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Efficient Lewis Acid-Catalyzed Stereocontrolled Radical Polymerization of Acrylamides

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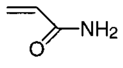
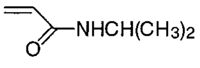
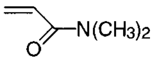
The stereoregularity (tacticity) of olefinic or vinyl polymers often significantly affects the properties and functions of the polymers. Therefore, stereocontrol during polymerization is very important not only in synthetic polymer chemistry but also in the polymer industry. Stereocontrolled polymerization has usually been attained via an ionic or coordination process with metal-based initiators or catalysts, which can provide a countercationic or anionic species at the growing end. On the other hand, radical polymerization is the most versatile process that can be applied to almost all vinyl monomers, and many industrial polymers such as polystyrene, poly(vinyl chloride), polyacrylates, and polyacrylamide have been produced by this process. However, because of the absence of a counterion in this process, it is difficult to control the polymerization stereochemistry, and even now only atactic or slightly syndiotactic-rich polymers can be produced. Highly stereocontrolled radical polymerization has been attained only in a very few examples.[1] Therefore, a more general method for controlling the tacticity during radical polymerization continues to be highly desired.

More than thirty years ago, Lewis acids were found to significantly affect monomer reactivity during radical copolymerization,[2] and afterward, its stereochemistry.[3] However, until very recently, the influence of Lewis acids on the stereochemistry during radical homopolymerization had not been reported, probably because almost no effect on tacticity had been observed,[4] although recently a remarkable advance has been made in the field of radical transformation.[5] We reported the clear effect of Lewis acids such as scandium trifluoromethanesulfonate (Sc(OTf)$_3$) on the stereospecific radical polymerization of a designed monomer, benzyl α-methoxymethylacrylate,[6] and Porter et al. seemed to find an analogous effect for a cyclic *N*,*N*-disubstituted acrylamide.[7] However, this Lewis acid effect has been less significantly observed for the polymerization of conventional monomers such as methyl methacrylate[8] and vinyl acetate.[9] We now report efficient stereocontrol during the radical polymerization of acrylamide (AM) and its derivatives, *N*-isopropylacrylamide (NIPAM) and *N*,*N*-dimethylacrylamide (DMAM), by using a catalytic amount of Lewis acids. AM and NIPAM can be polymerized only via a radical process to give atactic polymers. Poly(AM) is an industrial product with various applications and poly(NIPAM) has been attracting great interest due to its unique properties as a gel.[10]


AM


NIPAM


DMAM

The radical polymerization of NIPAM was examined in the presence of a catalytic amount ([monomer]/[triflate] = 12) of various rare earth metal trifluoromethanesulfonates (triflates), Sc(OTf)$_3$, Y(OTf)$_3$, La(OTf)$_3$, Ce(OTf)$_3$, Pr(OTf)$_3$, Nd(OTf)$_3$, Sm(OTf)$_3$, Eu(OTf)$_3$, Gd(OTf)$_3$, Tb(OTf)$_3$, Ho(OTf)$_3$, Er(OTf)$_3$, Tm(OTf)$_3$, Yb(OTf)$_3$, and Lu(OTf)$_3$. In the absence of Lewis acids, the tacticity of the polymer is only slightly influenced by the polymerization conditions such as temperature (−20 to 60 °C) and solvents ($CHCl_3$, CH_3OH, H_2O), and a slightly syndiotactic-rich polymer (meso diad (m) = 44−46, racemo diad (r) = 54−56) has been obtained. However, in the presence of the Lewis acids, the isotactic content (m) of the polymer remarkably increased as shown in Table 1.[11] In methanol at 60 °C, the m contents of the obtained polymers were in the range of 79−84% for most triflates except for Sc(OTf)$_3$ and La(OTf)$_3$, which gave the polymers with lower m contents, 62 and 72%, respectively. A remarkable solvent effect on the tacticity was observed in marked contrast to the polymerization in the absence of the Lewis acids. The polymerization systems looked homogeneous in polar solvents, but in nonpolar solvents such as $CHCl_3$, the acids were not completely dissolved. Methanol seems to be the best solvent for the isotactic-specific polymerization, and even in water, the effect was observed to some extent. However, dimethyl sulfoxide was not an isospecific solvent. This solvent may very tightly coordinate to Y(OTf)$_3$, which prevents the interaction of the monomer with the acid. The polymerization temperature was also an important factor and the optimized temperature seems to be around −20 °C. At this temperature, the isotacticity increased to m = 92%, which leads to the triad isotacticity mm = 84.6% by assuming the Bernoulli process of polymerization. This value may be the highest one for the homogeneous radical polymerization of commercially available monomers. Temperatures lower than −20 °C decreased the isotacticity.

The [Y(OTf)$_3$]/[NIPAM] ratio affected the tacticity (Figure 1). The isotacticity initially increased as the content of the Lewis acid increased up to the ratio about 0.20, and a further increase in the acid content slightly reduced the isospecificity. This indicates that the Lewis acid can catalytically affect the polymerization stereochemistry. The coordination of NIPAM to Y(OTf)$_3$ was detected by ^{1}H NMR measurement in methanol-d_4. The monomer seemed to more preferentially coordinate to the Lewis acid than the poly(NIPAM) chain. This coordination may activate the monomer, which allows preferent addition to the growing radical end. Therefore, immediately after the addition the Lewis acid can exist around the growing end and influence the polymerization stereochemistry. After a few monomer additions, the acid is probably detached from the polymer chain to coordinate to the monomer again.

When $ScCl_3$ and $YbCl_3$ were used as Lewis acids in methanol, the m content of the obtained polymers were 57 and 67%, indicating that the triflates are more effective in enhancing the isotacticity.

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Table 1. Radical Polymerization of NIPAM in the Presence of Lewis Acids[a]

entry	Lewis acid ([Lewis acid]$_0$)	solvent	temp (°C)	yield[b] (%)	tacticity[c] *m*/*r*
1	none	$CHCl_3$	60	65	45/55
2	$Yb(OTf)_3$ (0.2 M)	$CHCl_3$	60	39	58/42
3	$Y(OTf)_3$ (0.2 M)	CH_3OH	60	94	80/20
4	$Y(OTf)_3$ (0.2 M)	H_2O	60	94	57/43
5	$Y(OTf)_3$ (0.2 M)	DMSO	60	96	47/53
6	none	CH_3OH	−20	61	44/56
7	$Y(OTf)_3$ (0.2 M)	CH_3OH	−20	85	90/10
8	$Y(OTf)_3$ (0.5 M)	CH_3OH	−20	72	92/8
9	$Lu(OTf)_3$ (0.5 M)	CH_3OH	−20	62	92/8
10	$Y(OTf)_3$ (0.2 M)	CH_3OH	−40	85	89/11
11	$Y(OTf)_3$ (0.2 M)	CH_3OH	−78	98	80/20

[a] $[NIPAM]_0 = 2.4$ M. Initiator: AIBN (entries 1−3, 5), AIBN with UV irradiation (entries 6−9) ($[AIBN]_0 = 0.02$ M), $Na_2SO_3 + K_2S_2O_8$ ($[initiator]_0 = 0.02$ M) (entry 4), $(n\text{-}Bu)_3B$ with air ($[(n\text{-}Bu)_3B]_0 = 0.1$ M) (entries 10−11). Time = 3 h (entries 1−5), 24 h (entries 6−11). [b] Hot water-insoluble part. [c] Determind by ^1H NMR measurement in DMSO-d_6 at 170 °C.

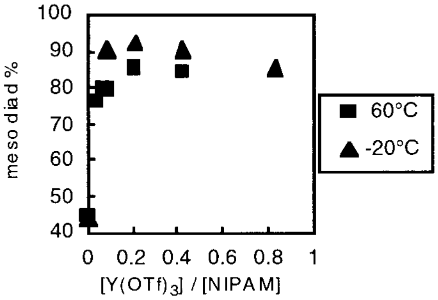

Figure 1. Relationship between the $[Y(OTf)_3]$/[NIPAM] ratio and the tacticity of obtained poly(NIPAM); the polymerizations were carried out in methanol.

The isotactic polymer (m = 92) had a much lower solubility in water compared with the conventional radically obtained polymer and exhibited a high crystallinity under a polarized microscope. The properties of the polymer seem to significantly depend on the tacticity. Many optically active poly(*N*-substituted acrylamides) have been synthesized by a radical process and used as chiral stationary phases in HPLC to separate enantiomers, particularly chiral drugs.[12] The preparation of stereoregular polymers would provide the chiral stationary phases with quite different properties.

Poly(AM) has been industrially produced by radical polymerization in water. The polymer is atactic with a triad tacticity mm:mr:rr = 19:49:33.[13] It appears very difficult to change the polymer stereoregularity by the conventional radical polymerization. However, by using Lewis acids the tacticity can be significantly varied (Table 2). The polymer obtained with $Yb(OTf)_3$ in methanol at 0 °C was isotactic-rich (mm = 65%). $Sc(OTf)_3$ and $Y(OTf)_3$ were less isospecific.

Table 2. Radical Polymerization of AM and DMAM in the Presence of Lewis Acids in Methanol[a]

entry	monomer	Lewis acid	temp (°C)	yield[b] (%)	tacticity[c] *m*/*r* (*mm*/*mr*/*rr*)
1	AM	none	0	60	46/54 (22/49/29)
2	AM	$Sc(OTf)_3$	0	71	62/38 (40/43/17)
3	AM	$Yb(OTf)_3$	0	50	80/20 (65/29/6)
4	AM	$Y(OTf)_3$	0	91	75/25 (58/33/9)
5	DMAM	none	60	73	46/54
6	DMAM	$Sc(OTf)_3$	60	76	78/22
7	DMAM	$Yb(OTf)_3$	60	86	84/16
8	DMAM	$Y(OTf)_3$	60	90	84/16
9	DMAM	$Lu(OTf)_3$	60	85	85/15
10	DMAM	none	0	81	49/51
11	DMAM	$Yb(OTf)_3$	0	76	88/12
12	DMAM	none	−78	62	55/45
13	DMAM	$Yb(OTf)_3$	−78	76	65/35

[a] $[Monomer]_0 = 1.0$ M. $[Lewis\ acid]_0 = 0.1$ M. Initiator: AIBN (entries 5−9), AIBN with UV irradiation (entries 1−4, 10−11) ($[AIBN]_0 = 0.02$ M), $(n\text{-}Bu)_3B$ with air ($[(n\text{-}Bu)_3B]_0 = 0.1$ M) (entries 12 and 13). Time = 24 h. [b] Polymers were purified by dialysis with cellophane in water. [c] Determined by ^{13}C NMR measurement in D_2O at 80 °C (entries 1−4), and ^1H NMR measurement in DMSO-d_6 at 170 °C (entries 5−13).

The isotactic-specific effect of the Lewis acids was also observed for the polymerization of the *N*,*N*-disubstituted monomer, DMAM, in methanol (Table 2). The m content was increased by about 40% using $Yb(OTf)_3$ at 60 and 0 °C. However, this effect was significantly reduced at −78 °C.

The efficient stereocontrolled radical polymerization of three different acrylamides was attained by using a catalytic amount of Lewis acids. The effect was strongly dependent on the polymerization conditions, such as the Lewis acid, solvent, and temperature, suggesting that even a higher level of stereocontrol would be realized by optimizing the polymerization conditions as has been successfully done in ionic or coordination polymerizations. This procedure may be applicable to many other polar monomers which can be polymerized by a radical process. The preparation of stereoregular polymers from these monomers is expected to provide new materials with superior properties and functionalities, and may open a new field of polymer science and industry which has been expected for many years.

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Supporting Information Available: Experimental details including NMR spectra of obtained polymers (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) The number-average molecular weights (M_n) of less isotactic polymers shown in Table 1 could be determined by size exclusion chromatography in DMSO (0.1 M LiCl) at 40 °C. For example, the M_n of the poly(NIPAM) (entry 2) prepared in $CHCl_3$ in the presence of $Y(OTf)_3$ at 60 °C was 68 500.

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