Stereospecific Anionic Polymerization of α -(*N,N*-Dialkylaminomethyl)acrylates

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(Received March 10, 1997)

ABSTRACT: α -(*N,N*-Dialkylaminomethyl)acrylates bearing various amino groups at the α -position of acrylate, such as ethyl α -(1-pyrrolidinylmethyl)acrylate, ethyl α -(*N,N*-diethylaminomethyl)acrylate, ethyl α -(*N*-benzyl-*N*-methylethylaminomethyl)acrylate, and ethyl α -[[(*S*)-2-methoxymethyl-1-pyrrolidinyl]methyl]acrylate, were synthesized, and stereospecific polymerization with anionic initiators was investigated. Highly isotactic polymers were obtained using Grignard reagent-(–)-sparteine complex as well as lithium amide as initiators. Isotactic specific anionic polymerization took place regardless of the polarity of solvents.

KEY WORDS Stereospecific Polymerization / Anionic Polymerization / Isotactic Polymer / α -(Amino-methyl)acrylate / Lithium Amide / Optically Active Polymer /

Control of stereoregularity in the polymerization of vinyl monomers is most important in the field of synthetic polymer chemistry. In anionic polymerization, tacticity is often greatly affected by polymerization conditions such as polarity of solvents and initiators.¹ Therefore, the introduction of a polar functional group to a vinyl monomer which can interact with a counter cation may greatly influence the stereoregulation of the polymerization. Recently, we found that the anionic polymerization of benzyl α -(alkoxymethyl)acrylates, which have various alkoxy groups at the α -position of acrylate, with alkyl-lithium reagents gave highly isotactic polymers.² Further, we reported that highly isotactic polymers were obtained in the polymerization of ethyl α -(1-pyrrolidinylmethyl)acrylate (EPNMA, **1**) using lithium amides as initiators,³ although it has been reported that α -(*N,N*-dialkylaminomethyl)acrylate has no radical polymerizability due to steric hindrance of α -substituents.^{4,5} It is noteworthy that the isotactic specific anionic polymerization of the above monomers takes place regardless of the polarity of solvents. In this polymerization, strong intra- and intermolecular coordination of the polar groups of the growing polymer chain end and monomers to the counter cation (Li^+) may be the main factor in controlling the stereochemistry.⁶ Stereospecific synthesis of the polymers possessing a variety of polar groups may be particularly important for generating novel functions of polymers.

Reported herein is the anionic polymerization of EPNMA (**1**) and novel monomers, ethyl α -(*N,N*-diethylaminomethyl)acrylate (**2**), ethyl α -(*N*-benzyl-*N*-methylethylaminomethyl)acrylate (**3**), and ethyl α -[[(*S*)-2-methoxy-

methyl-1-pyrrolidinyl]methyl]acrylate (**4**). To investigate the generality of stereospecific polymerization of the acrylate bearing a aminomethyl group at the α -position which we reported previously,³ the effects of various amino groups on the reactivity and stereoregulation in the anionic polymerization are mainly examined.

EXPERIMENTAL

Measurements

¹H and ¹³C NMR spectra were measured on a Varian Gemini-2000 (400 and 100 MHz) or UNITY-INOVA (500 and 125 MHz) spectrometer in CDCl₃ at 60°C with tetramethylsilane as the internal standard. Infrared (IR) spectra were recorded on a JASCO FT/IR-7000 spectrometer. The circular dichroism (CD) spectrum was taken on a JASCO J-720L apparatus with 0.1-mm cell in CF₃CH₂OH solution. UV spectra were measured on a JASCO Ubest-55 spectrophotometer. Optical rotation was measured with a JASCO DIP-181 polarimeter. Gel permeation chromatographic (GPC) analysis was carried out on a JASCO 880-PU equipped with an RI (JASCO 830-RI) detector using dry CHCl₃ as an eluent. Two GPC columns, TSK G5000H and Shodex AC802.5, were connected in series.

Materials

The solvents, toluene and tetrahydrofuran (THF), used in polymerization were distilled from Na wire, and distilled again from butyllithium (*n*-BuLi) for toluene and LiAlH₄ for THF under high vacuum just before use. *n*-BuLi was prepared from 1-chlorobutane and lithium powder in heptane. Lithium 4-benzylpiperidide as an initiator was prepared from the corresponding secondary amine in toluene by adding an equimolar amount of *n*-BuLi at room temperature. Cyclohexylmagnesium bromide (cHexMgBr) was prepared from cyclohexyl bromide and magnesium turnings in diethyl ether. Sparteine (Sigma, (–)-Sp) was dried over CaH₂, distilled under reduced pressure, and used as a toluene solution. cHexMgBr-(–)-Sp complex was prepared by mixing the Grignard reagent with 1.1 equiv. of (–)-Sp in toluene at room temperature under dry nitrogen.

Novel monomers, ethyl α -(*N,N*-dialkylaminomethyl)-

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acrylates were prepared from ethyl α -(bromomethyl)-acrylate⁷ and the corresponding secondary amines as previously reported for **1**.³

Ethyl α -(*N,N*-Diethylaminomethyl)acrylate (2): ¹H NMR (400 MHz, CDCl₃) δ 1.01 (t, 6H, J =7.2 Hz, CH₃), 1.30 (t, 3H, J =7.2 Hz, CH₃), 2.51 (q, 4H, J =7.2 Hz, NCH₂), 3.24 (m, 2H, NCH₂), 4.21 (q, 2H, J =7.2 Hz, OCH₂), 5.77 (m, 1H, vinyl), 6.25 (m, 1H, vinyl); IR (neat, cm⁻¹) 1717, 1638, 1456, 1383, 1307, 1261, 1176, 1143, 1064, 1031; *Elemental Analysis*. Found: N=7.48%, C=64.75%, H=10.55%. Calcd for C₁₀H₁₉NO₂: N=7.56%, C=64.83%, H=10.34%.

Ethyl α -(*N*-Benzyl-*N*-methylaminomethyl)acrylate (3): ¹H NMR (400 MHz, CDCl₃) δ 1.30 (t, 3H, J =7.2 Hz, CH₃), 2.20 (s, 3H, NCH₃), 3.24 (m, 2H, NCH₂), 3.55 (s, 2H, NCH₂), 4.22 (q, 2H, J =7.2 Hz, OCH₂), 5.84 (m, 1H, vinyl), 6.27 (m, 1H, vinyl), 7.2–7.4 (m, 5H, aromatic); IR (neat, cm⁻¹) 1719, 1638, 1495, 1456, 1369, 1307, 1272, 1154, 1131, 1077, 1029; *Elemental Analysis*. Found: N=6.02%, C=72.07%, H=8.03%. Calcd for C₁₄H₁₉NO₂: N=6.00%, C=72.07%, H=8.21%.

Ethyl α -[(*S*)-2-Methoxymethyl-1-pyrrolidiny]methyl]acrylate (4): ¹H NMR (400 MHz, CDCl₃) δ 1.31 (t, 3H, J =7.2 Hz, CH₃), 1.56–1.70 (m, 3H, CH₂), 1.92 (m, 1H, CH₂), 2.18 (m, 1H, NCH₂), 2.68 (m, 1H, NCH₂), 3.05 (m, 1H, NCH), 3.11 (m, 1H, CH₂), 3.25 (m, 1H, CH₂), 3.35 (s, 3H, OCH₃), 3.45 (m, 1H, CH₂), 3.76 (m, 1H, CH₂), 4.21 (q, 2H, J =7.2 Hz, OCH₂), 5.76 (m, 1H, vinyl), 6.22 (m, 1H, vinyl); IR (neat, cm⁻¹) 1721, 1634, 1462, 1383, 1307, 1263, 1178, 1123, 1031; *Elemental Analysis*. Found: N=6.17%, C=63.40%, H=9.44%. Calcd for C₁₂H₂₁NO₃: N=6.16%, C=63.41%, H=9.31%; $[\alpha]_D^{25} = -64^\circ$, $[\alpha]_{365}^{25} = -188^\circ$ (c =1.03, CHCl₃).

Polymerization Procedure

Polymerization was carried out in a glass ampule equipped with a three-way stopcock. The purified reagents were transferred into the ampule with syringes under a dry nitrogen atmosphere. The polymerization was initiated by adding initiator solution to the monomer solution. The polymerization was typically carried out using the monomer (1.50 mmol), an initiator (0.15

mmol), and a solvent (1.5 mL). The termination of the polymerization was accomplished by adding a small amount of methanol and a polymer was precipitated in a large amount of methanol. The polymer was separated by centrifugation and dried *in vacuo*.

GPC analysis of obtained poly[α -(*N,N*-dialkylaminomethyl)acrylates]s using CHCl₃ as an eluent was not successful, probably due to the characteristic basic or hygroscopic property of the polymer.^{3,8} Number-average molecular weight (M_n) of the polymers obtained with lithium 4-benzylpiperidide was estimated from the relative intensities of the phenyl proton signal (initiator fragment) and the signal of ester proton in ¹H NMR spectra.

RESULTS AND DISCUSSION

The previous paper reported that the anionic polymerizations of **1** using lithium amides proceeded in good yields, although *n*-BuLi gave no polymer.³ In the anionic polymerization with *n*-BuLi, a side reaction, 1,2-addition (carbonyl attack) appears to prevent the initiation of the polymerization. The radical polymerization of **1** did not proceed. This has been explained by the bulkiness of the amino group as well as difficulty of the radical polymerization of α -(alkoxymethyl)acrylates having bulky alkoxy groups.^{2b,5}

Anionic polymerizations of α -(*N,N*-dialkylaminomethyl)acrylates (**1**–**4**) were carried out using lithium 4-benzylpiperidide and cHexMgBr as initiators. The results are listed in Table I. The effects of polymerization temperature and initiator having different counter cation on polymerizability and stereoregularity were studied for the monomer **1** (entries 1–6). Polymerization temperature greatly affected polymer yield. Polymerizations at 0°C using lithium 4-benzylpiperidide in toluene and in THF provided no polymer (entries 2 and 4), in contrast to the polymerization at –78°C which proceeded in good yields (entries 1 and 3). Although cHexMgBr gave no polymer at –78°C in toluene (entry 5), its complex with (–)-sparteine provided the polymer with a small negative optical rotation ($[\alpha]_{365}^{25} = -22^\circ$) in good yield

Table I. Anionic polymerization of ethyl α -(*N,N*-dialkylaminomethyl)acrylates^a

Entry	Monomer	Initiator	Solvent	Temp.	Time	Yield ^b	$\bar{M}_n^c$
				°C	h	%	$\times 10^{-4}$
1 ^d	1	BPnLi ^e	Toluene	–78	24	84	2.3
2	1	BPnLi	Toluene	0	48	0	—
3 ^d	1	BPnLi	THF	–78	24	94	4.0
4	1	BPnLi	THF	0	48	0	—
5	1	cHexMgBr ^f	Toluene	–78	24	0	—
6	1	cHexMgBr-(–)-Sp ^g	Toluene	–78	24	89 ^h	—
7	2	BPnLi	Toluene	–78	30	27	1.7
8	2	BPnLi	THF	–78	30	5	0.71
9	2	cHexMgBr	Toluene	–78	30	0	—
10	2	cHexMgBr-(–)-Sp	Toluene	–78	30	8 ⁱ	—
11	3	BPnLi	Toluene	–78	48	25	—
12	3	BPnLi	THF	–78	48	20	—
13	4	BPnLi	Toluene	–78	96	7 ^j	0.74
14	4	BPnLi	THF	–78	96	46 ^k	0.77

^a[monomer]/[initiator]=10. ^bMethanol insoluble part. ^cDetermined by ¹H NMR. ^dData in ref 3. ^eLithium 4-benzylpiperidide. ^fCyclohexylmagnesium bromide. ^g(–)-Sparteine. ^h $[\alpha]_{365}^{25} = -22^\circ$ (CHCl₃, c =0.5). ⁱ $[\alpha]_{365}^{25} = -3^\circ$ (CHCl₃, c =0.5). ^j $[\alpha]_{365}^{25} = -285^\circ$, $[\alpha]_D^{25} = -89^\circ$ (CHCl₃, c =0.1). ^k $[\alpha]_{365}^{25} = -272^\circ$, $[\alpha]_D^{25} = -88^\circ$ (CHCl₃, c =0.1).

Figure 1. 400 MHz ^1H NMR spectra of poly(1) obtained with Grignard reagent-($-$)-Sp complex in toluene at -78°C (entry 6) (a) and poly(2) obtained with lithium 4-benzylpiperidide in toluene at -78°C (entry 7) (b) (CDCl_3 , 60°C).

Figure 2. 125 MHz ^{13}C NMR spectra of the carbonyl carbon in poly(1) obtained with lithium 4-benzylpiperidide in toluene (entry 1) (a), in THF (entry 3) (b), and with Grignard reagent-($-$)-Sp complex in toluene at -78°C (entry 6) (c) (CDCl_3 , 60°C).

(entry 6). The diamine ligand may inhibit side reactions or enhance its reactivity.

In the anionic polymerization of α -(alkoxymethyl)acrylates, counter cations are important to control of stereoregularity.^{2b} Figure 1(a) shows the ^1H NMR spectrum of poly(1) obtained with the complex of cHexMgBr and ($-$)-sparteine. The spectral pattern of the main chain methylene protons around 2.2 ppm shows a typical AB quartet and is almost the same as that of the polymer obtained with lithium amide in toluene.³ An isotactic polymer was also produced in the anionic polymerization with the complex of cHexMgBr and ($-$)-sparteine. Figure 2 shows the ^{13}C NMR spectra of the carbonyl

Figure 3. 125 MHz ^{13}C NMR spectra of the carbonyl carbon in poly(2) obtained with lithium 4-benzylpiperidide in toluene at -78°C (entry 7) (a), poly(3) obtained with lithium 4-benzylpiperidide in toluene (entry 11) (b), in THF (entry 12) (c), and poly(4) obtained with lithium 4-benzylpiperidide in THF (entry 14) (d) (CDCl_3 , 60°C).

carbon of poly(1)s obtained by anionic method (entries 1, 3, and 6). A sharp singlet with the same chemical shift is observed for each polymer, indicating that the anionic polymerization of **1** proceeds in a highly isotactic-specific manner regardless of the difference of the counter cation, Li^+ and Mg^{2+} , as well as the polarity of solvents. These results are in contrast to those of the anionic polymerization of α -alkylacrylates.^{1,9}

Anionic polymerization of monomers **2** and **3**, using lithium 4-benzylpiperidide and cHexMgBr at -78°C resulted in lower yields than those of monomer **1** (entries 7–12). The low reactivity may be ascribed to the bulkiness of the α -substituents. The α -substituent amino group also affected stereoregularity of the polymers. The ^1H NMR spectrum of the poly(2) obtained with lithium 4-benzylpiperidide in toluene is shown in Figure 1(b). The AB quartet spectral pattern of β -methylene protons (2.0–2.4 ppm) is observed together with the other small shoulder peaks. The isotacticity appears lower than that of the poly(1). The ^{13}C NMR spectrum of the carbonyl carbon of the poly(2) shows multiplets (Figure 3(a)), again indicating lower isotacticity. The ^{13}C NMR spectra of the carbonyl carbon of poly(3) obtained with the lithium amide in toluene and in THF are also shown in Figures 3(b) and 3(c). These spectra indicate that the stereoregularity (isotacticity) of poly(3)s is not as high as those of poly(1)s but higher than that of poly(2).

Optically active monomer **4** was polymerized using lithium 4-benzylpiperidide in toluene and in THF (entries 13 and 14) to generate the optically active polymers possessing $[\alpha]_{365}^{25} = -285$ and -272° ($c = 0.1$, CHCl_3) respectively. These values are higher than those of the model compound ($[\alpha]_{365}^{25} = -158^\circ$), ethyl 3-((S)-2-me-

Figure 4. CD and UV spectra of poly(**4**) obtained with lithium 4-benzylpiperidide (entry 14) (—) and the model compound **5** (-----) in $\text{CF}_3\text{CH}_2\text{OH}$.

thoxymethyl-1-pyrrolidinyl)-2,2-dimethylpropionate (**5**)¹⁰ and the monomer ($[\alpha]_{365}^{25} = -188^\circ$). Figure 3(d) shows the ^{13}C NMR spectrum of the carbonyl carbon of poly(**4**) obtained in THF. The spectral pattern suggests that the polymer is rich in isotacticity but possibly slightly lower than those of poly(**1**)s. The increase of specific rotation of poly(**4**)s relative to the model compound and the monomer may be caused by a higher order structure of polymer main chain originated in the high isotacticity. The CD spectra of (–)-poly(**4**) obtained in THF (entry 14) and model compound **5** in 2,2,2-trifluoroethanol are shown in Figure 4. The absorption around 220 nm is due to ester groups. The polymer appears to exhibit an exciton-type splitting, and its spectral pattern is quite different from that of **5**, indicating that the polymer may

exist under quite different chiral circumstances from that of **5**, which must be ascribed to a regular arrangement of the ester group of the isotactic polymer.

In conclusion, the anionic polymerization of ethyl α -(*N,N*-dialkylaminomethyl)acrylates (**1**–**4**) provided polymers with a high isotacticity regardless of differences in counter cations, Li^+ and Mg^{2+} , or polarity of solvents. The polymers may show characteristic features as polymeric bases or ligands due to the stereoregular structure.

Acknowledgment. This work was partially supported by a Grant-in-Aid for Scientific Research on Priority Areas (Reactive Organometallics No. 05236103) from the Ministry of Education, Science, Sports, and Culture of Japan, and by CREST (Core Research for Evolutional Science and Technology) of Japan Science and Technology Corporation (JST).

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- 5** was prepared by addition of the corresponding lithium amide to ethyl methacrylate followed by methylation with iodomethane: ^1H NMR (400 MHz, CDCl_3) δ 1.16 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.26 (t, 3H, $J=7.2$ Hz, CH_3), 1.53 (m, 1H, CH_2), 1.70 (m, 2H, CH_2), 1.84 (m, 1H, CH_2), 2.25 (m, 1H, NCH_2), 2.65 (m, 1H and d, 1H, $J=13.2$ Hz, NCH_2), 2.84 (d, 1H, $J=13.2$ Hz, NCH_2), 3.00 (m, 1H, NCH), 3.13 (dd, 1H, $J=7.6$ and 9.2 Hz, OCH_2), 3.34 (s, 3H, OCH_3), 3.36 (dd, 1H, $J=4.4$ and 9.2 Hz, OCH_2), 4.11 (m, 2H, OCH_2); IR (neat, cm^{-1}) 1731, 1473, 1390, 1365, 1315, 1261, 1176, 1149, 1114, 1033; $[\alpha]_D^{25} = -54^\circ$, $[\alpha]_{365}^{25} = -158^\circ$ ($c=1.0$, CHCl_3).