Substituent Effect on Ring-Opening Polymerization of Regioselectively Acylated α-D-Glucopyranose 1,2,4-Orthopivalate Derivatives

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ABSTRACT: To investigate the substituent effects at the 3-*O* and 6-*O* positions on ring-opening polymerization, 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**1**), 3-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**2**), 6-*O*-benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**3**), and 3,6-di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**4**) were selected as starting monomers and were polymerized under various reaction conditions. It was concluded from the results of monomer **1** reported previously and from those of monomers **2**−**4** in our present study that the benzyl group at the 3-*O* position is indispensable for yielding stereoregular (1→4)-*β*-D-glucopyranan derivatives, *i.e.*, cellulose derivatives. The mechanisms of ring-opening polymerizations are discussed.

Introduction

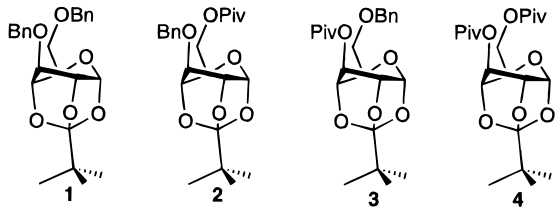
The selection of the best combination of protective groups is extremely important for a highly stereoselective glycosylation in high yield.[1−3] We have investigated the substituent effect on *β*-glycosylation in the synthesis of cellooligosaccharide by a stepwise method[1−3] and stereoregular polysaccharide by ring-opening polymerization.[4−6] As the results of our experiments from the synthesis of cellooligosaccharides, both 3-*O*-benzyl and 2-*O*-pivaloyl groups are indispensable for the synthesis of highly stereoselective *β*-glucoside in high yield, and we succeeded in the first synthesis of a celloeicosaose derivative.[3] Furthermore, this basic idea on the substituent effect has been applied to the first synthesis of stereoregular (1→5)-*β*-D-glucofuranan by the ring-opening polymerization of 1,4-anhydroglucose derivatives[5,6] and also the first chemical synthesis of cellulose by ring-opening polymerization of a glucose 1,2,4-orthopivalate derivative using 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate as a starting monomer.[4]

Here, we describe substituent effects on ring-opening polymerizations of regioselectively acylated α-D-glucopyranose 1,2,4-orthopivalate derivatives in detail.

Results and Discussion

Syntheses of α-D-Glucopyranose 1,2,4-Orthopivalate Derivatives. In order to systematically study the effect of acyl groups on ring-opening polymerization of α-D-glucopyranose 1,2,4-orthopivalate derivatives, three α-D-glucopyranose 1,2,4-orthopivalate derivatives, 3-*O*-benzyl-6-*O*-pivaloyl- (**2**), 6-*O*-benzyl-3-*O*-pivaloyl- (**3**), and 3,6-di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**4**), were newly selected in addition to 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**1**) whose polymerization has been reported.[4]

A synthetic method for α-D-glucopyranose 1,2,4-orthoacetate has been found by a previous investigation of Bochkov *et al.*:[7] 1-halogenized D-glucopyranose peracetate was converted to 1,2-methylorthoacetyl-3,4,6-tri-*O*-acetyl-α-D-glucopyranose, which was then deacetylated, orthoesterified, and finally acetylated to give a 3,6-di-*O*-acetyl-α-D-glucopyranose 1,2,4-orthoacetate. However, the above synthetic method applied to glucose[7] and xylose,[8] particularly the final step in the synthetic route, may not be applied to the syntheses of **2** and **3** because selective protection of the C_3- or C_6-positions would be difficult.



Our newly developed orthoesterification method using *N*,*N*′-carbonyldiimidazole seems to be quite useful for the synthesis of a series of orthoester derivatives.

Four glucose orthopivalate derivatives **1**−**4** were prepared by the synthetic routes shown in Scheme 1.

3,6-Di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**1**) was afforded from 3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (**5**)[9] in a 62.8% yield as described in our previous paper.[4] Glucose orthopivalate derivatives **2** and **3** were prepared from 3-*O*-benzyl-2,6-di-*O*-pivaloyl-α-D-glucopyranose (**6**)[6] in a 57.6% yield and from 6-*O*-benzyl-2,3-di-*O*-pivaloyl-α-D-glucopyranose (**7**)[6] in a 35.1% yield, respectively. 3,6-Di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**4**) was prepared from 4,6-*O*-benzylidene-1,2,3-tri-*O*-pivaloyl-*β*-D-glucopyranose (**8**)[6] by four reaction steps: debenzylidenation with *p*-TsOH, selective 6-*O*-pivaloylation with pivaloyl chloride and pyridine, selective 1-*O*-depivaloylation with hydrazine hydrate, and orthoesterification with *N*,*N*′-carbonyldiimidazole.

^{1}H-NMR Chemical Shifts of α-D-Glucopyranose 1,2,4-Orthopivalate Derivatives. The assignments of proton peaks are summarized in Table 1. C_4-proton resonances of 3-*O*-pivaloyl derivatives **3** and **4** are shifted to a low magnetic field (*δ* 5.08 and 5.12 ppm, respectively) compared with those of the 3-*O*-benzyl derivatives **1** and **2** (*δ* 3.95 and 3.95 ppm, respectively), although C_3-proton resonances of the 3-*O*-pivaloyl derivatives are little shifted. The reason for the difference of these chemical shifts is obscure, but it is predicted that the electron density of a C_4-oxygen of the 3-*O*-pivaloyl derivatives **3** and **4** becomes lower than those

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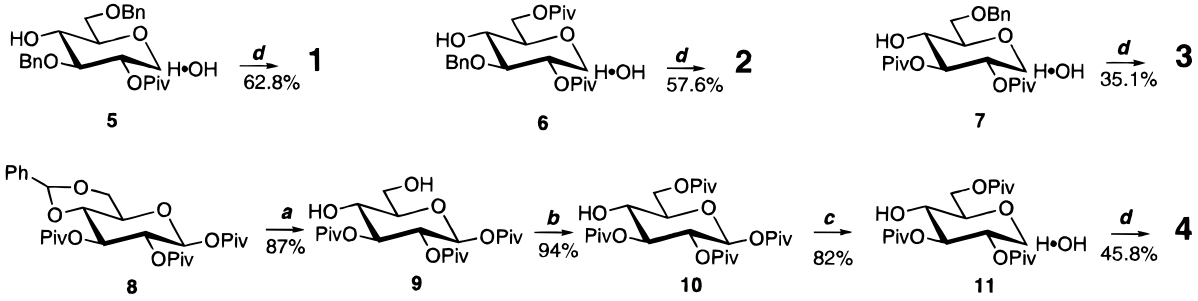
Scheme 1. Syntheses of Orthoester Derivatives



[a] p-TsOH / MeOH / r.t. / 2h, [b] PivCl / pyridine / r.t. / 1h, [c] $NH_2NH_2•H_2O$ / THF / r.t. / 8h, [d] *N,N'*-carbonyldiimidazole / reflux

Table 1. ^{1}H-NMR Chemical Shifts of α-D-Glucopyranose 1,2,4-Orthopivalate Derivatives

monomer no.	δ (ppm)									
	C_1−H	C_2−H	C_3−H	C_4−H	C_5−H	C_6−H		R_2	R_3	R_6
1	5.79	4.42	4.31	3.95	4.60	3.83	3.75	Piv	Bn	Bn
2	5.76	4.39−4.43	4.16	3.95	4.45−4.52	4.31−4.41		Piv	Bn	Piv
3	5.73	4.38	4.31	5.08	4.62	3.61	3.72	Piv	Piv	Bn
4	5.75	4.43	4.25	5.12	4.56	4.38	4.21	Piv	Piv	Piv

Table 2. Polymerizations of α-D-Glucopyranose 1,2,4-Orthopivalate Derivatives[a]

exp no.	monomer	initiator	temp, °C	time, h	yield, %	$[\alpha]^{26}_D$, deg	$10^{-3}M_{GPC}$	$\overline{DP}_n$
1	**1**	Ph_3CBF_4	−30	16	50	−20.1	2.9	6.9
2	**1**	Ph_3CBF_4	0	18	96	−32.9	3.8	8.9
3	**1**	Ph_3CBF_4	20	14	93	−35.2	4.5	10.5
4	**2**	Ph_3CBF_4	−30	96	21	−1.4	4.1	9.7
5	**2**	Ph_3CBF_4	0	22	51	−3.7	4.9	11.6
6	**2**	Ph_3CBF_4	20	2	60	+1.9	3.2	7.5
7	**3**	Ph_3CBF_4	−30	96	33	−26.8	2.9	6.9
8	**3**	Ph_3CBF_4	0	49	47	−12.6	3.7	8.8
9	**3**	Ph_3CBF_4	20	15	58	−18.8	3.0	7.1
10[b]	**4**	Ph_3CBF_4	−30	97	trace			
11[b]	**4**	Ph_3CBF_4	0	96	trace			
12[b]	**4**	Ph_3CBF_4	20	17	17	−24.8	1.4	3.5

[a] Initiator concentration, 5 mol %; solvent, CH_2Cl_2; monomer/solvent, 50 g/100 mL. [b] Monomer/solvent, 25 g/100 mL.

of the 3-*O*-benzyl derivatives **1** and **2**, owing to the electron-withdrawing effect of the 3-*O*-pivaloyl group. A relationship between these ^{1}H-NMR chemical shifts and the structure of polysaccharides yielded is mentioned in a later section.

Polymerization of Glucose Orthoester Derivatives. The results of polymerizations are summarized in Table 2. In our previous experiment, polymerization using Ph_3CBF_4 and dichloromethane was best among all polymerization conditions tried.[4] Therefore, in order to compare the polymerizability among the four monomers, all polymerizations were carried out under Ph_3CBF_4 as an initiator, the same initiator concentration (5 mol %), and the same monomer concentration (50 g/100 mL) except for those of monomer **4**. Monomer **4** was difficult to dissolve at the same monomer concentration, because monomer **4** has a poor solubility in dichloromethane. Thus, monomer **4** was dissolved in a lower monomer concentration (25 g/100 mL).

Polymerizations of **1**−**3** gave polysaccharides with almost the same degrees of polymerization ($\overline{DP}_n$). Number-averaged molecular weights of poly(**1**)s, poly(**2**)s, and poly(**3**)s, determined by gel permeation chromatography using polystyrene standards, ranged from 2.9×10^3 to 4.9×10^3. However, the polymerizability of **4** was extremely low among the four monomers: when compound **4** was polymerized at 20 °C, unreacted monomer remained in a reaction ampule (approximately over 70%); other monomers, **1**−**3**, did not remain under the reaction conditions. Polymerization of **4** only afforded an oligosaccharide in low yield.

We have already reported that all poly(**1**) were levorotatory and an absolute value of $[\alpha]_D$ of stereoregular poly(**1**) gradually increases with an increase of molecular weight.[4] Poly(**2**)s tend to have a specific rotation of almost 0°. These results coincide with the data of cellooligosaccharides having the same protective group system (benzyl group at the 3-*O* position and pivaloyl groups at the 2-*O* and 6-*O* positions).[3] Furthermore, poly(**2**)s were found to have a stereoregular structure by the ^{13}C-NMR analysis. On the other hand, poly(**3**)s have a nonstereoregular structure, although poly(**3**) has a relatively high negative specific rotation, between *ca.* −12° and −27°.

Structural Determination of Polysaccharides. In general, there are four possible structural units in the poly(D-glucose) prepared by ring-opening polymerization of tricyclic α-D-glucopyranose 1,2,4-orthoester derivatives, namely, the (1→4)-*β*- and (1→4)-α-D-glucopyranosidic ((1→4)-*β*-P and (1→4)-α-P) units and the (1→2)-*β*- and (1→2)-α-D-glucopyranosidic ((1→2)-*β*-P and (1→2)-α-P) units.

We have already reported that polymerization of **1** gave a stereoregular (1→4)-*β*-D-glucopyranan derivative which had a single anomeric peak at 99.6 ppm in the ^{13}C-NMR spectrum.[4]

On the other hand, the ^{13}C-NMR spectrum in Figure 1A of poly(**2**) having $[\alpha]^{26}_D$ −3.7° (Table 2, experiment no. 5) shows a single anomeric peak at 100.1 ppm, indicating a stereoregular poly(**2**). The C-1 peak of the

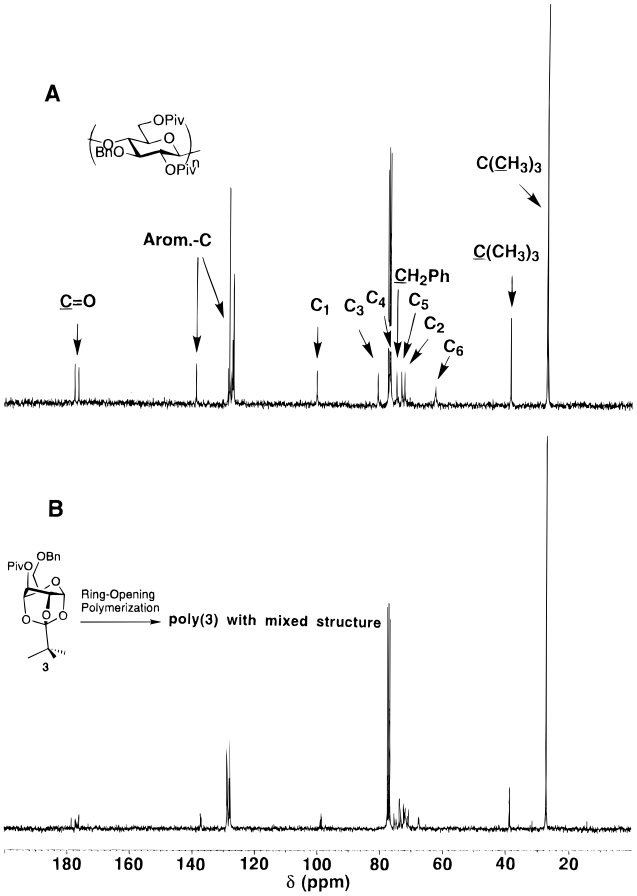


Figure 1. 75-MHz ^{13}C-NMR spectra of (A) poly(**2**) at °C (Table 2, experement no. 5) and (B) poly(**3**) polymerized at −30 °C (Table 2, experiment no. 7) ($CDCl_3$ as solvent).

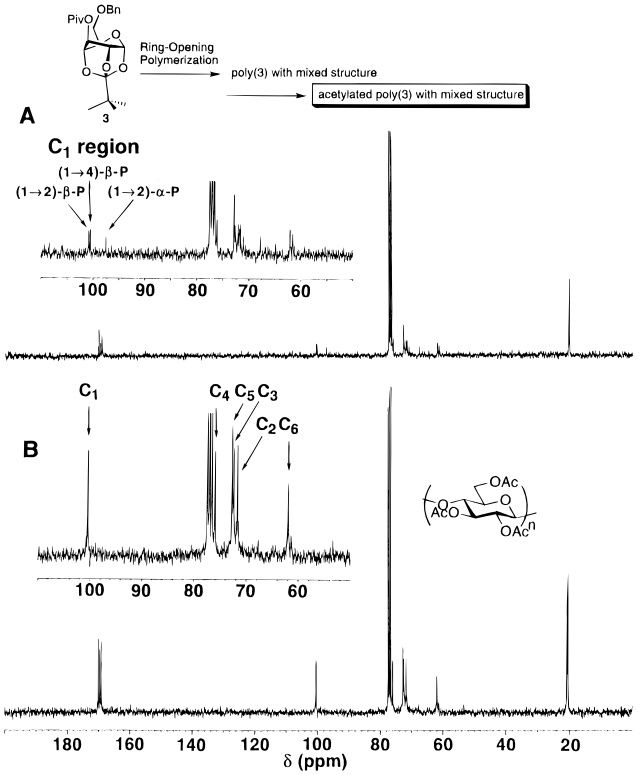


Figure 2. 75-MHz ^{13}C-NMR spectra of (A) acetylated poly(**3**) polymerized at −30 °C (Table 2, experiment no. 7) and (B) cellulose triacetate synthesized from poly(**1**) polymerized at 20 °C ($CDCl_3$ as solvent).

celloeicosaose derivative (DP = 20) with the same protective group system (benzyl group at the 3-*O* position and pivaloyl groups at the 2-*O* and 6-*O* positions) appears at 100.1 ppm.[3c] In addition, other carbon resonances of the stereoregular poly(**2**) completely agreed with those of the celloeicosaose derivative. Thus, it is concluded that the stereoregular poly(**2**) is a (1→4)-*β*-D-glucopyranan derivative, *i.e.*, cellulose derivative.

The ^{13}C-NMR spectrum in Figure 1B of poly(**3**) having $[\alpha]^{26}_D$ −26.8° (Table 2, experiment no. 7) shows three anomeric peaks at 98.6 ppm (major), 98.3, and 98.9 ppm (minor; their heights are almost identical), indicating a nonstereoregular poly(**3**). Poly(**3**) was converted to an acetyl derivative in order to determine its structure. The anomeric peaks of the acetylated poly(**3**) appeared at 97.6, 100.5, and 100.8 ppm, as shown in Figure 2A. The anomeric peaks of an amylose acetate ((1→4)-α-P) and a cellulose acetate ((1→4)-*β*-P) (Figure 2B) appear at 95.7[10] and 100.5 ppm, respectively. In addition, an anomeric peak of methyl 3,4,6-tri-*O*-acetyl-2-*O*-methyl-α-D-glucopyranoside, corresponding to a (1→2)-α-P unit, appears at 97.7 ppm,[11] and an anomeric peak of the nonreducing end group of *β*-sophorose octaacetate (1,3,4,6-tetra-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-*β*-D-glucopyranose), corresponding to a (1→2)-*β*-P unit, appears at 100.8 ppm.[12] Therefore, the anomeric peaks of the acetylated poly(**3**) at 97.6, 100.5, and 100.8 ppm were assigned to (1→2)-α-P, (1→4)-*β*-P, and (1→2)-*β*-P units, respectively, as shown in Figure 2. Polymerization of **3** produced no (1→4)-α-P unit. The structure of poly(**4**) was unidentified because polymerization of **4** only afforded a low molecular weight polymer in low yield.

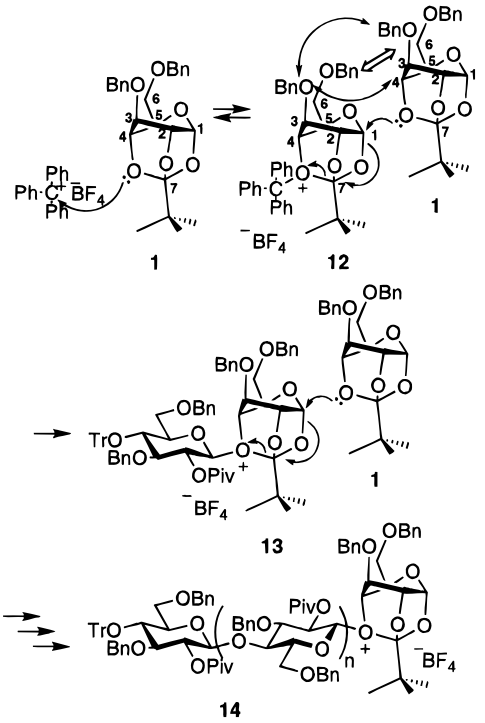
Substituent Effect on Ring-Opening Polymerization. Influence of the Number of Benzyl Groups. Molecular weights of poly(**1**)s, poly(**2**)s, and poly(**3**)s are almost the same as each other, but those of poly(**4**)s were low and the starting monomer was recovered in *ca.* 70% yield under all reaction conditions tried. The polymerization conditions of **4**, especially the concentration of monomer **4**, was different from those of other monomers so that the polymerizability of **4** may not be compared exactly with those of **1**−**3**.

Monomers having one benzyl group and two pivaloyl groups (including an orthopivaloyl group), that is monomers **2** and **3**, had the same polymerizability as monomer **1** having two benzyl groups and one pivaloyl group. Monomer **4**, however, had remarkably low polymerizability among the four monomers. After all, it is found that a starting monomer should have at least one benzyl group for yielding a polysaccharide.

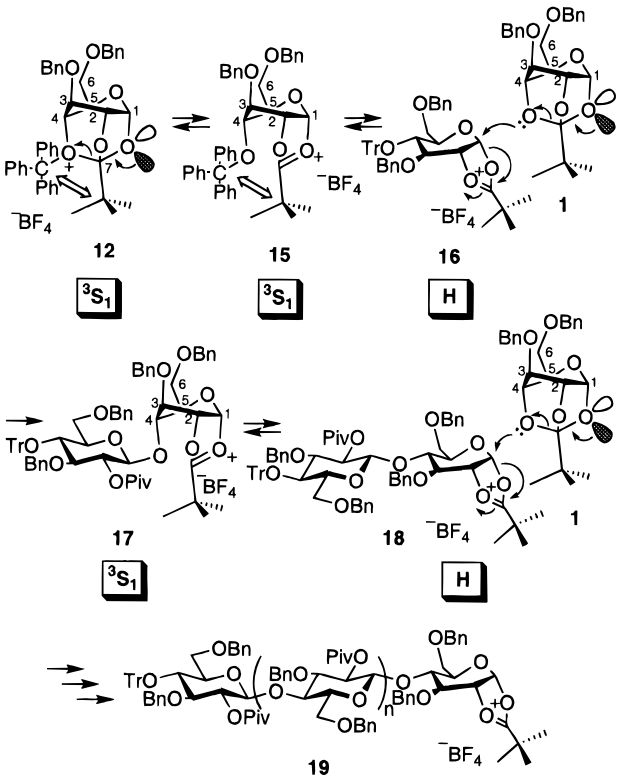
Influence of Position of the Benzyl Group. Polymerizations of **1** and **2** having a 3-*O*-benzyl group gave stereoregular (1→4)-*β*-D-glucopyranan derivatives (Table 2, experiment nos. 1−6). However, polymerizations of **3** having a 3-*O*-pivaloyl group afforded a stereo-irregular polysaccharide consisting of (1→2)-α-P, (1→4)-*β*-P, and (1→2)-*β*-P units. The product ratio can be determined by the peak areas of the corresponding anomeric carbons, as shown in Figure 2. A (1→2)-bond formation increased with a decrease in temperature. That is, at 0 and 20 °C, the probability of coordination of Ph_3CBF_4 with a C_2-oxygen was equal to that with a C_4-oxygen, and at −30 °C, the coordination with the C_2-oxygen took place in preference to that with the C_4-oxygen: (1→2)-α-P/(1→4)-*β*-P/(1→2)-*β*-P = 1/2/1 (Table 2, experiment nos. 8 and 9); (1→2)-α-P/(1→4)-*β*-P/(1→2)-*β*-P = 3/4/3 (Table 2, experiment no. 7).

Mechanism of Polymerization. The trialkyloxonium ion mechanism shown in Scheme 2 has been

Scheme 2. Trialkyloxonium Ion Mechanism



Scheme 3. Dioxalenium Ion Mechanism



proposed for the stereoregular ring-opening polymerization of 1,4- and 1,6-anhydro sugars.[13,14] First of all, in the initiation step of this mechanism, an oxonium ion intermediate **12** is formed by the complexation of a triphenylcarbenium ion with oxygen at the C_4-position (C_4−O). Then, the β-side attack of the next monomer **1** with Walden inversion at the C_1-position of the oxonium ion intermediate **12**, accompanied by the scissions of the C_4O-C_7 and C_1-OC_7 bonds, results in the formation of a dimeric trialkyloxonium ion **13**. Subsequently, in the propagation step, the continuous attacks of the monomer **1** on the trialkyloxonium ion afford a polymeric trialkyloxonium ion **14** consisting of a (1→4)-β-D-glucopyranan chain.

However, the β-side attack of the next monomer **1** on the oxonium ion **12** may be difficult because of the steric hindrance of the axial 3-*O*-benzyl group in the oxonium ion **12** having an $^3S_1$-conformation; the situation is also the same at the propagation step. Consequently, the present ring-opening polymerization may be explained by the dioxalenium ion mechanism (Scheme 3)[13] rather than the trialkyloxonium ion mechanism (Scheme 2).

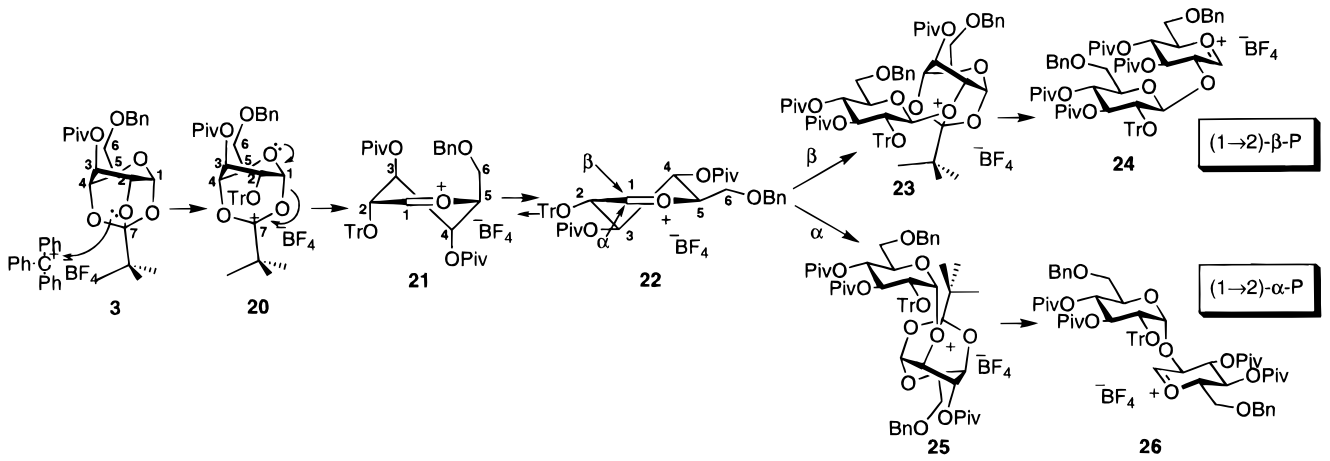
In the latter mechanism, the oxonium ion intermediate **12** formed at the initiation step is thought to be immediately converted to a dioxalenium ion **15** by the intramolecular backside attack of a lone pair orbital on the C_1- or C_2-oxygens oriented antiperiplanar to the C_4O-C_7 bond in preference to the attack of monomer **1** because of its instability caused by the large steric repulsion between the C_4O−trityl and the C_7−*tert*-butyl groups. The metastable ion **15** with the $^3S_1$-conformation seems to stabilize to another dioxalenium ion **16** with a half-chair (H) conformation, where both the 3-*O*- and 6-*O*-benzyl groups have the more stable equatorial orientation. The intermediate **16** can then undergo an intermolecular reaction with the next monomer **1** without any hindrance from the axial 3-*O*-benzyl group like that in Scheme 2, resulting first in a dimeric dioxalenium ion **17** with $^3S_1$, which then stabilizes to **18** in the H-form.

In the propagation step, the β-side attack of the next monomer **1** on the reducing end of the elongating chain and conformational transformation of $^3S_1$ into the H-conformation are alternatively repeated stepwise to afford a polymeric dioxalenium ion **19**. Finally, 1 mol of water is introduced into **19** at the workup step to give a completely stereoregular (1→4)-β-D-glucopyranan derivative. The mechanism in Scheme 3 is quite similar to that of the exclusive formation of low molecular weight 1,2-*trans*-glycoside using the neighboring participation of a 2-*O*-acyl group.[13,15] The trityl group of the nonreducing end may be removed by hydrolysis with strong acid formed during the workup.

Generally, there are two possible ring-opening modes, 1,2 and 1,4 scissions on the cationic ring-opening polymerization of tricyclic 1,2,4-orthoester. Quantum chemical calculations showed that an electrophilic attack at these two centers, C_2-*O*- and C_4-*O*-positions giving (1→2)- and (1→4)-glucans, respectively, is expected to be of nearly equal probability.[16] In fact, Bochkov *et al.* prepared xylan from 3-*O*-acetyl-α-D-xylopyranose 1,2,4-orthoacetate under optimum conditions containing an approximately equal number of (1→2)-α- and (1→4)-β-glycosidic linkages.[13,17] Furthermore, the production of 1,4-anhydro sugar and its polymerization also has been reported as a side reaction of the ring-opening polymerization of 1,2,4-orthoester.[8] However, none of these side reactions occurred in the polymerization of monomer **1**: if the conversion of monomer **1** into an anhydro sugar derivative occurred, the product should have a stereoregular (1→5)-β-D-glucofuranan derivative, but such a possibility was eliminated by the analyses of the ^1H- and ^{13}C-NMR spectra of the product.

In addition, Scheme 4 illustrated the proposed mechanism of polymerization of **3**, resulting in poly(**3**)s with mixed structures. In the case of (1→2)-bond formation, the coordination of the initiator with the C_2-oxygen affords a seven-membered ring carbonium ion intermediate **20**, which is unstable so that C_1-OC_7 bond breaking must precede an attack of the next monomer to afford the subsequent planar carboxonium ion inter-

Scheme 4



mediate **21**. However, the intermediate **21** having all axial substituent groups would be rapidly converted to the twist-boat form **22** because of stabilization. The next monomer attacks the C_1 carbon from both sides of the planar intermediate **22**, basically with equal probability because neighboring participations caused by both C_3- and C_4-pivaloyl groups are no longer expected. Then, the next monomer attacks the C_1 carbon from the α- and β-sides to form dimeric carboxonium ion intermediates **24** ((1→2)-β-P) and **26** ((1→2)-α-P) *via* dimeric trialkyloxonium ion intermediates **23** and **25**, respectively. Thus, the production of almost the same amount of (1→2)-α-P and (1→2)-β-P units would be explained.

A decrease of electron density of the C_4-oxygen due to introduction of a pivaloyl group at the 3-*O* position is expected from the ^{1}H-NMR data of the orthoester derivatives (Table 1). The decrease of electron density of the C_4-oxygen may cause an undesirable coordination of the initiator with the C_2-oxygen, resulting in the polysaccharide being stereo-irregular.

Thus, the benzyl group at the 3-*O* position is indispensable for yielding a stereoregular cellulose derivative, *i.e.*, a (1→4)-β-D-glucopyranan derivative.

Conclusions. Polymerizations of four regioselectively acylated α-D-glucopyranose 1,2,4-orthopivalate derivatives were discussed in order to clarify the effects of substituents at the 3-*O* and 6-*O* positions on those ring-opening polymerizations. Polymerizations of **1** and **2** having the benzyl group at the 3-*O* position afforded stereoregular (1→4)-β-D-glucopyranan derivatives, *i.e.*, cellulose derivatives. However, polymerization of **3** having a pivaloyl group at the 3-*O* position did not afford stereoregular polysaccharide.

Thus, it was concluded from the results of ring-opening polymerizations of monomers **1**−**4** that a monomer having one benzyl group is essential for obtaining a polysaccharide and that the benzyl group at the 3-*O* position is indispensable for yielding stereoregular (1→4)-β-D-glucopyranan derivatives, *i.e.*, cellulose derivatives. Finally, the 3-*O*-benzyl group has a special function for yielding a stereoregular polysaccharide not only in polymerizations of 1,4-anhydro-α-D-glucopyranose derivatives[6] but also in those of α-D-glucopyranose 1,2,4-orthopivalate derivatives.

Experimental Section

General Methods. Preparative thin layer chromatography (PTLC) was performed on silica-gel plates (Kieselgel 60 F_{254}, Merck). The standard workup procedure included diluting with ethyl acetate, washing with aqueous $NaHCO_3$ and brine, drying over Na_2SO_4, and evaporating *in vacuo*.

3-*O*-Benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-Orthopivalate (2). 3-*O*-Benzyl-2,6-di-*O*-pivaloyl-D-glucopyranose (**6**)[6] (576 mg, 1.32 mM) was dissolved in benzene (50 mL), and then *N*,*N*′-carbonyldiimidazole (228 mg, 1.05 equiv) was added. The solution was stirred at reflux temperature for 5 days. The reaction mixture was concentrated *in vacuo*. Compound **2** was purified on a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/4, v/v) to give colorless crystals (318 mg, 57.6%), mp 73.1−73.6 °C (recrystallized from methanol), $[\alpha]^{26}_D$ +31.2° (*c* 1.35, chloroform). ^{1}H-NMR ($CDCl_3$): δ 1.03 (9H, piv-H), 1.23 (9H, piv-H), 3.95 (dt, 1H, J = 3.5, C_4−H), 4.16 (dd, 1H, $J_{2,3}$ = 2.2, $J_{3,4}$ = 4.7, C_3−H), 4.31−4.41 (2H, C_6−H), 4.39−4.43 (1H, C_2−H), 4.45−4.52 (1H, C_5−H), 5.76 (d, 1H, $J_{1,2}$ = 4.9, C_1−H), 4.63 (s, 2H, J = 12.0, $CH_2C_6H_5$), 7.30−7.40 (5H, aromatic). ^{13}C-NMR: δ 97.6 (C-1), 64.4, 71.3, 71.5, 72.0, 72.2, 75.3 (C-2, C-3, C-3, C-4, C-5, C-6, $CH_2C_6H_5$), 123.1 ($(-O)_3C(CH_3)_3$), 27.2 (pivaloyl-C(CH_3)$_3$), 38.8 (pivaloyl-C(CH_3)$_3$), 24.9 (orthopivalate-C(CH_3)$_3$), 35.7 (orthopivalate-C(CH_3)$_3$), 127.7, 128.1, 128.7, 137.4 (aromatic).

6-*O*-Benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-Orthopivalate (3). 6-*O*-Benzyl-2,3-di-*O*-pivaloyl-D-glucopyranose (**7**)[6] (307.8 mg, 0.703 mM) was dissolved in benzene (50 mL), and then *N*,*N*′-carbonyldiimidazole (120 mg, 1.05 equiv) was added. The solution was stirred at reflux temperature for 1 week. The reaction mixture was concentrated *in vacuo*. Compound **3** was purified on a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/4, v/v) to give colorless crystals (103.7 mg, 35.1%), mp 85.9−86.9 °C (recrystallized from methanol), $[\alpha]^{26}_D$ +10.1° (*c* 1.07, chloroform). ^{1}H-NMR ($CDCl_3$): δ 1.06 (9H, piv-H), 1.11 (9H, piv-H), 3.61 (dd, 1H, J_{gem} = 9.6, $J_{5,6a}$ = 6.5, C_6-H_a), 3.72 (dd, 1H, $J_{5,6b}$ = 6.5, C_6-H_b), 4.31 (dd, 1H, $J_{2,3}$ = 2.2, $J_{3,4}$ = 4.7, C_3−H), 4.62 (t, 1H, C_5−H), 5.08 (dt, 1H, J = 3.5, C_4−H), 5.73 (d, 1H, $J_{1,2}$ = 4.9, C_1−H), 4.51, 4.60 (d, d, 1H, 1H, respectively, J = 12.0, $CH_2C_6H_5$), 7.20−7.40 (5H, aromatic). ^{13}C-NMR: δ 97.4 (C-1), 65.7, 69.6, 70.7, 72.0, 73.3, 75.5 (C-2, C-3, C-3, C-4, C-5, C-6, $CH_2C_6H_5$), 123.3 ($(-O)_3C(CH_3)_3$), 27.0 (pivaloyl-C(CH_3)$_3$), 38.7 (pivaloyl-C(CH_3)$_3$), 24.8 (orthopivalate-C(CH_3)$_3$), 35.7 (orthopivalate-C(CH_3)$_3$), 127.7, 127.8, 128.4, 137.7 (aromatic).

1,2,3-Tri-*O*-pivaloyl-β-D-glucopyranose (9). To a suspension of 4,6-*O*-benzylidene-1,2,3-tri-*O*-pivaloyl-β-D-glucopyranose (**8**)[6] (1.04 g, 2.0 mM) in methanol (10 mL) was added *p*-toluenesulfonic acid (172 mg, 1.0 mM) at room temperature. After 2 h, the suspension turned to a clear solution. The solution was worked up by the standard procedure. Compound **9** was crystallized from *n*-hexane (756 mg, 87% yield), mp 147.6−148.6 °C, $[\alpha]^{26}_D$ −1.7° (*c* 0.838, chloroform). ^{1}H-NMR ($CDCl_3$): δ 1.13, 1.186, 1.194 (9H, 9H, 9H, piv-H), 3.58 (m, 1H, C_5−H), 3.76−3.88 (m, 1H, C_4−H), 3.76−3.82 (1H, C_6-H_a), 3.91−3.98 (m, 1H, C_6-H_b), 5.10−5.20 (2H, C_2−H, C_3−H), 5.72 (d, 1H, $J_{1,2}$ = 8.1, C_1−H).

1,2,3,6-Tetra-*O*-pivaloyl-β-D-glucopyranose (10). To a solution of **9** (756 mg, 1.75 mM) in pyridine (5 mL) was added pivaloyl chloride (0.323 mL, 2.63 mM) at room temperature. After 1 h, the reaction mixture was diluted with ethyl acetate and washed successively with a saturated sodium hydrogen

carbonate solution, aqueous hydrochloric acid, and brine. The organic phase was dried over Na_2SO_4 and concentrated to dryness. Compound **10** was crystallized from *n*-hexane (851 mg, 94% yield), mp 147.9−148.8 °C, $[\alpha]^{26}_D$ −12.4° (*c* 0.709, chloroform). ^{1}H-NMR ($CDCl_3$): δ 1.19, 1.20, 1.23 (9H, 9H, 9H, piv-H), 3.50 (m, 1H, C_4−H), 4.07 (m, 1H, C_5−H), 4.36 (dd, 1H, J_{gem} = 12.2, $J_{5,6a}$ = 2.6, C_6−H_a), 4.42 (dd, 1H, $J_{5,6b}$ = 4.0, C_6−H_b), 4.80 (d, 1H, $J_{1,2}$ = 10.1, J = 3.7, C_1−H), 5.40 (t, 1H, $J_{2,3}$ = 10.1, C_2−H), 5.45 (1H, C_3−H).

2,3,6-Tri-*O*-pivaloyl-D-glucopyranose (11). To a solution of **10** (696.4 mg, 1.35 mM) in THF (10 mL) was added hydrazine hydrate (*ca.* 90%, 131 μL, 2.8 mM) at room temperature. After 8 h, the reaction mixture was worked up by the standard method to give a colorless syrup. Compound **11** was crystallized from *n*-hexane (478.8 mg, 82% yield), mp 68.8−69.4 °C, $[\alpha]^{26}_D$ +65.1° (*c* 0.767, chloroform). ^{1}H-NMR ($CDCl_3$): δ 1.13, 1.17, 1.19, 1.22 (9H, 9H, 9H, 9H, piv-H), 3.50−3.57 (m, 1H, C_4−H), 3.64−3.70 (m, 1H, C_5−H), 4.32 (dd, 1H, J_{gem} = 12.2, $J_{5,6a}$ = 2.5, C_6−H_a), 4.45 (dd, 1H, $J_{5,6b}$ = 4.7, C_6−H_b), 5.08−5.18 (2H, C_2−H, C_3−H), 5.68 (d, 1H, $J_{1,2}$ = 8.1, C_1−H).

3,6-Di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-Orthopivalate (4). Compound **11** (44.9 mg, 0.104 mM) was dissolved in benzene (40 mL), and then *N,N′*-carbonyldiimidazole (116.9 mg, 1.05 equiv) was added. The solution was stirred at reflux temperature for 9 days. The reaction mixture was concentrated *in vacuo*. Compound **4** was purified on a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/4, v/v) to give colorless crystals (19.7 mg, 45.8%), mp 127.3−128.7 °C (recrystallized from methanol), $[\alpha]^{26}_D$ +20.5° (*c* 0.77, chloroform). ^{1}H-NMR ($CDCl_3$): δ 1.06, 1.22, 1.23 (9H, 9H, 9H, piv-H), 4.21 (dd, 1H, J_{gem} = 9.6, $J_{5,6a}$ = 6.8, C_6−H_a), 4.25 (dd, 1H, $J_{2,3}$ = 2.2, $J_{3,4}$ = 4.7, C_3−H), 4.38 (dd, 1H, $J_{5,6b}$ = 6.5, C_6−H_b), 4.43 (m, 1H, C_2−H), 4.56 (t, 1H, C_5−H), 5.12 (dt, 1H, $J_{4,5}$ = 1.1, C_4−H), 5.75 (d, 1H, $J_{1,2}$ = 4.8, C_1−H). ^{13}C-NMR: δ 97.4 (C-1), 63.8, 65.6, 70.8, 72.0, 74.9 (C-2, C-3, C-3, C-4, C-5, C-6), 123.5 ((−O)$_3$*C*(CH$_3$)$_3$), 27.2 (pivaloyl-C(*C*H$_3$)$_3$), 38.8, 38.9 (pivaloyl-*C*(CH$_3$)$_3$), 24.8 (orthopivalate-C(*C*H$_3$)$_3$), 35.8 (orthopivalate-*C*(CH$_3$)$_3$).

Polymerization. Polymerizations were carried out under high vacuum at −30, 0, and +20 °C as described previously.[4]

Conversion of Poly(3) into Acetylated Poly(3). To a solution of poly(**3**) (9.2 mg) (Table 2, experiment no. 7) in THF/methanol (10/1, v/v) (3.3 mL) was added 28% sodium methoxide (0.1 mL). The reaction mixture was kept at reflux temperature for 27 h. Then, MeOH (*ca.* 2 mL) was added to the reaction mixture. After 5 h, the reaction mixture was treated with Amberlyst 15 ion-exchange resin for neutralization and then filtered off. The resin was washed with MeOH. The combined washings and filtrate were concentrated to dryness. The product was treated with acetic anhydride and pyridine at 50 °C overnight to give a crude 2,3-di-*O*-acetyl-6-*O*-benzyl derivative. The product was purified on a silica gel column (Wakogel C-200; eluent, $CHCl_3$, and then 20% MeOH/$CHCl_3$) and by PTLC (eluent, 10% MeOH/$CHCl_3$) to give 2,3-di-*O*-acetyl-6-*O*-benzyl derivative (7.1 mg, 96%). ^{13}C-NMR: δ 100.2, 99.9, 97.3 (C_1 region). To a solution of the 2,3-di-*O*-acetyl-6-*O*-benzyl derivative (7.1 mg) in THF (1 mL) was added palladium hydroxide on carbon (40 mg). The reaction mixture was kept at room temperature for about 1 day. Palladium hydroxide on carbon was filtered off and washed with chloroform. The combined washings and filtrate were concentrated to dryness. The product was treated with acetic anhydride and pyridine at 50 °C overnight to give a crude triacetylated poly(**3**). The product was purified on a silica gel column (Wakogel C-200; eluent, $CHCl_3$, and then 20% MeOH/$CHCl_3$) and by PTLC (eluent, 10% MeOH/$CHCl_3$) to give a triacetylated poly(**3**) (5.8 mg, 95%). ^{13}C-NMR: δ 100.8, 100.5, 97.6 (C_1 region).

Measurements. All melting points (mp) are uncorrected. ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded with a Bruker AC300 FT-NMR (300 MHz) spectrometer, in chloroform-*d* with tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) and coupling constants (J) are given in δ values (ppm) and Hz, respectively. Some chemical shift assignments were made using a decoupling method; others were made by an analogy with values in the literature and by analogy with model compounds. Optical rotations were measured at 26 °C using a JASCO Dip-1000 digital polarimeter. Molecular weight distributions of the substituted polymer were analyzed by gel permeation chromatography (GPC) in tetrahydrofuran. Calibration curves were obtained by using polystyrene standards (Shodex). A Waters universal liquid chromatograph injector (model U6K), a Waters solvent delivery system (model 6000A), a Waters refractive index detector (series R-400), a Waters absorbance detector (model 440), and Shodex columns (KF802 and KF803) were used. The flow rate was 1.0 mL/min.

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