SHORT COMMUNICATIONS

Effect of Tacticity of Poly(*N*-isopropylacrylamide) on the Phase Separation Temperature of Its Aqueous Solutions

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An aqueous solution and cross-linked gel of poly-(*N*-isopropylacrylamide) (PNIPAM) undergo phase separation upon heating around $32\,°C$.[1] Heskins and Guillet[2] studied the phase separation behavior of one unfractionated PNIPAM sample using a visible observation method. Later Fujishige *et al.*[3] studied the phase transition temperature of an aqueous solution of fractionated PNIPAM samples using 500 nm wavelength light transmission and concluded that the phase separation temperature was independent of either the molecular weight (within the range of 50,000–8,400,000) or its concentration (within the range of 0.01–1%). However, Schild and Tirrell[4] observed the effect of the molecular weight and the concentration on the phase separation temperature of aqueous PNIPAM samples. Recently, using two well characterized samples ($M_w = 49,400$ with $M_w/M_n = 1.21$ and $M_w = 101,000$ with $M_w/M_n = 1.23$) studied over the wide concentration range of 0.58–70 wt %, Tong *et al.*[5] reported that the phase separation temperature inversely depends on the molecular weight and concentration of PNIPAM. Thus, there have been relatively large numbers of papers dealing with the effects of molecular weights on the phase separation of PNIPAM. It has been reported earlier that the phase separation is due to the formation of hydrophobic bonding among the side chains of a polymer in an aqueous solution.[6–9] However, there is no report about the effect of tacticity on the phase separation temperature of aqueous PNIPAM solutions. One of our groups recently reported the effect of tacticity on the phase transition temperature of PNIPAM.[10]

Very recently, one of our groups has also reported the synthesis of stereo and molecular weight controlled PNIPAM using the RAFT polymerization in the presence and absence of Lewis acids.[11] Using the same technique, we prepared a series of PNIPAM samples with different meso diad (*m*) values in the range of 45–72% having the molecular weight (M_n) of $37,000 \pm 3000$ and polydispersity (M_w/M_n) in the range of 1.2–1.3. These polymers were used for the determination of the phase separation temperature of aqueous PNIPAM solutions and the novel inverse dependency of the tacticity on the phase separation temperature was observed.

EXPERIMENTAL

N-Isopropylacrylamide (NIPAM) (Wako, > 98%) was recrystallized twice from hexane. AIBN (Kishida, 99%) was recrystallized from methanol. Y(OTf)$_3$ (Aldrich, 98%) and Sc(OTf)$_3$ (Aldrich, 98%) were dried under vacuum before use. Dehydrated methanol (Kanto, > 99.8%) and dehydrated toluene (Kanto, > 99.5%) were used as received. 1-Phenylethyl phenyldithioacetate (PEPD)[12] was synthesized according to the literature. The polymerizations were performed in a methanol–toluene mixture at $60\,°C$ using 2.23 M NIPAM monomer, 0.80 mM AIBN as the initiator and 8.94 mM PEPD as the RAFT agent in the absence

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Table I. Synthesis of poly(NIPAM) samples with different isotacticity using RAFT technique[a]

Sample ID	Lewis Acid (M)	Yield (%)[d]	M_n ($\times 10^{-4}$)[e]	M_w/M_n[e]	Tacticity (m/r)[f]	T_{PS} (°C)[g]
m-45[b]	—	91	3.40	1.20	45/55	31.1
m-47[b]	Sc(OTf)$_3$ (0.016)	96	3.75	1.20	47/53	30.5
m-49[b]	Sc(OTf)$_3$ (0.035)	95	3.72	1.20	49/51	30.1
m-51[c]	Sc(OTf)$_3$ (0.057)	98	3.90	1.21	51/49	29.5
m-53[b]	Y(OTf)$_3$ (0.007)	99	3.69	1.23	53/47	28.5
m-57[c]	Sc(OTf)$_3$ (0.1)	99	3.52	1.25	57/43	27.7
m-62[c]	Y(OTf)$_3$ (0.019)	98	3.98	1.21	62/38	24.7
m-66[c]	Y(OTf)$_3$ (0.035)	99	3.93	1.24	66/34	17.0
m-72[c]	Y(OTf)$_3$ (0.076)	99	3.57	1.30	72/28	—

[a][NIPAM]$_o$ = 2.23 M, [AIBN]$_o$ = 0.80 mM, [PEPD]$_o$ = 8.4 mM, polymerization temperature = 60 °C, medium = 4 mL methanol–toluene (1/1,v/v) mixture. [b]Polymerization time = 48 h. [c]Polymerization time = 36 h. [d]Deteremined gravimetrically from diethyl ether-insoluble part. [e]Determined by SEC (PS standard, 0.1 M LiCl solution of dimethylformamide at 40 °C). [f]Determined by ^{1}H NMR in DMSO-d_6 at 170 °C. [g]T_{PS} = Phase separation temperature.

and the presence of varying concentrations of Sc(OTf)$_3$ or Y(OTf)$_3$ (Table I). The resulting polymer was purified from the Lewis acids by repeated dissolution in methanol and precipitation from hot water. The polymer prepared in the absence of the Lewis acid was purified by precipitation from hot diethyl ether. Table I shows the results of the polymerization and characterization data of nine PNIPAM samples.

The average molecular weights and polydispersities of the PNIPAM samples were measured by size exclusion chromatography (SEC) against polystyrene standards in *N,N*-dimethylformamide containing 0.1 mol/L LiCl with a flow rate of 0.5 ml/min at 40 °C on two polystyrene gel columns: TSK gel *α*-M (Bead size: 13 µm and measurable molecular weight range: $10^{2.5}$–10^7) and TSK gel *α*-3000 (Bead size: 7 µm and measurable molecular weight range: $10^{2.5}$–10^5) using JASCO RI-930 and JASCO UV-970 detectors.

The ^{1}H NMR spectra were recorded on a Varian Gemini 2000 spectrometer (400 MHz). The diad tacticities of the PNIPAM samples were determined from the methylene proton peaks of the polymer recorded in DMSO-d_6 at 170 °C.[11,13]

Aqueous solutions of the polymers were prepared by dissolving the polymer in deionized water and diluting the sample to a 1 wt % concentration. The phase separation temperatures of the solutions were measured by monitoring the transmittance of a 500 nm light beam through a 1 cm quartz sample cell at the rate of 1 °C/min during the heating and cooling scans.[14] The transmittance was recorded using a JASCO V-500 UV/vis spectrometer equipped with a Peltier-type ETC-505 thermostatic cell holder.

RESULTS AND DISCUSSION

The PNIPAM samples used here are soluble in water, except two with m = 66 and 72%. However, the sample with m = 66% could be dissolved by ultrasonication. The solubility of these polymers in water decreased with an increase in the meso diad value. Figure 1 shows the phase diagrams of 1 wt % aqueous solutions of PNIPAMs with the different tacticities of m = 45, 47, 49, 51, 53, 57, 62 and 66%. It is clear from these thermograms that the phase transition temperature gradually decreased with an increase in the meso diad value of the corresponding PNIPAM sample. As the molecular weight and the polydispersity of all the polymers are very close, the effect of the molecular weight and polydispersity may be negligible in the present study. The transition curve became broad with the increasing m value. The hysteresis also became larger with the higher m value. Figure 2 shows the plots of the meso diad value of the polymer versus its phase transition temperature. The transition temperature decreased with the increasing m value. Therefore, the tacticity of PNIPAM also has an effect on the phase transition temperature of its aqueous solution apart from the effect of the molecular weight and concentration as previously reported.[5]

This is the first report of the effect of tacticity on the phase separation temperature of PNIPAM. It is well known that at the phase transition temperature of an aqueous atactic PNIPAM solution, the hydrogen bonding among the side chain amide groups and water molecules is broken and water molecules are released from the polymer, and consequently, the hydrophobic bonding becomes stronger among the isopropyl groups and the polymer chain collapses from a coil to globule state and is followed by aggregation of the collapsed chains which leads to the phase separation. In the present study, the number of side chains on the same side of the polymer backbone increases in the poly(NIPAM) sample with an increase in the meso
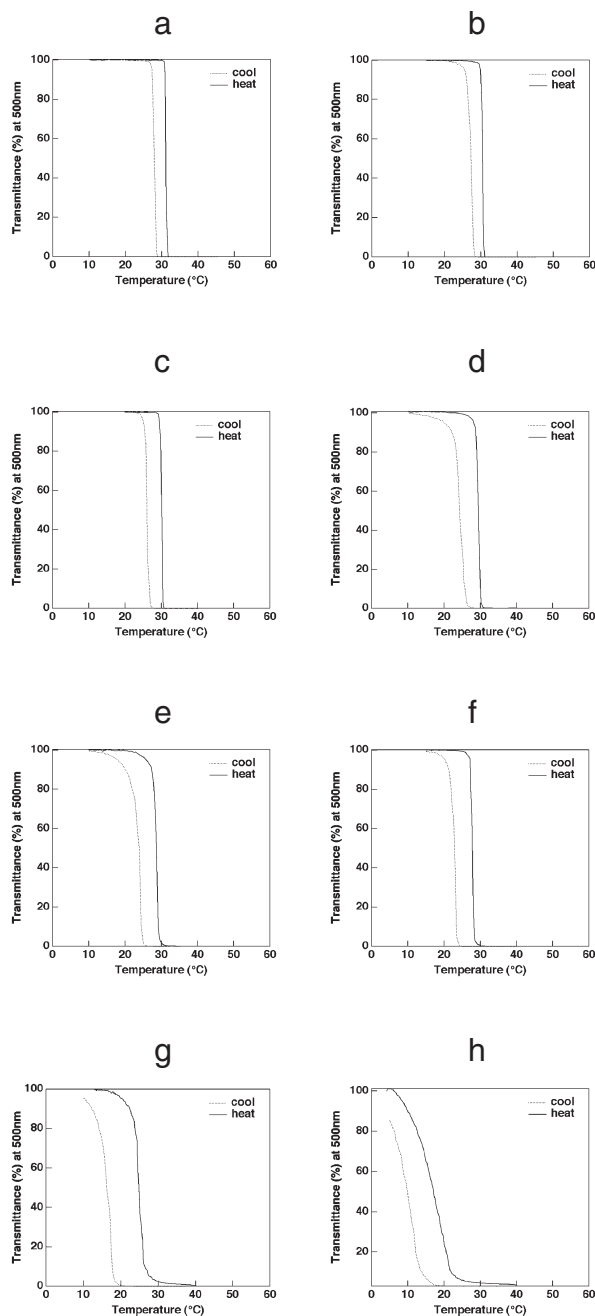
Figure 1. Temperature dependence of the transmittance at 500 nm of 1.0 wt % aqueous solution of PNIPAMs with (a) $m = 45\%$, (b) $m = 47\%$, (c) $m = 49\%$, (d) $m = 51\%$, (e) $m = 53\%$, (f) $m = 57\%$, (g) $m = 62\%$, and (h) $m = 66\%$. Heating or coolig rate is $1\,°C/min$.

Figure 2. Plot of phase separation temperature ($°C$) *vs.* the meso diad value of the PNIPAMs.

m value may also be responsible for the decrease in the solubility of the polymer in water with the increasing m value. A detailed study of the effect of tacticity on the polymer conformation and the hydration state of the polymer with a change in temperature close to the phase transition temperature is now in progress. At present, we can conclude that the phase separation temperature of PNIPAM depends on the tacticity of the polymer. This property may find application in a drug release or delivery system.

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diad value of the polymer. At the phase transition temperature, the interaction among the side chain groups (hydrogen bonding among amide groups and hydrophobic bonding among isopropyl groups) may become stronger with an increase in the isotacticity of the polymer, and the hydrogen bonding between the side chain amide groups with the water molecules may be broken at the cost of the formation of hydrogen bonding between the side chain amide groups. This stronger interaction within the polymer chains with a higher
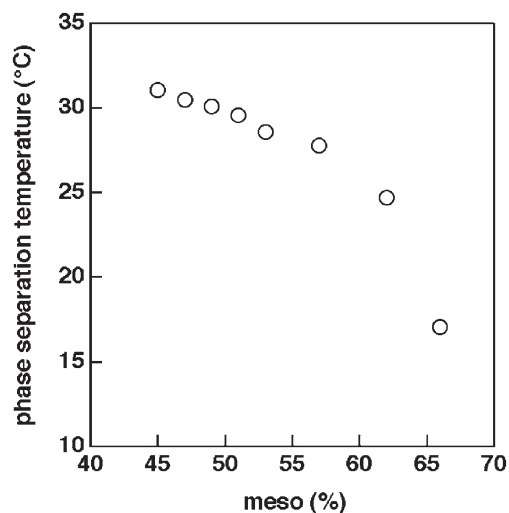
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