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Stereocontrolled radical polymerization of acrylamides and methacrylamides using Lewis acids

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Abstract—The isotactic-specific radical polymerization of various acrylamides and methacrylamides was attained in the presence of a catalytic amount of Lewis acids, such as $Y(OTf)_3$ and $Yb(OTf)_3$, whereas the normal radical process generally affords slightly syndiotactic polymers for acrylamides and syndiotactic ones for methacrylamides. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Stereocontrol during radical polymerization is very important because it has been widely used for producing various polymers in industry, and the polymer properties are often significantly influenced by stereoregularlity. Many stereocontrolled methods in ionic and coordination polymerizations have been reported. However, it is generally quite difficult to control the stereochemistry in the radical system, and only a few stereospecific radical polymerizations have been reported.[1–3] Although it is known that Lewis acids affect the monomer reactivity and stereochemistry during the radical copolymerization,[4] the influence of Lewis acids on the stereochemistry during radical homopolymerization had not been reported until very recently, probably because no clear effect on tacticity had been observed.[5,6]

We recently found that Lewis acids, such as zinc halides and scandium trifluoromethanesulfonate [$Sc(OTf)_3$], as an additive to the radical polymerization of the designed monomers, the α-(alkoxymethyl)acrylates, catalytically affected the main-chain tacticity, and the polymers rich in isotacticity, syndiotacticity, and heterotacticity to a certain extent were synthesized by controlling the intra- and intermolecular coordinations of the α-substituents to a Lewis acid catalyst.[7] On the other hand, the radical polymerization of the conventional monomers, the methacrylates, in the presence of $Sc(OTf)_3$ afforded polymers with a lower syndiotacticity than that of the polymers produced by the radical system without Lewis acids.[8] Here, we report our recent work on the stereoregulation during the radical polymerization of (meth)acrylamides, such as acrylamide (AM), *N*-isopropylacrylamide (NIPAM), *N*,*N*-dimethylacrylamide (DMAM), *N*-methylmethacrylamide (MMAM), and *N*-isopropylmethacrylamide (IPMAM) (Fig. 1), in the presence of various metal triflates [$M(OTf)_3$].[9,10]

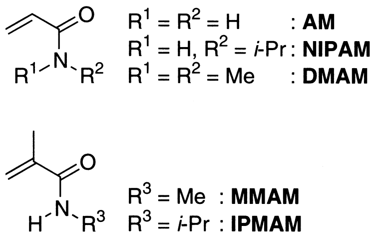

Figure 1. Structure of monomers.

Poly(acrylamide) and poly(methacrylamide) derivatives are often used as water-soluble polymers with various applications like biomedical materials, etc. AM, methacrylamide, and their *N*-monosubstituted derivatives can be polymerized only by the radical method because of the acidic amide proton. In addition, the *N*,*N*-disubstituted methacrylamide, except for methacryloylaziridine,[11] cannot be polymerized by any methods due to steric reasons. Therefore, little data are available for the stereochemical control during the polymerization of (meth)acrylamides.[12] The development of an effective and facile stereocontrol method is very important in the areas of polymer chemistry and industry.

2. Results and discussion

The radical polymerization of NIPAM was carried out in the presence of various rare earth metal salts at 60°C in methanol (initiator: α,α-azobisisobutyronitrile (AIBN),

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Keywords: radical polymerization; acrylamide; methacrylamide; Lewis acid; isotactic polymer.

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Table 1. Radical polymerization of NIPAM in the presence of various Lewis acids in methanol

Entry	Lewis acid	Temperature (°C)	Yield (%)[a]	Tacticity[b] *m*/*r*
1	None	60	82	45/55
2	None	−20[c,d]	78	44/56
3	$Sc(OTf)_3$	60	86	62/38
4	$Y(OTf)_3$	60	94	80/20
5	$Y(OTf)_3$	−20[c,d]	85	90/10
6	$Y(OTf)_3$	−40[c,e]	85	89/11
7	$Y(OTf)_3$	−78[c,e]	98	71/29
8	$Yb(OTf)_3$	60	89	82/18
9	$Lu(OTf)_3$	60	97	84/16
10	$ScCl_3$	60	85	57/43
11	$YbCl_3$	60	95	67/33

$[NIPAM]_0$=2.40 M, $[\text{Lewis acid}]_0$=0.20 M, $[AIBN]_0$=0.02 M, time=3 h.

[a] Hot water-insoluble part.

[b] Determined by ^1H NMR measurement in DMSO-d_6 at 170°C.

[c] Time=24 h.

[d] Initiator: AIBN with UV irradiation.

[e] Initiator: *n*-Bu_3B with air ($[n\text{-}Bu_3B]_0$=0.1 M).

[NIPAM]/[Lewis acid]=12). The clear effect of the Lewis acids, especially the triflate salts, on the stereocontrol was found and some of the results are summarized in Table 1. For example, the diad tacticity of poly(NIPAM) obtained by the polymerization with $Y(OTf)_3$ was meso (*m*)=80% (entry 4), while the polymer prepared by the normal radical method was slightly rich in sindiotacticity (racemo diad (*r*)=55%) (entry 1). The polymers rich in isotacticity (*m*=79–84%) were obtained using most triflate salts except for $Sc(OTf)_3$ (entry 3) and $La(OTf)_3$, which afforded polymers with lower isotacticities. The rare earth metal chlorides, such as $ScCl_3$ and $YbCl_3$ (entries 10 and 11), were less effective than the triflate salts in enhancing the isotacticity.

This effect of the metal triflates was quite dependent on the polymerization conditions, such as solvent and temperature, whereas, in the absence of a Lewis acid, the tacticity of poly(NIPAM) is only slightly influenced by the polymerization conditions. The *m* content of the polymers obtained in the presence of $Y(OTf)_3$ in methanol at −20°C remarkably increased and reached 90% (entry 5), although a temperature effect was hardly observed for the polymer prepared by the normal radical method (entry 2). The optimized polymerization temperature seems to be around −20°C, and the polymerization at lower temperature (entries 6 and 7) gave a polymer with a lower isotacticity.

A significant solvent effect on the stereoregularity was also observed for the NIPAM polymerization using $Y(OTf)_3$, in contrast to the normal radical process (Fig. 2). The polymerization systems were homogeneous in polar solvents, such as tetrahydrofuran (THF), methanol, methyl sulfoxide (DMSO), and water, and heterogeneous in chloroform. Methanol was the best solvent for the isotactic-specific polymerization, and the effect was observed to some extent even in water. However, the effect almost disappeared in DMSO, which may very tightly coordinate to the Lewis acid and prevent any interaction of the monomer with the Lewis acid.

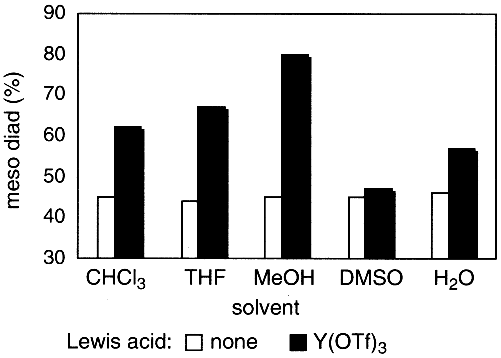

Figure 2. Solvent effect on the radical polymerization of NIPAM in the presence of $Y(OTf)_3$ at 60°C for 3 h ($[NIPAM]_0$=2.4 M, $[Y(OTf)_3]_0$=0.2 M, $[AIBN]_0$=0.02 M, Na_2SO_3 and $K_2S_2O_8$ were used as an initiator system in H_2O).

Fig. 3 shows the influence of the ratio of $[Y(OTf)_3]_0$ to $[NIPAM]_0$ on the isotacticity of the obtained polymers. A catalytic amount of Lewis acid was enough to control the stereoregularity in this system. The monomer may be activated by the coordination of a Lewis acid to preferentially polymerize the non-coordinated monomer. This leads to the selective existence of the Lewis acid around the ω-end of the propagating polymer, and the stereochemistry of the polymerization can be influenced. The Lewis acid is probably detached from the polymer chain after adding some monomers to coordinate to the free monomer again.[7d] The polymer obtained in the presence of 20 mol% of $Y(OTf)_3$ at −20°C showed an isotacticity of *m*=92%. This value may be the highest one for the homogeneous radical polymerization of conventional vinyl monomers.

The stereocontrolled radical polymerization using Lewis acid catalysts was successfully applied to the polymerization of methacrylamides. Table 2 shows the results of the radical polymerization of MMAM in the presence of various Lewis acids in methanol at 60°C (initiator: AIBN). The polymers were obtained as a THF-insoluble part with a molecular weight of $>2.2\times10^4$ in good yield. A significant increase in isotacticity was observed for the polymers obtained with metal triflates, such as $Yb(OTf)_3$, $Y(OTf)_3$, $Tm(OTf)_3$, and $Lu(OTf)_3$ (triad isotacticity (*mm*)>42%

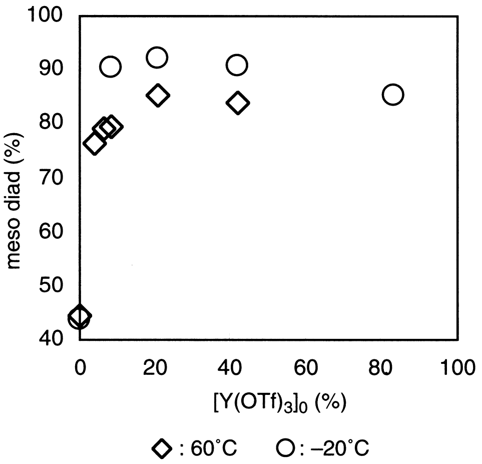

Figure 3. Relationship between the mol ratio of $Y(OTf)_3$ to NIPAM and the diad tacticity (*m*) of the obtained polymer (solvent: methanol, initiator: AIBN (60°C) and AIBN with UV irradiation (−20°C), $[NIPAM]_0$=2.4 M, $[AIBN]_0$=0.02 M).

Table 2. Radical polymerization of MMAM in the presence of various Lewis acids in methanol at 60°C

Entry	Lewis acid	Yield (%)[a]	M_n×10^{-4} (M_w/M_n)[b]	Tacticity[c] *mm*/*mr*/*rr*
1	None	97	2.2 (3.3)	2/29/69
2	$Sc(OTf)_3$	92	4.3 (2.2)	28/55/17
3	$Yb(OTf)_3$	89	4.0 (4.8)	46/44/10
4	$Y(OTf)_3$	91	7.5 (3.1)	46/40/14
5	$Tm(OTf)_3$	94	6.9 (2.9)	45/44/11
6	$Lu(OTf)_3$	74	4.8 (4.5)	42/46/12
7	$YbCl_3$	85	6.2 (2.8)	27/49/24

$[MMAM]_0$=2.0 M, [Lewis acid]$_0$=0.2 M, $[AIBN]_0$=0.02 M, time=24 h.

[a] THF-insoluble part.

[b] Determined by SEC (poly(ethylene oxide) standard) in water containing 0.1 M LiCl at 40°C.

[c] Determined by ^{1}H NMR measurement in DMSO-d_6 at 170°C.

(*m*>65%), entries 3–6), while the polymerization in the absence of a Lewis acid afforded a syndiotactic polymer (triad syndiotacticity (*rr*)=69% (*r*=83.5%), entry 1). $Sc(OTf)_3$ and $YbCl_3$ showed a much lower effect on the stereocontrol as observed for the polymerization of NIPAM (entries 2 and 7).

The solvent effect of the MMAM polymerization using $Yb(OTf)_3$ (10 mol%) at 60°C was investigated (Fig. 4). Solvents greatly influenced the stereochemistry, and methanol was again the best solvent. The obtained polymer in methanol had a tacticity of *mm*/*mr*/*rr*=46/44/10 (*m*/*r*=68/32), whereas almost no effect was observed for the polymerization in toluene and water. On the other hand, the temperature effect was hardly found for the radical polymerization of MMAM using a Lewis acid in contrast to the NIPAM polymerization.

The polymerization was carried out for various $[Yb(OTf)_3]_0/[MMAM]_0$ ratios in methanol at 60°C, and the tacticity of the obtained polymer was affected by the Lewis acid concentration (Fig. 5). The *mm* value significantly increased as the concentration of the Lewis acid increased up to about 20 mol%, but the further addition of a Lewis acid slightly reduced the effect. The polymerization using 20 mol% of $Yb(OTf)_3$ to the monomer ($[MMAM]_0$=0.5 or 1.0 M) produced a polymer with the highest isotacticity of *mm*=59%.

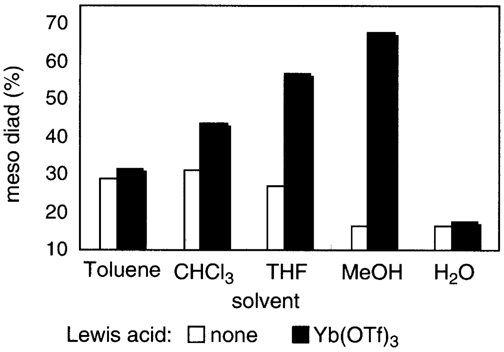

Figure 4. Solvent effect on the radical polymerization of MMAM in the presence of $Yb(OTf)_3$ at 60°C for 24 h ($[MMAM]_0$=2.0 M, $[Yb(OTf)_3]_0$=0.2 M, $[AIBN]_0$=0.02 M, Na_2SO_3 and $K_2S_2O_8$ were used as an initiator system in H_2O).

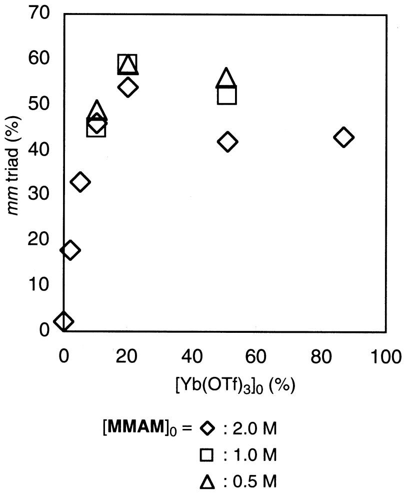

Figure 5. Relationship between the mol ratio of $Yb(OTf)_3$ to MMAM and the triad tacticity (*mm*) of the obtained polymer (solvent: methanol, temperature: 60°C, initiator: AIBN).

Table 3 shows the results of the radical polymerization of (meth)acrylamides, AM, DMAM, and IPMAM, in the absence and presence of $Yb(OTf)_3$ in methanol. The isotactic-specific effect of the Lewis acid was also observed for the polymerization of these monomers. Poly(AM) has been industrially produced by the radical method in water, and it is very difficult to change its stereoregularity by the conventional polymerization methods.[13c] The polymer obtained with $Yb(OTf)_3$ was rich in isotacticity (*mm*=65%) (entry 2), indicating that this method using Lewis acids is very effective. The *m* content of poly(DMAM) was increased by 38% using $Yb(OTf)_3$ at 60°C (entries 3 and 4). Furthermore, the polymer having *m*=88% was synthesized at 0°C (entry 6). The isotactic-rich poly(IPMAM) (*mm*=58%) was obtained as a hot water-insoluble fraction using $Yb(OTf)_3$ at 60°C (entry 10), whereas the radical polymerization without the Lewis acid gave a polymer rich in syndiotacticity (*rr*=68%, entry 9).

Table 3. Radical polymerization of AM, DMAM, and IPMAM in the presence of $Yb(OTf)_3$ in methanol

Entry	Monomer	Lewis acid	Temperature (°C)	Yield (%)[a]	Tacticity[b] *m*/*r* (*mm*/*mr*/*rr*)
1	AM	None	0[c]	60	(22/49/29)
2	AM	$Yb(OTf)_3$	0[c]	50	(65/29/6)
3	DMAM	None	60	73	46/54
4	DMAM	$Yb(OTf)_3$	60	86	84/16
5	DMAM	None	0[c]	81	49/51
6	DMAM	$Yb(OTf)_3$	0[c]	76	88/12
7	DMAM	None	−78[d]	62	55/45
8	DMAM	$Yb(OTf)_3$	−78[d]	76	65/35
9	IPMAM	None	60	50	(1/31/68)
10	IPMAM	$Yb(OTf)_3$	60	77	(58/37/5)
11	IPMAM	None	20[c]	16	(~0/20/80)
12	IPMAM	$Yb(OTf)_3$	−20[c,e]	13	(67/29/4)

[Monomer]$_0$=1.0 M, [Lewis acid]$_0$=0.1 M, $[AIBN]_0$=0.02 M, time=24 h.

[a] Polymers were purified by dialysis with cellophane in water (entries 1–8) and hot water-insoluble part (entries 9–12).

[b] Determined by ^{13}C NMR measurement in D_2O at 80°C (entries 1 and 2), ^{1}H NMR measurement DMSO-d_6 at 170°C (entries 3–8), and ^{13}C NMR measurement in DMSO-d_6 at 80°C (entries 9–12).

[c] Initiator: AIBN with UV irradiation.

[d] Initiator: *n*-Bu_3B with air ($[n\text{-}Bu_3B]_0$=0.1 M).

[e] Time=48 h.

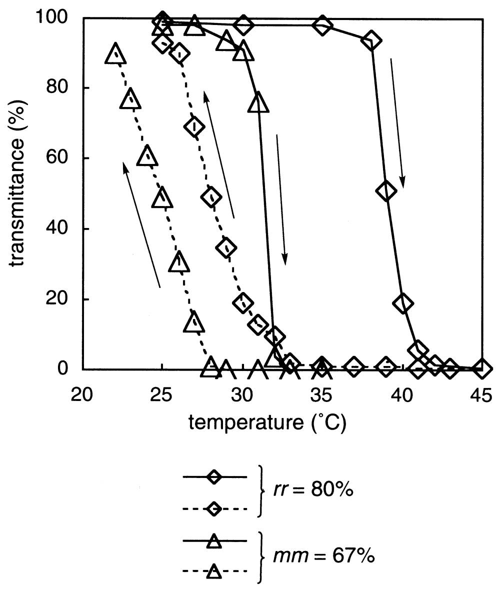

Figure 6. Temperature effect on the transmittance (500 nm) of the isotactic (*mm*=67%) and syndiotactic (*rr*=80%) poly(IPMAM) aqueous solutions (2 mg/ml).

The polymerization at lower temperature afforded polymers with higher stereoselectivities (entries 11 and 12). The difference in bulkiness of the side chains of MMAM and IPMAM should be responsible for the different temperature effects.

The difference in the main-chain tacticity of the obtained polymers clearly affected the polymer properties. For example, the isotactic (*mm*=76%, Table 3, entry 12) and syndiotactic (*rr*=80%, Table 3, entry 11) poly(IPMAM)s show a different thermosensitive phase transition in water (Fig. 6). The transmittance change of a water solution of the polymers at 500 nm was investigated at 20–45°C. The turbidity was observed at 38–42°C for the syndiotactic polymer during the heating process, and upon cooling from 33°C to 25°C, the transmittance was increased to be transparent. On the other hand, the cloud point of the isotactic polymer was lower than that of the syndiotactic one during both the heating (30–33°C) and cooling (<28°C) processes.

3. Conclusions

The efficient isotactic-controlled radical polymerizations of acrylamides and methacrylamides, NIPAM, AM, DMAM, MMAM, and IPMAM, were accomplished by using a catalytic amount of Lewis acids, such as $Y(OTf)_3$ and $Yb(OTf)_3$, in methanol, whereas the normal radical process generally affords slightly syndiotactic polymers for the acrylamides and syndiotactic ones for the methacrylamides. The effect was strongly dependent on the polymerization conditions, such as the Lewis acid, solvent, and temperature. The difference in the stereoregularity of the obtained polymers clearly influenced the phase transition temperature of poly(IPMAM) in water. This method should be applicable to many other polar vinyl monomers and may provide novel materials with superior properties.

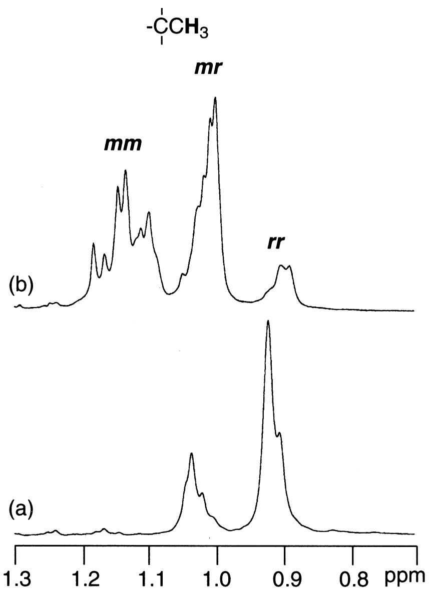

Figure 7. The 400 MHz ^1H NMR spectra of α-methyl protons of poly(MMAM) obtained in the absence (Table 2, entry 1) (a) and presence of $Yb(OTf)_3$ (Table 2, entry 3) (b) (in DMSO-d_6 at 170°C).

4. Experimental

4.1. General

The ^1H and ^{13}C NMR spectra were measured using Varian Gemini-2000 (400 MHz for ^1H) and Varian INOVA-500 (500 MHz for ^1H) spectrometers. The diad tacticities of poly(NIPAM) and poly(DMAM) were determined on the bases of the peaks of the main-chain methylene protons.[13] The triad tacticities were determined from the peaks of the α-methyl protons for poly(MMAM) (Fig. 7), the α-carbon for poly(AM) (Fig. 8), and the quaternary carbon for poly(IPMAM).[13] Ultraviolet (UV) absorption spectra were

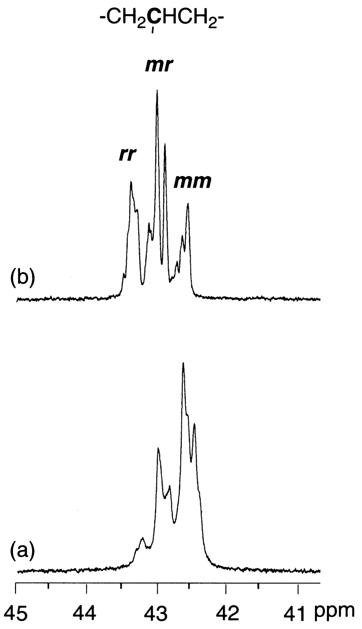

Figure 8. The 125 MHz ^{13}C NMR spectra of α-carbon of poly(AM) obtained in the presence (Table 3, entry 2) (a) and absence of $Yb(OTf)_3$ (Table 3, entry 1) (b) (in D_2O at 80°C).

obtained using a JASCO V-570 spectrometer. The size exclusion chromatographic (SEC) analyses were performed on a JASCO PU-980 equipped with JASCO RI-930 and JASCO UV-970 detectors using TSK α-M and α-3000 columns connected in series (eluent: water containing 0.1 M LiCl, temperature=40°C, flow rate=1.0 ml/min). Calibration was carried out using standard poly(ethylene oxide)s. The monomers, NIPAM (Wako) and IPMAM (Aldrich), were recrystallized from hexane/toluene (10/1) and hexane, respectively. MMAM (TCI) and DMAM (Wako) were distilled before use. AM (TCI) was used as received. AIBN was purified by recrystallization from methanol. Commercially available Lewis acids, such as $Sc(OTf)_3$, $Y(OTf)_3$, and $Yb(OTf)_3$ (Aldrich), were used after drying in vacuo. Dry solvents, toluene, THF, methanol, and DMSO (Kanto), were used for the polymerizations without further purification.

4.2. Polymerization procedure

The radical polymerization was carried out according to the following procedure. A Lewis acid, a monomer, and AIBN were placed in a glass ampoule equipped with a three-way stopcock under a dry nitrogen atmosphere. A solvent was introduced with a syringe, and the polymerization was initiated by heating. The reaction mixture was then poured into a large excess of hot water (>70°C) for the NIPAM and IPMAM polymerization systems, THF for the AM and MMAM, and ether for the DMAM. The resulting polymers were isolated by decantation or centrifugation, and purified by reprecipitation from a solution or by dialysis with a cellophane tube in water, and then dried under vacuum.

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