreed well with the DLS studies. The same general aggregation behavior was also observed for DLS and turbidimetry studies of the PDEA$_{25}$-(PSEMA$_{11}$)$_2$ and PDEA$_{25}$-(PSEMA$_{17}$)$_2$ aqueous copolymer solutions.

Given the polydispersity and compositional heterogeneity of the zwitterionic block copolymers and the associated experimental error in determining the onset of precipitation/redissolution, the midpoints of the pH ranges for precipitation are consistent with the calculated IEP's of these zwitterionic block copolymers. Clearly, further work will be required to determine the precise effect of the Y-shaped architecture of these zwitterionic block copolymers on their aqueous solution properties, but this is beyond the scope of the present study.

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References and Notes

(1) Lowe, A. B.; McCormick, C. L. *Chem. Rev.* **2002**, *102*, 4177.
(2) Creutz, S.; Jérôme, R.; Kaptijn, G. M. P.; van der Werf, A. W.; Akkerman, J. M. *J. Coat. Technol.* **1998**, *70*, 41.
(3) Creutz, S.; Jérôme, R. *Prog. Org. Coat.* **2000**, *40*, 21.
(4) Partrickios, C. S.; Yamasaki, E. N. *Anal. Biochem.* **1995**, *231*, 82.
(5) Lowe, A. B.; Billingham, N. C.; Armes, S. P. *Chem. Commun.* **1997**, 1035.
(6) Lowe, A. B.; Billingham, N. C.; Armes, S. P. *Macromolecules* **1998**, *31*, 5991.
(7) Liu, S. Y.; Armes, S. P. *Angew. Chem., Int. Ed.* **2002**, *41*, 1413.

(8) Liu, S. Y.; Armes, S. P. *Langmuir* **2003**, *19*, 4432.
(9) Bories-Azeau, X.; Armes, S. P.; van den Haak, H. J. W. *Macromolecules* **2004**, *37*, 2348.
(10) Arotcarena, M.; Heise, B.; Ishaya, S.; Laschewsky, A. *J. Am. Chem. Soc*. **2002**, *124*, 3787.
(11) Weaver, J. V. M.; Bütün, V.; Armes, S. P. *Chem. Commun*. **2002**, 2122.
(12) Liu, S. Y.; Billingham, N. C.; Armes, S. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 2328.
(13) Ramzi, A.; Prager, M.; Richter, D.; Efstratiadis, V.; Hadjichristidis, N.; Young, R. N.; Allgaier, J. B. *Macromolecules* **1997**, *30*, 7171.
(14) Pispas, S.; Hadjichristidis, N.; Potemkin, I.; Khokhlov, A. *Macromolecules* **2000**, *33*, 1741.
(15) Yun, J.; Faust, R.; Szilágyi, L. S.; Kéki, S.; Zsuga, M. *Macromolecules* **2003**, *36*, 1717.
(16) Sotiriou, K.; Nannou, A.; Velis, G.; Pispas, S. *Macromolecules* **2002**, *35*, 4106.
(17) Hadjichristidis, N.; Iatrou, H.; Pispas, S.; Pitsikalis, M. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 3211.
(18) Reutenauer, S.; Hurtrez, G.; Dumas, P. *Macromolecules* **2001**, *34*, 755.
(19) Gibanel, S.; Forcada, J.; Heroguez, V.; Schappacher, M.; Gnanou, Y. *Macromolecules* **2001**, *34*, 4451.
(20) Gibanel, S.; Heroguez, V.; Forcada, J.; Gnanou, Y. *Macromolecules* **2002**, *35*, 2467.
(21) Francis, R.; Lepoittevin, B.; Taton, D.; Gnanou, Y. *Macromolecules* **2002**, *35*, 9001.
(22) Bon, S. A. F., Ohno, K., Haddleton, D. M., McCormick, C. L., Ed.; ACS Symposium Series 780; American Chemical Society: Washington, DC, 2001; Chapter 9, p 148.
(23) He, T.; Li, D.; Sheng, X.; Zhao, B. *Macromolecules* **2004**, *37*, 3128.
(24) Cai, Y. L.; Burguiere, C.; Armes, S. P. *Chem. Commun.* **2004**, 802.
(25) Wang, J. S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **1995**, *117*, 5614.
(26) McDonald, S.; Rannard, S. P. *Macromolecules* **2001**, *34*, 8600.
(27) Liu, S. Y.; Tang, Y. Q.; Weaver, J. V. M.; Billingham, N. C.; Armes, S. P.; Tribe, K. *Macromolecules* **2002**, *35*, 6121.
(28) Coessens, V.; Matyjaszewski, K. *Macromol. Rapid Commun.* **1999**, *20*, 66.
(29) Zhao, B.; He, T. *Macromolecules* **2003**, *36*, 8599.
(30) Schön, F.; Hartenstein, M.; Müller, A. H. E. *Macromolecules* **2001**, *34*, 5394.
(31) Bednarek, M.; Biedron, T.; Kubisa, P. *Macromol. Chem. Phys.* **2000**, *201*, 58.
(32) Cai, Y. L.; Hartenstein, M.; Müller, A. H. E. *Macromolecules* **2004**, *37*, 7484.
(33) Bories-Azeau, X.; Armes, S. P. *Macromolecules* **2002**, *35*, 10241.
(34) Li, Z.; Liu, G. J.; Law, S.; Sells, T. *Biomacromolecules* **2002**, *3*, 984.
(35) Bories-Azeau, X. Ph.D. Thesis, University of Sussex, 2004.
(36) Alfrey, T.; Morawetz, H.; Fitzgerald, E. B.; Fuoss, R. M. *J. Am. Chem. Soc.* **1950**, *72*, 1864.

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