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Anionic Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol Leading to (6→1)-2,5-Anhydro-3,4-di-*O*-methyl-D-glucitol

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ABSTRACT: The anionic cyclopolymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol (**3**) was carried out using *t*-BuOK and KOH. The resulting polymer **4** consisted of 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol as a five-membered repeating unit, which was identical with that of polymer **2** obtained from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**). The copolymerization of **1** with **3** produced a random copolymer consisting of (1→6)-, (6→1)-, (1→1)-, and (6→6)-linked 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol. These facts elucidated the presence of two linkages during the homopolymerization of **1** and **3**, i.e., the (1→6) and (6→1)-bonded 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units in polymers **2** and **4**, respectively.

Introduction

Optically active oxiranes are important chiral building blocks for the syntheses of natural products and other stereocontrolled compounds. The regio- and stereoselective synthesis of chiral compounds using cyano epoxides, hydroxy epoxides and diepoxides is a particularly useful synthetic strategy.[1−7] Nicolaou et al. reported a stereospecific route to synthesize tetrahydropyrans and tetrahydrofurans from 5-substituted-4,5-epoxy-1-alcohol via the 6-endo and 5-exo modes of epoxide opening, respectively.[1,2] Kuszmann reported that the regio- and stereoselective cyclizations of 3,4-di-*O*-alkyl-1,2:5,6-dianhydro-D-mannitol and -L-iditol with hydrogen bromide produced the corresponding 2,5-anhydro-6-bromo-6-deoxy-D-glucitol and 2,5-anhydro-1-bromo-1-deoxy-D-glucitol, respectively.[4] We are concerned with the regio- and stereoselective cyclopolymerization of 1,2:5,6-dianhydrohexitol.

Previous papers have reported that the cationic and anionic cyclopolymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) were controlled through a regio- and stereoselective mechanism.[8−10] The resultant polymers consisted of a (1→6)-linked five-membered constitutional unit, that is, (1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol (**2**), which is a novel polymeric sugar lacking the anomeric linkage. The cyclopolymerization presents a new preparative method for polymeric carbohydrates.[11−14]

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (**3**), which is a diastereomer of **1**, was polymerized with a cationic initiator to give a polymer which contained 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol as a major part and six- and/or seven-membered units as a minor part, together with oligomers in fairly large quantities. In order to obtain further information on the regio- and stereoselective cyclopolymerization of 1,2:5,6-dianhydrohexitol, this paper reports the anionic cyclopolymerization of monomer **3**. The configurational relationships between the homopolymers (**2** and **4**) obtained from **1** and **3** are also discussed on the basis of the copolymerization between these monomers.

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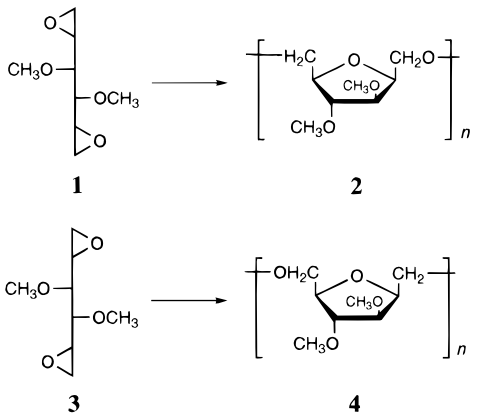
Scheme 1



Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded using a JEOL JNM-A400 II spectrometer using chloroform-*d* ($CDCl_3$) with tetramethylsilane as the internal standard. The molecular weights of the resulting polymers were measured by gel permeation chromatography (GPC) in tetrahydrofuran on a JASCO HPLC system equipped with three polystyrene gel columns (Shodex KF-804L). The number-average molecular weight (M_n) and the molecular weight distribution (M_w/M_n) were calculated on the basis of polystyrene calibration. Optical rotations were determined in chloroform solutions using a JASCO DIP-140 digital polarimeter.

Materials. Toluene and tetrahydrofuran were purified by the usual methods and distilled from sodium benzophenone ketyl. Monomers **1** and **3**, prepared according to the reported procedures, were freshly distilled from calcium hydride just before use.[15] 2,5-Anhydro-1,3,4-tri-*O*-methyl-D-glucitol (**5**) was synthesized from **3** as in the previous report.[8] Commercial potassium *tert*-butoxide (*t*-BuOK) was purified by sublimation before use. Potassium hydroxide (KOH) was purified by the usual methods.

Polymerization. All the polymerizations of **3** were carried out in dry toluene and tetrahydrofuran in an H-shaped glass ampule. A typical polymerization procedure is as follows: monomer **3** (0.771 g, 4.43 mmol) was added to the one side of the ampule, and *t*-BuOK (25.3 mg, 0.226 mmol) and dry toluene (4.5 mL) were added to the other side of the ampule under a nitrogen atmosphere. After sealing, the monomer and the catalyst solution were mixed at 60 °C. After 85 h, the reaction mixture was poured into a large amount of methanol, and the solution was neutralized with diluted hydrochloric acid. After evaporation of the solvent, the residue was purified by reprecipitation from chloroform−*n*-hexane to yield the polymer in 98.6% (0.76 g). The M_n and M_w/M_n were 3390 and 1.54, respectively. $[\alpha]_D$ +77.5°, $[\alpha]_{577}$ +80.7°, $[\alpha]_{546}$ +91.5°, and $[\alpha]_{435}$ +149.6° (*c* 1.0 in $CHCl_3$ at 23 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11−4.15 (m), 4.09 (td, J = 5.5 Hz and J = 3.9 Hz, H-5), 3.93 (td, J = 6.0 Hz and J = 3.0 Hz, H-2), 3.74 (dd, J = 10.3 Hz and J = 5.2 Hz, H-6), 3.70−3.86 (m), 3.61−3.69 (m, H-3, H-4, H-1, and H-6), 3.45−3.51 (m, H-1), 3.40−3.43 (m), 3.38 (s, CH_3O), 3.36 (s, CH_3O) and 1.19 ppm (s, CH_3, *t*-BuO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.37 (C3), 84.63 (C4), 84.33 (CH), 84.18 (CH), 82.23 (C2), 79.82 (C5), 73.07 (C, *t*-BuO), 71.68 (C1), 69.28 (C6), 62.96 (CH_2), 57.51 (CH_3), 57.33 (CH_3O), 57.28 (CH_3O), and 27.47 ppm (CH_3, *t*-BuO).

The copolymerization of **1** and **3** was carried out using *t*-BuOK in toluene at 1 h. The copolymer was obtained using a [**1**]/[**3**] molar ratio of 0.5/0.5 in the feed (run 7): yield 10.3%. The M_n and M_w/M_n were 1990 and 1.37, respectively. The molar ratio ($[m_1]/[m_3]$) in copolymer was 0.42/0.58, which was evaluated using ^{1}H NMR measurement from the molar ratio of residual monomers in the copolymerization system. $[\alpha]_D$ +67.7° and $[\alpha]_{546}$ +87.3° (c 1.0 in $CHCl_3$ at 22 °C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.13 (CH), 85.69 (CH), 85.56 (CH), 85.44 (CH), 84.92 (CH), 84.78 (CH), 84.64 (CH), 84.40 (CH), 84.14 (CH), 82.21 (CH), 81.44 (CH), 81.36 (CH), 79.92 (CH), 79.84 (CH), 73.02 (C, *t*-BuO), 71.87 (CH_2), 71.71 (CH_2), 69.35 (CH_2), 69.27 (CH_2), 62.93 (CH_2), 61.43 (CH_2), 57.67 (CH_3), 57.59 (CH_3), 57.37 (CH_3), 57.24 (CH_3), and 27.44 ppm (CH_3, *t*-BuO).

Table 1. Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (3)[a]

run	catalyst	[**3**]/[cat.]	solvent	time (h)	yield (%)	M_n[b] × 10^{-3}	M_w/M_n[b]	DP
1	*t*-BuOK	10	toluene	85	98.5	2.56	1.37	14.7
2		20	toluene	85	98.6	3.39	1.54	19.5
3		20	THF	85	95.0	2.95	1.31	17.0
4	KOH	5	THF	100	92.5	6.11	1.60	35.1
5		5	toluene	100	60.4	6.00	1.59	34.5

[a] [**3**] = 1.0 mol L^{-1}; temperature, 60 °C. [b] Measured in THF by GPC using polystyrene as the standard.

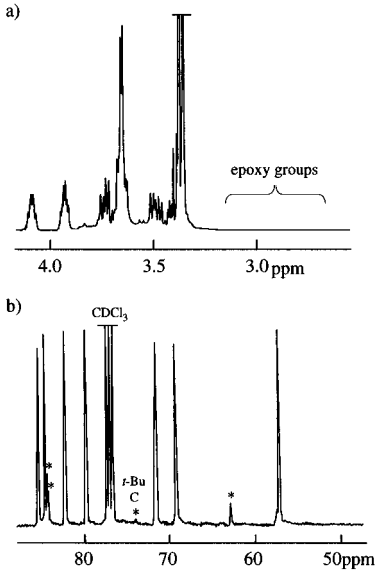
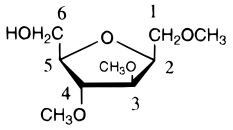


Figure 1. (a) ^{1}H and (b) ^{13}C NMR spectra of the polymer prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol (**3**) using *t*-BuOK in toluene: [**3**]/[*t*-BuOK] = 20; time 85 h; M_n = 3390; M_w/M_n = 1.54. The asterisked signals correspond to the carbons of the polymer chain-ends.

Chart 1



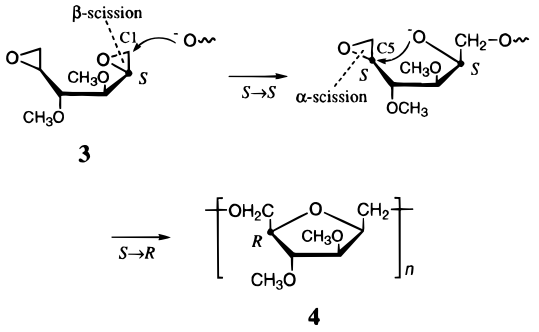
5

C	δ/ppm
1	70.66
2	79.70
3	84.47
4	84.29
5	84.22
6	62.85
CH_3O	59.20
CH_3O	57.71
CH_3O	57.65

Results and Discussion

The anionic polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol (**3**) was carried out using *t*-BuOK and KOH. The typical results are shown in Table 1. Both catalysts were effective at relatively high temperatures. The KOH catalyst in toluene was less active than the other reaction conditions due to its lower solubility in the solvent. The polymerization systems were homogeneous up to a very high conversion. The obtained polymers (**4**) were yellowish brown viscous liquids which were soluble in chloroform and tetrahydrofuran and insoluble in *n*-hexane. Polymer **4** has a number-average molecular weight (M_n) ranging from 2.6 × 10^3 to 6.1 × 10^3, which corresponds to a number-average degree of polymerization (DP) from 15 to 35.

Scheme 2



3 **4**

Figure 1 shows the ^{1}H and ^{13}C NMR spectra of polymer **4**. The characteristic absorption at 2.6−3.2 ppm due to the epoxy proton of **3** disappeared, as shown in Figure 1a. Since all epoxy groups participated in the polymerization, polymer **4** essentially consisted of cyclic repeating units. The signals newly appeared at 3.3−4.1 ppm resembled with those observed in the ^{1}H NMR spectrum of polymer **2** prepared from monomer **1** using *t*-BuOK. The NMR spectrum of **4** consisted of sharp signals, indicating that polymerization of **3** with *t*-BuOK is highly regio- and stereoselective. In Figure 1b, eight large and several small peaks were observed. The large signals agreed fairly well with the chemical shifts of the eight carbons for polymer **2** prepared from monomer **1** using *t*-BuOK. The cyclic constitutional unit in polymer **4**, thereby, is recognized as 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol, analogous to polymer **2**. The small signals asterisked in the figure are entirely attributable to both of the end units in the polymer chain, because the intensities decrease with the increasing M_n of polymer **4**. The signals at 84.33 (CH), 84.18 (CH), 62.96 (CH_2), and 57.51 ppm (CH_3O) belonging to the small signals were very similar to those of the C4, C5, C6, and CH_3O carbons for 2,5-anhydro-1,3,4-tri-*O*-methyl-D-glucitol (**5**), respectively, thus being attributable to the terminating end of the polymer chain (Chart 1). In addition, the two signals at 73.07 and 27.47 ppm were assigned to the quaternary and methyl carbons of the *tert*-butoxy group, respectively, being an initiating end. Polymer **4** consists of a 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol unit as the five-membered repeating unit, as well as polymer **2**.

The formation of the 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol unit is based on the alternative reactions of an intermolecular propagation and an intramolecular cyclization through *β*- and α-scissions of the two epoxy groups in monomer **3**, respectively, as indicated in Scheme 2. The intermolecular reaction through *β*-scission retains the *S* configuration of the C2 carbon. On the other hand, the intramolecular cyclization through α-scission inverts the configuration from *S* to *R* for the C5 carbon. The nucleophilic substitution at the α-carbon converted the L-iditol unit in monomer **3** to a D-glucitol unit in polymer **4**. The anionic cyclopolymerization of **3**, thus, is regio- and stereoselective, like that of **1**.

There is an essential difference in structure between polymers **2** and **4**. Although both polymers have apparently the same constitutional repeating unit, their units differ from one another in direction. Polymer **2** is constructed by the (1→6)-bonded unit, but polymer **4** by the (6→1)-bonded unit, as shown in Scheme 3. For

Table 2. Anionic Copolymerization of 1,2;5,6-Dianhydro-3,4-di-*O*-methyl-D-mannitol (1) and 1,2;5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (3) using *t*-BuOK[a]

run	[**1**]/[**3**] in feed	yield (%)	M_n[b] × 10^{-3}	M_w/M_n[b]	DP_n	$[m_1]/[m_3]$[c] in copolymer'
6	0.1/0.9	15.6	2.06	1.47	11.8	0.09/0.91
7	0.5/0.5	10.3	1.99	1.37	11.4	0.42/0.58

[a] [**1** + **3**] = 1.0 mol L^{-1}; [**1** + **3**]/[cat.] = 20; temperature, 60 °C; time, 1 h; solvent, toluene. [b] Measured in THF by GPC using polystylene as the standard. [c] Determiend by a molar ratio of residual monomers in the copolymerization system.

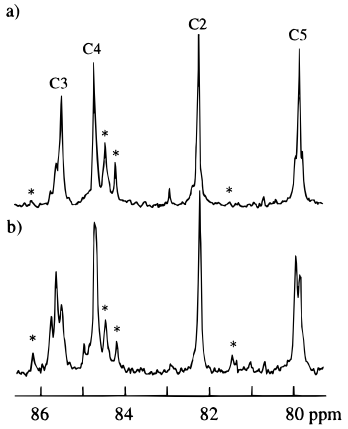
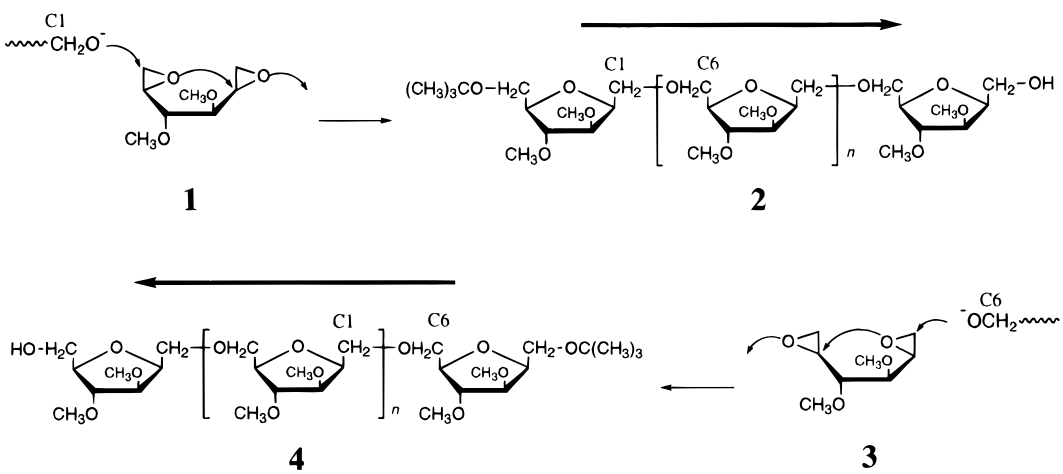


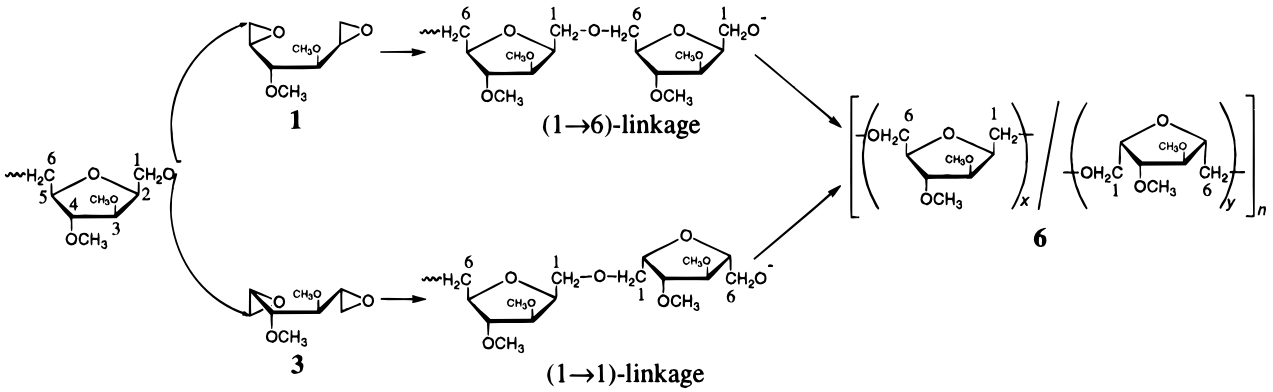
Figure 2. ^{13}C NMR spectra of the copolymers prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) and 1,2:5,6-dianhydro-3,4-di-*O*-methyl-L-iditol (**3**) using *t*-BuOK in toluene. (A) $[m_1]/[m_3]$ molar ratio in copolymer = 0.09 / 0.91 and (B) $[m_1]/[m_3]$ = 0.42/0.58. The asterisked signals correspond to the carbons of the polymer chain ends.

Scheme 3



1 **2** **4** **3**

Scheme 4



the intermolecular propagation of **1**, the attack by the growing alkoxide ion, which is attached at the C1 carbon, occurs at the β-carbon of a monomer, whereas, for **3**, the alkoxide ion, which is bound to the C6 carbon, attacked a monomer. The spectral analysis of the homopolymers, however, are useless for clarifying the presence of the two linkages. The copolymerization between monomers **1** and **3** offers a solution to the problem of direction.

The result of the copolymerization between **1** and **3** carried out using *t*-BuOK in toluene is shown in Table 2. The reaction was terminated at a lower conversion to attempt an analysis of the sequences in the resulting copolymer (**6**). The copolymerization at a [**1**]/[**3**] molar ratio of 0.5/0.5 in the feed produced the copolymer with a ratio ($[m_1]/[m_3]$) of 0.42/0.58. Monomer **3** had a higher reactivity during the copolymerization than monomer **1**. Figure 2 shows the ^{13}C NMR spectra of copolymers **6** in the range of 80−86 ppm. Each of the singlet signals due to the C3, C4, and C5 carbons was split into two or three peaks. Variation of their relative intensities with the copolymer composition was found by comparison of parts a and b of Figure 2. Therefore, copolymer **6** is constructed by (1→6)-, (6→1)-, (1→1)-, and (6→6)-bonded 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units, as shown in Scheme 4. The splitting is caused by the difference in the sequences of the 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units. These facts elucidates the presence of two linkages during the homopolymerization of **1** and **3**, that is, the (1→6)- and (6→1)-bonds in polymers **2** and **4**, respectively. Further details of the copolymerization, i.e., the kinetic studies of the copolymerization and the structural analysis of the copolymer, are currently in progress.

Conclusions

1,2:5,6-Dianhydro-3,4-di-*O*-methyl-L-iditol (**3**) was cyclopolymerized by anionic catalysts to afford a polymer which has only 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units as a result of the regio- and stereoselective mechanism. On the other hand, the anionic copolymerization of these monomers produced a random copolymer (**6**) consisting of (1→6)-, (6→1)-, (1→1)-, and (6→6)-linked 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol. For the intermolecular propagation of **1**, the attack by the growing alkoxide ion, which is attached at the C1 carbon, occurs at the β-carbon of the monomer, whereas, for **3**, the alkoxide ion, which is bound to the C6 carbon, attacked the monomer. These results clarify the presence of two linkages during the homopolymerization of **1** and **3**, that is, polymers **2** and **4** consist of the (1→6) and (6→1)-bonded 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units, respectively.

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References and Notes

(1) Nicolaou, K. C.; Duggan, M. E.; Hwang, C-K.; Somers, P. K. *J. Chem. Soc. Chem. Commun.* **1985**, 1359.
(2) Nicolaou, K. C.; Prassad, C. V. C.; Somers, P. K.; Hwang, C-K. *J. Am. Chem. Soc.* **1989**, *111*, 5330.
(3) Stork, G.; Maldonado, L. *J. Am. Chem. Soc.* **1974**, *96*, 5270.
(4) Kuszmann, J. *Carbohydr. Res.* **1979**, *73*, 93.
(5) Suzuki, T.; Sato, O.; Hirawa, M. *Tetrahedron Lett.* **1990**, *31*, 4747.
(6) Mukai, C.; Ikeda, Y.; Sugimoto, Y.; Hanaoka, M. *Tetrahedron Lett.* **1994**, *35*, 2179.
(7) Fujiwara, K.; Tokiwano, T.; Murai, A. *Tetrahedron Lett.* **1995**, *36*, 8063.
(8) Kakuchi, T.; Satoh, T.; Umeda, S.; Hashimoto, H.; Yokota, K. *Macromolecules* **1995**, *28*, 5643.
(9) Satoh, T.; Yokota, K.; Kakuchi, T. *Macromolecules* **1995**, *28*, 4762.
(10) Satoh, T.; Hatakeyama, T.; Umeda, S.; Hashimoto, H.; Yokota, K.; Kakuchi, T. *Macromolecules* **1996**, *29*, 3447.
(11) Kakuchi, T.; Satoh, T.; Umeda, S.; Hashimoto, H.; Yokota, K. *Macromolecules* **1995**, *28*, 4062.
(12) Kakuchi, T.; Umeda, S.; Satoh, T.; Hashimoto, H.; Yokota, K. *J. Macromo. Sci., Pure Appl. Chem.* **1995**, *A32*, 1007.
(13) Kakuchi, T.; Satoh, T.; Mata, J.; Umeda, S.; Hashimoto, H.; Yokota, K. *J. Macromol. Sci., Pure Appl. Chem* **1995**, *A33* (3), 325.
(14) Satoh, T.; Hatakeyama, T.; Umeda, S.; Yokota, K.; Kakuchi, T. *Polym. J.* **1996**, *28*, 520.
(15) Kuszmann, J. *Carbohydr. Res.* **1979**, *71*, 123.

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