Effect of Polymerization Conditions on the Syndiotactic-Specificity in Radical Polymerization of *N*-Isopropylacrylamide and Fractionation of the Obtained Polymer According to the Stereoregularity

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Abstract

Radical polymerization of *N*-isopropylacrylamide (NIPAAm) was examined in the presence of hexamethylphosphoramide (HMPA). The addition of an excess amount of HMPA induced syndiotactic-specificity that gradually enhanced as the feed monomer was consumed. The syndiotacticity of the obtained poly(NIPAAm)s was improved by increasing the $[HMPA]_0/[NIPAAm]_0$ ratio to 5 and prolonging the polymerization time to 96h (*racemo* = 72%). It was also revealed that more stereoregulated poly(NIPAAm) could be fractionated by reprecipitating the resulting polymers from hexane-THF mixture. This result suggested that more stereoregulated poly(NIPAAm) showed a lower solubility than less stereoregulated poly(NIPAAm)s. Furthermore, unusual hysteresis was observed in transmittance analysis of an aqueous solution of the fractionated syndiotactic poly(NIPAAm).

Keywords: hydrogen bond; *N*-isopropylacrylamide; stereospecific radical polymerization

1. Introduction

The stereostructure of poly(N-isopropylacrylamide) [poly(NIPAAm)] has attracted less attention so far, because the synthetic route of poly(NIPAAm) has been limited via the free-radical polymerization of N-isopropylacrylamide (NIPAAm). Recently, both isotactic [1] and syndiotactic [2] poly(NIPAAm)s were prepared by deprotection of stereoregular polymers obtained by an anionic polymerization of protected NIPAAm monomer.   Furthermore, isotactic poly(NIPAAm)s with *meso* (*m*) diad over 90% were directly prepared even by radical polymerization of NIPAAm in the presence of Lewis acids such as yttrium trifluoromethanesulfonate [3,4].   It is assumed that the interest in the stereoregularity of poly(NIPAAm) is increasing in recent years.

More recently, we found that stereospecificity of radical polymerization of NIPAAm could be controlled, even under metal-free conditions, by utilizing a hydrogen-bond-assisted complex formation of NIPAAm monomer with Lewis bases such as phosphoric acid derivatives [5-8].   In the polymerization system, the syndiotactic-specificity seemed induced by the steric repulsion between the Lewis base coordinating at the propagating chain-end and that coordinating at the incoming monomer [6,7].
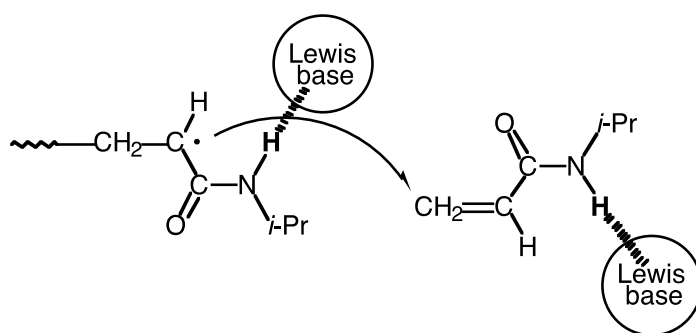
Among the examined Lewis bases, hexamethylphosphoramide (HMPA) induced the highest syndiotactic-specificity and the syndiotacticity reached up to *racemo* (*r*) diad = 70% [7].   In this study, the effect of polymerization conditions such as the ratio of $[\text{HMPA}]_0/[\text{NIPAAm}]_0$ and polymerization time on the induced

syndiotactic-specificity was examined in more detail and isolation of more stereoregulated fraction was attempted by reprecipitating the resulting poly(NIPAAm).

2. Experimental Section

2.1 Materials

N-Isopropylacrylamide (NIPAAm) (Tokyo Kasei Kogyo Co.) was recrystallized from hexane-benzene mixture. Toluene was purified through washing with sulfuric acid, water, and 5% aqueous NaOH; this was followed by fractional distillation. Tri-*n*-butylborane (*n*-Bu$_3$B) as a tetrahydrofuran (THF) solution (1.0M) and hexamethylphosphoramide (HMPA) were obtained from Aldrich Chemical Co. and used without further purification for polymerization reaction.

2.2 Polymerization

Typical polymerization procedure is as follows; NIPAAm (0.628 g, 5.5 mmol) was dissolved in toluene to prepare the 5 mL solution of 1.1 mol/L. Four milliliter of the solution was transferred to the glass ampoule and cooled at –60°C. The polymerization was initiated by adding *n*-Bu$_3$B solution (0.44 ml) into the monomer solution. After 24h, the reaction was terminated with a small amount of THF solution of 2,6-di-*t*-butyl-4-methylphenol at polymerization temperature. The polymerization mixture was poured into a large amount of diethyl ether or hexane : ethyl acetate mixtures (9 : 1 v/v), and the precipitated polymer was collected by filtration, and dried *in vacuo*. The polymer yield was determined from the weight ratio of the obtained polymer and the feed monomer.

2.3 Measurements

The ^{1}H NMR spectra were measured on an EX-400 spectrometer (JEOL Ltd.) operated at 400MHz. The tacticities of the poly(NIPAAm)s were determined from ^{1}H NMR

signals due to methylene group in chain measured in deuterated dimethyl sulfoxide (DMSO-d_6) at 150°C.   The molecular weights and molecular weight distributions of the polymers were determined by size exclusion chromatography (SEC) (HLC 8220 instrument (Tosoh Co.)) equipped with TSK gels (SuperHM-M and SuperHM-H (Tosoh Co.)) using dimethylformamide (LiBr 10 mmol/L) as an eluent at 40°C ([polymer] = 1.0 mg/mL, flow rate = 0.35 mL/min).   The SEC chromatogram was calibrated with standard polystyrene samples.   The transmittance of a poly(NIPAAm) solution (0.5 w/v %) was monitored at 500nm as a function of temperature with an UV-spectrophotometer (V-550 (JASCO Co.)).   The temperature was changed at 0.5 °C/min.

3. Results and discussion

3.1 The effect of polymerization conditions on the stereoregularity of the obtained poly(NIPAAm)s

First, we conducted radical polymerization of NIPAAm ($[NIPAAm]_0$ = 1.0 mol/l) for 24h in the presence of various amounts of HMPA (Table 1, Runs 1-4 and 13). The syndiotacticity gradually increased with an increase in the ratio of $[HMPA]_0/[NIPAAm]_0$, although the addition of HMPA less than the NIPAAm monomer hardly induced syndiotactic-specificity.   This result indicates that at least an equimolar amount of HMPA should be required for the induction of syndiotactic-specificity.   In the previous paper [7], we estimated, from a van't Hoff relationship, that the equilibrium constant (K) for 1:1 complex between NIPAAm and HMPA in toluene at –60°C is 446 l/mol.   Thus, we evaluated the degree of association (α) of NIPAAm with HMPA for the actual polymerization systems (Table 1).   It was found that NIPAAm monomer quantitatively formed 1:1 complex, except for the addition of half amount of HMPA, although the syndiotacticity gradually increased as the $[HMPA]_0/[NIPAAm]_0$ ratio increased.   Furthermore, the syndiotacticity of the obtained poly(NIPAAm)s

reduced with a decrease in [NIPAAm]$_0$ even when NIPAAm monomer quantitatively formed 1:1 complex in the presence of a twofold amount of HMPA (Table 1, Runs 5-7). These results contrast with a HMPA-improving enantioselectivity in deprotonation reaction of 4-substituted cyclohexanone derivatives, that is, the enantioselectivity increased with an increase in the fraction of monomeric chiral bidentate lithium amide coordinated by HMPA [9-12].

We have proposed that the propagation reaction between propagating radical and incoming monomer, both of which are coordinated by HMPA, proceeds in a syndiotactic-specific manner [6,7]. If the equilibrium between free and complexed monomers and that between free and complexed propagating species are enough slower than the rate of the propagation reaction, syndiotacticity should increase in proportion to the degree of association. However, these equilibriums would be fast, taking into account that free and complexed NIPAAm monomers were not distinguished for the timescale of NMR. Therefore, it is thought that concernment of free propagating radical and/or free incoming monomer, both of which should favor a non-specific propagation, increased as the concentration of HMPA decreased, even though the degree of association was estimated at unity.

<Table 1>

Next, we conducted NIPAAm polymerization for shorter time under the conditions where the highest syndiotactic polymer was obtained ([NIPAAm]$_0$ = 1.0 mol/l and [HMPA]$_0$ = 2.0 mol/l) (Table 1, Runs 8-13). Over half of monomer was consumed within 1 hour. Fig. 1 portrays a relationship between the polymer yield and the syndiotacticity of the obtained poly(NIPAAm)s. The syndiotacticity linearly increased from 62% to 70% with an increase in the polymer yield. This result indicates that the induced syndiotactic-specificity was more enhanced at the later stage

of polymerization.

<Fig.1>

Consequently, it is suggested that the induction of a significant syndiotactic-specificity requires two factors, an excess amount of HMPA and a quantitative consumption of NIPAAm monomer, at the same time. Thus, polymerizations at a reduced $[NIPAAm]_0$ were carried out for longer time in the presence of a large excess amount of HMPA ($[NIPAAm]_0$ = 0.4 mol/l, $[HMPA]_0/[NIPAAm]_0$ = 5). The syndiotacticity of the polymer obtained for 48h was r = 70%, although *ca.* 40% of NIPAAm monomer remained unconsumed (Table 1, Run 14). Furthermore, the syndiotacticity reached up to 72% by prolonging the polymerization time to 96h (Table 1, Run 15).

3.2 Fractionation of syndiotactic poly(NIPAAm) by reprecipitation

As mentioned above, the induced syndiotactic-specificity was more enhanced at the later stage of polymerization. This means that the obtained poly(NIPAAm)s consisted of polymers having different syndiotacticities. In general, stereoregulated polymers have poorer solubilities than non-stereoregulated polymers. For instance, isotactic poly(NIPAAm)s were insoluble in water, although atactic poly(NIPAAm) is one of representative water-soluble polymers [1, 3]. Thus, we tried isolating more stereoregulated poly(NIPAAm)s by reprecipitation from hexane-THF mixture as follows (Scheme 1); 1.4 ml of hexane was slowly added into THF solution (2.0 ml) of syndiotactic poly(NIPAAm) (10.6 mg) (Table 1, run 13). The precipitate was collected by centrifugation as an insoluble part. The supernatant was poured into a large amount of hexane and the precipitate was collected by centrifugation as a soluble part.

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<Scheme 1>

<Fig. 2>

Fig. 2 displays ^{1}H NMR spectra of the soluble and insoluble parts after reprecipitation, together with that of the original syndiotactic poly(NIPAAm). Syndiotacticity of the insoluble part slightly increased and that of the soluble part slightly decreased compared with that of the original poly(NIPAAm). This result indicates that poly(NIPAAm) could be discriminated by solubility depending on the tacticity, as expected.

It is well known that poly(NIPAAm) shows a lower critical solution temperature (LCST) that lies between 30 and 35°C [13-16]. Thus, we investigated a thermosensitive property of syndiotactic poly(NIPAAm) with r = 75% [17]. Interestingly, it took a couple of days to completely dissolve it in water, suggesting that highly syndiotactic poly(NIPAAm) exhibited poor solubility as well as isotactic poly(NIPAAm)s. Figure 3a shows the temperature dependence of the light transmittance of an aqueous solution of the syndiotactic poly(NIPAAm) on both the heating and cooling processes. On the heating process, the light transmittance drastically decreased at ca. 32°C, corresponding to the typical behavior of atactic poly(NIPAAm)s (Figure 3b) [18]. However, on the cooling process, the light transmittance drastically increased around 15°C, although it rippled within 10% until ca. 15°C. Thus, it is assumed that the tacticity of poly(NIPAAm) influenced the interaction between macromolecules more than hydrophobic hydration and consequently only its dissolving process was made difficult.

<Fig. 3>

4. Conclusions

Radical polymerization of NIPAAm was examined in the presence of HMPA. Syndiotactic-specificity was induced by adding an excess amount of HMPA and gradually enhanced as the feed monomer was consumed. More stereoregulated poly(NIPAAm)s could be fractionated by reprecipitating the obtained syndiotactic poly(NIPAAm) from hexane-THF mixture. The aqueous solution of the fractionated syndiotactic poly(NIPAAm) showed a large hysteresis in transmittance analysis between the heating and cooling processes. This suggests that higher-level control of stereoregularity of poly(NIPAAm) brings about unexpected properties. Now, further work is under way to investigate the effect of tacticity of poly(NIPAAm) on the solution property in more detail.

References and Notes

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[17] The used polymer ($r = 75\%$, $M_n = 1.11$ x 10^4, $M_w/M_n = 1.4$) was fractionated from poly(NIPAAm) ($r = 72\%$, $M_n = 0.99$ x 10^4, $M_w/M_n = 1.4$) that was prepared under the same conditions as Table 1, Run 15.

[18] The atactic polymer was prepared with dimethyl 2,2'-azobisisobutyrate in toluene at 60°C ($r = 55\%$, $M_n = 11.6$ x 10^4, $M_w/M_n = 2.4$).

Table 1
Radical Polymerization of NIPAAm in toluene at –60°C for various time in the presence of HMPA

Run	[NIPAAm]$_0$ mo/l	[HMPA]$_0$ mol/l	Time h	Yield %	Diad tacticity/%[a] m	r	M_n[b] $\times 10^4$	M_w/M_n[b]	α[c]
1[d]	1.0	0.0	24	10	43	57	0.74	1.8	-
2	1.0	0.5	24	>99	42	58	1.22	2.1	0.50
3	1.0	1.0	24	>99	35	65	1.18	1.7	0.95
4	1.0	1.5	24	>99	33	67	1.63	1.8	1.00
5	0.25	0.5	24	50	38	62	0.91	1.7	0.99
6	0.50	1.0	24	84	34	66	1.03	1.6	1.00
7	0.75	1.5	24	97	34	66	1.14	1.6	1.00
8	1.0	2.0	0.25	23	38	62	1.28	2.1	1.00
9	1.0	2.0	0.5	41	35	65	1.52	2.0	1.00
10	1.0	2.0	0.75	55	34	66	1.62	1.7	1.00
11	1.0	2.0	1.0	63	34	66	1.49	1.7	1.00
12	1.0	2.0	1.5	71	33	67	1.51	1.8	1.00
13	1.0	2.0	24	>99	30	70	1.02	1.9	1.00
14	0.40	2.0	48	58	30	70	1.18	1.4	1.00
15	0.40	2.0	96	88	28	72	1.13	1.4	1.00

[NIPAAm]$_0$ / [n-Bu$_3$B]$_0$ = 10.

[a] Determined by ^{1}H NMR signals due to methylene group.

[b] Determined by SEC (polystyrene standards).

[c] Degree of association estimated with K = 446 l/mol.

[d] Monomer, polymer, or both were precipitated during the polymerization reaction.

Captions for Fig.s and Scheme

Fig. 1. The yield dependence of r diad in poly(NIPAAm)s prepared in toluene at –60°C in the presence of twofold amounts of HMPA.

Fig. 2. Expanded ^{1}H NMR spectra of main-chain methine and methylene groups of poly(NIPAAm)s; (a) original (Table 1, Run 13), (b) insoluble part, and (c) soluble part. Measured in DMSO-d_6 at 150°C. * denotes ^{13}C satellite peak of (C$\underline{H}_3$)$_2$CH- and × denotes impurities.

Fig. 3. Temperature dependence of the light transmittance (500nm) of the aqueous solutions of (a) syndiotactic poly(NIPAAm) with r = 75% and (b) atactic poly(NIPAAm)s prepared conventional radical polymerization at 60°C (r = 55%).

Scheme 1. Flowchart for fractionation of syndiotactic poly(NIPAAm) according to stereoregularity.
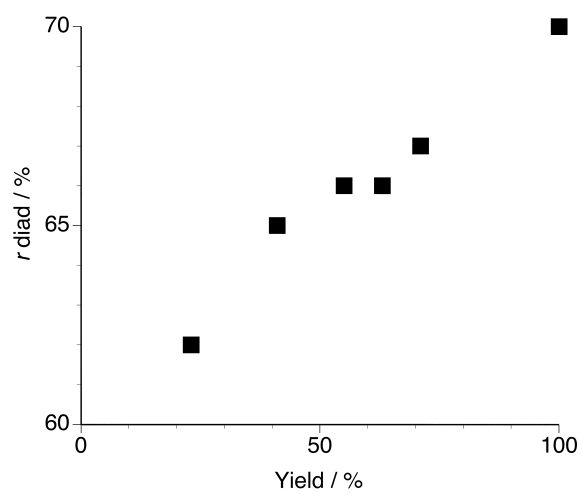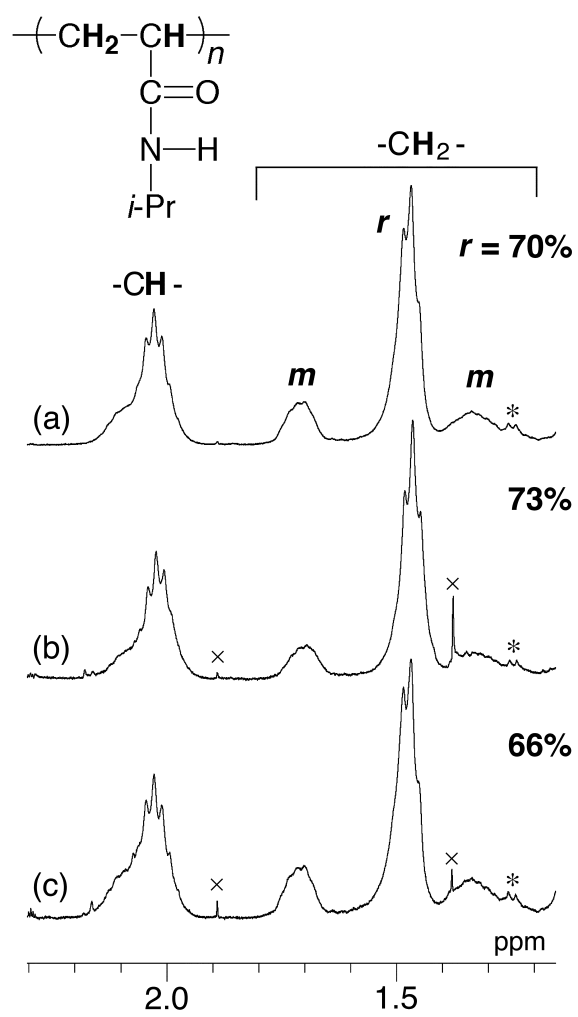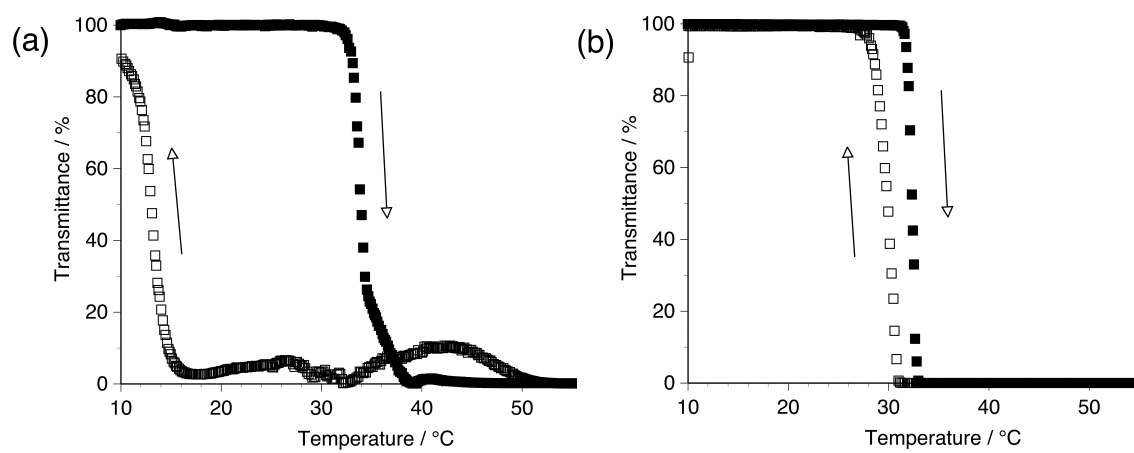
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original (10.6 mg)

THF 2.0 ml
Hexane 1.4 ml

insoluble part
(4.0 mg, 38%)

supernatant

Hexane

soluble part
(4.7 mg, 44%)