Carbohydrate Research, 104 (1982) 55–67
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

THE REGIOSELECTIVITY OF THE REDUCTIVE RING-CLEAVAGE OF THE ACETAL RING OF 4,6-*O*-BENZYLIDENEHEXOPYRANOSIDES

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(Received July 20th, 1981; accepted for publication, November 11th, 1981)

ABSTRACT

The hydrogenolytic ring-cleavage of benzyl 4,6-*O*-benzylidene-β-D-glucopyranoside derivatives with $LiAlH_4$–$AlCl_3$ was investigated in relation to the bulk of the C-3 substituents (H, OMe, OEt, OPr, OBzl). In ether–dichloromethane (2:1), 4-benzyl ethers were the major products, and the ratio of the 4- and 6-benzyl ethers was strongly dependent on the steric requirement of the C-3 substituent. Hydrogenolytic ring-cleavage with various reducing agents (AlH_2Cl, AlH_2Br, AlH_2I, Bu^i_2AlH, and borane) was also studied and the best selectivity was found with AlH_2Br. The donor ability of the solvent has significant effects on the product ratios and the reaction rates in some reductions.

INTRODUCTION

The reductive ring-cleavage of carbohydrate benzylidene acetals having either 1,3-dioxane[1–5] or 1,3-dioxolane[6–10] rings proceeds with high regioselectivity to give partially benzylated derivatives, and a great number of synthetically useful derivatives have been prepared in this way. For dioxolane-type benzylidene acetals, the direction of the reaction is determined by the configuration of the acetal carbon[6–10], whereas the factors that influence the reduction of acetals of the 1,3-dioxane type are not obvious.

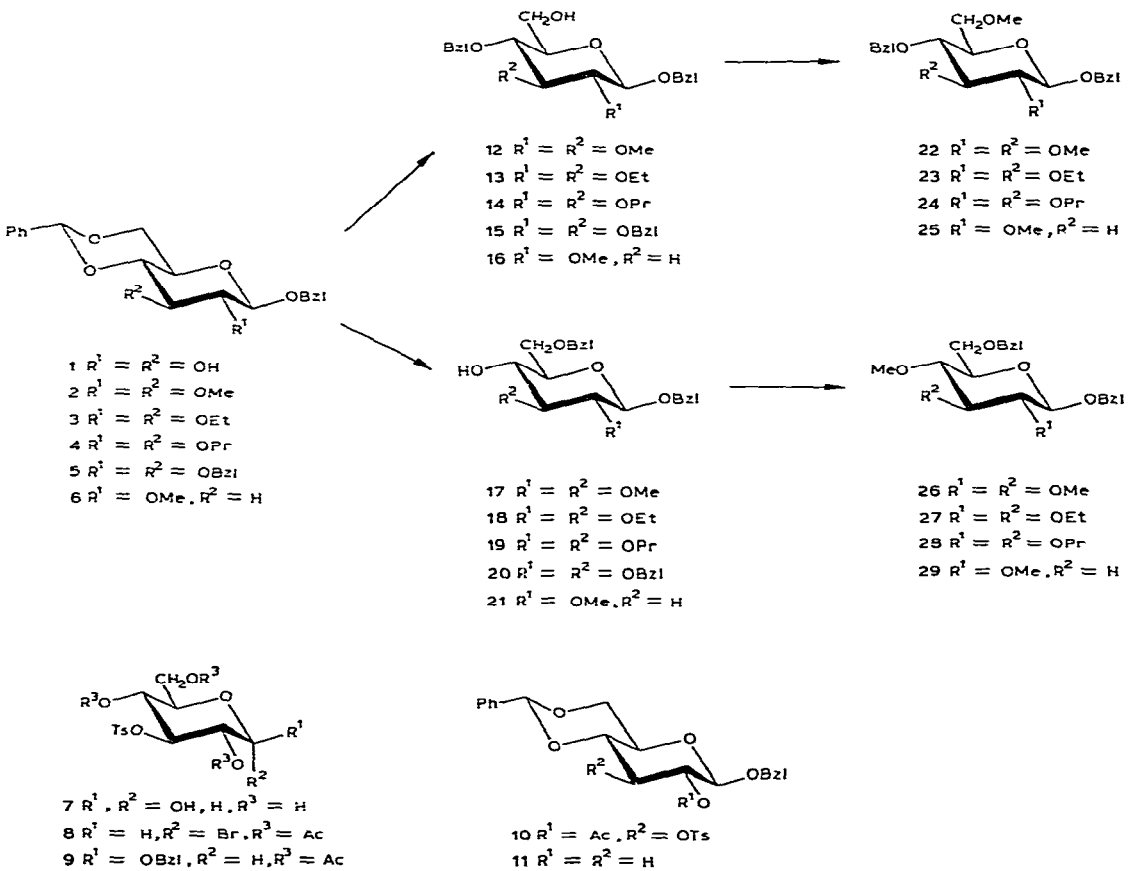
Reduction of several 4,6-*O*-benzylidene derivatives of mono-[1,2,4,5] and disaccharides[3] with $LiAlH_4$–$AlCl_3$ gave the 4-*O*-benzyl derivative as the major product in almost every case, accompanied by various amounts of the 6-benzyl ether. For example, various 4,6-*O*-benzylidene-3-*O*-methylglucopyranosides gave the 6-*O*-benzyl derivatives as by-products in yields of ~30%, but no 6-benzyl ethers were detected in the reduction of 3-*O*-benzyl-4,6-*O*-benzylideneglucopyranosides[1–3]. It was suggested[1,2] that the product ratio is determined by the bulk of the 3-substituent, *i.e.*, by the steric accessibility of the acetal oxygen atoms to the chloroalane[11] reagent.

We now describe a systematic study of the effect of the 3-substituent on the product ratios of ring cleavage, as well as the reduction of the benzylidene ring with various reducing agents.

RESULTS AND DISCUSSION

To study the effect of the bulk of the 3-substituent, a series of 3-*O*-alkyl-4,6-*O*-benzylideneglucopyranosides was required. Since 2-substituents have no influence on the product ratio of the reductive ring-cleavage, 2,3-di-*O*-alkyl-4,6-*O*-benzylidene-glucopyranosides were synthesised; these are more easily accessible than the former compounds.

Benzyl 4,6-*O*-benzylidene-β-D-glucopyranoside[12] (**1**) was alkylated by the method of Kuhn[13], to give the 2,3-di-*O*-methyl (**2**), 2,3-di-*O*-ethyl (**3**), and 2,3-di-*O*-propyl (**4**) derivatives, and benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**5**) was prepared as previously described[12]. Alternatively, these alkylations were performed by using powdered potassium hydroxide and the appropriate alkyl halide in dimethyl sulfoxide.



The compound possessing the substituent of minimum steric requirement at C-3 was benzyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-methyl-β-D-*ribo*-hexopyranoside (**6**). 2,4,6-Tri-*O*-acetyl-3-*O*-tosyl-β-D-glucopyranosyl bromide[14] (**8**), prepared from 3-*O*-tosyl-D-glucose[15] (**7**), was converted into the benzyl glucoside **9** with benzyl alcohol in the presence of mercuric oxide and mercuric bromide. Deacetylation of **9** with catalytic amounts of sodium methoxide gave a mixture of products. The reaction was stopped when the starting material had disappeared, and the crude product, when treated with benzaldehyde and zinc chloride, gave the crystalline 2-acetate-3-tosylate **10**. Reduction[16] of **10** with $LiAlH_4$ in tetrahydrofuran afforded mainly the 3-deoxy derivative **11**. Methylation of **11** then gave **6**.

Hydrogenolytic ring-cleavage of the alkylated 4,6-*O*-benzylideneglucopyranoside derivatives was performed with the $LiAlH_4$–$AlCl_3$ (1:1) reagent (using 10% excess of $LiAlH_4$, to allow for possible traces of moisture) in ether–dichloromethane (2:1) at reflux temperature. Reactions were complete within 2 h, and the position of the benzyl group in the products was determined by n.m.r. spectroscopy. For the 4-*O*-benzyl derivatives **12–16**, the signals of the hydroxyl groups were triplets because of the coupling with the methylene protons, whereas the corresponding signals for the 6-*O*-benzyl derivatives **17–21** were doublets. This multiplicity of signals was observed for solutions in deuteriochloroform or in $(CD_3)_2SO$ where the proton exchange is slow[17]. The benzyl protons of the 4-*O*-benzyl derivatives appeared as AB quartets, whereas those for the 6-*O*-benzyl derivatives appeared as singlets.

The products **12–21** were methylated to give the fully substituted derivatives **22–29**. For permethylated sugars, the methyl groups attached to primary hydroxyl groups generally resonate[18–21] at higher field than the other methyl groups. This finding was confirmed with other sugar derivatives[2,3,22] and is also valid in the present case. The only exceptions were **25** and **29**; for **25**, the methoxyl group assignable to C-6 resonated at 3.37 p.p.m., whereas, for **29**, the 4-methoxyl resonance was at 3.30 p.p.m. This anomaly may be explained by the absence of a 3-substituent.

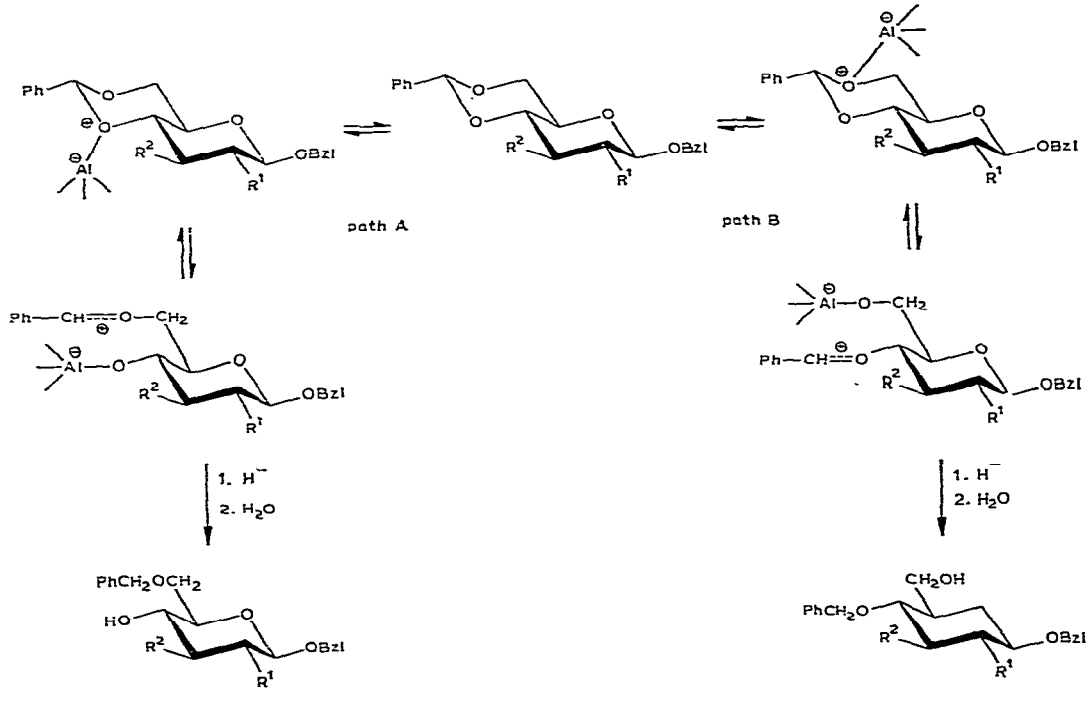
Considering the product ratios in Table I, it is evident that the bulkier the 3-substituent, the higher the proportion of the 4-benzyl ether. This increase in the regioselectivity can be explained on mechanistic grounds (Scheme 1). The first step involves complexation of the Lewis-acid chloroalane[11] with one of the acetal oxygen atoms[23]. Complex formation at O-4 (path A) is hindered by bulky 3-substituents because of steric reasons, but complexation at O-6 (path B) is not influenced by these substituents. Thus, path B will be favoured, resulting in the formation of a higher proportion of the 4-*O*-benzyl derivative. Only scattered data are available on the basicity of acetal oxygen atoms[24,25], but similar steric effects that influence the basicity of ethereal oxygen atoms towards Lewis acids are known[26] and were used to explain the product distribution of some acetal reductions[27]. It is apparent from Table I that some 6-*O*-benzyl derivative was formed even in the reduction of the 3-*O*-propyl (**4**) and 3-*O*-benzyl (**5**) derivatives. These compounds give nearly the same product ratios, indicating that the reaction does not become completely regioselective by increasing the length of the *O*-alkyl groups.

TABLE I

$LiAlH_4$–$AlCl_3$ REDUCTION OF 4,6-*O*-BENZYLIDENE-D-GLUCOPYRANOSIDES

Starting material	*3-Substituent*	*Product ratio*[a]	*Isolated yield (%) of derivative*	
			4-O-Benzyl	*6-O-Benzyl*
2	OMe	77:23	68	14
3	OEt	91:9	75	7
4	OPr	94:6	91	3
5	OBzl	93:7	91	4
6	H	53:47	43	41

[a]4-*O*-Benzyl derivative/6-*O*-benzyl derivative



Scheme 1

The above explanation is in agreement with the earlier findings[2–4] that the reductive ring-cleavage of 4,6-*O*-benzylidenegalactopyranoside derivatives always resulted in a higher proportion of 6-benzyl ethers than for the corresponding glucopyranoside derivatives, as shielding of O-4 by the 3-substituents is less effective in the former.

The polarity of substituents near the acetal oxygen atoms generally plays a definitive role in the product distribution of acetal reductions[22] by stabilising or

TABLE II

HYDROGENOLYSIS OF **2** WITH VARIOUS REDUCING AGENTS

Reagent	*Solvent*	*Temperature*[a] *(degrees)*	*Reaction time (h)*	*Product ratios* (2:12:17)	*Isolated yield* (%) 2	12	17
$LiAlH_4$–$AlCl_3$	Ether–dichloromethane (2:1)	45	2	0:77:23	—	68	14
$LiAlH_4$–$AlBr_3$	Ether–dichloromethane (2:1)	45	2	0:84:16	—	73	12
Bu^i_2AlH	Benzene	0	3	0:46:54	—	34	43
Bu^i_2AlH	Ether–dichloromethane (9:1)	45	8	0:71:29	—	68	25
Borane	Tetrahydrofuran	75	72	100:0:0	91	—	—
Borane	Benzene	90	120	32:57:11	28	46	7

[a]Bath temperature.

destabilising one of the alternative oxocarbonium ions. These effects can be neglected in comparing the 3-*O*-alkyl derivatives, but must be taken into account in comparing the reduction of the 3-deoxy derivative **6** with that of the 3-*O*-alkyl derivatives **2**–**5**.

Electron-withdrawing substituents near to an acetal oxygen atom destabilise the oxocarbonium ion, and electron-donating substituents have the opposite effect, so that cleavage occurs away from the electron donor and towards the electron-acceptor substituent[22]. Thus, reduction of a 3-*O*-alkyl derivative, in comparison with the 3-deoxy derivative, should favour path A, giving a higher ratio of the 6-benzyl ether. This was clearly not the case, so that any electron-donating or -withdrawing property of the substituents is overshadowed by the steric hindrance of complexation as a consequence of the bulk of the 3-substituents.

The reduction of a 4,6-*O*-benzylideneglucopyranoside derivative with various agents was also examined. For this purpose, compound **2** was chosen, where the steric hindrance is relatively small, so that changes in the product ratio should be maximal. The results are summarised in Table II.

Reduction with $LiAlH_4$–$AlBr_3$ (1:1), *i.e.*, by bromoalane[11], gave a higher ratio of the 4-*O*-benzyl derivative than that found with $LiAlH_4$–$AlCl_3$. This observation may be explained by the greater bulk of the reagent, although the different nature of the reagents may also have to be considered. Reductions with iodoalane generated either from $LiAlH_4$ and commercial AlI_3[11] or by the reaction of alane with iodine[28] were not conclusive, because the reactions were incomplete and significant amounts of by-products were formed.

Acetals are generally stable towards di-isobutylaluminium hydride[29], but reduction may occur[29,30] at elevated temperatures. Compound **2** was readily reduced with this reagent in benzene solution at 0°, to give a 46:54 mixture of the 4- and 6-benzyl ethers. When ether containing 10% of dichloromethane (for solubility reasons)

was used as solvent, a longer reaction time at reflux temperature was required, and a higher proportion of the 4-*O*-benzyl derivative was formed. In benzene solution, the reagent is relatively poorly solvated and behaves as a strong Lewis-acid that attacks both of the acetal oxygen atoms. On the other hand, in ether solution, the effective complexation of the solvent with the reagent results in slower reaction and increased selectivity.

Borane in tetrahydrofuran was reported to reduce acetals[31,32] and was considered to have advantages over the $LiAlH_4$–$AlCl_3$ system. However, there was no reduction during treatment of **2** for 72 h with an excess of borane in tetrahydrofuran. On performing the reaction in benzene at elevated temperature, a slow reaction took place, but, even after 120 h, much **2** was still present. The major product was the 4-benzyl ether, formed with good regioselectivity, but the low rate of this method makes it insuitable for practical purposes.

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter for solutions in chloroform. I.r. spectra were recorded for KBr pellets with a Perkin–Elmer 700 instrument. N.m.r. spectra were recorded with a JEOL MH-100 spectrometer for solutions in $CDCl_3$ (internal Me_4Si). Gas chromatography was performed on a Hewlett-Packard 5830 A instrument with a stainless-steel column (180 cm × 2 mm i.d.) coated with 3% of ECNSS-M on Gas Chrom Q (80–100 mesh). The operation conditions were injection port, 250°; flame-ionisation detector, 300°; nitrogen flow-rate, 26 ml/min; column temperature, 210° (isothermal). H.p.l.c. was performed with a Hewlett-Packard 1081 A instrument, a column (250 × 4.6 mm) of SI-100 (10 μm), and hexane–2-propanol mixtures: *A*, 99.5:0.5; *B*, 98:2, *C*, 96:4.

Processed solutions were dried with sodium sulfate, and evaporations were conducted *in vacuo* with the bath temperature below 40°. Short-column chromatography was performed on Kieselgel G. T.l.c. was carried out with precoated plates of Kieselgel 60 F_{254} (Merck) with *D*, benzene–methanol (96:4); *E*, chloroform–methanol (9:1); *F*, light petroleum–ethyl acetate (3:1); *G*, dichloromethane–acetone (19:1). Detection was effected under u.v. light and by charring with 50% aqueous sulfuric acid. Light petroleum refers to the fraction having b.p. 60–80°. Glassware for the reduction reactions was dried overnight at 160° and the equipment was assembled whilst hot under dry nitrogen.

*Benzyl 4,6-*O*-benzylidene-2,3-di-*O*-methyl-β-*D*-glucopyranoside* (**2**). — To a solution of **1** (5.37 g) in dimethyl sulfoxide (20 mL) was added powdered potassium hydroxide (6.73 g, 4 equiv.) followed by methyl iodide (3.75 mL, 2 equiv.) dropwise with stirring and external cooling. The product precipitated within 5 min, and stirring was continued for 30 min. Dichloromethane (300 mL) and water (50 mL) were added, and the organic phase was separated, washed with water (4 × 50 mL), dried, and evaporated. Recrystallisation of the residue from ethyl acetate–light petroleum gave **2**

(5.57 g, 96%), m.p. 119–120° (after resolidification, the m.p. was 130–131°), $[\alpha]_D$ −71° (*c* 1), R_F 0.66 (*D*). N.m.r. data: δ 7.6–7.2 (m, 10 H, aromatic), 5.49 (s, 1 H, PhC*H*), 4.74 (q, 2 H, PhCH_2), 4.48 (d, 1 H, H-1), 4.32 (dd, 1 H, H-6*eq*), 3.8–3.0 (m, 5 H, ring protons), 3.61 and 3.59 (2 s, 6 H, 2 OCH_3).

Anal. Calc. for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.47; H, 6.82.

*Benzyl 4,6-*O*-benzylidene-2,3-di-*O*-ethyl-β-*D*-glucopyranoside* (**3**). — To a solution of **1** (5.37 g) in *N,N*-dimethylformamide (30 mL) was added ethyl iodide (9.0 mL) followed by silver oxide (9.0 g). The mixture was protected from light with aluminium foil and stirred at room temperature for 18 h. Chloroform (200 mL) was added, the mixture was filtered through Celite, and the filtrate was washed with 5% aqueous KCN (3 × 50 mL) and then with water (3 × 50 mL), dried, and evaporated. Crystallisation from ethanol afforded **3** (5.29 g, 85%), m.p. 121–122°, $[\alpha]_D$ −74° (*c* 1), R_F 0.70 (*D*). N.m.r. data: δ 7.6–7.2 (m, 10 H, aromatic), 5.49 (s, 1 H, PhC*H*), 4.74 (q, 2 H, PhCH_2), 4.48 (d, 1 H, H-1), 4.31 (dd, 1 H, H-6*eq*), 4.0–3.1 (m, 9 H, ring protons and 2 OCH_2CH$_3$), and 1.13 (t, 6 H, 2 OCH$_2$CH_3).

Anal. Calc. for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30. Found: C, 69.41; H, 7.24.

*Benzyl 4,6-*O*-benzylidene-2,3-di-*O*-propyl-β-*D*-glucopyranoside* (**4**). — Treatment of **1** (5.37 g) in dimethyl sulfoxide (20 mL) with potassium hydroxide (6.73 g) and propyl iodide (5.90 mL) for 2 h as described for **2**, followed by crystallisation of the product from ethyl acetate–light petroleum, gave **4** (6.02 g, 91%), m.p. 114–115°, $[\alpha]_D$ −72° (*c* 1), R_F 0.74 (*D*). N.m.r. data: δ 7.5–7.2 (m, 10 H, aromatic), 5.50 (s, 1 H, PhC*H*), 4.76 (q, 2 H, PhCH_2), 4.48 (d, 1 H, H-1), 4.32 (dd, 1 H, H-6*eq*), 3.9–3.1 (m, 9 H, ring protons and 2 OCH_2CH$_2$CH$_3$), 1.76–1.40 (m, 4 H, 2 OCH$_2$-CH_2CH$_3$), and 0.88 (t, 6 H, 2 OCH$_2$CH$_2$CH_3).

Anal. Calc. for $C_{26}H_{34}O_6$: C, 70.57; H, 7.74. Found: C, 70.55; H, 7.65.

*Benzyl 2,4,6-tri-*O*-acetyl-3-*O*-tosyl-β-*D*-glucopyranoside* (**9**). — Mercuric oxide (10.4 g), mercuric bromide (1 g), Drierite (10 g), calcium carbonate (10 g), and benzyl alcohol (37 mL) were stirred in dichloromethane (200 mL) for 30 min. Compound **8** (27 g) was then added and stirring was continued overnight. The mixture was filtered through Celite, insoluble material was washed with dichloromethane, and the filtrate was subjected to steam distillation. A solution of the residue in dichloromethane (200 mL) was washed with 5% aqueous potassium iodide (3 × 50 mL) and water (50 mL), dried, and evaporated. Two crystallisations of the residue from 2-propanol–chloroform afforded **9** (21.7 g, 76%), m.p. 169–170°, $[\alpha]_D$ −30° (*c* 1), R_F 0.52 (*D*). N.m.r. data: δ 7.48 (q, 4 H, tosyl), 7.4–7.2 (m, 5 H, Ph), 5.3–3.5 (m, 9 H, ring protons and PhCH_2), 2.36 (s, 3 H, tosyl CH_3), 2.03, 1.93, and 1.85 (3 s, 9 H, 3 OAc).

Anal. Calc. for $C_{26}H_{30}O_{11}S$: C, 56.72; H, 5.49. Found: C, 56.88; H, 5.61.

*Benzyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-*O*-tosyl-β-*D*-glucopyranoside* (**10**). — To a mixture of **9** (20.7 g), methanol (100 mL), and chloroform (100 mL) was added M methanolic sodium methoxide repeatedly to maintain a pH of ~9. When t.l.c. showed that **9** (R_F 0.85, solvent *E*) had been replaced by a major product (R_F 0.60), the solution was neutralised with Amberlite IR-120 (H^+) resin, filtered, and evapo-

rated. The residue was shaken overnight with freshly fused zinc chloride (12 g) and benzaldehyde (40 mL). The mixture was poured into water, the aqueous phase was decanted, and the residue was triturated with light petroleum. The resulting solid was recrystallised from dichloromethane–light petroleum, to give **10** (10.2 g, 49%), m.p. 157–158°, $[\alpha]_D$ −109° (*c* 0.9), R_F 0.69 (*D*), ν_{max} 1750 cm^{-1} (C=O). N.m.r. data: δ 7.29 (q, 4 H, tosyl), 7.4–7.2 (m, 10 H, 2 Ph), 5.35 (s, 1 H, PhC*H*), 5.16 (dd, 1 H, $J_{1,2}$ 7.7, $J_{2,3}$ 9.4 Hz, H-2), 4.90 (t, 1 H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H-3), 4.72 (q, 2 H, PhCH_2), 4.60 (d, 1 H, H-1), 4.36 (dd, 1 H, H-6*eq*), 3.9–3.3 (m, 3 H, ring protons), 2.23 (s, 3 H, tosyl CH_3), and 2.00 (s, 3 H, OAc).

Anal. Calc. for $C_{29}H_{30}O_9S$: C, 62.80; H, 5.45. Found: C, 62.88; H, 5.51.

*Benzyl 4,6-*O*-benzylidene-3-deoxy-β-*D*-ribo-hexopyranoside* (**11**). — Lithium aluminium hydride (2.0 g) was added to tetrahydrofuran (25 mL), and the mixture was boiled under reflux with stirring. After 1 h, **10** (5.54 g) was added, and stirring and boiling were continued for 7 h. Ethyl acetate and then water were added, the mixture was diluted with dichloromethane (100 mL) and filtered through Celite, and the solid was washed with dichloromethane (2 × 100 mL). The filtrate was washed with water, dried, and evaporated. Column chromatography on Kieselgel G (100 g) gave, first, **11** (2.20 g, 64%), m.p. 171–172° (from dichloromethane–light petroleum), $[\alpha]_D$ −76° (*c* 1), R_F 0.47 (*D*). N.m.r. data: δ 7.5–7.2 (m, 10 H, aromatic), 5.48 (s, 1 H, PhC*H*), 4.74 (q, 2 H, PhCH_2), 4.48 (d, 1 H, H-1), 4.33 (dd, 1 H, H-6*eq*), 3.9–3.2 (m, 4 H, ring protons), 2.48 (s, 1 H, exchangeable with deuterium, OH), 2.6–2.3 (m, 1 H, H-3*eq*), and 1.9–1.5 (m, 1 H, H-3*ax*).

Anal. Calc. for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.05; H, 6.54.

The second fraction (0.51 g, 14%) was indistinguishable from **1** (t.l.c., m.p., mixture m.p.).

*Benzyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-methyl-β-*D*-ribo-hexopyranoside* (**6**). — Compound **11** (1.71 g) was methylated as described for **2**. Recrystallisation of the product from ethyl acetate–light petroleum gave **6** (1.55 g, 87%), m.p. 135–136°, $[\alpha]_D$ −74° (*c* 0.7), R_F 0.61 (*D*). N.m.r. data: δ 7.5–7.2 (m, 10 H, aromatic), 5.50 (s, 1 H, PhC*H*), 4.78 (q, 2 H, PhCH_2), 4.50 (d, 1 H, H-1), 4.33 (dd, 1 H, H-6*eq*), 3.8–3.1 (m, 4 H, ring protons), 3.46 (s, 3 H, OMe), 2.46 (dt, 1 H, $J_{3ax,3eq} = 12$, $J_{2,3eq} = J_{3eq,4} = 4.5$ Hz, H-3*eq*), and 1.63 (dd, 1 H, $J_{2,3ax} = J_{3ax,3eq} = J_{3ax,4} = 12$ Hz, H-3*ax*).

Anal. Calc. for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.71; H, 6.82.

*Benzyl 4-*O*-benzyl-2,3-di-*O*-methyl-* (**12**) *and benzyl 6-*O*-benzyl-2,3-di-*O*-methyl-β-*D*-glucopyranoside* (**17**). — To a solution of **2** (3.67 g) in dry ether (30 mL) and dry dichloromethane (30 mL) was added lithium aluminium hydride (0.50 g) with stirring, and the mixture was heated to reflux. A solution of aluminium chloride (1.90 g) in dry ether (30 mL) was added dropwise and stirring was continued under reflux for 2 h. After cooling, ethyl acetate was added, followed by water until precipitation was complete. The mixture was diluted with ether (200 mL) and decanted, the precipitate was washed with ether (2 × 50 mL), and the combined organic phase was washed with water (3 × 50 mL), dried, and evaporated. A sample (10 mg) of

the crude product was analysed by g.l.c. after acetylation. Two components were detected having *T* 23.37 (77%) and 26.03 min (23%). The crude product was recrystallised twice from ethanol, to give **12** (2.02 g, 55%), m.p. 113–114°, $[\alpha]_D$ −26° (*c* 1.7), R_F 0.49 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.75 and 4.73 (2 q, 4 H, 2 PhCH_2), 4.38 (d, 1 H, H-1), 3.9–3.0 (m, 6 H, ring protons), 3.60 and 3.57 (2 s, 6 H, 2 OMe), and 2.40 (t, 1 H, OH).

Anal. Calc. for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26. Found: C, 67.94; H, 7.21.

Column chromatography of the mother liquors gave 0.48 g of **12** (total yield, 2.50 g, 68%). The second fraction was syrupy **17** (0.50 g, 14%), $[\alpha]_D$ −56° (*c* 2), R_F 0.36 (*D*). N.m.r. data: δ 7.4–7.1 (m, 10 H, aromatic), 4.71 (q, 2 H, PhCH_2O-1), 4.54 (s, 2 H, PhCH_2O-6), 4.34 (d, 1 H, H-1), 3.9–3.0 (m, 7 H, ring protons and OH), 3.57 and 3.54 (2 s, 6 H, 2 OMe). N.m.r. data [$(CD_3)_2SO$]: δ 5.06 (d, 1 H, exchangeable with deuterium, OH).

Anal. Found: C, 68.14; H, 7.20.

*Benzyl 4-*O*-benzyl-2,3-di-*O*-ethyl-* (**13**) *and benzyl 6-*O*-benzyl-2,3-di-*O*-ethyl-β-*D*-glucopyranoside* (**18**). — Compound **3** (4.14 g) was treated with $LiAlH_4$ (0.63 g) and $AlCl_3$ (2.00 g), as described above. G.l.c. of the acetylated, crude product showed two peaks (*T* 21.96 and 23.27) in the ratio 91:9. Two recrystallisations from ethanol gave **13** (1.92 g, 46%), m.p. 95–96°, $[\alpha]_D$ −25° (*c* 1.2), R_F 0.40 (*F*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.74 (q, 4 H, 2 PhCH_2), 4.39 (d, 1 H, H-1), 4.1–3.0 (m, 10 H, ring protons and 2 OCH_2CH_3), 2.22 (t, 1 H, OH), 1.23 and 1.20 (2 t, 6 H, 2 OCH$_2$CH_3).

Anal. Calc. for $C_{24}H_{32}O_6$: C, 69.21; H, 7.74. Found: C, 69.08; H, 7.71.

Column chromatography of the mother liquor (solvent *F*) gave 0.79 g of **13** (total yield, 2.71 g, 75%), followed by syrupy **18** (0.28 g, 7%), $[\alpha]_D$ −52° (*c* 2.5), R_F 0.35 (*F*). N.m.r. data [$(CD_3)_2SO$]: δ 7.1–6.9 (m, 10 H, aromatic), 4.59 (d, 1 H, OH), 4.54 (q, 2 H, PhCH_2O-1), 4.38 (s, 2 H, PhCH_2O-6), 4.24 (d, 1 H, H-1), 3.8–2.7 (m, 10 H, ring protons and 2 OCH_2CH_3), 1.12 and 1.10 (2 t, 6 H, 2 OCH$_2$CH_3).

Anal. Found: C, 69.05; H, 7.65.

*Benzyl 4-*O*-benzyl-2,3-di-*O*-propyl-* (**14**) *and benzyl 6-*O*-benzyl-2,3-di-*O*-propyl-β-*D*-glucopyranoside* (**19**). — Compound **4** (4.42 g) was hydrogenolysed as described above. G.l.c. of the acetylated, crude product showed two peaks (*T* 19.50 and 21.48) in the ratio 94:6. The same ratio was found by h.p.l.c. analysis of the crude product (solvent *A*). Recrystallisation from ethyl acetate–light petroleum afforded **14** (3.74 g, 84%), m.p. 86–87°, $[\alpha]_D$ −23° (*c* 1.3), R_F 0.28 (*G*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.73 (q, 4 H, 2 PhCH_2), 4.38 (d, 1 H, H-1), 4.0–3.0 (m, 10 H, ring protons and 2 OCH_2CH$_2$CH_3), 2.16 (t, 1 H, OH), 1.8–1.4 (m, 4 H, 2 OCH$_2$CH_2CH$_3$), 0.92 and 0.90 (2 t, 6 H, 2 OCH$_2$CH$_2$CH_3).

Anal. Calc. for $C_{26}H_{36}O_6$: C, 70.24; H, 8.16. Found: C, 70.37; H, 8.08.

Column chromatography of the mother liquor (solvent *G*) gave **19** (0.14 g, 3%) as a syrup, $[\alpha]_D$ −53° (*c* 0.95), R_F 0.32 (*G*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.71 (q, 2 H, PhCH_2O-1), 4.52 (s, 2 H, PhCH_2O-6), 4.34 (d, 1 H, H-1),

3.9–3.1 (m, 10 H, ring protons and 2 $OCH_2CH_2CH_3$), 2.76 (s, 1 H, OH), 1.8–1.2 (m, 4 H, 2 $OCH_2CH_2CH_3$), and 0.88 (t, 6 H, 2 $OCH_2CH_2CH_3$).

Anal. Found: C, 70.41; H, 8.17.

The second fraction was **14** (0.29 g; total yield, 4.03 g, 91%).

*Benzyl 2,3,4-tri-*O*-benzyl-* (**15**) *and benzyl 2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**20**). — Compound **5** (2.69 g) was hydrogenolysed as described above. H.p.l.c. of the crude product (solvent *B*) showed two peaks (*T*, 1.72 and 2.05) in the ratio 7:93. Recrystallisation (ethyl acetate–light petroleum) and column chromatography (solvent *D*) gave **15** (2.47 g, 91%) and **20** (0.12 g, 4%); **15** had m.p. 104–105°, $[\alpha]_D$ −10° (*c* 1.35), R_F 0.47 (*D*); lit.[2] m.p. 104–105°, $[\alpha]_D$ −11.5°; lit.[33] m.p. 105–106°, $[\alpha]_D$ −9.2°; **20** had m.p. 64–65°, $[\alpha]_D$ −41° (*c* 1), R_F 0.56 (*D*); lit.[34] m.p. 66–67°, $[\alpha]_D$ −42°; lit.[35] m.p. 66–67°, $[\alpha]_D$ −44°.

*Benzyl 4-*O*-benzyl-3-deoxy-2-*O*-methyl-* (**16**) *and benzyl 6-*O*-benzyl-3-deoxy-2-*O*-methyl-β-*D*-ribo-hexopyranoside* (**21**). — Compound **6** (1.07 g) was hydrogenolysed as described above. H.p.l.c. of the crude product (solvent *C*) gave two peaks (*T* 1.57 and 3.20) in the ratio 53:47. The products were separated by column chromatography (solvent *D*). Eluted first was **16** (0.46 g, 43%), m.p. 69–70°, $[\alpha]_D$ −11° (*c* 1.2), R_F 0.34 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.75 and 4.49 (2 q, 4 H, 2 $PhCH_2$), 4.41 (d, 1 H, H-1), 4.0–3.0 (m, 5 H, ring protons), 3.44 (s, 3 H, OMe), 2.54 (dt, 1 H, H-3*eq*), 2.04 (t, 1 H, OH), and 1.42 (dd, 1 H, H-3*ax*).

Anal. Calc. for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.32; H, 7.44.

Eluted second was syrupy **21** (0.44 g, 41%), $[\alpha]_D$ −31° (*c* 0.5), R_F 0.20 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.74 (q, 2 H, $PhCH_2$O-1), 4.54 (s, 2 H, $PhCH_2$O-6), 4.40 (d, 1 H, H-1), 3.8–3.0 (m, 6 H, ring protons and OH), 3.41 (s, 3 H, OMe), 2.32 (dt, 1 H, H-3*eq*), and 1.44 (dd, 1 H, H-3*ax*).

Anal. Found: C, 70.24; H, 7.22.

*Benzyl 4-*O*-benzyl-2,3,6-tri-*O*-methyl-β-*D*-glucopyranoside* (**22**). — Compound **12** (0.50 g) was treated conventionally with silver oxide (0.92 g) and methyl iodide (0.40 mL). Recrystallisation of the product from hexane gave **22** (0.37 g, 72%), m.p. 48–49°, $[\alpha]_D$ −35° (*c* 0.95), R_F 0.66 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.97–4.50 (2 q, 4 H, 2 $PhCH_2$), 4.32 (d, 1 H, H-1), 3.7–3.0 (m, 6 H, ring protons), 3.62 and 3.59 (2 s, 6 H, 2 OMe), and 3.37 (s, 3 H, MeO-6).

Anal. Calc. for $C_{23}H_{30}O_6$: C, 68.64; H, 7.51. Found: C, 68.41; H, 7.68.

*Benzyl 4-*O*-benzyl-2,3-di-*O*-ethyl-6-*O*-methyl-β-*D*-glucopyranoside* (**23**). — Kuhn methylation of **13** (0.60 g) gave **23** (0.58 g, 93%), m.p. 49–50°, $[\alpha]_D$ −30° (*c* 1.35), R_F 0.65 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.96–4.52 (2 q, 4 H, 2 $PhCH_2$), 4.34 (d, 1 H, H-1), 4.0–3.0 (m, 10 H, ring protons and 2 OCH_2CH_3), 3.36 (s, 3 H, MeO-6), 1.23 and 1.19 (2 t, 6 H, 2 OCH_2CH_3).

Anal. Calc. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.71; H, 7.78.

*Benzyl 4-*O*-benzyl-6-*O*-methyl-2,3-di-*O*-propyl-β-*D*-glucopyranoside* (**24**). — Compound **14** (0.89 g) in dimethyl sulfoxide (5 mL) was treated with potassium hydroxide (0.45 g) and methyl iodide (0.25 mL) for 1 h. Recrystallisation of the product from hexane yielded **24** (0.87 g, 95%), m.p. 32–33°, $[\alpha]_D$ −28° (*c* 1.1),

R_F 0.68 (*D*). N.m.r. data: δ 7.4–7.1 (m, 10 H, aromatic), 4.96–4.50 (2 q, 4 H, 2 PhCH_2), 4.32 (d, 1 H, H-1), 3.9–3.1 (m, 10 H, ring protons and 2 OCH_2CH$_2$CH$_3$), 3.35 (s, 3 H, MeO-6), 1.7–1.4 (m, 4 H, 2 OCH$_2$CH_2CH$_3$), 0.90 and 0.88 (2 t, 6 H, 2 OCH$_2$-CH$_2$CH_3).

Anal. Calc. for $C_{27}H_{38}O_6$: C, 70.71; H, 8.35. Found: C, 70.75; H, 8.32.

*Benzyl 4-O-benzyl-3-deoxy-2,6-di-O-methyl-β-*D-ribo-*hexopyranoside* (**25**). — Methylation of **16** (0.179 g) in dimethyl sulfoxide (2 mL) with potassium hydroxide (0.11 g) and methyl iodide (0.12 mL) gave syrupy **25** (0.162 g, 87%), $[\alpha]_D$ −26° (*c* 0.9), R_F 0.58 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.76 and 4.50 (2 q, 4 H, 2 PhCH_2), 4.36 (d, 1 H, H-1), 3.8–3.0 (m, 5 H, ring protons), 3.46 (s, 3 H, MeO-2), 3.37 (s, 3 H, MeO-6), 2.50 (dt, 1 H, H-3*eq*), and 1.40 (dd, 1 H, H-3*ax*).

Anal. Calc. for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58. Found: C, 71.07; H, 7.61.

*Benzyl 6-O-benzyl-2,3,4-tri-O-methyl-β-*D-*glucopyranoside* (**26**). — Kuhn methylation of **17** (0.20 g) gave syrupy **26** (0.15 g, 71%), $[\alpha]_D$ −36° (*c* 0.6), R_F 0.64 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.76 and 4.60 (2 q, 4 H, 2 PhCH_2), 4.32 (d, 1 H, H-1), 3.8–3.0 (m, 6 H, ring protons), 3.62 and 3.60 (2 s, 6 H, 2 OMe), and 3.49 (s, 3 H, MeO-4).

*Benzyl 6-O-benzyl-2,3-di-O-ethyl-4-O-methyl-β-*D-*glucopyranoside* (**27**). — Methylation of **18** (0.20 g), as described above, yielded **27** (0.20 g, 97%) as a syrup, $[\alpha]_D$ −30° (*c* 1.4), R_F 0.65 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.76 and 4.59 (2 q, 4 H, 2 PhCH_2), 4.34 (d, 1 H, H-1), 4.0–3.0 (m, 10 H, ring protons and 2 OCH_2CH$_3$), 3.49 (s, 3 H, OMe), 1.23 and 1.19 (2 t, 6 H, 2 OCH$_2$CH_3).

*Benzyl 6-O-benzyl-4-O-methyl-2,3-di-O-propyl-β-*D-*glucopyranoside* (**28**). — Methylation of **19** (0.054 g) in dimethyl sulfoxide (1 mL) with potassium hydroxide (0.1 g) and methyl iodide (0.10 mL) afforded syrupy **28** (0.048 g, 86%), $[\alpha]_D$ −33° (*c* 0.4), R_F 0.66 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.73 (q, 2 H, PhCH_2O-1), 4.57 (s, 2 H, PhCH_2O-6), 4.32 (d, 1 H, H-1), 3.9–3.1 (m, 10 H, ring protons and 2 OCH_2CH$_2$CH$_3$), 3.49 (s, 3 H, OMe), 1.8–1.4 (m, 4 H, 2 OCH$_2$CH_2CH$_3$), 0.90 and 0.87 (2 t, 6 H, 2 OCH$_2$CH$_2$CH_3).

*Benzyl 6-O-benzyl-3-deoxy-2,4-di-O-methyl-β-*D-ribo-*hexopyranoside* (**29**). — Methylation of **21** (0.183 g), as described above, gave **29** as a syrup (0.183 g, 96%), $[\alpha]_D$ −29° (*c* 1.1), R_F 0.56 (*D*). N.m.r. data: δ 7.4–7.2 (m, 10 H, aromatic), 4.81 (q, 2 H, PhCH_2O-1), 4.60 (s, 2 H, PhCH_2O-6), 4.38 (d, 1 H, H-1), 3.9–3.0 (m, 5 H, ring protons), 3.48 (s, 3 H, MeO-2), 3.30 (s, 3 H, MeO-4), 2.56 (dt, 1 H, H-3*eq*), and 1.32 (dd, 1 H, H-3*ax*).

Reduction of **2**. — (*a*) *with LiAlH$_4$–AlBr$_3$*. Compound **2** (1.93 g) was treated with LiAlH$_4$ (0.31 g) and AlBr$_3$ (2.00 g) as described for **12** and **17**. G.l.c. of the acetylated, crude product showed the same peaks in the ratio 84:16. Column chromatography (solvent *D*) gave **12** (1.41 g, 73%) and **17** (0.23 g, 12%).

(*b*) *With di-isobutylaluminum hydride*. (*i*) A solution of **2** (0.386 g) in dry benzene was stirred under dry nitrogen at 0°. A 25% solution of reductant in toluene (1.2 mL) was injected, and stirring was continued for 3 h at 0°. Water was added dropwise, the resulting gel was thoroughly stirred with methanol, filtered through Celite, and

washed with dichloromethane, and the filtrate was evaporated. G.l.c. showed **12** and **17** in the ratio 46:54. Column chromatography gave **12** (0.132 g, 34%) and **17** (0.165 g, 43%).

(*ii*) A solution of **2** (0.966 g) in ether (45 mL) and dichloromethane (5 mL) was stirred at room temperature under dry nitrogen, and a 25% solution of reductant in dry toluene (3.0 mL) was injected. After boiling under reflux for 8 h, the solution was cooled and water was added dropwise followed by dichloromethane and processing as described above. G.l.c. of the acetylated, crude product revealed **12** and **17** in the ratio 71:29. Column chromatography gave **12** (0.66 g, 68%) and **17** (0.241 g, 25%).

(*c*) *With borane.* Compound **2** (0.966 g) was stirred in dry benzene (10 mL) under nitrogen. A M solution of borane in tetrahydrofuran (10 mL) was injected, and, after 10 min, the solution was heated to 90°, ~10 mL of solvent were distilled off, and stirring under reflux was continued at this temperature. Additional amounts (5 mL) of borane solution were added after 24, 48, and 72 h, followed by distillation of the solvent. After 120 h, water (50 mL) was added, the mixture was extracted with ether (4 × 100 mL), and the combined organic phase was washed with water (2 × 50 mL), dried, and evaporated. G.l.c. of the acetylated, crude product revealed **2**, **12**, and **17** in the ratios 32:57:11. Column chromatography gave the above compounds in yields of 28, 46, and 7%, respectively.

NOTE ADDED IN PROOF (3 April, 1982)

After submission of this paper for publication, the reduction of 4,6-*O*-benzylideneglucopyranosides with $NaBH_3CN$–HCl was reported by P. J. Garegg and H. Hultberg, *Carbohydr. Res.*, 93 (1981) C10–C11.

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