Heat-Induced Association and Dissociation Behavior of Amphiphilic Diblock Copolymers Synthesized via Reversible Addition−Fragmentation Chain Transfer Radical Polymerization

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ABSTRACT: A water-soluble diblock copolymer was prepared from sodium 2-(acrylamido)-2-methylpropanesulfonate (NaAMPS) and *N*-isopropylacrylamide (NIPAM) via reversible addition−fragmentation chain transfer (RAFT) controlled radical polymerization. The RAFT "living" radical polymerization process of NIPAM using an NaAMPS-based macrochain transfer agent was confirmed by the fact that the number-average molecular weight increased linearly with monomer consumption while the molecular weight distribution remained to be narrow for the polymerization. The NIPAM block exhibited a lower critical solution temperature (LCST) in water. Both the NaAMPS and NIPAM blocks are soluble in water at room temperature. At temperatures above the LCST, the NIPAM blocks associated into a polymer aggregate. The polymer aggregate was assumed to be an elongated micelle or a multiple aggregate due to intermicellar association of the spherical core−corona micelles based on characterization data obtained from ^{1}H NMR, turbidity, light scattering, and fluorescence probe experiments. A hydrophobic compound such as 8-anilino-1-naphthalenesulfonic acid, ammonium salt hydrate (ANS), was incorporated into the hydrophobic aggregate of the NIPAM blocks above LCST and released from the aggregate when temperature was reduced below LCST. The capture and release of ANS triggered by temperature change were completely reversible.

Introduction

Controlled radical polymerization has been the subject of continued interest for the past decade because it allows one to synthesize block copolymers of well-controlled block lengths with a wide range of monomer selection.[1−3] Controlled radical polymerization techniques including atom transfer radical polymerization (ATRP),[4−6] nitroxide radical mediated radical polymerization,[7,8] and reversible addition−fragmentation chain transfer (RAFT) radical polymerization[9−13] have been extensively studied and found to be useful in the synthesis of block copolymers with controlled molecular weight and narrow molecular weight distribution. The RAFT process has a distinct advantage over the other controlled radical polymerization processes in that it can be used for a wide range of monomers that can be polymerized in a wide range of solvents including water. Indeed, the RAFT process can be applied to the polymerization of many water-soluble monomers such as sodium 2-(acrylamido)-2-methylpropanesulfonate (NaAMPS),[14] sodium 4-styrenesulfonate,[15] (*ar*-vinylbenzyl)trimethylammonium chloride,[15] *N,N*-dimethylacrylamide,[16] and *N*-isopropylacrylamide (NIPAM).[17−21] Recently, Lowe and McCormick[22] have reviewed the ability of controlled radical polymerizations in homogeneous aqueous media regarding the RAFT process.

Aqueous solutions of PNIPAM undergo a thermally reversible phase separation.[23] PNIPAM dissolves in water to form coils at room temperature, but it separates from aqueous solutions when heated to 31−32 °C, which is the lower critical solution temperature (LCST). Feijen et al.[24] and Zhu et al.[25] have reported the synthesis and aggregation behavior of block copolymers of NIPAM and poly(ethylene oxide) (PEO). The synthesis of block copolymers of NIPAM and PEO (PNIPAM-*b*-PEO) was carried out using a redox system consisting of ceric ion and PEO.[26] LCST for PNIPAM-*b*-PEO is 30−31 °C, and the block copolymers form micelles in water. Laschewsky et al.[27] have reported the synthesis of block copolymers of NIPAM and 3-[*N*-(3-methacrylamidopropyl)-*N,N*-dimethyl]ammoniopropanesulfonate (SPP) by the RAFT process. The NIPAM and SPP blocks exhibit an LCST and an upper critical solution temperature (UCST), respectively. Therefore, both the NIPAM and SPP blocks in these copolymers are soluble in water at intermediate temperatures, whereas the NIPAM blocks form hydrophobic aggregates at high temperatures and the SPP blocks form aggregates at low temperatures. These thermal stimulus-responsive block copolymers have attracted considerable interest because of their potential ability to encapsulate and transport various kinds of materials.[28,29]

Here, we report the controlled synthesis of a diblock copolymer of NaAMPS and NIPAM (pNaAMPS−NIPAM) (Chart 1) by the RAFT process using the NaAMPS macro-chain transfer agent. The diblock copolymer exhibits heat induced self-association due to selective

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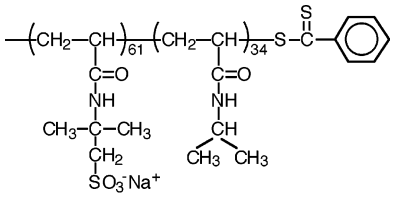
Chart 1. Diblock Copolymer Used in This Study



pNaAMPS–NIPAM

dehydration of the NIPAM blocks above LCST. We mainly focus on the thermoresponsive association behavior of the diblock copolymer in aqueous solutions as characterized by ^{1}H NMR, turbidity, light scattering, and fluorescence probe techniques.

Experimental Section

Materials. 4-Cyanopentanoic acid dithiobenzoate used as a chain transfer agent (CTA) was synthesized according to the method reported by McCormick and co-workers.[15] Methanol was dried over 4 Å molecular sieves and distilled. *N*-Isopropylacrylamide (NIPAM) (97%) from Aldrich was purified by recrystallization from a mixture of benzene and *n*-hexane (3/7, v/v). 2-(Acrylamido)-2-methylpropanesulfonic acid (98%) from Tokyo Kasei Kogyo Co., 4,4′-azobis(4-cyanopentanoic acid) (75%) from Aldrich, and 8-anilino-1-naphthalenesulfonic acid, ammonium salt hydrate (ANS) (97%) from Aldrich were used as received without further purification. Water was purified with a Millipore Mill-Q system. Other reagents were used as received.

Preparation of Macro-CTA. 2-(Acrylamido)-2-methylpropanesulfonic acid (50.0 g, 242 mmol) was neutralized with NaOH (9.62 g, 242 mmol) in 120 mL of water, and 4-cyanopentanoic acid dithiobenzoate (464 mg, 1.66 mmol) and 4,4′-azobis(4-cyanopentanoic acid) (92.8 mg, 0.332 mmol) were added to this solution. The mixture was degassed by purging with Ar gas for 30 min. Polymerization was carried out at 70 °C for 4 h. The polymer was dialyzed against pure water for a week, changing the water twice a day, and recovered by a freeze-drying technique. The obtained polymer (42.1 g, 84.2% conversion) could be used as a macro-CTA. ^{1}H NMR (500 MHz, D_2O): δ 1.30−1.91 (br, 8H, CH_2CH, CH_3), 1.91−2.38 (br, 1H, CH_2C*H*), 3.09−3.63 (br, 2H, CCH_2). $M_n = 1.39 \times 10^4$; $M_w/M_n = 1.28$ (GPC).

Preparation of Diblock Copolymer. Sodium 2-(acrylamido)-2-methylpropanesulfonate (NaAMPS) macro-CTA (4.50 g, 0.324 mmol), NIPAM (2.15 g, 19.0 mmol), and 4,4′-azobis(4-cyanopentanoic acid) (13.8 mg, 0.0490 mmol) were dissolved in a 38 mL mixed solvent of methanol and water (8/2, v/v). The solution was deoxygenated by purging with Ar gas for 30 min. Block copolymerization was carried out at 70 °C for 4 h. The diblock copolymer was purified by dialysis against pure water for a week, changing the water twice a day. The diblock copolymer was recovered by a freeze-drying technique (5.36 g, 39.8% conversion). $M_n = 4.09 \times 10^4$ (SLS); $M_w/M_n = 1.27$ (GPC).

To monitor the extent of polymerization of NIPAM using NaAMPS macro-CTA, predetermined amounts of NaAMPS macro-CTA, NIPAM, and initiator were dissolved in a mixed solvent of methanol-d_4 and D_2O (8/2, v/v). The solutions were added to NMR tubes and degassed by purging with Ar gas for 30 min. The cap was sealed and tubes placed in the temperature equipped probe (70 °C) of the NMR spectrometer. Proton NMR and gel permeation chromatography (GPC) for the reaction mixture were measured to estimate the conversion and molecular weight, respectively.

Measurements. ^{1}H NMR. Proton NMR spectra were obtained with a Bruker DRX-500 spectrometer operating at 500 MHz. Chemical shifts were determined by using 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid, sodium salt, as an internal reference.

GPC. GPC analysis was performed with a JASCO GPC-900 equipped with a Shodex 7.0 μm bead size GF-7M HQ column (molecular weight range of 10^7−10^2) using a 0.2 M $LiClO_4$ methanol solution as an eluent at a flow rate of 0.6 mL/min at 40 °C and a refractive index (RI) detector. The number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) for the sample polymers were calibrated with standard poly(ethylene oxide) samples.

Thin-Layer Chromatography (TLC). TLC experiments were performed with silica gel 60 F_{254} TLC plates (Merck) at room temperature using ethyl acetate/methanol (7/3, v/v) as eluent. Methanol solutions of the polymers were spotted at the TLC plate.

Percent Transmittance (%*T*). %*T* of 0.1 M NaCl aqueous solutions for the diblock copolymer was recorded on a Hitachi U-1500 spectrophotometer with a 1.0 cm path length quartz cell at various temperatures.

Quasi-Elastic Light Scattering (QELS). QELS data were obtained with an Otsuka Electronics Photal DLS-7000DL light scattering spectrometer equipped with an ALV-5000E multi-τ digital time correlator at various temperatures. An Ar^+ laser (30.0 mW at 488 nm) was used as a light source. Sample solutions were filtered with a 0.2 μm pore size PTFE membrane filter prior to measurements. The solutions were permitted to stand for at least 10 min at a constant temperature. The intensity−intensity time correlation function $g^{(2)}(t)$ in the self-beating mode was measured, and $g^{(2)}(t)$ is related to the normalized autocorrelation function of the scattered electric field $g^{(1)}(t)$:

$$g^{(2)}(t) = B(1 + \beta|g^{(1)}(t)|^2) \tag{1}$$

where B is a baseline, β is a factor which takes into account deviations from ideal correlation, and t is the delay time. To obtain $\tau A(\tau)$, the inverse Laplace transform (ILT) analysis was performed using a constrained regularization routine, REPES.[30,31]

$$g^{(1)}(t) = \int \tau A(\tau) \exp(-t/\tau)\, \mathrm{d} \ln \tau \tag{2}$$

Here, τ is the relaxation time. The average diffusion coefficient ($\langle D \rangle$) is calculated from $\langle D \rangle = \langle \Gamma \rangle / q^2$, where Γ (= $1/\tau$) is the relaxation rate and q is the scattering vector. The symbol "$\langle\ \rangle$" means an average value. The q value is calculated from $q = (4\pi n/\lambda) \sin(\theta/2)$, where n is the refractive index of the solvent, λ is the wavelength (= 488 nm), and θ is the scattering angle fixed at 90°. The intensity-average hydrodynamic radius ($\langle R_h \rangle$) is calculated using the Einstein−Stokes relation $\langle R_h \rangle = k_B T / 6\pi\eta\langle D \rangle$, where k_B is Boltzmann's constant, T is the absolute temperature, and η is the solvent viscosity.

Static Light Scattering (SLS). SLS measurements were performed with an Otsuka Electronics Photal DLS-7000DL light scattering spectrometer equipped with an Ar^+ laser (30.0 mW at 488 nm). Weight-average molecular weight (M_w), z-average radius of gyration (R_g), and the second virial coefficient (A_2) values were estimated from the relation[32]

$$\frac{KC_p}{R_\theta} = \frac{1}{M_w}\left(1 + \frac{1}{3}\langle R_g^2 \rangle q^2\right) + 2A_2 C_p \tag{3}$$

where C_p is the polymer concentration, R_θ is the reduced Rayleigh ratio, and $K = 4\pi^2 n^2 (\mathrm{d}n/\mathrm{d}C_p)^2 / N_A \lambda^4$ with $\mathrm{d}n/\mathrm{d}C_p$ being the refractive index increment against C_p and N_A being Avogadro's number. Values of $\mathrm{d}n/\mathrm{d}C_p$ were determined with an Otsuka Electronics Photal DRM-1020 differential refractometer at a wavelength of 488 nm.

Fluorescence. Steady-state fluorescence spectra were recorded on a Hitachi F-2500 fluorescence spectrophotometer at various temperatures. Fluorescence emission spectra of ANS were measured with excitation at 350 nm. The slit widths for the excitation and emission side were kept at 20 and 5.0 nm, respectively, during measurement. Sample solutions were

Table 1. Characteristic Data of the Diblock Copolymer

	DP_n of NaAMPS block[a]	DP_n of NIPAM block[b]	M_w[c] $\times 10^{-4}$	R_g[c] (nm)	$A_2 \times 10^4$ [c] (mol mL g^{-2})	M_w/M_n[a]	LCST[d] (°C)
PNaAMPS−NIPAM	61	34	4.09	10.3	9.72	1.27	35

[a] Determined from GPC. [b] Estimated by ^{1}H NMR. [c] Determined by static light scattering (SLS) in 0.1 M NaCl aqueous solutions at 25 °C. [d] Lower critical solution temperature (LCST) in 0.1 M NaCl aqueous solution was determined by % transmittance, where the diblock copolymer concentration is 5.0 g/L.

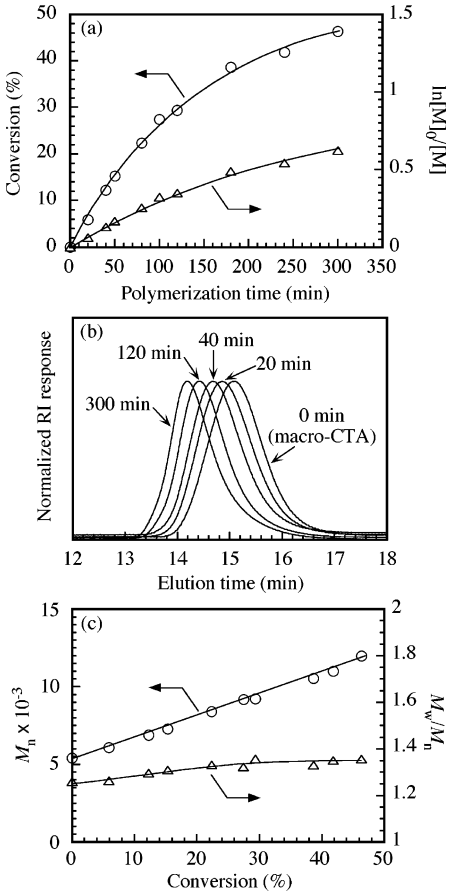


Figure 1. (a) Time−conversion (circles) and the first-order kinetic plots (triangles) for the polymerization of *N*-isopropylacrylamide (NIPAM) (0.50 M) in the presence of sodium 2-(acrylamido)-2-methylpropanesulfonate macro-chain transfer agent (NaAMPS macro-CTA) (8.5 mM) in a mixed solvent of methanol-d_4 and D_2O (8/2, v/v) at 70 °C under an inert atmosphere. (b) GPC elution curves demonstrating evolution of molecular weight during the synthesis of [poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)-*block*-poly(*N*-isopropylacrylamide)] using NaAMPS macro-CTA and NIPAM. Polymerization times are shown for each peak. (c) Dependence of number-average molecular weight (M_n) (circles) and molecular weight distribution (M_w/M_n) (triangles) on the monomer conversion in the polymerization of NIPAM (0.50 M) in the presence of NaAMPS macro-CTA (8.5 mM) in a mixed solvent of methanol-d_4 and D_2O (8/2, v/v) at 70 °C under an inert atmosphere.

prepared by dissolving the polymer in 0.1 M NaCl aqueous solutions of ANS (0.02 mM).

Results and Discussion

Synthesis of the NaAMPS−NIPAM Diblock Copolymer. Figure 1a exhibits a time−conversion relationship along with the pseudo-first-order kinetic plot for the polymerization of NIPAM in the presence of NaAMPS macro-CTA and 4,4′-azobis(4-cyanopentanoic acid) at 70 °C under an Ar atmosphere. A mixed solvent of methanol-d_4 and D_2O (8/2, v/v) was used for the polymerization to obtain a homogeneous polymerization solution. The polymerization mixture was subjected to NMR measurements as a function of polymerization time to obtain the time−conversion curve. Values of M_n and M_w/M_n for the NaAMPS macro-CTA used were predetermined to be 5.40×10^3 relative to standard poly(ethylene oxide) and 1.26, respectively, by GPC using a 0.2 M $LiClO_4$ methanol solution as eluent. The pseudo-first-order kinetic plot is consistent with a "living" polymerization mechanism over the first 100 min; the concentration of active propagating radical species remains nearly constant during this part of the polymerization. Beyond 100 min, downward curvature is observed, which may indicate a decrease in the concentration of propagating radicals. As can be seen from GPC data shown in Figure 1b, the molecular weight of the polymer yielded increases progressively with polymerization time. The GPC elution profiles are unimodal with no indication of the presence of lower molecular weight NIPAM homopolymer newly formed.

Figure 1c plots M_n and M_w/M_n for the polymers obtained by RAFT polymerization of NIPAM in the presence of NaAMPS macro-CTA as a function of the conversion of the NIPAM monomer. The M_n and M_w/M_n values and the monomer conversion were estimated from GPC and ^{1}H NMR, respectively. However, the M_n values estimated by GPC are only apparent values mainly because PEO, an uncharged polymer with no bulky side chain, was used as standard for molecular weight calibration. The increase in the apparent M_n with conversion is practically linear with the M_w/M_n values being in a somewhat narrow range of 1.25−1.35 nearly independent of the conversion. These observations indicate that the polymerization is reasonably well controlled as "living" in nature.

To investigate heat-induced association behavior of the diblock copolymer, an NaAMPS macro-CTA of $M_n = 1.39 \times 10^4$ and $M_w/M_n = 1.28$ was used to synthesize a diblock copolymer of NaAMPS and NIPAM (pNaAMPS−NIPAM) (Chart 1). The number-average degrees of polymerization (DP_n) of the NaAMPS and NIPAM blocks are 61 and 34, respectively, calculated from GPC and ^{1}H NMR data listed in Table 1. On the basis of GPC and thin-layer chromatography (TLC) data,[33] it was confirmed that no NIPAM homopolymer coexists with pNaAMPS−NIPAM. The GPC elution profile of pNaAMPS−NIPAM was unimodal with no indication of the presence of higher or lower molecular weight NIPAM homopolymer. In TLC, rate of flow (R_f) values for NaAMPS macro-CTA and NIPAM homopolymer were confirmed to be 0 and 0.83, respectively, in a separate experiment. The sample of pNaAMPS−NIPAM showed only one spot at $R_f = 0.78$ with no sign of spots existing at $R_f = 0$ and 0.83.

^{1}H NMR. Heat-induced association of pNaAMPS−NIPAM was observed in ^{1}H NMR spectra measured at different temperatures in D_2O containing 0.1 M NaCl. Figure 2 compares the ^{1}H NMR spectra of pNaAMPS−NIPAM measured at 25 and 60 °C. The HOD resonance peak shifts to higher fields at elevated temperatures as

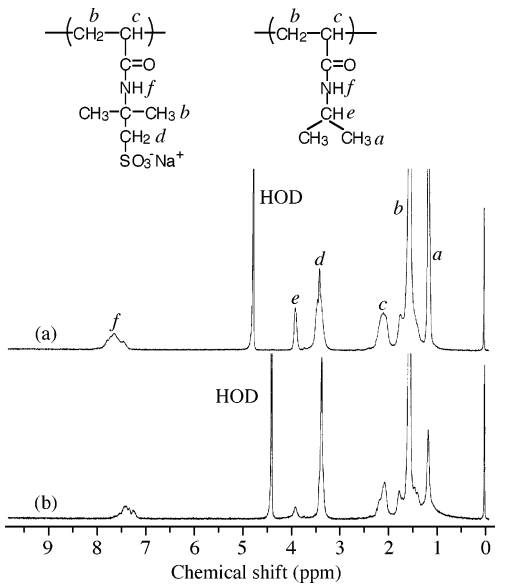


Figure 2. Comparison of 500 MHz ^{1}H NMR spectra of [poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)-*block*-poly(*N*-isopropylacrylamide)] ($M_w = 4.09 \times 10^4$ (SLS), $M_w/M_n = 1.27$ (GPC)) in D_2O containing 0.1 M NaCl at 25 (a) and 60 °C (b), where the block copolymer concentration is 5.0 g/L.

reported by Gottlieb and co-workers.[34] The resonance bands in the 1.28−2.38 ppm region, observed at 25 °C, are attributed to the sum of the main chain protons and the methyl protons in the NaAMPS unit. The side-chain methylene protons in the NaAMPS unit are observed at 3.41 ppm. The resonance peaks at 1.16 and 3.91 ppm are attributed to the methyl and methine protons, respectively in the pendent isopropyl group in the NIPAM unit. The bands around 7.4 ppm are assigned to amide protons. The composition of the diblock copolymer was determined from the intensity ratio of the resonance bands due to the methylene protons in the side chain of the NaAMPS unit at 3.41 ppm and the methine protons in the side chain of the NIPAM unit at 3.91 ppm in D_2O at 25 °C. An important observation is that the intensities of the resonance peaks due to the isopropyl protons in the NIPAM unit (1.16 and 3.91 ppm) relative to the intensity of the peak due to the side chain methylene protons in the NaAMPS unit (3.41 ppm) are considerably lower at 60 °C than at 25 °C. These observations are indicative of restricted motions of the NIPAM block at an elevated temperature of 60 °C, a temperature higher than LCST for PNIPAM.

Figure 3 plots the peak intensities for the methyl protons in the NIPAM side chain (1.16 ppm) and AMPS side chain (1.55 ppm) in the diblock copolymer at a constant polymer concentration (C_p) of 5.0 g/L in D_2O containing 0.1 M NaCl against temperature. The peak intensities are normalized with the peak intensity at 25 °C. When the temperature is increased from 21 °C, the normalized peak intensity for the AMPS block increases gradually and then saturates or turns slightly to decrease at a temperature near 44 °C. The increase in the intensity for the AMPS block at ≤44 °C should be due to an increase in the motion of the AMPS block with increasing temperature. On the other hand, the normalized peak intensities for the NIPAM side chain are practically constant below 35 °C, but the intensity starts to decrease slightly with increasing temperature from 35 to 44 °C, followed by a rapid decrease above 44 °C, reaching a small value of ca. 0.25 at 60 °C. The decrease in the peak intensity for the methyl protons

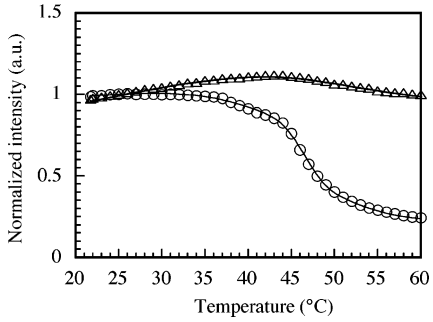


Figure 3. Plots of the intensities of 500 MHz ^{1}H NMR peaks at 1.16 (circles) and 1.55 ppm (triangles) normalized to the intensity at 25 °C for [poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)-*block*-poly(*N*-isopropylacrylamide)] in D_2O containing 0.1 M NaCl as a function of temperature, where the block copolymer concentration is 5.0 g/L.

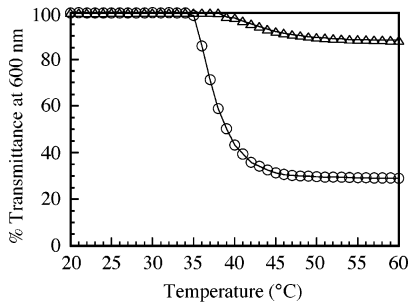


Figure 4. Percent transmittance (%*T*) at 600 nm for 0.1 M NaCl aqueous solutions of [poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)-*block*-poly(*N*-isopropylacrylamide)] at 5.0 (circles) and 1.0 g/L (triangles) as a function of temperature.

of *N*-isopropyl groups above 35 °C indicates a restricted motion of the NIPAM block at temperatures > LCST. Above 44 °C, the mobility for the NIPAM block is more restricted because of the collapse of the NIPAM block.

Changes in Transmittance of Aqueous Solutions. The diblock copolymer is completely soluble in 0.1 M NaCl aqueous solutions at 25 °C and exhibits an LCST which is markedly dependent on C_p. As shown in Figure 4, the %*T* (transmittance) values for 0.1 M NaCl aqueous solutions of the diblock copolymer at $C_p = 1.0$ and 5.0 g/L are practically 100% at temperatures below 39 and 35 °C, respectively. The %*T* values at $C_p = 1.0$ and 5.0 g/L decrease with increasing temperature, reaching small values of 86% at >50 °C and 25% at >45 °C, respectively. It is apparent that the LCST values increase with decreasing polymer concentration. Turbid solutions above LCST become clear again when the solutions are cooled below LCST. The presence of LCST indicates a collapse of the NIPAM block in the diblock copolymer above LCST in 0.1 M NaCl aqueous solution. The LCST value at $C_p = 5.0$ g/L estimated from a break in the %*T* vs temperature plot (Figure 4) is given in Table 1.

Light Scattering. Intermolecular self-association of the diblock copolymer in 0.1 M NaCl aqueous solution was evidenced by light scattering data. Figure 5 compares QELS relaxation time distributions for pNaAMPS−NIPAM at $C_p = 5.0$ g/L observed at different temperatures. The QELS measurement was performed with a sample solution after allowing it to stand for at least 10 min at each temperature. The unimodal relaxation peak at 25 °C (Figure 5a) is attributed to a single polymer chain, i.e., a unimer with an intensity-average hydrodynamic radius ($\langle R_h \rangle$) of 5.8 nm. When tempera-

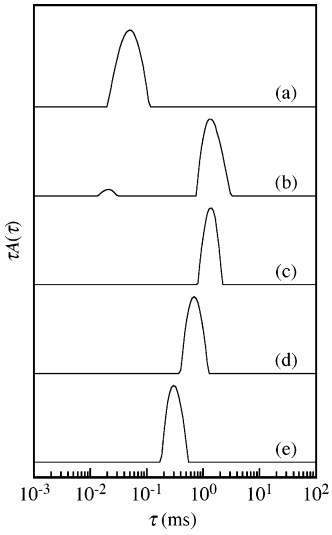


Figure 5. Typical examples of quasi-elastic light scattering (QELS) relaxation time distributions for [poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)-*block*-poly(*N*-isopropylacrylamide)] at 5.0 g/L in 0.1 M NaCl aqueous solutions at 25 (a), 36 (b), 38 (c), 50 (d), and 60 °C (e), where the scattering angle is 90°.

ture is raised to 36 °C, a temperature higher than LCST observed from a change in solution transmittance (Figure 4), a bimodal distribution with a small peak due to a fast mode and a much larger peak due to a slow mode was observed. The fast relaxation mode may be attributed to a unimer state of the diblock copolymers and the slow mode to multipolymer aggregates formed from hydrophobic associations of the NIPAM blocks. When the temperature is increased to 38 °C or higher, the fast mode peak disappears completely while the slow mode peak remains as a single component. The peak for the slow mode shifts toward faster relaxation times with increasing temperature above 38 °C. These observations suggest that the aggregate of the NIPAM blocks becomes more compact at higher temperatures. It was confirmed that the relaxation time distribution remained the same after the sample solution was kept at 60 °C for 12 h.

Figure 6a plots $\langle R_h \rangle$ of the diblock copolymer at C_p = 1.0 and 5.0 g/L in 0.1 M NaCl aqueous solutions against temperature. Below LCST, the diblock copolymer is dissolved molecularly in water with an $\langle R_h \rangle$ of approximately 4.8−6.3 nm. As temperature is increased at C_p = 5.0 g/L, the $\langle R_h \rangle$ value starts to increase abruptly at a temperature of 34 °C, reaching a maximum value of 350 nm at 37 °C, and then rapidly decreases, reaching a value of ca. 90 nm at 60 °C. These observations suggest two possibilities: (i) the aggregate of the NIPAM blocks becomes more compact due to further dehydration of the NIPAM blocks as the temperature is further increased beyond LCST, and (ii) the aggregation number of the multipolymer aggregate decreases with increasing temperature. As temperature is increased at C_p = 1.0 g/L, the $\langle R_h \rangle$ value starts to increase at >40 °C, reaching a value of ca. 90 nm at 60 °C. The $\langle R_h \rangle$ values at C_p = 1.0 and 5.0 g/L are almost the same at 60 °C, which indicates the $\langle R_h \rangle$ value is independent of the polymer concentration at 60 °C.

Values of M_w, R_g, and A_2 for a unimer state of the diblock copolymer determined by static light scattering (SLS) in 0.1 M NaCl aqueous solution at 25 °C in the concentration range 1.0−10 g/L are listed in Table 1.

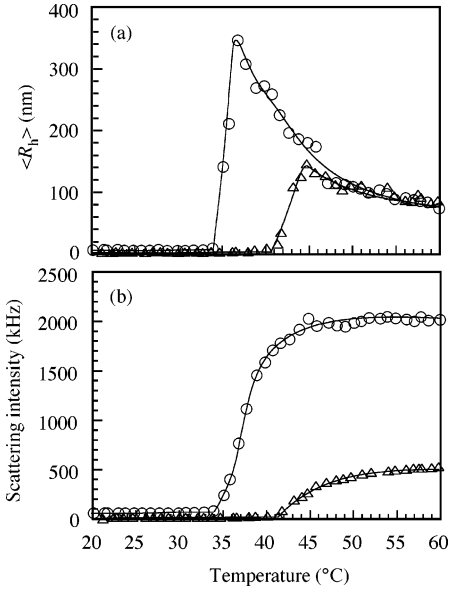


Figure 6. (a) Intensity-average hydrodynamic radius ($\langle R_h \rangle$) and (b) scattering intensity for [poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)-*block*-poly(*N*-isopropylacrylamide)] at 5.0 (circles) and 1.0 g/L (triangles) in 0.1 M NaCl aqueous solutions as a function of temperature, where the scattering angle is 90°.

The value of dn/dC_p for the solution of the diblock copolymer was 0.151 mL/g at 25 °C. Figure 6b plots scattering intensities for the aqueous solution of the diblock copolymer containing 0.1 M NaCl at C_p = 1.0 and 5.0 g/L against temperature. As the temperature is increased, the scattering intensities for pNaAMPS−NIPAM at C_p = 1.0 and 5.0 g/L begin to increase abruptly at 40 and 34 °C, respectively. These temperatures agree well with those at which $\langle R_h \rangle$ starts to increase abruptly (Figure 6a). The abrupt increase in $\langle R_h \rangle$ and scattering intensity at a certain temperature is a manifestation that the diblock copolymers form the multipolymer aggregate at temperatures near LCST or higher while the polymer dissolves molecularly at lower temperatures. Since the polymer solutions are turbid, we were unable to determine apparent M_w for the multipolymer aggregate formed at temperatures above LCST by SLS. The scattering intensity is proportional to M_w because the intensity is linearly related to R_θ/C_p (i.e., $R_\theta/C_p \propto M_w$). Therefore, the observation that the scattering intensities are nearly constant at temperatures above 55 and 44 °C (Figure 6b) suggests that the aggregation numbers of the multipolymer aggregates (N_{agg}) at C_p = 1.0 and 5.0 g/L are practically constant at temperatures above 55 and 44 °C, respectively.

It is expected that pNaAMPS−NIPAM forms a spherical core−corona type micelle with an aggregate of collapsed NIPAM blocks forming a core and charged NaAMPS blocks forming coronas above LCST. Namely, above LCST, dehydrated PNIPAM blocks form a swollen core and the charged NaAMPS blocks form a corona layer. At further elevated temperatures, however, the micelle core becomes more compact due to further dehydration of the NIPAM blocks. According to this model, N_{agg} is constant while $\langle R_h \rangle$ decreases with increasing temperature above LCST. Tenhu et al.[35] reported thermal behavior of PNIPAM grafted with poly(ethylene oxide) (PNIPAM-*g*-PEO) in aqueous solutions. Above LCST, loosely packed aggregates shrink with increasing temperature because the interchain

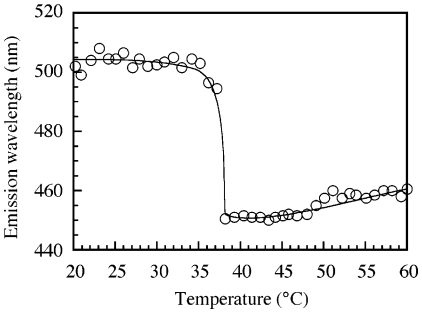


Figure 7. Wavelength of emission maximum in 8-anilino-1-naphthalenesulfonic acid, ammonium salt hydrate (ANS) ([ANS] = 0.02 mM), fluorescence spectra excited at 350 nm in the presence of [poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)-*block*-poly(*N*-isopropylacrylamide)] at 5.0 g/L in 0.1 M NaCl aqueous solutions as a function of temperature.

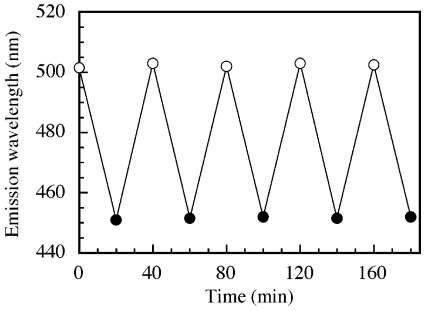


Figure 8. Heat-induced reversible incorporation and release of 8-anilino-1-naphthalenesulfonic acid, ammonium salt hydrate (ANS) ([ANS] = 0.02 mM), by [poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)-*block*-poly(*N*-isopropylacrylamide)] at 5.0 g/L in response to temperature changes for 20 min cycles between 25 (open circles) and 60 °C (closed circles) in 0.1 M NaCl aqueous solution.

aggregation of the PNIPAM chain in PNIPAM-*g*-PEO occurs prior to the intrachain coil-to-globule transition of the PNIPAM chain with a raise in temperature. Similarly, in the case of the pNaAMPS−NIPAM block copolymer, interchain associations of NIPAM block chains may occur prior to the intrachain collapse of the NIPAM block. However, the $\langle R_h \rangle$ value for pNaAMPS−NIPAM at C_p = 5.0 g/L at 37 °C is 350 nm, which is obviously too large for a single spherical core−corona micelle (Figure 6a). These findings suggest that above LCST pNaAMPS−NIPAM may form elongated micelles or multiple aggregates due to intermicellar association of the spherical core−corona micelles.

Fluorescence. ANS is commonly used as a fluorescence probe to investigate molecular assemblies of surfactants and amphiphilic polymers because a blue shift of the emission maximum indicates that the probe is located in less polar media.[36−40] Laschewsky and coworkers[25] have reported that block copolymers of NIPAM and 3-[*N*-(3-methacryloylamidopropyl)-*N*,*N*-dimethyl]-ammoniopropanesulfonate (SPP) form hydrophobic microdomains comprising dehydrated NIPAM blocks which can solubilize a probe such as 2-anilinonaphthalene above LCST.

We confirmed that the emission maximum for ANS in 0.1 M NaCl aqueous solutions in the absence of the diblock copolymer was scarcely influenced by changes in temperature. The emission maxima in the absence of the polymer were 512 and 508 nm at 25 and 60 °C, respectively. Figure 7 shows the emission maximum for ANS fluorescence in the presence of the diblock copolymer plotted against temperature. The maximum wavelength in the presence of pNaAMPS−NIPAM is in the neighborhood of 505 nm at low temperatures (<35 °C), which is practically the same as that for ANS in aqueous solution. As the temperature is increased, the maximum wavelength commences to shift toward shorter wavelengths at 35 °C, reaching a nearly constant wavelength of 450 nm. This observation implies that pNaAMPS−NIPAM is able to incorporate ANS molecules into hydrophobic microdomains formed from the self-association of the NIPAM blocks at high temperatures (>38 °C). QELS data (Figure 6a) indicate that the aggregate of the NIPAM blocks is further dehydrated, and the hydrodynamic size of the multipolymer aggregate becomes smaller with increasing temperature above 37 °C.

When the temperature was increased from 25 to 60 °C and subsequently decreased back to 25 °C, heat-induced fluorescence spectral changes were found to be completely reversible. Figure 8 shows the heat-induced changes of the emission maximum of the ANS fluorescence in 0.1 M NaCl aqueous solution in the presence of pNaAMPS−NIPAM observed at 25 and 60 °C cycled with a 20 min interval. The changes in emission maximum between the two temperatures were completely reproducible, indicating that the capture and release of ANS by a temperature change are reversible over many cycles. These results suggest that the diblock copolymer may find applications as a temperature-responsive controlled capture−release system.

Conclusions

A diblock copolymer of NaAMPS and NIPAM was synthesized via RAFT controlled radical polymerization. The polymerization of NIPAM using an NaAMPS macro-CTA proceeded in a "living" fashion. This was confirmed by the fact that M_n increased linearly with the conversion. The diblock copolymer in 0.1 M NaCl aqueous solutions exhibited an LCST. The NIPAM blocks associated above LCST and formed a multipolymer aggregate. The aggregate was assumed to be an elongated micelle or a multiple aggregate due to intermicellar association of the spherical core−corona micelles on the basis of characterization data from ^{1}H NMR, turbidity, light scattering, and fluorescence probe experiments. The multipolymer aggregate can solubilize hydrophobic molecules, such as ANS, into its hydrophobic aggregate of the NIPAM blocks. The incorporated ANS molecules were released from the hydrophobic aggregate of the NIPAM blocks at temperatures below LCST. The capture and release of ANS by the multipolymer aggregate were triggered by changes in temperature. Further studies of the properties of the diblock copolymers with varying lengths of each block are underway in our laboratory.

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