Chemical Syntheses of Comb-Shaped Polysaccharide Derivatives via Cationic Ring-Opening Polymerization and Copolymerization of an Anhydrodisaccharide Monomer

Maria Carmelita Kasuya and Kenichi Hatanaka*

Department of Biomolecular Engineering, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8501, Japan

Received November 6, 1998; Revised Manuscript Received January 20, 1999

ABSTRACT: Cationic ring-opening polymerization of anhydrodisaccharide monomer (1,6-anhydro-3-*O*-benzyl-2-deoxy-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-α-D-glucopyranosyl)-*β*-D-*arabino*-hexopyranose), which was prepared by glycosylation of an anhydroglucose derivative, was carried out under high vacuum in dichloromethane with phosphorus pentafluoride as initiator. The Lewis acid catalyzed polymerization gave a cyclic oligosaccharide (thermodynamically preferred) and a (1→6)-α-linked comb-shaped polysaccharide (kinetically preferred) having an α-glucopyranosyl branching unit per sugar residue in the backbone chain. The branched polysaccharide has a number-average molecular weight of about 21 300 ($DP_n \sim 28$) and a specific rotation of +84.1° (c1, $CHCl_3$). Variations in reaction conditions significantly affected the course of polymerization. Copolymerization of the anhydrodisaccharide monomer with an anhydromonosaccharide monomer (1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy-*β*-D-*arabino*-hexopyranose) was also carried out under high vacuum in the presence of PF_5 initiator at −60 °C. The homopolymer and copolymer structures were determined by optical rotation and NMR spectroscopy. The mechanism of ring-opening polymerization of the anhydrodisaccharide monomer is discussed.

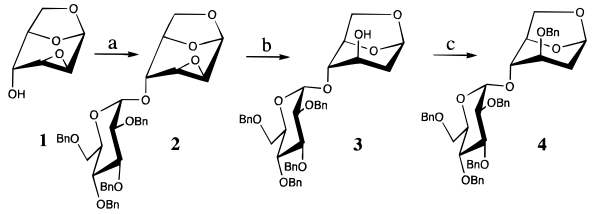
Introduction

The well-designed chemical synthesis of biologically active polysaccharide homologues has proven to be an effective strategy to investigate the relationship between carbohydrate structure and biological function. Recently, reports indicate that many of the biologically active polysaccharides are branched[1] and that the kind of branching unit, as well as the degree and position of branching, are essential for inducing the biological activity. For example, exceptionally high antitumor activity has been demonstrated by (1→3)-*β*-D-glucan having a *β*-D-glucopyranosyl group linked (1→6) to every third or fourth residue of the main chain, while linear (1→3)-*β*-D-glucopyranan shows no activity.[2] Moreover, the synthetic α-D-glucopyranose-branched (1→6)-α-D-glucopyranan[3] showed hypoglycaemic activity, i.e., lowering the blood glucose level, while α-D-mannopyranose-branched (1→6)-α-D-glucopyranan[4] and linear (1→6)-α-D-glucopyranan did not have any hypoglycaemic activity.

Cationic ring-opening polymerization of anhydrodisaccharide derivatives[5] having a bicyclic acetal skeleton has been one of the excellent methods for the chemical synthesis of branched polysaccharides with high molecular weight and well-defined structures. Kobayashi et al. reported the chemical synthesis of a comb-shaped stereoregular polysaccharide, 4-*O*-α-D-mannopyranosyl-(1→6)-α-D-mannopyranan, via cationic ring-opening polymerization of an anhydrodisaccharide monomer.[6] Schuerch and co-workers prepared comb-shaped polysaccharides and oligosaccharides from 1,6-anhydrocellobiose hexabenzyl ether[7] and from 1,6-anhydromaltose hexabenzyl ether.[8] A branched dideoxy polysaccharide 2,4-dideoxy-3-*O*-(*β*-galactosyl)−(1→6)-α-*threo*-hexopyranan was prepared by ring-opening polymerization of 1,6-anhydro-3-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-*β*-galactopyranosyl)-2,4-dideoxy-*β*-*threo*-hexopyranose.[9] Despite the regularly branched structure and the high stereoregularity of the polysaccharides prepared by the above-mentioned approach, a major drawback is the low number-average molecular weight of polymerization products due to the low polymerizability of the monomers with bulky branching unit.

In an attempt to synthesize a homologue of Panaxan A, a natural branched polysaccharide with hypoglycaemic activity,[10] this research was carried out to chemically synthesize a comb-shaped polysaccharide (having a pendant monosaccharide unit regularly substituted in each sugar unit in the main chain) via cationic ring-opening polymerization of an anhydrodisaccharide monomer. A deoxy monomer was prepared to facilitate the synthesis of deoxy branched polysaccharides with high molecular weight.

Scheme 1. Synthesis of Anhydrodisaccharide Monomer (4)[a]



[a] Reagents and conditions: (a) glycosyl donor: 2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl trichloroacetimidate, TBDMSOTf, CH_2Cl_2, $NaHCO_3$, room temperature, 5 h. (b) LAH, Et_2O, reflux, 4 h. (c) BnBr, NaH, DMF, room temperature, 4 h.

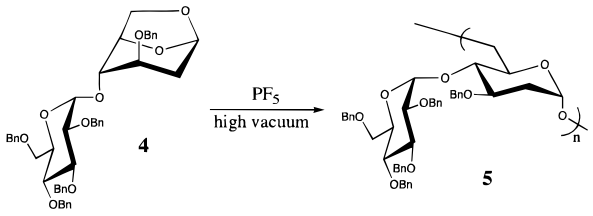
Results and Discussion

I. Homopolymerization. The monomer with the glucopyranosyl branching unit at the C-4 position was prepared (Scheme 1) using the trichloroacetimidate

* To whom corrrespondence should be addressed.

10.1021/ma981730i CCC: $18.00
Published on Web 03/11/1999

Scheme 2. Ring-Opening Polymerization of Anhydrodisaccharide Monomer (4)



Disaccharide Monomer **Comb-shaped Polysaccharide**

Table 1. Ring-Opening Polymerization of Anhydrodisaccharide Monomer (4)[a,d]

no.	initiator, mol %	temp, °C	time, h	conversion,[b] %	polymer vs trimer,[b] %	$\overline{M_n}^b \times 10^3$	$\overline{DP_n}$
1	20	−75	24	85.5	75:25	21.3	28
2	20	−60	24	96.1	60:40	10.9	14
3	20	−60	0.3	98.3	57:43	6.8	9
4[c]	10	−40	2	74.8	37:63	8.6	11
5	20	−40	24	88.7	34:66	6.1	8
6	20	−40	48	89.0	0:100	2.2	3
7	20	0	24	88.6	0:100	2.3	3

[a] Monomer (200 mg) was dissolved in 0.5 mL of CH_2Cl_2 and polymerized under high vacuum using PF_5 as initiator. [b] Determined by GPC with polystyrene as standard. [c] Monomer (300 mg) was dissolved in 1 mL of CH_2Cl_2. [d] The polymerization product gave a mixture of a polymer and a trimer which was separated by HPLC.

method of glycosylation[11] of a 1,6:2,3-dianhydromannose derivative (**1**) which has been prepared from 1,6-anhydro-β-D-glucopyranose[12] by the method developed by Cerny et al.[13] 2,3-Epoxide scission of the glycosylated anhydrosugar derivative (**2**) with lithium aluminum hydride[14] gave the anhydrodisaccharide derivative with a free hydroxyl group at the C-3 position (**3**). Finally, benzylation of the free hydroxyl group afforded the anhydrodisaccharide monomer 1,6-anhydro-3-*O*-benzyl-2-deoxy-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-α-D-glucopyranosyl)-β-D-*arabino*-hexopyranose (**4**).

The cationic ring-opening polymerization of the anhydrodisaccharide monomer (Scheme 2) was investigated under high vacuum with phosphorus pentafluoride as initiator. The results of polymerization are summarized in Table 1. Polymerization reaction required a high concentration of the initiator probably because of the large number of oxygen atoms in the structure which are possible complexation sites. Polymerization was undertaken in dichloromethane at different temperatures ranging from −75 to 0 °C. When the polymerization was started, the polymerization solution became viscous and pale yellow, but the color disappeared after termination of polymerization by the addition of methanol. Purification of the polymer was carried out by reprecipitation from the chloroform solution by adding methanol and by lyophilization to give a white powdery polymerization product.

The gel permeation chromatogram of the products resulting from the polymerization at lower temperatures (−60 to −40 °C) and at shorter period of time (15 min to 24 h) showed two peaks indicating a mixture of polymerization products. One of the products was a polysaccharide with a number-average molecular weight in the range 6000−11 000 ($DP_n = 8-14$), and the other product was an oligomer with a number-average molecular weight of about 2300 ($DP_n = 3$). At −60 and −40 °C, the polymer-to-trimer ratio was 60:40 and 34:66, respectively. A high molecular weight polymerization

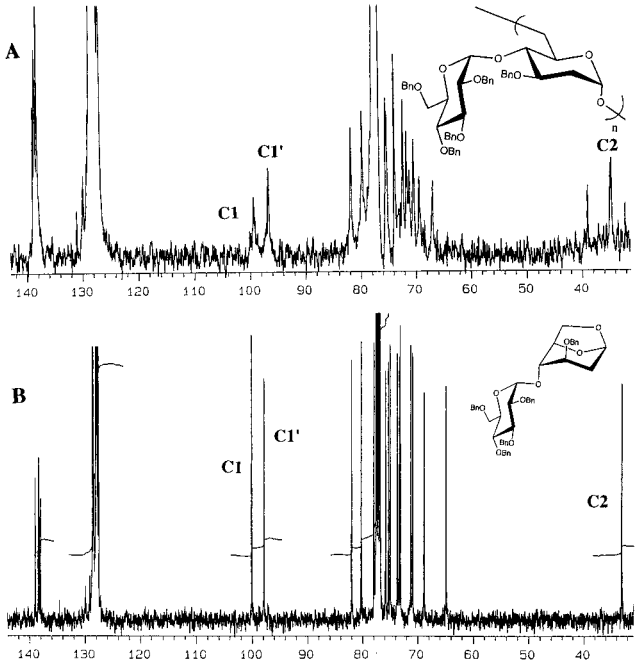


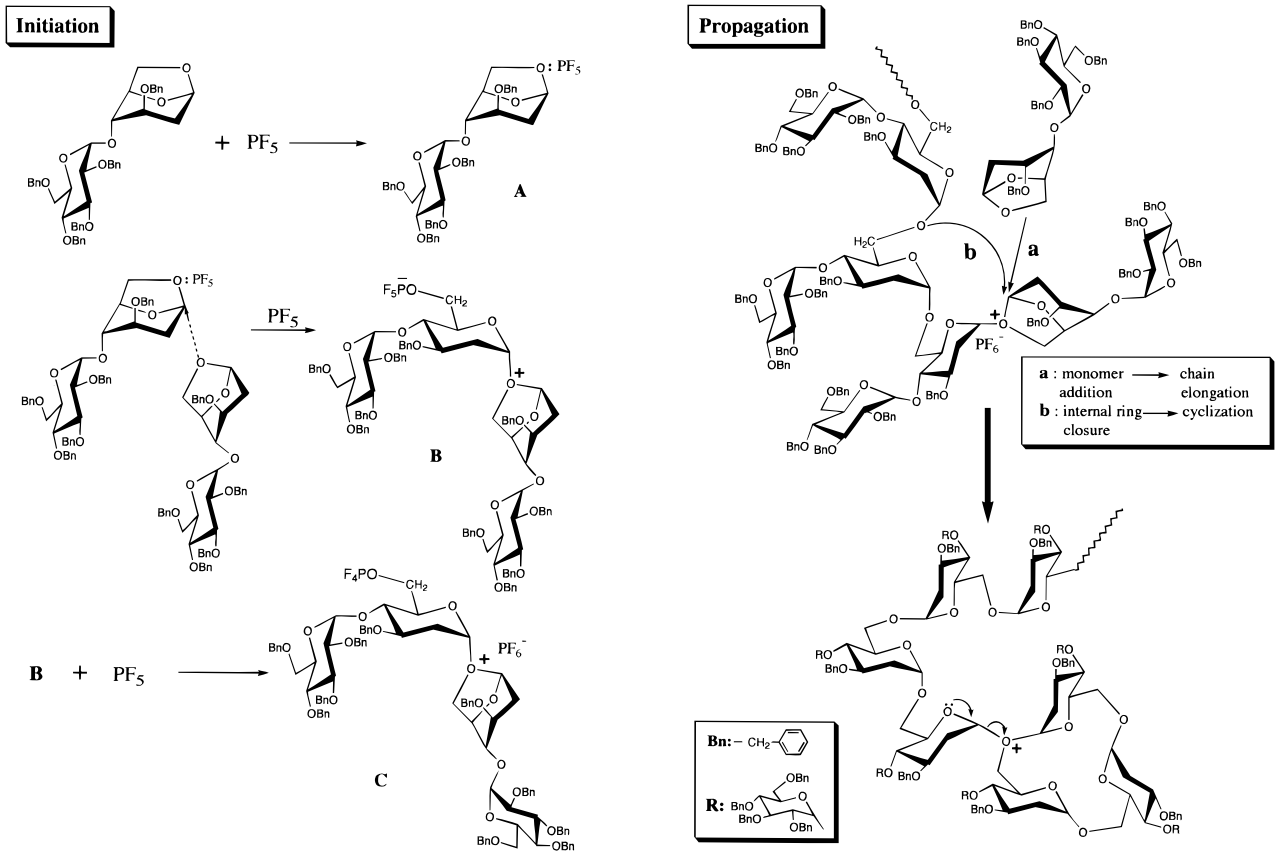
Figure 1. ^{13}C NMR spectra of (A) branched polysaccharide (**5**) and (B) anhydrodisccharide monomer (**4**) in $CDCl_3$.

product (M_n = 21 300; $DP_n = 28$) was obtained at −75 °C for 24 h with a polymer-to-trimer ratio of 75 to 25, respectively. However, at a higher temperature of 0 °C or at a reaction time of 48 h or even longer, no polysaccharide was detected, and the polymerization gave only the oligomer. These results highlight the dramatic effects of time and temperature in the polymerization reaction. Separation of the polysaccharide from the oligomer was accomplished by HPLC.

Polymer Structure. The polymer exhibited a relatively high specific rotation value of $[\alpha]^{25}_D$ +84.1° (c1,$CHCl_3$), which implies high α stereoregularity. The ^1H NMR spectrum of the polymer confirms high α stereoregularity as indicated by the presence of a single resonance at 5.78 ppm corresponding to the anomeric proton of the sugar residue of the main chain. The signals at 2.29 and 1.44 ppm correspond to the two protons at the deoxy position (C-2). Complete assignment in the ^1H NMR has not been made due to the excessive overlapping of similar resonances of the pendant and backbone moeities. The 100 MHz ^{13}C NMR spectral results (Figure 1) showed two resonances at 96.74 and 99.74 ppm corresponding to the anomeric carbon atoms of the branching unit and the sugar unit at the main chain, respectively. Taking into account the high positive specific rotation value and the structural analysis by NMR, it can be concluded that the polymer is a highly stereoregular (1→6)-α-linked comb-shaped polysaccharide (**5**) with a glucopyranosyl branching unit attached to the C-4 position of each sugar residue of the main chain. Inspection of the molecular models suggests that the polymer backbone is very crowded due to the large volume of pendant tetrabenzylated sugar units.

Mechanism of Polymerization. In the polymerization of 1,6-anhydro sugar derivatives protected by benzyl groups at low temperatures, the addition reaction of the monomer has already been established to proceed via the oxonium ion mechanism (S_N2).[15] Polymerization proceeds with configurational inversion of the anomeric carbon to give stereoregular (1→6)-α-D-glucopyranan derivatives. The mechanism of polymerization of the

Scheme 3. Mechanism of Polymerization



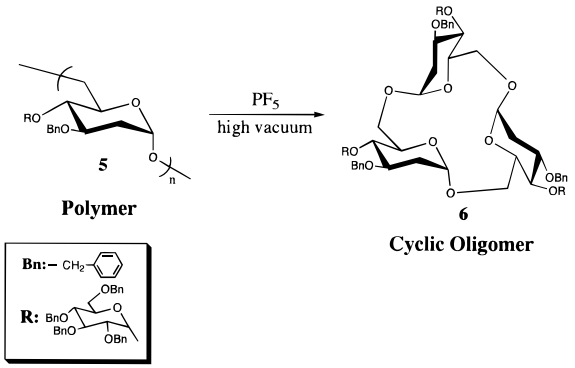
anhydrodisaccharide monomer can be described as follows (Scheme 3): Initiation process with phosphorus pentafluoride can be formulated as taking place in three stages: (i) initial complexation with the ring oxygen atom resulting in the partial electron deficiency at C-1; (ii) attack by the ring oxygen atom of a second monomer on the electron deficient C-1, with simultaneous bond breaking to form a terminal $-CH_2-O-PF_5$ anion and an active trialkyloxonium ion; (iii) transfer of the fluoride ion to PF_5 to give an uncharged terminal $-CH_2-O-PF_4$ and a hexafluorophosphate counterion that can migrate and remain close to the trialkyloxonium ion during propagation. Propagation consists of the repeated attack on C-1 of the trialkyloxonium ion of the growing chain end and migration of the phosphorus hexafluoride anion with the charging cation.

Generally, the rate of propagation is slow for bulky monomeric units. This makes side reactions possible and results in the formation of a mixture of products. In the formation of a mixture of polymerization products (a polysaccharide and an oligomer) in this study, a rational explanation can be proposed by looking into the crucial propagation step. During propagation, it is estimated that "competetive reaction"[16] may have taken place and that monomer concentration may have played a very significant role in the polymerization behavior. Two types of reactions can take place competitively on the chain end unit: one is monomer addition (arrow a), and the other is internal ring closure (arrow b). At the onset of polymerization, i.e., when the initial concentration of the monomer is high, elongation of the polymer chain by monomer addition proceeds to give the branched polysaccharide (**5**). Thus, during propagation reaction involving the propagating cation and monomer, the rate is substantially enhanced at high monomer concentration and the molecular weight of the polysaccharide is higher. On the other hand, when the disaccharide monomer concentration becomes sufficiently low (monomer consumed during polymerization), cyclization by internal ring closure (backbiting) is most likely to occur, thus giving the cyclic oligosaccharide (**6**)[17] as another polymerization product, which has been reported in detail elsewhere.

Initial monomer concentration as well as the length of polymerization time significantly affected the course of polymerization in a predictable manner. Monomer addition may proceed kinetically, i.e., elongation occurs fast, as indicated by the production of polysaccharides with relatively higher molecular weight even at a short polymerization time of 15 min. Ring closure is perceived to have occurred at the later part of polymerization. Interestingly, only the oligomer is detected at longer polymerization time (48 h or longer). Thus, it may be considered that when the polymerization has been completed, the polymer chain is very crowded such that, at longer periods of time, internal ring closure may have been favored to give only the thermodynamically preferred oligosaccharide.

Polymerization at lower temperature was governed by kinetic factors, rather than by thermodynamic factors, especially in the initial stage of polymerization. At −75 °C, the predominant product was the polysaccharide (polymer:oligomer ratio, 75:25). The amount of polysaccharide formed decreased with increasing temperature such that, at −40 °C, the polymer:trimer ratio became 34:66, and at 0 °C, the polymer:trimer ratio was 0:100. This indicates that thermodynamic factors predominate during polymerization at higher temperatures.

Scheme 4. Depolymerization



Although the absence of a substituent at the C-2 position might have facilitated the attack of a monomer, the electrophilic anomeric center C-1 in the bicyclic system of the oxonium ion can be attacked only from the rear with respect to the 1,6-anhydro ring leading to only an α linkage. Moreover, the absence of substituent at C-2 has been significant in the preparation of relatively high molecular weight branched polysaccharides from anhydrodisaccharide monomer without the need for a cocatalyst.[7,8]

To provide supporting evidence to the proposed mechanism of possible internal ring-closure during polymerization, i.e., backbiting taking place resulting in the formation of the cyclic trimer, depolymerization (Scheme 4) was carried out in the presence of 20 mol % phosphorus pentafluoride under high vacuum.

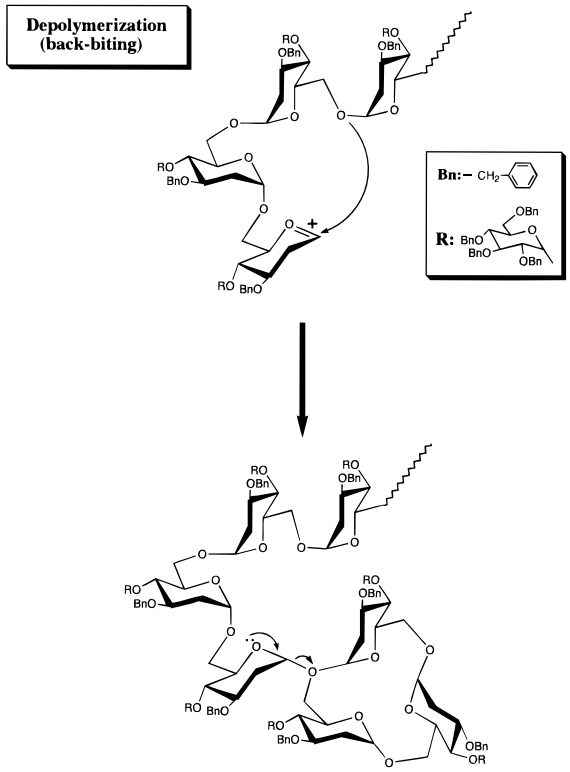
When PF_5 was added to a solution of the polymer (**5**) (product from the polymerization of the anhydrodisaccharide monomer) in dichloromethane, depolymerization occurred at −60 °C within 24 h as confirmed by gel permeation chromatography results. Molecular weight calculations showed that the depolymerization product was a trimer.

The spectral results obtained for the trimer from ring-opening polymerization of the anhydrodisaccharide monomer and the trimer from depolymerization of the polysaccharide were identical. These results confirmed that when polymerization has been completed, depolymerization further occurred in the presence of the catalyst to give the cyclic oligosaccharide.

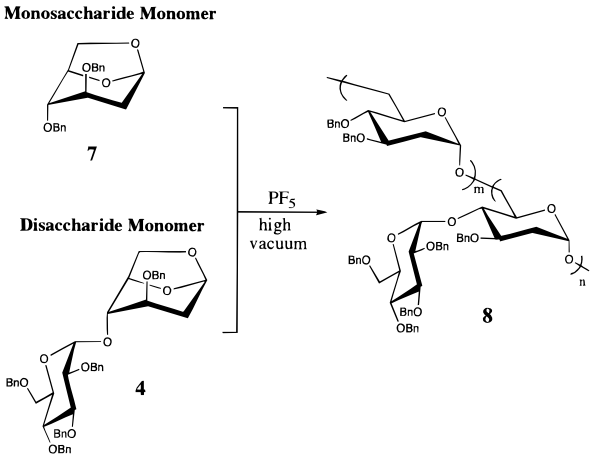
Depolymerization to give the cyclic oligosaccharide is considered to have taken place via the carbenium ion mechanism as shown in Scheme 5. Moreover, the same mechanism could also provide an explanation as to why the cyclic trimer was also produced even during polymerization at 0 °C—the temperature at which the carbenium ion mechanism predominates. Careful consideration of results has led to the conclusion that both the oxonium and carbenium ions were present during polymerization of the anhydrodisaccharide monomer to give a mixture of comb-shaped polysaccharide and a cyclic oligosaccharide.

II. Copolymerization. Copolymerization of the anhydrodisaccharide monomer (**4**) with an anhydromonosaccharide monomer 1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy-β-D-*arabino*-hexopyranose (**7**)[18] was carried out at −60 °C in dichloromethane using PF_5 as initiator (Scheme 6). The results are summarized in Table 2. Copolymerization proceeded to give products of 40.8−86.4% yield and with number-average molecular weight of about 2500−6100. Gel permeation chromatography results indicate that copolymerization at high anhydro-

Scheme 5. Mechanism of Depolymerization



Scheme 6. Copolymerization of Anhydrodisaccharide Monomer (4) with Anhydromonosaccharide Monomer (7)



disaccharide feed gave a mixture of products of copolymer and oligomer. On the other hand, at low anhydrodisaccharide monomer feed, only the copolymer was detected.

Copolymer Structure. The specific rotation obtained for the copolymerizations gave high positive values (+92.0 to +116.3), indicating that the copolymer has an α linkage. The ^{1}H NMR spectrum shows two resonances at 5.78 and 5.85 ppm which can be assigned to the anomeric protons of the two different sugar units (with and without branching unit, respectively) in the main chain. In the ^{13}C NMR spectrum (Figure 2) of the obtained copolymer, the signal for the anomeric carbon atoms of the monosacharide unit and the disaccharide unit in the main chain are overlapping at 98.15 ppm. The anomeric carbon atom of the glucose branching unit of the disaccharide residue appears at 96.72 ppm. The optical rotation results coupled with the NMR results

Table 2. Copolymerization of Anhydrodisaccharide Monomer (4) with Anhydromonosaccharide Monomer (7)[a]

no.	disaccharide monomer feed (mg)	disaccharide monomer feed mol fraction	monosaccharide monomer feed (mg)	catalyst, %	yield, %	mol fraction of disaccharide monomer in the copolymer[d]	$\overline{M_n}^e \times 10^3$	$[\alpha]_D^{25}$, deg
1[b]	49.3	0.25	63.6	10	56.1	0.18	4.5	+116.32
2[c]	100	0.50	43.0	20	40.8	0.41	2.5	+92.0
3[c]	148	0.75	21.2	10	86.4	0.59	6.1	+92.8

[a] Solvent, CH_2Cl_2 (0.5 mL); polymerization temperature, −60 °C. [b] Polymerization time, 1 h. [c] Polymerization time, 2 h. [d] Determined by ^{13}C NMR spectroscopy. [e] Determined by GPC using polystyrene as standard.

indicate that the product is a highly stereoregular (1→6)-α-linked copolymer (**8**).

The mole fraction of disaccharide monomer incorporated in the copolymerization product was determined by NMR spectroscopy with reference to the relative intensities of the C-2 signals from the two components. Results showed that the mole fraction of the disaccharide unit in the copolymer (0.18, 0.41, and 0.59) is relatively proportional to the feed (0.25, 0.50, and 0.75, respectively). However, at low anhydrodisaccharide feed (0.25), the disaccharide units were not efficiently taken into the copolymer probably due to its bulky branching units, and the main chain was dominated by monosaccharide units. At high anhydrodisaccharide feed (0.75), the cyclic oligomer was detected as another copolymerization product.

Experimental Section

Characterization. ^1H and ^{13}C NMR spectra were obtained with Varian Gemini-100 and UNITY plus 400 spectrometers on solutions in chloroform-*d* with tetramethylsilane as internal standard. Optical rotations were measured as solutions in chloroform at room temperature using a JASCO LIP 1000 digital polarimeter. Gel permeation chromatography (GPC) of the polymers were carried out on a Shimadzu LC9A liquid chromatograph (GPC-802, 803, and 804 columns) using THF as solvent and polystyrene standards. Melting points were determined with a Yanaco MP-S3 melting point apparatus. Merck Silica gel was used for column chromatography.

Preparation of 1,6-Anhydro-3-*O*-benzyl-2-deoxy-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-α-D-glucopyranosyl)-*β*-D-*arabino*-hexopyranose (Compound 4). The anhydrodisaccharide monomer was prepared by glycosylation of the 1,6:2,3-dianhydro mannose derivative (4.0 g, 27.8 mmol) using the trichloroacetimidate of tertabenzylglucose (28.5 g, 41.6 mmol) in 250 mL of dry dichloromethane and *tert*-butyldimethylsilyl triflate (2.5 mL) as catalyst. Glycosylation was carried out at room temperature for 5 h, and the resulting mixture was neutralized with $NaHCO_3$, washed with water, dried with anhydrous sodium sulfate, and concentrated in vacuo to afford 100% α-stereoselective product **2** (4.79 g, 12.6% yield). 2,3-Epoxide scission with lithium aluminum hydride according to Seib's procedure[14] gave compound **3** (82.6% yield). Finally, benzylation of the free hydroxyl group of compound **3** (3.0 g, 4.5 mmol) with benzyl bromide (1.53 g, 9.0 mmol) and sodium hydride (0.39 g) in 130 mL of DMF for 4 h at room temperature afforded the anhydrodisaccharide monomer **4**. Purification was carried out by column chromatography ($CHCl_3$:EtOAc, 9:1). Crystallization from butyl chloride solution and recrystallization twice using petroleum benzine and ether gave the pure, white crystals. Yield 88.1%; $[\alpha]^{25}_D = +1.1$ (c1, $CHCl_3$); melting point 84−85 °C. $C_{47}H_{50}O_9$ (758.9). Calcd: C, 74.38; H,6.65. Found: C,74.25; H,6.36.

Polymerization and Copolymerization. Cationic ring-opening polymerization and copolymerization were carried out under high vacuum using dichloromethane and phosphorus pentafluoride (generated by pyrolysis of a precursor, *p*-chlorobenzendiazonium hexafluorophosphate) as initiator.[19] Polymerization was carried out at different temperatures ranging from −75 to 0 °C. Copolymerization was carried out only at −60 °C. The polymerization/copolymerization reaction was terminated by the addition of MeOH. The products were purified by reprecipitation of the chloroform solution into methanol three times and then freeze-dried from benzene solution. Polymerization/copolymerization products were separated by HPLC using chloroform as eluting solvent.

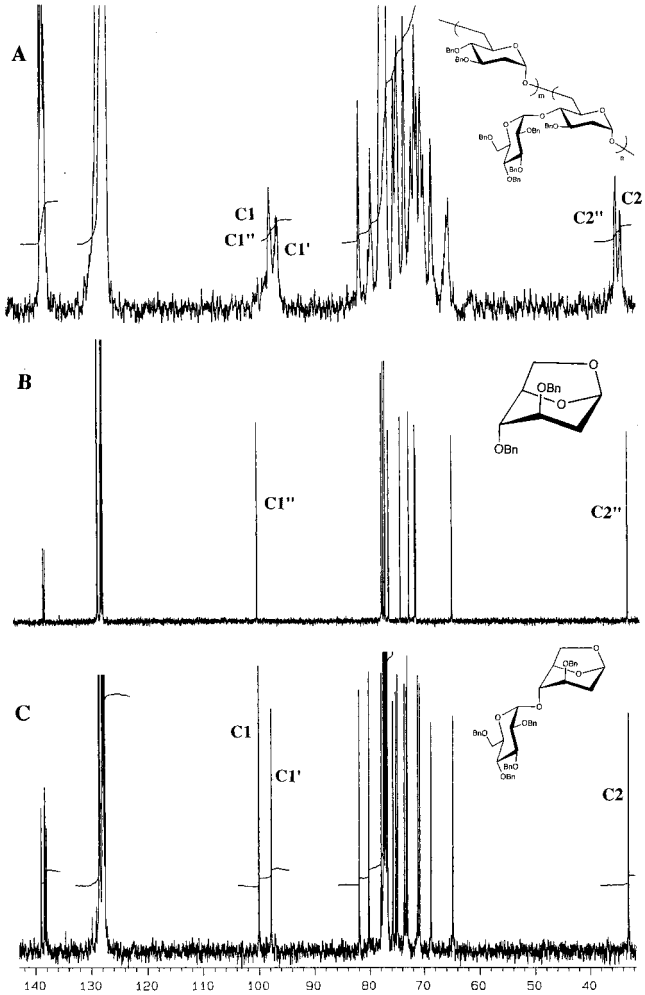


Figure 2. ^{13}C NMR spectra of (A) copolymerization product (**8**), (B) anhydromonosaccharide monomer (**7**), and (C) anhydrodisaccharide monomer (**4**) in $CDCl_3$.

Depolymerization. Depolymerization of the polysaccharide (**5**) obtained from ring-opening polymerization of the anhydrodisaccharide monomer was carried out under high vacuum using 0.5 mL of dichloromethane and 20 mol % phosphorus pentafluoride as initiator. Depolymerization was carried out for 24 h at −60 °C. The depolymerization reaction was terminated by the addition of MeOH. The depolymerization product was purified by reprecipitation of the chloroform solution into methanol three times and then freeze-dried from benzene solution.

Acknowledgment. This research was supported in part by the Sasakawa Scientific Research Grant from the Japan Science Society.

References and Notes

(1) Uryu, T.; Yamanaka, M.; Henmi, M.; Hatanaka, K.; Matsuzaki, K. *Carbohydr. Res.* **1986**, *157*, 157−169.
(2) Hatanaka, K. In *Polymeric Materials*; Salamone, J. C., Ed.; CRC Press: Boca Raton, Fl, 1996; Vol. 9, pp 6713−6717.
(3) Hatanaka, K. In *Polysaccharides in Medicinal Application*; Dumitriu, S., Ed.; Marcel Dekker: New York, 1996; pp 3−20.
(4) Hatanaka, K.; Hirobe, T.; Yoshida, T.; Yamanaka, M.; Uryu, T. *Polym. J.* **1990**, *22* (5), 435−441.
(5) (a) Kochetkov, N. K. *Tetrahedron* **1987**, *43*, 2389−2439. (b) Schuerch, C. *Adv. Carbohydr. Chem. Biochem.* **1981**, *39*, 157−212. (c) Uryu, T.; Hatanaka, K.; Matsuzaki, K.; Kuzuhara, H. *Macromolecules* **1983**, *16*, 853.
(6) Kobayashi, K.; Nomura, K.; Okada, M. *Carbohydr. Res.* **1993**, *242*, 161−166.
(7) Masura, V.; Schuerch, C. *Carbohydr. Res.* **1970**, *15*, 65−72.
(8) Veruovic, B.; Schuerch, C. *Carbohydr. Res.* **1970**, *14*, 199−206.
(9) Okada, M.; Sumitomo, H.; Ogasawara, K. *Polym. J.* **1982**, *14* (10), 815−821.
(10) (a) Tomoda, M.; Shimada, K.; Konno, C.; Sugiyama, K.; Hikino, H. *Planta Medica* **1984**, 436−438. (b) Oshima, Y.; Konno, C.; Hikino, H. *J. Etnopharmacol.* **1985**, *14*, 285−259. (c) Konno, C.; Murakami, M.; Oshima, Y.; Hikino, H. *J. Etnopharmacol.* **1985**, *14*, 69−74.
(11) (a) Schmidt, R. R.; Michel, J. *J. Carbohydr. Chem.* **1985,** *4*, 141−169. (b) Schmidt, R. R. *Adv. Carbohydr. Chem. Biochem.* **1994,** *50*, 21−123. (c) Schmidt, R.; Michel, J. *Tetrahedron Lett.* **1984**, *25*, 821. (d) Schmidt, R. R. In *Modern Methods of Carbohydrate Synthesis*; Khan, S., O'Neill, G., Eds.; Harwood Academic Publishers: Amsterdam, 1996; pp 20−54.
(12) Zottola, M. A.; Alonso, R.; Vite, G. D.; Fraser-Reid, B. *J. Org. Chem.* **1989**, *54*, 6123−6125.
(13) (a) Cerny, M.; Kaldova, L.; Pacak, J. *Collect. Czech. Chem. Commun.* **1968**, *33*, 1143−1156. (b) Trnka, T.; Cerny, M. *Collect. Czech. Chem. Commun.* **1971**, *36*, 2216−2225.
(14) Seib, P. A. *J. Chem. Soc. C* **1969**, 2552−2559.
(15) (a) Sumitomo, H.; Okada, M. In *Ring-Opening Polymerization*; Ivin, K. V., Saegusa, T., Eds.; Elsevier Applied Science: London, 1984; Vol. 1, pp 299−367. (b) Uryu, T. In *Models of Biopolymers by Ring-Opening Polymerization*; Penczek, S., Ed.; CRC Press: Boca Raton, Fl, 1990; pp 133−233.
(16) Hirasawa, T.; Okada, M.; Sumitomo, H. *Macromolecules* **1988**, *21*, 1566−1571.
(17) Kasuya, M. C.; Hatanaka, K. *Tetrahedron Lett.* **1998**, *39*, 9719−9722.
(18) Hatanaka, K.; Kanazawa, S.; Uryu, T. *J. Polym. Sci., Chem. Ed.* **1984,** *22*, 1987−1996.
(19) Kobayashi, K.; Sumitomo, H. *Macromolecules* **1981**, *14*, 250.

MA981730I