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Synthesis of Thermosensitive Water-Soluble Polystyrenics with Pendant Methoxyoligo(ethylene glycol) Groups by Nitroxide-Mediated Radical Polymerization

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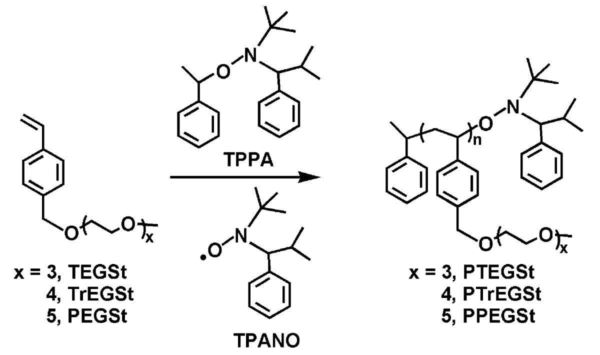
ABSTRACT: Nitroxide-mediated radical polymerizations of 4-vinylbenzyl methoxytris(oxyethylene) ether (TEGSt), 4-vinylbenzyl methoxytetrakis(oxyethylene) ether (TrEGSt), and 4-vinylbenzyl methoxypentakis-(oxyethylene) ether (PEGSt) were carried out at 120 °C using 2,2,5-trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane as initiator. Kinetics study and gel permeation chromatography analysis showed that the polymerizations were living processes yielding polymers with controlled molecular weights and narrow molecular weight distributions. The polymers can be dissolved in water forming transparent solutions and undergo phase transitions when the temperature is above a critical point. The cloud points of the homopolymers of TEGSt, TrEGSt, and PEGSt were around 13, 39, and 55 °C, respectively, which were also supported by variable temperature ^{1}H NMR spectroscopy analysis. The high level of alkoxyamine chain end retention allowed the synthesis of diblock copolymers with low polydispersities (<1.15). Cloud point measurements and ^{1}H NMR studies indicated that the diblock copolymers undergo phase transition in water at a temperature between the cloud points of the two corresponding homopolymers.

Introduction

Thermosensitive water-soluble polymers undergo a phase transition in aqueous solutions from a soluble to an insoluble state when the temperature is above a critical point (lower critical solution temperature, LCST) or below a certain point (upper critical solution temperature, UCST).[1,2] These types of polymers, especially those exhibiting the LCST behavior, have attracted considerable attention in the past several decades and have been intensively investigated from both scientific and technological points of view. A variety of applications have been reported ranging from the creation of smart surfaces (e.g., for manipulation of cells on the surface),[2,3] to drug delivery systems,[4,5] to the design of biomaterials,[2,4−6] and the use as intelligent chromatographic supports.[7] A classic example is poly(*N*-isopropylacrylamide),[1−3] one of the most intensively studied and most widely used temperature-sensitive polymers.

By introducing nonionizable hydrophilic moieties, for example, methoxyoligo(ethylene glycol), to the polymer backbone as pendant groups, one can design new thermosensitive water-soluble polymers. This concept has been demonstrated in recent reports on the preparation of thermoresponsive polymers of methoxyoligo(ethylene glycol) methacrylates by living anionic polymerization[8] and of oligo(ethylene glycol) vinyl ether by living cationic polymerization.[9−12] Both homopolymers and block copolymers with controlled molecular weights and narrow molecular weight distributions have been synthesized, and interesting solution behavior has been observed.[8−12] Living free radical polymerizations, most notably, atom transfer radical polymerization (ATRP), nitroxide-mediated radical polymerization (NMRP), and reversible addition−fragmentation chain transfer process (RAFT), have been widely used in recent years to prepare various polymers[13−18] and polymer brushes[19−21] with controlled molecular weights, narrow polydispersities, and well-defined architectures. Owing to the nature of radical reaction and the less strict requirements of the polymerization conditions (e.g., the tolerance of some impurity in the monomers and solvents) compared with living anionic and cationic polymerizations, living radical polymerizations can be applied to a broad range of functional monomers. A variety of stimuli-responsive water-soluble polymers have been synthesized, mostly by ATRP and RAFT.[22−34]

Scheme 1. Synthesis of Thermosensitive Water-Soluble Polystyrenics by Nitroxide-Mediated Radical Polymerization Using 2,2,5-Trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane (TPPA) as Initiator in the Presence of 0.05 equiv of 2,2,5-Trimethyl-4-phenyl-3-azahexane-3-nitroxide (TPANO)



In this article, we report on the synthesis of thermosensitive water-soluble polystyrenics containing pendant methoxyoligo(ethylene glycol) groups by NMRP and the study of their thermoresponsive properties in aqueous solutions. Three monomers with different lengths of oligo(ethylene glycol), TEGSt, TrEGSt, and PEGSt as shown in Scheme 1, were synthesized and polymerized by use of 2,2,5-trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane (TPPA), a α-hydrido alkoxyamine, as initiator (Scheme 1). α-Hydrido alkoxyamines that

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contain a hydrogen atom attached to a carbon located α to the nitrogen atom have been proven to be highly effective in the controlled polymerizations of a wide variety of monomers including styrenics, acrylates, and acrylamides.[16] The advantage of these second-generation NMRP initiators over TEMPO-based systems is also shown by the very low polydispersities, typically 1.05−1.15. In the present work, we used TPPA to prepare homopolymers and diblock copolymers of TEGSt, TrEGSt, and PEGSt. Although the polymerization of TrEGSt by α,α′-azobis(isobutyronitrile) was reported for making biocompatible materials[35] and similar polystyrenics containing oligo(ethylene glycol) groups (x = 3 and 7 in Scheme 1) were grown from the surface by surface-initiated TEMPO-mediated radical polymerization to form protein-resistant polymer brushes,[36] the thermosensitive properties of the polymers in water were not investigated. In the current work, the phase transitions of homopolymers and diblock copolymers of the three monomers were studied by cloud point measurements and variable temperature ^{1}H NMR spectroscopy.

Experimental Section

Materials. Tri(ethylene glycol) monomethyl ether (95%), ethylene glycol, di(ethylene glycol) (99%), and anisole (99.7%) were purchased from Aldrich and used as received. 4-Vinylbenzyl chloride (tech., 90%), *p*-toluenesulfonyl chloride (p.a), and NaH (60% dispersion in mineral oil) were obtained from Acros and used as received. Tetrahydrofuran (THF) was distilled from sodium and benzophenone and stored in a solvent storage bottle prior to use. All other chemical reagents were purchased from either Aldrich or Fisher and used without further purification.

Characterization. Gel permeation chromatography (GPC) was carried out at room temperature using a PL-GPC 20 (an integrated GPC system from Polymer Laboratories, Inc.) with a refractive index detector, one PLgel 5 μm guard column (50 × 7.5 mm), and two PLgel 5 μm mixed-C columns (each 300 × 7.5 mm, linear range of molecular weight from 200 to 2 000 000 according to Polymer Laboratories). The data were processed using Cirrus GPC/SEC software (Polymer Laboratories). THF was used as the carrier solvent at a flow rate of 1.0 mL/min. Standard monodisperse polystyrenes (Polymer Laboratories) were used for calibration. The ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian Mercury 300 NMR spectrometer, and the residual solvent proton signal was used as the internal standard. Mass spectroscopy was performed in the Mass Spectroscopy Center in the Chemistry Department at the University of Tennessee at Knoxville on a Micromass Quattro II tandem electrospray spectrometer run in the positive ion electrospray mode or using fast atom bombardment (FAB). Variable temperature ^{1}H NMR (400 MHz) spectra were recorded on a thermoregulated Bruker Avance 400 using solutions of polymers in $\mathrm{D_2O}$ (99.9 D atom %) with a concentration of 10 mg/mL. An acquisition of 32 scans was performed with an acquisition time of 4 s per scan, a pulse of 10 μs, and a recycle delay of 1 s. For each temperature, the solution was equilibrated for 20 min. Cloud points of thermosensitive homopolymers and diblock copolymers in aqueous solutions (0.5% (w/w) for homopolymers and 1.0% for diblock copolymers) were measured by placing the solutions in the water bath of a Fisher Scientific Isotemp refrigerated circulator. Temperature was increased at a step of 1 °C. At each temperature, the polymer solutions were allowed to equilibrate with the water bath for 3 min. The cloud point was recorded when the polymer solution became cloudy. IR spectra were recorded on a BIO-RAD FTS-60A Fourier transform infrared instrument. The samples were prepared by adding several drops of a solution of the compound in chloroform on a NaCl plate and drying in a vacuum at room temperature for 10 min.

α-(*p*-Toluenesulfonyl)-ω-methoxytris(oxyethylene), tetra(ethylene glycol) monomethyl ether (α-hydro-ω-methoxytetrakis(oxyethylene), TrEG), and penta(ethylene glycol) monomethyl ether (α-hydro-ω-methoxypentakis(oxyethylene), PEG) were prepared by use of the same procedures reported in the literature.[37]

α-(*p*-Toluenesulfonyl)-ω-methoxytris(oxyethylene). ^{1}H NMR ($\mathrm{CDCl_3}$) δ (ppm): 7.77 (d, 2H, $\mathrm{RO_3SC(C\mathit{H})_2}$), 7.32 (d, 2H, $\mathrm{H_3CC(C\mathit{H})_2}$), 4.14 (t, 2H, $\mathrm{SO_3C\mathit{H}_2}$), 3.67 (t, 2H, $\mathrm{SO_3CH_2C\mathit{H}_2}$), 3.61−3.49 (m, 8H, $\mathrm{OC\mathit{H}_2}$), 3.35 (s, 3H, $\mathrm{OC\mathit{H}_3}$), 2.43 (s, 3H, $\mathrm{ArC\mathit{H}_3}$). ^{13}C NMR ($\mathrm{CDCl_3}$) δ (ppm): 144.75 ($\mathrm{CH_3\mathit{C}(CH)_2}$), 132.97 ($\mathrm{SO_2\mathit{C}(CH)_2}$), 129.78 ($\mathrm{CH_3C(\mathit{C}H)_2}$), 127.95 ($\mathrm{SO_2C(\mathit{C}H)_2}$), 71.86 ($\mathrm{CH_3O\mathit{C}H_2}$), 70.71, 70.53, 70.51, 69.20 ($\mathrm{O\mathit{C}H_2}$), 68.64 ($\mathrm{SO_3\mathit{C}H_2}$), 59.00 ($\mathrm{O\mathit{C}H_3}$), 21.6 ($\mathrm{\mathit{C}H_3C(CH)_2}$). MS (ES) *m/z* 341.1 ($\mathrm{[M + Na]^+}$).

Tetra(ethylene glycol) Monomethyl Ether (α-Hydro-ω-methoxytetrakis(oxyethylene), TrEG). ^{1}H NMR ($\mathrm{CDCl_3}$) δ (ppm): 3.78−3.41 (m, 16H, $\mathrm{OC\mathit{H}_2}$), 3.35 (s, 3H, $\mathrm{OC\mathit{H}_3}$), 2.60 (t, 1H, $\mathrm{-O\mathit{H}}$). ^{13}C NMR ($\mathrm{CDCl_3}$) δ (ppm): 72.66 ($\mathrm{\mathit{C}H_2OCH_3}$), 71.73 ($\mathrm{HOCH_2\mathit{C}H_2O}$), 70.45, 70.36, 70.33, 70.26, 70.03 ($\mathrm{-CH_2O\mathit{C}H_2\mathit{C}H_2O\mathit{C}H_2\mathit{C}H_2O\mathit{C}H_2CH_2OCH_3}$), 61.51 ($\mathrm{HO\mathit{C}H_2-}$), 58.84 ($\mathrm{-O\mathit{C}H_3}$). MS (ES) *m/z* 231.1 ($\mathrm{[M + Na]^+}$).

Penta(ethylene glycol) Monomethyl Ether (α-Hydro-ω-methoxypentakis(oxyethylene), PEG). ^{1}H NMR ($\mathrm{CDCl_3}$) δ (ppm): 3.73−3.51 (m, 20H, $\mathrm{OC\mathit{H}_2}$); 3.36 (s, 3H, $\mathrm{-OC\mathit{H}_3}$), 2.67 (t, 1H, $\mathrm{-O\mathit{H}}$). ^{13}C NMR ($\mathrm{CDCl_3}$) δ (ppm): 72.57 ($\mathrm{\mathit{C}H_2OCH_3}$), 71.59 ($\mathrm{HOCH_2\mathit{C}H_2O}$), 70.33, 70.30, 70.21, 69.92 ($\mathrm{CH_2O(\mathit{C}H_2\mathit{C}H_2O)_3O\mathit{C}H_2CH_2OCH_3}$), 61.32 ($\mathrm{HO\mathit{C}H_2CH_2O}$), 58.75 ($\mathrm{O\mathit{C}H_3}$). MS (ES) *m/z* 275.1 ($\mathrm{[M + Na]^+}$).

Synthesis of 4-Vinylbenzyl Methoxytris(oxyethylene) Ether (TEGSt). Tri(ethylene glycol) monomethyl ether (16.58 g, 0.101 mol) was added into a three-necked flask containing dry THF (50 mL) followed by addition of NaH (6.08 g, 0.152 mol). After the mixture was stirred at room temperature under $\mathrm{N_2}$ atmosphere for 1 h, a solution of 4-vinylbenzyl chloride (10.76 g, 70.5 mmol) in dry THF (20 mL) was added dropwise. The reaction mixture was refluxed for 20 h. The mixture was then poured into a 250 mL beaker and neutralized by adding a dilute HCl aqueous solution. The mixture was then placed in a separatory funnel to allow phase separation. The organic phase was separated, and the aqueous layer was extracted with diethyl ether four times. The organic phase and extracts were combined and dried over anhydrous $\mathrm{Na_2SO_4}$. The solvents were removed by a rotavapor, and purification by column chromatography (1:1 ethyl acetate/hexanes) afforded 9.99 g of pure product as a nearly colorless liquid (51% yield). ^{1}H NMR ($\mathrm{CDCl_3}$) δ (ppm): 7.36 (d, 2H, aromatic), 7.28 (d, 2H, aromatic), 6.69 (dd, 1H, $\mathrm{CH_2{=}C\mathit{H}-}$), 5.72 (dd, 1H, $\mathrm{C\mathit{H}H{=}CH-}$), 5.21 (dd, 1H, $\mathrm{CH\mathit{H}{=}CH-}$,), 4.53 (s, 2H, $\mathrm{(CH)_2C-C\mathit{H}_2-}$), 3.51−3.67 (m, 12H, $\mathrm{-OC\mathit{H}_2C\mathit{H}_2O-}$), 3.35 (s, 3H, $\mathrm{OC\mathit{H}_3}$). ^{13}C NMR ($\mathrm{CDCl_3}$) δ (ppm): 137.85 ($\mathrm{OCH_2\mathit{C}(CH)_2}$), 136.90 ($\mathrm{CH_2\mathit{C}HC(CH)_2}$), 136.51 ($\mathrm{CH_2CH\mathit{C}(CH)_2}$), 127.90 ($\mathrm{((\mathit{C}H)_2CCH_2O)}$), 126.16 ($\mathrm{CH_2CHC(\mathit{C}H)_2}$), 113.70 ($\mathrm{\mathit{C}H_2CHC(CH)_2}$), 72.90 ($\mathrm{((CH)_2C\mathit{C}H_2O)}$), 71.90 ($\mathrm{CH_3O\mathit{C}H_2}$), 70.60, 70.51, 69.34 ($\mathrm{\mathit{C}H_2O}$), 59.01 ($\mathrm{\mathit{C}H_3OCH_2}$). IR ($\mathrm{cm^{-1}}$): 2870 ($\mathrm{CH_2}$ and $\mathrm{CH_3}$, ether), 1628 ($\mathrm{CH{=}CH_2}$), 1512 (aromatic C=C), 1454 ($\mathrm{CH_2}$), 1107 (C−O−C). MS (ES) *m/z* 303.1 ($\mathrm{[M + Na]^+}$).

Synthesis of 4-Vinylbenzyl Methoxytetrakis(oxyethylene) Ether (TrEGSt). A procedure similar to the synthesis of TEGSt was used to prepare TrEGSt. The crude product was purified by column chromatography (4:1 ethyl acetate/hexanes), giving a nearly colorless liquid (72% yield). ^{1}H NMR ($\mathrm{CDCl_3}$) δ (ppm): 7.37 (d, 2H, aromatic), 7.28 (d, 2H, aromatic), 6.69 (dd, 1H, $\mathrm{CH_2{=}C\mathit{H}-}$), 5.72 (dd, 1H, $\mathrm{C\mathit{H}H{=}CH-}$), 5.21 (dd, 1H, $\mathrm{CH\mathit{H}{=}CH-}$), 4.53 (s, 2H, $\mathrm{(CH)_2C-C\mathit{H}_2-}$), 3.67−3.50 (m, 16H, $\mathrm{-OC\mathit{H}_2C\mathit{H}_2O-}$), 3.35 (s, 3H, $\mathrm{OC\mathit{H}_3}$). ^{13}C NMR ($\mathrm{CDCl_3}$) δ (ppm): 137.83 ($\mathrm{((CH)_2\mathit{C}CH_2O)}$), 136.89 ($\mathrm{CH_2\mathit{C}HC(CH)_2}$), 136.48 ($\mathrm{CH_2CH\mathit{C}(CH)_2}$), 127.88 ($\mathrm{((\mathit{C}H)_2CCH_2O)}$), 126.14 ($\mathrm{CH_2CHC(\mathit{C}H)_2}$), 113.68 ($\mathrm{\mathit{C}H_2CHC(CH)_2}$), 72.88 ($\mathrm{((CH)_2C\mathit{C}H_2O)}$), 71.87 ($\mathrm{\mathit{C}H_2OCH_3}$), 70.58, 70.55, 70.46, 69.33 ($\mathrm{\mathit{C}H_2O}$), 58.97 ($\mathrm{\mathit{C}H_3OCH_2}$). IR ($\mathrm{cm^{-1}}$): 2870 ($\mathrm{CH_2}$ and $\mathrm{CH_3}$, ether), 1628 ($\mathrm{CH{=}CH_2}$), 1512 (aromatic C=C), 1454 ($\mathrm{CH_2}$), 1107 (C−O−C); MS (ES) *m/z* 347.2 ($\mathrm{[M + Na]^+}$).

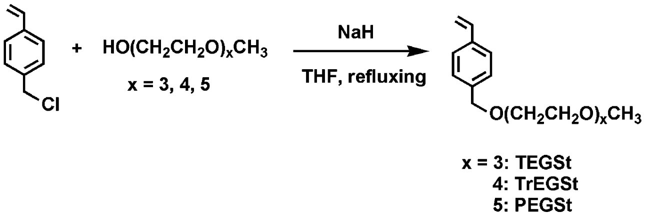
Synthesis of 4-Vinylbenzyl Methoxypentakis(oxyethylene) Ether (PEGSt). A procedure similar to the synthesis of TEGSt was used to prepare PEGSt. The crude product was purified by column chromatography (ethyl acetate as eluent), affording a colorless liquid (35% yield). ^{1}H NMR ($CDCl_3$) δ (ppm): 7.36 (d, 2H, aromatic), 7.27 (d, 2H, aromatic), 6.68 (dd, 1H, $CH_2{=}C\mathit{H}{-}$), 5.71 (d, 1H, $C\mathit{H}H{=}CH{-}$), 5.21 (d, 1H, $CH\mathit{H}{=}CH{-}$), 4.53 (s, 2H, $(CH)_2C{-}C\mathit{H}_2{-}$), 3.67−3.50 (m, 20H, $-OC\mathit{H}_2C\mathit{H}_2O-$), 3.35 (s, 3H, $OC\mathit{H}_3$). ^{13}C NMR ($CDCl_3$) δ (ppm): 137.80 ($(CH)_2\mathit{C}CH_2O$), 136.83 ($CH_2\mathit{C}HC(CH)_2$), 136.44 ($CH_2CH\mathit{C}(CH)_2$), 127.83 ($(\mathit{C}H)_2CCH_2O$), 126.10 ($CH_2CHC(\mathit{C}H)_2$), 113.63 ($\mathit{C}H_2CHC(CH)_2$), 72.83 ($(CH)_2C\mathit{C}H_2O$), 71.83 ($CH_3O\mathit{C}H_2$), 70.55, 70.49, 70.47, 70.41, 69.29 ($\mathit{C}H_2O$), 58.92 ($\mathit{C}H_3OCH_2$). IR (cm^{-1}): 2870 (CH_2 and CH_3, ether), 1628 ($CH{=}CH_2$), 1512 (aromatic C=C), 1454 (CH_2), 1103 (C−O−C). MS (ES) *m/z* 391.3 ($[M + Na]^+$).

Synthesis of 2,2,5-Trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane (TPPA). 2,2,5-Trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane (TPPA) was synthesized by use of the same procedure described in the literature.[16] A colorless liquid was obtained after purification by flash column chromatography (10:1 hexanes/methylene chloride). ^{1}H NMR ($CDCl_3$, both diastereomers) δ (ppm): 7.5−7.1 (m, 20H), 4.90 (q, 2H, both diastereomers), 3.41 (d, 1H, major diastereomer), 3.29 (d, 1H, minor diastereomer), 2.32 (m, 2H, both diastereomer), 1.63 (d, 3H, major diastereomer), 1.54 (d, 3H, minor diastereomer), 1.31 (d, 3H, major diastereomer), 1.04 (s, 9H, minor diastereomer), 0.90 (t, 3H, minor diastereomer), 0.76 (s, 9H, major diastereomer), 0.54 (d, 3H, major diastereomer), 0.21 (d, 3H, minor diastereomer). ^{13}C NMR ($CDCl_3$) δ (ppm): 145.75, 144.98 ($(CH)_2\mathit{C}CHN$, both diastereomers), 142.44, 142.25 ($(CH)_2\mathit{C}CHO$, both diastereomers), 130.94, 128.22, 128.04, 128.02, 127.36, 127.26, 127.17, 126.98, 126.60, 126.32, 126.15, 126.14 (aromatic carbons), 83.47, 82.81 ($CH_3\mathit{C}HO$, both diastereomers), 72.19, 72.10 ($C\mathit{C}HN$, both diastereomers), 60.49, 60.35 ($N\mathit{C}(CH_3)_3$, both diastereomers), 32.00, 31.58 ($CH\mathit{C}H(CH_3)_2$, both diastereomers), 28.38, 28.19, 28.58 ($NC(\mathit{C}H_3)_3$), 24.69, 23.16 ($\mathit{C}H_3CHO$, both diastereomers), 22.12, 21.96, 21.16, 21.04 ($NCHCH(\mathit{C}H_3)_2$, both diastereomers). MS (FAB) *m/z* 326.4 ($[M + 1]^+$).

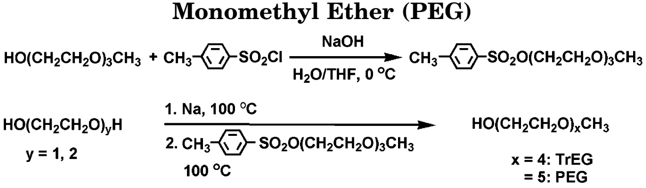
Nitroxide-Mediated Radical Polymerization of TEGSt, TrEGSt, and PEGSt. A typical procedure for nitroxide-mediated radical polymerization of TEGSt is described below. Similar procedures were used to polymerize TrEGSt and PEGSt. TPPA (15.0 mg, 0.0462 mmol), TEGSt (1.543 g, 5.51 mmol), anisole (0.843 g), and 100 μL of a solution of 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (TPANO) in anisole (concentration: 0.54 mg/100 μL) were added into a 25 mL two-necked flask. The concentrations were $[TEGSt]_0 = 2.226$ M, $[I]_0 = 18.7$ mM, and $[TPANO]_0 = 1.0$ mM. The flask was then degassed by freeze−pump−backfilling with nitrogen six times. After warming to room temperature, the reaction flask was placed in a 120 °C oil bath. A sample was taken immediately ($t = 0$ min) for kinetics study. During the polymerization, samples were taken via an argon-exchanged syringe at regular intervals for ^{1}H NMR spectroscopy and GPC analysis. After polymerization proceeded for 351 min, the flask was removed from the oil bath. The mixture was allowed to cool naturally to room temperature, diluted with THF (1 mL), and precipitated in hexanes (100 mL). The polymer was purified by reprecipitation of its THF solution in hexanes (100 mL). The polymer was then transferred to a flask and dried in a vacuum for 15 h at room temperature. A viscous polymer (0.352 g, 23% yield) was obtained. GPC analysis results: $M_n = 10\,500$ g/mol; polydispersity index (PDI) = 1.07.

Synthesis of Diblock Copolymers by Nitroxide-Mediated Radical Polymerization. A typical procedure for the synthesis of PPEGSt-*b*-PTEGSt is described below. Similar procedures were used to synthesize other diblock copolymers. Dry PPEGSt (0.473 g, 0.0358 mmol, $M_n = 8800$ g/mol, PDI = 1.08), TEGSt (2.022 g, 7.22 mmol), anisole (1.03 g), and 85 μL of the solution of TPANO in anisole (concentration: 0.54 mg/100 μL) were added into a 25 mL two-necked flask. The concentrations were $[M]_0 = 2.02$ M, $[PPEGSt]_0 = 10.0$ mM, and $[TPANO]_0 = 0.58$ mM. The flask was then degassed by freeze−pump−backfilling with nitrogen six times. After warming to room temperature, the flask was placed in a 120 °C oil bath. Samples were taken by use of an argon-exchanged syringe at regular intervals for ^{1}H NMR spectroscopy and GPC analysis. After polymerization proceeded for 242 min, the flask was removed from the oil bath. The mixture was cooled to room temperature, diluted with THF (2 mL), and precipitated in hexanes (100 mL). The polymer was purified by precipitation in hexanes (100 mL) again. The polymer was then transferred to a flask and dried in a vacuum at room temperature for 15 h. 0.957 g (38% yield) of polymer was obtained ($M_n = 19\,900$ g/mol, PDI = 1.11).

Scheme 2. Synthesis of 4-Vinylbenzyl Methoxytris(oxyethylene) Ether (TEGSt), 4-Vinylbenzyl Methoxytetrakis(oxyethylene) Ether (TrEGSt), and 4-Vinylbenzyl Methoxypentakis(oxyethylene) Ether (PEGSt)



Scheme 3. Synthesis of Tetra(ethylene glycol) Monomethyl Ether (TrEG) and Penta(ethylene glycol) Monomethyl Ether (PEG)



Results and Discussion

Monomer Synthesis. 4-Vinylbenzyl methoxytris(oxyethylene) ether (TEGSt), 4-vinylbenzyl methoxytetrakis(oxyethylene) ether (TrEGSt), and 4-vinylbenzyl methoxypentakis(oxyethylene) ether (PEGSt) were synthesized by reaction of 4-vinylbenzy chloride with sodium salts of tri(ethylene glycol) monomethyl ether (TEG), tetra(ethylene glycol) monomethyl ether (TrEG), and penta(ethylene glycol) monomethyl ether (PEG), respectively, in dry THF (Scheme 2). TrEG and PEG were prepared according to Scheme 3 by following the procedures described in the literature.[37] The monosodium salts of ethylene glycol and di(ethylene glycol) were reacted with α-(*p*-toluenesulfonyl)-ω-methoxytris(oxyethylene), yielding TrEG and PEG, respectively. All three monomers were thoroughly purified by silica gel column chromatography, and the molecular structures were confirmed by ^{1}H NMR, ^{13}C NMR, infrared spectroscopy, and mass spectroscopy.

Nitroxide-Mediated Radical Polymerizations of TEGSt, TrEGSt, and PEGSt Using 2,2,5-Trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane as Initiator. 2,2,5-Trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane (TPPA) and the corresponding nitroxide radical, 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (TPANO), were prepared according to the procedures reported in the literature.[16] The molecular structures were confirmed by ^{1}H NMR, ^{13}C NMR, and mass spectroscopy. TPPA is a second-generation NMRP initiator and has been used for the polymerization of styrenics, acrylates, and acrylamides in a living manner, yielding polymers with controlled molecular weights and narrow polydispersities. The key feature of NMRP is the

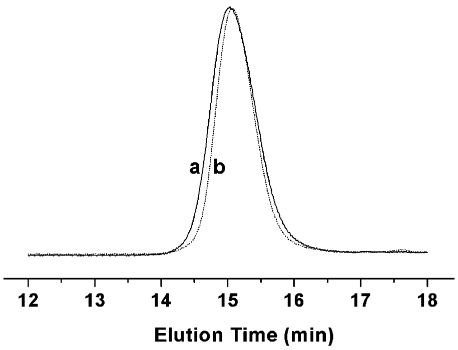


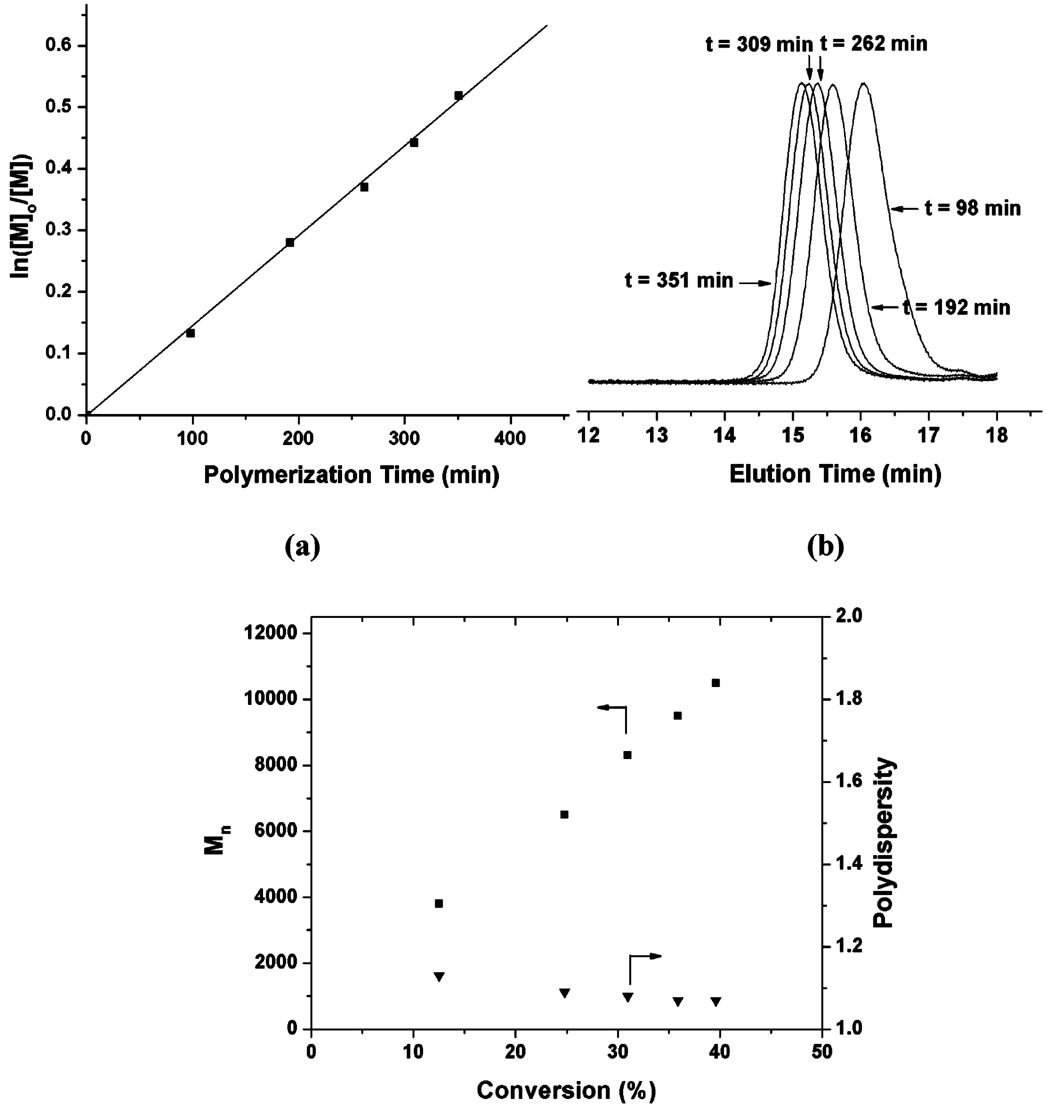
Figure 1. Gel permeation chromatography analysis of the polymers synthesized by nitroxide-mediated radical polymerizations of 4-vinylbenzyl methoxytris(oxyethylene) ether (TEGSt). Curve a (—) represents the polymer obtained at $t = 250$ min from a polymerization in anisole (50% (w/w), to the monomer) at 120 °C without free nitroxide. Number-average molecular weight (M_n) = 10 800 g/mol, polydispersity index (PDI) = 1.11. $[M]_0 = 2.43$ M, $[M]_0/[I]_0 = 152$. Curve b (···) is the polymer obtained at $t = 370$ min from a polymerization in anisole (50% (w/w), to the monomer) at 120 °C in the presence of 0.05 equiv of 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (TPANO). $M_n = 10\,700$ g/mol, PDI = 1.08. $[M]_0 = 2.28$ M, $[M]_0/[I]_0 = 155$, $[TPANO]_0 = 0.73$ mM.

operation of a special kinetic phenomenon termed the persistent radical effect. According to the mechanism, a small fraction of the initiating radicals formed from decomposition of the initiator undergo radical−radical coupling reaction in the initial stages of the polymerization, leading to a small amount of excess mediating free radical (persistent radical) that gives rise to the persistent radical effect and to eventual control over the polymerization process. An artificial persistent radical effect may be created by addition of a few percent of mediating radical relative to the initiator.[16] In the present work, 0.05 equiv of nitroxide TPANO with respect to the initiator TPPA was added into the reaction mixture. The polymerizations were carried out in anisole (50% (w/w), to the monomer) at 120 °C. The effect of addition of free nitroxide on the control of the polymerization of TEGSt can be appreciated from Figure 1. GPC curve a represents the polymer obtained without free nitroxide radical, and the polydispersity was 1.11. Addition of 0.05 equiv of TPANO decreased the polydispersity to 1.08 for the polymer with a similar molecular weight (GPC curve b). The rate of polymerization was slightly decreased by addition of TPANO. For the polymerization in the presence of free nitroxide radical, it took 370 min in this particular experiment to reach a number-average molecular weight of 10 700 g/mol, while a similar M_n (10 800 g/mol) was obtained after 250 min without free nitroxide.

To confirm that the NMRPs of TEGSt, TrEGSt, and PEGSt with addition of 0.05 equiv of free nitroxide radical were living processes, ^{1}H NMR spectroscopy was employed to monitor the polymerizations using the peaks located at 4.30−4.64 ppm, which are from $-CH_2-$ of the benzyl groups of the monomer and the polymer, as internal standard. (The sum of the integral values of the two peaks was a constant during the course of polymerization.) The monomer conversions were calculated by use of the integral value of the peaks at 5.72 ppm (1H from the monomer) at time t and the value of the same peaks at $t = 0$. The samples for kinetics study were also analyzed by GPC relative to polystyrene standards to give the molecular weights and polydispersities. After desired conversions/molecular weights were reached, the polymerizations were stopped by cooling the flask naturally to room temperature. Figures 2−4 show the kinetics plots and GPC results for the polymerizations of TEGSt, TrEGSt, and PEGSt, respectively. A linear relationship between $\ln([M]_0/[M])$ and the reaction time was observed for all three polymerizations, indicating that the polymerizations were a first-order reaction with respect to the monomer and the number of growing polymer chains was a constant during the course of the polymerization. GPC analysis shows that the molecular weight increased with the reaction time and monomer conversion and the polydispersity decreased progressively. For example, for the NMRP of TEGSt, the M_n increased from 3800 ($t = 98$ min), to 6500 ($t = 192$ min), to 8300 ($t = 262$ min), to 9500 ($t = 309$ min), to 10 500 g/mol ($t = 351$ min), while the polydispersity decreased gradually from 1.13 ($t = 98$ min), to 1.09 ($t = 192$ min), to 1.08 ($t = 262$ min), to 1.07 ($t = 309$ and 351 min). No significant differences in the polymerization rates were observed for the three monomers when the molar ratios of monomer to initiator were similar.

In the experiments, we found that if the ratio of the monomer to the initiator was ≥100 and the monomer conversion was relatively high (>55%), a shoulder appeared in the high molecular weight side of the peak. Figure 5 shows the evolution of GPC peaks in a polymerization of TrEGSt ($[M]_0/[I]_0 = 150$) at relatively high monomer conversions. At conversions of 44.1% (curve a, $M_n = 15\,700$ g/mol) and 53.4% (curve b, $M_n = 18\,300$ g/mol), the GPC peaks were symmetric. However, when the conversion reached 64.0%, the shoulder peak became noticeable (curve c). Presumably, the viscosity of the reaction mixture became high at relatively high conversions, causing some propagating chains to combine with each other or not to be effectively terminated by mediating nitroxide radicals. This shoulder peak can be avoided by control of the monomer conversion below 50%. If the molar ratio of monomer to initiator was small, e.g. 43, no high molecular weight shoulder peak was observed even when the monomer conversion reached 74.0%.

Synthesis of Diblock Copolymers by NMRP. Encouraged by the controlled polymerizations of all three monomers using α-hydrido alkoxyamine TPPA along with free nitroxide radical TPANO, we began to pursue the synthesis of diblock copolymers. To mitigate the effects associated with viscosity, a molar ratio of monomer to macroinitiator of ca. 200 was employed, and anisole was used as solvent. The polymerization was carried out at 120 °C with addition of 0.05 equiv of TPANO (relative to the macroinitiator). Both the monomer and macroinitiator were dried in a vacuum (<100 mTorr) overnight prior to polymerization. Figure 6 shows the GPC analysis of a block copolymerization of TEGSt using PPEGSt as macroinitiator ($M_n = 8800$ g/mol, $M_w = 9500$ g/mol, degree of polymerization (DP) = 35 calculated from the conversion). The monomer conversion was determined by ^{1}H NMR spectroscopy. From Figure 6, one can see that the GPC peak shifted to the high molecular weight region from the original position of the macroinitiator with the increase of monomer conversion, indicating that the block copolymerization efficiency was very high. The molecular weight increased from 8800 to 15 700 g/mol at the conversion of 22.7% and to 19 900 g/mol at the conver-



(a) **(b)**

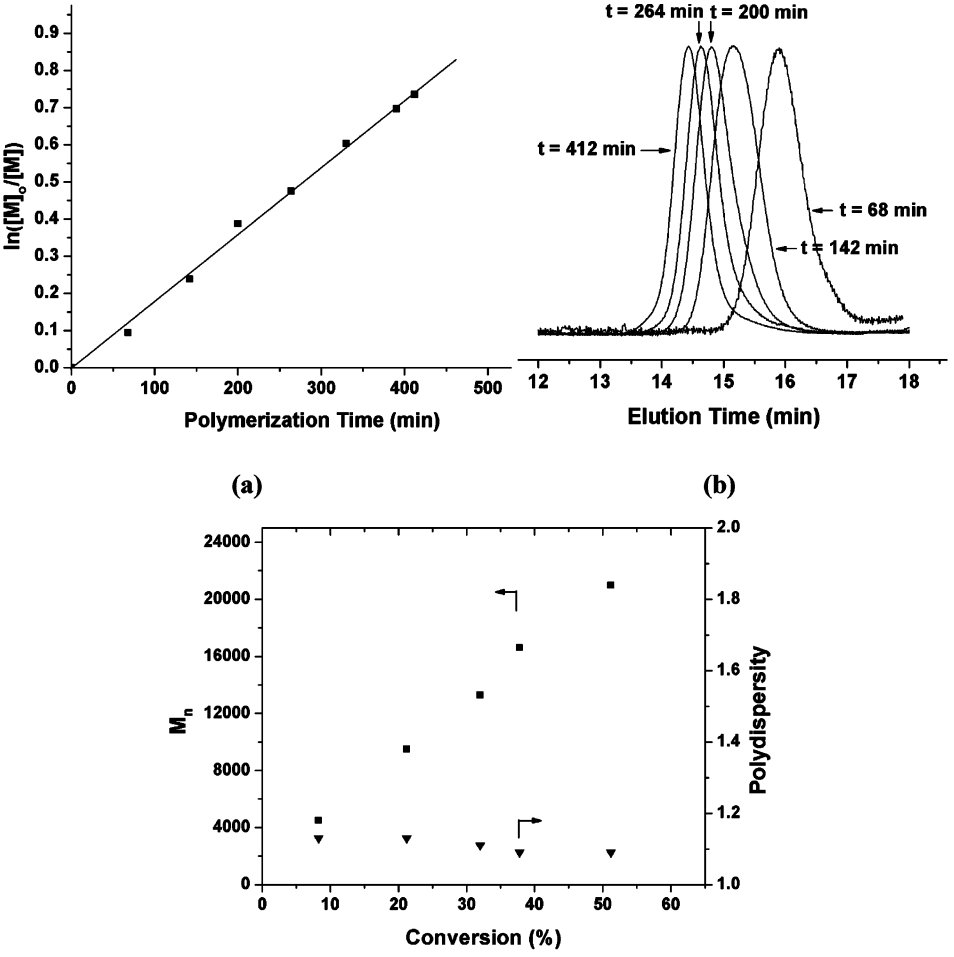
(c)

Figure 2. (a) Relationship between ln([M]$_0$/[M]) and time for the polymerization of 4-vinylbenzyl methoxytris(oxyethylene) ether (TEGSt) in anisole (50% (w/w), relative to TEGSt) at 120 °C. [M]$_0$ = 2.23 M, [M]$_0$/[I]$_0$ = 119, [2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide]$_0$ = 1.01 mM. (b) Evolution of gel permeation chromatography curves with the polymerization time. (c) Number-average molecular weight (M_n, ■) and polydispersity (▼) vs monomer conversion.

sion of 30.4%. The polydispersity index remained low, 1.11. Although 0.05 equiv of free nitroxide radical relative to the macroinitiator was added into the reaction mixture to create an artificial persistent radical effect, tailing at the low molecular weight side of the main peak was observed, indicating that some polymer chains were dead. It is not clear whether the dead polymer chains formed in the synthesis of macroinitiator, or in the process of the isolation of macroinitiator, or in the block copolymerization. Assuming that all macroinitiator molecules have initiated the polymerization, one can calculate the degree of polymerization of the second block by use of the ratio of monomer to initiator and the conversion. In this particular experiment, the calculated DP of PTEGSt was 61.

A series of diblock copolymers were synthesized by NMRP using PTEGSt, PTrEGSt, and PPEGSt as macroinitiators and are summarized in Table 1. All these diblock copolymers have a relatively narrow molecular weight distribution (PDI < 1.15). By use of the peak located at 4.42 ppm (the $-CH_2-$ of the benzyl group) as reference, the molar ratio of the two blocks was calculated by use of the integral value of the peaks in the range of 3.2–4.0 ppm ($CH_3(OCH_2CH_2)_x-$, x = 3, 4, 5). The results are summarized in Table 1. Given the limitation of ^{1}H NMR analysis, these values are reasonably close to those calculated from conversions.

Thermoresponsive Properties of PTEGSt, PTrEGSt, and PPEGSt. As expected, all homopolymers of TEGSt, TrEGSt, and PEGSt can be dissolved in water forming clear solutions as long as the temperature is below a critical point. To determine the cloud points, aqueous solutions of three homopolymers (M_n of PTEGSt = 10 500 g/mol, PDI = 1.07; PTrEGSt M_n = 10 600 g/mol, 1.09; PPEGSt M_n = 9900 g/mol, 1.08) with a concentration of 0.5 wt % were prepared. For PTEGSt, the solution was transparent at 12 °C and suddenly became cloudy at 13 °C during the course of increasing the temperature. The solutions of PTrEGSt and PPEGSt became cloudy at 39 and 55 °C, respectively. Apparently, the cloud point increases with the length of the methoxyoligo(ethylene glycol) group. The longer the side chain, the stronger the interaction between the polymer molecules and water.



(a) **(b)**

(c)

Figure 3. (a) Relationship between ln([M]$_0$/[M]) and time for the polymerization of 4-vinylbenzyl methoxytetrakis(oxyethylene) ether (TrEGSt) in anisole (50% (w/w), relative to the monomer) at 120 °C. [M]$_0$ = 1.90 M, [M]$_0$/[I]$_0$ = 203, [2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide]$_0$ = 0.49 mM. (b) Evolution of gel permeation chromatography curves with the polymerization time. (c) Number-average molecular weight (M_n, ■) and polydispersity index (▼) vs monomer conversion.

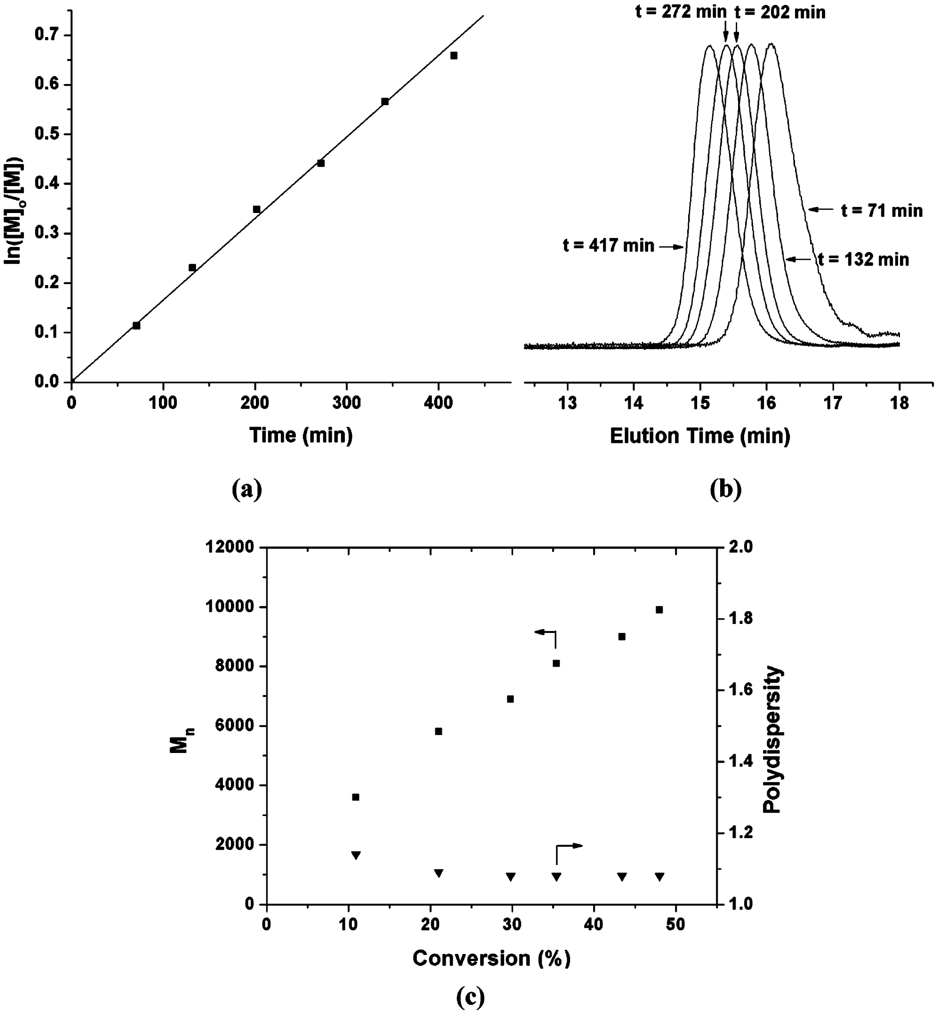
Table 1. Synthesis of Diblock Copolymers of 4-Vinylbenzyl Methoxytris(oxyethylene) Ether (TEGSt), 4-Vinylbenzyl Methoxytetrakis(oxyethylene) Ether (TrEGSt), and 4-Vinylbenzyl Methoxypentakis(oxyethylene) Ether (PEGSt) by Nitroxide-Mediated Radical Polymerization in Anisole at 120 °C

no.	macroinitiator (M_n, PDI, DP)[a,b]	monomer ([M]$_0$/[I]$_0$)	conv, % (DP)[b]	copolymer (M_n, PDI)[a]	molar ratio[c] of two blocks	molar ratio[d] of two blocks
1	PTEGSt (10 500, 1.07, 48)	TrEGSt (221)	25.8 (57)	21 400, 1.11	45.7:54.3	42.8:57.2
2	PTrEGSt (10 600, 1.09, 44)	TEGSt (207)	24.8 (51)	18 500, 1.12	46.3:53.7	47.5:52.5
3	PTrEGSt (9300, 1.08, 36)	TEGSt (204)	44.8 (91)	24 500, 1.13	28.3:71.7	31.0:69.0
4	PPEGSt (8800, 1.08, 35)	TEGSt (201)	30.4 (61)	19 900, 1.11	36.5:63.5	37.3:62.7
5	PPEGSt (9900, 1.08, 41)	TrEGSt (205)	39.6 (81)	23 200, 1.13	33.6:66.4	30.5:69.5

[a] Number-average molecular weight (M_n) and polydispersity index (PDI) were obtained from gel permeation chromatography analysis relative to polystyrene standards. [b] DP represents degree of polymerization; conversions were determined by ^{1}H NMR spectroscopy. [c] Molar ratio of the two blocks calculated from conversions. [d] Molar ratio calculated from ^{1}H NMR analysis of diblock copolymers.

^{1}H NMR spectroscopy was employed to study the phase transitions of the three polymers in D_2O. Figures 7−9 show the ^{1}H NMR spectra of the polymer solutions (1.0% (w/w)) at different temperatures. The height and position of water peak were used as references. For PTEGSt, at temperatures in the range 5−11 °C, the peaks from phenyl ring were visible and the peaks of methoxytris(ethylene glycol) group were sharp. When the temperature was raised from 11 to 14 °C, the height of the aromatic peaks decreased noticeably. While at 17 °C, the aromatic peaks almost disappeared, the peaks from the side chain in the range of 2.5−3.5 ppm remained visible but became broadened. Clearly, the polymer underwent a phase transition from a soluble to an insoluble state at around 14 °C, consistent with cloud point measurement.

For PTrEGSt, the peaks from the polymer backbone in the range of 1.5−2.0 ppm were visible at 30 and 35 °C, but completely disappeared at 40 °C. In the meantime, the intensity of the aromatic peaks decreased significantly, indicating that the transition occurred somewhere between 35 and 40 °C. This is also in good agreement with the result (39 °C) obtained in the cloud point measurements. For PPEGSt, when the temperature was raised from 50 to 55 °C, the aromatic peaks decreased slightly but became smoother and broader, while the peaks from the polymer backbone (δ = 1.0−2.0 ppm) almost disappeared. This observation is con-



(a) **(b)**

(c)

Figure 4. (a) Relationship between $\ln([M]_0/[M])$ and time for the polymerization of 4-vinylbenzyl methoxypentakis(oxyethylene) ether (PEGSt) in anisole (50% (w/w), relative to the monomer). $[M]_0 = 1.78$ M, $[M]_0/[I]_0 = 86$, [2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide]$_0 = 1.0$ mM. (b) Evolution of gel permeation chromatography curves with the polymerization time. (c) Number-average molecular weight (M_n, ■) and polydispersity index (▼) vs monomer conversion.

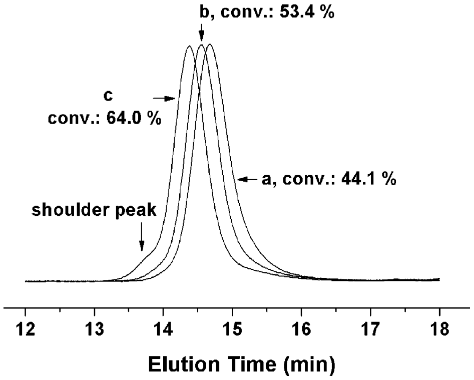


Figure 5. Gel permeation chromatography analysis of the polymers obtained at conversions of 44.1% (curve a), 53.4% (curve b), and 64.0% (curve c) in a polymerization of 4-vinylbenzyl methoxytetrakis(oxyethylene) ether (TrEGSt) in anisole (50% (w/w) relative to the monomer) at 120 °C. $[M]_0 = 2.00$ M, $[M]_0/[I]_0 = 150$, [2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide]$_0 = 0.70$ mM.

sistent with the cloud point (55 °C) of the same polymer in water. From these three sets of ^{1}H NMR spectra, one can also easily find that the two aromatic peaks of PPEGSt were more discernible than those of PTEGSt and PTrEGSt at temperatures below LCST, suggesting that the interaction between the PPEGSt and water is the strongest among the three polymers. The small decrease in the height of the aromatic peaks of PPEGSt

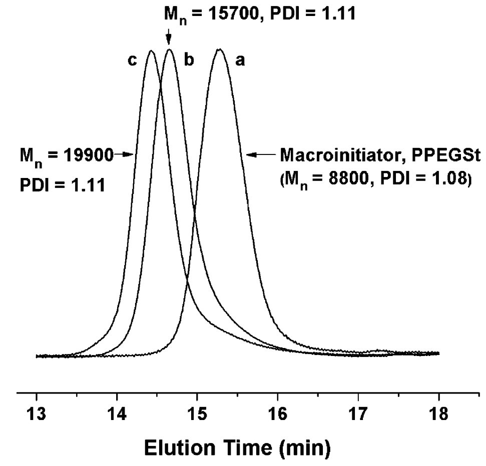


Figure 6. Gel permeation chromatography analysis of a block copolymerization of 4-vinylbenzyl methoxytris(oxyethylene) ether using poly(4-vinylbenzyl methoxypentakis(oxyethylene) ether) (PPEGSt) as macroinitiator ($M_n = 8800$ g/mol, polydispersity index (PDI) = 1.08) in anisole (50% (w/w) relative to the monomer) at 120 °C. $[M]_0 = 2.02$ M, $[M]_0/[I]_0 = 202$, [2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide]$_0 = 0.58$ mM. Curve a: macroinitiator PPEGSt; curve b: at conversion of 22.7%; curve c: at conversion of 30.4%.

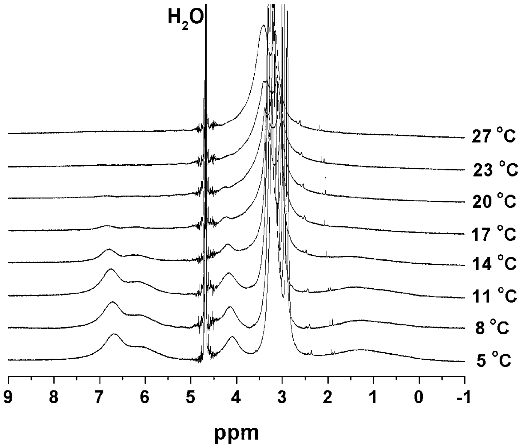


Figure 7. ^{1}H NMR spectra of poly(4-vinylbenzyl methoxytris(oxyethylene) ether) (number-average molecular weight = 10 500 g/mol, polydispersity index = 1.07) in D_2O (1% (w/w)) at various temperatures.

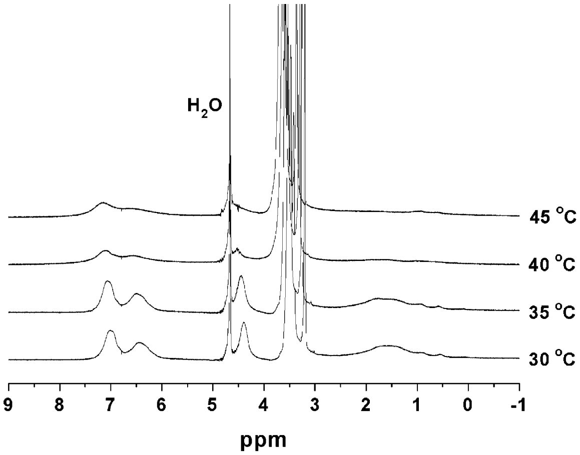


Figure 8. ^{1}H NMR spectra of poly(4-vinylbenzyl methoxytetrakis(oxyethylene) ether) (number-average molecular weight = 10 600 g/mol, polydispersity index = 1.09) in D_2O (1% (w/w)) at various temperatures.

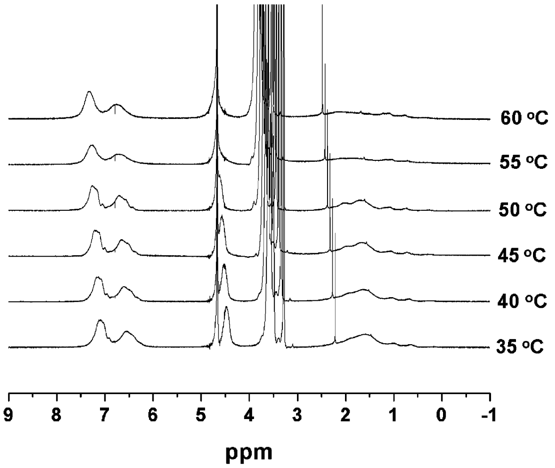


Figure 9. ^{1}H NMR spectra of poly(4-vinylbenzyl methoxypentakis(oxyethylene) ether) (number-average molecular weight = 9900 g/mol, polydispersity index = 1.08) in D_2O (1% (w/w)) at different temperatures.

in the transition shown in Figure 9 indicates that the hydrophilicity is still very high even at temperatures above LCST.

Thermoresponsive Properties of Diblock Copolymers in Water. Cloud point measurements indicated that the diblock copolymers undergo phase transition in water at a temperature between the cloud points of the two corresponding homopolymers (Table 2). For example, the cloud point of PTEGSt$_{48}$-*b*-PTrEGSt$_{57}$ (sample no. 1 in Table 2) was 29 °C, which lies between those of PTEGSt (13 °C) and PTrEGSt (39 °C). These results were consistent with those reported by Han et al. in the study of diblock copolymers of oligo(ethylene glycol) monomethyl ether methacrylates synthesized by living anionic polymerization.[8] The phase transitions were also studied by variable temperature ^{1}H NMR spectroscopy. Figure 10 shows the ^{1}H NMR spectra of PTrEGSt$_{44}$-*b*-PTEGSt$_{51}$ (sample no. 2 in Table 2) in D_2O (1.0%) at various temperatures. The aromatic peaks decreased in the height from 20 to 25 °C and almost disappeared at 30 °C, indicating that the transition occurred at around 25 °C, consistent with the observation in the cloud point measurements (25 °C). A closer examination shows that the transition point is very close to the block-length-averaged cloud point of the two homopolymers. Except the first diblock copolymer, the experimental cloud points were essentially identical to (≤1 °C) the calculated values for the other

Table 2. Cloud Points of a Series of Diblock Copolymers of 4-Vinylbenzyl Methoxytris(oxyethylene) Ether (TEGSt), 4-Vinylbenzyl Methoxytetrakis(oxyethylene) Ether (TrEGSt), and 4-Vinylbenzyl Methoxypentakis(oxyethylene) Ether (PEGSt)

no.	diblock copolymers[a]	M_n, PDI[b]	cloud point (°C) exptl[c]	cloud point (°C) calcd[d]
1	PTEGSt$_{48}$-*b*-PTrEGSt$_{57}$	21400, 1.11	29	27
2	PTrEGSt$_{44}$-*b*-PTEGSt$_{51}$	18500, 1.12	25	25
3	PTrEGSt$_{36}$-*b*-PTEGSt$_{91}$	24500, 1.13	19	20
4	PPEGSt$_{35}$-*b*-PTEGSt$_{61}$	19900, 1.11	28	28
5	PPEGSt$_{41}$-*b*-PTrEGSt$_{81}$	23200, 1.13	45	44

[a] PTEGSt: poly(4-vinylbenzyl methoxytris(oxyethylene) ether); PTrEGSt: poly(4-vinylbenzyl methoxytetrakis(oxyethylene) ether); PPEGSt: poly(4-vinylbenzyl methoxypentakis(oxyethylene) ether). [b] M_n: number-average molecular weight; PDI: polydispersity index. [c] Experimentally determined cloud points (the concentration of the solution was 1.0 wt %). [d] Cloud points calculated by use of the equation $CP_{cal} = DP_1/(DP_1 + DP_2) \times CP_1 + DP_2/(DP_1 + DP_2) \times CP_2$, where DP_1 and DP_2 represent the DPs of the first and second blocks and CP_1 and CP_2 represent the cloud points of the corresponding homopolymers.

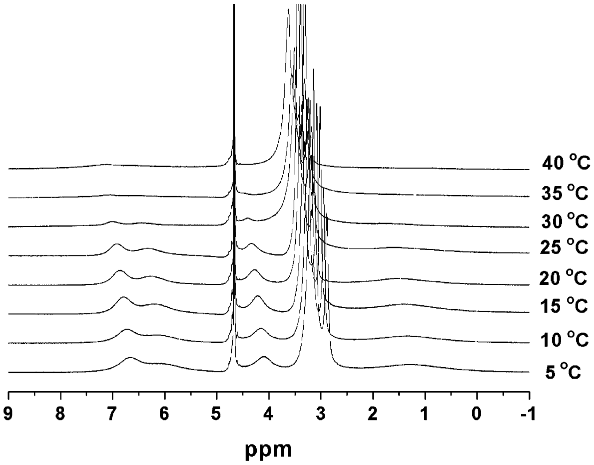


Figure 10. ^{1}H NMR spectra of a diblock copolymer of 4-vinylbenzyl methoxytetrakis(oxyethylene) ether (TrEGSt) and 4-vinylbenzyl methoxytris(oxyethylene) ether (TEGSt) (sample no. 2 in Table 2, PTrEGSt$_{44}$-*b*-PTEGSt$_{51}$, number-average molecular weight = 18 500, polydispersity index = 1.12) in D_2O (1.0%) at various temperatures.

four diblock copolymers. These observations imply that the cloud points of diblock copolymers in water were determined by both blocks. A further investigation is underway.

The transition points of the diblock copolymers in water were also compared with those of the mixtures of the two corresponding homopolymers. An aqueous solution of a mixture of PTrEGSt (M_n = 22 400 g/mol) and PTEGSt (M_n = 13 600 g/mol) with the same molar ratio as in PTrEGSt$_{44}$-*b*-PTEGSt$_{51}$ was made, and the concentration was 1%. The cloud point of this mixed polymer solution was found to be 15 °C, close to the cloud point of this particular PTEGSt (M_n = 13 600 g/mol) with a similar concentration (0.55%) as in the mixture (14 °C). The difference was 1 °C. On the other hand, the difference between the cloud points of PTrEGSt$_{44}$-*b*-PTEGSt$_{51}$ and PTEGSt is $>$10 °C. We also found that the transition point of a mixture of PPEGSt (M_n = 12 900 g/mol) and PTrEGSt (M_n = 22 400 g/mol) in water (1.0%) with the similar molar ratio as in PPEGSt$_{41}$-*b*-PTrEGSt$_{81}$ (sample no. 5 in Table 2) was at 41 °C, only 1 °C difference from the cloud point of this particular PTrEGSt with a concentration of 0.67% (w/w) in water (40 °C). These observations further confirmed that our polymers from block copolymerizations were predominantly diblock copolymers, although some dead homopolymer chains were present from GPC analysis. We are currently using dynamic light scattering to study how the diblock copolymers respond to the temperature change in aqueous solutions.

Conclusions

We successfully synthesized thermosensitive water-soluble polymers of *p*-methoxyoligo(ethylene glycol)-substituted styrenes with controlled molecular weights and narrow molecular weight distributions by nitroxide-mediated radical polymerization using a second-generation initiator along with free nitroxide. Kinetics study and GPC analysis showed that the polymerizations were living producing well-controlled polymer structures. The thermoresponsive properties of three homopolymers in aqueous solutions were studied by cloud point measurements and variable temperature ^{1}H NMR spectroscopy. The cloud points of PTEGSt, PTrEGSt, and PPEGSt in aqueous solutions were ~13, 39, and 55 °C, which were confirmed by variable temperature ^{1}H NMR spectroscopy analysis. The living polymerizations of the three monomers allowed the synthesis of diblock copolymers. GPC analysis showed that the molecular weight distribution remained narrow ($<$1.15). Cloud point measurements and ^{1}H NMR analysis indicated that the diblock copolymers undergo a phase transition in water at a temperature between the cloud points of the two corresponding homopolymers.

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References and Notes

(1) Gil, E. S.; Hudson, S. M. *Prog. Polym. Sci.* **2004**, *29*, 1173−1222.
(2) Nath, N.; Chilkoti, A. *Adv. Mater.* **2002**, *14*, 1243−1247.
(3) Kushida, A.; Yamato, M.; Konno, C.; Kikuchi, A.; Sakurai, Y.; Okano, T. *J. Biomed. Mater. Res.* **1999**, *45*, 355−362.
(4) Langer, R. *Nature (London)* **1998**, *392*, 5−10 (suppl).
(5) Chen, G. H.; Hoffman, A. S. *Nature (London)* **1995**, *373*, 49−52.
(6) Sakiyama-Elbert, S. E.; Hubbell, J. A. *Annu. Rev. Mater. Res.* **2001**, *31*, 183−201.
(7) Kanazawa, H.; Matsushima, Y.; Okano, T. *Adv. Chromatogr.* **2001**, *41*, 311−336.
(8) Han, S.; Hagiwara, M.; Ishizone, T. *Macromolecules* **2003**, *36*, 8312−8319.
(9) Sugihara, S.; Kanaoka, S.; Aoshima, S. *Macromolecules* **2005**, *38*, 1919−1927.
(10) Aoshima, S.; Sugihara, S.; Shibayama, M.; Kanaoka, S. *Macromol. Symp.* **2004**, *215*, 151−163.
(11) Sugihara, S.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 2601−2611.
(12) Aoshima, S.; Sugihara, S. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 3962−3965.
(13) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921−2990.
(14) Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661−3688.
(15) Bosman, A. W.; Vestberg, R.; Heumann, A.; Fréchet, J. M. J.; Hawker, C. J. *J. Am. Chem. Soc.* **2002**, *125*, 715−728.
(16) Benoit, D.; Chaplinski, V.; Braslau, R.; Hawker, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3904−3920.
(17) Sessions, L. B.; Miinea, L. A.; Ericson, K. D.; Glueck, D. S.; Grubbs, R. H. *Macromolecules* **2005**, *38*, 2116−2121.
(18) He, T.; Li, D. J.; Sheng, X.; Zhao, B. *Macromolecules* **2004**, *37*, 3128−3135.
(19) Zhao, B.; He, T. *Macromolecules* **2003**, *36*, 8599−8602.
(20) Zhao, B.; Haasch, R. T.; MacLaren, S. *J. Am. Chem. Soc.* **2004**, *126*, 6124−6134.
(21) Li, D. J.; Sheng, X.; Zhao, B. *J. Am. Chem. Soc.* **2005**, *127*, 6248−6256.
(22) Ding, S.; Radosz, M.; Shen, Y. *Macromol. Rapid Commun.* **2004**, *25*, 632−636.
(23) Ali, M. M.; Stöver, H. D. H. *Macromolecules* **2004**, *37*, 5219−5227.
(24) Xia, Y.; Yin, X.; Burke, N. A. D.; Stöver, H. D. H. *Macromolecules* **2005**, *38*, 5937−5943.
(25) Arotcarena, M.; Heise, B.; Ishaya, S.; Laschewsky, A. *J. Am. Chem. Soc.* **2002**, *124*, 3787−3793.
(26) Huang, J.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 3577−3583.
(27) Wang, X. S.; Ames, S. P. *Macromolecules* **2000**, *33*, 6640−6647.
(28) Li, Y.; Narain, R.; Ma, Y.; Lewis, A. L.; Armes, S. P. *Chem. Commun.* **2004**, 2746−2747.
(29) Perruchot, C.; Khan, M. A.; Kamitsi, A.; Armes, S. P. *Langmuir* **2001**, *17*, 4479−4481.
(30) Donovan, M. S.; Sanford, T. A.; Lowe, A. B.; Sumerlin, B. S.; Mitsukami, Y.; McCormick, C. L. *Macromolecules* **2002**, *35*, 4570−4572.
(31) Convertine, A. J.; Ayres, N.; Scales, C. W.; Lowe, A. B.; McCormick, C. L. *Biomacromolecules* **2004**, *5*, 1177−1180.
(32) Ayres, L.; Vos, M. R. J.; Adams, P. J. H. M.; Shklyarevskiy, I. O.; van Hest, J. C. M. *Macromolecules* **2003**, *36*, 5967−5973.
(33) Maeda, Y.; Mochiduki, H.; Ikeda, I. *Macromol. Rapid Commun.* **2004**, *25*, 1330−1334.
(34) Schilli, C. M.; Zhang, M.; Rizzardo, E.; Thang, S. H.; Chong, Y. K.; Edwards, K.; Karlsson, G.; Müller, A. H. E. *Macromolecules* **2004**, *37*, 7861−7866.
(35) Kros, A.; Gerritsen, M.; Murk, J.; Jansen, J. A.; Sommerdijk, N. A. J. M.; Nolte, R. J. M. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 468−474.
(36) Andruzzi, L.; Senaratne, W.; Hexemer, A.; Sheets, E. D.; Ilic, B.; Kramer, E. J.; Baird, B.; Ober, C. K. *Langmuir* **2005**, *21*, 2495−2504.
(37) Lauter, U.; Meyer, W. H.; Wegner, G. *Macromolecules* **1997**, *30*, 2092−2101.

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