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2-BROMO-2-DEOXY SUGARS AS STARTING MATERIALS FOR THE SYNTHESIS OF α- OR β-GLYCOSIDES OF 2-DEOXY SUGARS*

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ABSTRACT

3,4-Di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-α-D-gluco- (**1**) and -D-manno-pyranosyl bromide (**18**) gave, in glycosidation reactions, 1,2-*trans*-glycosides. β-D-Glycosides were formed as the main products from **1** in moderate yields, whereas **18** gave α-D-glycosides exclusively and in high yields. The 2,6-dibromo-2,6-dideoxy-β-D-glucosides were converted into the 2,6-dideoxy-β-D-glycosides by treatment with tributylstannane, and removal of the bromine atoms from 2,6-dibromo-2,6-dideoxy-α-D-mannosides to give 2,6-dideoxy-α-D-glycosides could also be effected by catalytic hydrogenolysis.

INTRODUCTION

Glycosides of 2-deoxy sugars are integral moieties of several naturally occurring products, and their synthesis is therefore of interest. Various methods through which 2-deoxy-α-glycosides can be synthesized in good yields have been described[1–3], whereas few efficient procedures are available for the preparation of the corresponding β-glycosides[4]. In order to obtain good yields of anomerically homogeneous 2-deoxyglycosides, it is advantageous to use a glycosyl halide having a substituent at C-2 helping to direct the aglycon group into the α- or β-anomeric position. This substituent should, subsequently, be readily removable. In fact, this is the principle in previous methods for the preparation of both 2-deoxy-α- and -β-glycosides[1–4]. We have previously described convenient methods for synthesizing various 2-bromo-2-deoxy- and 2,6-dibromo-2,6-dideoxyglycosyl bromides[5,6]; since a 2-bromo substituent may have a directing effect in the glycosidation reaction and can be easily removed, it became of interest to study the conversion of the aforementioned compounds into 2-deoxyglycosides.

*Dedicated to Professor Raymond U. Lemieux.

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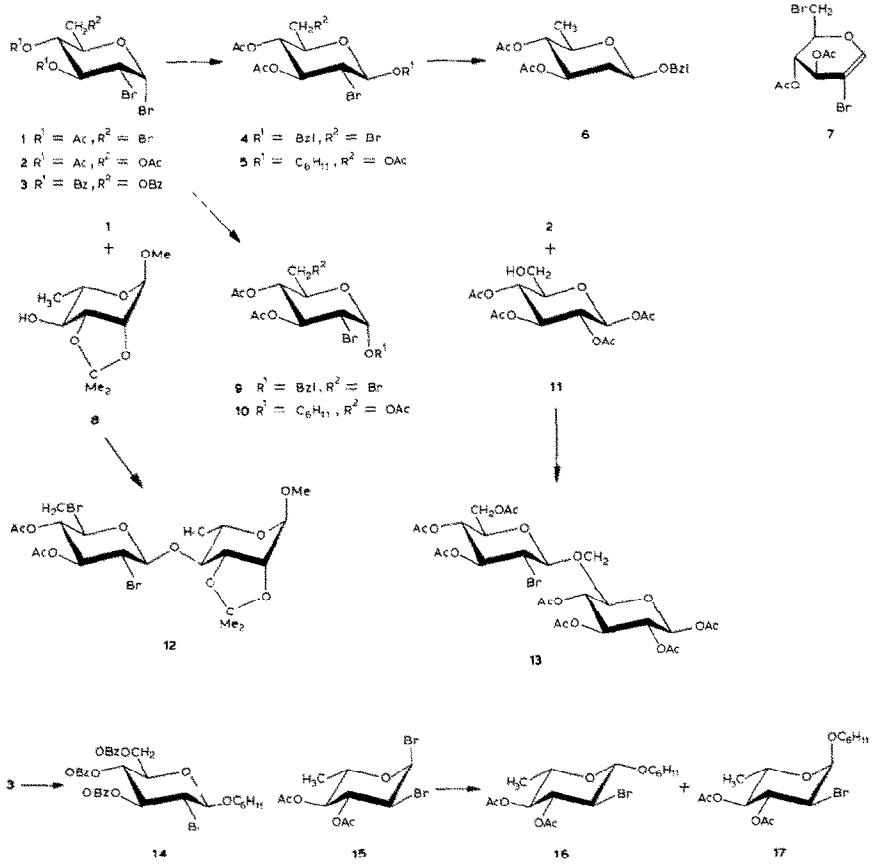
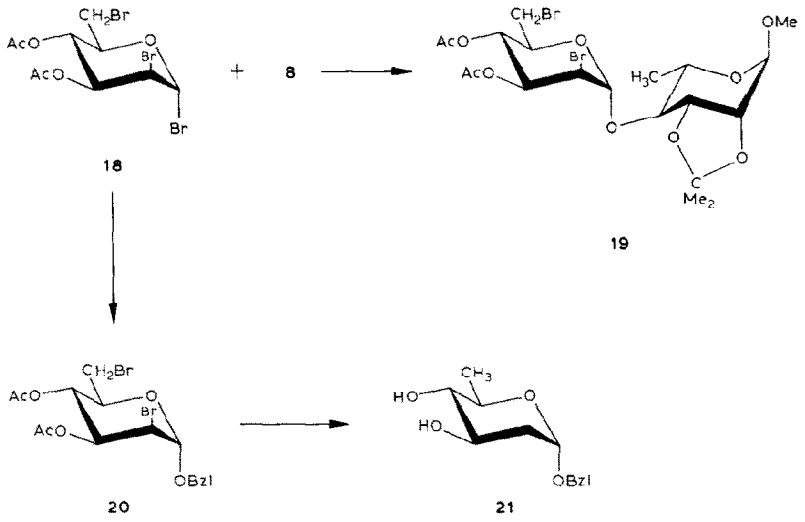
DISCUSSION AND RESULTS

The reaction of 3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-α-D-glucopyranosyl bromide (**1**) with benzyl alcohol in dichloromethane was studied with various promoters. It had been previously shown that when glycosyl bromides, devoid of an acyl group at C-2, react with alcohols, the ratio of the anomeric glycosides formed depends on the alcohol, as well as on the promoter and solvent[7]. Silver silicate, when used in dichloromethane, has been reported[7,8] to give inversion at C-1. Reaction of **1** in the presence of silver silicate gave the benzyl β-D-glycoside **4** in 47% yield; no α-D-anomer was detected. Other promoters gave mixtures of anomers; thus, when silver oxide was used, an α-to-β ratio of 1:4 was obtained. Mercury(II) iodide[9] gave a 1:2 ratio, and soluble silver triflate yielded a 1:1 mixture of anomers, accompanied by some unsaturated product **7**. Reaction of **1** with less reactive methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**8**) in dichloromethane gave, both with silver silicate and with silver triflate as promoter,





the β-D-glycoside **12** as the only glycoside, although in rather low yield. In a more polar solvent (nitromethane–toluene), a mixture of α- and β-D-anomers was obtained.

Similar condensations of 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide (**2**) with alcohols, in dichloromethane solution in the presence of silver carbonate, were carried out. With cyclohexanol, **2** gave a 4.5:1 mixture of the β- (**5**) and the α-D-glycoside (**10**), from which **5** could be crystallized in 48% yield. Reaction of **2** with 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (**11**) under the same conditions gave a product from which 37% of the (1→6)-β-D-linked disaccharide **13** could be crystallized. An analogous reaction of 3,4,6-tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide (**3**) with cyclohexanol gave a product that contained only traces of the α-D anomer; the β-D-glycoside (**14**) could be crystallized in 63% yield. Finally, treatment of 3,4-di-*O*-acetyl-2-bromo-2,6-dideoxy-α-L-glucopyranosyl bromide (**15**) with cyclohexanol, under the same conditions, gave a mixture of anomers from which the β-L anomer (**16**) was isolated in 48% yield and the corresponding α-L anomer (**17**) in 19% yield.

Hence, it may be concluded that glycosidation of the rather unreactive bromide **1** with a reactive alcohol gives a pure β-D-glycoside only when a less active promoter (silver silicate) is used in a nonpolar solvent. With a less reactive alcohol, the β selectivity is high, even with an active promoter. A similar β selectivity was found for the glycosyl bromide **2** and for its benzoylated analog **3**. Hence, these bromides may be used for the synthesis of β-glycosides if the proper conditions are selected.

Treatment of the C-2 epimeric 2,6-dibromo-2,6-dideoxy-α-D-mannopyranosyl bromide (**18**) with benzyl alcohol in dichloromethane using silver oxide or silver triflate as the promoter gave high yields of the benzyl α-D-glycoside

20. With methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**8**) as the aglycon, the α-L-glycoside **19** was the only product obtained, and when a polar solvent (nitromethane–toluene) was used, the yield was 67%; with dichloromethane only 33% of **19** was formed. The high yields obtained in these reactions indicate that the Br-2 of **18** directs the aglycon group into the α-anomeric position. Whether the corresponding bromine atom in the *gluco* isomers **1** and **2** participates in the formation of the β-D anomers, or whether the reaction takes place *via* a direct replacement at C-1 is not known.

In order to obtain 2-deoxyglycosides, it is necessary to remove the bromine atom from the bromoglycosides described earlier. Upon catalytic hydrogenolysis, followed by deacetylation the 2,6-dibromomannoside **20** gave the crystalline 2,6-dideoxy-α-D-glycoside **21** in high yield. With the *gluco* isomers (**4** and **9**), this procedure was less satisfactory since by-products were formed, and the dideoxyglycosides (**6** and **21**) could only be isolated in moderate yields. The benzyl glycosides (**4** and **9**) could, however, be reduced in high yields to the dideoxyglycosides **6** and **21**, respectively, on treatment with tributylstannane[1].

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. N.m.r. spectra were recorded with Bruker WH-90, HX-90, HX-270, and WM-400 instruments. For ^{1}H-n.m.r. spectra recorded on (^{2}H)chloroform solutions, tetramethylsilane was used as internal reference, and 1,4-dioxane (δ 67.4) for ^{13}C-n.m.r. spectra recorded on deuterium oxide solutions. Preparative t.l.c. was performed on 1-mm layers of silica gel (Merck PF_{254}), and column chromatography on silica gel 60 (40–63 Merck 9385) using the "flash" technique[10]. Microanalyses were performed by NOVO microanalytical laboratory.

Reaction of 2,6-dibromo-2,6-dideoxy-α-D-glucopyranosyl bromide (**1**) *with benzyl alcohol using different promoters. — (A) Silver silicate.* Bromide[6] **1** (200 mg, 0.44 mmol) in dry dichloromethane (3 mL) was added at −20° to a solution of benzyl alcohol (50 μL, 0.48 mmol) in dichloromethane (5 mL) containing powdered 4A molecular sieve and silver silicate[7] (400 mg). The mixture was stirred for 2 h at −20°, then filtered and evaporated. ^{1}H-N.m.r. spectrum of the residue showed only the β anomer and benzyl alcohol. Preparative t.l.c. (1:4 ethyl acetate–pentane) gave benzyl 3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-β-D-glucopyranoside (**4**, 100 mg, 47%) as a syrup, $[\alpha]_D^{20}$ +5.7° (*c* 1.5, chloroform); ^{1}H-n.m.r.: δ 4.57 (H-1), 3.82 (H-2), 5.18 (H-3), 4.83 (H-4), 3.67 (H-5), 3.53 (H-6), 3.31 (H-6′), 4.93 and 4.68 ($CH_2C_6H_5$), 2.06 and 2.02 (OAc). $J_{1,2}$ 8.5, $J_{2,3}$ 10.5, $J_{3,4}$ 9.0, $J_{4,5}$ 9.5, $J_{5,6}$ 3.0, $J_{5,6'}$ 6.5, $J_{6,6'}$ 11.0, and $J_{CH_2C_6H_5}$ 12.0 Hz.

Anal. Calc. for $C_{17}H_{20}Br_2O_6$: C, 42.52; H, 4.20; Br, 33.29. Found: C, 42.46; H, 4.22; Br, 33.22.

(B) Mercury(II) iodide. Bromide **1** (222 mg, 0.49 mmol) in dry, ethanol-free

chloroform (3 mL) was added to a mixture of benzyl alcohol (0.3 mL, 2.9 mmol), chloroform (5 mL), mercury(II) iodide (230 mg, 0.5 mmol) and 4A molecular sieve. The mixture was stirred at room temperature for 2 days. It was then filtered, and the filtrate washed with aqueous potassium iodide and sodium hydrogencarbonate, dried, and evaporated. Preparative t.l.c. (1:4 ethyl acetate–pentane) gave benzyl 3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-α-D-glucopyranoside (**9**, 39 mg, 17%) as the fastest moving component. Crystallisation and recrystallisation from ether–pentane gave a product having m.p. 94–95°, $[\alpha]_D^{20}$ +165° (*c* 0.4, chloroform); ^{1}H-n.m.r.: δ 5.01 (H-1), 3.91 (H-2), 5.51 (H-3), 4.89 (H-4), 4.09 (H-5), 3.44 (H-6), 3.27 (H-6'), 4.80 and 4.58 ($CH_2C_6H_5$), 2.02 and 1.97 (OAc), $J_{1,2}$ 3.3, $J_{2,3}$ 11.0, $J_{3,4}$ 9.0, $J_{4,5}$ 9.5, $J_{5,6}$ 3.5, $J_{5,6'}$ 5.7, $J_{6,6'}$ 11.5, and $J_{CH_2C_6H_5}$ 12.0 Hz.

Anal. Calc. for $C_{17}H_{20}Br_2O_6$: C, 42.52; H, 4.20; Br, 33.29. Found: C, 42.30; H, 4.21; Br, 33.44.

The next fraction gave the β-glycoside (**4**, 78 mg, 33%), identical with the product described under (*A*).

(C) Silver oxide. A mixture of bromide **1** (200 mg, 0.44 mmol), benzyl alcohol (0.2 mL, 2.0 mmol), and silver oxide (1 g) in dichloromethane (8 mL) was stirred at room temperature for 20 h in the presence of molecular sieve. Work-up and chromatography as just described gave the α-glycoside **9** (29 mg, 14%) and the β-glycoside **4** (99 mg, 47%).

(D) Silver triflate. Bromide **1** (1.0 g) in dichloromethane (5 mL) was dried for 4 h with molecular sieve. Benzyl alcohol (1.1 mL, 11 mmol) in dichloromethane (5 mL) and 2,4,6-trimethylpyridine (0.44 mL, 3.3 mmol) was similarly dried for 3 h. Silver triflate (848 mg, 3.3 mmol) was added, and the mixture stirred for 1 h and then cooled to −70°. The solution of the bromide **1** was then added at −70° during 30 min and the temperature allowed to rise to room temperature overnight. After filtration, the solution was washed successively with aqueous sodium thiosulfate, 4M hydrochloric acid, and aqueous sodium hydrogencarbonate, dried, and evaporated to give 940 mg of residue. Preparative t.l.c. (1:2 ether–pentane) gave, as the fastest moving fraction, 3,4-di-*O*-acetyl-2,6-dibromo-1,2,6-trideoxy-D-*arabino*-hex-1-enopyranose (**7**, 36 mg, 4%), which was only identified through its ^{1}H-n.m.r. spectrum. The second fraction gave the α-glycoside **9** (324 mg, 31%), m.p. 91–92°, and the third fraction the β-anomer **4** (351 mg, 33%); both were identified through the ^{1}H-n.m.r. spectra. Finally, a small amount (32 mg, 3%) of 1,3,4-tri-*O*-acetyl-2,6-dibromo-2,6-dideoxy-α-D-glucopyranose, m.p. 147–148°, was obtained; it was only identified through its ^{1}H-n.m.r. spectrum.

Reaction of bromide **1** *with methyl 2,3-O-isopropylidene-α-*L*-rhamnopyranoside* (**8**). — *(A) With silver silicate.* Rhamnoside[11] **8** (60 mg, 0.33 mmol) in dichloromethane (3 mL) and silver silicate[7] (200 mg) were stirred for 1 h with 4A molecular sieve, and then cooled to −20°. A solution of bromide **1** (180 mg, 0.4 mmol) in dry dichloromethane (4 mL) was added during 15 min at −20°. This temperature was kept for 2 h, and the mixture then kept overnight at room temperature. Filtration, evaporation, and preparative t.l.c. (1:4 ethyl acetate–pentane)

gave the unsaturated product **7** (6 mg, 4%), followed by methyl 4-*O*-(3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-β-D-glucopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**12**, 40 mg, 22%), which contained a trace of the α anomer as seen from the ^{1}H-n.m.r. spectrum. Rechromatography gave pure **12** as a sirup, $[\alpha]_D^{20}$ +16.5° (*c* 0.9, chloroform); ^{1}H-n.m.r. (400 MHz): δ 4.86 (H-1), 4.11 (H-2), 4.31 (H-3), 3.71 (H-4), 3.69 (H-5), 1.32 (H-6), 5.18 (H-1'), 3.70 (H-2'), 5.33 (H-3'), 4.86 (H-4'), ~3.7 (H-5'), 3.44 (H-6'a), 3.37 (H-6'b), 2.10 and 2.05 (OAc), 3.38 (OMe), 1.56 and 1.38 (CMe_2), $J_{1,2}$ 0.5, $J_{2,3}$ 5.6, $J_{3,4}$ 5.6, $J_{4,5}$ 10.0, $J_{5,6}$ 5.6, $J_{1',2'}$ 8.7, $J_{2',3'}$ 10.6, $J_{3',4'}$ 9.0, $J_{4',5'}$ 10.0, $J_{5',6'a}$ 2.6, $J_{5',6'b}$ 3.4, and $J_{6',6'}$ 11.0 Hz.

Anal. Calc. for $C_{20}H_{30}Br_2O_{10}$: C, 40.69; H, 5.12; Br, 27.08. Found: C, 40.69; H, 5.22; Br, 27.07.

(B) With silver triflate. Bromide **1** (214 mg, 0.47 mmol) was stirred with molecular sieve in dichloromethane (2 mL) for 2 h. Rhamnoside **8** (77 mg, 0.43 mmol) in dichloromethane (5 mL) was treated in the same way. Silver triflate (166 mg, 0.64 mmol) was then added to the latter solution and, after 30 min, the mixture was cooled to −70° and the solution of the bromide was added during 15 min. The mixture was allowed to reach room temperature overnight. It was then filtered and the filtrate washed with aqueous sodium thiosulfate and sodium hydrogencarbonate, dried, and evaporated. Preparative t.l.c. (1:2 ethyl acetate–pentane) gave the β anomer **12** (68 mg, 29%), identical with the material described under (A). The α anomer was not observed.

When the same experiment was carried out in 1:4 nitromethane–toluene, the product isolated after t.l.c. (33%) consisted of a 3:1 mixture of **12** and its α anomer.

*Cyclohexyl 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-β-*D*-glucopyranoside* (**5**). — Bromide[5] **2** (2.0 g, 4.6 mmol) in dichloromethane (20 mL) was stirred for 2 h with 4A molecular sieve. This solution was added in one portion to a mixture of cyclohexanol (0.53 mL, 5.1 mmol) in dichloromethane (10 mL) and silver carbonate (8 g) which had also been stirred with molecular sieve. Stirring was continued overnight. Filtration and evaporation left a syrup (2 g) that contained an 4.5:1 mixture of α- and β-glycosides as seen from the ^{1}H-n.m.r. spectrum. Crystallization from ethanol gave the β-glycoside **5** (1.0 g, 48%), m.p. 102–104°. Recrystallization from ethanol gave a product having m.p. 103.5–104°, $[\alpha]_D^{20}$ +33.8° (*c* 0.4, chloroform); ^{1}H-n.m.r. (270 MHz): δ 4.65 (H-1), 3.78 (H-2), 5.30 (H-3), 4.98 (H-4), 3.6–3.8 (H-5), 4.30 (H-6), 4.10 (H-6'), 3.6–3.8 (cyclohexyl), 2.09, 2.07, 2.02 (OAc), $J_{1,2} = J_{2,3} = J_{3,4} = J_{4,5}$ 9.0, $J_{5,6}$ 5.0, $J_{5,6'}$ 2.0, and $J_{6,6'}$ 12.0 Hz.

Anal. Calc. for $C_{18}H_{27}BrO_8$: C, 47.90; H, 6.03; Br, 17.71. Found: C, 47.69; H, 5.90; Br, 18.18.

Preparative t.l.c. of the material in the mother liquors (1:2 ethyl acetate–pentane) gave, as the first fraction, the α anomer **10** (300 mg, 14%) which crystallized, m.p. 94–95°. Recrystallization from ethanol gave a pure product, m.p. 97–97.5°; $[\alpha]_D^{20}$ +154.4° (*c* 0.8, chloroform); ^{1}H-n.m.r. (90 MHz): δ 5.04 (H-1), 3.92 (H-2), 5.48 (H-3), 4.95 (H-4), 4.4–4.3 (H-5, -6, -6'), 3.6–3.8 (1 H, cyclohexyl), $J_{1,2}$ 3.5, $J_{2,3}$ 11.0, $J_{3,4}$ 9.0, and $J_{4,5}$ 9.0.

Anal. Calc. for $C_{18}H_{27}BrO_8$: C, 47.90; H, 6.03; Br, 17.71. Found: C, 48.04; H, 6.20; Br, 17.78.

1,2,3,4-Tetra-O-acetyl-6-O-(3,4,6-tri-O-acetyl-2-bromo-2-deoxy-β-D-glucopyranosyl)-β-D-glucopyranose (**13**). — 1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyranose[12] (**11**, 2.42 g, 6.94 mmol) was stirred in dichloromethane (20 mL) with silver carbonate (12 g) and molecular sieve for 2 h. Bromide **2** (3.0 g, 6.94 mmol) in dry dichloromethane (20 mL) was added in one portion and the mixture stirred for 2 days. Filtration and evaporation gave 4.5 g which was crystallized from ethanol yielding **13** (1.8 g, 37%), m.p. 155–156°. Recrystallization from ethyl acetate–pentane gave a product having m.p. 157–158°, $[\alpha]_D^{20}$ +32.7° (*c* 0.7, chloroform); ^{1}H-n.m.r. (270 MHz): δ 5.72 (H-1), 5.11 (H-2), 5.26 (H-3), 5.07 (H-4), 3.6–3.7 (H-5), 3.8–4.0 (H-6), 4.64 (H-1′), 3.75 (H-2′), 5.27 (H-3′), 4.96 (H-4′), 3.6–3.7 (H-5′), 4.28 and 4.12 (H-6′a and -6′b), $J_{1,2}$ 8.5, $J_{2,3}$ 9.5, $J_{3,4} = J_{4,5}$ 9.5, $J_{1',2'}$ 8.5, $J_{2',3'}$ 10.5, $J_{3',4'} = J_{4',5'}$ 9.0, $J_{5',6'a}$ 5.0, $J_{5',6'b}$ 2.5, and $J_{6',6'}$ 12.0 Hz.

Anal. Calc. for $C_{26}H_{35}BrO_{17}$: C, 44.65; H, 5.04; Br, 11.42. Found: C, 44.95; H, 5.03; Br, 11.79.

Cyclohexyl 3,4,6-tri-O-benzoyl-2-bromo-2-deoxy-β-D-glucopyranoside (**14**). — 3,4,6-Tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide[5] (**3**, 2.0 g, 3.0 mmol) in dichloromethane (20 mL) was dried with molecular sieve for 2 h. The solution was added to a dried solution of cyclohexanol (0.35 mL, 3.4 mmol) in dichloromethane (10 mL) which contained silver carbonate (7 g) and molecular sieve. The mixture was stirred for 20 h, filtered, and evaporated. The crystalline residue (2.1 g) was recrystallized from ethanol to give **14** (1.3 g, 63%), m.p. 115–116°, $[\alpha]_D^{20}$ −6.7° (*c* 0.9, chloroform); ^{13}C-n.m.r.: δ 101.0 (C-1), 78.6, 79.9, 71.9, 70.9 (C-3, -4, -5, and OC_6H_{11}), 63.2 (C-6), 50.3 (C-2), 33.2, 31.4, 25.4, and 23.7 (cyclohexyl).

Anal. Calc. for $C_{33}H_{33}BrO_8$: C, 62.17; H, 5.22; Br, 12.53. Found: C, 61.74; H, 5.04; Br, 13.03.

Cyclohexyl 3,4-di-O-acetyl-2-bromo-2,6-dideoxy-β-L-glucopyranoside (**16**). — 3,4-Di-*O*-acetyl-2-bromo-2-deoxy-α-L-glucopyranosyl bromide[5] (**15**, 2.0 g, 5.1 mmol) in dry dichloromethane (20 mL) was treated, as described for the preparation of **14**, with cyclohexanol (0.55 mL, 5.3 mmol) in dichloromethane (10 mL) containing silver carbonate (8 g) and molecular sieve for 20 h. The crude product (2 g) was chromatographed on a column with 1:2 ether–pentane as eluant. The first fraction to be eluted was cyclohexyl 3,4-di-*O*-acetyl-2-bromo-2-deoxy-α-L-glucopyranoside (**17**, 400 mg, 19%) which crystallized. Recrystallization from pentane gave a pure product, m.p. 59–61°, $[\alpha]_D^{20}$ −181.6° (*c* 1.0, chloroform); ^{13}C-n.m.r.: δ 96.3 (C-1), 48.5 (C-2), 76.6, 74.9, 72.0, 65.3 (C-3, -4, -5, and OC_6H_{11}), 17.0 (C-6), 32.9, 30.7, 25.4, 23.6, 23.3 (cyclohexyl), and 20.4 (OAc).

Anal. Calc. for $C_{16}H_{25}BrO_6$: C, 48.86; H, 6.41; Br, 20.32. Found: C, 49.24; H, 6.55; Br, 20.64.

The next fraction was the β anomer **16** (1.0 g, 48%) which crystallized from ethanol, m.p. 92–94°, $[\alpha]_D^{20}$ −50.6° (*c* 1.2, chloroform); ^{13}C-n.m.r.: δ 100.2 (C-1),

77.6, 74.8, 74.2. 69.6 (C-3, -4, -5, and OC_6H_{11}), 50.2 (C-2), 17.0 (C-6), 33.0, 31.1, 25.3, 23.5, 23.4 (cyclohexyl), and 20.3 (OAc).

Anal. Calc. for $C_{16}H_{25}BrO_6$: C, 48.86; H, 6.41; Br, 20.32. Found: C, 48.99; H, 6.51; Br, 20.81.

*Benzyl 3,4-di-O-acetyl-2,6-dibromo-2,6-dideoxy-α-*D*-mannopyranoside* (**20**). — *(A) With silver oxide.* Bromide[5] **18** (1.0 g, 2.2 mmol) in dichloromethane (5 mL) was stirred with molecular sieve for 4 h. Benzyl alcohol (1.1 mL, 11 mmol) in dichloromethane (5 mL) containing silver oxide (3 g) was similarly dried, and the two mixtures were mixed and stirred overnight. The mixture was filtered, and the filtrate washed with aqueous sodium hydrogencarbonate, dried, and evaporated. The crystalline residue (900 mg) was recrystallized from ethanol to give **20** (880 mg, 83%), m.p. 106–109°. Further recrystallization gave a product having m.p. 110–111°, $[\alpha]_D^{20}$ +54 3° (*c* 1.5, chloroform); ^{1}H-n.m.r. (400 MHz): δ 5.12 (H-1), 4.46 (H-2), 5.24 (H-3), 5.30 (H-4), 4.09 (H-5), 3.44 (H-6, -6′), 4.80 and 4.60 ($CH_2C_6H_5$), 2.08 (OAc), $J_{1,2}$ 1.8, $J_{2,3}$ 4.0, $J_{3,4}$ 9.0, $J_{4,5}$ 9.0, $J_{5,6}$ 5.5, and $J_{CH_2C_6H_5}$ 12.0 Hz.

Anal. Calc. for $C_{17}H_{20}Br_2O_6$: C, 42.52; H, 4.20.; Br, 33.29. Found: C, 42.54; H, 4.26; Br, 33.23.

(B) With silver triflate. Bromide **18** (1.0 g, 2.2 mmol) in dichloromethane was dried as described earlier. Benzyl alcohol (1.1 mL, 17 mmol) in dichloromethane (7 mL) containing 2,4,6-trimethylpyridine (0.44 mL, 3.3 mmol) was stirred with molecular sieve for 2 h. Silver triflate (848 mg, 3.3 mmol) was added and the mixture stirred for 1 h. It was then cooled to −70°, and the solution of bromide **18** added during 30 min. The stirring was continued overnight at room temperature. The mixture was filtered, and the filtrate washed successively with aqueous sodium thiosulfate, 4M hydrochloric acid, and aqueous sodium hydrogencarbonate, dried, and evaporated at 70° *in vacuo* (0.1 kPa) to remove benzyl alcohol. The residue crystallized from ether–pentane to give **20** (790 mg, 75%), m.p. 104–107°, identical with the product described under (*A*).

*Methyl 4-O-(3,4-di-O-acetyl-2,6-dibromo-2,6-dideoxy-α-*D*-mannopyranosyl)-2,3-O-isopropylidene-α-*L*-rhamnopyranoside* (**19**). — Methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside[11] (**8**, 133 mg, 0.73 mmol) in toluene (4 mL) and nitromethane (1 mL) was stirred with molecular sieve for 2 h. Silver triflate (281 mg, 1.09 mmol) was added, and the mixture stirred for 1 h and then cooled to −70°. A dried solution of bromide **18** (366 mg, 0.81 mmol) in toluene (1.5 mL) and nitromethane (1.5 mL) was added during 30 min. The mixture was kept overnight at room temperature and filtered. The filtrate was washed as described earlier and evaporated to give a residue that crystallized from ethanol (273 mg, 67%), m.p. 130–132°. Recrystallization gave **19** having m.p. 133–134°, $[\alpha]_D^{20}$ +33.4° (*c* 0.25, chloroform); ^{1}H-n.m.r. (400 MHz): δ 4.85 (H-1), 4.21 (H-2), 4.25 (H-3), 3.40 (H-4), 3.69 (H-5), 1.28 (H-6), 5.41 (H-1′), 4.43 (H-2′), 5.40 (H-3′), 5.53 (H-4′), 4.34 (H-5′), 3.56 (H-6′a), 3.48 (H-6′b), 3.37 (OCH_3), 2.10 and 2.08 (OAc), 1.55, 1.35 (CMe_2), $J_{1,2}$ ~0.5, $J_{2,3}$ 5.4, $J_{3,4}$ 7.0, $J_{4,5}$ 10.0, $J_{5,6}$ 6.0, $J_{1',2'}$ 1.3, $J_{2',3'}$ 3.8, $J_{3',4'}$ 9.4, $J_{4',5'}$ 9.7, $J_{5',6'a}$ 3.5, $J_{5',6'b}$ 3.2, and $J_{6',6'}$ 11.4 Hz.

Anal. Calc. for $C_{20}H_{30}Br_2O_{10}$: C, 40.69; H, 5.12; Br, 27.08. Found: C, 40.60; H, 5.18; Br, 27.11.

When the reaction was performed in dichloromethane solution, the yield of **19** was only 33%. In none of the two experiments was the β anomer detected.

*Benzyl 2,6-dideoxy-α-*D-arabino-*hexopyranoside* (**21**). — *(A) From* **20**. 2,6-Dibromo compound **20** (240 mg, 0.53 mmol) was hydrogenolyzed overnight at 0.1 MPa pressure in ethyl acetate (10 mL) containing triethylamine (0.2 mL) and 10% palladium-on-carbon (50 mg). The mixture was filtered, the filtrate evaporated, and the residue in dichloromethane washed with 4M hydrochloric acid, dried, and evaporated. This gave chromatographically homogenous benzyl 3,4-di-*O*-acetyl-2,6-dideoxy-α-D-*arabino*-hexopyranoside (145 mg, 90%); ^{1}H-n.m.r. (90 MHz): δ 4.93 (H-1), 2.27 (H-2*e*), 1.79 (H-2*a*), 5.29 (H-3), 4.73 (H-4), 3.89 (H-5), 1.16 (H-6), 4.64 and 4.44 ($CH_2C_6H_5$), 2.04 and 2.01 (OAc), $J_{1,2e}$ 1.4, $J_{1,2a}$ 3.5, $J_{2,2}$ 12.8, $J_{2e,3}$ 5.5, $J_{2a,3}$ 11.5, $J_{3,4}$ 9.5, $J_{4,5}$ 9.5, $J_{5,6}$ 6.0, and $J_{CH_2C_6H_5}$ 12.0 Hz.

The product was deacetylated with sodium methoxide in methanol for 1 h to give **21** (91 mg, 85%) which crystallized from ethyl acetate–pentane, m.p. 108–110°, $[\alpha]_D^{20}$ +89.3° (*c* 0.3, water); lit.[13] m.p. 112°, $[\alpha]_D$ +88.9° (*c* 0.2, water); ^{13}C-n.m.r.: δ 96.3 (C-1), 77.5, 68.7, 68.7, 67.7 (C-3, -4, -5, and $CH_2C_6H_5$), 37.5 (C-2), 17.6 (C-6), and $J_{C\text{-}1,H\text{-}1}$ 165 Hz.

(B) From **9**. A similar hydrogenolysis of **9** gave a mixture of products from which only 39% of **21** could be isolated after chromatography.

Alternatively, the dibromoglucoside **9** (180 mg, 0.38 mmol) and α,α′-azobisisobutyronitrile (30 mg, 0.18 mmol) in toluene (15 mL) was stirred for 15 min under an argon atmosphere. Tributylstannane (0.32 mL, 1.2 mmol) was then added and the mixture heated at 70° for 3 h. Evaporation and column chromatography (1:3 ethyl acetate–pentane) gave pure benzyl 3,4-di-*O*-acetyl-2,6-dideoxy-α-D-*arabino*-hexopyranoside (96 mg, 80%), identical with the product described under (*A*).

*Benzyl 3,4-di-*O*-acetyl-2,6-dideoxy-β-*D-arabino-*hexopyranoside* (**6**). — The dibromo compound **4** (205 mg, 0.45 mmol) was treated with tributylstannane as just described. Column chromatography (1:3 ethyl acetate–pentane) gave **6** (122 mg, 89%) as a syrup, $[\alpha]_D^{20}$ −58.4° (*c* 1.4, chloroform); ^{1}H-n.m.r. (270 MHz): δ 4.59 (H-1), 2.31 (H-2*e*), 1.76 (H-2*a*), 4.94 (H-3), 4.74 (H-4), 3.46 (H-5), 1.26 (H-6), 4.88 and 4.58 ($CH_2C_6H_5$), 2.04 and 2.00 (OAc), $J_{1,2e}$ 2.2, $J_{1,2a}$ 9.6, $J_{2,2}$ 12.8, $J_{2e,3}$ 5.2, $J_{2a,3}$ 12.0, $J_{3,4}$ 9.2, $J_{4,5}$ 9.2, $J_{5,6}$ 6.0, and $J_{CH_2C_6H_5}$ 12.0 Hz.

Anal. Calc. for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.31; H, 6.86.

Catalytic hydrogenolysis of **4** as described earlier gave a mixture of products from which **6** could be isolated in 48% yield after chromatography.

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