NOTE

Effects of surfactants on cloud points in aqueous poly(*N*-isopropylacrylamide) solutions

Masashi Osa¹, Hirotada Shiraki¹, Udai Morinaga¹ and Takenao Yoshizaki²

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INTRODUCTION

Poly(*N*-isopropylacrylamide) (PNIPA) has long been attractive to polymer scientists because aqueous solutions of PNIPA exhibit lower-critical-solution-temperature miscibility behavior near the human body temperature and also because PNIPA seems to have potential applications in drug delivery and smart materials. In recent years, it has been reported that the behavior of cloud-point curves for aqueous PNIPA solutions is considerably affected by the kind of chain-end group of the PNIPA sample used and also by the degree of branching of the sample.^{1–5} It is also known that the phase behavior of aqueous PNIPA solutions is influenced by the addition of surfactants.^{6–8} Given that many biomolecules exhibit surfactant behavior, an understanding of the way surfactants affect the phase behavior of the aqueous PNIPA solutions is essential to employing PNIPA in drug delivery.

Schild and Tirrell⁶ have studied the phase behavior of aqueous mixtures of PNIPA and a series of sodium *n*-alkyl sulfates. They have shown that, in aqueous PNIPA solutions, the addition of sodium *n*-dodecyl sulfate (SDS) causes the cloud point to increase relative to its value in aqueous PNIPA solution that does not contain SDS. Having closely studied this phenomenon using calorimetric and fluorescence probe methods, Schild and Tirrell⁶ suggested that the surfactant molecules bind to the PNIPA chains in water in the form of adsorbed micelles and that electrostatic repulsion between the micelles results in the elevation of the cloud point.

The surfactants used by Schild and Tirrell⁶ were limited to anionic varieties. In addition, they used one PNIPA sample having a high-molecular-weight ($>4 \times 10^5$), so that the effects of the chain-end group on the cloud point could not be detected. To investigate the surfactant effects on the cloud point more deeply, it may be valuable to conduct an experiment using low-molecular-weight samples and a cationic surfactant. Thus, in this study, we study the cloud point in aqueous solutions of low-molecular-weight PNIPA samples with additions of anionic SDS and cationic *n*-dodecyltrimethylammonium chloride (DTAC); this experimental setup is designed, to clarify whether the cationic surfactant affects the cloud point in aqueous PNIPA solutions in the same manner as does the anionic surfactant.

Furthermore, we use two low-molecular-weight PNIPA samples with hydrophobic and hydrophilic chain-end groups to examine, the effect of the chain-end group on the behavior of the cloud point.

EXPERIMENTAL PROCEDURE

Materials

The PNIPA sample M6 was the same as that used in our previous study¹ of the cloud points in aqueous solutions; that is, M6 was the fraction separated by fractional precipitation from the original sample, which was synthesized by radical polymerization in methanol, using AIBN (azobisisobutyronitrile) as an initiator. We note that almost all of the initiating and terminating chain ends of the sample M6 are considered to be isobutyronitrile groups derived from AIBN.

A new PNIPA sample, R3, was prepared by aqueous redox polymerization using a redox catalyst consisting of ammonium persulfate, (NH₄)₂S₂O₈ (Nacalai Tesque, Inc., Kyoto, Japan), as the oxidative part, and sodium metabisulfite, Na₂S₂O₅ (Nacalai Tesque, Inc.), as the reductive part; this was consistent with the procedure reported by Wooten *et al.*⁹ The detailed procedure for the polymerization and purification of the sample was the same as that described in our previous paper,⁵ except the present sample was not fractionated. We note that almost all of the initiating chain ends of the sample R3 are considered to be sulfonate groups.⁵ As for the terminating chain-end group of the sample R3, we do not have any detailed information. However, at least, it may be considered that the terminating chain-end group of the sample is not positively charged. For the sample R3, the ratio of the weight-average molecular weight M_w to the number-average molecular weight M_n was determined from analytical gel permeation chromatography with two serially connected columns, SB-805HQ and SB-804HQ (Showa Denko KK, Tokyo, Japan), connected to a solvent delivery pump L-7100 (Hitachi Ltd, Tokyo, Japan) and a refractive index detector RI-930 (JASCO Corporation, Tokyo, Japan); *N,N*-dimethylformamide containing 10 mM lithium bromide at 50 °C was used as an eluent, and 12 standard polystyrene samples (Tosoh Corporation, Tokyo, Japan, $M_w = 550 - 5.46 \times 10^6$) were used as reference standards. For the sample R3, the values of M_w determined from light-scattering (LS) measurements and M_w/M_n are given in Table 1, along with the values previously determined for the sample M6.¹ The chemical structures of SDS and DTAC, and those of the PNIPA samples M6 and R3, are shown in

¹Department of Chemistry, Aichi University of Education, Aichi, Japan and ²Department of Polymer Chemistry, Kyoto University, Kyoto, Japan
Correspondence: Dr M Osa, Department of Chemistry, Aichi University of Education, 1 Hirosawa, Igaya-cho, Kariya, Aichi 448-8542, Japan.
E-mail: mosa@aeu.ac.jp

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Table 1 Values of M_w and M_w/M_n for poly(*N*-isopropylacrylamide)

Sample	M_w	M_w/M_n^a
M6	6.45×10^4	1.19
R3	3.26×10^4	1.51

Abbreviation: GPC, gel permeation chromatography.

^aThe values of M_w/M_n were determined by analytical GPC using standard polystyrene samples as reference standards. **Figure 1** Chemical structures of SDS and DTAC, and the PNIPA samples M6 and R3.

Figure 1. We note that both samples M6 and R3 are atactic.^{1,5} We also note that both samples are considered to have small numbers of branch points.^{1,5}

The surfactants SDS (Wako Pure Chemical Industries, Ltd) and DTAC (Tokyo Chemical Industry Co., Ltd, Tokyo, Japan) that were added into the aqueous PNIPA solutions in the measurements of the cloud point were of reagent grade.

Light scattering

The LS measurement was carried out to determine the M_w for the sample R3 in methanol at 25.0 °C. The apparatus, experimental procedure and data analysis method were the same as those described in the previous papers.^{1–5} For the refractive index increment $\partial n/\partial c$ for R3 in methanol at 25.0 °C and at a wavelength of 436 nm, we used the value $0.186 \text{ cm}^3 \text{ g}^{-1}$.⁵ As for the refractive index n_0 of methanol at 25.0 °C at a wavelength of 436 nm, we used the literature value 1.3337.¹⁰

Transmittance of light

For both samples, M6 and R3, the intensity of light was monitored as it passed through aqueous solutions of the samples, to which SDS or DTAC was added. The PNIPA concentration c_p was chosen to be 10 mg ml^{-1} in all the measurements, and the surfactant concentration c_s was varied between 0 and 6.9 mM ($= 2.0 \text{ mg ml}^{-1}$) for SDS and between 0 and 38 mM ($= 10 \text{ mg ml}^{-1}$) for DTAC. All measurements were carried out using a home-made apparatus, which was constructed previously,^{1,3–5} with an incident light of wavelength 650 nm that was emitted from a laser diode module.

To determine the cloud point in each solution, the temperature of the test solution was increased at a rate of *ca.* 1.5 °C per hour. During continuous temperature elevation from 30 °C to 40 °C, the intensity of light passing through the test solution was monitored by a photodiode. The output of the photodiode, along with the solution temperature measured simultaneously,

Figure 2 Temperature dependence of the (relative) transmittance of light passing through aqueous solutions of the PNIPA sample M6 ($c_p = 10 \text{ mg ml}^{-1}$) with an addition of the surfactants SDS (a) or DTAC (b). The heavy curves represent the values for the solution without surfactant, and the light curves represent those for the solutions with SDS at $c_s = 0.35$, 0.87, 1.7, 3.5 and 6.9 mM or DTAC at $c_s = 3.8$, 27, 30, 34 and 38 mM.

was recorded on a personal computer. Then, the (relative) transmittance, defined as the ratio of the intensity of light through the test solution at a given temperature to the intensity at a lower temperature (for which the test solution is transparent) was determined as a function of temperature.

RESULTS AND DISCUSSION

Figures 2a and b show plots of the (relative) transmittance against temperature for the aqueous solutions of the sample M6 with additions of the surfactants SDS and DTAC, respectively, each at $c_p = 10 \text{ mg ml}^{-1}$. We note that the shape of the transmittance curve for each solution is almost independent of the rate of temperature elevation, for rates lower than 1.5 °C per hour. In these figures, the heavy curves represent the values for the solution without surfactant, and the light curves represent those for the solutions with surfactants at the indicated values of c_s . For the solutions of the sample M6 with SDS shown in Figure 2a, the transmittance curve shifts toward the high-temperature side as c_s is increased for values of $c_s \geq 0.87 \text{ mM}$. As for the solutions of the sample M6 with DTAC, shown in Figure 2b, the transmittance curve is almost independent of c_s for values of $c_s \leq 27 \text{ mM}$ but shifts toward the high-temperature side with increasing c_s for values of $c_s \geq 27 \text{ mM}$. For all the solutions of M6, the transmittance decreases from 100 to 0% with increasing temperature, and no macroscopic precipitate can be observed.

Figures 3a and b show plots of the (relative) transmittance against temperature for the aqueous solutions of the sample R3 with the addition of the surfactants SDS and DTAC, respectively, each at $c_p = 10 \text{ mg ml}^{-1}$. As in Figures 2a and b, the heavy curves represent the values for the solution without surfactant, and the light curves

Figure 3 Temperature dependence of the (relative) transmittance of light passing through aqueous solutions of the PNIPA sample R3 ($c_p = 10 \text{ mg ml}^{-1}$) with an addition of the surfactants SDS (a) or DTAC (b). The heavy curves represent the values for the solution without surfactant, and the light curves represent those for the solutions with SDS at $c_s = 0.35, 0.87, 1.7, 3.5$ and DTAC at $c_s = 0.95, 1.9, 3.8, 11, 30, 34, 38 \text{ mM}$.

represent those for the solutions with surfactants at the indicated values of c_s . For the solutions of the sample R3 with SDS, shown in Figure 3a, the transmittance curve shifts toward the high-temperature side with increasing c_s , as in the case of the sample M6 (Figure 2a), but the decrease in the transmittance for the solutions with SDS is much slower than that for the solution without SDS. In our previous study,⁴ we showed that the decrease in the transmittance in aqueous PNIPA solution arises from the formation of PNIPA aggregates in the solution. Therefore, the above result implies that the aggregation of PNIPA may be suppressed by the addition of SDS for the sample R3. On the other hand, for the solutions of the sample R3 with DTAC, it is seen from Figure 3b that the transmittance curve first shifts toward the low-temperature side with increasing c_s for values of $c_s \lesssim 11 \text{ mM}$ and then shifts toward the high-temperature side for values of $c_s \gtrsim 11 \text{ mM}$. It is interesting to see that the transmittance for the aqueous solutions of R3 with DTAC for values of $c_s \lesssim 11 \text{ mM}$ first decreases from 100% with increasing temperature and then passes through a minimum before finally achieving a finite value for higher temperature. It should be noted that macroscopic precipitates appear in the solutions of R3 with DTAC for values of $c_s \lesssim 11 \text{ mM}$ above the temperature at which the transmittance takes the minimum value, although no macroscopic precipitate can be observed in the other solutions of the sample R3 as in the case of the sample M6.

The cloud point in each solution was then determined as the temperature at which the transmittance becomes 90%, as in our previous studies.^{1,3,5} The cloud points so determined are plotted against c_s in Figure 4. In this figure, the symbols $\circ$ and $\bullet$ represent

Figure 4 Plots of the cloud point in aqueous PNIPA solutions against the concentration c_s of the added surfactants: ($\circ$), the sample M6 with SDS; ($\bullet$), the sample M6 with DTAC; (Δ), the sample R3 with SDS; ($\blacktriangle$), the sample R3 with DTAC. In all solutions, the concentration c_p of the PNIPA samples is 10 mg ml^{-1} . The solid curves connect smoothly the respective data points. The dotted curve represents the literature data for aqueous PNIPA solutions with SDS reported by Schild and Tirrell.⁶

the values for the sample M6 with SDS and DTAC, respectively, and the symbols Δ and $\blacktriangle$ represent those for the sample R3 with SDS and DTAC, respectively. The solid curves smoothly connect the respective data points. The cloud point in the aqueous solution of R3 without surfactant is higher than that of M6 because the hydrophilicity of the chain-end group is stronger for the former than for the latter, as pointed out in our previous study.⁵ For comparison, the literature data (as reported by Schild and Tirrell⁶) for aqueous PNIPA solutions with an addition of SDS are also shown in the figure by the dotted curve. We note that the PNIPA sample used by Schild and Tirrell was prepared by radical polymerization in benzene with AIBN as an initiator and its molecular weight ($M_w = 4.4 \times 10^5$, $M_n = 1.6 \times 10^5$) is appreciably larger than those of our samples. We also note that Schild and Tirrell determined the cloud point by monitoring scattered light intensity from 0.40 mg ml^{-1} solutions of PNIPA at a scattering angle of 90° .

As expected from the results shown in Figures 2a and 3a, the cloud points in the solutions with additions of SDS ($\circ$ and Δ) increase monotonically with increasing c_s , as in the case of the literature data produced by Schild and Tirrell.⁶ As suggested by Schild and Tirrell,⁶ the monotonic elevation of the cloud point with increasing values of c_s in the solutions containing SDS results from the electrostatic repulsion between negatively charged PNIPA-SDS micelles that are formed by the binding of the SDS molecules to the PNIPA chain in water. This electrostatic repulsion suppresses the aggregation of the PNIPA chains. On the other hand, the cloud point is almost independent of c_s in the solutions of M6 with DTAC ($\bullet$) for

values of $c_s \lesssim 27$ mM and then increases with increasing c_s for values of $c_s \gtrsim 27$ mM. These results indicate that the electrostatic repulsion between positively charged PNIPA-DTAC micelles, which are formed by the binding of the DTAC molecules to the PNIPA chain, is not as strong as that between the above-mentioned PNIPA-SDS micelles.

As for the solutions of R3 with DTAC ($\blacktriangle$), the cloud point first decreases, then passes through a minimum value at $c_s \simeq 11$ mM, and finally increases with increasing c_s for values of $c_s \gtrsim 11$ mM. The increase in the cloud point in the range of large values of c_s occurs for the same reason as in the case of the solutions of M6 containing DTAC, whereas the decrease in the cloud point for small values of c_s is characteristic of this case. In consideration of the fact that the sample R3 has the anionic sulfonate group at its chain end, the cationic DTAC molecules are expected to be adsorbed selectively onto the negatively charged chain end if c_s is small. Then the hydrophobic alkyl chains of DTAC around the chain end diminish its hydrophilicity, and the cloud point may, therefore, be lowered. As c_s is further increased, the cloud point in the aqueous solutions increases because of the electrostatic repulsion between the PNIPA-DTAC micelles, as mentioned above.

CONCLUDING REMARKS

For the two PNIPA samples, M6, which has a hydrophobic chain-end group, and R3, which has a (negatively charged) hydrophilic chain-end group, the cloud points were determined in their aqueous solutions with the addition of surfactants—either anionic SDS or cationic DTAC. The cloud points in the solutions of both samples containing SDS increased monotonically and rather steeply with increasing values of c_s , as in the case of the literature data reported by Schild and Tirrell.⁶ On the other hand, the cloud point in the solutions of the sample M6 containing DTAC was found to be almost independent of c_s for values of $c_s \lesssim 27$ mM and then increase with increasing c_s for values of $c_s \gtrsim 27$ mM. As for the solutions of the sample R3 with DTAC, it was found that the cloud point first decreased with increasing c_s , then passed through a minimum at

$c_s \simeq 11$ mM, and finally increased for values of $c_s \gtrsim 11$ mM. The increase in the cloud point in all the solutions arises from the electrostatic repulsion between the charged PNIPA-surfactant micelles formed by the binding of the surfactant molecules to the PNIPA chains. The decrease in the cloud point observed for the solutions of the sample R3 with DTAC for a small c_s is considered to arise because the cationic DTAC molecule bound to the negatively charged PNIPA chain end diminishes the hydrophilicity of the chain end.

Finally, we remark on the structure of the PNIPA-surfactant micelles. The structural information on micelles formed from polymers and surfactants may be obtained by LS measurements.¹¹ An investigation of the PNIPA-surfactant micelles using LS techniques is one of the problems in the future.

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