

Heterotactic-Specific Radical Polymerization of *N*-Isopropylacrylamide and Phase Transition Behavior of Aqueous Solution of Heterotactic Poly(*N*-isopropylacrylamide)

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ABSTRACT: Radical polymerization of *N*-isopropylacrylamide (NIPAAm) in toluene at low temperatures, in the presence of fluorinated alcohols, produced heterotactic polymer comprising an alternating sequence of *meso* and *racemo* dyads. The heterotacticity reached 70% in triads when polymerization was carried out at -40°C using nonafluoro-*tert*-butanol as the added alcohol. NMR analysis revealed that formation of a 1:1 complex of NIPAAm and fluorinated alcohol through $\text{C}=\text{O}\cdots\text{H}-\text{O}$ hydrogen bonding

induces the heterotactic specificity. A mechanism for the heterotactic-specific polymerization is proposed. Examination of the phase transition behavior of aqueous solutions of heterotactic poly(NIPAAm) revealed that the hysteresis of the phase transition between the heating and cooling cycles depended on the average length of *meso* dyads in poly(NIPAAm).

Keywords: stereospecific polymers; radical polymerization; stimuli-sensitive polymers; hydrogen bonding; *N*-isopropylacrylamide; heterotactic

Running head: Heterotactic poly(*N*-isopropylacrylamide)

INTRODUCTION

Isotactic and syndiotactic polymers are representative stereoregular polymers that are composed of contiguous *meso* (*m*) and *racemo* (*r*) dyads. In principle, control of the configurational relationship between neighboring constitutional repeating units is sufficient for isotactic- and syndiotactic-specific polymerizations. Heterotactic polymer is another kind of stereoregular polymer that has an alternating sequence of *m* and *r* dyads. Formation of heterotactic polymer requires two different types of stereoregulation, *m*- and *r*-additions, to occur in an alternating manner. Thus the dyad configuration at the propagating chain end should affect the stereoselectivity of propagating species in heterotactic-specific polymerization as follows: *m*-ended radical prefers *r*-addition and

r-ended radical prefers *m*-addition (Scheme 1). Consequently, the formation of heterotactic polymer requires a higher level of stereoregulation than is the case for isotactic and syndiotactic polymers.¹

<Scheme 1>

Recently, we have reported stereospecific radical polymerization of *N*-alkylacrylamides by controlling the structures of hydrogen bonding-assisted complexes of the monomers with added reagents.²⁻⁷ *N*-Alkylacrylamides behaved as hydrogen donors in the presence of Lewis bases such as phosphoric acid derivatives^{2,3} or pyridine *N*-oxide derivatives⁴: syndiotactic or isotactic polymer was obtained through 1:1 or 2:1 complex formation. Moreover, *N*-alkylacrylamides behaved as hydrogen donor and acceptor simultaneously with the addition of alkyl alcohols, and syndiotactic polymer was obtained through complex formation with cooperative hydrogen bonding.⁵

It is known that fluorinated alcohols (RfOHs) exhibit stereocontrolling power in radical polymerization of vinyl monomers such as vinyl esters,⁸ methacrylates⁹⁻¹¹ and *N*-vinyl amides,^{12,13} through a hydrogen bonding interaction. Our investigation of the effect of fluorinated alcohols on the stereospecificity of NIPAAm polymerization⁶ showed that heterotactic polymer was obtained by adding fluorinated alcohols to reaction mixtures for radical polymerization of *N*-isopropylacrylamide (NIPAAm). In the present study we have investigated in detail the heterotactic-specific radical polymerization of NIPAAm, and the structure of the complex between NIPAAm and fluorinated alcohols, to

understand the mechanism of the stereoregulation.

The phase transition behavior of aqueous solutions of poly(NIPAAm) has been extensively studied.¹⁴⁻¹⁶ It was reported recently that isotactic poly(NIPAAm) exhibited a lower phase transition temperature than the atactic polymer.^{17,18} We have also reported that increase in syndiotacticity of poly(NIPAAm) increased both the phase transition temperature and the cooperativity of phase transition, and reduced the hysteresis between heating and cooling cycles.^{5(a)} Thus in the present study the phase transition behavior of heterotactic poly(NIPAAm) was investigated and significant insight was obtained into the relationship between the phase transition behavior and the stereoregularity of poly(NIPAAm).

Experimental

Materials

NIPAAm (Tokyo Kasei Kogyo Co.) was recrystallized from hexane-toluene mixture. Toluene was purified by washing with sulfuric acid, water and 5% aqueous NaOH, then fractional distillation. Tri-*n*-butylborane (*n*-Bu₃B) as a tetrahydrofuran (THF) solution (1.0 M), 2,2,2-trifluoroethanol (**1**) (Aldrich Chemical Co.), 1,1,1,3,3,3-hexafluoro-2-propanol (**2**) (supplied by DAIKIN INDUSTRIES Ltd.), nonafluoro-*tert*-butanol (**3**) (Tokyo Kasei Kogyo Co.), and 2,2,3,3,4,4,5,5-octafluoro-1-pentanol (PenOH-F₈, supplied by DAIKIN INDUSTRIES Ltd) were used without further purification.

Polymerization

A typical polymerization procedure was as follows. NIPAAm (0.314 g, 2.8 mmol) and **1** (1.120 g, 11.2 mmol) were dissolved in toluene to prepare 5 mL solution. Four milliliters of the solution was transferred to a glass ampoule and cooled to -40°C . Polymerization was initiated by adding *n*-Bu₃B solution (0.22 mL) to the monomer solution.¹⁹ Monomer, polymer or both were precipitated during the polymerization in the presence of fluorinated alcohols. Reaction was terminated after 24 h by adding a small amount of a solution of 2,6-di-*t*-butyl-4-methylphenol in THF at the polymerization temperature. The reaction mixture was poured into a large amount of diethyl ether, and the precipitated polymer collected by filtration or centrifugation then dried *in vacuo*. The polymer yield was determined gravimetrically.

Measurements

¹H and ¹³C NMR spectra were obtained using an EX-400 or ECX-400 spectrometer (JEOL Ltd.) operated at 400 MHz for ¹H and 100 MHz for ¹³C. Molecular weights and molecular weight distributions of the polymers were determined by size exclusion chromatography (SEC); the chromatograph was calibrated with standard polystyrene samples. SEC was performed with an HLC 8220 chromatograph (Tosoh Co.) equipped with TSK gel columns (SuperHM-M and SuperHM-H, both 6.5 mm IDx150 mm long; Tosoh Co.). Dimethylformamide containing LiBr (10 mmol L⁻¹) was used as eluent at 40°C with flow rate 0.35 mL min⁻¹. The polymer concentration was 1.0 mg mL⁻¹. The

transmittance of an aqueous solution of poly(NIPAAm) (0.1 w/v%) was monitored at 500 nm as a function of temperature using a UV/VIS spectrophotometer (V-550, JASCO Co.) equipped with a Peltier thermostatted single cell holder (ETC-505, JASCO Co.). The temperature was varied at $0.5^{\circ}\text{C min}^{-1}$. The cloud point (T_c) was taken as the temperature at which the transmittance was 50% in the heating and cooling cycles.

NMR evaluation of stereoregularity of poly(NIPAAm) at triad level

The dyad tacticity of the polymer obtained was determined from ^1H NMR signals from the methylene groups in the main chain, measured in deuterated dimethyl sulfoxide ($\text{DMSO-}d_6$) at 150°C . As reported previously,⁶ the signals due to the main-chain methine carbons of poly(NIPAAm) measured in $\text{DMSO-}d_6$ at 100°C split into three broad peaks, but triad tacticity could not be determined accurately because of low resolution of the resonances. For that reason we conducted ^{13}C NMR measurement in various solvents to evaluate the tacticity at triad level.

Figure 1 displays expanded scale NMR spectra of the methine carbons of poly(NIPAAm). Use of CD_3OD as a solvent or as a component of a mixed solvent improved the resolution even at 55°C (Figure 1(b) and 1(c)), although the signal due to the methine carbons of the isopropyl side groups overlapped with the splittings due to the in-chain methine carbons. This suggested that a protic solvent is suitable for determining the triad tacticity of poly(NIPAAm), and $\text{DMSO-}d_6:\text{D}_2\text{O}$ (90:10 wt%) was used as a mixed solvent at 100°C , giving well-resolved splitting without signal overlap (Figure 1(d)). However, the solubility of poly(NIPAAm) was drastically reduced, probably

because of co-nonsolvency.^{20,21} PenOH-F₈ was added as a third component²², improving the solubility of poly(NIPAAm) and well-resolved splitting was observed (Figure 1(e)). The *r* dyad tacticity calculated from the triad tacticity via the equation ($r = rr+mr/2$) agreed well with the *r* dyad tacticity determined by ¹H NMR. Thus we chose that mixed solvent as the solvent for NMR analysis of poly(NIPAAm) to determine the tacticity at triad level.

<Figure 1>

RESULTS AND DISCUSSION

Radical Polymerization of NIPAAm in the Presence of Fluorinated Alcohols

Radical polymerization of NIPAAm was carried out in toluene at low temperatures in the presence of fluorinated alcohols (**1-3**), to investigate the effect of polymerization temperature on the heterotactic specificity (Table 1). Polymers were obtained in moderate yields, although polymerization below -40°C in the presence of **3** was not achieved due to the insolubility of the monomer. The addition of fluorinated alcohols tended to increase the number average molecular weights of the polymers obtained. A similar tendency was observed for NIPAAm polymerization in the presence of alkyl alcohols; in that case significant syndiotactic specificity was induced.^{5(a)}

<Table 1>

Triad tacticity distribution of the polymer obtained was determined using ^{13}C NMR signals from the main-chain methine carbons. The heterotacticity of poly(NIPAAm) prepared in the presence of **3** gradually increased with decrease in the polymerization temperature, whereas very little temperature dependence was observed for polymerization in the presence of **1** or **2**. Fluorinated alcohol **3** induced the highest heterotactic specificity, up to 70 % by lowering the temperature to -40°C (Figure 1(f)), among the alcohols examined. To the best of our knowledge, the extent of heterotacticity was the highest so far reported for radically prepared homopolymers.

NIPAAm polymerization at -40°C was carried out with different amounts of **1-3**. Significant induction of heterotactic specificity required excess amounts of **2** or **3**, whereas the heterotacticity gradually increased with the added amount of **1** (Figure 2).

<Figure 2>

Hydrogen Bonding Interaction between NIPAAm and Fluorinated Alcohols

To confirm the involvement of a hydrogen bonding interaction in stereocontrol of NIPAAm polymerization, we conducted an NMR analysis of a mixture of NIPAAm and **3**, in which the concentration of NIPAAm was kept at 0.2 mol L^{-1} , in toluene- d_8 at 0°C . Some signals, in particular those due to $-\text{NH}$ and $-\text{OH}$ groups, significantly shifted with changes in the added amount of **3**. Even without NIPAAm monomer, the chemical shift of the $-\text{OH}$ proton of **3** varied with the concentration, because the alcohol self-associated through a hydrogen bonding interaction. Thus the differences in the chemical shift of the

–OH proton of **3** [$\Delta\delta(-OH)$] between the signals of the sample and **3** alone, at corresponding concentrations, were plotted against the $[3]_0/[NIPAAm]_0$ ratio, as shown in Figure 3. Figure 3 also displays the changes in the chemical shifts of the –NH proton of NIPAAm [$\Delta\delta(-NH)$] and of the C=O carbon of NIPAAm [$\Delta\delta(C=O)$], respectively, versus the $[3]_0/[NIPAAm]_0$ ratio. The –OH signal of **3** showed a downfield shift from mixing with NIPAAm, regardless of the concentration of **3**. The signal from the C=O carbon of NIPAAm also exhibited a downfield shift with increase in the added amount of **3**. These results indicate that NIPAAm and **3** form a C=O•••H-O hydrogen bond as in the case of NIPAAm and non-fluorinated alkyl alcohols.^{5(a)}

<Figure 3>

The signal due to the –NH proton of NIPAAm showed an upfield shift with increasing concentration of **3**. This contrasts with the result in the NIPAAm/alkyl alcohol system where a downfield shift was observed in the presence of excess alkyl alcohol.^{5(a)} Taking into account NIPAAm self-association through a hydrogen bonding interaction, it is concluded that NIPAAm monomer behaved only as a proton acceptor, probably because the basicities of the oxygen atoms of fluorinated alcohols are much lower than those of alkyl alcohols.

To investigate the stoichiometry of the NIPAAm-**3** complex, ¹H NMR analysis was carried out on solutions with $[NIPAAm]_0+[3]_0=0.25 \text{ mol L}^{-1}$ in toluene-*d*₈ at 0°C. Figure 4(a) shows changes in the chemical shift of the methine proton in the vinyl group

(=CH) of NIPAAm resulting from variation of the initial proportion of NIPAAm. The plots roughly obeyed a quadratic equation. The stoichiometry of the complex was evaluated by Job's method (Figure 4(b)) via eq. (1):²³

$$[\text{NIPAAm} - \mathbf{3}] = \frac{\delta(=CH) - \delta(=CH)_f}{\delta(=CH)_c - \delta(=CH)_f} \times [\text{NIPAAm}]_0 \quad (1)$$

where $\delta(=CH)$ and $\delta(=CH)_f$ are the chemical shifts of the sample mixture and NIPAAm alone, respectively. As mentioned above, $\delta(=CH)_f$ also varies with $[\text{NIPAAm}]_0$ owing to its self-association. Thus the chemical shift of NIPAAm alone at the corresponding concentration was equated to $\delta(=CH)_f$ (Figure 4(a)). The chemical shift for the saturated mixture, $\delta(=CH)_c$, was calculated from the intercept of a quadratic fit to the data in Figure 4(a), since the saturation value should be independent of NIPAAm concentration. The maximum observed at an initial proportion of NIPAAm=0.5 (Figure 4(b)), indicates that NIPAAm and **3** formed a 1:1 complex through C=O...H-O hydrogen bonding.

<Figure 4>

The equilibrium constant (K) of the NIPAAm-**3** complex was determined from the changes in the ¹H NMR chemical shift of the methine proton of NIPAAm. Figure 5 shows the relationship between the change in the chemical shift and the $[\mathbf{3}]_0/[\text{NIPAAm}]_0$ ratio at constant $[\text{NIPAAm}]_0$ ($5.0 \times 10^{-2} \text{ mol L}^{-1}$) in toluene-*d*₈ at several temperatures. K was determined from the data in Figure 5 by nonlinear least squares fitting of the data to eq (2):²⁴

$$\Delta\delta = \frac{\Delta\delta'}{2} (b - \sqrt{b^2 - 4X}) \quad (2)$$

$$b = 1 + X + \frac{1}{(K[\text{NIPAAm}]_0)}$$

$$X = [\mathbf{3}]_0 / [\text{NIPAAm}]_0$$

where $\Delta\delta$ and $\Delta\delta'$ are the changes in the chemical shift of =CH of NIPAAm for the given solution and a saturated solution, respectively (Table 2).²⁵

A van't Hoff plot for the K values obtained is shown in Figure 6. The enthalpy (ΔH) and entropy (ΔS) for complex formation were evaluated as $-16.6 \pm 1.4 \text{ kJ mol}^{-1}$ and $-12.8 \pm 4.3 \text{ J mol}^{-1} \text{ K}^{-1}$, respectively, from eq (3):

$$\ln K = \frac{\Delta S}{R} - \frac{\Delta H}{RT} \quad (3)$$

where R is the gas constant and T is absolute temperature. The K values at temperatures below 25°C were calculated on the assumption that ΔH was constant.

<Table 2>

<Figure 5>

<Figure 6>

Application of the K values for the polymerization conditions gives the values shown in Table 2 for the degree of association (α) of NIPAAm. When an equimolar amount of **3** was added, 4% of NIPAAm was uncomplexed even at -40°C . However, NIPAAm formed the complex quantitatively in the presence of excess amounts of **3**. This result corresponds with the polymerization result that excess amounts of **3** were required to induce significant heterotactic specificity (cf. Figure 2).²⁷

Proposed Mechanism for Heterotactic-specific Radical Polymerization of NIPAAm Induced by Fluorinated Alcohols

The formation of heterotactic polymer requires alternating stereoselection of the propagating radical, that is, *r*-addition to *m*-ended radical and *m*-addition to *r*-ended radical. The stereochemical process of the heterotactic-specific polymerization can thus be characterized by two parameters; the probability of *r*-addition to *m*-ended radical ($P_{m/r}$) and that of *m*-addition to *r*-ended radical ($P_{r/m}$) in first-order Markovian statistics.

Figure 7 shows a plot of the two parameters for NIPAAm polymerization at -40°C in the presence of different amounts of RfOH. $P_{m/r}$ values gradually increased with increase in the $[\text{RfOH}]_0/[\text{NIPAAm}]_0$ ratio, except for **2**. In particular, $P_{m/r}$ reached 0.81 with addition of a fourfold amount of **3**. On the other hand, the changes in $P_{r/m}$ values appear smaller compared with $P_{m/r}$. However, $P_{r/m}$ values decreased at $[\text{RfOH}]_0/[\text{NIPAAm}]_0=1$ and increased in the presence of excess amounts of RfOH, except for **1**. In particular, $P_{r/m}$ varied from 0.42 to 0.61 with increasing amount of **3**. These results suggest that the addition of fluorinated alcohols should induce syndiotactic specificity in principle. However, the stereoselectivity of *r*-ended radical tends to be inverted in the presence of excess amounts of fluorinated alcohols, leading to induction of heterotactic specificity. In other words, *m*-addition to *r*-ended radical is identified as the key step for heterotactic specificity. Thus we propose the following mechanism for the polymerization.

<Figure 7>

First, NIPAAm forms the 1:1 complex with the added fluorinated alcohol. When the complexed NIPAAm undergoes a propagating reaction, the fluorinated alcohol binding to the NIPAAm monomer remains at the newly formed propagating chain end. The single bond near the propagating chain end of the *r*-ended radicals rotates to reduce the repulsion of fluorine atoms in fluorinated alcohols bound to the amide groups at the antepenultimate and chain-end monomeric units (Scheme 2). The conformationally rotated radicals can react with a new incoming monomer via two possible pathways: pathway **a** should form an *r* dyad and pathway **b** should form an *m* dyad. However, the amide group at the penultimate monomeric unit bound to RfOH limits the approach via pathway **a** by the next incoming monomer, so that *r*-ended radical favors *m*-addition via pathway **b**.

<Scheme 2>

In the *m*-ended radicals, the single bond at the second dyad from the end rotates to reduce the repulsion of fluorine atoms in RfOHs bound to the amide groups at the antepenultimate and penultimate monomeric units (Scheme 3). These conformationally rotated radicals also can undergo the next propagating reaction via two possible pathways. However, amide groups not only at the penultimate monomeric unit but also at the antepenultimate monomeric unit sterically prevent the radicals from propagating via

pathway **b** so that *m*-ended radical favors *r*-addition via pathway **a**. As a result, *m*-addition to *r*-ended radicals and *r*-addition to *m*-ended radicals both take place in an alternating manner, resulting in the formation of heterotactic stereosequences.

<Scheme 3>

Phase Transition Behavior of Aqueous Solution of Heterotactic Poly(NIPAAm)

We previously reported^{5(a)} significant effects of increase in the dyad syndiotacticity on the phase transition behavior of aqueous solutions of poly(NIPAAm), as follows: (1) the phase transition temperature increased slightly; (2) the phase transition behavior was sharpened; (3) hysteresis between the heating and cooling cycles was reduced. In the present study, we obtained heterotactic polymer composed of an alternating stereosequence of *m* and *r* dyads. Thus we investigated the phase transition behavior of heterotactic poly(NIPAAm) to examine the effect of stereoregularity at triad level.

Figures 8 and 9 display the temperature dependences of the transmittance of aqueous solutions of poly(NIPAAm) with *r* dyad content 50% (**C**, **D** in Table 3) or 58% (**F**, **G**, **H** in Table 3) in heating and cooling cycles. In the heating cycle (Figures 8(a) and 9(a)), T_c of each series of polymers was observed within 1.0°C, although the triad tacticity distributions of the polymers were quite different. Figure 10 shows the relationship between T_c (heating) and the *r* dyad content of poly(NIPAAm). The data for poly(NIPAAm)s with *r* dyads of 41 % to 71 % (**A**, **B**, **E**, **I** in Table 3) are also plotted. The observed value of T_c (heating) gradually increased with increase in *r* dyad content,

although the temperature dependence changed at around $r=50\%$. These results indicate that the phase transition temperature of poly(NIPAAm) solution in the heating cycle was determined by the r dyad content of the polymer examined. In addition, the phase transition behavior of heterotactic polymer was further sharpened as compared with the syndiotactic polymer (Figure 9). Similar tendencies were observed more clearly in the cooling cycles (Figures 8(b) and 9(b)).

<Figure 8>

<Figure 9>

<Figure 10>

The hysteresis between the heating and cooling cycles in the phase transition of heterotactic polymer was significantly reduced, compared with atactic polymer and even syndiotactic polymer. This result indicates that the phase transition behavior of poly(NIPAAm) solution in the cooling cycle depended not on the dyad tacticity but on the triad tacticity distributions of the polymer examined. Figure 11 displays the differences in the values of T_c between the heating and cooling cycles (ΔT_c) versus the average length of m dyad, n_m , or r dyad, n_r , calculated from the triad distributions.²⁸ ΔT_c tended to increase with increase in n_m , whereas no clear dependence was observed with n_r . Thus it is assumed that contiguous m dyads impeded the re-dissolution process of poly(NIPAAm), probably because of cooperative hydrogen bonding interactions between the amide groups in isotactic sequences.²⁹

<Figure 11>

CONCLUSIONS

Heterotactic polymer was successfully synthesized by radical polymerization of NIPAAm in the presence of fluorinated alcohols. The heterotacticity reached 70% with the addition of nonafluoro-*tert*-butanol at -40°C , which to the best of our knowledge is the highest heterotacticity so far reported for radically prepared polymers. NMR analysis revealed that NIPAAm forms a 1:1 complex with fluorinated alcohols through $\text{C}=\text{O}\cdots\text{H}-\text{O}$ hydrogen bonding. Based on the complex structure, a mechanism for the heterotactic-specific radical polymerization is proposed. The effect of stereoregularity on the phase transition behavior of poly(NIPAAm) solution was also examined. It appears that the hysteresis between the heating and cooling cycles depends on the average length of *m* dyad. It should be noted that that effect was found only after the preparation of heterotactic poly(NIPAAm). Further work is now under way to examine the effect of *N*-substituent on the stereospecificity of radical polymerization of *N*-alkylacrylamides in the presence of fluorinated alcohols, and on the phase transition behavior of the resulting polymers.

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27. As described at the section on mechanism, the heterotactic-specificity would be induced when propagating reaction proceeds between the NIPAAm complexed with RfOH and the radical bound with RfOHs at the antepenultimate, penultimate, and chain-end monomeric units. If assuming that degree of association between **3** and monomeric unit near the propagating chain-end is the same as that for the NIPAAm-**3** complex, probability of the above-mentioned propagating reaction in the presence of an equimolar amount of **3** is calculated to be 0.85. Furthermore, it is assumed that the radicals bound with RfOHs favor propagating reaction with uncomplexed monomer more than complexed monomer, because of the repulsion of fluorine atoms in complexed radicals and complexed monomers. Therefore, it is reasonable that the heterotactic-specificity induced by an equimolar amount of **3** significantly decreased compared with that by a twofold amount of **3**, although the difference in degree of association of the NIPAAm-**3** complex was only 4%.
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Table 1. Radical Polymerization of NIPAAm in Toluene at Low Temperatures for 24 h in the Absence or Presence of Fluorinated Alcohols^a

Added Alcohol	[Alcohol] ₀ mol L ⁻¹	Temp. °C	Yield %	<i>r</i> Dyad/% ^b Obsd.	Triad tacticity/% ^c			<i>r</i> Dyad/% ^d Calcd.	<i>M_n</i> ^e x10 ⁻⁴	<i>M_w</i> ^e <i>M_n</i>
					<i>mm</i>	<i>mr</i>	<i>rr</i>			
None	0.0	0	92	53	20	53	27	53	4.54	2.0
None	0.0	-40	89	54	23	52	25	51	2.72	1.8
1	2.0	0	85	58	18	59	23	52.5	2.66	1.6
1	2.0	-20	77	58	15	58	27	56	3.34	1.5
1	0.5	-40	96	58	18	55	27	54.5	4.00	1.7
1	1.0	-40	94	58	14	57	29	57.5	3.90	1.7
1	2.0	-40	96	58	12	60	28	58	4.29	1.4
1	2.0	-60	53	58	11	62	27	58	6.39	3.1
1	2.0	-80	60	58	14	57	29	57.5	11.52	3.2
2	2.0	0	>99	50	21	59	20	49.5	5.60	1.3
2	2.0	-20	>99	49	21	58	21	50	5.17	1.4
2	0.5	-40	96	53	26	49	25	50.5	5.37	1.7
2	1.0	-40	87	49	26	53	21	47.5	5.13	2.1
2	2.0	-40	93	50	22	59	19	48.5	5.01	1.3
2	2.0	-60	84	48	22	59	19	48.5	5.48	1.6
2	2.0	-80	81	47	28	55	17	44.5	4.42	1.7
3	2.0	0	75	57	12	67	21	54.5	4.53	1.4
3	2.0	-20	66	59	9	69	22	56.5	7.75	1.3
3	0.5	-40	96	56	16	50	34	59	5.64	1.8
3	1.0	-40	>99	61	9	66	25	58	8.33	2.0
3	2.0	-40	86	58	8	70	22	57	7.21	3.1

a. [NIPAAm]₀=0.5 mol L⁻¹, [*n*-Bu₃B]₀=5.0x10⁻² mol L⁻¹, [fluorinated alcohol]₀=2.0 mol L⁻¹.

b. Determined from ¹H NMR signals due to the main-chain methylene groups, measured in DMSO-*d*₆ at 150°C.

c. Determined from ¹³C NMR signals due to the main-chain methine groups, measured in mixed solvent (DMSO-*d*₆:D₂O:PenOH-F₈=75:10:15 wt%) at 100°C.

d. Calculated from the triad tacticities with the equation: $r=mr/2+rr$.

e. Determined by SEC (polystyrene standards).

Table 2. Equilibrium constants (K) for the interaction between NIPAAm and **3**, and degree of association (α) in the polymerization system^a

Temperature °C	K L mol ⁻¹	α ^b			
		3 =	1 equiv.	2 equiv.	4 equiv.
60	87.5		0.86	0.98	0.99
40	122		0.88	0.98	0.99
25	177		0.90	0.99	1.00
0	(321) ^c		0.92	0.99	1.00
-20	(572) ^c		0.94	1.00	1.00
-40	(1126) ^c		0.96	1.00	1.00

a. NMR conditions: [NIPAAm]₀=5.0×10⁻² mol L⁻¹, in toluene-*d*₈.

b. Calculated with [NIPAAm]₀=0.5 mol L⁻¹.

c. Calculated from van't Hoff relationship.

Table 3. Poly(NIPAAm) Samples in Phase Transition Experiments

Sample Code	r Dyad/% ^a Obsd.	Triad tacticity/% ^b			r Dyad/% ^c Calcd.	n_m ^d	n_r ^d	T_c (heating) °C	ΔT_c ^e °C	M_n ^f x10 ⁻⁴	M_w ^f M_n
		mm	mr	rr							
A ^g	41	39	38	23	42	3.05	2.21	24.7	-	1.55	1.5
B ^h	45	34	43	23	44.5	2.58	2.07	28.3	9.7	1.86	1.4
C ⁱ	50	29	41	30	50.5	2.41	2.46	33.0	7.7	2.56	1.3
D	50	22	59	19	48.5	1.75	1.64	33.3	2.8	5.01	2.1
E	54	23	52	25	51	1.88	1.96	33.5	2.8	2.72	1.8
F ^j	58	14	50	36	61	1.56	2.44	34.0	2.6	6.74	1.3
G	58	12	60	28	58	1.40	1.93	34.6	1.3	4.29	1.4
H	58	8	70	22	57	1.23	1.63	34.4	1.1	7.21	3.1
I ^k	71	8	44	48	70	1.36	3.18	35.9	1.5	8.87	1.5

a. Determined from ¹H NMR signals due to the main-chain methylene groups, measured in DMSO-*d*₆ at 150°C.

b. Determined from ¹³C NMR signals due to the main-chain methine groups, measured in mixed solvent DMSO-*d*₆:D₂O:PenOH-F₈=75:10:15 wt%) at 100°C.

c. Calculated from the triad tacticities with the equation: $r=mr/2+rr$.

d. Calculated from the triad tacticities with the following equations: $n_m=(mm+mr/2)/(mr/2)$, $n_r=(rr+mr/2)/(mr/2)$.²⁷

e. $\Delta T_c=T_c(\text{heating})-T_c(\text{cooling})$.

f. Determined by SEC (polystyrene standards).

g. Prepared in CHCl₃ at -60°C ([NIPAAm]₀=1.0 mol L⁻¹, [3,5-dimethylpyridine *N*-oxide]₀=0.75 mol L⁻¹).^{4(b)}

h. Prepared in CHCl₃ at -60°C ([NIPAAm]₀=1.0 mol L⁻¹, [3,5-dimethylpyridine *N*-oxide]₀=0.5 mol L⁻¹).^{4(b)}

i. Prepared in CHCl₃ at -40°C ([NIPAAm]₀=1.0 mol L⁻¹, [2,6-dimethylpyridine *N*-oxide]₀=1.0 mol L⁻¹).^{4(b)}

j. Prepared in toluene at -40°C ([NIPAAm]₀=0.5 mol L⁻¹, [3Me3PenOH]₀=0.25 mol L⁻¹).^{5(a)}

k. Prepared in toluene at -60°C ([NIPAAm]₀=0.5 mol L⁻¹, [3Me3PenOH]₀=2.0 mol L⁻¹).^{5(a)}

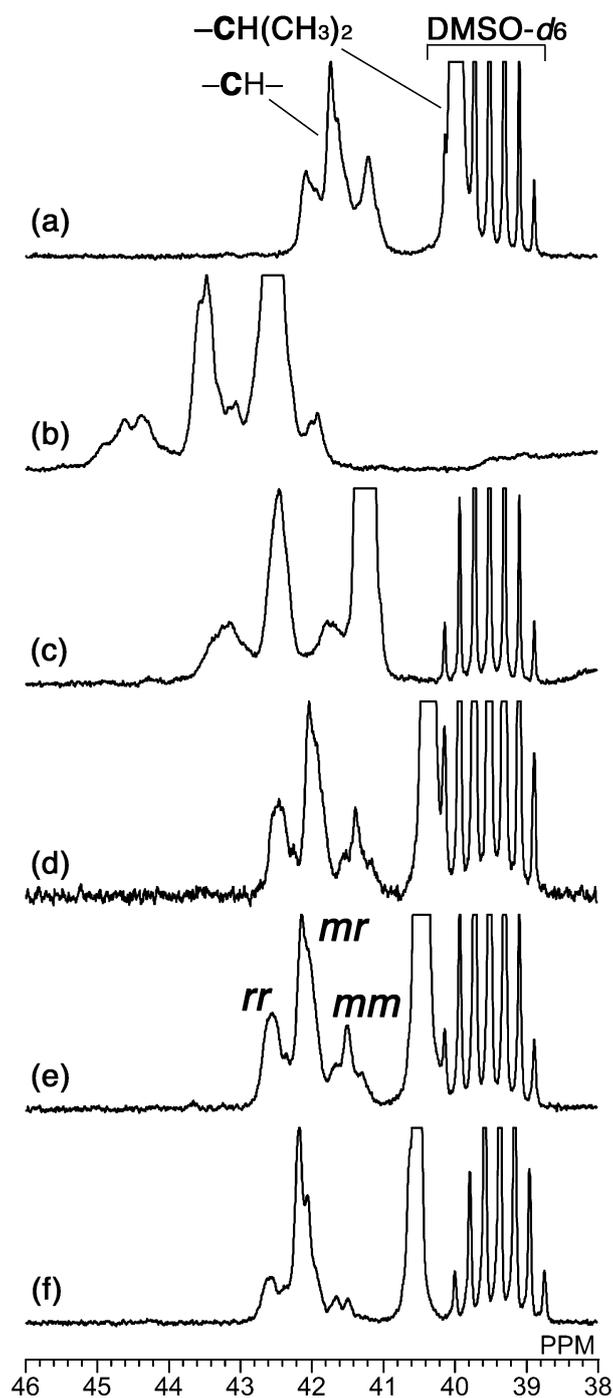


Figure 1. Expanded ^{13}C NMR spectra of the methine carbons of poly(NIPAAm) prepared at -40°C in the absence of fluorinated alcohols, as measured in (a) $\text{DMSO-}d_6$ at 100°C , (b) CD_3OD at 55°C , (c) $\text{DMSO-}d_6:\text{CD}_3\text{OD}$ (1:1 vol/vol) at 55°C , (d) $\text{DMSO-}d_6:\text{D}_2\text{O}$ (90:10 wt%) at 100°C , and (e) $\text{DMSO-}d_6:\text{D}_2\text{O}:\text{PenOH-F}_8$ (75:10:15 wt%) at 100°C , and (f) poly(NIPAAm) with $mr=70\%$, as measured in $\text{DMSO-}d_6:\text{D}_2\text{O}:\text{PenOH-F}_8$ (75:10:15 wt%) at 100°C .

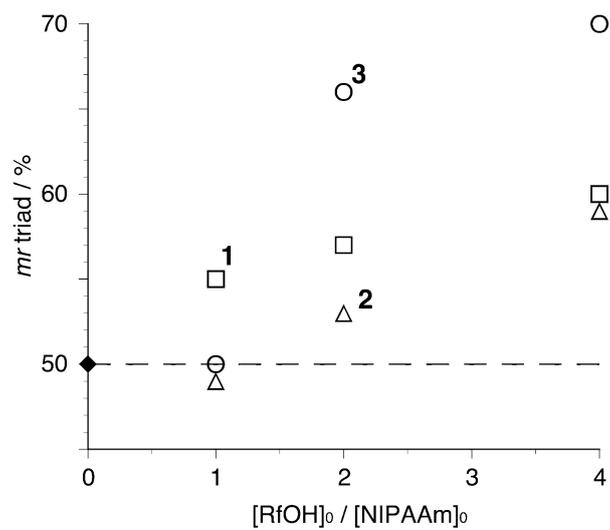


Figure 2. Relationship between the $[RfOH]_0/[NIPAAm]_0$ ratio and *mr* triad content of poly(NIPAAm) prepared in toluene at -40°C in the presence of fluorinated alcohols.

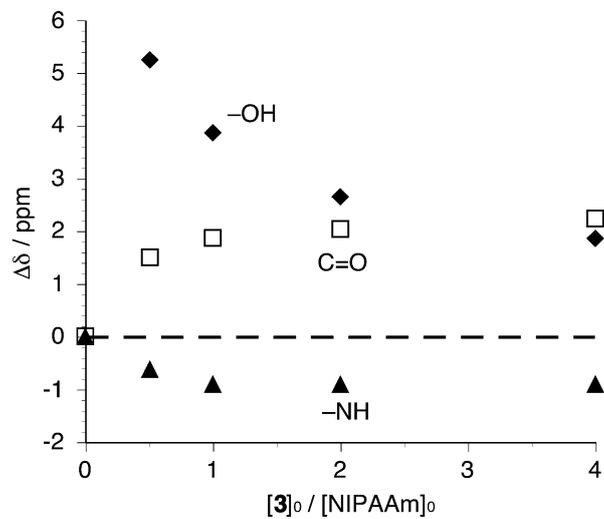


Figure 3. ^1H NMR chemical shift difference of the $-\text{OH}$ protons of **3** between the sample mixture and **3** alone at corresponding concentrations (\blacklozenge), changes in ^1H NMR chemical shift of the $-\text{NH}$ protons (\blacktriangle), and changes in ^{13}C NMR chemical shift of the $\text{C}=\text{O}$ carbons (\square) of NIPAAm monomer, resulting from variation of the $[3]_0/[\text{NIPAAm}]_0$ ratio.

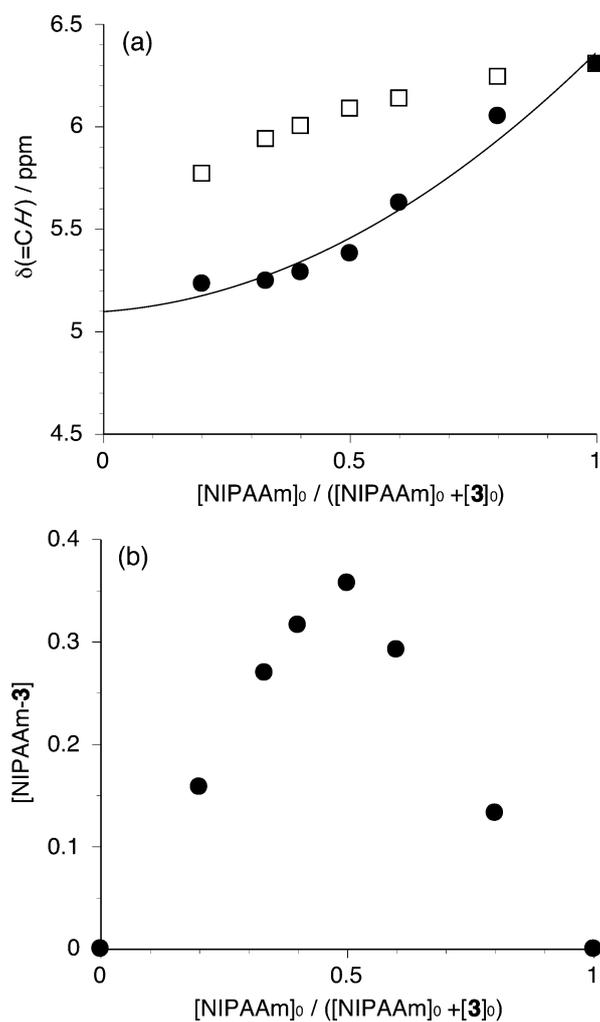


Figure 4. Job's plots for the association of NIPAAm with **3** in toluene- d_8 at 0°C evaluated from the changes in the =CH chemical shifts of NIPAAm in the presence of **3** (●) ($[NIPAAm]_0 + [3]_0 = 0.25 \text{ mol L}^{-1}$). (□) denotes chemical shift of NIPAAm alone at the corresponding concentration.

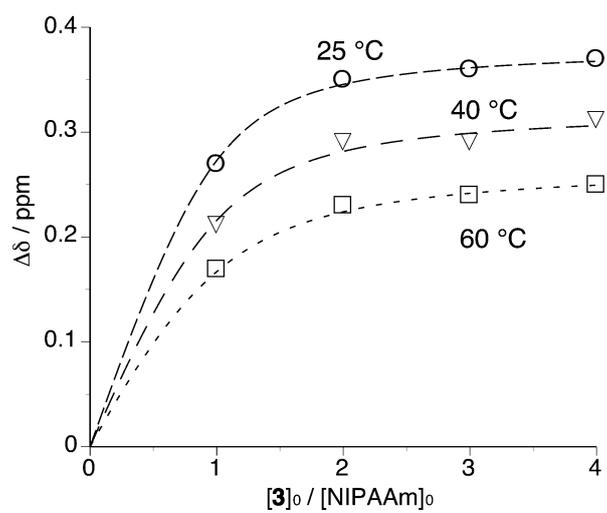


Figure 5. Changes in the chemical shifts of the =CH protons of NIPAAm in toluene-*d*₈ at various temperatures resulting from variation of the $[3]_0/[NIPAAm]_0$ ratio.

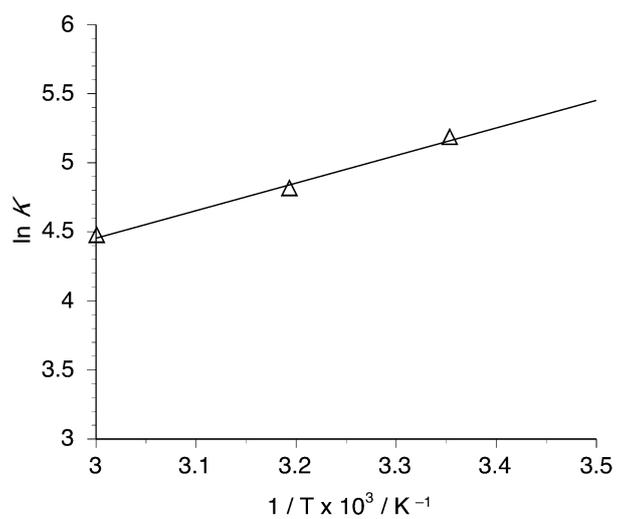


Figure 6. van't Hoff plot for 1:1 complex formation between NIPAAm and **3** in toluene- d_8 .

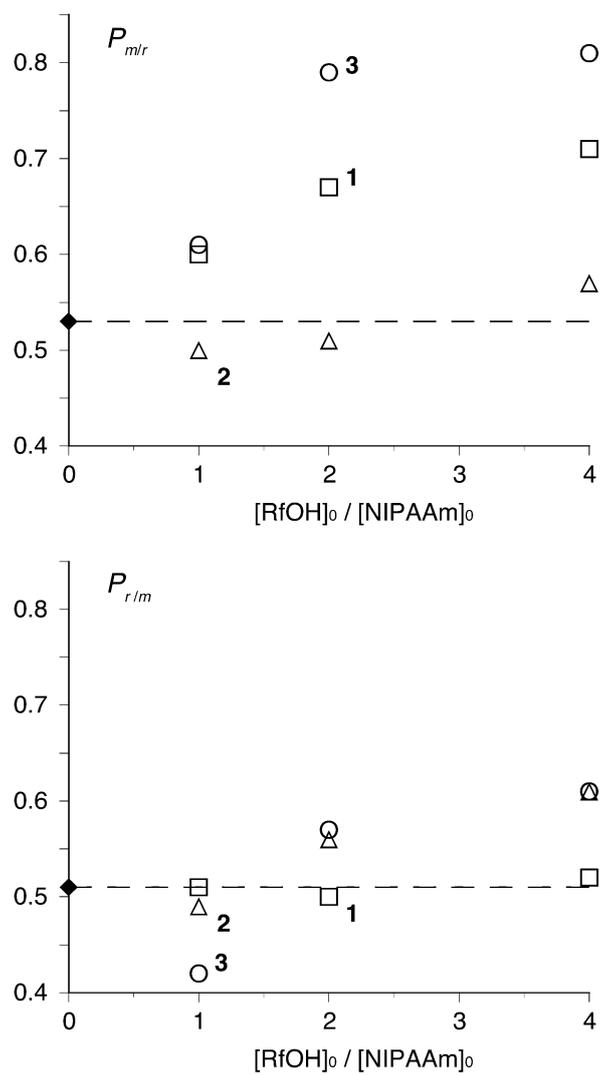


Figure 7. Dependence of probabilities of r -addition to m -ended radicals ($P_{m/r}$) and of m -addition to r -ended radicals ($P_{r/m}$) on the $[RfOH]_0/[NIPAAm]_0$ ratio.

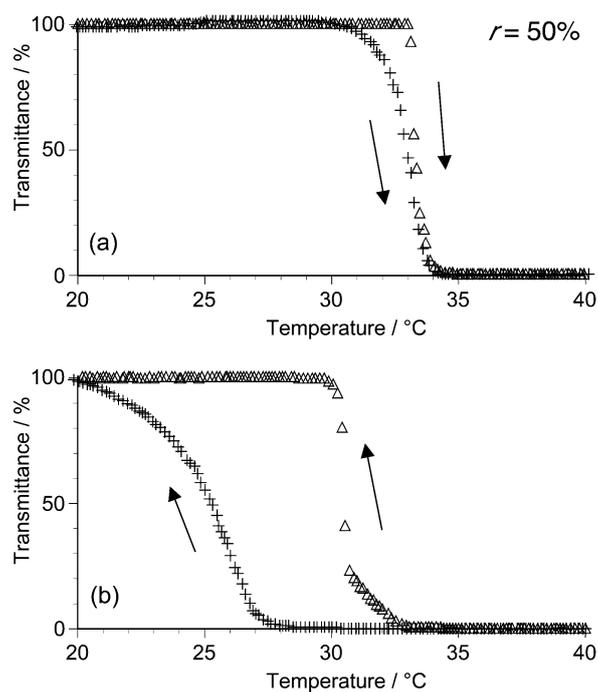


Figure 8. Temperature dependence of the transmittance at 500 nm of the aqueous solution of poly(NIPAAm) with $r=50\%$ with different triad tacticity distributions [(+): **C** in Table 3, (Δ): **D** in Table 3] in (a) heating and (b) cooling cycles. (0.1 w/v%, heating and cooling rates= $0.5^{\circ}\text{C min}^{-1}$).

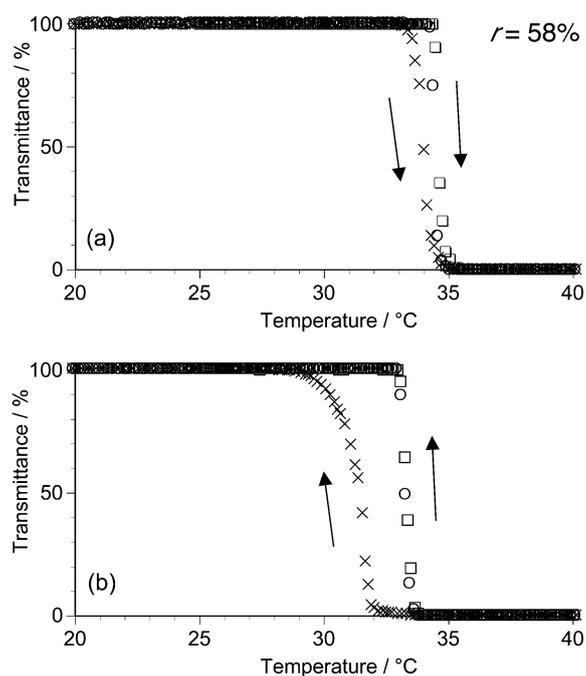


Figure 9. Temperature dependence of the transmittance at 500 nm of the aqueous solution of poly(NIPAAm) with $r=58\%$ with different triad tacticity distributions [(x): **F** in Table 3, (□): **G** in Table 3, (O): **H** in Table 3] in (a) heating and (b) cooling cycles. (0.1 w/v%, heating and cooling rates= $0.5^{\circ}\text{C min}^{-1}$).

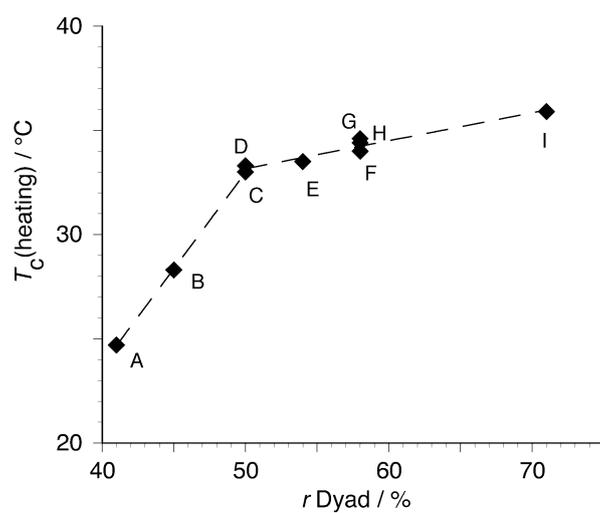


Figure 10. Relationship between $T_c(\text{heating})$ and the r dyad content of poly(NIPAAm) (0.1 w/v%, heating rate= $0.5^\circ\text{C min}^{-1}$).

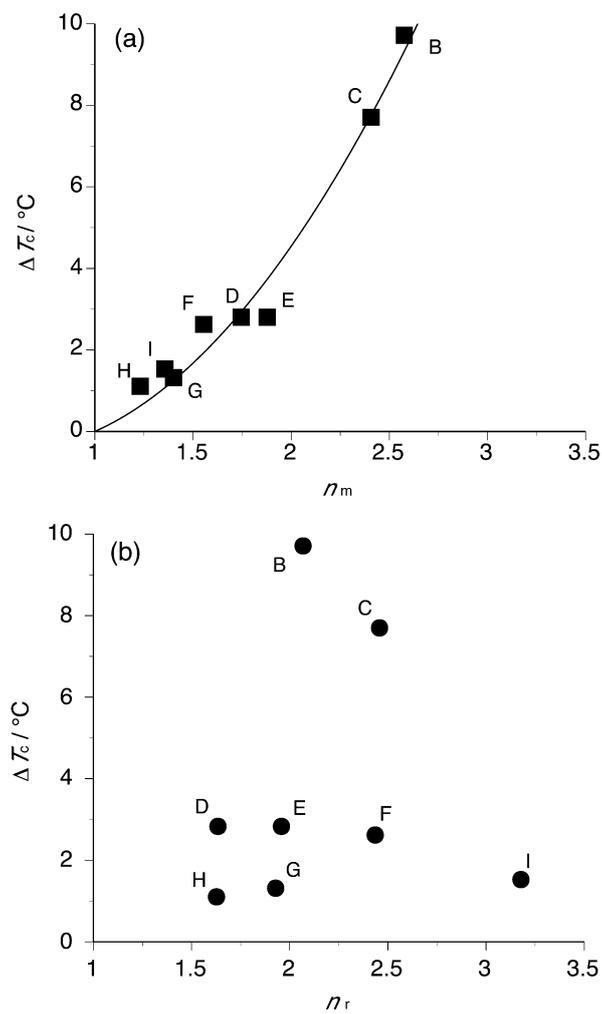
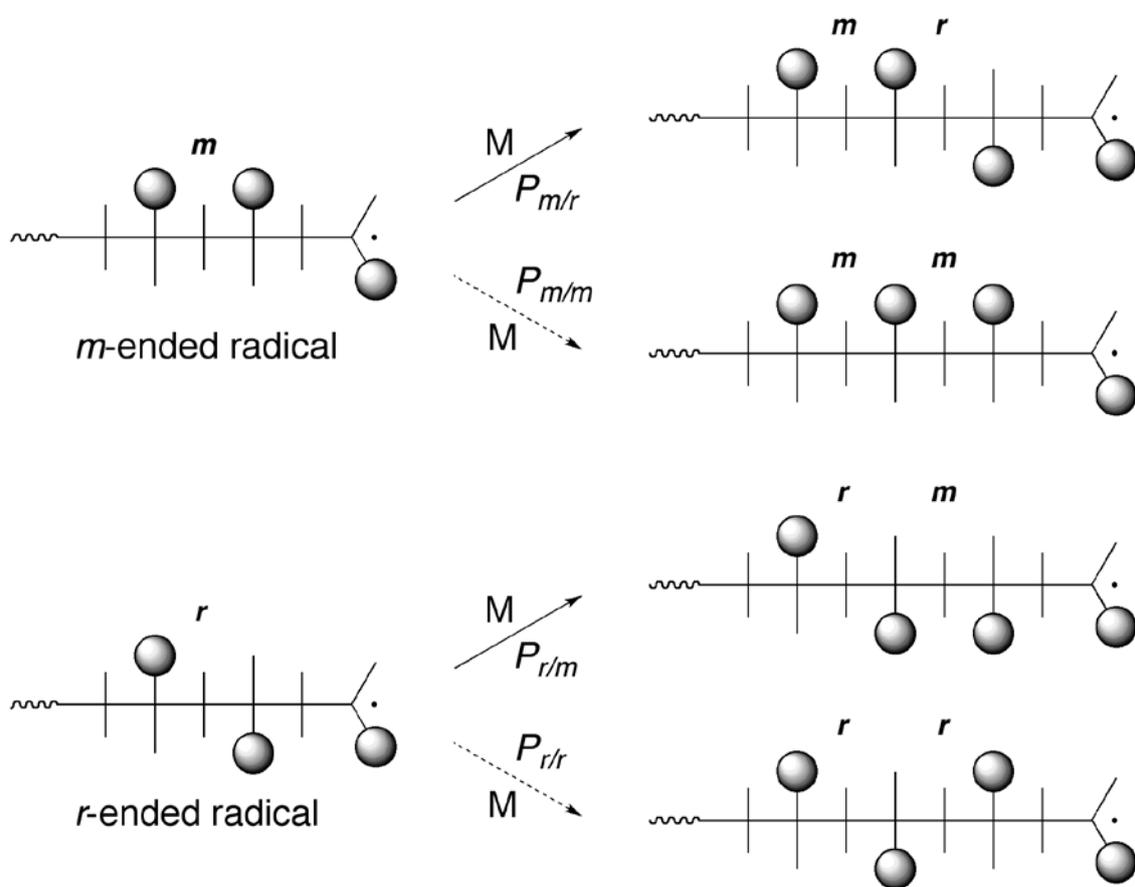
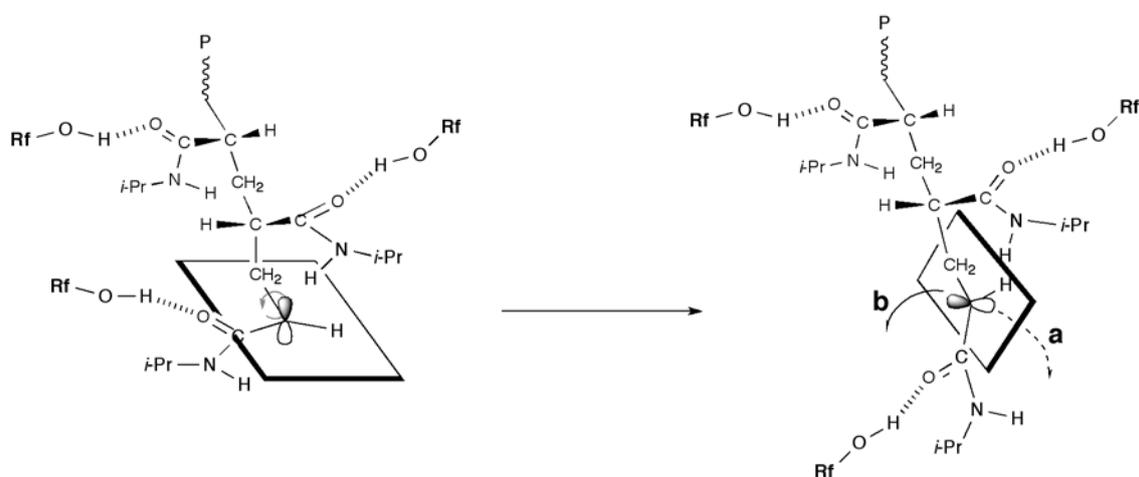


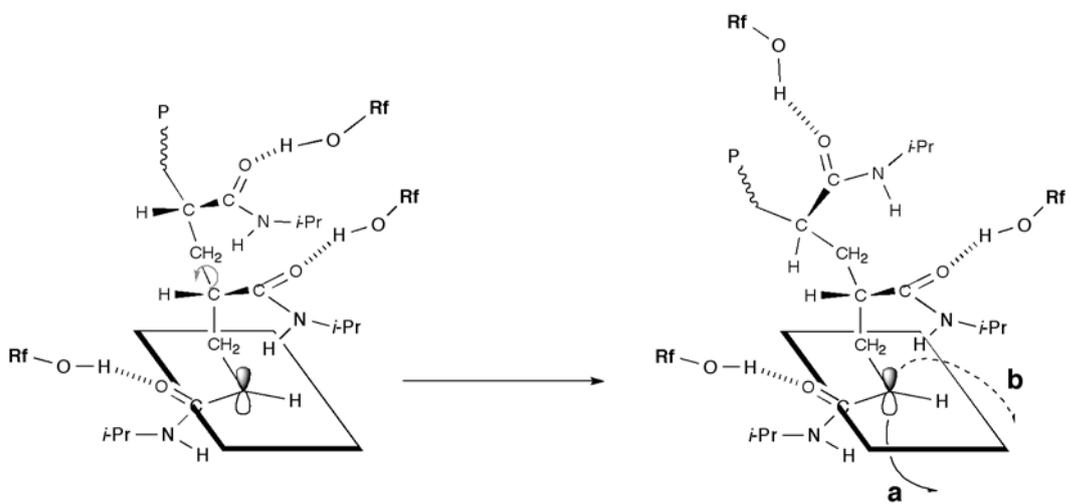
Figure 11. Relationship of ΔT_c to the average length of (a) m dyad (n_m) or (b) r dyad (n_r) in poly(NIPAAm).



Scheme 1. Favored stereoselections in the propagating reaction by *m*-ended or *r*-ended radicals in heterotactic-specific polymerization.



Scheme 2. Proposed mechanism for *m*-addition to *r*-ended radicals.



Scheme 3. Proposed mechanism for *r*-addition to *m*-ended radicals.