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Tacticity Effects on the Phase Diagram for Poly(*N*-isopropylacrylamide) in Water

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Stimuli-responsive polymers, which undergo relatively large and abrupt physical or chemical changes in response to a small external stimulus, have received increasing attention during recent years in both academic and industrial contexts.[1–4] Temperature is the most widely used stimulus in these polymer systems, and poly(N-substituted acrylamide) is representative of the group of temperature-responsive polymers.[1,5] The phase diagram for these polymers in water is very important to provide fundamental insights into the temperature responsiveness. Especially, many efforts have been devoted to complete the phase diagram for poly(*N*-isopropylacrylamide) (PNiPA) in aqueous media.[6–9] However, the phase diagram for PNiPA is still controversial. Heskins and Guillet[6] reported the phase diagram for PNiPA in water with lower critical solution temperature (LCST), in which an unfractionated polymer sample was used. On the other hand, Fujishige et al.[7] revealed by using fractionated PNiPA samples that the cloud point (T_c) of the polymer in water is concerned neither with the molecular weight of the polymer (from 5.0×10^4 to 8.4×10^6 g mol^{-1}) nor with its concentration (from 0.01 to 1 wt %). Tong et al.[8] suggested that T_c monotonically decreases with increasing polymer concentration from 0.58 to 70 wt % and that the critical point cannot be identified. These contradictions may arise from insufficient information on the characterization of polymer samples.

Several researchers have recently suggested that the tacticity affects the temperature responsiveness of PNiPA in aqueous media.[10,11] Ray et al.[10] clarified that the increase in the meso diad (*m*) content of PNiPA is responsible for the decrease in T_c; for example, T_c of the aqueous solutions of PNiPAs with m = 45 and 66% is 31.1 and 17.0 °C, respectively. On the contrary, Hirano et al.[11] revealed that T_c goes up with the increase in the racemo diad (*r*) content of PNiPA. These results imply that the phase diagram of the PNiPA aqueous solution is significantly influenced by the tacticity. However, the tacticity effect on the phase boundary curve for PNiPA has not been investigated. In the present paper, therefore, we explore the phase diagram for the aqueous solution of stereocontrolled PNiPAs. To discuss the tacticity effect in detail, we have to prepare well-defined polymer samples. The recent developments in stereoregulation in living radical polymerization enable us to control the molecular weight, polydispersity, and diad tacticity of PNiPA samples.[12,13]

PNiPAs were prepared by stereospecific living radical polymerization using a reversible addition−fragmentation chain transfer (RAFT) agent and Lewis acid catalyst.[12] 1-Phenylethylphenyl dithioacetate (PEPD) used as a RAFT agent was synthesized according to the literature.[14] NiPA monomer and 2,2′-azobis(isobutyronitrile) (AIBN) initiator were recrystallized from benzene/hexane. The number-averaged molecular weight (M_n) and polydispersity (M_w/M_n) of the prepared samples were determined by size exclusion chromatography (SEC) (Jasco Intelligent HPLC system) equipped with a guard column (SB-807HQ, Shodex), two linear poly(hydroxy methacrylate) beads columns (Shodex SB-802.5HQ and SB-806M), and a differential refractive-index detector (RI-2031, Jasco). The eluent was *N*,*N*-dimethylformamide (LiBr 10 mM) at 60 °C with a flow rate of 0.35 mL min^{-1}. The SEC chromatogram was calibrated with standard polystyrene samples. ^{1}H NMR spectra were recorded on a JEOL JNM-LAMBDA spectrometer (500 MHz). The tacticity of the polymers was represented by the diad ratio (*m*:*r*), which is determined from the methylene proton peaks of the polymer measured in DMSO-d_6 at 140 °C.[10,11] The temperature dependence of transmittance of 650 nm light was monitored using a homemade apparatus equipped with a Si photodiode detector (S2386-18K, Hamamatsu photonics). The temperature was controlled by a homemade thermostat with an accuracy of ±0.1 °C. Heating and cooling rates were less than 0.2 °C min^{-1}. The T_c was estimated by the first derivative of the transmittance curves.

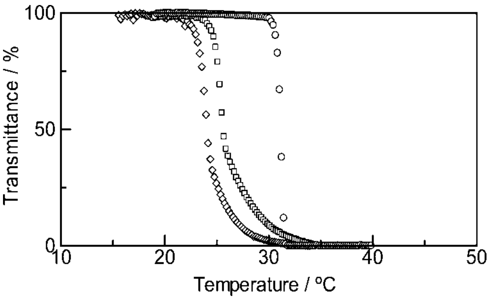

Figure 1. Temperature dependence of transmittance of 650 nm light for the aqueous solutions of PNiPAs with *m*-46 (circle), *m*-60 (rectangle), and *m*-64 (diamond).

Table 1 compiles the characterization results of the stereocontrolled PNiPAs used in the present study. By carrying out RAFT polymerization, well-defined polymers were obtained; M_n is determined to be about 3×10^4 g mol^{-1}, and M_w/M_n ranges from 1.12 to 1.30. Since it has been known that T_c of PNiPA in water is not very sensitive to the molecular weight and the polydispersity,[7,8,15] we expect that the tacticity effect on the phase diagram for PNiPA in water can be examined by using these samples. Figure 1 depicts the transmittance curves for the 1 wt % aqueous solutions of PNiPAs *m*-46, *m*-60, and *m*-64. The T_c decreases with increasing *m*. This tendency is in good agreement with the results reported previously.[10,11] It has been considered that an attractive interaction between the PNiPA chain and water is weakened at higher temperature, resulting in the LCST phase separation.[16,17] Thus, the result implies that the isotactic-rich PNiPA is more hydrophobic than the atactic one. The shape of the transmittance curve is also influenced by the tacticity of PNiPA. The curves for *m*-60 and *m*-64 are broader than that for *m*-46, suggesting that the collapse and

Table 1. Characterization of Stereocontrolled PNiPAs

ID	*m*:*r*	M_n/g mol^{-1}	M_w/M_n	Lewis acid
m-46[a]	46:54	3.2×10^4	1.12	none
m-60[a]	60:40	3.0×10^4	1.30	Y(OTf)$_3$[b]/0.007 M
m-64[a]	64:36	3.4×10^4	1.29	Sc(OTf)$_3$[b]/0.186 M

[a] [NiPA] = 2.23 M, [AIBN] = 0.8 mM, [PEPD] = 8.94 mM in methanol/toluene (1/1, v/v) mixture at 60 °C. [b] Metal trifluoromethanesulfonate.

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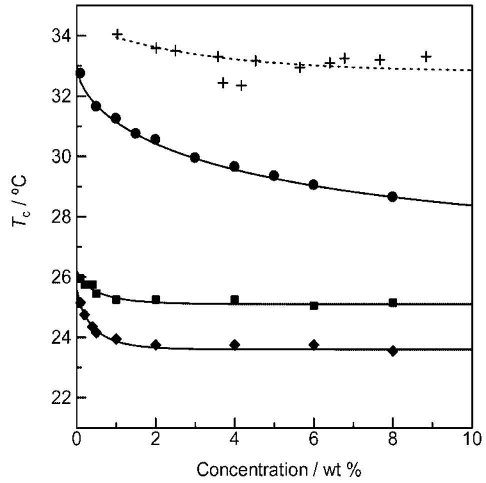

Figure 2. Cloud point (T_c) plotted against the concentration of PNiPAs *m*-46 (circle), *m*-60 (rectangle), and *m*-64 (diamond) in water. The values represented by cross ($M_w = 6.15 \times 10^5$, $M_w/M_n = 2.04$) symbols are obtained from the ref 9. The solid and dotted lines are drawn as guides for the eyes.

aggregation of the polymers are influenced by the tacticity. For the transmittance curves of *m*-60 and *m*-64 in water, the curvature seems to change around 50% of transmittance, and then the broadening becomes significant. Since the curvature of the first stage for *m*-60 and *m*-64 is similar to that of the whole range for *m*-46, the second stage may be characteristic for the phase separation of isotactic-rich PNiPAs in water. The following two hypotheses may explain the difference in the transmittance curves. First, the hydrophobic interactions among the PNiPA segments are possibly strengthened by the stereoregularity of the polymer chain. Second, the interaction among the side-chain groups becomes stronger with increasing *m*, modifying the hydration state of the polymer chain.[10]

Figure 2 shows the phase boundary curves for the aqueous solutions of PNiPAs *m*-46, *m*-60, and *m*-64, which are obtained by plotting T_c against the polymer concentration. For comparison, the phase boundary curve for PNiPA reported by de Azevedo et al.[9] is also plotted in Figure 2. It should be notified that the tacticity of the polymer samples was not characterized in their reports. Several researchers have suggested that the *m* value is about 45% for an atactic PNiPA prepared by free radical polymerization.[18] Thus, it is inferred that the diad tacticity of PNiPAs used in the refs 8 and 9 is similar to that of *m*-46 used in the present study.

Tong et al.[8] revealed that the phase boundary curve for the aqueous solution of PNiPA with higher M_w is located above that with lower M_w, which is in contrast to the LCST phase separation occurring in most synthetic polymer solutions. The result obtained here may be consistent with their conclusion; the phase boundary curve for *m*-46 with ca. $M_w = 3.4 \times 10^4$ g mol^{-1} is located below those for PNiPA with $M_w = 4.91 \times 10^4$ to 6.15×10^5 g mol^{-1} reported previously.[8,9] As shown in Figure 2, T_c for *m*-46 keeps decreasing from ca. 33 to 29 °C with increasing polymer concentration, and the critical point cannot be determined in this concentration region on account of the shape of the phase boundary curve. Although the phase boundary curve for *m*-46 is similar to those reported previously for an atactic PNiPA,[8,9] the concentration dependence of T_c for *m*-46 is larger.

The phase boundary curve for PNiPA shifts to lower temperature with increasing *m* (see Figure 2). Thus we conclude that the phase boundary curve for the PNiPA aqueous solution is influenced by the tacticity of the polymer. Moreover, the effect of the tacticity on the phase boundary curve is much larger than that of the molecular weight. Interestingly, the shape of the phase boundary curve also varies depending upon the tacticity of PNiPA; the curves for *m*-60 and *m*-64 are very flat compared with that for *m*-46. Okada and Tanaka[16] have theoretically reproduced a very flat phase boundary for an aqueous polymer solution, in which the formation of sequential hydrogen bonds of water molecules along the polymer chain (so-called "cooperative hydration") is considered. According to their theory, the shape of the phase boundary curve depends upon the strength of the cooperative hydration; the phase boundary curve shifts to lower temperature and changes from a convex downward form to concentration-independent one with an increase in the cooperativity of hydration. When the cooperativity of hydration is very strong, the phase boundary curve decreases monotonically with increasing polymer concentration. It is therefore likely that the result shown in Figure 2 indicates the changes in hydration of PNiPA depending upon the tacticity. However, the result of the present study seems to be deviated from the theory mentioned above. As shown in Figure 2, the phase boundary curve for PNiPA changes from a monotonic decreasing form to concentration-independent one, when it shifts to lower temperature. This discrepancy cannot be explained in the current state.

The present study has clarified that a small change in tacticity causes a large shift in the phase boundary curve for the PNiPA aqueous solution. That is to say, the tacticity is one of the important factors for understanding the phase separation behavior and stimuli responsiveness of PNiPA in water. The solubility of poly(N-substituted acrylamide) may be influenced not only by the balance between the hydrophilic amide group and hydrophobic group in the monomer but also by the stereosequence in the polymer chain. In the very near future the stereoregulation of synthetic polymers may be a major concern to us for designing novel stimuli-responsive polymers in the near future.

Supporting Information Available: SEC chromatograms and ^{1}H NMR spectra for the PNiPA samples; concentration dependence of the transmittance curves for the aqueous solutions of PNiPA *m*-46, *m*-60, and *m*-64. This materials is available free of charge via the Internet at http://pubs.acs.org.

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