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Regioselectively Modified Stereoregular Polysaccharide. 1. Polymerization of 1,6-Anhydro-3-*O*-acetyl-2,4-di-*O*-benzyl-β-D-glucopyranose and Synthesis of 2,4-Di-*O*-benzyl-(1→6)-α-D-glucopyranan

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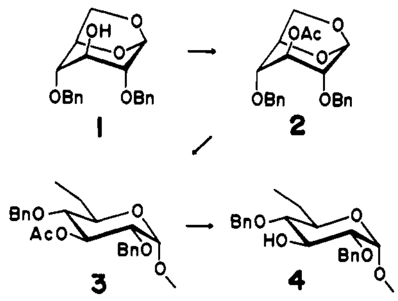
ABSTRACT: An anhydro sugar having two different blocking groups, 1,6-anhydro-3-*O*-acetyl-2,4-di-*O*-benzyl-β-D-glucopyranose, was polymerized with PF$_5$ as catalyst at temperatures ranging from 0 to −78 °C. Polymerization at −60 °C or below gave a highly stereoregular polymer. Subsequent deacetylation was successful with the use of DMF–methanol containing a small amount of sodium methoxide. Physical and spectral properties of these stereoregular, linear, polysaccharide derivatives were presented. A characteristic relationship was observed for the ^{13}C NMR chemical shifts of 1,6-anhydro-β-D-glucopyranose and the corresponding (1→6)-α-D-glucopyranan derivatives. The 2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan obtained will serve as a starting material for synthesis of new, useful polysaccharides.

Several stereoregular polysaccharides have been synthesized[1-4] and used as valuable model compounds for the investigation of the physical properties and the physiological and biochemical interactions of natural polysaccharides.[5-10] The properties and functions of polysaccharides change significantly with a slight change of the chemical structure. A well-defined modification of the polymer unit, therefore, will serve in elucidating the relation between the structure and function. One modification of interest is regio- and stereoselective introduction of functional groups and other sugar moieties onto stereoregular polysaccharides. Reactions of polysaccharides, however, are usually not regioselective because the three hydroxyl groups of a sugar unit have similar reactivities.[11,12] One of the possible procedures to avoid this difficulty involves the ring-opening polymerization of anhydro sugars, which are substituted regioselectively by two different types of blocking groups, and the subsequent reactions of the resulting polymer. We have given attention to 1,6-anhydro-2,4-di-*O*-benzyl-β-D-glucopyranose (1),[13,14] which is obtainable through the regioselective benzylation of 1,6-anhydro-2,3,4-tri-*O*-acetyl-β-D-glucopyranose. The benzyl ether substituents are typically used as removable blocking groups for synthesis of polysaccharides, but the hydroxyl group in position 3 must be substituted by an appropriate protecting group. The protecting group must not interfere with cationic polymerization but be removed easily from the resulting polymer under conditions where no debenzylation occurs.

We have attempted the polymerization of the acetylated product, 1,6-anhydro-3-*O*-acetyl-2,4-di-*O*-benzyl-β-D-glucopyranose (2). The stereoregular 3-*O*-acetyl-2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan (3) has been obtained and deacetylated to yield the regioselectively blocked polysaccharide, 2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan (4). The polysaccharide 4 has a free hydroxyl group only in position 3 of the pyranose ring. Reactions of the hydroxyl group will open a way to synthesize a variety of new stereoregular polysaccharides.

Scheme I
Stereoselective Synthesis of Regioselectively Substituted Polysaccharide



Bn, CH$_2$C$_6$H$_5$; Ac, COCH$_3$

Recently, Ito and Schuerch[15] reported the polymerization of 1,6-anhydro-2,4-di-*O*-benzyl-3-*O*-but-2-enyl-β-D-glucopyranose and the synthesis of α-(1→3)-branched dextrans through the reactions of its polymer.

Experimental Section

Characterization. NMR spectra were recorded with Japan Electro-Optic Laboratory JNM-MH-100 NMR and JNM-FX-100

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Table I
Polymerization of 1,6-Anhydro-3-*O*-acetyl-2,4-di-*O*-benzyl-β-D-glucopyranose (2)[a]

expt no.	feed, $\times 10^{-3}$ mol	catalyst, mol %	temp, °C	time, h	yield, %	$[\alpha]_D$,[b] deg	$[\eta]$[c]	α form,[d] %
A-3	1.10	9.1	0	48	43.9	84.4	0.02_2	60
A-5	1.04	9.6	−20	17	43.0	112.4	0.05_9	76
A-2	1.12	8.9	−40	24	61.0	131.7	0.10_2	93
A-1	1.16	8.6	−60	61	40.7	130.7	0.15_6	~100
A-4	1.00	10.0	−78	78	24.8	131.2	0.15_5	~100

[a] Solvent, methylene chloride 1 mL; *p*-chlorobenzenediazonium hexafluorophosphate, 29 mg. [b] Determined in chloroform (1 g/100 mL) at 25 °C. [c] Determined in chloroform at 25 °C. [d] Determined from the ^{13}C NMR spectrum.

Fourier transform NMR spectrometers on solutions in chloroform-*d* with tetramethylsilane as internal standard. IR spectra were measured as KBr disk with a JASCO IR-G grating infrared spectrophotometer. Optical rotations were determined in a JASCO DIP-4 automatic polarimeter by using a 1-dm cell. UV spectra were recorded with a JASCO UVIDEC-1 digital double-beam spectrophotometer. CD spectra were recorded on a JASCO J-40A automatic spectropolarimeter in the wavelength regions from 300 to 240 nm at room temperature. The concentration of the solution was 0.06 g/5 mL in dioxane, and the path length of the quartz cell was 0.1 cm. Gel-permeation chromatography was carried out by using a Shodex 802A (8 mm i.d. × 1000 mm) column on a Hitachi high-speed liquid chromatography Model 634A (solvent, chloroform). Vapor-pressure osmometry was carried out in benzene at 37 °C by use of a Hewlett-Packard Model 302. Viscosity was measured in chloroform in an Ubbelohde viscometer at 25 °C. TLC was carried out on Merck silica gel 60 F_{254} coated plates, and detection was effected by irradiating a UV lamp and by charring with a $CeSO_4$–3.6 N sulfuric acid mixture.

Monomer. The monomer 2 was prepared from 1,6-anhydro-2,3,4-tri-*O*-acetyl-β-D-glucopyranose[16] according to the Zemplen's procedure.[14] Tribenzyl byproduct was removed by fractional crystallization. The residual syrup was purified by chromatography over silica gel with benzene–ether (9/2 v/v) as solvent. The eluate having a single TLC spot at an R_f value of 0.57 (benzene–ether, 9/2 v/v) was collected, concentrated, and dried in a rotary evaporator under vacuum (1 mmHg) for 1 day: $[\alpha]^{24}{}_D$ −31.8° (*c* 1.0 in chloroform); $n^{25}{}_D$ 1.5428. Anal. Calcd for $C_{22}H_{24}O_6$ (mol wt 384.4): C, 68.74; H, 6.29. Found: C, 68.92; H, 6.24; mol wt 391 (VPO in benzene at 37 °C).

Polymerization. Polymerization was carried out according to the Schuerch's procedure, using high-vacuum techniques (2×10^{-5} mmHg).[17,18] The polymerization tube was allowed to stand with occasional shaking in a thermostat controlled at −78, −60, −40, −20, and 0 °C. The cold mixture of methanol and petroleum ether was added to the solution to terminate the polymerization. The precipitated polymer was centrifuged and purified by reprecipitation from its chloroform solution into petroleum ether four times. Finally, its benzene solution was freeze-dried, and a white fine powdery polymer was isolated. It was kept in a brown desiccator under vacuum.

The monomer was not detected in the purified polymer as judged by the ^{1}H and ^{13}C NMR spectra and the TLC of the polymer. On the other hand, the pure monomer was recovered from the supernatant of centrifugation as judged by its rotation ($[\alpha]^{25}{}_D$ −32.7°). The separation of the polymer and the unreacted monomer was complete. The following analysis was made on the stereoregular 3-*O*-acetyl-2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan. Anal. Calcd for $(C_{22}H_{24}O_6)_n$: C, 68.74; H, 6.29. Found: C, 69.47; H, 6.39.

Deacetylation of Stereoregular 3-*O*-Acetyl-2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan (3). After polymer 3 (0.41 g) was dissolved in 24 mL of DMF, dry methanol (20 mL) containing 14 mg of sodium methoxide was added. The solution was stirred magnetically at room temperature for 5 days. The solvents were distilled off under reduced pressure, and the residue was poured into 170 mL of methanol. The precipitated polymer (methanol insoluble fraction) was separated by centrifugation and purified by reprecipitation from chloroform solution into petroleum ether. The yield of the methanol insoluble polymer was 0.18 g (49%). The supernatant containing the methanol soluble polymer was concentrated, dissolved in 50 mL of chloroform, and washed with 30 mL of water. The chloroform solution was concentrated to dryness. A white powdery polymer was obtained by freeze-drying of its benzene solution (0.13 g, 36%).

Results and Discussion

Polymerization of 1,6-Anhydro-3-*O*-acetyl-2,4-di-*O*-benzyl-β-D-glucopyranose (2). The polymerization of monomer 2 was carried out under high vacuum with use of 10 mol % phosphorus pentafluoride as catalyst in methylene chloride solution. Table I gives the results of the polymerization at temperatures ranging from 0 to −78 °C. When the polymerization proceeded, the polymerization solution became viscous. The lower the temperature, the more viscous the solution became. The solution was pale yellow, but the color disappeared when the polymerization was terminated. After the reprecipitation procedure, the polymer was completely free of the unreacted monomer.

A white powdery polymer was obtained at all temperatures attempted. The polymer yields were in the range of 20–60%. At the higher polymerization temperature, the resulting polymer was of lower molecular weight. The molecular weight determined by vapor pressure osmometry was 3300 (DP 8.6) for the polymer prepared at −20 °C. As the polymerization temperature was lowered, the intrinsic viscosity of the resulting polymer went up. The polymer of the intrinsic viscosity of 0.10 (chloroform, 25 °C) had a molecular weight (M_n) of 1.7×10^4 ($\overline{DP}_n$, 44; $\bar{M}_w$, 3.6×10^4; $\overline{DP}_w$, 94), which was estimated from the GPC retention time–molecular weight relationship derived for standard polystyrenes. If the molecular size could be estimated from a viscosity–number average molecular weight relationship derived for corresponding 2,3,4-tri-*O*-benzyl-(1→6)-α-D-glucopyranan,[17] the viscosity number of 0.16 would correspond to the $\bar{M}_n$ value of about 2×10^4 or the $\overline{DP}_n$ value of 50.

Schuerch et al. attempted the polymerization of 1,6-anhydro-2,3,4-tri-*O*-acetyl-β-D-glucopyranose (triacetyllevoglucosan)[19] and 1,6-anhydro-2,3,4-tri-*O*-acetyl-β-D-mannopyranose (triacetyllevomannosan).[20] Both triacetyl monomers polymerized at 0 °C to yield low molecular weight and nonstereoregular polymer, but no polymerization occurred at −78 °C. Compared with them, the present monomer 2 exhibited higher polymerizability. However, in spite of the large amount of catalyst used, the polymer yield was lower than that from tribenzyllevoglucosan. Noncrystallizability of 2 may be responsible for the low yield. It may be expected that the polymer yield and the molecular weight will be enhanced if the purification and drying of the liquid monomer can be improved. Nevertheless, the following order of the polymerizability seems valid: tribenzyllevoglucosan > 2 > triacetyllevoglucosan. The intermediate reactivity of the present monomer would be understandable as follows. The probable coordination of the Lewis acid catalyst with the acetyl group may lower the catalyst efficiency and result in slow initiation. Acetyl substituents lower the nucleophilicity

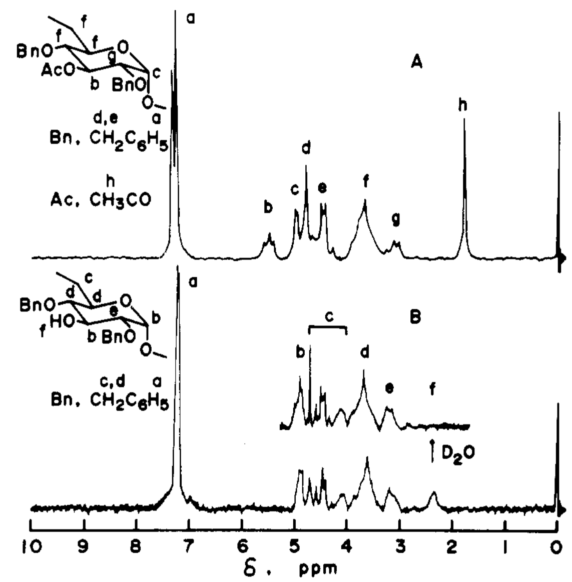


Figure 1. ^{1}H NMR spectra of 3-*O*-acetyl-2,4-di-*O*-benzyl- (3) (A) and 2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan (4) (B) in $CDCl_3$: concentration 10% (A) and 5% (B) [100 MHz].

of the acetal oxygen of the monomer as well as the reactivity of the propagating oxonium ion. Particularly, the neighboring participation of the C-2 acetate of triacetyllevoglucosan was assumed to stabilize the propagating oxonium ion.[19]

The Structure and Stereoregularity of 3-*O*-Acetyl-2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan (3). ^{1}H NMR spectra of the polymer prepared at −60 °C are shown in Figure 1. Compared with the chemical shifts of the monomer, some characteristic migrations were observed. Most remarkable were the signals due to the proton in position 3 of the pyranose ring (H-3 proton) and the anomeric proton. The H-3 signal appeared as an isolated peak of rather lower magnetic field, owing to the acetyl group. In contrast to the singlet at δ 5.08 of the monomer, the signal of 3 was δ 0.5 downfield (δ 5.54) and triplet (J = 9 Hz). The splitting was attributable to the coupling of the H-3 proton with the H-2 and H-4 protons. This coupling resulted from the conformational change from the $^1C_4$ conformation of the monomer to the $^4C_1$ conformation of the polymer. The anomeric proton was found to migrate from δ 5.42 of the monomer to δ 5.00 of the polymer. The signal of the polymer was a slightly broad singlet and assignable to the α-anomeric structure. The ^{1}H NMR spectra could not tell us if the β-anomeric structure was present in the polymer sequence or not, because the predicted chemical shift of β-anomeric proton should be overlapped with the neighboring signals.

A clear discussion on the stereoregularity of the polymer can be made on the basis of the ^{13}C NMR spectra. The spectra of polymer 3 prepared at −60 and −78 °C were simple, as shown in Figure 2. Around the region of the anomeric carbon was observed only one signal of the α-anomeric carbon at δ 97.2. The β-anomeric structure was practically absent in the polymer sequence. The polymer was highly stereoregular. That was also confirmed by the treatment of the polymer with sodium–liquid ammonia. Both deacetylation and debenzylation proceeded to give unsubstituted (1→6)-α-D-glucopyranan. The ^{13}C NMR spectrum of the product was the same as that of the debenzylation product starting from the stereoregular 2,3,4-tri-*O*-benzyl-(1→6)-α-D-glucopyranan.[21-23]

As the polymerization temperature was raised to over −60 °C, however, each peak became broad and some extra signals were detectable in the region between δ 65 and 100. Among them, the absorption at δ 100.3 was assignable to the β-anomeric carbon. The α/β anomer ratios estimated from the peak areas were 0.93:0.07 at −40 °C, 0.76:0.24 at −20 °C, and 0.60:0.40 at 0 °C. The stereoregularity of the polymer was lowered with an increase in temperature. The imperfect stereoregularity was also revealed by the optical rotations of the polymers as listed in Table I. The optical rotation was almost constant at +131 to +132° for the polymer prepared below −40 °C but decreased with increasing temperature.

The UV spectrum of 3 was comparable with that of 2,3,4-tri-*O*-benzyl-(1→6)-α-D-glucopyranan. The absorption maximum due to the phenyl group appeared at 258.4 nm in both spectra. The molar absorbance (ϵ_{max}) was proportional to the number of phenyl groups in a glucose unit: 400 for 3 and 640 for 2,3,4-tri-*O*-benzyl-(1→6)-α-D-glucopyranan. Their CD spectra in the region between 240 and 280 nm were shown in Figure 3. The spectra were well resolved, compared with those previously published.[24] Four peaks at 269, 263, 259, and 254 nm were observed for

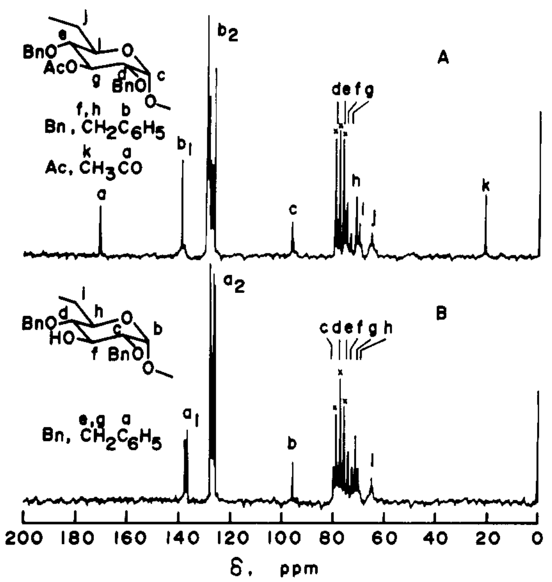


Figure 2. ^{13}C NMR spectra of 3-*O*-acetyl-2,4-di-*O*-benzyl- (3) (A) and 2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan (4) (B) in $CDCl_3$, concentration ca. 7% [25 MHz].

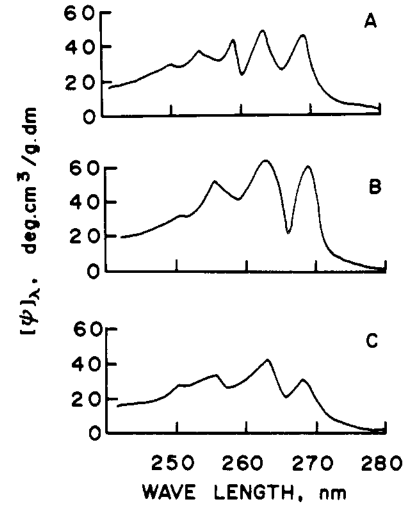
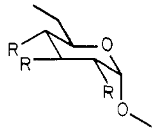


Figure 3. CD spectra of 2,3,4-tri-*O*-benzyl- (A), 3-*O*-acetyl-2,4-di-*O*-benzyl- (3) (B), and 2,4-di-*O*-benzyl-(1→6)-α-D-glucopyranan (4) (C): solvent, dioxane; path length, 1 mm; concentration 1.56 × 10^{-2} (A), 1.35 × 10^{-2} (B), and 1.86 × 10^{-2} g/mL.

Table II
^{13}C Chemical Shift Parameters (δ) of (1→6)-α-D-glucopyranan upon Replacement of the Hydroxyl Group by Benzyl and Acetyl Substituents



	R, OH → OBn	R, OH → OAc
α	8.3 ± 0.9	1.1 ± 1.1
β	0.4 ± 0.6	−1.9 ± 0.6
γ	−0.2 ± 0.4	−0.1 ± 0.8

2,3,4-tri-*O*-benzyl-(1→6)-α-D-glucopyranan (Figure 3A) and three peaks at 269, 263, and 255 nm for **3** (Figure 3B). The peak at 259 nm was absent in the spectrum of the latter polymer, suggesting that it was assignable to the benzyl group in position 3. The other peaks were assumed to arise from the benzyl groups in positions 2 and 4 and their coupling.

Stereoregular 2,4-Di-*O*-benzyl-(1→6)-α-D-glucopyranan (4). The deacetylation of stereoregular polymer **3** was carried out in a DMF–methanol mixture containing a small amount of sodium methoxide at room temperature. The reaction went essentially to completion after 5 days. Product **4** was isolated as the methanol insoluble fraction and the soluble one. The total yield was 67–99%.

The completion of deacetylation was ascertained by IR, ^1H NMR (Figure 1), and ^{13}C NMR (Figure 2) spectroscopy. Instead of the acetyl bands at 1745 and 1230 cm^{-1}, a hydroxyl stretching band appeared at 3500 cm^{-1} in the IR spectrum of **4**. Instead of the acetyl absorption of δ 1.84, a new absorption appeared at δ 2.34 in the ^1H NMR spectrum of **4**. It was assigned to the hydroxyl proton because it disappeared when a drop of heavy water was added. Figure 2 showed that the absorption at δ 170.1 and 21.2 of **3** disappeared after deacetylation. There was only one absorption at δ 96.7 in the anomeric region of ^{13}C NMR spectrum of **4**, suggesting that no configurational change occurred during the reaction. It was also supported by the high optical rotation ($[\alpha]_D$) of 138.5°. The intrinsic viscosity of the methanol-insoluble fraction in DMF was 0.16, which was higher than that of the parent polymer (0.10 in benzene). Although the increase may be attributable partly to fractionation and to different solvent, it is probable that no scission at the main chain occurred. In conclusion, complete deacetylation was achieved in high yield, without scission of the main chain and without any configurational change.

Comparison of phenyl signals in the ^1H and ^{13}C NMR spectra of **3** and **4** led to a finding. The ^1H NMR spectrum of **3** had two separated signals at δ 7.25 and 7.12, which almost degenerated to one at δ 7.44 after deacetylation. On the contrary, the ^{13}C NMR signal due to the substituted carbons of the benzene rings was observed at δ 138.2 for **3** but was separated to δ 138.6 and 138.1 for **4**. The NMR behavior could not be attributable to inductive effects of acetyl and hydroxyl groups when considered with the monomeric derivatives **1** and **2**. Both **1** and **2** had the singlet peaks at δ 7.32 in the ^1H NMR and at δ 137.7 in the ^{13}C NMR spectra. We assumed that the conformation of the polymer sequence was changed slightly by deacetylation. The following CD spectral data of **4** (cf. Figure 3C) might be evidence in support of the conformational change. The wavelengths of the ellipticity maxima (268, 262, and 256 nm) were similar to those of **3**, but the relative intensity at 268 nm became weak.

Comparison of the ^{13}C NMR Spectra between 1,6-Anhydro-β-D-glucopyranose and (1→6)-α-D-Glucopyranan Derivatives. ^{13}C NMR spectra of unsubstituted polysaccharides have been widely investigated, but little has been reported on the assignment of ^{13}C NMR spectra of substituted polysaccharides because of the chemical heterogeneity of the polysaccharides and the complexity of the spectra. Recently, Gagnaire et al.[23] reported the ^1H and ^{13}C NMR studies on stereoregular 2,3,4-tri-*O*-benzyl- and 2,3,4-tri-*O*-acetyl-(1→6)-α-D-glucopyranan. This paper encouraged us to assign the regioselectively-substituted stereoregular polysaccharides **3** and **4**. With the use of the off-resonance technique, the methylene carbon signals of the benzyl and of position 6 could be distinguished from methine carbons. The assignment of the methine carbons in the pyranose ring was attempted by applying the additivity property of substituent contributions.[25,26] The contributions of the benzyl group to α-, β-, and γ-carbons were estimated from the differences in chemical shift between unsubstituted and 2,3,4-tri-*O*-benzyl-(1→6)-α-D-glucopyranan.[23] The acetyl contributions were estimated likewise from 2,3,4-tri-*O*-

Table III
^{13}C NMR Chemical Shifts (δ) of (1→6)-α-D-Glucopyranan Derivatives

substance	C-1	C-2	C-3	C-4	C-5	C-6	CH_2 in benzyl group
(1→6)-α-D-glucopyranan[a,b]	97.9	71.5	73.5	70.0	70.4	66.2	
2,3,4-tri-*O*-benzyl-[a,c]	97.7	80.8	81.8	77.8	71.2	66.0	75.3, 74.9, 72.0
2,3,4-tri-*O*-acetyl-[a,d]	95.6	70.9	70.2	68.8	68.7	65.8	
2,4-di-*O*-benzyl- (4)[e]	96.7	79.6	73.2	77.0	70.3	65.6	74.5, 71.7
3-*O*-acetyl-2,4-di-*O*-benzyl- (3)[e]	97.2	77.7	73.2	75.7	71.0	65.0	74.5, 71.7

[a] Data by D. Gagnaire et al.[23] [b] Solvent, D_2O; internal reference, sodium 2,2,3,3-tetradeuterio-3-(trimethylsilyl)propionate (TSP); external reference, Me_4Si; 62.84 MHz. [c] Solvent, 1,1,2,2-tetrachloroethane; internal reference, Me_4Si; 62.84 MHz. [d] Solvent, $CDCl_3$; internal reference, Me_4Si; 62.84 MHz. [e] Solvent, $CDCl_3$; internal reference, Me_4Si; 25 MHz.

Table IV
^{13}C NMR Chemical Shifts (δ) of 1,6-Anhydro-β-D-glucopyranose Derivatives

substance	C-1	C-2	C-3	C-4	C-5	C-6	CH_2 in benzyl group
1,6-anhydro-β-D-glucopyranose[a]	102.2	71.8	73.4	71.2	76.9	65.8	
2,3,4-tri-*O*-benzyl-[b]	100.6	76.3	76.9	76.1	74.4	65.1	72.0, 71.7, 71.1
2,3,4-tri-*O*-acetyl-[c]	99.5	70.1[d]	69.6[d]	71.0	74.0	65.5	
2,4-di-*O*-benzyl- (1)[b]	101.1	79.6	70.4	79.4	75.0	66.3	71.9, 71.6
3-*O*-acetyl-2,4-di-*O*-benzyl- (2)[b]	100.3	74.2	68.6	74.2	74.8	64.8	71.6, 71.0

[a] Data by H. Paulsen et al.;[27] solvent, D_2O–acetone 9:1; 67.88 MHz. [b] Solvent, $CDCl_3$; internal standard, Me_4Si; 25 MHz. [c] Data by R. G. S. Ritchie et al.;[28] solvent, $CDCl_3$; 22.63 MHz. [d] Assignments may be reversed.[28]

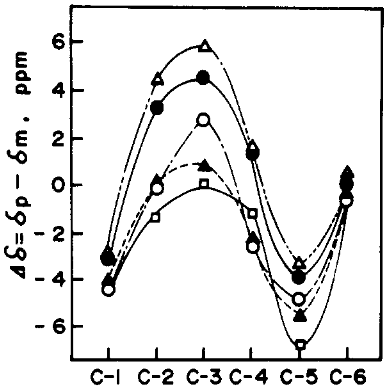


Figure 4. Differences in ^{13}C NMR chemical shifts between (1→6)-α-D-glucopyranan (δ_p) and 1,6-anhydro-β-D-glucopyranose (δ_m) derivatives: —□—, unsubstituted; —△- -, 2,3,4-tri-*O*-benzyl; - -▲- -, 2,3,4-tri-*O*-acetyl; —○- -, 2,4-di-*O*-benzyl; —●—, 3-*O*-acetyl-2,4-di-*O*-benzyl.

acetyl-(1→6)-α-D-glucopyranan.[23] The contributions, given in Table II as independent of the positions in the pyranose ring, were applied to **3** and **4**. The calculated chemical shifts agreed well with the observed ones. The assignments were summarized in Table III.

The 1,6-anhydro derivatives **1** and **2** could be assigned in the same procedure[27,28] (Table IV), but the agreements between the calculated and observed values were poor. It was impossible to obtain excellent agreement so long as parameters independent of the positions were used. Especially, the deviation of the carbon in position 3 was large. That was probably due to steric repulsion of the large substituents through 1,3 interaction on the bicyclic ring.

The differences (Δδ) in chemical shifts between the corresponding carbons of (1→6)-α-D-glucopyranan (δ_p) and 1,6-anhydro-β-D-glucopyranose (δ_m) derivatives were of interest. The Δδ values were plotted against each carbon in the pyranose ring in Figure 4. Characteristic analogous curves having a maximum at C-3 and a minimum at C-5 were given for all five pairs, regardless of substituents. The same tendency was observed even for the pair of 6,8-dioxabicyclo[3.2.1]octane and its polymer, poly(tetrahydropyran-2,6-diyloxymethylene),[29] both of which had the same frameworks as the compounds in Figure 4 but no oxy substituents. Carbon 6 showed little differences between the monomeric and polymeric forms. The upfield shift ($\Delta\delta < 0$) of the anomeric carbons was assigned to the configurational change of β to α anomers. The Δδ values for the other pyranose carbons should be attributable to the conformational change from the monomeric ($^1C_4$) to polymeric ($^4C_1$) forms. It is well known that chemical shifts of sterically perturbed carbon atoms, in general, appear at higher field than similar carbons which are not spatially crowded.[25,30] Since the substituents on the pyranose ring of the present 1,6-anhydro-β-D-glucopyranose derivatives are all axial and closely crowded, one might presume that downfield shift ($\Delta\delta > 0$) was brought about by ring opening and flipping of the pyranose ring. Actually, positive Δδ was obtained for all of the C-3 carbons and some of the C-2 and C-4 carbons. The C-5 carbons, however, showed an opposite tendency ($\Delta\delta < 0$). It is important to point out that the C-5 signals of all eight diastereoisomeric 1,6-anhydro-β-D-hexopyranoses appeared downfield of all except the C-1 signals.[27,28] Ritchie et al.[28] suggested that this downfield shift at C-5 was attributable to the bridgehead of the bicyclic structure. That would be a main factor of the characteristic negative Δδ at C-5. These tendencies in Figure 4 should serve as a tool for the ^{13}C NMR assignment of analogous compounds.

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