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THE PREPARATION OF SOME BROMODEOXY- AND DEOXY-HEXOSES FROM BROMODEOXYALDONIC ACIDS*

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ABSTRACT

The reduction of 2,6-dibromo-2,6-dideoxy-D-mannono- and 2,6-dibromo-2,6-dideoxy-D-glucono-1,4-lactone with sodium borohydride affords 2,6-dibromo-2,6-dideoxy-D-mannose and 2,6-dibromo-2,6-dideoxy-D-glucose, respectively, which may be isolated as their acetates. Similarly, 2-bromo-2,6-dideoxy-L-glucono-1,4-lactone yields 2-bromo-2,6-dideoxy-L-glucose. Hydrogenolysis of 2,6-dibromo-2,6-dideoxy-D-mannono-1,4-lactone gives 6-bromo-2,6-dideoxy-D-*arabino*-hexono-1,4-lactone and, subsequently, 2,6-dideoxy-D-*arabino*-hexono-1,4-lactone. Reduction of the latter with bis(1,2-dimethylpropyl)borane leads to 2,6-dideoxy-D-*arabino*-hexose, which may be converted into methyl 2,6-dideoxy-3,4-di-*O*-*p*-nitrobenzoyl-D-*arabino*-hexopyranoside.

INTRODUCTION

The reaction of calcium D-gluconate with hydrogen bromide in acetic acid readily yields 2,6-dibromo-2,6-dideoxy-D-mannono-1,4-lactone (**4**); similarly, 2,6-dibromo-2,6-dideoxy-D-glucono-1,4-lactone (**10a**) can be prepared from D-mannono-1,4-lactone[1]. These dibromolactones are useful synthetic intermediates which may be converted into other derivatives of aldonic acids or into derivatives of reducing sugars. We now describe a number of such reactions.

DISCUSSION AND RESULTS

The preparation of the acetylated lactone (**10b**) from D-mannono-1,4-lactone, or from its di-*O*-isopropylidene derivative, has been described[1]. The deacetylated lactone **10a** has now been obtained crystalline, and it has been found that it is best prepared from 2,3:5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone by treatment with hydrogen bromide in acetic acid followed by deacetylation. D-Mannono-1,4-lactone also gives **10b** in high yield under these conditions, but crystallisation of the product is difficult. In contrast, L-rhamnono-1,4-lactone (**13**) is easily converted, in 61% yield, into crystalline 2-bromo-2,6-dideoxy-L-glucono-1,4-lactone (**14**).

*Reaction of Aldonic Acids with Hydrogen Bromide, Part II. For Part I, see ref. 1.

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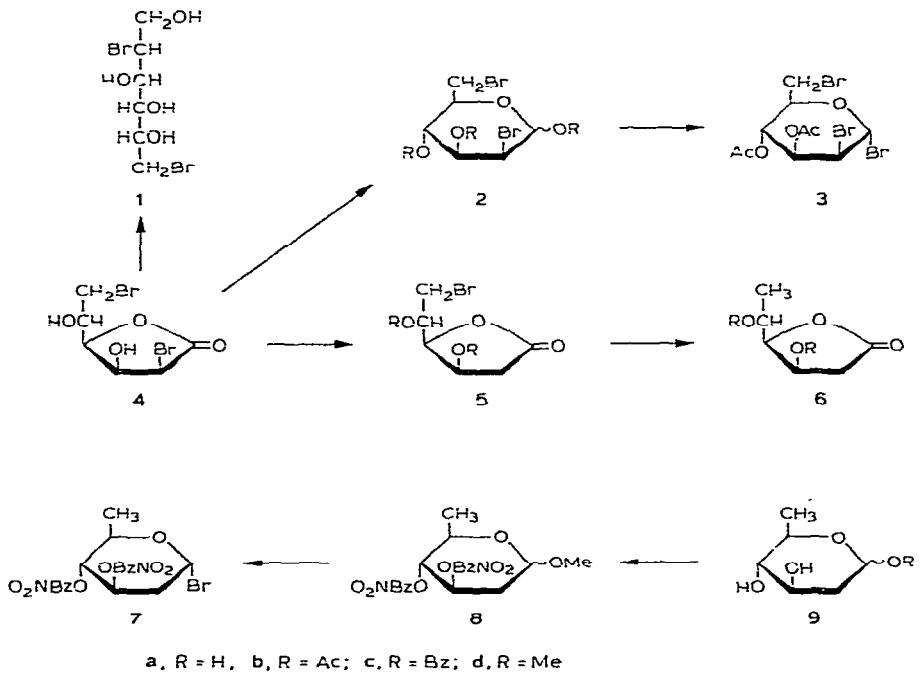

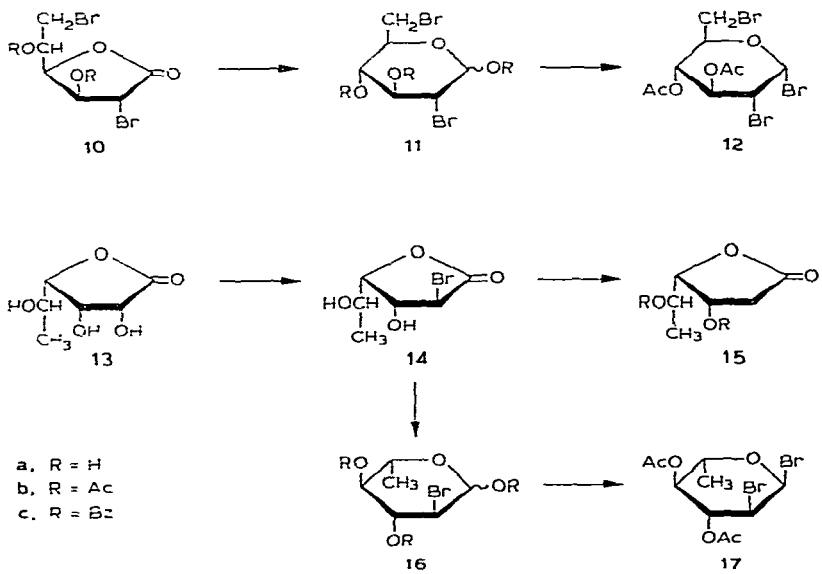

Reduction of the dibromolactone[1] **4** with sodium borohydride in the presence of an acidic ion-exchange resin, to keep[2] the pH value below 6, gave the non-crystalline 2,6-dibromo-2,6-dideoxy-D-mannose (**2a**) together with some 2,6-dibromo-2,6-dideoxy-D-mannitol (**1**). Compound **1** was the main product when the reduction was

performed at a higher pH. Acetylation converted the pyranose mixture into the crystalline α-triacetate (**α-2b**), which could be further converted into the bromide **3**. Similarly, reduction of the dibromolactone **10a** gave 2,6-dibromo-2,6-dideoxy-D-glucose (**11a**) as a syrup, which was converted into the bromide **12** *via* the acetate **11b**. The same procedure converted the monobromolactone **14** into 2-bromo-2,6-dideoxy-L-glucose (**16a**), which was characterised as the acetylated bromide **17**. The structures of the acetylated bromodeoxyhexose **α-2b** and the glycosyl bromides **3**, **12**, and **17** were unambiguously derived from their ^{1}H-n.m.r. spectra. Consequently, the previously proposed structures[1] of the corresponding lactones (**4**, **10**, and **14**) are firmly established.

When the dibromolactone **4** was subjected to hydrogenolysis in the presence of triethylamine, one molar equivalent of hydrogen was rapidly consumed and 6-bromo-2,6-dideoxy-D-*arabino*-hexono-1,4-lactone (**5a**) was obtained. The crystalline diacetate (**5b**) of **5a** was identical with that obtained previously by reduction of the diacetate of **4** with iodide[1]. On prolonged exposure of **4** to hydrogen, both bromine atoms were removed and 2,6-dideoxy-D-*arabino*-hexono-1,4-lactone (**6a**) was obtained; **6a** gave a crystalline diacetate (**6b**) and dibenzoate (**6c**). Hydrogenolysis of the 2-bromolactone **14** gave 2,6-dideoxy-L-*arabino*-hexono-1,4-lactone (**15a**), *i.e.*, the enantiomer of **6a**, which was readily converted into the crystalline diacetate **15b**.

A dihydroxylactone, forming a diacetate with m.p. 113°, and assigned the structure 2,6-dideoxy-D-*ribo*-hexonolactone on the basis of spectroscopic data, has been reported as a hydrolysis product of the antibiotic flambamycin[3]. From another antibiotic, avilamycin, a 3,5-diacetoxycapronolactone, m.p. 102°, was obtained[4]. No optical rotations were reported for the two acetates; the m.p. of the latter is identical with that of **6b** (or **15b**). The ^{1}H-n.m.r. data for the three diacetates are almost identical. The optical rotation of the non-acetylated, flambamycin-derived lactone was reported[3] to be +50°; **6a** has a rotation of +53°. The reported ^{1}H-n.m.r. spectrum of the naturally derived lactone[3] is identical with that of **6a**. Furthermore, 2,6-dideoxy-D-*ribo*-hexono-1,4-lactone, prepared by oxidation of D-digitoxose, is reported[5] to have a specific rotation of −32.1° (acetone). Together, these data suggest that the lactone isolated from flambamycin possesses the D-*arabino* rather than the reported D-*ribo* configuration.

The foregoing lactones are potentially useful materials for the synthesis of derivatives of reducing sugars. In contrast to the dibromolactones **4** and **10a**, the 2-deoxylactones could not be reduced with borohydride or with sodium amalgam. Dyong *et al.* have converted a number of deoxylactones into hemiacetals by reduction with either di-isobutylaluminium hydride[6] or bis(1,2-dimethylpropyl)borane[7]. The latter reagent, which was first used for the reduction of acylated sugar lactones by Lerner *et al.*[8], has also been applied[9] to the reduction of unprotected 2-deoxylactones. The reduction of **6a** proceeded smoothly with bis(1,2-dimethylpropyl)borane in tetrahydrofuran and gave 2,6-dideoxy-D-*arabino*-hexose (**9a**) as a syrupy mixture of the two pyranoses; this compound has been isolated from naturally occurring glycosides[10,11] and has been crystallised[10]. When treated with methanol and acid, it

yielded the methyl glycosides **9d** with the α anomer preponderating[11]. The products **9a** and **9d** were characterised only through their ^{13}C-n.m.r. spectra. *p*-Nitrobenzoylation of crude **9d** gave a crystalline bis(*p*-nitrobenzoate) mixture (**8**) obtainable from **4** in 48% overall yield. Chromatography of **8** gave the pure α anomer (**α-8**) possessing ^{1}H-n.m.r. data closely similar to those of the corresponding dibenzoate[12]. Treatment of crude **8** with hydrogen bromide gave the crystalline α-bromide **7**, well suited for the preparation of glycosides.

EXPERIMENTAL

N.m.r. spectra (^{1}H, ^{13}C) were recorded with Bruker HX 90, WH 90, and HX 270 instruments. For spectra measured on solutions in $CDCl_3$, Me_4Si was used as internal standard. ^{13}C-Chemical shifts for solutions in D_2O were measured relative to that of internal 1,4-dioxane (67.40 p.p.m.). Optical rotations were measured with a Perkin–Elmer 141 instrument. Melting points are uncorrected.

2,6-Dibromo-2,6-dideoxy-D-*glucono-1,4-lactone* (**10a**). — To 2,3:5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone[13] (4 g) was added a saturated solution (25 ml) of hydrogen bromide in acetic acid, and the mixture was stirred for 3 h at room temperature. Methanol (50 ml) was added, the solution was kept overnight and then concentrated, and water (2 × 20 ml) was distilled from the residue. A solution of the residue in water (20 ml) was extracted with ether (5×). The combined extracts were concentrated, and the residue was crystallised from dichloromethane, to give **10a** (3.16 g, 67%), m.p. 91–94°. Recrystallisation from ether–pentane gave a product with m.p. 90–92°, $[\alpha]_D^{20}$ +29° (*c* 2, ethyl acetate). ^{13}C-N.m.r. data (D_2O): 172.4 (C-1), 80.9 (C-4), 73.7 (C-3), 67.2 (C-5), 40.9 (C-2), and 35.8 p.p.m. (C-6).

Anal. Calc. for $C_6H_8Br_2O_4$: C, 23.71; H, 2.65; Br, 52.58. Found: C, 23.77; H, 2.66; Br, 52.23.

When D-mannono-1,4-lactone was treated as described above, the crude, syrupy product contained ~80% of **10a**, as estimated by ^{13}C-n.m.r. spectroscopy. However, crystallisation of the product was difficult and pure **10a** could be obtained only in ~30% yield.

2-Bromo-2,6-dideoxy-L-*glucono-1,4-lactone* (**14**). — L-Rhamnono-1,4-lactone[14] (5 g) was treated with a saturated solution of hydrogen bromide in acetic acid (30 ml) for 3 h. Methanol (75 ml) was added and the solution was kept overnight. Work-up as described above and crystallisation of the product from ether–pentane gave a crude product (4.5 g) which was recrystallised from ethyl acetate–pentane, to give **14** (4.1 g, 61%), m.p. 111–113°. An additional recrystallisation gave a product with m.p. 111–113°, $[\alpha]_D^{20}$ −19° (*c* 2.2, ethyl acetate). ^{13}C-N.m.r. data (D_2O): 175.6 (C-1), 86.1 (C-4), 74.3 (C-3), 67.4 (C-5), 42.5 (C-2), and 19.9 p.p.m. (C-6).

Anal. Calc. for $C_6H_9BrO_4$: C, 32.02; H, 4.03; Br, 35.51. Found: C, 32.22; H, 4.09; Br, 35.39.

2,6-Dibromo-2,6-dideoxy-D-*mannopyranose* (**2a**). — A solution of 2,6-dibromo-2,6-dideoxy-D-mannono-1,4-lactone[1] (5 g) in water (50 ml) and ethanol (25 ml)

was cooled in ice and stirred with Amberlite IR-120 (H^+) resin (~10 ml). Sodium borohydride (600 mg, 1 mol. equiv.) was added in portions at such a rate that the pH did not rise above 6. After the addition was complete (~30 min), stirring was continued for an additional 30 min. The resin was then collected and washed with methanol, and the combined filtrate and washings were concentrated. Methanol was twice distilled from the residue to remove boric acid. The syrupy residue (5.0 g) was shown by ^{13}C-n.m.r. spectroscopy to consist of **2a** (as a mixture of the two pyranoses) and dibromomannitol (**1**) in the ratio 2.5:1; no **4** could be detected.

The mixture was eluted from a column of silica gel with ether, to give syrupy **2a** (3.5 g, 70%). A proton-decoupled, ^{13}C-n.m.r. spectrum (D_2O) of **2a** showed two sets of signals corresponding to an $\alpha\beta$-pyranose ratio of 2:1. No other signals were seen. α Anomer: 94.9 (C-1), 72.1 and 70.1 (C-3,5), 68.8 (C-4), 56.3 (C-2), and 34.6 p.p.m. (C-6). β Anomer: 92.3 (C-1), 75.7 and 71.8 (C-3,5), 69.7 (C-4), 60.8 (C-2), and 33.8 p.p.m. (C-6). A proton-coupled, ^{13}C-n.m.r. spectrum showed $J_{C\text{-}1,H\text{-}1}$ values of 176.3 and 160.3 Hz for the α and β anomers, respectively, in agreement with the anomeric assignment[15]. The β anomer had $J_{C\text{-}2,H\text{-}1}$ ~10 Hz, as found in *β-manno* compounds[16].

2,6-Dibromo-2,6-dideoxy-D-*mannitol* (**1**). — To a solution of **4** (5 g) in water (100 ml) was added Amberlite IR-120 (H^+) resin (~10 ml). The mixture was cooled in ice and stirred while sodium borohydride (0.75 g) was added at such a rate that the pH was kept below 6 (more resin was added, if necessary). More (0.75 g) sodium borohydride was then added, allowing the pH to increase to ~9. The stirring was continued for 30 min and excess of resin was added until a pH of ~3 was obtained. The mixture was filtered and concentrated, and boric acid was removed by evaporation of methanol from the residue which was then crystallised from ethanol, to give **1** (3.9 g, 77%), m.p. 85–89°. Recrystallisation from ethyl acetate–pentane gave a product with m.p. 92–93°, $[\alpha]_D^{20}$ −9° (*c* 1.6, ethyl acetate). ^{13}C-N.m.r. data (D_2O): 72.2, 70.4, and 70.1 (C-3,4,5), 64.0 (C-1), 56.2 (C-2), and 39.1 p.p.m. (C-6).

Anal. Calc. for $C_6H_{12}Br_2O_4$: C, 23.40; H, 3.93; Br, 51.89. Found: C, 23.38; H, 3.91; Br, 51.89.

1,3,4-Tri-O-*acetyl-2,6-dibromo-2,6-dideoxy*-α-D-*mannopyranose* (**α-2b**). — Reduction of **4** (10 g) with sodium borohydride (1 mol. equiv.), as described above, gave a mixture of **2a** and **1**, which was treated with acetic anhydride (25 ml) and 60% aqueous perchloric acid (1 ml) for 1 h. Ice and water were added and, after 0.5 h, the mixture was extracted with dichloromethane. The extract was washed with water and aqueous $NaHCO_3$, dried, and concentrated. The syrupy residue (~13 g) crystallised from ether–pentane, to give **α-2b** (5.0 g, 35%), m.p. 80–84°. Further recrystallisations gave material having m.p. 85–87°, $[\alpha]_D^{20}$ +36° (*c* 3, chloroform). ^{1}H-N.m.r. data (90 MHz, $CDCl_3$): δ 6.27 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 5.38 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-4), 5.16 (q, 1 H, $J_{2,3}$ 3.6 Hz, H-3), 4.22 (q, 1 H, H-2), 4.10 (m, 1 H, $J_{4,5}$ 9.5 Hz, H-5), and 3.44 (2 H, ABX pattern, H-6). A proton-coupled, ^{13}C-n.m.r. spectrum gave $J_{C\text{-}1,H\text{-}1}$ 179.5 Hz, proving[15] that **α-2b** had H-1 equatorial.

Anal. Calc. for $C_{12}H_{16}Br_2O_7$: C, 33.35; H, 3.73; Br, 36.99. Found: C, 33.51; H, 3.72; Br, 36.93.

The combined mother liquors were concentrated and to a solution of the residue in dichloromethane (15 ml) was added a saturated solution (15 ml) of hydrogen bromide in acetic acid. The mixture was kept for 0.5 h at room temperature, and then diluted with dichloromethane, washed with water and aqueous $NaHCO_3$, dried, and concentrated. The residue was crystallised from ether–pentane, to give **3** (2.7 g, 18%), m.p. 118–121° (see below).

3,4-Di-O-acetyl-2,6-dibromo-2,6-dideoxy-α-D-mannopyranosyl bromide (**3**). — To a solution of **α-2b** (3 g) in dichloromethane (5 ml) was added a saturated solution (5 ml) of hydrogen bromide in acetic acid. After 0.5 h, the mixture was diluted with dichloromethane, washed with water and aqueous $NaHCO_3$, dried, and concentrated. The residue crystallised from ether–pentane, to give **3** (2.7 g, 86%), m.p. 119–121°. An additional recrystallisation gave a sample having m.p. 121–122°, $[\alpha]_D^{20}$ +91° (*c* 2.1, chloroform). ^{1}H-N.m.r. data (270 MHz, $CDCl_3$): δ 6.62 (bs, 1 H, H-1), 5.49 (m, 2 H, H-3,4), 4.82 (dd, 1 H, $J_{1,2}$ 1.5, $J_{2,3}$ 3.0 Hz, H-2), 4.30 (m, 1 H, H-5), and 3.45 (2 H, ABX pattern, $J_{5,6}$ 2.9, $J_{5,6'}$ 5.5, $J_{6,6'}$ 11.8 Hz, H-6,6').

Anal. Calc. for $C_{10}H_{13}Br_3O_5$: C, 26.53; H, 2.89; Br, 52.93. Found: C, 26.51; H, 2.88; Br, 52.66.

2,6-Dibromo-2,6-dideoxy-D-glucopyranose (**11a**). — 2,6-Dibromo-2,6-dideoxy-D-glucono-1,4-lactone[1] (**10a**, 2 g) was reduced with sodium borohydride as described above. A ^{13}C-n.m.r. spectrum of the crude, syrupy product showed that it consisted of 70% of **11a** (as a mixture of the anomeric pyranoses) and 30% of a product assumed to be 2,6-dibromo-2,6-dideoxy-D-glucitol.

Elution of the mixture from a column of silica gel with ether gave syrupy **11a** (1.4 g). A proton-decoupled, ^{13}C-n.m.r. spectrum (D_2O) of **11a** showed two sets of signals corresponding to an αβ-pyranose ratio of 4:5; no other signals were seen. α Anomer: 93.1 (C-1), 73.6, 73.3, 70.9 (C-3,4,5), 53.5 (C-2), and 34.4 p.p.m. (C-6). β Anomer: 96.6 (C-1), 76.7, 74.9, 73.0 (C-3,4,5), 56.3 (C-2), and 33.6 p.p.m. (C-6). A proton-coupled, ^{13}C-n.m.r. spectrum showed $J_{C\text{-}1,H\text{-}1}$ 172.5 and 164.0 Hz, for the α and β anomer, respectively[15].

3,4-Di-O-acetyl-2,6-dibromo-2,6-dideoxy-α-D-glucopyranosyl bromide (**12**). — The dibromolactone **10a** (4.6 g) was reduced with sodium borohydride, and the crude product was treated with acetic anhydride as described above. Work-up gave a syrup (**11b**) which was dissolved in a saturated solution (20 ml) of hydrogen bromide in acetic acid. After 30 min, the solution was concentrated and toluene was twice evaporated from the residue, which then crystallised from ether–pentane to give **12** (2.5 g, 36%), m.p. 155–161°. Recrystallisation gave a product with m.p. 159–161°, $[\alpha]_D^{20}$ +255° (*c* 0.7, chloroform). ^{1}H-N.m.r. data (270 MHz, $CDCl_3$): δ 6.45 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.54 (dd, 1 H, $J_{2,3}$ 10.7, $J_{3,4}$ 9.2 Hz, H-3), 5.15 (t, 1 H, $J_{4,5}$ 9.8 Hz, H-4), 4.45 (m, 1 H, H-5), 4.15 (dd, 1 H, H-2), 3.54 (dd, 1 H, $J_{5,6}$ 3.0 Hz, H-6), and 3.42 (dd, 1 H, $J_{5,6'}$ 4.8, $J_{6,6'}$ 11.8 Hz, H-6').

Anal. Calc. for $C_{10}H_{13}Br_3O_5$: C, 26.53: H, 2.89: Br, 52.93. Found: C, 26.63; H, 2.91; Br, 53.85.

2-Bromo-2,6-dideoxy-L-*glucopyranose* (**16a**). — The bromolactone **14** (2 g) was reduced with sodium borohydride (0.34 g) in water (20 ml) and ethanol (10 ml) in the presence of Amberlite IR-120 (H^+) resin as described above. The crude product was eluted from a column of silica gel (100 g) with ethyl acetate. The main fraction (1.4 g) was almost pure, syrupy **16a** with an $\alpha\beta$-pyranose ratio of 2.5:1 as seen from a ^{13}C-n.m.r. spectrum (D_2O). α Anomer: 92.9 (C-1), 77.3 (C-4), 73.4 (C-3), 68.6 (C-5), 54.1 (C-2), and 17.7 p.p.m. (C-6). β Anomer: 96.5 (C-1), 77.0 and 76.5 (C-3,4), 72.8 (C-5), 56.9 (C-2), and 17.7 p.p.m. (C-6). A proton-coupled, ^{13}C-n.m.r. spectrum gave $J_{C\text{-}1,H\text{-}1}$ values of 172.0 Hz for the α anomer and 163.8 for the β anomer[15].

3,4-Di-O-acetyl-2-bromo-2,6-dideoxy-α-L-*glucopyranosyl bromide* **17**. — The bromolactone **14** (1 g) was reduced with sodium borohydride as described above. The crude product was treated, essentially as described above, with acetic anhydride (5 ml) containing a few drops of 60% aqueous perchloric acid. The syrupy product was dissolved in dichloromethane (5 ml), and hydrogen bromide in acetic acid (5 ml) was added. After 2 h at room temperature, the mixture was diluted with dichloromethane, washed with water and aqueous $NaHCO_3$, dried, and concentrated. The residue was crystallised from pentane, to give **17** (650 mg, 39%), m.p. 129–131°, $[\alpha]_D^{20}$ −305° (*c* 0.7, chloroform). ^{1}H-N.m.r. data (90 MHz, $CDCl_3$): δ 6.37 (bd, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.49 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 9.0, $J_{1,3}$ ~0.4 Hz, H-3), 4.83 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 4.28 (dq, 1 H, $J_{1,5}$ ~0.5 Hz, H-5), 4.10 (dd, 1 H, H-2), 2.06 and 2.08 (6 H, OAc), and 1.26 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6).

Anal. Calc. for $C_{10}H_{14}Br_2O_5$: C, 32.11; H, 3.77: Br, 42.73. Found: C, 32.02: H, 3.94; Br, 42.62.

6-Bromo-2,6-dideoxy-D-arabino-*hexono-1,4-lactone* (**5a**). — A solution of the dibromolactone **4** (5 g) in ethyl acetate (75 ml) containing triethylamine (3 ml) was hydrogenated over 5% palladium-on-charcoal (1 g) at room temperature and 1 atmos. until 1 mol. equiv. (~400 ml) of hydrogen was consumed (~20 min). The mixture was filtered and concentrated. The residue, which consisted almost exclusively of **5a** as seen from a ^{13}C-n.m.r. spectrum, was dissolved in 2M hydrochloric acid (20 ml), and the solution was extracted several times with ethyl acetate. The extract was dried and concentrated, to give syrupy **5a** (3.2 g, 86%). ^{13}C-N.m.r. data (D_2O): 179.8 (C-1), 84.9 (C-4), 68.3 and 67.2 (C-3,5), 39.8 (C-2), and 38.2 (C-6).

Crude **5a** (from 5 g of **4**) was treated with acetic anhydride (15 ml) and a few drops of 60% perchloric acid, essentially as described above. The product was crystallised from ether–pentane, to give the 3,5-diacetate[1] **5b** (3.3 g, 65%), m.p. 97–100°. Further recrystallisation gave a product with m.p. 99–100°.

2,6-Dideoxy-D-arabino-*hexono-1,4-lactone* (**6a**). — A solution of **4** (5 g) in ethyl acetate (75 ml) and triethylamine (8 ml) was hydrogenated over 5% palladium-on-charcoal (1 g) for 16 h at room temperature and 1 atmos, and then filtered. The precipitate was washed with ethyl acetate, and the combined filtrate and washings were concentrated. The residue was a colourless syrup containing **6a** and a small

amount of triethylamine hydrobromide as seen from a ^{13}C-n.m.r. spectrum. ^{13}C-N.m.r. data (D_2O): 180.2 (C-1), 88.3 (C-4), 68.4 (C-3), 64.8 (C-5), 39.8 (C-2), and 20.3 p.p.m. (C-6).

A sample was eluted from a column of silica gel with ethyl acetate, to give **6a** as a colourless syrup, $[\alpha]_D^{20}$ +53° (*c* 3.3, ethanol). ^1H-N.m.r. data (90 MHz, pyridine-d_5): δ 4.99 (m, 1 H, H-3), 4.63 (m, 1 H, H-5), 4.37 (dd, 1 H, $J_{3,4}$ 3.4, $J_{4,5}$ 8.2 Hz, H-4), 3.04 (dd, H-1, $J_{2,2'}$ 17.5, $J_{2',3}$ 4.7 Hz, H-2'), 2.78 (dd, 1 H, $J_{2,3}$ 1.2 Hz, H-2), and 1.54 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6).

Crude **6a** (from 5 g of **4**) was acetylated with acetic anhydride and perchloric acid as described above. The product was crystallised from ether–pentane, to give the 3,5-diacetate **6b** (2.55 g, 67%), m.p. 99–101°. An additional recrystallisation gave material having m.p. 101–102° $[\alpha]_D^{20}$ +25° (*c* 1.1, chloroform). ^1H-N.m.r. data (90 MHz, $CDCl_3$): δ 5.61 (septet, 1 H, $J_{2,3}$ 1.2, $J_{2',3}$ 5.5 Hz, H-3), 5.11 (dq, 1 H, H-5), 4.40 (dd, 1 H, $J_{3,4}$ 4.0, $J_{4,5}$ 8.8 Hz, H-4), 2.87 (dd, 1 H, $J_{2,2'}$ 18.0 Hz, H-2'), 2.56 (dd, 1 H, H-2), and 1.40 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6).

Anal. Calc. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.46; H, 6.15.

3,5-Di-O-acetyl-2,6-dideoxy-L-arabino-*hexono-1,4-lactone* (**15b**). — The bromolactone **14** (1 g) was hydrogenolysed essentially as described above. The resulting crude dideoxylactone[5] **15a** was treated with acetic anhydride and perchloric acid essentially as described above. Crystallisation of the product from ether–pentane gave **15b** (700 mg, 69%), m.p. 100–101°, $[\alpha]_D^{20}$ −26° (*c* 1.8, chloroform). The ^1H-n.m.r. spectrum was identical with that of the enantiomer.

Anal. Calc. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.39; H, 6.14.

Crude **6a** (from 2.5 g of **4**) was stirred with pyridine (15 ml) and benzoyl chloride (4 ml) for a few min and then kept overnight at 5°. Water was then added followed by dichloromethane, and the organic phase was washed with 2 M sulfuric acid and aqueous $NaHCO_3$, dried, and concentrated. Recrystallisation of the residue from ether–pentane gave the 3,5-dibenzoate **6c** (2.0 g, 69%), m.p. 130–132°. Two recrystallisations gave a product with m.p. 132–133°, $[\alpha]_D^{20}$ −143° (*c* 0.8 chloroform). ^1H-N.m.r. data (90 MHz, $CDCl_3$): δ 5.86 (m, 1 H, $J_{2,3}$ 1.2, $J_{2',3}$ 5.6 Hz, H-3), 5.57 (dq, 1 H, H-5), 4.74 (dd, 1 H, $J_{3,4}$ 4.3, $J_{4,5}$ 8.0 Hz, H-4), 3.07 (dd, 1 H, $J_{2,2'}$ 18.5 Hz, H-2'), 2.77 (dd, 1 H, H-2), and 1.59 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6).

Anal. Calc. for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12. Found: C, 67.59; H, 5.04.

2,6-Dideoxy-D-arabino-*hexose* (**9a**). — A solution of borane–methyl sulfide complex (Aldrich, 8 ml) in tetrahydrofuran (20 ml) was cooled in ice and stirred under argon while 2-methyl-2-butene (17.5 ml) was added, and then kept for 5 h at room temperature. The resulting solution of di-isoamylborane[17] was then cooled in ice and stirred, and a solution of crude **6a** (2.4 g) in tetrahydrofuran (15 ml) was added during a few min. The solution was kept at room temperature for 18 h, water (10 ml) was added, the mixture was boiled under reflux for 1 h and then partly concentrated, more water was added, and the mixture was extracted thrice with dichloromethane to remove borinic acids. The aqueous phase was concentrated, to give crude, syrupy **9a** (2.3 g). A ^{13}C-n.m.r. spectrum (D_2O) showed that the product was a mixture of

pyranoses (α:β ratio 2:3) and ~10% of another product, probably a deoxypolyol. ^{13}C-N.m.r. data (D_2O). α Anomer: 92.0 (C-1), 77.8 (C-5), 72.7 (C-3), 68.7 (C-4), 38.5 (C-2), and 17.9 p.p.m. (C-6). β Anomer: 94.0 (C-1), 77.2 (C-5), 71.1 (C-3), 68.6 (C-4), 40.7 (C-2), and 17.9 p.p.m. (C-6). The two sets of signals were assigned to the anomers on the basis of their intensities and the $J_{C\text{-}1,H\text{-}1}$ values, which were 167.5 Hz for the α anomer and 160.0 Hz for the β anomer[15].

Methyl 2,6-dideoxy-D-arabino-*hexopyranoside* (**9d**). — To a solution of crude **9a** (2.3 g) in methanol (50 ml) were added a few drops of conc. sulfuric acid. The mixture was kept overnight, neutralised ($BaCO_3$), filtered through carbon, and concentrated to a colourless syrup (2.0 g) which consisted mainly of **α-9d** and **β-9d** in the ratio 5:1 as seen from a ^{13}C-n.m.r. spectrum. ^{13}C-N.m.r. data (D_2O): α Anomer: 98.9 (C-1), 77.4 (C-5), 68.7 (C-3,4), 55.3 (OMe), 37.7 (C-2), and 17.8 p.p.m. (C-6); $J_{C\text{-}1,H\text{-}1}$ 167.6 Hz. β Anomer: 101.4 (C-1); $J_{C\text{-}1,H\text{-}1}$ 159.0 Hz.

Crude **9d** from 5 g of **4** was treated conventionally with pyridine (25 ml) and *p*-nitrobenzoyl chloride (6 g). Crystallisation of the product from ethanol gave crude 3,4-bis(*p*-nitrobenzoate) **8** (3.7 g, 48%), m.p. 140–145°, which was sufficiently pure for the preparation of **7** (see below).

Preparative t.l.c. (ether–pentane, 1:1) of crude **8** gave **α-8** with m.p. 149–151° (from dichloromethane–pentane), $[\alpha]_D^{20}$ −72° (*c* 1.4, chloroform). ^{1}H-N.m.r. data (270 MHz, $CDCl_3$): δ 5.60 (m, 1 H, H-3), 5.15 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 4.83 (bd, 1 H, $J_{1,2a}$ 3.5 Hz, H-1), 4.07 (dq, 1 H, H-5), 3.37 (s, 3 H, OMe), 2.44 (octet, 1 H, $J_{1,2e}$ 1.2, $J_{2e,3}$ 5.3, $J_{2e,2a}$ 12.0 Hz, H-2*e*), 1.98 (octet, 1 H, $J_{2a,3}$ 11.2 Hz, H-2*a*), and 1.30 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6).

Anal. Calc. for $C_{21}H_{20}N_2O_{10}$: C, 54.78; H, 4.38; N, 6.09. Found: C, 54.57; H, 4.35; N, 6.00.

2,6-Dideoxy-3,4-di-O-p-*nitrobenzoyl*-α-D-arabino-*hexopyranosyl bromide* (**7**). — A solution of crude **8** (500 mg) in dichloromethane (5 ml) and acetic acid saturated with hydrogen bromide (2 ml) was kept for 1 h at room temperature. More dichloromethane was then added and the solution was washed with water, aqueous $NaHCO_3$, dried, and concentrated. The residue was crystallised from ether–pentane, to give **7** (420 mg, 80%), m.p. 110–114°. Two recrystallisations from dichloromethane–ether–pentane gave a product with m.p. 120–122° $[\alpha]_D^{20}$ −5° (*c* 2.2, chloroform). ^{1}H-N.m.r. data (90 MHz, $CDCl_3$): δ 6.62 (bd, 1 H, $J_{1,2a}$ 3.7, $J_{1,2e}$ ~1 Hz, H-1) 5.89 (m, 1 H, H-3), 5.29 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 4.40 (dq, 1 H, H-5), 2.73 (octet, 1 H, $J_{2e,3}$ 5.0, $J_{2a,2e}$ 14.0 Hz, H-2*e*), 2.49 (octet, 1 H, $J_{2a,3}$ 10.6 Hz, H-2*a*), and 1.36 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6).

Anal. Calc. for $C_{20}H_{17}BrN_2O_9$: C, 47.16; H, 3.37; Br, 15.69. Found: C, 47.54; H, 3.43; Br, 15.58.

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