Substituent Effects of the Orthoester Group on Ring-Opening Polymerization of α-D-Glucopyranose 1,2,4-Orthoester Derivatives

Michiko Hori, Hiroshi Kamitakahara, and Fumiaki Nakatsubo*

Forest and Biomaterials Science, Graduate School of Agriculture, Kyoto University, Sakyo-ku, Kyoto 606-01, Japan

Received December 23, 1996; Revised Manuscript Received March 3, 1997[⊗]

ABSTRACT: The first chemical synthesis of cellulose derivatives, (1→4)-*β*-D-glucopyranan derivatives has been accomplished by cationic ring-opening polymerization using 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**1**) as a starting monomer, taking into account substituent effects.[1] Here, three orthoester derivatives as starting materials for the polymerization, 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopropionate (**2**), 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthoacetate (**3**), and 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthobenzoate (**4**), were selected to investigate the substituent effects of orthoester group on the ring-opening polymerization. These three monomers were polymerized under the same reaction conditions as those of monomer **1**, yielding stereoregular (1→4)-*β*-D-glucopyranan derivatives, previously reported. As the result, monomers **2**−**4** gave non-regioregular polymers consisting of (1→4)- and (1→2)-*β*-pyranose units, although they gave high stereoregularity, *i.e.*, *β*-glucosidic linkage. Thus, it was concluded from the polymerizations of the monomers **1**−**4** that the orthopivaloyl group of the starting monomer is indispensable for regiospecificity of the polymerization, yielding only the (1→4)-glycosidic bond, not the (1→2)-bond.

Introduction

The chemical synthesis of a series of cellooligosaccharides up to celloeicosaose derivatives with a degree of polymerization of 20 by a stepwise synthetic route has succeeded.[2] The most important findings obtained from the stepwise synthesis are the substituent effects on the *β*-glycosylation; that is, both benzyl and pivaloyl groups introduced into 3-*O*- and 2-*O*-positions of glucose, respectively, are indispensable for highly stereoselective (1→4)-*β*-glycosidic bond formation in a high yield.[3]

These substituent effects were applied to the ring-opening polymerization of 1,4-anhydroglucose derivatives and the first chemical synthesis of stereoregular (1→5)-*β*-D-glucofuranan[4] was accomplished. The effectiveness of the substituent effects was also verified by the polymerizations of several 1,4-substituted anhydroglucose derivatives.[5]

Furthermore, the substituent effects were applied to the cationic ring-opening polymerization of glucose 1,2,4-orthoester derivatives, and we succeeded in the first chemical synthesis of cellulose via polymerization of 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**1**).[1] In the polymerization, the 3-*O*-benzyl group also proved to be essential for obtaining the stereoregular (1→4)-*β*-D-glucopyranan derivatives,[6] but the significance of the 2-*O*-pivaloyl group on the orthoester polymerization is still unknown.

In this paper, we describe electronic and steric effects of the orthoester group on the ring-opening polymerization of glucose 1,2,4-orthoester for obtaining (1→4)-*β*-D-glucopyranan.

Results and Discussion

Selection of the Starting Monomers. Generally, electron-donating substituents increase both reactivities of glycosyl donor and acceptor, resulting in the highly stereoselective glycosylation with high yield, but on electron-withdrawing one exhibits the opposite effect.[7] This means that ether groups are superior to acyl groups. Thus, the pivaloyl (trimethylacetyl) group with relatively small electron-withdrawing effects in acyl groups is highly effective as a protective group of sugar hydroxyl groups on the glycosylation. The electron-withdrawing abilities of acyl groups are associated with the pK_a values of the corresponding carboxylic acids.

We selected three additional orthoesters as starting monomers for the ring-opening polymerization, 1,2,4-orthopropionate (**2**), orthoacetate (**3**), and orthobenzoate (**4**), prepared from propionic (pK_a 4.88), acetic (pK_a 4.76), and benzoic (pK_a 4.20) acids, respectively, to investigate the electronic effects of the orthoester groups on the ring-opening polymerization and to compare with that of orthopivalate (**1**) (pK_a of pivalic acid, 5.05), whose polymerization gave a completely stereoregular cellulose derivative as reported in our previous paper.[1]

Synthesis of 3,6-Di-*O*-benzyl-α-D-glucopyranose 1,2,4-Orthoester Derivatives. Three new glucose orthoester derivatives **2**, **3**, and **4** were prepared by the synthetic route for orthopivalate (**1**) reported previously (Scheme 1). 2-*O*-Acyl groups in these orthoesters were introduced by utilizing various acylating reagents, propionic and acetic anhydrides, and benzoyl chloride, respectively, at the reaction step of acylation of 2-*O*-position (Scheme 1, reaction a). The overall yields of orthoesters **2**, **3**, and **4** from 3-*O*-benzyl-4,6-*O*-benzylidene-D-glucopyranose (**5**)[8] were 32, 31, and 28%, respectively.

^{1}H-NMR Chemical Shifts of 3,6-Di-*O*-benzyl-α-D-glucopyranose 1,2,4-Orthoester Derivatives 1−4. The assignments of proton peaks are summarized in Table 1. All proton peaks of orthobenzoate (**4**) are shifted to a little lower magnetic field comparing with those of orthoester derivatives **1**−**3** whose chemical shifts are almost the same. This is supposed to be attributable to the larger inductive effect of the phenyl group in orthobenzoate. The difference of pK_a values of the corresponding acids in orthoesters **1**−**3** does not affect those of ^{1}H-chemical shifts. From these NMR data, monomers **2** and **3** are expected to give the same

[⊗] Abstract published in *Advance ACS Abstracts,* April 15, 1997.

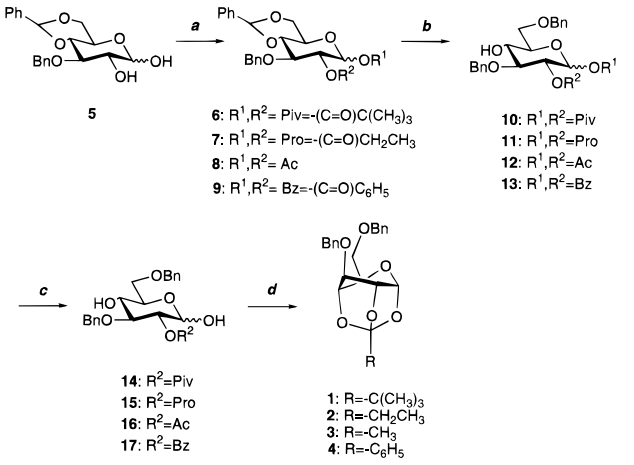
S0024-9297(96)01883-9 CCC: $14.00

Table 1. ^{1}H-HMR Chemical Shifts of Orthoester Derivatives

		δ (ppm)						
monomer	pK_a[a]	C_1−H	C_2−H	C_3−H	C_4−H	C_5−H	C_6−H	
1	5.05	5.79	4.42	4.31	3.95	4.60	3.75	3.83
2	4.88	5.78	4.40	4.27	3.96	4.60	3.72	3.81
3	4.76	5.79	4.39	4.25	3.96	4.63	3.72	3.80
4	4.20	5.97	4.59	4.48	4.13	4.79	3.79	3.86

[a] pK_a values are those of the carboxylic acid groups introduced at the 2-*O*-positions of the monomers.

Scheme 1. Synthesis of Orthoester Derivatives



[a]various acylating reagents/ pyridine/ r.t., [b]$NaCNBH_3$/ $(CH_3)_3SiCl$/ MS 4 Å / CH_3CN/ r.t., [c] $H_2NNH_2 \cdot H_2O$/ THF/ r.t., [d] *N,N'*-carbonyldiimidazol/ benzene/ reflux

Table 2. Polymerization of Orthoester Derivatives[a]

monomer	temp (°C)	time (h)	yield[b] (%)	$[\alpha]_D^{25}$ (deg)	$\overline{DPn}$[c]	10^{-3} M_{GPC}	M_w/M_n
1	20	2	62	−37.2	19.3	8.3	1.3
2	20	6	56	+1.56	15.8	6.4	1.6
3	20	1.5	72	+12.9	10.4	4.0	1.7
4	20	1.5	94	+11.8	9.4	4.2	1.9

[a] Initiator: Ph_3CBF_4. Initiator concentration: 5 mol %. Solvent: CH_2Cl_2. Monomers/solvent: 100 g/100 mL. [b] Polymer was insoluble fraction in chloroform/*n*-hexane (ca. 1/5, v/v). [c] Molecular weight was calculated from polystyrene standard.

stereoregular polymer as monomer **1**, except for monomer **4**.

Polymerizations of 3,6-Di-*O*-benzyl-α-D-glucopyranose 1,2,4-Orthoester Derivatives. Polymerizations of 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthoester derivatives **2**−**4** were carried out under the same reaction conditions as those of polymerization of **1**, which gave cellulose derivative with the degree of polymerization ($\overline{DPn}$) of 19.3 in our previous experiments,[1] in order to compare polymerizability among the four monomers; *i.e.*, all polymerizations were carried out at 20 °C in the presence of triphenylcarbenium tetrafluoroborate as an initiator, in the same initiator concentration (5 mol %), and in the same monomer concentration (100 g/100 mL). The results are summarized in Table 2. Interestingly, the specific rotations of Poly(**2**)−Poly(**4**) were positive values, +1.56°, +12.9°, and +11.8°, respectively, as compared with Poly(**1**), a cellulose derivative which has large negative specific rotation. These specific rotation values suggest that all polymers newly obtained from monomers **2**−**4** are not stereoregular. In fact, the structures of all these polymers were determined to be nonregioregular by ^{13}C-NMR analysis as described in a later section.

Structures of Poly(2)−Poly(4). Generally, there are four possible structural units in the polymer prepared by cationic ring-opening polymerization of tricyclic α-D-glucopyranose 1,2,4-orthoester derivatives, namely, the (1→4)-α- and (1→4)-β-D-glucopyranose ((1→4)-α-P and (1→4)-β-P) units and the (1→2)-α- and (1→2)-β-D-glucopyranose ((1→2)-α-P and (1→2)-β-P) units.[6]

All ^{1}H-NMR spectra of Poly(**2**)−Poly(**4**) suggest that these polymers are not stereo- and/or regioregular. For example, Poly(**3**) is clearly not stereo- and/or regioregular by comparing the ^{1}H-NMR spectra of Poly(**3**) (Figure 1B) with that of Poly(**1**) (Figure 1A).

^{13}C-NMR spectra A, B, C, and D in Figure 2 correspond to those of Poly(**1**)−Poly(**4**). These ^{13}C-NMR spectra can be classified into two categories by their resonance pattern of pyranose-ring carbons appearing at δ *ca.* 66 to *ca.* 82 ppm, that is, A−C and B−D groups.

Poly(**1**) has been found to be a stereoregular (1→4)-β-P. Thus, Poly(**3**) may consist of mainly (1→4)-β-P, but the group B−D is supposed to be mainly (1→2)-β-P from analyses of these ^{13}C-NMR spectra, although these ^{13}C-NMR spectra suggest that all of these Poly(**2**)−Poly(**4**) are nonstereo- and/or nonregioregular because peak overlapping is found in each peak.

Conversions of Poly(2)−Poly(4) into Their Acetyl Derivatives. The structures of Poly(**2**)−Poly(**4**) were furthermore determined by the analyses of ^{13}C-NMR spectrum of their acetyl derivatives obtained after deprotection and subsequent acetylation as shown in Scheme 2. It was found by their GPC analyses that the depolymerization of these Polys did not occur during the deprotection processes.

Structures of Acetyl Poly(2)−Poly(4). All ^{1}H-NMR spectra of the acetylated polymers obtained via reactions shown in Scheme 2 were compared with that of authentic cellulose triacetate[9] prepared from low molecular weight cellulose. It was found that Poly(**2**)−Poly(**4**) all were mixtures mainly consisting of (1→4)-β-P, contrary to the expectation from the ^{13}C-NMR spectrum of Polys (Figure 2) discussed in the above section.

The composition ratio in the Poly(**2**)−Poly(**4**) was calculated by the peak ratio corresponding to the anomeric ^{13}C-carbons appeared at δ *ca.* 97 to *ca.* 102 ppm, as reported in the previous paper and as shown in Figure 3A.[6]

The ^{13}C-NMR spectrum of acetyl Poly(**3**) (Figure 3B) shows only two anomeric peaks at 100.5 (major) and 100.8 (minor) ppm. These peaks correspond to (1→4)-β-P and (1→2)-β-P units, respectively, judging from the comparison with Figure 3A. Interestingly, an anomeric peak at 97.6 ppm corresponding to (1→2)-α-P in Figure 3A did not appear in Figure 3B. Consequently, Poly(**3**) was determined to be a mixture consisting of only β-anomer, *i.e.*, (1→4)- and (1→2)-β-P, units without any α-anomer units. Similarly, both Poly(**2**) and Poly(**4**) were also found to be a mixture consisting of only (1→4)- and (1→2)-β-P units by their ^{13}C-NMR analyses. The results are summarized in Table 3.

These data indicate that there is no distinct relationship between the production of (1→4)-β-P unit and the pK_a values of their carboxylic acid groups introduced at 2-*O*-positions of the monomers.

Therefore, only the 2-*O*-pivaloyl group has a characteristic effect on the fate of the ring-opening polymerization, resulting in the formation of stereoregular (1→4)-β-pyranan. The characteristic may originate in its large steric effects but not in its electronic effects.

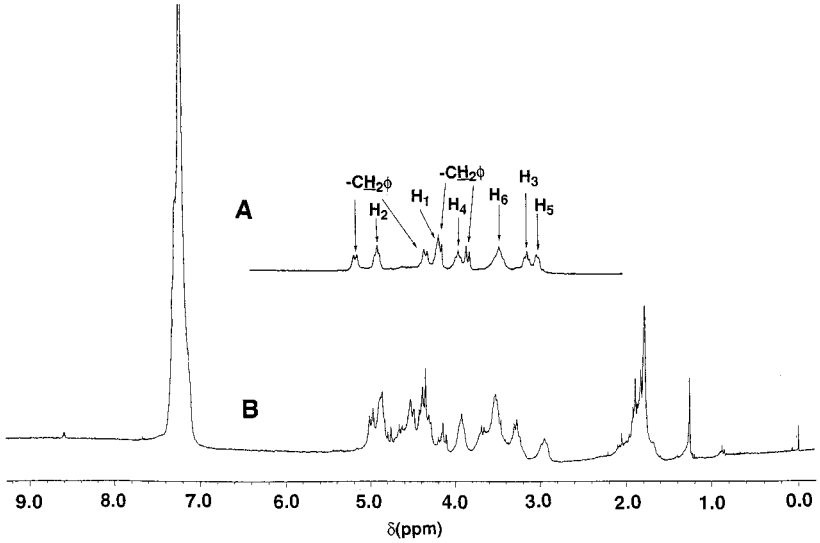


Figure 1. 300 MHz ^{1}H-NMR spectra of (A) the (1→4)-β-D-glucopyranan derivative, Poly(**1**), and (B) Poly(**3**) ($CDCl_3$ as solvent).

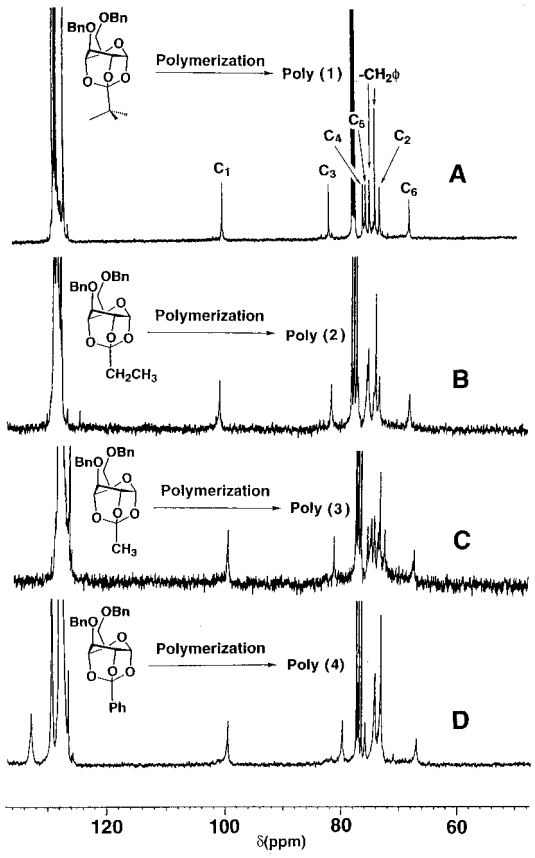


Figure 2. 300 MHz ^{13}C-NMR spectra of (A) Poly(**1**), (B) Poly(**2**), (C) Poly(**3**), and (D) Poly(**4**) ($CDCl_3$ as solvent).

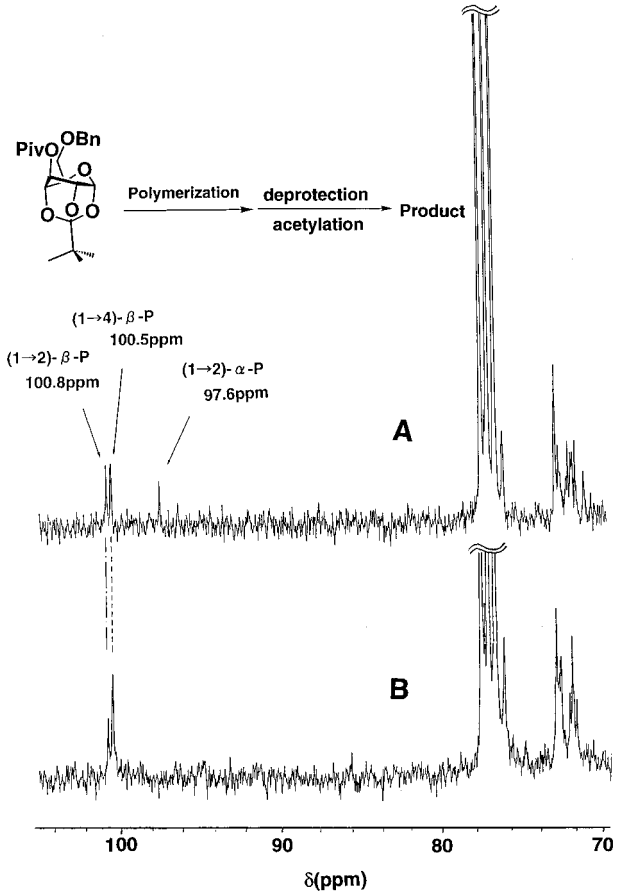
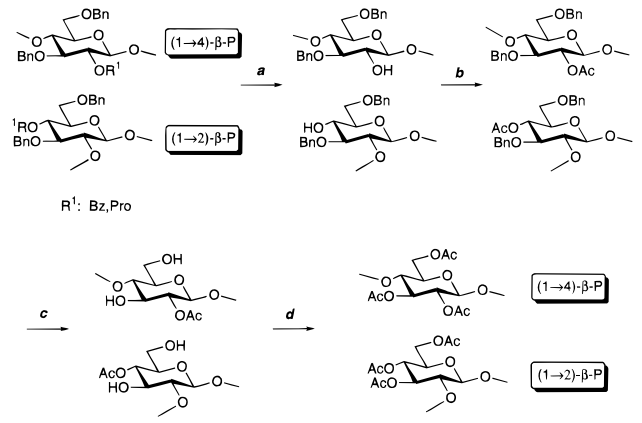


Figure 3. 300 MHz ^{13}C-NMR spectra of (A) a nonstereoregular polymer synthesized from 6-*O*-benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate and (B) acetyl Poly(**3**) ($CDCl_3$ as solvent).

Substituent Effect on Stereoregularity of Polysaccharide. The polymerized products of orthoester derivatives having 3-*O*-pivaloyl group consist of almost the same amount of (1→2)-α- and (1→2)-β-P units in the case of (1→2)-glycosidic bond formation (Figure 3A). This was because the next monomer could attack the C_1-carbon with equal possibility from both α- and β-sides of the planar intermediate having a half-chair form.[6]

However, the present polymerizations of orthoesters **2**−**4** having the 3-*O*-benzyl group gave only β-glucosidic linkages on the (1→2)-bond formation. These results can be explained as follows (Figure 4). In the case of (1→2)-bond formation, the initiator, triphenylcarbenium ion, preferentially attacks the C_2-oxygen to afford the oxonium ion intermediate (A), which is then coverted to the seven-membered ring dioxalenium ion intermediate (B), via O_2-C_7 bond breaking. In the case of the orthoester derivatives having 3-*O*-pivaloyl group (upper route), this seven-membered ring structure is labilized, probably, by the electron-withdrawing effect of the 3-*O*-pivaloyl group, so that C_1-O bond breaking must precede an attack of the next monomer to give both (1→2)-α,β-bond formations via S_N1 attack. On the other hand, in the case of the orthoester derivatives having 3-*O*-benzyl group (lower route), the dioxalenium ion

Scheme 2. Conversion of the Synthesized Polymers into the Triacetates



[a]$NaOCH_3$/ Dioxane:MeOH(10:1)/ 50℃/ over night, [b,d]$(CH_3CO)_2O$/ pyridine/ 50℃/ over night, [c]H_2/ $Pd(OH)_2$ on carbon/ THF:AcOH(1:1)/ 80℃/ over night

Table 3. Structure of Polymers Synthesized from Orthoester Derviatives

		polymer structure[b] (%)	
monomer	pK_a[a]	(1→4)-β-P	(1→2)-β-P
1	5.05	100	0
2	4.88	67	33
3	4.76	77	23
4	4.20	81	19

[a] pK_a values are those of the carboxylic acid groups introduced at 2-*O*-positions of monomers. [b] Determined from the proportion of anomeric peaks in ^{13}C-NMR spectra of polymers.

intermediate (B) is stabilized by the electron-donating effect of the 3-*O*-benzyl group to result in only (1→2)-*β*-bond formation via S_N2 attack of the next monomer.

Consequently, the benzyl group at the 3-*O*-position has a great electronic effect upon the stereospecificity in polymerizations of α-D-glucopyranose 1,2,4-orthoester derivatives.

Conclusions. Polymerization of orthopivalate (**1**) has afforded stereoregular (1→4)-*β*-D-glucopyranan derivatives, *i.e.*, cellulose derivatives.[1] However, any polymerizations of orthopropionate (**2**), orthoacetate (**3**), and orthobenzoate (**4**), newly prepared in the present study, did afford stereoregular polysaccharides consisting of only *β*-glucosidic bonds, but not regioregular: these gave a mixture consisting of (1→4)-*β*- and (1→2)-*β*-P units.

Thus, it was concluded that 2-*O*-acyl groups affect highly stereoselective *β*-glucosidic bond formation, and, in addition, the pivaloyl group in their acyl groups also affects further highly regioselective, (1→4)-glycosidic bond formation, probably due to steric effects and not electronic effects. On the other hand, on the polymerization of orthopivalates, the 3-*O*-pivaloyl derivative yielded nonstereo- and nonregioregular moieties, *i.e.*, a mixed polymer consisting of *β*-(1→4)- and α,*β*-(1→2)-glucans,[6] because of the electron-withdrowing effects, but the 3-*O*-benzyl derivative gave stereoregular *β*-(1→4)-glucan, cellulose.

Thus, both the 3-*O*-benzyl group and orthopivaloyl group are indispensable substituents for the synthesis of stereoregular (1→4)-*β*-D-glucopyranan derivatives (cellulose derivatives) in the ring-opening polymerization of α-D-glucopyranose 1,2,4-orthoester derivatives.

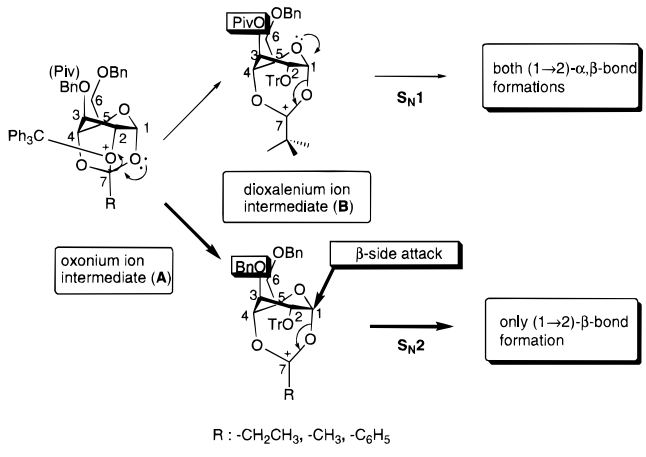


Figure 4. Mechanism of the (1→2)-*β*-bond formation.

Experimental Section

General Methods. Anhydrous dichloromethane was distilled from CaH_2. 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*.

1,2-Di-*O*-propionyl-3-*O*-benzyl-4,6-*O*-benzylidene-D-glucopyranoside (7). To a solution of 3-*O*-benzyl-4,6-*O*-benzylidene-D-glucopyranose (**5**)[8] (0.5 g, 1.4 mM) in pyridine (8 mL) was added propionic anhydride (0.54 mL, 4.2 mM) at room temperature. The solution was kept at room temperature for 12 h. The reaction mixture was concentrated *in vacuo*. Compound **7** was purified on a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/2, v/v) to give a colorless syrup (544.8 mg, 83% yield). Compound **7** was a mixture of α- and *β*-anomers: $[\alpha]_D^{25}$ +50.3° (*c* = 1, in chloroform). ^{1}H-NMR (300 MHz, $CDCl_3$): *δ* 6.31 (d, 1H, $J_{1,2}$ = 3.85 Hz; α-C_1−H), 5.10 (dd, 1H, $J_{2,3}$ = 9.64 Hz; α-C_2−H), 5.72 (d, 1H, $J_{1,2}$ = 8.15 Hz; *β*-C_1−H), 5.16 (m, 1H; *β*-C_2−H), 4.71, 4.91 (d, d, 1H, 1H, respectively, *J* = 11.9 Hz; α-C$H_2C_6H_5$), 4.68, 4.88 (d, d, 1H, 1H, respectively, *J* = 12.0 Hz; *β*-C$H_2C_6H_5$), 5.60 (s, 1H; α-CHC_6H_5), 5.58 (s, 1H; *β*-CHC_6H_5), 2.27, 2.41 (dd, dd, 2H, 2H, *J* = 7.54 Hz; α-C=OCH_2CH$_3$) 2.23, 2.35 (dd, dd, 2H, 2H, *J* = 7.54 Hz; *β*-C=OCH_2CH$_3$), 1.11, 1.17 (t, t, 3H, 3H; α-C=OCH$_2$CH_3), 1.08, 1.13 (t, t, 3H, 3H; *β*-C=OCH$_2$CH_3). ^{13}C-NMR: *δ* 101.4 (α-C-1), 101.4 (*β*-C-1), 8.89, 9.0 (α-C=OCH$_2$CH_3), 8.75, 9.10 (*β*-C=OCH$_2$CH_3), 27.3, 27.6 (α-C=OCH_2CH$_3$), 172.5, 27.5 (*β*-C=OCH_2CH$_3$), 173.1 (α-C=O), 172.8 (*β*-C=O).

1,2-Di-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (8). Acetylation of compound **5** (0.5 g, 1.4 mM) with acetic anhydride (3 mL) by the same manner as described for propionylation of compound **5**. Compound **8** was purified on a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/4, v/v) to give a colorless syrup (617.3 mg, 100% yield): $[\alpha]_D^{25}$ +68.4° (*c* = 1, in chloroform). ^{1}H-NMR (300 MHz, $CDCl_3$): *δ* 5.08 (dd, 1H, $J_{2,3}$ = 9.65 Hz; C_2−H), 6.28 (d, 1H, $J_{1,2}$ = 3.88 Hz; C_1−H), 4.71, 4.91 (d, d, 1H, 1H, respectively, *J* = 11.9 Hz; C$H_2C_6H_5$), 5.60 (s, 1H; CHC_6H_5), 2.02, 2.15 (s, s, 3H, 3H; C=OCH$_3$). ^{13}C-NMR: *δ* 101.4 (C-1), 64.9, 68.6, 71.2, 74.7, 75.9, 81.5, 90.0 (C-2, C-3, C-4, C-5, C-6, C$H_2C_6H_5$, CHC_6H_5), 20.6, 20.9 (C=OCH$_3$), 137.1, 138.3, 126.0−129.0 (aromatic), 169.0, 169.8 (C=O).

1,2-Di-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-D-glucopyranoside (9). Benzoylation of compound **5** (0.5 g, 1.4 mM) with benzoyl chloride (0.49 mL, 4.2 mM) was performed in the same manner as described for propionylation of compound **5**. The reaction mixture was worked-up by the standard method to afford a yellow syrup. Compound **9** was purified on a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/4, v/v) to give colorless syrup (766.8 mg, 97% yield). Compound **9** gave a mixture of α- and *β*-anomers: $[\alpha]_D^{25}$ +87.9° (*c* = 3, in chloroform). ^{1}H-NMR (300 MHz, $CDCl_3$): *δ* 6.65 (d, 1H, $J_{1,2}$ = 3.81 Hz; α-C_1−H), 6.06 (d, 1H, $J_{1,2}$ = 8.06 Hz; *β*-C_1−H), 5.46 (dd, 1H, $J_{2,3}$ = 9.68 Hz; α-C_2−H), 5.62 (t, 1H, $J_{2,3}$ = 5.62 Hz; *β*-C_2−H), 4.81, 4.94 (d, d, 1H,

1H, respectively, J = 11.8 Hz; α-CH_2C$_6$H$_5$), 4.75, 4.87 (d, d, 1H, 1H, respectively, J = 12.0 Hz; β-CH_2CH$_5$), 5.67 (s, 1H; α-CHC$_6$H$_5$), 5.64 (s, 1H; β-CHC$_6$H$_5$). ^{13}C-NMR: δ 101.4 (a-C-1), 101.5 (β-C-1), 164.5, 165.4 (α-C═O), 164.8, 165.1 (β-C═O).

1,2-Di-*O*-propionyl-3,6-di-*O*-benzyl-D-glucopyranoside (11). To a solution of compound **7** (544.8 mg, 1.16 mM) in acetonitrile (6 mL) were added powdered molecular sieves 4 Å (500 mg) and sodium cyanoborohydride (383.7 mg, 5.8 mM). Trimethylchlorosilane (1.47 mL, 11.6 mM) was added dropwise over a period of 4 h to the reaction mixture. The reaction mixture was kept at room temperature for 30 min and filtered by the use of Celite 535, and the residue was washed with ethyl acetate. The combined filtrate and washing was worked-up by the standard method to afford yellow syrup. Compound **11** was purified on a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/4, v/v) to give a colorless syrup (459.6 mg, 84% yield): $[\alpha]_D^{25}$ +46.8° (c = 2, in chloroform). ^{1}H-MMR (300 MHz, CDCl$_3$): δ 6.33 (d, 1H, $J_{1,2}$ = 3.63 Hz; C$_1$−H), 5.01 (dd, 1H, $J_{2,3}$ = 9.65 Hz, C$_2$−H), 4.71, 4.91 (d, d, 1H, 1H, respectively, J = 11.9 Hz; CH_2C$_6$H$_5$), 2.18, 2.35 (dd, dd, 2H, 2H, J = 7.54 Hz; C═OCH_2H$_3$) 1.03, 1.13 (t, t, 3H, 3H; C═OCH$_2$CH_3). ^{13}C-NMR: δ 89.4 (C-1), 68.1, 70.4, 71.3, 72.7, 73.3, 74.6, 78.9 (C-2, C-3, C-4, C-5, C-6, CH$_3$C$_6$H$_5$), 8.55, 8.74 (C═OCH$_2$$CH_3$), 27.0, 27.3 (C═O$CH_2CH_3$), 137.5, 138.1, 127.2−128.1 (aromatic), 172.2, 172.9 (C═O).

1,2-Di-*O*-acetyl-3,6-di-*O*-benzyl-α-D-glucopyranoside (12). Reductive cleavage of the benzylidene acetal of compound **8** (617.3 mg, 1.4 mM) as described for the preparation of compound **11**, and then purification by a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/4, v/v) of the products gave a colorless syrup of compound **12** (558 mg, 90% yield): $[\alpha]_D^{25}$ +58.3° (c = 1, in chloroform). ^{1}H-NMR (300 MHz, CDCl$_3$): δ 6.28 (d, 1H, $J_{1,2}$ = 3.66 Hz; C$_1$−H), 5.00 (dd, 1H, $J_{2,3}$ = 9.81 Hz, C$_2$−H), 3.68−3.83 (5H, C$_3$−H, C$_4$−H, C$_5$−H, C$_6$−H$_{a,b}$), 4.53, 4.60 (d, d, 1H, 1H, respectively, J = 12.1 Hz; CH_2C$_6$H$_5$), 1.97, 2.13 (s, s, 3H, 3H, C═OCH$_3$). ^{13}C-NMR: δ 89.8 (C-1), 69.6, 71.1, 71.5, 72.5, 73.7, 75.0, 79.2 (C-2, C-3, C-4, C-5, C-6, CH$_2$C$_6$H$_5$), 20.62, 20.98 (C═OCH$_3$), 137.6, 138.4, 127.5−128.5 (aromatic), 169.1, 169.8 (C═O).

1,2-Di-*O*-benzoyl-3,6-di-*O*-benzyl-D-glucopyranoside (13). Reductive cleavage of the benzylidene acetal of compound **9** (766.8 mg, 1.35 mM), as described for the preparation of compound **11**, and then purification by a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/4, v/v) of the products gave a colorless syrup of compound **13** (761.8 mg, 99% yield): $[\alpha]_D^{25}$ +63.2° (c = 1, in chloroform). ^{1}H-NMR (300 MHz, CDCl$_3$): δ 5.41 (dd, 1H, $J_{2,3}$ = 9.91 Hz; α-C$_2$−H), 6.68 (d, 1H, $J_{1,2}$ = 3.63 Hz; α-C$_1$−H), 4.81, 4.94 (d, d, 1H, 1H, respectively, J = 11.8 Hz; α-CH_2C$_6$H$_5$), 5.58 (dd, 1H, $J_{2,3}$ = 9.28 Hz; β-C$_2$−H), 5.99 (d, $J_{1,2}$ = 8.25 Hz; β-C$_1$−H), 4.36, 4.53, 4.60, 4.61 (d, d, d, d, 1H, 1H, 1H, 1H, respectively, J = 12.0 Hz; α,β-CH_2C$_6$H$_5$), 7.17−7.49, 7.89−8.04 (20H; α,β-aromatic). ^{13}C-NMR: δ 90.6 (α-C-1), 92.8 (β-C-1), 164.4, 164.9, 165.2, 165.4 (α,β-C═O).

3,6-Di-*O*-benzyl-2-*O*-propionyl-D-glucopyranose (15). To a solution of compound **11** (459.6 mg, 0.97 mM) in tetrahydrofuran (4 mL) was added hydrazine hydrate (*ca*. 90%, 52.3 mL, 0.97 mM) at room temperature. After 5 h, the reaction mixture was diluted with ethyl acetate, washed with H_2O and brine, dried over Na_2SO_4, and the solvent evaporated off *in vacuo*. Compound **15** was purified by PTLC (1/1, v/v, ethyl acetate/*n*-hexane) to afford a colorless oil (314.4 mg, 78% yield): $[\alpha]_D^{25}$ +34.4° (c = 1, in chloroform). ^{1}H-NMR (300 MHz, CDCl$_3$): δ 5.40 (d, 1H, $J_{1,2}$ = 3.48 Hz; C$_1$−H), 4.83 (dd, 1H, $J_{2,3}$ = 9.89 Hz; C$_2$−H), 4.54, 4.59, 4.72, 4.81 (d, d, d, d, 1H, 1H, 1H, 1H, respectively, J = 12.2 Hz, 11.7 Hz; CH_2C$_6$H$_5$), 1.13 (t, 3H, J = 7.45 Hz; C═OCH$_2$CH_3), 2.34 (dd, 2H; C═OCH_2-CH$_3$). ^{13}C-NMR: δ 95.9 (C-1), 70.0, 71.4, 73.5, 73.7, 75.1, 79.3, 90.6 (C-2, C-3, C-4, C-5, C-6, CH$_2$C$_6$H$_5$), 9.0 (C═OCH$_2$CH$_3$), 27.5 (C═OCH$_2$CH$_3$), 137.7, 138.5, 127.7−128.6 (aromatic), 173.7 (C═O).

3,6-Di-*O*-benzyl-2-*O*-acetyl-D-glucopyranose (16). The products were obtained from compound **12** (558 mg, 1.26 mM) by the same manner as described for the preparation of compound **15**. Compound **16** was purified by PTLC (1/1, v/v, ethyl acetate/*n*-hexane) to afford a colorless oil (495 mg, 98% yield): $[\alpha]_D^{25}$ +27.0° (c = 1, in chloroform). ^{1}H-NMR (300 MHz, CDCl$_3$): δ 5.40 (d, 1H, $J_{1,2}$ = 3.12 Hz; C$_1$−H), 4.79 (m, 1H, $J_{2,3}$ = 10.6 Hz; C$_2$−H), 4.51, 4.56, 4.72, 4.79 (d, d, d, d, 1H, 1H, 1H, 1H, respectively, J = 12.2 Hz, 11.7 Hz; CH_2C$_6$H$_5$), 2.02 (s, 3H; C═OCH_3). ^{13}C-NMR: δ 95.6 (C-1), 69.9, 71.3, 73.5, 74.9, 79.3, 82.0, 90.4 (C-2, C-3, C-4, C-5, C-6, CH$_2$C$_6$H$_5$), 20.89 (C═OCH$_3$), 138.5, 137.7, 127.6−128.7 (aromatic), 170.3 (C═O).

3,6-Di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranose (17). The products were obtained from compound **13** (761.8 mg, 1.34 mM) by the same manner as described for the preparation of compound **15**. Compound **17** was purified by PTLC (1/2, v/v, ethyl acetate/*n*-hexane) to afford a colorless oil (435.6 mg, 70% yield): $[\alpha]_D^{25}$ +74.6° (c = 1, in chloroform). ^{1}H-NMR (300 MHz, CDCl$_3$): δ 5.49 (d, 1H, $J_{1,2}$ = 3.63 Hz; C$_1$−H), 5.05 (dd, 1H, $J_{2,3}$ = 9.95 Hz; C$_2$−H), 4.50, 4.56, 4.71, 4.82 (d, d, d, d, 1H, 1H, 1H, 1H, respectively, J = 12.1 Hz, 11.4 Hz; CH_2C$_6$H$_5$). ^{13}C-NMR: δ = 95.8 (C-1), 69.9, 71.4, 73.6, 74.0, 75.1, 79.3, 90.5 (C-2, C-3, C-4, C-5, C-6, CH$_2$C$_6$H$_5$), 137.6, 138.2, 133.2, 127.8−129.8 (aromatic), 165.9 (C═O).

3,6-Di-*O*-benzyl-α-D-glucopyranose 1,2,4-Orthopropionate (2). Compound **15** (314.4 mg, 0.76 mM) was dissolved in benzene (80 mL), and then *N*,*N*′-carbonyldiimidazole (128.2 mg, 0.78 mM) was added. The solution was stirred at reflux temperature for 31 h. 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 (1/2, v/v) to give a colorless syrup (171.5 mg, 57% yield): $[\alpha]_D^{25}$ +20.9° (c = 1, in chloroform). ^{1}H-NMR (300 MHz, CDCl$_3$): δ 1.0 (3H, CH$_2$CH_3), 1.26 (2H, CH_2CH$_3$), 3.72 (dd, 1H, J_{gem} = 9.68 Hz, $J_{5,6a}$ = 7.51 Hz; C$_6$−H$_a$), 3.81 (dd, 1H, $J_{5,6b}$ = 6.51 Hz; C$_6$−H$_b$), 3.96 (dt, 1H, $J_{4,5}$ = 0 Hz; C$_4$−H), 4.27 (dd, 1H, $J_{3,4}$ = 4.63 Hz; C$_3$−H), 4.40 (dt, 1H, $J_{2,3}$ = 2.13 Hz, $J_{2,4}$ = 1.31 Hz; C$_2$−H), 4.60 (t, 1H; C$_5$−H), 5.78 (d, 1H, $J_{1,2}$ = 4.88 Hz; C$_1$−H), 4.48, 4.53, 4.62 (d, s, d, 1H, 2H, 1H, respectively, J = 12.0 Hz; CH_2C$_6$H$_5$), 7.26−7.32 (10H, aromatic). ^{13}C-NMR: δ 97.6 (C-1), 120.3 (CC$_2$H$_5$), 69.9, 71.3, 71.4, 71.9, 72.1, 73.2, 75.8 (C-2, C-3, C-4, C-5, C-6, CH$_2$C$_6$H$_5$), 7.64 (CCH$_2$$CH_3$), 26.9 (C$CH_2$-CH$_3$), 137.4, 138.0, 127.4−128.5 (aromatic).

3,6-Di-*O*-benzyl-α-D-glucopyranose 1,2,4-Orthoacetate (3). Orthoesterification of compound **16** (495 mg, 1.23 mM), as described for the preparation of compound **2**, and then purification by a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/1, v/v) gave a colorless syrup of compound **3** (151.3 mg, 32% yield): $[\alpha]_D^{25}$ +20.1° (c = 1, in chloroform). ^{1}H-NMR (300 MHz, CDCl$_3$): δ 1.62 (3H, CH$_3$), 3.72 (dd, 1H, J_{gem} = 9.61 Hz, $J_{5,6a}$ = 6.53 Hz; C$_6$−H$_a$), 3.80 (dd, 1H, $J_{5,6a}$ = 7.52 Hz; C$_6$−H$_b$), 3.96 (dt, 1H, $J_{4,5}$ = 0 Hz; C$_4$−H), 4.25 (dd, 1H, $J_{3,4}$ = 4.64 Hz; C$_3$−H), 4.39 (dt, 1H, $J_{2,3}$ = 2.23 Hz, $J_{2,4}$ = 0.66 Hz; C$_2$−H), 4.63 (t, 1H; C$_5$−H), 5.79 (d, 1H, $J_{1,2}$ = 4.89 Hz; C$_1$−H), 4.47, 4.53, 4.62 (d, s, d, 1H, 2H, 1H, respectively, J = 12.0 Hz; CH_2C$_6$H$_5$), 7.26−7.34 (10H, aromatic). ^{13}C-NMR: δ 97.8 (C-1), 118.9 (CCH$_3$), 20.2 (CCH$_3$), 69.9, 71.1, 71.4, 72.3, 73.2, 75.8 (C-2, C-3, C-4, C-5, C-6, CH$_2$C$_6$H$_5$), 137.3, 138.0, 127.5−128.6 (aromatic).

3,6-Di-*O*-benzyl-α-D-glucopyranose 1,2,4-Orthobenzoate (4). Orthoesterification of compound **17** (435.6 mg, 0.94 mM), as described for the preparation of compound **2**, and then purification by a silica gel column (Wakogel C-200) eluted with ethyl acetate/*n*-hexane (1/2, v/v) gave a colorless syrup of compound **4** (201 mg, 48% yield): $[\alpha]_D^{25}$ +35.8° (c = 1, in chloroform). ^{1}H-NMR (300 MHz, CDCl$_3$): δ = 3.79 (dd, 1H, J_{gem} = 9.67 Hz, $J_{5,6a}$ = 7.57 Hz; C$_6$−H$_a$), 3.86 (dd, 1H, $J_{5,6b}$ = 6.53 Hz; C$_6$−H$_b$), 4.13 (dt, 1H, $J_{4,5}$ = 0 Hz; C$_4$−H), 4.48 (dd, 1H, $J_{3,4}$ = 4.62 Hz; C$_3$−H; C$_3$−H), 4.59 (dt, 1H, $J_{2,3}$ = 2.18 Hz, $J_{2,4}$ = 1.55 Hz; C$_2$−H), 4.79 (t, 1H, C$_5$−H), 5.97 (d, 1H, $J_{1,2}$ = 4.84 Hz; C$_1$−H), 4.50, 4.58, 4.64 (d, s, d, 1H, 2H, 1H, respectively, J = 12.0 Hz; CH_2C$_6$H$_5$), 7.26−7.39 (10H; aromatic). ^{13}C-NMR: 97.8 (C-1), 117.9 (C C$_6$H$_5$), 69.8, 71.1, 72.0, 72.5, 73.1, 75.8, 77.2 (C-2, C-3, C-4, C-5, C-6, CH$_2$C$_6$H$_5$), 133.2, 133.7, 137.2, 137.9, 125.9−129.8 (aromatic).

Polymerization. All polymerizations were carried out in a high-vacuum system.[10] The monomer was dried in a polymerization ampule by evacuating for *ca*. a day. Methylene chloride was distilled from CaH_2 and degassed by freezing and

thawing three times in a high-vacuum line. The solvent was transferred under high vacuum. Triphenylcarbenium tetrafluoroborate was placed on a small glass plate in the reaction ampule with the monomer. The reaction apparatus was then separated by melting off and placed in a water bath at 20 °C. The reaction mixture was diluted with chloroform, washed with saturated aqueous $NaHCO_3$, water, and brine, dried over anhydrous sodium sulfate, and concentrated to dryness. The polymer mixture was dissolved in a small amount of chloroform. To the solution was added *n*-hexane, and then residual polymer was collected by filtration and finally dried *in vacuo*. Poly(**2**) had $[\alpha]_D^{25}$ +1.56° (c = 1, in chloroform). Anal. Calcd for $C_{368}H_{416}O_{96}$: C, 69.19; H, 6.58. Found: C, 69.23; H, 6.73. Poly(**3**) had $[\alpha]_D^{25}$ +12.9° (c = 1, in chloroform). Anal. Calcd for $C_{132}H_{144}O_{36}{\cdot}2H_2O$: C, 67.68; H, 6.36. Found: C, 67.66; H, 6.35. Poly(**4**) had $[\alpha]_D^{25}$ +11.8° (c = 1, in chloroform). Anal. Calcd for $C_{243}H_{234}O_{54}$: C, 72.63; H, 5.87. Found: C, 72.37; H, 5.96.

Conversions of Poly(2)−Poly(4) into Acetyl Poly(2)−Poly(4). To a solution of Poly(**2**) or Poly(**4**) (35 mg) in dioxane/methanol (10/1, v/v) (5 mL), 28% sodium methoxide (0.35 mL) was added. The reaction mixture was kept at room temperature for 24 h. Then, the reaction mixture was treated with Amberlyst 15 ion exchange resin for neutralization, which was then filtered off. The resin was washed with $CHCl_3$. The combined washings and filtrate were concentrated to dryness. The product was treated with acetic anhydride and pyridine at 50 °C overnight. The reaction mixture was concentrated *in vacuo*. To the concentrated mixture (36.4 mg) in THF/acetic acid (1/1, v/v) (7 mL) was added palladium hydroxide on carbon (50 mg). The reaction mixture was kept under hydrogen at room temperature for about 1 day. The reaction mixture was concentrated and treated with acetic anhydride and pyridine at 50 °C overnight. The palladium hydroxide on carbon was filtered off and washed with chloroform. The combined washings and filtrate were concentrated to dryness. The product was purified by a silica gel column (Wakogel C-200; eluent: 20% MeOH/$CHCl_3$) to give acetylated polymers (18.3 mg). Debenzylation and acetylation of Poly(**3**) (40 mg) and then purification, as described above, gave acetyl Poly(**3**) (21.6 mg). Acetyl Poly(**2**) ^{13}C-NMR: δ 100.4, 100.7 (C-1 region). Acetyl Poly(**3**) ^{13}C-NMR: δ 100.4, 100.7 (C-1 region). Acetyl Poly(**4**) ^{13}C-NMR: δ = 100.4, 100.7 (C-1 region), 169.3, 169.6, 169.7, 170.2 (C═O region), 20.5, 20.6, 20.8, (C═OCH_3 region).

Measurements. ^{1}H- 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 25 °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.

Acknowledgment. This investigation was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture of Japan (No. 07456080).

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MA961883A