Helix-Sense-Selective Anionic Polymerization of a Bulky Methacrylamide Using Organozincates Having Sugar Residues[†]

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The precise design and control of polymer structures, such as stereoregularity, molecular weight, and its distribution, are the ultimate goals in polymer synthesis.[1−5] Anionic polymerization is one of the most powerful processes for controlling the polymer structure.[6−8] Methacrylates having bulky side groups, such as triphenylmethyl methacrylate and 1-phenyldibenzosuberyl methacrylate, are known to produce highly isotactic one-handed helical polymers through not only an anionic process using a chiral organolithium complex or a chiral organolithium[9−11] but also a radical process under chiral conditions.[12,13] The methacrylamides having bulky side groups, such as *N*-triphenylmethylmethacrylamide (TrMAM), *N*-[(4-butyl)triphenylmethyl]methacrylamide (BuTrMAM), and *N*-[(4,4′-dibutyl)triphenylmethyl]methacrylamide (DBuTrMAM), can also produce analogous helical polymers during the radical polymerization in the presence of (+)- or (-)-menthol.[14,15] However, because of the acidic NH proton of TrMAM, its anionic polymerization with *n*-butyllithium (*n*-BuLi) did not proceed.[14]

Recently, Uchiyama et al. found that dilithium tetra-*tert*-butylzincate (t-Bu_4ZnLi_2), possessing a high nucleophilicity as well as a low basicity, is able to anionically polymerize *N*-isopropylacrylamide.[16] In the present study, the anionic polymerization of BuTrMAM was examined using the chiral initiator systems consisting of t-Bu_4ZnLi_2 or dilithium tetra-*n*-butylzincate (n-Bu_4ZnLi_2) and halogeno sugars, i.e., 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (Glu-Br), 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (Gal-Br), or 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide[17] (Man-Br) as a chiral additive.

The anionic polymerization of BuTrMAM was carried out using an organozincate with a chiral additive[18] in toluene or tetrahydrofurn (THF) at 30 °C for 24 h,[19] and these results are shown in Table 1 (runs 1−7). The polymers were obtained in passable yields, except for run 3 using the n-Bu_4ZnLi_2/Glu-Br initiator system in THF. The polymer yield and the molecular weight ($M_{n,SEC}$) of the poly(BuTrMAM)s obtained in toluene were higher than those in THF. The obtained polymers were soluble in chloroform and partially soluble in THF.

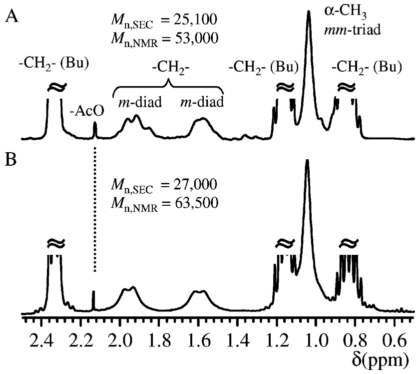

Figure 1. ^{1}H NMR spectra (300 MHz) of PMAMs in D_2SO_4 at 60 °C (A, derived from the poly(BuTrMAM) obtained by n-Bu_4ZnLi_2/Glu-Br in toluene at 30 °C (lists in Table 1, run 2); B, derived from the poly(BuTrMAM) obtained by n-Bu_4ZnLi_2/Gal-Br in toluene at 30 °C (lists in Table 1, run 5)).

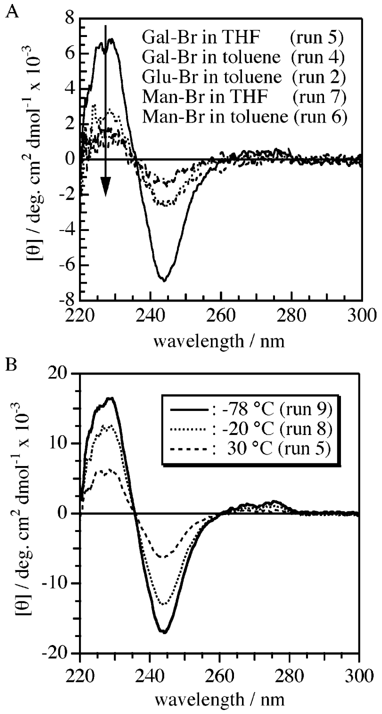

Figure 2. CD spectra of poly(BuTrMAM)s in $CHCl_3$ at room temperature (A, lists in Table 1, runs 2, 4−7; B, lists in Table 1, runs 5, 8, and 9).

The poly(*N*-methacrylamide)s having bulky side groups are quantitatively convertible into poly(methacrylamide) (PMAM) by dissolving them in concentrated sulfuric acid for a few minutes at room temperature.[14,15] Therefore, the tacticity of poly(BuTrMAM) was estimated from the ^{1}H NMR spectrum of the derived PMAM in D_2SO_4. The ^{1}H NMR spectra of the PMAMs derived from the poly(BuTrMAM)s using the n-Bu_4ZnLi_2/Glu-Br initiator system (run 2 in Table 1) and the n-Bu_4ZnLi_2/Gal-Br initiator system (run 5 in Table 1) are shown in Figure 1. In both spectra, a methyl peak due to a meso−meso−triad (isotactic) sequence at 1.05 ppm and two methylene peaks due to a meso−diad sequence at 1.6 and 1.9 ppm are clearly observed, indicating that the original poly(BuTrMAM)s were highly isotactic (mm >99%). In addition, the signal due to the acetyl protons of the sugar residue, which is hydrolyzed by concentrated D_2SO_4, is observed at 2.12 ppm, indicating that the initiating chain end of the poly(BuTrMAM)s has a sugar residue. The molecular weights ($M_{n,NMR}$) of the poly(BuTr-

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[†] This communication is dedicated in the memory of the late Prof. Yoshihiko Ito.

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Table 1. Polymerization of BuTrMAM Using Organozincate/Halogeno Sugar Initiator Systems[a]

run	organozincate	halogeno sugar	solvent	temp (°C)	time (day)	yield[b] (%)	$M_{n,SEC}$ (M_w/M_n)[c]	$[\alpha]_{365}$[d] (deg)
1	t-Bu_4ZnLi_2	Glu-Br	toluene	30	1	7.5	9400 (1.08)	ca. 0
2	n-Bu_4ZnLi_2	Glu-Br	toluene	30	1	13.5	25100 (4.54)	+13.0
3	n-Bu_4ZnLi_2	Glu-Br	THF	30	1	ca. 0		
4	n-Bu_4ZnLi_2	Gal-Br	toluene	30	1	62.0	51000 (4.76)	+13.7
5	n-Bu_4ZnLi_2	Gal-Br	THF	30	1	41.5	27000 (4.67)	+32.8
6	n-Bu_4ZnLi_2	Man-Br	toluene	30	1	40.0	113000 (3.09)	+7.8
7	n-Bu_4ZnLi_2	Man-Br	THF	30	1	34.0	38600 (3.55)	+8.6
8	n-Bu_4ZnLi_2	Gal-Br	THF	-20	2	67.5	49000 (5.71)	+67.1
9	n-Bu_4ZnLi_2	Gal-Br	THF	-78	2	2.0	248000 (3.00)	+94.9[e]

[a] $[BuTrMAM]_0 = 1.0$ mol L^{-1}; $[BuTrMAM]_0/[organozincate]_0/[halogeno\ sugar]_0 = 20/1/4$. [b] Methanol-insoluble part. [c] Determined by SEC in THF at 40 °C using PMMA standards. [d] Measured in $CHCl_3$ (conc, 0.35 g dL^{-1}; 25 °C; cell length, 5 cm). [e] Measured in $CHCl_3$ (conc, 0.067 g dL^{-1}; 25 °C; cell length, 5 cm).

MAM)s were estimated from the peak intensity ratio of the methylene protons of the main chain (1.40−2.10 ppm) to the acetyl protons of the sugar unit (2.12 ppm) assuming that one sugar unit is attached to one polymer chain. This was also confirmed by the MALDI-TOF-MS spectra of these polymers. The $M_{n,NMR}$ was higher than the $M_{n,SEC}$ estimated from SEC, probably because the latter was determined on the basis of the poly(methyl methacrylate) calibration.[20]

The specific rotation of poly(BuTrMAM)s was strongly influenced by the initiator systems. The polymers obtained using the n-Bu_4ZnLi_2/Glu-Br initiator system at 30 °C were optically active showing a specific rotation $[\alpha]_{365}$ +13.0° (*c* 0.35, $CHCl_3$) in run 2, while the polymer prepared using the t-Bu_4ZnLi_2/Glu-Br initiator system (run 1) was optically inactive. In addition, the specific rotations of the poly(BuTrMAM)s prepared by n-Bu_4ZnLi_2 (runs 2, 4−7) were also significantly influenced by the halogeno sugars and solvents. The sugar residue attached to the chain end does not seem to be the main reason for the specific rotation of the polymer. In other words, assuming that the specific rotation of the 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose unit is similar to that of Gal-Br ($[\alpha]_{365}$ +720°, *c* 3.17, $CHCl_3$), if the main reason for the specific rotation of the polymer is the sugar unit, the specific rotation of the poly(BuTrMAM) with $M_{n,NMR} = 63\,500$ (run 5) is estimated to be only $[\alpha]_{365}$ +3.8°. The actual value of the obtained poly(BuTrMAM) was $[\alpha]_{365}$ +32.8°. Therefore, the large specific rotation may be attributed to the helical conformation of the polymer.

The circular dichroism (CD) spectra of the optically active poly(BuTrMAM)s in THF at room temperature are shown in Figure 2A. Split-type CD peaks were observed at 230 and 244 nm, and their patterns are similar to that of the helical poly(BuTrMAM) obtained by the radical polymerization of BuTrMAM in a toluene/(−)-menthol mixture,[15] suggesting that the polymers prepared using the n-Bu_4ZnLi_2/halogeno sugar initiator systems have a helical conformation with an excess of the right- or left-handed helicity. The CD intensity of the poly(BuTrMAM)s proportionally increased with an increase in the optical rotation. The influence of the terminal chiral groups on the optical activity of the polymers is attributed to the excess of the right- or left-handed helicity arising from the chiral chain end originating from the chiral initiator.[21] THF was found to be a better solvent than toluene for producing the polymer with a higher CD intensity. When the same solvent was used for the

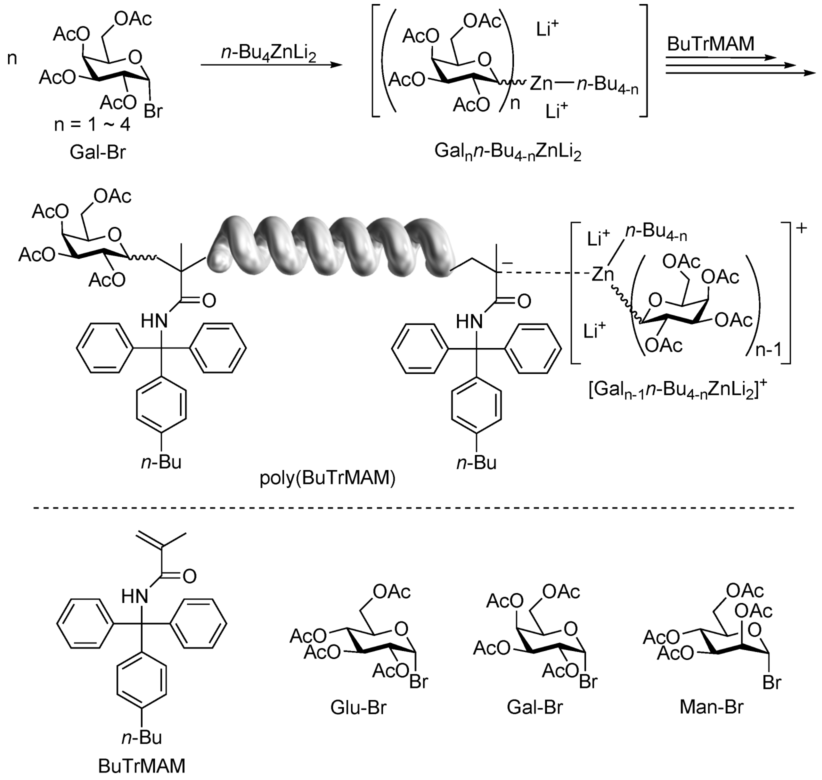

Figure 3. Possible mechanism for the polymerization of BuTrMAM using the n-Bu_4ZnLi_2/Gal-Br initiator system.

polymerization, the CD intensity of the poly(BuTrMAM)s increased in the order of Man-Br < Glu-Br < Gal-Br.

The polymerization of BuTrMAM was also carried out using the *n*-Bu_4ZnLi_2/Gal-Br initiator system in THF at −78 and −20 °C (Table 1, runs 8 and 9). The polymer obtained at −78 °C showed the highest optical activity ($[\alpha]_{365}$ +94.9°, $[\alpha]_D$ +28.6°), which is much higher than the poly(BuTrMAM) obtained by the asymmetric radical polymerization in the presence of (+)-menthol at 0 °C ($[\alpha]_{365}$ +29.4°),[15] although the polymer yield was very low (run 9). Figure 2B shows the CD spectra of the poly(BuTrMAM)s prepared using the *n*-Bu_4ZnLi_2/Gal-Br initiator system in THF at −78, −20, or 30 °C (Table 1, runs 9, 8, and 5). The CD intensity of poly(BuTrMAM) increased with a decrease in the polymerization temperature.

Figure 3 shows the possible mechanism for the initiation reaction and the propagation. The initiation reaction takes place by a two-step reaction; e.g., the halogen−metal exchange reaction first occurs between the halogeno sugar and the organozincate that forms a chiral initiator system ($Gal_n n\text{-}Bu_{4-n}ZnLi_2$),[22−24] followed by the addition of the BuTrMAM to the chiral initiator system to form one of two diastereomers in excess due to the chirality of the sugar residue, and the subsequent addition of BuTrMAM probably proceeds with the significant retention of configuration because the produced poly(BuTrMAM) is highly isotactic.[11] Furthermore, the subsequent addition may also be restricted by the steric hindrance of the countercation ($[Gal_{n-1} n\text{-}Bu_{4-n}ZnLi_2]^+$) having sugar residues.

In summary, the asymmetric anionic polymerization of the bulky methacrylamide, BuTrMAM, was performed using the chiral anionic initiator systems consisting of the organozincates and halogeno sugars, such as *n*-Bu_4ZnLi_2/Glu-Br, Gal-Br, or Man-Br. The obtained polymers were optically active. The specific rotation of the polymers increased in the order of Man-Br < Glu-Br < Gal-Br and with a decrease in the polymerization temperature. The CD spectra of poly(BuTrMAM)s showed Cotton effects duo to a helical conformation with an excess right- or left-handed helicity. To the best of our knowledge, this is the first example of the helix-sense-selective anionic polymerization of a bulky methacrylamide.

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(18) Preparation of *n*-Bu_4ZnLi_2/Gal-Br: The *n*-BuLi (2.62 mol L^{-1} hexane solution, 0.31 mL, 0.8 mmol) was added to a mixture of dry THF (0.93 mL) and $ZnCl_2$ (0.5 mol L^{-1} THF solution, 0.4 mL, 0.2 mmol) at 0 °C under dry N_2. The mixture was then stirred for 30 min at the same temperature. Gal-Br (330 mg, 0.8 mmol) was added to the THF solution of *n*-Bu_4ZnLi_2 at 0 °C, and the mixture was stirred at the same temperature for 30 min.

(19) Polymerization: The polymerization reactions were carried out under dry N_2 in a glass ampule sealed with a three-way stopcock. A typical procedure is described for run 5 in Table 1. The THF solution of *n*-Bu_4ZnLi_2/Gal-Br (0.26 mL, 0.026 mmol) was added to a THF solution (0.058 mL) of BuTrMAM (200 mg, 0.52 mmol) at 30 °C. The reaction mixture was allowed to stand in a 30 °C oil bath for 24 h and then quenched with 0.2 mL of 0.1 N HCl. The reaction mixture was poured into a large amount of methanol. The precipitated polymer was purified by reprecipitation twice from $CHCl_3$/MeOH, and the polymer was recovered from the $CHCl_3$/benzene solution by freeze-drying.

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