A Novel Polymeric Carbohydrate. Synthesis of (1→6)-2,5-Anhydro-D-glucitol by Regio- and Stereoselective Anionic Cyclopolymerization of 1,2:5,6-Dianhydro-D-mannitol

Toshifumi Satoh,[†] Takeshi Hatakeyama, Satoshi Umeda, Hisaho Hashimoto,[‡] and Kazuaki Yokota*

Division of Molecular Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo 060, Japan

Toyoji Kakuchi*

Division of Bioscience, Graduate School of Environmental Earth Science, Hokkaido University, Sapporo 060, Japan

Received December 13, 1995; Revised Manuscript Received February 20, 1996[⊗]

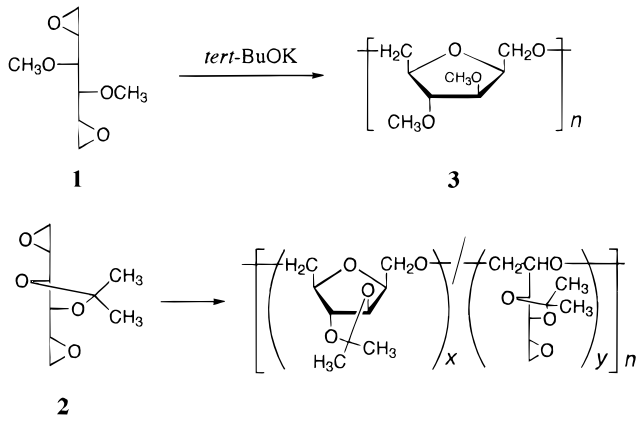
ABSTRACT: The anionic cyclopolymerizations of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) and 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (**2**) have been carried out using potassium *tert*-butoxide (*t*-BuOK) and potassium hydroxide (KOH). For the polymerization of **1**, a well-defined carbohydrate polymer consisting of (1→6) linked 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol units was synthesized through a regio- and stereoselective mechanism. When a [**1**]/[*t*-BuOK] molar ratio of 20 was used in toluene for 48 h, the yields and number-average molecular weights (M_n) of the polymers gradually increased with polymerization time. The M_n of the polymer varied with the molar ratio of monomer to initiator, and a linear relationship between them was found. The degree of polymerization was larger than that estimated from the molar ratio, resulting in an initiator efficiency of about 55%. KOH was also effective for converting monomer **1** to a gel-free polymer but was not as active as *t*-BuOK. The rate of polymerization was rather slow, and the polymerization was not complete, even after 100 h. The presence of a crown ether, 18-crown-6, in the cyclopolymerization allowed the M_n of the polymer to approach the value estimated from the [**1**]/[*t*-BuOK] molar ratio. On the other hand, monomer **2** tended to form a gel in the polymerization process, so soluble polymers were isolated only at early stages of the polymerization.

Introduction

Naturally occurring polysaccharides such as cellulose and chitin are widely used and have received considerable attention as raw materials for antiviral, biomedical, and other applications. Therefore, continuous effort has been made in the studies of structure analysis and chemical modification. The preparation of synthetic polysaccharides with structures that mimic those of a natural polymers is of interest. Recently, Kobayashi et al. reported that (1→4)-*β*-D-glucopyranan, i.e., cellulose, was synthesized by the enzymatic polymerization of *β*-cellubiosyl fluoride.[1,2]

Ring-opening polymerization of an anhydromonosaccharide is an established method for preparing various types of polysaccharides. Schuerch and Ruckel reported the synthesis of 1,6-α-linked polyglucose, dextran, by ring-opening polymerization with 1,6-anhydro-*β*-D-glucopyranose.[3,4] It was the first synthetic polysaccharide having a highly stereoregular structure similar to that of a natural polysaccharide. Using the ring-opening polymerization method, new types of polysaccharides have been synthesized, i.e., (1→3)-α-D-glucopyranan from 1,3-anhydro-*β*-D-glucopyranose,[5,6] (1→4)-*β*-D-ribopyranan and (1→5)-α-D-ribofuranan from 1,4-anhydro-α-D-ribopyranose,[7,8] and (1→6)-α-D-mannopyranan from 1,6-anhydro-*β*-D-mannopyranose.[9] These polysaccharides are termed artificial polysaccharides. On the other hand, Thiem et al. reported the synthesis of a polymeric carbohydrate by ring-opening polymerization of carbohydrate-derived dialkoxyoxolanes and 1,4:2,5:3,6-trianhydro-D-mannitol.[10−12]

Scheme 1



Recently, we presented the cyclopolymerization of 1,2:5,6-dianhydrohexitol as a new method for synthesizing polymeric carbohydrates.[13−20] 3,4-Di-*O*-alkyl substituted 1,2:5,6-dianhydro-D-mannitols and L-iditol were found to polymerize using cationic initiators, and the resulting polymers consisted of 2,5-anhydro-D-glucitols as the main repeating cyclized units, together with other cyclic units as minor components.[14−16] Moreover, we reported the successful synthesis of (1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol (**3**) by the anionic cyclopolymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) using potassium *tert*-butoxide (Scheme 1).[18] Both cyclopolymerizations proceeded through regio- and stereoselective mechanisms, respectively. On the other hand, 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-manni-

* To whom all correspondence should be addressed.

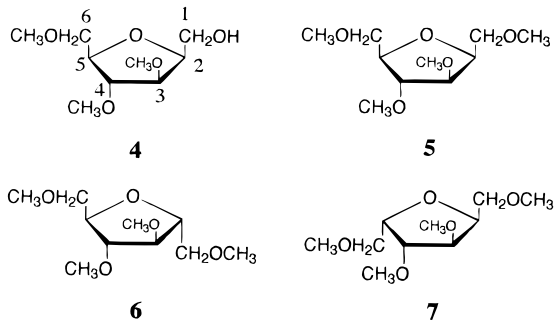
[†] Research Fellow of the Japan Society for the Promotion of Science.

[‡] Present address: Department of Industrial Chemistry, Tomakomai National College of Technology, Nishikioka 443, Tomakomai 059-12, Japan.

[⊗] Abstract published in *Advance ACS Abstracts,* April 15, 1996.

S0024-9297(95)01842-0 CCC: $12.00

Chart 1



4 **5** **6** **7**

tol (**2**) was polymerized with a cationic initiator to yield polymers with cyclic and acyclic units due to the restricted free rotation of bonds between the carbons at the 3,4-positions (Scheme 1).[15]

The difference between the cyclopolymerization and ring-opening polymerization methods is not only the polymerization manner but also the resulting polymer structure. The (1→6)-linked 2,5-anhydro-D-glucitol is a novel polymeric carbohydrate which lacks the anomeric linkage. Therefore, it is important to elucidate the cyclopolymerization tendency of the dianhydro monomer and to characterize the polymer structure. The present study focuses on the cyclopolymerization of dianhydro-D-mannitols using an anionic initiator.

In this paper, we report the cyclopolymerization of **1** using potassium *tert*-butoxide and potassium hydroxide as the anionic initiator, changing the molar ratio of **1** and the initiator, polymerization time, and solvent. In addition, to enhance the activation of the catalyst and the growing chain end, the anionic polymerization of **1** is performed in the presence of 18-crown-6. The polymerization of **2** is also carried out in order to determine the effect of substituents at the 3,4-positions on the anionic cyclopolymerization. The regio- and stereoselectivities of the cyclopolymerizations of **1** and **2** are discussed by comparing the characteristics of the resulting polymers with those of cyclic model compounds **4**−**7** (Chart 1).

Experimental Section

Measurement. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-A400 II and JEOL JNM-EX 270 spectrometers using chloroform-*d* ($CDCl_3$) with tetramethylsilane as internal standard. The absorptions in the ^{1}H and ^{13}C NMR spectra of the obtained polymer are assigned on the basis of the results with two-dimensional NMR measurements such as COSY and H−C COSY. Optical rotation measurements were carried out in chloroform solutions using a Jasco DIP-140 digital polarimeter. 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 molecular weight distribution (M_w/M_n) of the polymers were calculated on the basis of polystyrene calibration. To confirm the reliability of these M_n values, we carried out an additional measurement using field-desorption mass spectrometry (FD-MS). The values (M_n = 1150 and 1680) determined using FD-MS were, fortunately, similar to those using GPC (M_n = 1100 and 1590). FD-MS was obtained with a JEOL JMS-SX102A mass spectrometer.

Materials. Potassium *tert*-butoxide (*t*-BuOK) was purified by sublimation of the commercial product under reduced pressure. Potassium hydroxide (KOH) was purified by the following method: 2 g of KOH was dissolved in 20 mL of pure ethanol, and the solution was filtered under nitrogen gas. The solution was concentrated under vacuum using mild heating and then vacuum-dried at 50 °C for 30 h. Tetrahydrofuran, 1,4-dioxane, benzene, and toluene were purified by the usual methods and distilled from sodium benzophenone. 18-Crown-6 was purified by recrystallization from acetonitrile when necessary. 1,2;5,6-Dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) was prepared from D-mannitol according to the method of Kuszmann.[21] The method of Merrer et al. was used to synthesize 1,2;5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (**2**).[22] Monomers **1** and **2** were distilled over CaH_2 under reduced pressure before polymerization runs. 2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (**4**) and 2,5-anhydro-3,4,6-tri-*O*-methyl-D-glucitol (**5**) were synthesized from **1** as in the previous reports.[16] 2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol (**6**) was prepared by methylation of 2,5-anhydro-D-mannitol purchased from Aldrich.[19] Similarly, 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-L-iditol (**7**) was synthesized from 2,5-anhydro-L-iditol, which was prepared according to the method of Bock et al.[19,23]

Polymerization. All the polymerizations of **1** and **2** were carried out in dry benzene, toluene, tetrahydrofuran, and 1,4-dioxane in an H-shaped glass ampule. A typical polymerization procedure is as follows: Monomer **1** (0.862 g, 4.95 mmol) was added to one side of the ampule, and *t*-BuOK (110.4 mg, 0.986 mmol) and dry toluene (4.95 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 48 h, the reaction mixture was poured into a large amount of methanol, and the solution was neutralized with diluted hydrochloric acid. After evaporating the solvent, the residue was purified by reprecipitation from chloroform−*n*-hexane to yield the polymer in 96.5% (0.832 g). The M_n and M_w/M_n were 1590 and 1.27, respectively: $[\alpha]_D$ +64.7°, $[\alpha]_{577}$ +67.6°, $[\alpha]_{546}$ +76.2°, $[\alpha]_{435}$ +125.6°, and $[\alpha]_{405}$ +147.5° (c = 1.0 in $CHCl_3$ at 23 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.09 (td, J = 5.6 and 4.2 Hz, H5, 1H), 3.93 (td, J = 6.0 and 2.9 Hz, H2, 1H), 3.74 (dd, J = 10.2 and 5.4 Hz, H6, 1H), 3.62−3.69 (m, H3, H4, H1, and H6, each 1H, total 4H), 3.46−3.52 (m, H1, 1H), 3.38 (s, CH_3O, 3H), 3.36 (s, CH_3O, 3H), and 1.19 (s, *t*-BuO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.10 (CH), 85.55 (CH), 85.42 (C3), 84.97 (CH), 84.86 (CH), 84.70 (C4), 82.94 (CH), 82.23 (C2), 81.39 (CH), 80.04 (CH), 79.84 (C5), 79.70 (CH), 73.04 (C, *t*-BuO), 71.92 (CH_2), 71.70 (C1), 69.44 (CH_2), 69.38 (CH_2), 69.31 (C6), 61.46 (CH_2), 57.68 (CH_3), 57.34 (CH_3O), 57.27 (CH_3O), 57.09 (CH_3), and 27.48 (CH_3, *t*-BuO).

The polymerization of **2** (407 mg, 2.20 mmol) was carried out according to the above procedure to obtain 87 mg (21.4%) of the polymer with an M_n of 3560 and M_w/M_n of 2.19: $[\alpha]_D$ +17.2°, $[\alpha]_{577}$ +17.3°, $[\alpha]_{546}$ +20.3°, $[\alpha]_{435}$ +32.1°, and $[\alpha]_{405}$ +36.0° (c = 1.0 in $CHCl_3$ at 23 °C).

Results and Discussion

Anionic Polymerization. Table 1 summarizes the results of the polymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) using *t*-BuOK and KOH at 60 °C. All polymerizations proceeded homogeneously until the monomers were completely consumed. The reaction mixtures always exhibited a color change from colorless to dark brown as the reaction progressed. the obtained polymers were a yellow-brown sticky semisolid, soluble in toluene, chloroform, tetrahydrofuran, methanol, and water but insoluble in *n*-hexane. The solubility of the polymers was similar to that for the polymers obtained using cationic initiators.[16]

For the polymerization with a [**1**]/[*t*-BuOK] molar ratio of 20 (runs 4−8), the yields and number-average molecular weights (M_n) of polymers gradually increased with polymerization time. After prolonged polymerization for 48 h, the conversion came close to 100%. This polymerization, in which the M_n increases with conversion, shows characteristics typical of the stepwise anionic polymerization of alkylene oxides. The ultimate M_n of the polymer varied with the molar ratio of monomer to initiator, and a linear relationship between

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

run	catalyst	[**1**]/[cat.]	solvent	time (h)	yield (%)	M_n[b]	M_w/M_n[b]	DP	$[\alpha]^{23}_{546}$[c] (deg)
1	*t*-BuOK	2	toluene	48	52.1[d]	1100	1.09	6.3	+69.4
2		5	toluene	48	96.5	1590	1.27	9.1	+76.2
3		10	toluene	48	97.0	3030	1.41	17.4	+79.8
4		20	toluene	1	23.0	2110	1.22	12.1	+72.8
5		20	toluene	2	37.4	3070	1.28	17.6	+65.3
6		20	toluene	6	62.9	4140	1.30	23.8	+68.8
7		20	toluene	12	75.7	4930	1.43	28.3	+66.1
8		20	toluene	48	98.5	6410	1.53	36.8	+84.5
9		40	toluene	48	94.1	12900	1.65	74.1	+72.2
10		20	benzene	48	95.4	6400	1.64	36.8	+84.9
11		20	1,4-dioxane	48	96.1	7960	1.48	45.7	+93.9
12		20	THF	48	84.3	5100	1.31	29.3	+78.0
13[e]		20	toluene	48	92.5	2980	1.38	17.1	+90.4
14	KOH	5	THF	100	69.5	7680	1.91	44.1	+70.5
15		5	toluene	60	44.8	3860	1.76	22.1	+74.0
16		10	toluene	60	21.4	4260	1.75	24.5	+75.5

[a] [**1**] = 1.0 mol L^{-1}; temp, 60 °C. [b] Measured in THF by GPC using polystyrene as the standard. [c] c = 1.0 in chloroform. [d] Perhaps some low molecular weight polymer was lost in the precipitation. [e] [Crown]/[*t*-BuOK] = 2.0; 18-crown-6 in the polymer was removed by reprecipitation from chloroform−*n*-butyl ether.

Table 2. Cyclopolymerization of 1,2:5,6-Dianhydro-3,4-*O*-isopropylidene-D-mannitol (2) Using *t*-BuOK[a]

run	solvent	time (h)	yield (%)	M_n[b]	M_w/M_n[b]	DP	f_c[c]	$[\alpha]^{23}_{546}$[d] (deg)
17	benzene	2	21.4	3560	2.19	19.1	0.65	+20.3
18	benzene	24	gel					
19	THF	3	22.9	8210	2.62	44.1	0.65	+16.0
20	THF	24	gel					

[a] [**2**] = 1.0 mol L^{-1}; [**2**]/[catalyst] = 20; temp, 60 °C. [b] Measured in THF by GPC using PSt as the standard. [c] Mole fraction of the cyclic structure units in the polymer. [d] c = 1.0 in chloroform.

them was found. The degree of polymerization was larger than that estimated from the molar ratio, resulting in an initiator efficiency of about 55%. The reason for the loss of the initiator is obscure. The M_n was slightly increased with decreasing dipole moment of the solvent, by which the chain transfer reaction should be depressed. The specific rotation of the polymer varied in the range from +65.3° to +93.9°. However, the obvious relation between the specific rotation and the M_n was not observed.

KOH was also effective for converting monomer **1** to a gel-free polymer but was not as active as *t*-BuOK. The rate of polymerization was rather slow, and the polymerization was not complete, even after a long time (100 h). The M_n was far larger than that estimated from the [**1**]/[KOH] molar ratio. These results are interpreted as being caused by the lower basicity and solubility of KOH in comparison with *t*-BuOK.

The addition of crown ether was reported to introduce the activation of initiation and propagation in the anionic polymerization of alkylene oxides with *t*-BuOK.[24,25] The presence of a crown ether, 18-crown-6, in the cyclopolymerization allowed the M_n of the polymer to approach the value estimated from the [**1**]/[*t*-BuOK] molar ratio. The complexing agent promoted the dissociation of *t*-BuOK to an initiating anion.

Table 2 summarizes the results of the polymerization of 1,2;5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (**2**) using *t*-BuOK. Monomer **2** tended to form a gel in the polymerization process, so soluble polymers were isolated only at early stages of the polymerization. Such a polymer was powdery and soluble in toluene, chloroform, tetrahydrofuran, and methanol but insoluble in *n*-hexane. The restriction of free rotation at the C3 and C4 positions of the monomer strongly influences the decrease in its tendency to undergo cyclization.

The Vandenberg catalyst system, $2AlEt_3/H_2O$/acetylacetone in toluene, was suitable for the cyclopolymerization of α,β-diepoxides, leading to polymeric crown ethers.[26] In the systems for **1** and **2**, no polymer was obtainable. Other coordinated catalytic systems, such as $ZnEt_2/H_2O$ and $ZnEt_2/CH_3OH$, yielded only a trace of oligomers.

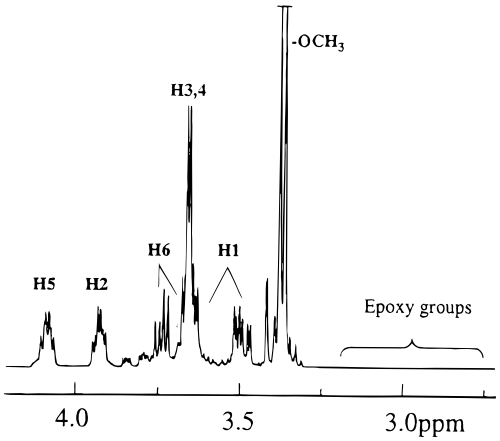


Figure 1. ^1H NMR spectrum of the polymer prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) using *t*-BuOK in toluene: [**1**]/[*t*-BuOK] = 20; time, 48 h; M_n = 6410; M_w/M_n = 1.53.

Polymer Structure. 1,2:5,6-Diepoxyhexane and 1,2-epoxyethylbenzene capable of forming 5- or 6-membered rings were polymerized to form polymers consisting of tetrahydropyran or tetrahydrofuran recurring units, depending upon the conditions.[27−30] The cationic cyclopolymerization of **1** mainly formed 5-membered rings, (1→6)-bonded 2,5-anhydro-D-glucitol units. Figures 1 and 2 show the ^1H and ^{13}C NMR spectra of polymer **3** prepared by the anionic polymerization of **1**, respectively. Because the characteristic absorption due to the epoxy protons (2.5−3.3 ppm) and carbons (50.02 and 46.51 ppm) completely disappeared and polymer **3** was soluble in common organic solvents, the polymerization proceeded according to a cyclopolymerization mechanism leading to polymers consisting of cyclic constitu-

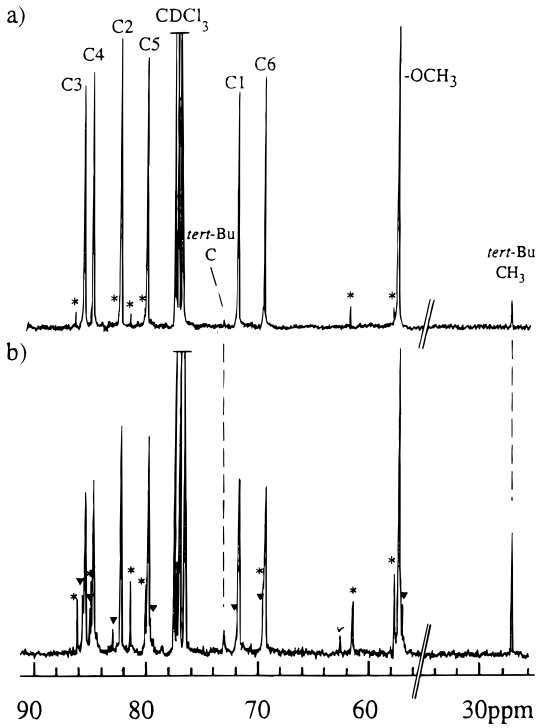


Figure 2. ^{13}C NMR spectra of the polymers prepared from 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol (**1**) using *t*-BuOK in toluene: (a) [**1**]/[*t*-BuOK] = 20; time, 48 h; $M_n = 6410$; $M_w/M_n = 1.53$; (b) [**1**]/[*t*-BuOK] = 5; time, 48 h; $M_n = 1590$; $M_w/M_n = 1.27$. Signals marked with asterisks and solid triangles correspond to the carbons for terminal end unit and initiating end unit, respectively.

Table 3. Comparison of the Signals in Polymer 3 with Those of the Model Compounds 4 and 5 in ^{13}C NMR Chemical Shifts[a]

polymer				
major signals	minor signals		model compounds	
	A[b]	B[c]	**4**	**5**
85.42 (CH)	85.55 (CH)	86.10 (CH)	86.04 (C3)	85.69 (C3)
84.70 (CH)	84.97 (CH)	84.86 (CH)	84.97 (C4)	84.75 (C4)
82.23 (CH)	82.94 (CH)	81.39 (CH)	81.32 (C5)	82.26 (C2)
79.84 (CH)	79.70 (CH)	80.04 (CH)	80.06 (C2)	79.83 (C5)
71.70 (CH_2)	71.92 (CH_2)	69.38 (CH_2)	73.20 (C6)	73.15 (C1)
69.31 (CH_2)	69.44 (CH_2)	61.46 (CH_2)	61.47 (C1)	70.66 (C6)
57.34 (CH_3)		57.68 (CH_3)	57.71 (CH_3)	57.42 (CH_3)
57.27 (CH_3)	57.09 (CH_3)		57.65 (CH_3)	57.35 (CH_3)

[a] All values were measured in $CDCl_3$ solution using tetramethylsilane as reference. [b] The signals, marked with solid triangles in Figure 2, correspond to initiating end unit. [c] The signals, marked with asterisks in Figure 2, correspond to terminal end unit.

tional repeating units, i.e., the extent of cyclization is 100%, regardless of the initiator used.

Figure 2, parts a and b shows the ^{13}C NMR spectra of the polymers obtained at [**1**]/[*t*-BuOK] ratios of 20 and 5, respectively. The former spectrum contained eight major signals and eight minor ones. In the latter spectrum, eight more signals were added to the minor ones. Because their intensity decreased with increasing M_n of the polymer, the minor signals should be due to the two end units in the chain. Table 3 compares the major and minor signals with those of 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-glucitol (**4**) and 2,5-anhydro-3,4,6-tri-*O*-methyl-D-glucitol (**5**) in the ^{13}C NMR chemical shift. The major signals very closely agreed with **5** corresponding to the constitutional unit in the polymer prepared by cationic polymerization. The minor signals

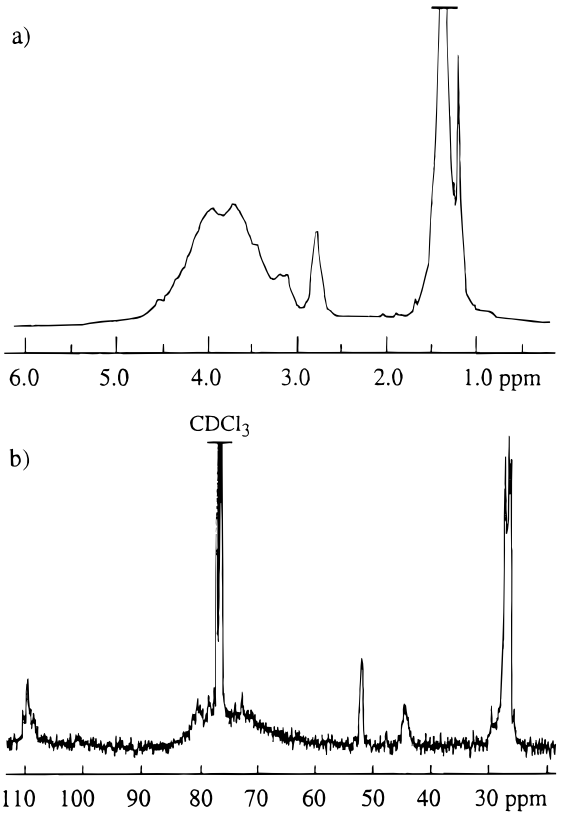
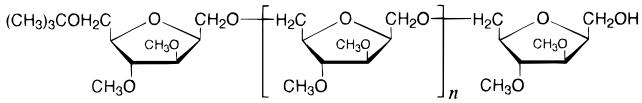


Figure 3. (a) ^1H and (b) ^{13}C NMR spectra of the polymer prepared from 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol (**2**) using *t*-BuOK in THF: [**2**]/[*t*-BuOK] = 20; time, 3 h; $M_n = 8210$; $M_w/M_n = 2.62$.

Chart 2



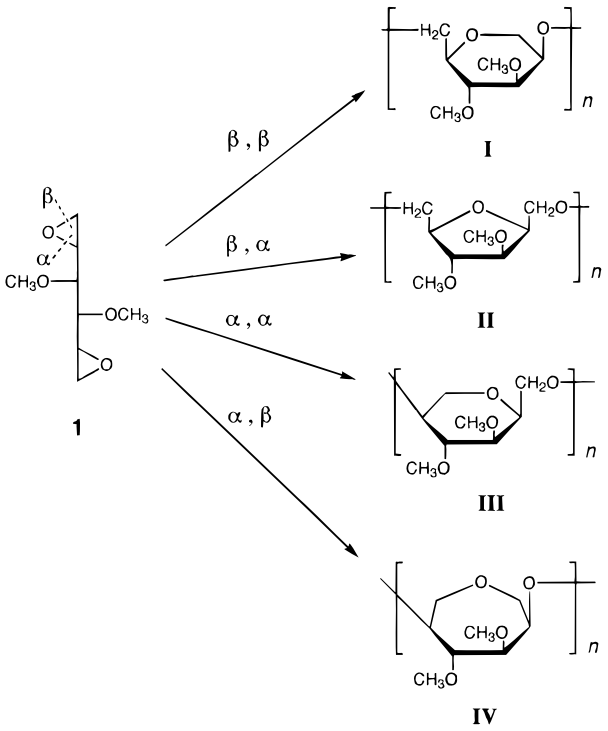
3

marked with asterisks in Figure 2a exactly agreed with those in **4**, thus being attributable to a terminal end. Minor signals at 27.48 and 73.04 ppm are assigned to the methyl carbon and the quaternary carbon in the *tert*-butoxy group, being an initiating end, respectively. Each of the additional minor signals, marked with the solid triangles in Figure 2b, was slightly shifted from the corresponding major signals. The additional signals, therefore, are attributable to the first cyclic unit bonding to the *tert*-butoxy group.

Moreover, in order to confirm the stereochemistry, the ^{13}C NMR spectrum of polymer **3** was compared with those of 2,5-anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol (**6**) and L-iditol (**7**), the stereoisomers of **5**. The configurations of the asymmetric carbons at the C2 and C5 positions are *S*,*S* in **6** and *R*,*R* in **7**, compared to *S*,*R* in **5**. The characteristic resonances at 81.30 and 86.70 ppm due to C2 and C3 for **6** and at 78.53 and 83.29 ppm for **7** were not found in the spectrum of polymer **3**. Conclusively, the anionic cyclopolymerization of **1** is highly stereoselective and produces a polymer consisting of stereochemically controlled repeating units. The polymer molecule is pictured in Chart 2. The polymer is (1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol, having hydroxymethyl and *tert*-butoxy groups at each of the chain ends.

Figure 3 shows the ^1H and ^{13}C NMR spectra of the polymer prepared from **2**. Broadening of these spectra

Scheme 2[a]



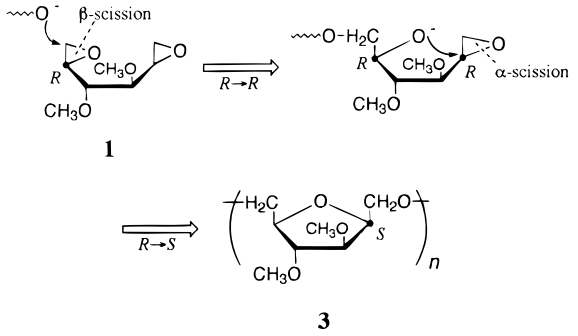
[a] The former and latter symbols (α or *β*) correspond to the intermolecular and intramolecular scissions, respectively.

is reflected from the indistinct structure. The signals at 2.6−3.0 ppm in Figure 3a indicate the presence of unreacted epoxy groups in the polymer. The extent of cyclization was about 65% which was estimated from the relative areas of the two regions at 2.6−3.0 and at 1.1−1.7 ppm due to the isopropylidene group. This group bonding to the C3 and C4 positions restricted the free rotation around the C−C bond, thus inducing a decreased tendency to undergo cyclization. The structure of cyclic units in the polymer is obscure in the NMR study.

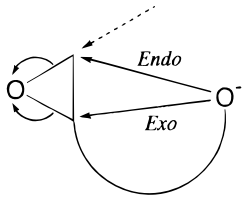
Cyclopolymerization Mechanism. Ring-opening of monosubstituted epoxides occurs in two ways, i.e., by α- or *β*-scission. In general, the polymerization using an anionic catalyst (ROK) cleaves predominantly the CH_2−O bond (*β*-scission) via S_N2 displacement to form the regular head-to-tail linkage.[31] In the cyclopolymerization of **1**, there are four possible cyclic units by combination of the inter- and intramolecular reactions via the S_N2 reaction, as shown in Scheme 2. *β*,*β*- or α,α-scissions of the two epoxides in a molecule form 6-membered rings (I and III), whereas and *β*,α- and α,*β*-scissions lead to the formation of 5- and 7-membered rings (**II** and **IV**), respectively.

Because polymer **3** consists of (1→6)-linked 2,5-anhydro-3,4-di-*O*-methyl-D-glucitol repeating units (**II**), the anionic polymerization of **1** proceeded through the mechanism with *β*,α-scissions, as shown in Scheme 3. For the intermolecular reaction, the growing alkoxy anion attacked the *β*-carbon of the first epoxide. On the other hand, for the intramolecular cyclization, the alkoxy anion produced from the first epoxide cleaved the α-bond of the second epoxide to form a 5-membered ring. It is noteworthy that the attack in the intramolecular reaction occurs not at the *β*-carbon but at the α-carbon. The cyclization along with α-scission is contrary to the usual anionic ring-opening of monosubstituted epoxides with *β*-scission. The regioselectivity

Scheme 3



Scheme 4



in the cyclization, however, can be explained by the Baldwin rule which is applicable to ring closure on the basis of a stereoelectronic effect in general.[32,33] The rule clarifies that the cyclization process accompanying the ring opening of a 3-membered ring prefers the formation of a 5-membered ring via an *exo* reaction rather than the formation of a 6-membered ring via an *endo* reaction. In such a case, the positioning of the alkoxy ion along the broken line representing the collinear approach requires considerable bond distortion, as shown in Scheme 4. Hence, the occurrence of α-scission is suitable for intramolecular reaction in the anionic polymerization of **1**. The α-scission inverts the configuration from *R* to *S* in the carbon at the C2 position. The *β*-scission in the intermolecular reaction retains the *R* configuration in the carbon at the C5 position. Thus, polymer **3** with only the D-glucitol unit as the constitutional unit is formed from monomer **1** with D-mannitol, and the anionic cyclopolymerization is highly regio- and stereoselective in comparison with the cationic polymerization.

Conclusions

The anionic cyclopolymerization of 1,2:5,6-dianhydro-3,4-di-*O*-methyl-D-mannitol using potassium *tert*-butoxide and potassium hydroxide was highly regio- and stereoselective and produced a well-defined polymer, (1→6)-2,5-anhydro-3,4-di-*O*-methyl-D-glucitol, which has hydroxymethyl and *tert*-butoxy groups at each of the chain ends. The polymer yields and molecular weights are affected by both the monomer-to-catalyst molar ratio and the polymerization time. The presence of a crown ether, 18-crown-6, in the cyclopolymerization allowed the M_n of the polymer to approach the value estimated from the [**1**]/[*t*-BuOK] molar ratio. On the other hand, 1,2:5,6-dianhydro-3,4-*O*-isopropylidene-D-mannitol tended to form a gel in the polymerization process. The restriction of free rotation at the C3 and C4 positions of the monomer strongly influences the decrease in its tendency to undergo cyclization. The selective cyclopolymerization of 1,2:5,6-dianhydrohexitol is a new synthetic method for preparing an artificial polymeric carbohydrate.

Acknowledgment. This work was supported by the Special Grant-in-Aid for Promotion of Education and

Science in Hokkaido University, provided by the Ministry of Education, Science and Culture, and by a Research Fellowship of the Japan Society for the Promotion of Science for Young Scientists.

References and Notes

(1) Kobayashi, S.; Kashiwa, K.; Kawasaki, T.; Shoda, S. *J. Am. Chem. Soc.* **1991**, *113*, 3079.
(2) Lee, J. H.; R. M. Brown, J.; Kuga, S.; Shoda, S.; Kobayashi, S. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 7425.
(3) Ruckel, E. R.; Schuerch, C. *J. Org. Chem.* **1966**, *31*, 2233.
(4) Ruckel, E. R.; Schuerch, C. *J. Am. Chem. Soc.* **1966**, *88*, 2605.
(5) Ito, H.; Kramer, S. R.; Schuerch, C. *Carbohydr. Res.* **1980**, *86*, 193.
(6) Ito, H.; Schuerch, C. *Macromolecules* **1981**, *14*, 246.
(7) Uryu, T.; Kitano, K.; Ito, K.; Yamanouchi, J.; Matsuzaki, K. *Macromolecules* **1981**, *14*, 1.
(8) Uryu, T.; Yamanouchi, J.; Kato, T.; Higuchi, S.; Matsuzaki, K. *J. Am. Chem. Soc.* **1983**, *105*, 6865.
(9) Frechet, J.; Schuerch, C. *J. Am. Chem. Soc.* **1969**, *91*, 1161.
(10) Thiem, J.; Häring, T. *Makromol. Chem.* **1987**, *188*, 711.
(11) Thiem, J.; Strietholt, W. A.; Häring, T. *Makromol. Chem.* **1989**, *190*, 1737.
(12) Strietholt, W. A.; Thiem, J.; Höweler, U. F. B. *Makromol. Chem.* **1991**, *192*, 317.
(13) Hashimoto, H.; Kakuchi, T.; Yokota, K. *J. Org. Chem.* **1991**, *56*, 6471.
(14) Kakuchi, T.; Umeda, S.; Satoh, T.; Hashimoto, H.; Yokota, K. *Macromol. Rep.* **1995**, *A32*, 1007.
(15) Kakuchi, T.; Satoh, T.; Umeda, S.; Hashimoto, H.; Yokota, K. *Macromolecules* **1995**, *28*, 4062.
(16) Kakuchi, T.; Satoh, T.; Umeda, S.; Hashimoto, H.; Yokota, K. *Macromolecules* **1995**, *28*, 5643.
(17) Kakuchi, T.; Satoh, T.; Mata, J.; Umeda, S.; Hashimoto, H.; Yokota, K. *J. Macromol. Sci.—Pure Appl. Chem.* **1996**, *A33*, 325.
(18) Satoh, T.; Yokota, K.; Kakuchi, T. *Macromolecules* **1995**, *28*, 4762.
(19) Satoh, T.; Hatakeyama, T.; Umeda, S.; Yokota, K.; Kakuchi, T. *Polym. J.*, in press. 2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-D-mannitol; ^{13}C NMR (68 MHz, $CDCl_3$) δ 86.70 (C-3,4), 81.30 (C-2,5), 72.78 (C-1,6), 59.21 ($2CH_3O$), and 57.52 ($2CH_3O$). 2,5-Anhydro-1,3,4,6-tetra-*O*-methyl-L-iditol; ^{13}C NMR (68 MHz, $CDCl_3$) δ 83.29 (C-3,4), 78.53 (C-2,5), 70.71 (C-1,6), 59.14 (2 CH_3O), and 58.03 ($2CH_3O$).
(20) Yokota, K.; Haba, O.; Satoh, T.; Kakuchi, T. *Macromol. Chem. Phys.* **1995**, *196*, 2383.
(21) Kuszmann, J. *Carbohydr. Res.* **1979**, *71*, 123.
(22) Merrer, Y. L.; et al., *Heterocycles* **1987**, *25*, 541.
(23) Bock, K.; Pedersen, C.; Thogersen, H. *Acta Chem. Scand.* **1981**, *B35*, 441.
(24) Stolarzewicz, A.; Grobelny, Z. *Makromol. Chem.* **1992**, *193*, 531.
(25) Stolarzewicz, A.; Neugebauer, D.; Grobelny, Z. *Macromol. Chem. Phys.* **1995**, *195*, 1295.
(26) Yokota, K.; Hashimoto, H.; Kakuchi, T.; Takada, Y. *Makromol. Chem., Rapid Commun.* **1984**, *5*, 115.
(27) Stille, J. K.; Culbertson, B. M. *J. Polym. Sci., Part A, Polym. Chem.* **1964**, *2*, 405.
(28) Stille, J. K.; Hillman, J. J. *J. Polym. Sci. A-1* **1967**, *5*, 2067.
(29) Aso, C.; Aito, Y. *Makromol. Chem.* **1964**, *73*, 141.
(30) Bauer, R. S. *J. Polym. Sci. A-1* **1967**, *5*, 2192.
(31) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 758.
(32) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.
(33) Stork, G.; Cohen, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 5270.

MA951842Z