Synthesis of Hyperbranched Polysaccharide by Thermally Induced Cationic Polymerization of 1,6-Anhydro-β-D-mannopyranose

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ABSTRACT: The thermally induced cationic polymerization of 1,6-anhydro-β-D-mannopyranose (**1**) as a latent cyclic AB_4-type monomer was carried out using 2-butenyltetramethylenesulfonium hexafluoroantimonate (**2**) as the initiator. The solution polymerization in propylene carbonate proceeded without gelation to produce the water-soluble hyperbranched polysaccharides (**3**) with controlled molecular weights and narrow polydispersities. The weight-average molecular weight ($M_{w,SLS}$) values of **3** measured by static laser light scattering (SLS) varied in the range 6.5×10^3 to 6.4×10^5, which were significantly higher than the weight-average molecular weight ($M_{w,SEC}$) values by size exclusion chromatography (SEC). The viscosity of the solution of **3** was very low, and the intrinsic viscosities were from 0.032 to 0.047 $dL \cdot g^{-1}$. Polymer **3** was composed of α- and β-linked hyperbranched polysaccharides consisting of 19 kinds of D-mannopyranosyl and D-mannofuranosyl repeating units, which had numerous nonreducing D-mannopyranosyl terminal units. The degree of branching (DB), estimated by the methylation analysis of **3**, was in the range of 0.38−0.44. The thermally induced cationic polymerization of **1** using **2** is a facile method leading to the hyperbranched polysaccharide with a high DB value.

Introduction

The spherical architectures of highly branched macromolecules, such as dendrimers and hyperbranched polymers, have attracted much attention from the viewpoint of nanotechnology, because their numerous terminal units can be converted into various functional groups leading to novel nanomaterials.[1−19] In general, the synthetic method of making hyperbranched polymers is easier than that of dendrimers, because they can be prepared through a one-pot procedure using AB_m-type monomers. For the preparation of hyperbranched polymers, there are three synthetic strategies, such as "polycondensation" of AB_m-type monomers as the most common method,[7,20,21] "self-condensing vinyl polymerization" based on a vinyl monomer bearing an initiating group,[22−25] and "ring-opening multibranching polymerization" of cyclic latent AB_m-type monomers.[26−31] Thus, various types of hyperbranched polymers have been synthesized, and their properties, such as the hydrodynamic volume and viscosity, were compared with the linear analogues.[32−34]

Most of the naturally occurring and chemically synthesized polysaccharides are recognized as linear macromolecules or those with short branches, so that it is of great interest to synthesize and characterize the hyperbranched polysaccharides. So far, although the apparent concept of hyperbranched macromolecular architecture was lacking in the 1950s, Schuerch et al. and other groups have reported pioneering research on highly branched polysaccharides prepared by the acid-catalyzed ring-opening polymerization of the 1,6-anhydrohexopyranoses.[35−42] However, it was insufficient to elucidate the properties of spherical molecules such as the degree of branching of the highly branched polysaccharides. Recently, on the basis of the synthetic strategy of ring-opening multibranching polymerization, Kadokawa et al. reported that a hyperbranched aminopolysaccharide was synthesized by the acid-catalyzed polymerization of an oxazoline sugar monomer having two hydroxyl groups.[43,44]

In this article, we describe the detailed research of the synthesis and characterization of a hyperbranched polysaccharide based on the strategy of ring-opening multibranching polymerization. The ring-opening polymerization of 1,6-anhydro-β-D-mannopyranose (**1**) as a latent AB_4-type monomer was carried out in propylene carbonate as a solvent using 2-butenyltetramethylenesulfonium hexafluoroantimonate (**2**) as a thermally induced cationic initiator, as shown in Scheme 1. In addition, the hyperbranched polysaccharide **3** is characterized by properties of spherical molecules, such as the hydrodynamic volume, viscosity, and degree of branching, in comparison with a linear polysaccharide of (1→6)-α-D-mannopyranan (**4**).

Experimental Section

Materials. D-(+)-Mannose was purchased from Junsei Chemical Co., Ltd. Anhydrous propylene carbonate, methyl α-D-mannopyranoside (**5a**), and methyl β-D-mannopyranoside (**5b**) were purchased from Sigma-Aldrich Co. 2-Butenyltetramethylenesulfonium hexafluoroantimonate (**2**) in propylene carbonate solution (66 wt %) was a gift from Asahi Denka

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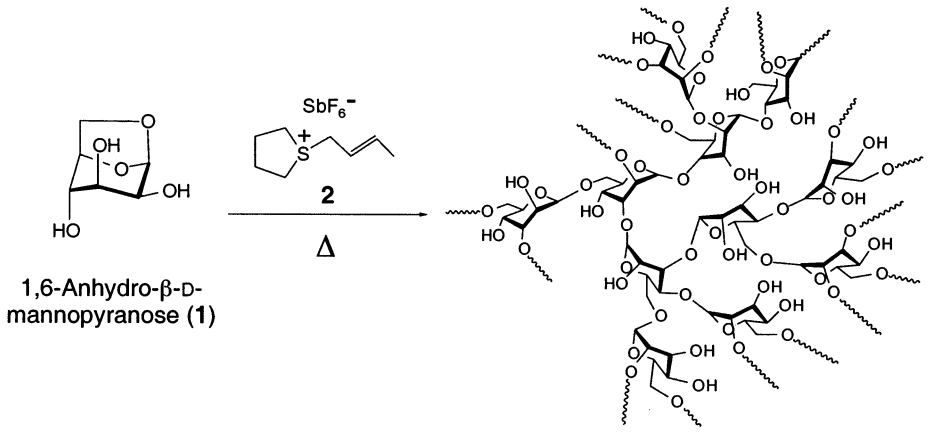
Scheme 1



Kogyo K.K., and used without further purification. 1,6-Anhydro-β-D-mannopyranose (**1**) was synthesized from D-(+)-mannose using a procedure similar to that reported by Fraser-Reid.[45] **1** was recrystallized twice from dry methanol and dried in a vacuum oven at 50 °C for 2 days. The synthesis of (1→6)-α-D-mannopyranan (**4**) was reported in a previous article.[46] The $M_{w,SLS}$ value of **4** was 11000.

Measurements. The ^{1}H and ^{13}C NMR spectra were recorded using a JEOL JNM-A400II instrument. The quantitative ^{13}C NMR spectra were obtained using a 20% (w/v) sample in deuterium oxide (D_2O) at 25 °C and 45° pulse angle, with 3-(trimethylsilyl)propyonic-2,2,3,3-d_4 acid sodium salt as the internal reference. Size exclusion chromatography (SEC) was performed at 40 °C in aqueous sodium nitrate ($NaNO_3$) solution (0.2 mol·L^{-1}) using a TOSOH HPLC system equipped with two TOSOH TSK gel GMPW$_{XL}$ columns. The weight-average molecular weight ($M_{w,SEC}$) and the molecular weight distribution ($M_{w,SEC}$ /$M_{n,SEC}$) of the polymer samples were calculated on the basis of poly(ethylene glycol) calibration. A static laser light scattering (SLS) measurement was performed in aqueous $NaNO_3$ solution (0.2 mol·L^{-1}) at 23 °C using an Otsuka Electronics DLS-7000 light scattering spectrometer (λ = 632.8 nm). The refractive index increment (dn/dc) was 0.1291, which was measured in aqueous $NaNO_3$ solution (0.2 mol·L^{-1}) at 23 °C using an Otsuka Electronics DRM-1021 double-beam differential refractometer (λ = 632.8 nm). The intrinsic viscosity ([η]) was determined in aqueous $NaNO_3$ solution (0.2 mol·L^{-1}) at 23 °C using a Canon-Fenske viscometer. The specific rotation was measured using a Jasco DIP-1000 digital polarimeter.

Thermally Induced Cationic Polymerization. To a solution of **1** (2.15 g, 13.3 mmol) in anhydrous propylene carbonate (4.3 mL) at 130 °C was added 2-butenyltetramethylenesulfonium hexafluoroantimonate in propylene carbonate solution (9.4 μL, 3.76 × 10^{-2} mmol) using a microsyringe under a nitrogen atmosphere. After 20 min, the reaction mixture was poured into a large amount of methanol. The residue was purified by reprecipitation with water and methanol to obtain the polymer in 56.6% yield. The $M_{w,SEC}$ and $M_{w,SEC}$ /$M_{n,SEC}$ values were 2170 and 1.30, respectively, and the $M_{w,SLS}$ value was 3.42 × 10^4. [α]$_D$ +50.2° (c 1.0, H_2O, 23 °C). ^{1}H NMR (400 MHz, D_2O): δ (ppm) 5.64−5.57 (m), 5.42 (unopened ring C-1), 5.25−4.72 (C-1, m), 4.62 (unopened ring C-5), and 4.23−3.35 ppm (C-2, C-3, C-4, C-5, C-6, m). ^{13}C NMR (100 MHz, D_2O): δ (ppm) 107.91 (C-1, mannofuranosyl unit), 102.91−100.04 (C-1, m), 79.83 (α,β-C-4, mannofuranosyl terminal unit), 76.88 (β-C-5, mannopyranosyl terminal unit), 73.95, (α-C-3, mannopyranosyl terminal unit), 73.35 (α-C-5, mannopyranosyl terminal unit), 71.21 (α-C-3, mannopyranosyl terminal unit), 70.99 (β-C-2, mannopyranosyl terminal unit), 70.63 (α-C-2, mannopyranosyl terminal unit), 67.40 (α,β-C-4, mannopyranosyl terminal unit), 66.78−66.68 (CH, m), 66.23−65.48 (CH_2, m), 63.67 (α,β-C-6 mannofuranosyl terminal unit), and 61.61 ppm (α,β-C-6, mannopyranosyl terminal unit).

Methylation Analysis. Methylation of the polysaccharide was carried out according to the method described by Tomoda et al.[47] The methylated polysaccharide was converted to partially methylated D-mannitol acetates (PMMA) as described by Kennedy et al.[48] The samples were analyzed by gas chromatography (GC) using a Shimadzu GC-17A chromatograph equipped with a BPX 70 capillary column (70% bis-(cyanopropyl)poly(silphenylenesiloxane), 30 m × 0.25 mm, 0.25 μm film thickness, SGE) and a flame-ionization detector. The oven was heated at 190 °C as the initial temperature, heated at a rate of 1.0 °C/min to a final temperature of 250 °C, and maintained for 10 min. The injection and detector temperatures were 260 °C. The PMMA was identified by gas chromatography and mass spectrometry (GC−MS) analyses using a JEOL JMS-AX-500 equipped with a BPX 70 capillary column and electron-impact ionization at 70 eV (GC−MS & NMR Laboratory, Graduate School of Agriculture, Hokkaido University), and also by their retention times relative to *myo*-inositol hexaacetate as described by Bacic et al.[49] For the quantitative PMMA analysis using GC, the relative molar response factors were estimated from theoretical calculations.[50] The calculated response factors were 0.70 for di-*O*-acetyl-tetra-*O*-methyl-D-mannitol, 0.74 for 1,2,5-, 1,3,5- and 1,4,5-tri-*O*-acetyl-tri-*O*-methyl-D-mannitol, 0.75 for 1,5,6- and 1,4,6-tri-*O*-acetyl-tri-*O*-methyl-D-mannitol, 0.79 for 1,2,3,5-, 1,3,4,5-, and 1,2,4,5-tetra-*O*-acetyl-di-*O*-methyl-D-mannitol, 0.80 for 1,2,5,6-, 1,3,5,6-, and 1,4,5,6-tetra-*O*-acetyl-di-*O*-methyl-D-mannitol, 0.84 for penta-*O*-acetyl-*O*-methyl-D-mannitol, and 0.89 for hexa-*O*-acetyl-D-mannitol.

Degree of Branching. The degree of branching (DB) of the polysaccharide prepared from a latent cyclic AB_4-type monomer **1** was calculated from the number of terminal units (T), linear units (L), semidendritic units (sD_1 and sD_2), and dendritic units (D), by Frey's equation (eq 1).[51]

$$DB = \frac{3D + 2\,sD_2 + sD_1}{0.75\,(4D + 3\,sD_2 + 2sD_1 + L)} \qquad (1)$$

The numbers of each unit were determined by the methylation analysis of the polysaccharide and the correction with molar response factors.[50]

Results and Discussion

Polymerization. Schuerch et al. and other groups have reported the synthesis of highly branched polysaccharides prepared from the 1,6-anhydrohexopyranoses using monochloroacetic acid.[35−41] This solid phase polymerization, however, has the disadvantage of the heterogeneous initiation reaction, which may lead to a broad polydispersity. To improve the problem, we chose the solution and melt polymerizations using a thermally induced cationic initiator. The ring-opening polymeri-

Table 1. Thermally Induced Cationic Polymerization of 1,6-Anhydro-β-D-mannopyranose (1) Using 2-Butenyltetramethylenesulfonium Hexafluoroantimonate (2)[a]

run no.	[**1**] (mol·L^{-1})	[**1**]/[**2**]	time (min)	temp (°C)	yield[b] (%)	$M_{w,SEC} \times 10^{-3}$ [c] ($M_{w,SEC}/M_{n,SEC}$)	$M_{w,SLS} \times 10^{-3}$	$[\alpha]_D$[d]
1	1.6	350	20	130	18.8	1.56 (1.22)	6.5	+49.9
2	3.2	350	20	130	56.6	2.17 (1.30)	34.2	+50.2
3	6.4	350	20	130	61.6	3.20 (1.35)	80.5	+64.7
4	6.4	700	40	130	57.0	2.48 (1.31)	69.4	+50.3
5	6.4	700	20	150	61.1	4.30 (1.49)	96.3	+65.3
6	6.4	700	40	150	63.0	10.50 (1.43)	637	+64.4
7	melt	350	<1	210	23.8	5.84 (1.84)	80.9	+51.9

[a] Solvent, propylene carbonate. [b] Water-soluble but methanol-insoluble parts. [c] Determined by size exclusion chromatography (SEC) in aqueous $NaNO_3$ solution (0.2 mol·L^{-1}) using poly(ethylene glycol) as standards. [d] Measured in H_2O at 23 °C (*c* 1.0).

zation of 1,6-anhydro-β-D-mannopyranose (**1**) was carried out using 2-butenyltetramethylenesulfonium hexafluoroantimonate (**2**) as a thermally induced cationic initiator at temperatures in the range 130−210 °C. Table 1 summarizes the results of the polymerization. When propylene carbonate was used as the solvent, the polymerization homogeneously proceeded for 5 min, and then the reaction system gradually became heterogeneous as the reaction proceeded. The polymeric products were isolated by precipitation using water and methanol. The resulting polysaccharide was a gel-free white solid that was completely soluble in water and dimethyl sulfoxide, slightly soluble in pyridine and 1,3-dimethyl-2-imidazolidinone, and insoluble in toluene, chloroform, acetone, and methanol.

For the solution polymerization of **1** in propylene carbonate, the weight-average molecular weights ($M_{w,SEC}$) measured by size exclusion chromatography (SEC) and the yields of the resulting polysaccharide (**3**) gradually increased with the increasing monomer concentration [**1**], i.e., when the [**1**]/[**2**] molar ratio of 350 was used at 130 °C for 20 min, the $M_{w,SEC}$s were 1.56×10^3 in 18.8% yield for 1.6 mol·L^{-1} of [**1**] (run 1), 2.17×10^3 in 56.6% yield for 3.2 mol·L^{-1} (run 2), and 3.20×10^3 in 61.6% yield for 6.4 mol·L^{-1} (run 3). The $M_{w,SEC}$s and the yields of **3** also increased with the rising polymerization temperature, i.e., when the [**1**] of 6.4 mol·L^{-1} and the [**1**]/[**2**] molar ratio of 700 were used for 40 min at 150 °C, **3** having the highest $M_{w,SEC}$ (1.05×10^4) was obtained in 63.0% yield (run 6), while the $M_{w,SEC}$ of 2.48×10^3 in 57.0% yield at 130 °C (run 4) was obtained. The extension of the polymerization time also led to an increase in the $M_{w,SEC}$ and the yield, as the comparison between runs 5 and 6. The polydispersities ($M_{w,SEC}/M_{n,SEC}$) for the solution polymerization were found to be relatively narrow values in the range of 1.22 to 1.49 and increased with the increasing monomer conversion. The melt polymerization using **2** at 210 °C immediately occurred to produce a brown cake, and the precipitated polysaccharide was a light brown solid with a $M_{w,SEC}$ of 5.84×10^3 in 23.8% yield (run 7). The $M_{w,SEC}/M_{n,SEC}$ was broader than those from the solution polymerizations in propylene carbonate.

In general, highly branched polymers, such as dendrimers, star polymers, and hyperbranched polymers, are known to have spherical conformations in a solution, and the $M_{w,SEC}$s of these polymers were often claimed to be too low because the hydrodynamic volumes of these polymers are smaller than the corresponding linear polymers used for the calibration. The weight-average molecular weight ($M_{w,SLS}$) of **3**, therefore, was also measured by the static laser light scattering (SLS) method in aqueous $NaNO_3$ solution (0.2 mol·L^{-1}). The $M_{w,SLS}$s of **3** ranged from 6.5×10^3 to 6.4×10^5, which were 4.2−60.7 times as many as the $M_{w,SEC}$s. These results suggest that **3** has a more compact form in solution when compared to the linear polymer.

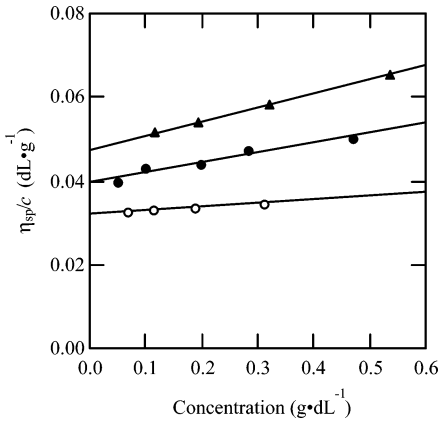


Figure 1. Viscosity-concentration plots for **3** in aqueous $NaNO_3$ solution (0.2 mol·L^{-1}) at 23 °C. Intrinsic viscosities [η]: 0.032 dL·g^{-1} for run 1, 0.040 dL·g^{-1} for run 3, and 0.047 dL·g^{-1} for run 6.

In the viscosity measurement of **3** in aqueous $NaNO_3$ solution (0.2 mol·L^{-1}), a linear dependence between the reduced viscosity and the concentration was observed in the polymer concentration range for the SLS measurement, as shown in Figure 1, meaning that no aggregation occurred, and therefore, the measured $M_{w,SLS}$ corresponded to the absolute molecular weight of the polysaccharide. The solution viscosity of **3** was very low; i.e., the intrinsic viscosities were in the range of 0.032 to 0.047 dL·g^{-1}. On the other hand, the intrinsic viscosities for the linear polymers of (1→6)-α-D-mannopyranan with the viscosity-average molecular weights of 53700 and 81200 were 0.31 and 0.41 dL·g^{-1}, respectively.[52] Therefore, these results of the SEC, SLS, and viscosity measurements suggested that **3** was a highly branched spherical molecule, i.e., hyperbranched polysaccharide.

Polymer Structure. To investigate the polymer structure, the ^{13}C NMR spectrum of polysaccharide **3** (run 2) was compared with that of the stereoregular (1→6)-α-D-mannopyranan (**4**), which was synthesized by the cationic polymerization of 1,6-anhydro-2,3,4-tri-*O*-allyl-β-D-mannopyranose using BF_3·OEt_2 and the following deallylation,[46] as shown in Figure 2. There was a distinct difference between the two spectra. For the spectrum of **4**, the six signals due to the α-D-mannopyranosyl units were observed and the signals at 100.13, 71.65, 71.47, 70.78, 67.40, and 66.30 ppm were assigned to the carbons at C-1, C-5, C-2, C-3, C-4, and C-6, respectively. On the other hand, the spectrum of **3** consisted of a number of split and broad peaks, though some peaks corresponded to those for **4**. The peaks in

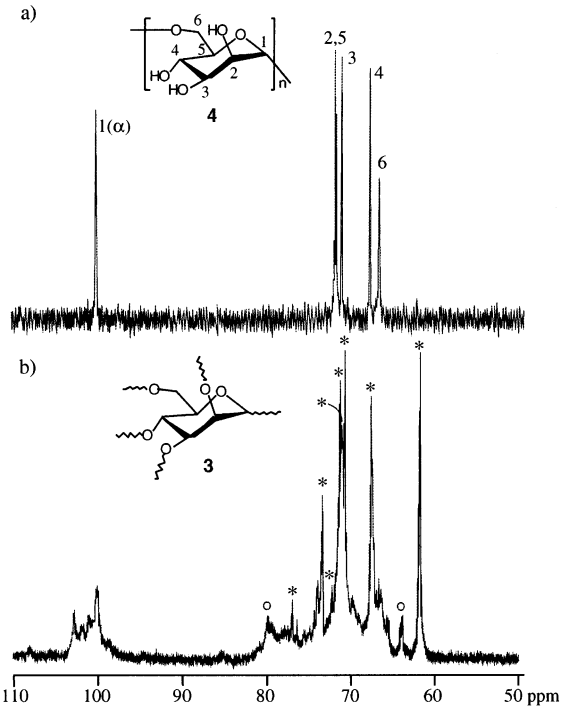
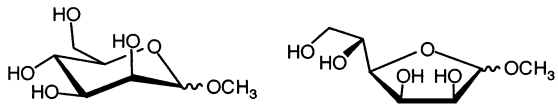


Figure 2. ^{13}C NMR spectra of (a) (1→6)-α-D-mannopyranan **4** and (b) polysaccharide **3** (run 2) prepared from **1**.

Figure 2b should be caused by the different sequences of the D-mannopyranosyl units, such as (1→2)-, (1→3)-, (1→4)-, and (1→6)-linkages, and so on. The major signals for **3**, which are asterisked in Figure 2b, fairly agreed with the chemical shifts of the carbons for methyl α-D-mannopyranoside (**5a**) and methyl *β*-D-mannopyranoside (**5b**), corresponding to the model compounds of terminal units in **3** (Chart 1).[53] These results indicated that **3** was a highly branched polymer having numerous nonreducing D-mannopyranosyl terminal units, which was a characteristic of a hyperbranched polymer. In addition, the ^{13}C NMR spectrum of **3** exhibited the presence of the D-mannofuranosyl units, as shown by

Chart 1



5a : α-form
5b : β-form

6a : α-form
6b : β-form

the open circle in Figure 2b; i.e., the peaks at 79.83 and 63.67 ppm fairly agreed with the chemical shifts of the C-4 and C-6 carbons for methyl α-D-mannofuranoside (**6a**) and methyl *β*-D-mannofuranoside (**6b**).[54] Therefore, these peaks should be assigned to the carbons of the nonreducing D-mannofuranosyl terminal units.

Previously, Goldstein et al. reported that the D-mannofuranosyl units were formed in a D-mannan by the polymerization of **1** using monochloroacetic acid.[40] The ratio of the mannopyranosyl terminal units to the mannofuranosyl ones in **3**, which was calculated using quantitative ^{13}C NMR measurements, varied with the monomer conversion and the molecular weight, as summarized in Table 2, i.e., 99.7 mol % of the mannopyranosyl terminal unit and 0.3 mol % of mannofuranosyl terminal unit for run 1 and 88.1 mol % and 11.9 mol % for run 6, respectively. The split and broad peaks at 96−105 ppm due to the C-1 carbons also indicated the presence of both α- and *β*-D-linkages in **3**, though the main peaks at 100 ppm were assigned to the (1→6)-α-D-linked C-1 carbons, as shown in the spectrum of **4**. Although the peaks at 5.42 and 4.62 ppm in the ^{1}H NMR spectrum of **3** indicated the presence of the 1,6-anhydro-*β*-D-mannopyranosyl end unit, the amount of the 1,6-anhydro units in the hyperbranched polysaccharide should be less than 1 mol %.

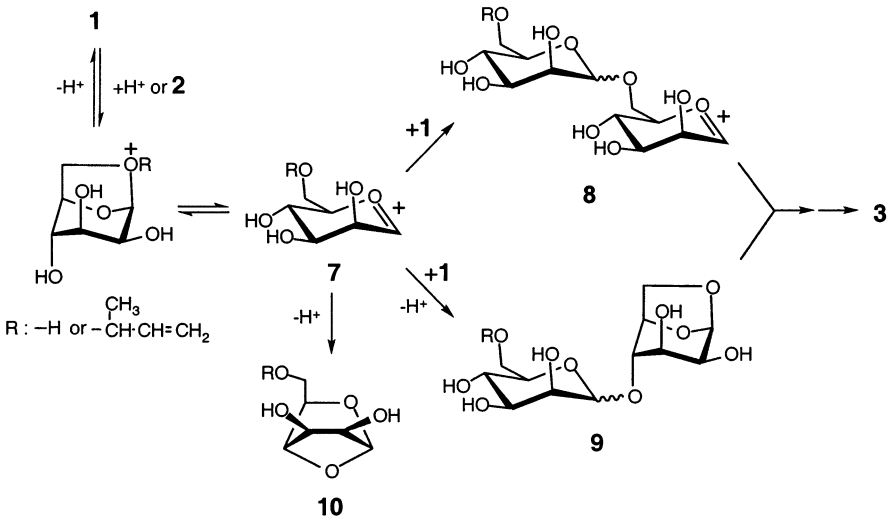
The specific rotations ($[\alpha]_D$, H_2O) of **3** were found in the range of +49.9 to +64.7°, which should be influenced by the difference in the sequences, the ratio of the α- to *β*-D-linkages between the sugar units, the ratio of the D-mannopyranosyl to D-mannofuranosyl units, and so on.

Table 2. Linkage Analysis of a Polysaccharide (3) Obtained by Thermally Induced Cationic Polymerization of 1,6-Anhydro-*β*-D-mannopyranose (1) Using 2-Butenyltetramethylenesulfonium Hexafluoroantimonate (2)[a]

unit	D-mannitol acetate[b]	type of linkage[c]	run 1	run 2	run 3	run 4	run 5	run 6	run 7
T	2,3,4,6- and 2,3,5,6-*O*-Me_4	T-*p* and T-*f*	26.8	28.9	29.1	28.2	30.4	31.5	36.2
		T-*p*/T-*f* [d]	99.7/0.3	94.3/5.7	93.0/7.0	92.4/7.6	90.6/9.4	88.1/11.9	88.0/12.0
L	2,4,6- and 3,4,6-*O*-Me_3	(1−2) and (1−3)-*p*	7.2	8.2	8.9	9.1	7.3	8.8	9.3
	2,3,6-*O*-Me_3	(1−4)-*p* and (1−5)-*f*	4.0	5.2	4.9	5.2	5.5	5.0	7.1
	2,3,4-*O*-Me_3	(1−6)-*p*	38.2	30.3	29.1	30.9	29.4	26.5	20.6
	2,3,5-*O*-Me_3	(1−6)-*f*	0.5	0.6	0.5	0.3	0.5	1.0	2.2
	total		50.0	44.3	43.4	45.5	42.6	41.3	39.2
sD_1	4,6-*O*-Me_2	(1−2−3)-*p*	<0.1	<0.1	0.9	0.3	0.7	0.8	1.1
	2,6-*O*-Me_2	(1−3−4)-*p*	<0.1	<0.1	0.7	0.3	0.6	0.8	1.2
	3,6-*O*-Me_2	(1−2−4)-*p*	0.7	0.8	1.0	0.4	1.2	0.9	0.9
	2,3-*O*-Me_2	(1−4−6)-*p*	6.0	6.5	6.4	5.9	6.6	6.4	6.5
	2,4-*O*-Me_2	(1−3−6)-*p*	4.4	6.1	5.8	5.4	5.0	5.0	4.6
	3,4-*O*-Me_2	(1−2−6)-*p*	6.5	7.7	7.0	8.2	7.4	6.8	4.8
	total		17.6	21.1	21.8	20.5	21.6	20.9	19.1
sD_2	6-*O*-Me	(1−2−3−4)-*p*	-	-	0.1	-	-	0.4	0.3
	2-*O*-Me	(1−3−4−6)-*p*	1.2	0.9	1.4	0.8	1.1	1.2	1.1
	3-*O*-Me	(1−2−3−6) and (1−2−4−6)-*p*	4.1	4.3	3.6	4.4	3.7	4.0	3.4
	total		5.3	5.2	5.1	5.3	4.8	5.6	4.8
D	hexaacetates	(1−2−3−4−6)-*p*	0.4	0.4	0.7	0.4	0.6	0.7	0.8
	degree of branching[e]		0.38	0.42	0.43	0.41	0.43	0.44	0.44

[a] Estimated by the methylation analysis of polysaccharide and the correction by molar response-factors.[50] The values were normalized by mol %. [b] 2,3,5,6-*O*-Me_4 means 1,4-di-*O*-acetyl-2,3,5,6-tetra-*O*-methyl-D-mannitol, etc. [c] T-*p* and T-*f* mean a nonreducing terminal D-mannopyranosyl and a D-mannofuranosyl residue, respectively. (1−4)-*p* and (1−5)-*f* mean a (1→4)-linked D-mannopyranosyl and a (1→5)-linked mannofuranosyl residue, respectively, etc. [d] Estimated by quantitative ^{13}C NMR measurement (mol %:mol %). [e] Calculated by Frey's equation (eq 1).[45]

Scheme 2



To confirm the branching and linkage manner of the D-mannosyl units, the methylation analysis of **3** was carried out according to a reported method.[47−49] These results are summarized in Table 2. Fifteen different peaks corresponding to the 19 repeating units were detected and classified into five categories of terminal units (T), linear units (L), two semi-dendritic units with three and four linkages (sD_1 and sD_2, respectively), and perfect dendritic units (D) with five linkages (Chart 2). The main components were terminal units and (1→6)-linked D-mannopyranosyl units, and the terminal units increased and the (1→6)-linked units decreased with the increasing molecular weight of **3**. For run 6, the T unit was 31.5 mol %, the L unit 41.3 mol %, the sD_1 unit 20.9 mol %, the sD_2 unit 5.6 mol %, and the D unit 0.7 mol %. The results of the methylation analysis showed that the reaction with the C-6 position was apparently favored. For the solution polymerization, the C-2 hydroxyl groups was more reactive than the C-3 and C-4 hydroxyl groups, i.e., the reactivity increased in the order C-6 ≫ C-2 > C-4 > C-3, while C-6 ≫ C-4 > C-2 = C-3 for the melt polymerization.

Polymerization Mechanism. Hyperbranched polysaccharides **3** consist of 19 kinds of α- and β-D-linked mannopyranosyl and mannofuranosyl repeating units. The mechanism for the thermally induced cationic polymerization, therefore, should proceed through the mechanism for the acid-catalyzed polymerization of 1,6-anhydro-β-D-glucopyranose proposed by Seib et al.,[41] as shown in Scheme 2. In the polymerization system, **1** was rapidly protonated at the 1,6-ether oxygen atom and the protonated **1** underwent the ring-opening to afford the carbonium−oxonium ion (**7**). When **7** reacted with the 1,6-ether oxygen atom of a second monomer, two kinds of α- and β-D-linked disaccharides (**8**) were formed. The process produced a terminal unit and a (1→6)-linkage. On the contrary, when **7** reacted with the hydroxyl group of another monomer, a disaccharide monomer (**9**) with a terminal residue and a (1→2)-, (1→3)-, or (1→4)-linkage was obtained along with the regeneration of a proton. A branched structure was obtained by the reaction of **7** (or **8**) with a hydroxyl group of the resulting oligo- and polysaccharides. Because the results of the NMR spectroscopic measurement and the methylation analysis indicated the presence of D-mannofuranosyl units, a portion of **7** was probably converted to a 1,4-anhydro-α-D-mannofuranose derivative (**10**), as shown in Scheme 2. These reactions mentioned above simultaneously occurred in the polymerization systems and consequently produced the hyperbranched polysaccharide **3**.

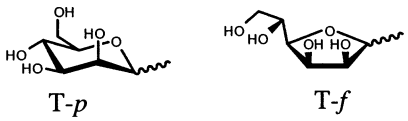
Degree of Branching. For determining the degree of branching (DB) for a hyperbranched polymer, we assumed **1** as a latent AB_4-type monomer, which has one anhydro moiety capable of ring-opening and three hydroxyl groups, even though the reactivity of their hydroxyl groups was expected to be different for each other. The DB of **3**, therefore, can be calculated from the numbers of T, L, sD_1, sD_2, and D units using eq 1 reported by Frey et al.[51] Table 2 summarizes the calculated DB values, where the DB values of 0 and 1 mean a linear polymer and a dendrimer, respectively. Assuming that the B groups has the same reactivity leading to the random polycondensation reaction, the DB value for the polymerization of the AB_4-type monomers is 0.42. For the thermally induced cationic polymerization of **1**, the DB values were in the range 0.38 to 0.44, which were approximately consistent with the theoretical value of 0.42 for the AB_4-type monomer.[51] The low DB value of **3** (run 1) should be due to its low molecular weight. As a result, the thermally induced cationic polymerization of **1** with **2** is a facile method leading to a hyperbranched polysaccharide with a high DB value.

Conclusions

The thermally induced cationic polymerization of 1,6-anhydro-β-D-mannopyranose (**1**) using 2-butenyltetramethylenesulfonium hexafluoroantimonate (**2**) proceeded without gelation to produce a water-soluble hyperbranched polysaccharide (**3**) with a high degree of branching. For the polymerization using propylene carbonate as the solvent, the weight-average molecular weights of **3** can be controlled by the polymerization conditions, such as the ratio of monomer to initiator, the monomer concentration, the polymerization time, and the temperature. The results of the SEC, SLS, and viscosity measurements indicated that **3** was a highly branched spherical macromolecule, i.e., a hyperbranched polysaccharide. The DB values determined by the methylation analysis of **3** were in the range of 0.38 to 0.44, which were approximately consistent with the value of 0.42 expected for the random polymerization of a AB_4-

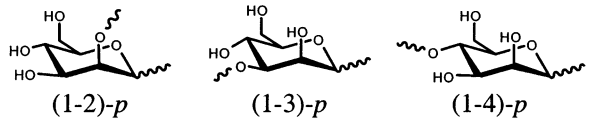
Chart 2

Terminal units (T)

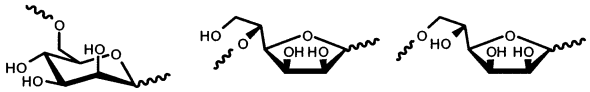


T-*p* T-*f*

Linear units (L)

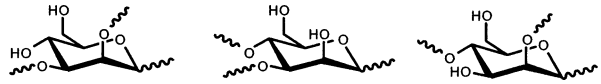


(1-2)-*p* (1-3)-*p* (1-4)-*p*

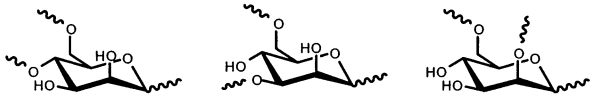


(1-6)-*p* (1-5)-*f* (1-6)-*f*

Semi-dendritic units with three linkages (sD_1)

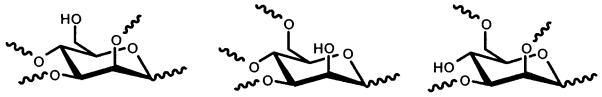


(1-2-3)-*p* (1-3-4)-*p* (1-2-4)-*p*



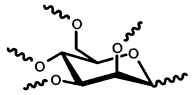
(1-4-6)-*p* (1-3-6)-*p* (1-2-6)-*p*

Semi-dendritic units with four linkages (sD_2)

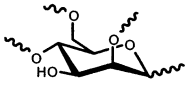


(1-2-3-4)-*p* (1-3-4-6)-*p* (1-2-3-6)-*p*

Perfect dendritic unit (D)



(1-2-3-4-6)-*p*



(1-2-4-6)-*p*

type monomer. Polymerization is a useful method for preparing a hyperbranched polysaccharide having numerous nonreducing D-mannopyranosyl terminal units, which can be expected for use in medical and medicinal applications.

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(53) **5a**. ^{13}C NMR (100 MHz, D_2O): δ (ppm) 101.51 (C-1), 73.20 (C-5), 71.20, (C-3), 70.57 (C-2), 67.42 (C-4), 61.61 (C-6), and 55.36 (−OMe). **5b**. ^{13}C NMR (100 MHz, D_2O): δ (ppm) 101.54 (C-1), 76.78 (C-5), 73.49, (C-3), 70.81 (C-2), 67.41 (C-4), 61.61 (C-6), and 57.34 (−OMe).
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