A Study of the Rapid Anomerization of Poly-*O*-benzyl-β-D-glucopyranosides with Titanium Tetrachloride

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Titanium tetrachloride rapidly anomerizes methyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside in dichloromethane at 25 °C. Evidence for the proposal that the benzyloxymethyl group on C-5 and the ring oxygen of the glucoside cooperate to prompt the reaction is described. The reagent anomerizes the interglycosidic linkage of several disaccharide derivatives.

The anomerization of per-*O*-acetyl-β-D-glucopyranosides,[1] as well as of per-*O*-benzoyl ones,[2] with titanium tetrachloride (**1**) is useful for preparing the corresponding α-D-glucopyranosides[3] and has been well studied.[4] In spite of this, no report about such a reaction of per-*O*-benzyl-β-D-glucopyranosides has appeared. As has been communicated, however, methyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (**2b**) was anomerized with an extraordinary rapidity into the α-anomer (**2a**) in the presence of **1** in dichloromethane at 25 °C.[5] This paper will present evidence for the mechanism previously proposed[5] in which the benzyloxymethyl group and the ring oxygen of **2b** play an important role in accelerating the reaction. The reagent was applied to the anomerization of the interglycosidic linkage of several disaccharide derivatives.

Results and Discussion

Table 1 shows the dependence of the anomerization reaction of **2b** on the molar ratio of **1** to **2b** and the time course of the reaction. The molar ratio should be greater than 0.5 to keep the efficiency of the reaction high. The equimolar amount of **1** completed the reaction within 10 s.

Table 1. Anomerization of methyl per-*O*-benzyl-β-D-glucopyranoside (**2b**) with titanium tetrachloride in dichloromethane

Mole ratio of $TiCl_4$ to the glucoside	Time/s	Content of the α-anomer/%[a]	Recovery of the glucosides/%[b]
0.2	300	42	96
0.2	3600	76	92
0.5	300	89	93
1.0	4	90	78
1.0	10	96	78
1.0	300	96	77

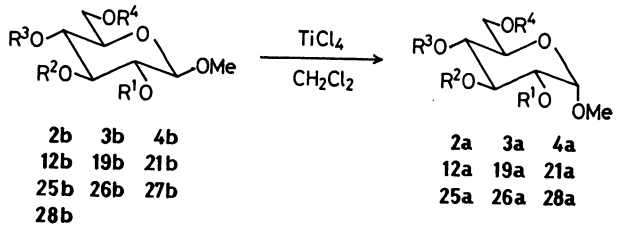
a) Mol% of α-glucoside to the sum of unchanged β-glucoside and anomerized α-one. b) Sum of yield of α-glucoside and recovery of unchanged β-one.

Interestingly, Table 2 shows that **2b** was anomerized much faster than was methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**3b**). The replacement of the acetyl group at C-6 of **3b** with a benzyl one (Compound **4b**) had remarkable accelerating effects on the reaction. However, the replacement of acetyl groups at C-2, -3, and -4 with a benzyl one (Compound **26b**) did not accelerate the reaction appreciably. Compounds **19b**, **21b**, and **25b**, all of them with a benzyloxyl group at C-6, showed fast anomerization rates.

Table 2. Effect of substituents on the anomerization[a]

Compd	R^1	R^2	R^3	R^4	Time/s	Content of the α-anomer/%[b]	Recovery of the glucosides/%[b]
2b	Bn	Bn	Bn	Bn	4	90	78
					300	96	78
3b	Ac	Ac	Ac	Ac	300	3	100
4b	Ac	Ac	Ac	Bn	4	59	88
					300	98	87
12b	Bn	Bn	Bn	Me	4	96	79
13b	Bn	Bn	Bn	—[c]	4	12	67
14b	Bn	Bn	Bn	—[d]	4	7	50
19b	Ac	Bn	Bn	Bn	300	100	67
21b	Bn	Ac	Bn	Bn	300	99	85
25b	Bn	Bn	Ac	Bn	300	100	80
26b	Bn	Bn	Bn	Ac	300	4	70
27b[e]	Bn	Bn	Ac	Ac	300	0	74
28b	Ac	Ac	Ac	Me	4	74	95

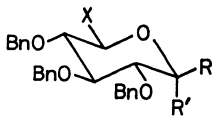
a) The mole ratio of $TiCl_4$ to the glucoside was 1.0. b) They are defined in Table 1. c) X=Me. d) X=H. e) A. P. Tulloch and A. Hill, *Can. J. Chem.*, **46**, 2485 (1968).



2b 3b 4b 12b 19b 21b 25b 26b 27b 28b

2a 3a 4a 12a 19a 21a 25a 26a 28a

	X	R	R′
13a	Me	H	OMe
13b	Me	OMe	H
14a	H	H	OMe
14b	H	OMe	H



Furthermore, the methoxyl group at C-6 considerably accelerates the reaction; the effect was even greater than that by a benzyloxyl group. This indicates that an ether group at C-6 is essential for the rapid anomerization. The slight retardation shown by **4b** and **28b** at 4 s seems to be due to electron-withdrawing acetoxyl groups, which might depress the affinity of O-5 to **1**

Table 3. Retarding effect of additives on the anomerization[a)]

Additives	Mole ratio to the glucoside, **2b**	Content of the α-anomer/%[b)]	Recovery of the glucosides/%[b)]
5	2.0	34	86
6	1.0	57	84
7	2.0	85	87
8	1.0	7	87
9	1.0	8	86
10	1.0	2	89
11	1.0	21	84

a) The mole ratio of $TiCl_4$ to the glucoside was 1.0; reactions were conducted for 4 s. b) They are defined in Table 1.

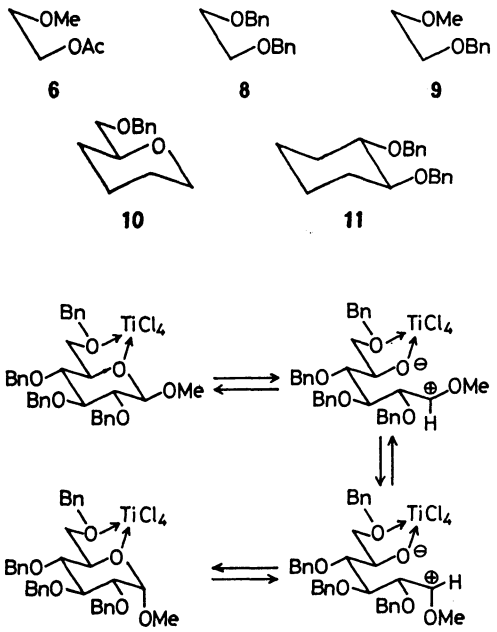


Fig. 1. A mechanism for the rapid anomerization reaction of methyl per-*O*-benzyl-β-D-glucopyranoside.

and/or the ability of C-1 to dissociate the bond between O-5 (Fig. 1).[6)]

These facts caused us to wonder if the benzyloxymethyl group in **2b** or **4b** has a special promoting function, possibly by assisting the interaction between the ring oxygen and **1**.[4a)] Additives which structurally resemble the $C_6H_5CH_2$–O–CH_2–C(5)–O(5)–moiety of **2b** are thought to compete with **2b** in capturing **1**, thus retarding the reaction. Table 3 shows how additives with benzyloxyl and/or acetoxyl group(s) in their structure retard the reaction of **2b**. Additives, such as ethyl acetate(**5**), 2-methoxyethyl acetate(**6**), and benzyl ethyl ether (**7**), did not clearly retard the anomerization of **2b**. This indicates that neither of these additives can be a ligand possessing more affinity to **1** than can **2b** Especially, the fact that **7** did not impede the reaction, while **4b** was anomerized rapidly, suggests that the benzyloxymethyl group of **4b**, and consequently of **2b**, is not fully responsible for the rapidity of the anomerization of **4b** and, hence, of **2b**. However, 1,2-bis(benzyloxy)ethane (**8**) and 1-benzyloxy-2-methoxyethane (**9**), as expected, inhibit the reaction clearly. 2-(Benzyloxymethyl)tetrahydropyran (**10**), whose structure is closely related to the pyranose ring system, hindered the reaction almost completely. This indicates that the $C_6H_5CH_2$–O–CH_2CH_2–O– moiety can effectively compete with **2b** in capturing **1**. It should also be noted that Compound **11**, in which the benzyloxyl groups are linked to the cyclohexane ring, showed a weaker inhibitory effect; this is apparently because benzyloxymethylene groups have lesser flexibility than the benzyloxymethyl one when they complex with **1**. From the things described so far there emerges the conclusion that the difunctional $C_6H_5CH_2$–O–CH_2–C(5)–O(5)– moiety of **2b** is the part which preferentially coordinates with **1**, in competition with other benzyloxyl groups, in the reaction where **1** assists the cleavage of the C(1)–O(5) bond[7,8b)] (Fig. 1). The fact that the 6-*O*-methyl glucoside derivative (**12b**) is rapidly anomerized, while the 6-deoxy one (**13b**) is not, is consistent with the above conclusion (Table 2). In this connection, it is remarkable that methyl 2,3,4-tri-*O*-benzyl-β-D-xylopyranoside (**14b**) was anomerized slower than **2b**, whereas methyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside was anomerized faster than **3b**.[8b)]

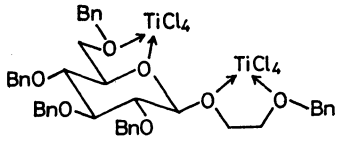
Table 4. Effect of aglycon on the anomerization

Compd	Aglycon	Time / s	Content of the α-anomer / %[a)]	Recovery of the glucosides / %[b)]
29b	Cyclohexylmethyl	4	100	80
30b	Cyclohexyl	2	100	87
31b	Benzyl	4	100	78
32b	2-Benzyloxyethyl	4	93	54
33b	3-Benzyloxypropyl	4	99	80
34b	6-Benzyloxyhexyl	4	100	76

a) The mole ratio of $TiCl_4$ to the glucoside was 1.0. b) They are defined in Table 1.

As for aglycon, **1** was even more effective for such alkyl groups as cyclohexylmethyl, cyclohexyl, and benzyl (Table 4). In some cases, no trace of β-glucoside was found in the reaction mixture.

The positional effect of the benzyloxyl group in aglycon was then studied in order to ascertain the scope of the reaction.[8a)] Table 4 shows that, when the benzyloxyl group is present at the carbon vicinal to the one which links with the glucosyloxyl residue, the efficiency of the reaction decreases and the recovery of the anomeric glucosides is seriously diminished. In this case, 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose was isolated in a fair yield after the chromatography of the reaction mixture. This seems to be produced *via* the hydrolysis of the complex (**15**). Therefore, the reaction is not suitable for anomerizing the interglycosidic linkage of per-*O*-benzylated disaccharides.



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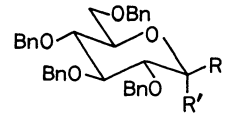
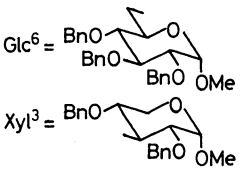
Nevertheless, the findings described so far stimulated us to try to anomerize the per-*O*-benzyl derivative of disaccharides.[3a,b] The gentiobiose derivative (**16b**) was rapidly transformed into the isomaltose one (**16a**) with **1** at room temperature. The per-*O*-benzyl derivative (**17b**) of methyl 3-*O*-(β-D-glucopyranosyl)-α-D-xylopyranoside, the aglycon monosaccharide of which has no benzyloxymethyl group, inverted the configuration of its interglycosidic linkage, though the recovery was not so high. To our knowledge, the latter is the first case of the anomerization of the interglycosidic β-linkage of a secondary hydroxyl group of disaccharide.[3a]

	R	R′
16a	H	$OGlc^6$
16b	$OGlc^6$	H
17a	H	$OXyl^3$
17b	$OXyl^3$	H
29a	H	OCm
29b	OCm	H
30a	H	OCh
30b	OCh	H
31a	H	OBn
31b	OBn	H
32a	H	$O(CH_2)_2OBn$
32b	$O(CH_2)_2OBn$	H
33a	H	$O(CH_2)_3OBn$
33b	$O(CH_2)_3OBn$	H
34a	H	$O(CH_2)_6OBn$
34b	$O(CH_2)_6OBn$	H



Bn = benzyl
Ch = cyclohexyl
Cm = cyclohexylmethyl



Experimental

The melting points were determined on an MP-1 melting point apparatus (Yanagimoto) and are uncorrected. The optical rotations were measured with a DIP-180 automatic polarimeter (Japan Spectroscopic) in a jacketed 1-dm cell at 20 °C. The ^1H NMR spectra were recorded with a Varian S-60T spectrometer, and the ^{13}C NMR spectra, with a JEOL-PS-100, using TMS as the internal standard. The refractive indexes were determined with an Abbe refractometer, Model 3 (Atago), at 20 °C. Column chromatography was carried out on silica gel (Kanto Kagaku), using an appropriate solvent system of Solvent A (benzene–2-butanone), B (hexane–ethyl acetate), or C (chloroform–methanol); each fraction was examined by means of TLC on silica gel (Merck, 7731). The dichloromethane (Wako) was distilled and stored over a molecular sieve (Linde 3A). The catalyst **1** (Wako) was distilled before use. The ethyl acetate (**5**, Wako), 2-methoxyethyl acetate (**6**, Tokyo Kasei), benzyl ethyl ether (**7**, Wako), and 1,2-bis(benzyloxy)ethane (**8**, Tokyo Kasei) were used without any pre-treatment.

General Procedure for Anomerization. The β-glucoside (0.1 mmol) was dissolved in dichloromethane (1.0 ml) in a stoppered vial, into which **1** was then injected under stirring at room temperature. The reaction was quenched by the addition of a mixture of aq sodium hydrogencarbonate (5%, 1.0 ml) and ice (≈5 g). In the case of the reaction within 4 s, an open vessel was used: dichloromethane was injected into a stoppered vial containing the β-glucoside, and then, just after the removal of the stopper, **1** was shot into the solution under efficient stirring, with care taken to avoid any bubbling. The mixture was extracted with benzene (15 ml), and the organic layer was washed with water (5 ml) and evaporated to give the product mixture, which was then chromatographed.

The additive, when necessary, was injected into the vessel before the addition of **1**.

*Preparation of β-Glucosides and Isolation of α-Glucosides Formed by Anomerization. Methyl 2,3,4,6-Tetra-O-benzyl-α-D-glucopyranoside (**2a**)*: The treatment of **2b**[9] with **1**, followed by processing and chromatography (Solvent A, 30 : 1), gave **2a** as a syrup, identified with an authentic sample.[10]

*Methyl 2,3,4-Tri-O-acetyl-6-O-benzyl-β-D-glucopyranoside (**4b**)*: A mixture of methyl β-D-glucopyranoside (1.0 g, 5.2 mmol), sodium hydride (≈50% dispersion, 0.39 g, ≈8.1 mmol), and benzyl chloride (Tokyo Kasei, 30 ml) was stirred for 1.5 h at 100 °C and then evaporated on a boiling water bath to give an oily product mixture. Column chromatography (Solvent C, gradient) and subsequent crystallization from diisopropyl ether containing ethanol gave methyl 6-*O*-benzyl-β-D-glucopyranoside (**18**, 0.28 g, 19%): mp 97—98 °C, $[\alpha]_D$ −36° (*c* 1.0, $CHCl_3$), NMR ($(CD_3)_2CO$) δ=3.51 (s, 3, CH_3O), 4.61 (s, 2, $PhCH_2$), and 7.36 (s, 5, C_6H_5). Found: C, 58.91; H, 7.08%. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09%.

The acetylation of **18** with acetic anhydride in pyridine and subsequent crystallization from diisopropyl ether gave **4b**: mp 104—105 °C, $[\alpha]_D$ −1° (*c* 0.7, $CHCl_3$): NMR (CCl_4) δ=1.84 (s, 3, CH_3CO), 1.94 (s, 3, CH_3CO), 1.98 (s, 3, CH_3CO), 3.45 (s, 3, CH_3O), 4.33 (d, 1, *J*=7.8 Hz, H-1), 4.48 (s, 2, $PhCH_2$), and 7.27 (s, 5, C_6H_5). Found: C, 58.24; H, 6.37%. Calcd for $C_{20}H_{26}O_9$: C, 58.53; H, 6.39%.

*Methyl 2,3,4-Tri-O-acetyl-6-O-benzyl-α-D-glucopyranoside (**4a**)*: The treatment of **4b** with **1**, followed by the aforementioned work-up and chromatographic separation (Solvent B, 6 : 1), gave **4a** as a syrup: $[\alpha]_D$ +131° (*c* 2.0, $CHCl_3$); NMR(CCl_4) δ=1.85 (s, 3, CH_3CO), 1.93 (s, 3, CH_3CO), 2.01 (s, 3, CH_3CO), 3.39 (s, 3, CH_3O), 3.86 (m, 1, H-5), 4.46 (s, 2, $PhCH_2$), 4.72 (dd, 1, *J*=3.5 and 9.0 Hz, H-2), 4.85 (d, 1, *J*=3.5 Hz, H-1), 4.92 (t, 1, *J*=9.0 Hz, H-4), 5.31 (t, 1, *J*=9.0 Hz, H-3), and 7.25 (s, 5, C_6H_5). Found: C, 58.48; H, 6.28%. Calcd for $C_{20}H_{26}O_9$: C, 58.53; H, 6.39%.

*Methyl 2-O-Acetyl-3,4,6-tri-O-benzyl-β-D-glucopyranoside (**19b**)*: A mixture of 3,4,6-tri-*O*-benzyl-1,2-*O*-(1-ethoxyethylidene)-α-D-glucopyranose[11] (0.88 g), methanol (68 μl), mercury(II) bromide (18 mg), and nitromethane (10 ml) was stirred for 1 h at 100 °C[12] and then evaporated after a few drops of pyridine had been added. The residue was chromatographed (Solvent B, 10 : 1), and the fractions (R_f=0.45, Solvent B, 5 : 1) were collected and crystallized from diisopropyl ether to give **19b** (0.24 g, 28%): mp 51.5—52 °C; $[\alpha]_D$ +4° (*c* 1.0, $CHCl_3$); NMR(CCl_4) δ=1.96 (s, 3, CH_3CO), 3.47 (s, 3, CH_3O), 4.32 (d, 1, *J*=8.0 Hz, H-1), 7.22—7.33 (15, $3C_6H_5$). Found: C, 70.90; H, 6.70%. Calcd for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77%.

*Methyl 2-O-Acetyl-3,4,6-tri-O-benzyl-α-D-glucopyranoside (**19a**)*: The treatment of **19b** with **1** and subsequent chromatographic separation (Solvent A, 30 : 1) gave **19a** as a syrup: $[\alpha]_D$ +83° (*c* 0.8, $CHCl_3$); NMR(CCl_4) δ=1.90 (s, 3, CH_3CO), 3.30 (s, 3, CH_3O), and 7.13—7.21 (15, $3C_6H_5$). Found: C, 70.70; H, 6.83%. Calcd for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77%.

*Methyl 3-O-Acetyl-2,4,6-tri-O-benzyl-β-D-glucopyranoside (**21b**)*: A mixture of methyl β-D-glucopyranoside hemihydrate (Tokyo Kasei, 1.02 g, 5 mmol), sodium hydride (≈60% dispersion, 0.80 g, ≈20 mmol), and benzyl chloride (10 ml) was heated under efficient stirring for 3 h at 100 °C. The mixture was processed and chromatographed (Solvent A, gradient) to afford **2b** (0.33 g, 12%, R_f=0.75, Solvent A, 10 : 1) and then methyl 2,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**20**, 0.56 g, 24%, R_f=0.45): $[\alpha]_D$ +19° (*c* 1.0, $CHCl_3$). Found: C,

72.23; H, 7.09%. Calcd for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94%.

The acetylation of **20** with acetic anhydride in pyridine and subsequent crystallization from hexane gave **21b**: mp 109.5—110 °C, $[\alpha]_D$ +18° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$) δ=1.83 (s, 3, CH_3CO), 3.56 (s, 3, CH_3O), 4.34 (d, 1, J=8.0 Hz, H-1), and 7.22—7.31 (15, $3C_6H_5$). Found: C, 71.29, H, 6.78%. Calcd for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77%.

Methyl 3-O-Acetyl-2,4,6-tri-O-benzyl-α-D-glucopyranoside (21a): The treatment of **21b** with **1** and subsequent chromatographic separation (Solvent A, 30 : 1) gave **21a**, whose ^1H NMR spectrum was identical with that of an authentic sample.[13]

Methyl 4-O-Acetyl-2,3,6-tri-O-benzyl-β-D-glucopyranoside (25b) and Methyl 6-O-Acetyl-2,3,4-tri-O-benzyl-β-D-glucopyranoside (26b): Methyl 2,3-di-*O*-benzyl-β-D-glucopyranoside[14] (**22**, 1.4 g, 3.74 mmol) was heated in benzyl chloride (14 ml) containing sodium hydride (≈50% dispersion, 0.22 g, ≈4.6 mmol) under stirring for 75 min at 75°C. The mixture was then processed and chromatographed (Solvent A, gradient) to afford **2b** (0.28 g, 13%), methyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**23**, 1.12 g, 60%, R_f=0.40, Solvent A, 10 : 1), and methyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranoside[15] (**24**, 0.34 g, 18%, R_f=0.25).

The acetylation of **23** with acetic anhydride in pyridine furnished **25b**: $[\alpha]_D$ −7° (*c* 2.0, $CHCl_3$); NMR($CDCl_3$) δ=1.73 (s, 3, CH_3CO), 3.51 (s, 3, CH_3O), 4.22 (d, 1, J=7.2 Hz, H-1), and 7.18—7.25 (15, $3C_6H_5$). Found: C, 70.41; H, 6.66%. Calcd for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77%.

The acetylation of **24** gave **26b**: mp 70—70.5 °C (from hexane); $[\alpha]_D$ +19° (*c* 1.0, $CHCl_3$) [lit,[16] mp 61—63 °C; $[\alpha]_D$ +26° ($CHCl_3$)]. Found: C, 70.91; H, 6.68%. Calcd for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77%.

Methyl 4-O-Acetyl-2,3,6-tri-O-benzyl-α-D-glucopyranoside (25a): The treatment of **25b** with **1** and subsequent chromatographic purification (Solvent A, 30 : 1) afforded 25a as a syrup: $[\alpha]_D$ +14° (*c* 2.0, $CHCl_3$); NMR(CCl_4) δ=1.74 (s, 3, CH_3CO), 3.36 (s, 3, CH_3O), and 7.21—7.26 (15, $3C_6H_5$). Found: C, 70.27; H, 6.40%. Calcd for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77%.

Methyl 6-O-Acetyl-2,3,4-tri-O-benzyl-α-D-glucopyranoside (26a): The treatment of **26b** with **1** and subsequent chromatographic separation (Solvent A, 20 : 1) gave **26a** as a syrup: $[\alpha]_D$ +28° (*c* 1.0, $CHCl_3$); NMR CCl_4) δ=1.96 (s, 3, CH_3CO), 3.34 (s, 3, CH_3O), and 7.23—7.27 (15, $3C_6H_5$). Found: C, 70.80; H, 6.79%. Calcd for $C_{30}H_{34}O_7$: C, 71.13; H, 6.77%.

Methyl 2,3,4-Tri-O-benzyl-6-O-methyl-β-D-glucopyranoside (12b): A mixture of **24** (0.41 g), methyl iodide (2.7 ml), and silver oxide (1.0 g) was vigorously stirred for 40 h at room temperature. Chromatography (Solvent A, 30 : 1) and subsequent crystallization from hexane afforded **12b** (0.31 g, 74%): mp 64—65.5 °C; $[\alpha]_D$ +5° (*c* 1.0, $CHCl_3$); NMR(CCl_4) δ=3.31 (s, 3, CH_3O), 3.48 (s, 3, CH_3O), 4.15 (d, 1, J=7.4 Hz, H-1), and 7.15—7.18 (15, $3C_6H_5$). Found: C, 72.69; H, 7.07%. Calcd for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16%.

Methyl 2,3,4-Tri-O-benzyl-6-O-methyl-α-D-glucopyranoside (12a): The treatment of **12b** with **1** and subsequent chromatographic separation (Solvent A, 30 :1) gave **12a** as a syrup: $[\alpha]_D$ +12° (*c* 2.0, $CHCl_3$) [lit,[17] $[\alpha]_D$ +8° (*c* 0.71, $CHCl_3$)]. Found: C, 72.48; H, 7.05%. Calcd for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16%.

Methyl 2,3,4-Tri-O-acetyl-6-O-methyl-β-D-glucopyranoside (28b): The hydrogenolysis of **12b** in acetic acid and methanol in the presence of palladium black at 340 kPa and subsequent acetylation with acetic anhydride and pyridine, followed by crystallization from diisopropyl ether, furnished **28b**: mp 113—113.5 °C; $[\alpha]_D$ −14° (*c* 0.4, $CHCl_3$); NMR ($CDCl_3$) δ=2.03 (s, 3, CH_3CO), 2.06 (s, 6, $2CH_3CO$), 3.40 (s, 3, CH_3O), 3.53 (s, 3, CH_3O), and 4.44 (d, 1, J=8.0 Hz, H-1). Found: C, 50.39; H, 6.75%. Calcd for $C_{14}H_{22}O_9$: C, 50.29; H, 6.63%.

Methyl 2,3,4-Tri-O-acetyl-6-O-methyl-α-D-glucopyranoside (28a): The treatment of **28b** with **1** and subsequent chromatography (Solvent B, 6 : 1) gave **28a**: mp 77.5—78.5 °C; $[\alpha]_D$ +137° (*c* 2.0, $CHCl_3$); +150° (*c* 1.0, MeOH) [lit,[18] mp 73.5—74 °C, $[\alpha]_D$ +145° (*c* 0.99, MeOH)], NMR($CDCl_3$) δ=2.00 (s, 3, CH_3CO), 2.03 (s, 3, CH_3CO), 2.07 (s, 3, CH_3CO), 3.36 (s, 3, CH_3O), and 3.42 (s, 3, CH_3O). Found: C, 50.02; H, 6.71%. Calcd for $C_{14}H_{22}O_9$: C, 50.29; H, 6.63%.

Methyl 2,3,4-Tri-O-benzyl-6-deoxy-β-D-glucopyranoside (13b): Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside[19] was benzylated with hot benzyl chloride containing powdered potassium hydroxide to afford **13b**: mp 106.5—107 °C (from hexane); $[\alpha]_D$ +8° (*c* 0.5, $CHCl_3$) [lit,[20] mp 98 °C; $[\alpha]_D$ +6.8° (*c* 0.7, $CHCl_3$)]. Found: C, 74.87; H, 7.14%. Calcd for $C_{28}H_{32}O_5$: C, 74.97; H 7.19%.

Methyl 2,3,4-Tri-O-benzyl-6-deoxy-α-D-glucopyranoside (13a): The treatment of **13b** with **1** and subsequent chromatography (Solvent A, 50 : 1) gave **13a** as a syrup: $[\alpha]_D$ +21° (*c* 0.6, $CHCl_3$) [lit,[20] $[\alpha]_D$ +20.8° (*c* 0.7, $CHCl_3$)]. Found: C, 74.01; H, 6.91%. Calcd for $C_{28}H_{32}O_5$: C, 74.97; H, 7.19%.

Methyl 2,3,4-Tri-O-benzyl-α-D-xylopyranoside (14a): The treatment of **14b**[21] with **1** and subsequent chromatography (Solvent A, 40 : 1), followed by crystallization from hexane, gave **14a**: mp 68—69 °C, $[\alpha]_D$ +16° (*c* 0.7, $CHCl_3$), +50° (*c* 0.7, CH_2Cl_2) [lit,[21] mp 61 °C; $[\alpha]_D$ +50.5° (*c* 5.22, CH_2Cl_2)]. Found: C, 74.41; H, 6.86%. Calcd for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96%.

Cyclohexylmethyl 2,3,4,6-Tetra-O-benzyl-α-D-glucopyranoside (29a): The treatment of **29b**[22] with **1** and subsequent chromatography (Solvent B, 15 : 1) gave **29a** as a syrup, identified with an authentic sample.[22]

Cyclohexyl 2,3,4,6-Tetra-O-benzyl-α-D-glucopyranoside (30a): The treatment of **30b**[10] with **1** and subsequent chromatography (Solvent B, 15 : 1) gave **30a** as a syrup, identified with an authentic sample.[10]

Benzyl 2,3,4,6-Tetra-O-benzyl-α-D-glucopyranoside (31b): The treatment of **31b**[23] with **1** and subsequent chromatography (Solvent B, 15 : 1) furnished **31a**: mp 94.5—95 °C (from hexane); $[\alpha]_D$ +53° (*c* 1.0, $CHCl_3$) [lit,[23] mp 93.5—94.5 °C; $[\alpha]_D^{28}$ +55.8° (*c* 1.63, $CHCl_3$)]. Found: C, 78.02; H, 6.70%. Calcd for $C_{41}H_{42}O_6$. C, 78.07; H, 6.71%.

2-Benzyloxyethyl, 3-Benzyloxypropyl, and 6-Benzyloxyhexyl 2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosides (32b, 33b, and 34b): A mixture of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide[24] (1.0 g, 2.4 mmol), 1,2-ethanediol (Wako, 0.27 ml), 4.8 mmol), silver oxide (1.1 g, 4.8 mmol), and benzene (10 ml) was agitated for 20 h at room temperature. The mixture was filtered, evaporated, and then chromatographed (Solvent A, 5 : 1) to afford 2-hydroxyethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[25] (0.80 g, 84%). This (0.26 g) was treated with hot benzyl chloride (5 ml) containing powdered potassium hydroxide (0.93 g) for 4 h at 100 °C. Usual work-up and chromatography (Solvent A, 30 : 1), followed by crystallization from hexane, gave **32b** (0.36 g, 81%); mp 67.5—68.5 °C; $[\alpha]_D$ +5° (*c* 1.0, $CHCl_3$). Found: C, 76.49; H, 6.88%. Calcd for $C_{43}H_{46}O_7$. C, 76.53; H, 6.87%.

The condensation of the bromide with 1,3-propanediol (Tokyo Kasei) and 1,6-hexanediol (Tokyo Kasei) afforded 3-hydroxypropyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[26] (80%) and 6-hydroxyhexyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[27] (46%) respectively. The yields were substantially improved. The subsequent benzylation of them furnished **33b** and **34b** respectively. **33b**: $[\alpha]_D$ +8° (*c* 2.8, $CHCl_3$). Found: C, 76.33; H, 6.96%. Calcd for $C_{44}H_{48}O_7$: C, 76.71; H, 7.02%. **34b**: $[\alpha]_D$ +4° (*c* 2.6, $CHCl_3$) Found: C, 76.79; H, 7.47%. Calcd for $C_{47}H_{54}O_7$: C, 77.23; H, 7.45%.

*2-Benzyloxyethyl, 3-Benzyloxypropyl, and 6-Benzyloxyhexyl 2,3,-4,6-Tetra-O-benzyl-α-D-glucopyranosides (**32a**, **33a**, and **34a**)*: The treatment of **32b**, **33b**, and **34b** with **1**, and subsequent chromatographic separation (Solvent B, 10 : 1) gave **32a**, **33a**, and **34a** respectively. **32a**: $[\alpha]_D$ +37° (*c* 0.3, $CHCl_3$). Found: C, 75.50; H, 6.61%. Calcd for $C_{43}H_{46}O_7$: C, 76.53; H, 6.87%. **33a**: $[\alpha]_D$ +42° (*c* 0.4, $CHCl_3$). Found: C, 75.85; H, 6.97%. Calcd for $C_{44}H_{48}O_7$: C, 76.71; H, 7.02%. **34a**: $[\alpha]_D$ +33° (*c* 1.0, $CHCl_3$). Found: C, 76.25; H, 7.21%. Calcd for $C_{47}H_{54}O_7$: C, 77.23; H, 7.45%.

In the case of the reaction of **32b**, 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (22%), whose IR and NMR spectra were superimposable with those of an authentic specimen,[28] was isolated on chromatography.

*Preparation of Additives. 1-Benzyloxy-2-methoxyethane (**9**)*: 2-Benzyloxyethanol (Tokyo Kasei) was methylated with methyl iodide in the presence of silver oxide to form **9**: bp 161—163 °C/123 mmHg,† n_D 1.4967 NMR(CCl_4) δ=3.33 (s, 3, CH_3O), 3.55 (s, 4, $(CH_2)_2$), 4.53 (s, 2, $PhCH_2$), and 7.25 (s, 5, C_6H_5). Found: C, 72.22; H, 8.30%. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%.

*2-(Benzyloxymethyl)tetrahydropyran (**10**)*: The benzylation of 2-(hydroxymethyl)tetrahydropyran[29] with hot benzyl chloride containing powdered potassium hydroxide afforded **10**: bp 169—172 °C/23—25 mmHg; n_D 1.5132; NMR($CDCl_3$) δ=23.2, 26.0, 28.3, 68.5, 73.4, 73.8, 76.8, 127.5, 127.7 (2C), 128.3 (2C), and 138.3. Found: C, 75.46; H, 8.82%. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79%.

trans-*1,2-Bis(benzyloxy)cyclohexane (**11**)*: The benzylation of *trans*-1,2-cyclohexanediol (Aldrich) with hot benzyl chloride and potassium hydroxide furnished **11**: bp 202—204 °C/2.5 mmHg; n_D 1.5470 [lit,[30] bp 182—183 °C/2 mmHg, n_D^{20}1.5468]; NMR(CCl_4) δ=0.93—2.23 (m, 8, $(CH_2)_4$), 3.31 (m, 2, H-1 and H-2), 4.56 (s, 4, $2PhCH_2$), and 7.21 (s, 10, $2C_6H_5$). Found: C, 81.09; H, 8.20% Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16%.

*Anomerization of Disaccharides. Anomerization of Methyl 6-O-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (**16b**) into the α-Disaccharide (**16a**)*: A solution of **16b**[31] (36.4 mg, 0.037 mmol) in dichloromethane (0.37 ml) was treated with **1** (4.1 μl 0.037 mmol). After 30 s, the reaction was quenched and the mixture was processed as usual. Subsequent chromatographic separation (Solvent A, 30 : 1) gave **16a** (16.6 mg, 46%): mp 105—106 °C; $[\alpha]_D$ +59° (*c* 1.0, $CHCl_3$) [lit,[32] mp 101.5 °C; $[\alpha]_D^{20}$ +59.3° (*c* 1.78, $CHCl_3$)]. Found: C, 75.38; H, 6.71%. Calcd for $C_{62}H_{66}O_{11}$. C, 75.43; H, 6.74%.

The slower-moving, unchanged **16b** (4.9 mg, 14%) was recovered.

*Anomerization of Methyl 3-O-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-2,4-di-O-benzyl-α-D-xylopyranoside (**17b**) into the α-Disaccharide (**17a**)*: A solution of **17b**[33] (297 mg, 0.34 mmol) in dichloromethane (3.4 ml) was treated with **1** (38 μl, 0.34 mmol). After 60 s, the reaction was quenched. The mixture was then processed and chromatographed (Solvent B, 4 : 1) to furnish **17a** (40 mg, 14%), which was identified with a sample prepared alternatively:[33] $[\alpha]_D$ +58° (*c* 1.0, $CHCl_3$); NMR($CDCl_3$) δ=96.7 (C_{glc}-1) and 97.7 (C_{xyl}-1). Found: C, 74.04; H, 6.93%. Calcd for $C_{54}H_{58}O_{10}$: C, 74.81; H, 6.94%.

The faster-moving, unchanged **17b** (42 mg, 14%) was recovered.

† 1 mmHg≈133.322 Pa.

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