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THE PREPARATION OF SOME BROMODEOXY- AND DIBROMODIDEOXY-PENTONOLACTONES*

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ABSTRACT

Brief reaction of D-lyxono-1,4-lactone (**1**) with hydrogen bromide in acetic acid (HBA) yields 2-bromo-2-deoxy-D-xylono-1,4-lactone (**2**), and a similar treatment of D-ribono-1,4-lactone (**8**) gives 2-bromo-2-deoxy-D-arabinono-1,4-lactone (**12**). On longer reaction with HBA, **1** is converted into 2,5-dibromo-2,5-dideoxy-D-xylono-1,4-lactone, whereas **8** forms a mixture of 2,5-dibromolactones. Reduction of **2** and **12** gives 2-bromo-2-deoxy-D-xylose and -D-arabinose, respectively. On hydrogenolysis, **2** and **12** are converted into 2-deoxy-D-*threo*- and 2-deoxy-D-*erythro*-pentono-1,4-lactone, respectively. The 2,5-dibromolactones can be selectively hydrogenolysed to 5-bromo-2,5-dideoxy-D-pentono-1,4-lactones.

INTRODUCTION

Bromodeoxylactones have been prepared[1–3] by treatment of hexonolactones, or salts of hexonic acids, with a solution of hydrogen bromide in acetic acid (HBA). In each reaction, the primary hydroxyl group was substituted with bromine to give 6-bromo-6-deoxylactones. With D-glucono-, D-mannono-, and L-rhamnono-lactone, bromine also reacted at C-2 with inversion of configuration; no other hydroxyl group was replaced by bromine. We now report on the reactions of D-lyxono- (**1**) and D-ribono-lactone (**8**) with HBA.

RESULTS AND DISCUSSION

When D-lyxono-1,4-lactone[4] (**1**) was treated with HBA for 1 h at room temperature, followed by deacetylation with methanol, 2-bromo-2-deoxy-D-xylono-1,4-lactone (**2**) was isolated in 75% yield, and the dibromolactone **3a** in 5% yield. Prolonged treatment (2–3 days) of **1** or **2** with HBA gave 2,5-dibromo-2,5-dideoxy-D-xylono-1,4-lactone (**3a**) as the sole reaction product. Both **2** and **3a** could be prepared equally well from the more readily available potassium D-lyxonate[4].

The reaction of D-ribono-1,4-lactone (**8**) with HBA for 4 h gave, after separa-

*Reaction of Aldonic Acids with Hydrogen Bromide, Part III. For Part II, see ref. 2.

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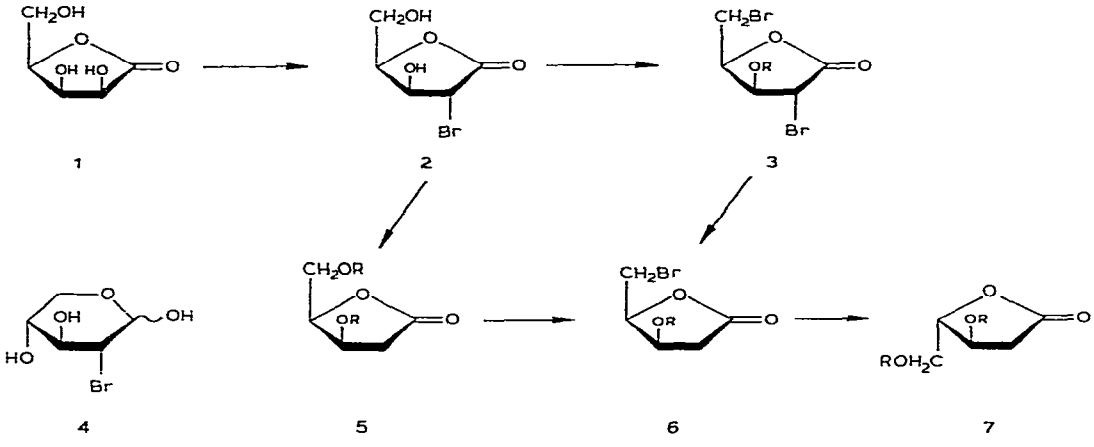
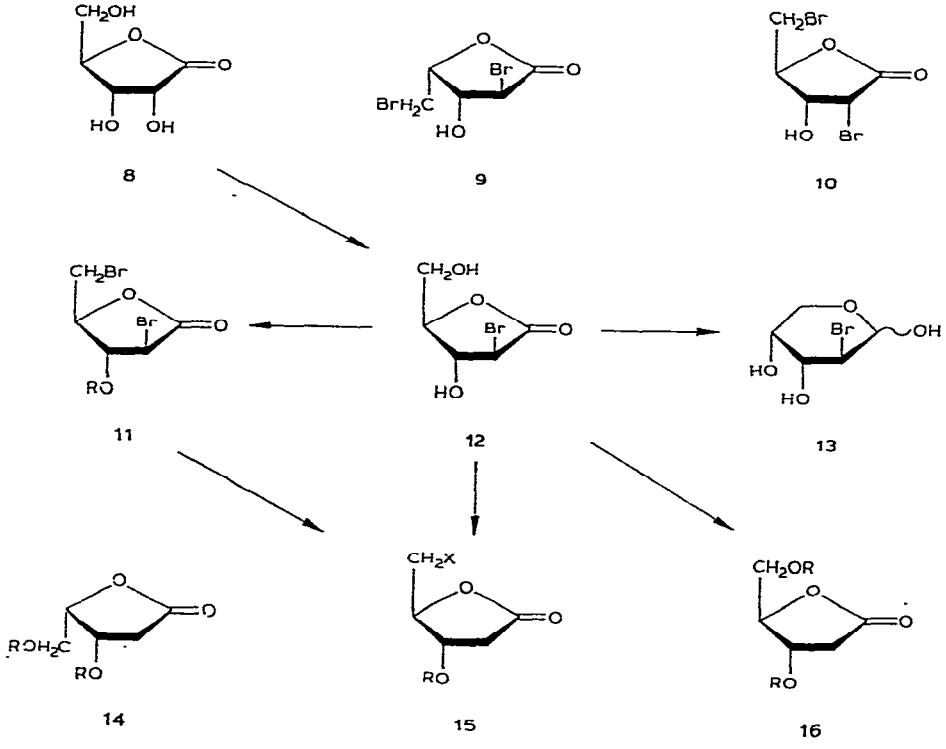


a R = H
b R = Ac
c R = Bz



a R = H
b R = Ac
c R = Bz

tion, 2-bromo-2-deoxy-D-arabinono-1,4-lactone (**12**, 64%) and 2,5-dibromo-2,5-dideoxy-D-arabinono-1,4-lactone (**11a**, 4%). In a series of experiments, **8** was treated with HBA for 1–7 days, and analysis of the crude products by ^{13}C-n.m.r. spectroscopy showed that the initially formed 2-bromolactone **12** slowly disappeared while increasing amounts of **11a** appeared. However, isomers of **11a** were also formed. When **8** was allowed to react with HBA for 60 h, 32% of the monobromolactone **12** and 57% of a mixture of dibromolactones were obtained. Fractionation of the latter yielded **11a** as the major product, accompanied by smaller amounts of 2,5-dibromo-2,5-dideoxy-L-xylono-1,4-lactone (**9**) and the corresponding D-ribonolactone **10**. Prolonged treatment of **12** with HBA gave a mixture of **11a**, **9**, and **10**. On the other hand, when the pure dibromolactone **11a** was treated with HBA for 4 days, the isomeric products **9** and **10** were not detected, showing that they are formed from **12** and not by isomerisation of **11a**.

The structures of the 2-bromo-2-deoxylactones **2** and **12** could not be derived unambiguously from their n.m.r. spectra. However, reduction with sodium borohydride in the presence of an acidic ion-exchange resin[5] gave 2-bromo-2-deoxy-D-xylose (**4**) and 2-bromo-2-deoxy-D-arabinose (**13**), respectively; **4** was converted into known 3,4-di-*O*-benzoyl-2-bromo-2-deoxy-α-D-xylopyranose[6]. Crystalline **13** was identical with a previously described product[7]. Thus, the structures of the lactones **2** and **12** were established.

Catalytic hydrogenolysis of **2** and **12** gave the corresponding 2-deoxylactones **5a**[8] and **16a**[9], respectively, isolated as their crystalline dibenzoates **5c** and **16c**. Reduction of 2-deoxy-D-*erythro*-pentono-1,4-lactone (**16a**) with di-isoamylborane yielded 2-deoxy-D-*erythro*-pentose, which was isolated as the anilide. Selective hydrogenolysis of the 2,5-dibromolactone **3a** gave 5-bromo-2,5-dideoxy-D-*threo*-pentono-1,4-lactone (**6a**), which was identical with a product obtained by total synthesis[9]. This result proves the configuration at C-3 and C-4 of **3a**, and since **3a** was prepared by treatment of the 2-bromolactone **2** with HBA, it seems likely that **3a** and **2** have the same configuration at C-2. Acetylation of **3a** followed by treatment with sodium iodide in acetone and trifluoroacetic acid[1] also resulted in selective removal of the bromine at C-2, to give the acetylated 5-bromo-2-deoxylactone **6b**. Treatment of 2-deoxy-D-*threo*-pentono-1,4-lactone (**5a**) with HBA also gave **6b** in good yield.

Selective hydrogenolysis of the dibromolactone **11a** produced 5-bromo-2,5-dideoxy-D-*erythro*-pentono-1,4-lactone (**15a**, X = Br), isolated as the crystalline acetate (**15b**, X = Br). Treatment of the acetate **11b** with sodium iodide in trifluoroacetic acid–acetone gave the 5-iodo compound (**15b**, X = I). The reaction of **16a** with HBA was slow and gave, in addition to the expected **15a** (X = Br), an isomeric product, either **6a** or its enantiomer as indicated by the ^{13}C-n.m.r. spectrum.

Nakaminami *et al.*[9] found that hydrolysis of the 5-bromolactone **6a** with aqueous base gave 2-deoxy-L-*erythro*-pentono-1,4-lactone (**7a**), subsequent to lactonisation of the initially formed carboxylate. In our hands, **7a**, produced from **6a** by reaction with base[9], gave a dibenzoate (**7c**) which proved to be the enantiomer of

16c. Similar treatment of **15a** (X = Br) with aqueous base yielded a mixture of **14a**, **16a**, and an unidentified, unsaturated product as indicated by the ^{13}C-n.m.r. spectra.

Whereas the dibromolactone **9** was identified as the enantiomer of **3a**, the isomer **10** was assumed to be the C-2 epimer of **11**, since selective hydrogenolysis and acetylation gave **15b** (X = Br).

Previous work indicates that the reaction of aldonolactones with HBA takes place *via* partial acetylation, formation of acetoxonium ions, and subsequent reaction of the latter with bromide ions[10]. The bromine at C-5 could possibly be introduced by a direct replacement. However, the formation of **9** from **12** with inversion at C-4 indicates that the lactone ring has opened during this reaction, and it seems likely that, in all cases, bromine is introduced at C-5 *via* a 4,5-acetoxonium ion derived from a ring-opened lactone. The introduction of bromine at C-2 in **1** and **8** could take place *via* 2,3-acetoxonium ions derived from the lactones. However, gluconolactone, having HO-2 and HO-3 *trans*-oriented, also yields[1] a 2-bromo derivative with HBA, and in this case an acetoxonium ion could not be formed without opening of the lactone ring.

EXPERIMENTAL

The ~35% solution of hydrogen bromide in acetic acid (HBA) was prepared by saturating glacial acetic acid with anhydrous hydrogen bromide at 0°. T.l.c. was performed on silica gel (Merck PF_{254}) with detection by charring with sulfuric acid or with the hydroxamic acid reagent[11]. The flash column-chromatography technique[12] was used with silica gel 60 (40–63 μm, Merck 9385). Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 instrument, and ^{1}H- and ^{13}C-n.m.r. spectra were recorded with Bruker HX-90, WH-90, and HX-270 instruments. Microanalyses were performed by NOVO microanalytical laboratory.

2-Bromo-2-deoxy-D-*xylono-1,4-lactone* (**2**). — A solution of D-lyxono-1,4-lactone[4] (5 g) in HBA (50 ml) was kept for 1 h at room temperature. Methanol (100 ml) was then added (exothermic reaction), and the solution was kept overnight and then concentrated. Water was twice distilled from the residue, a solution of which in water (50 ml) was then extracted with chloroform (6 × 20 ml). The extract was dried ($MgSO_4$) and concentrated, leaving the pure dibromolactone **3a** (0.5 g, 5%) as indicated by the ^{13}C-n.m.r. spectrum.

The aqueous phase was extracted continuously with ether for 3 h. The extract was dried ($MgSO_4$) and concentrated, and the residue (6.0 g) was crystallised from a small amount of ether, to give **2** (5.6 g, 78%), m.p. 81–84°. Recrystallisation from ethyl acetate–pentane gave a product with m.p. 86.5–87.5°, $[\alpha]_D^{20}$ +26° (*c* 2.5, ethyl acetate). N.m.r. data: ^{1}H (270 MHz, D_2O): δ 4.92 (q, 1 H, $J_{4,5}$ 4.5 Hz, H-4), 4.77 (t, 1 H, $J_{3,4}$ 4.5 Hz, H-3), 4.64 (d, 1 H, $J_{2,3}$ 4.2 Hz, H-2), and 3.95 (d, 2 H, H-5); ^{13}C (D_2O): 175.4 (C-1), 84.1 (C-4), 75.1 (C-3), 59.9 (C-5), and 43.7 p.p.m. (C-2).

Anal. Calc. for $C_5H_7BrO_4$: C, 28.46; H, 3.34; Br, 37.87. Found: C, 28.32; H, 3.35; Br, 37.81.

Alternatively, potassium D-lyxonate[4] (50 g) was stirred with HBA (250 ml) for 1 h. Further treatment as described above gave **3a** (8.6 g, 13%) and crude **2** (43 g) which, on crystallisation from ether, yielded material (29 g, 57%) having m.p. 82–86°.

2,5-Dibromo-2,5-dideoxy-D-*xylono-1,4-lactone* (**3a**). — (*a*) A suspension of potassium D-lyxonate (10 g) in HBA (75 ml) was stirred for 4 days at room temperature. Methanol (150 ml) was added, and the mixture was kept overnight, and then filtered and concentrated. Water was twice evaporated from the residue, and a solution of the residue in water (20 ml) was then extracted with chloroform (10 × 20 ml). The extract was dried and concentrated, leaving a syrup (10.7 g, 80%) which contained only **3a** as indicated by the ^{13}C-n.m.r. spectrum. The product, which was sufficiently pure for use in further reactions, crystallised on storage, and recrystallisation from chloroform at −78° gave **3a** (4.7 g, 45%), m.p. 60.5–62°. Recrystallisation from chloroform gave a product with m.p. 63–64.5°, $[\alpha]_D^{25}$ +12° (*c* 9.6, ethyl acetate). N.m.r. data: ^{1}H (270 MHz, $CDCl_3$): δ 5.00 (dt, 1 H, $J_{4,5}$ 7.0 Hz, H-4), 4.71 (d, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 4.32 (s, 1 H, $J_{2,3}$ ~0 Hz, H-2), and 3.69 (d, 2 H, H-5); ^{13}C ($CDCl_3$): 172.7 (C-1), 81.8 (C-4), 73.7 (C-3), 41.6 (C-2), and 26.2 p.p.m. (C-5).

Anal. Calc. for $C_5H_6Br_2O_3$: C, 21.91; H, 2.21; Br, 58.36. Found: C, 21.99; H, 2.18; Br, 58.84.

(*b*) Treatment of 2-bromo-2-deoxy-D-xylono-1,4-lactone (**2**, 783 mg) with HBA (10 ml) for 4 days, with work-up as described above, gave syrupy **3a** (835 mg, 82%), identified by its ^{13}C-n.m.r. spectrum. An ether extract of the aqueous phase gave crude **2** (143 mg, 18%).

2-Bromo-2-deoxy-D-*arabinono-1,4-lactone* (**12**). — A solution of D-ribono-1,4-lactone (**8**, 50 g) in HBA (250 ml) was kept for 4 h at room temperature, methanol (350 ml) was added, the solution was kept overnight and then concentrated, and water was evaporated from the residue. A solution of the crude product in water (40 ml) was extracted with chloroform (10 × 25 ml). The extract was dried and concentrated, leaving the crude dibromolactone **11a** (3.8 g, 4%). The aqueous phase was extracted continuously with ether overnight, and the extract was dried and concentrated, leaving a product (83 g) which, on crystallisation from ether, gave **12** (46 g, 64%), m.p. 75–79°. Further recrystallisation gave a product with m.p. 79–81°, $[\alpha]_D^{21}$ +72° (*c* 4.1, ethyl acetate). N.m.r. data: ^{1}H (270 MHz, D_2O): δ 4.90 (d, 1 H, $J_{2,3}$ 7.8 Hz, H-2), 4.56 (t, 1 H, $J_{3,4}$ 7.8 Hz, H-3), 4.50 (m, 1 H, $J_{4,5}$ 2.4, $J_{4,5'}$ 4.7 Hz, H-4), 3.98 (dd, 1 H, $J_{5,5'}$ 13.2 Hz, H-5), and 3.81 (dd, 1 H, H-5'); ^{13}C (D_2O): 173.6 (C-1), 85.6 (C-4), 75.3 (C-3), 60.2 (C-5), and 46.8 p.p.m. (C-2).

Anal. Calc. for $C_5H_7BrO_4$: C, 28.46; H, 3.34; Br, 37.87. Found: C, 28.40; H, 3.30; Br, 37.70.

2,5-Dibromo-2,5-dideoxy-D-*arabinono-1,4-lactone* (**11a**). — (*a*) D-Ribonolactone (20 g) was treated with HBA (200 ml) for 60 h and worked-up as described above. The chloroform extract gave a mixture (21 g, 57%) of dibromolactones **11a**, **9**, and **10** (as indicated by the ^{13}C-n.m.r. spectrum) in the ratios 9:3:1. An ether extract of the aqueous phase gave the monobromolactone **12** (9 g, 32%), m.p. 77–80°.

The mixture of dibromolactones was purified by column chromatography in 2.5-g portions, using ethyl acetate–pentane (1:2). Eluted first was 2,5-dibromo-2,5-dideoxy-L-xylono-1,4-lactone (**9**: 2.7 g, 7%), which was crystallised and recrystallised from chloroform at −78° to give a product with m.p. 63–65°, $[\alpha]_D^{25}$ −12° (*c* 3, ethyl acetate). The ^{1}H- and ^{13}C-n.m.r. spectra were identical with those of the enantiomer **3**.

Anal. Calc. for $C_5H_6Br_2O_3$: C, 21.91; H, 2.21; Br, 58.36. Found: C, 22.11; H, 2.21; Br, 58.51.

After a small fraction containing **11a** and **9**, pure (^{13}C-n.m.r.) **11a** was eluted (13.3 g, 36%); **11a** could be crystallised with difficulty from chloroform at −78° to give a product with m.p. 46–47°, $[\alpha]_D^{25}$ +62° (*c* 6, ethyl acetate). N.m.r. data: ^{1}H (270 MHz, $CDCl_3$): δ 4.6–4.5 (m, 3 H, H-2,3,4), 3.77 (dd, 1 H, $J_{5,5'}$ 11.5 Hz, H-5), and 3.67 (dd, 1 H, H-5'); ^{13}C ($CDCl_3$): 170.7 (C-1), 82.9 (C-4), 77.4 (C-3), 44.6 (C-2), and 30.3 p.p.m. (C-5).

Anal. Calc. for $C_5H_6Br_2O_3$: C, 21.91; H, 2.21; Br, 58.36. Found: C, 21.91; H, 2.14; Br, 58.62.

Eluted next was a mixture (0.85 g) of **11a** and **10**, followed by a syrupy product (0.32 g, ~1%) assumed to be 2,5-dibromo-2,5-dideoxy-D-ribono-1,4-lactone (**10**). N.m.r. data: ^{1}H (270 MHz, $CDCl_3$): δ 4.71 (d, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 4.62 (m, 1 H, $J_{4,5}$ 4.1, $J_{4,5'}$ 3.9 Hz, H-4), 4.40 (dd, 1 H, $J_{3,4}$ 5.7 Hz, H-3), 3.78 (dd, 1 H, $J_{5',5}$ 11.9 Hz, H-5), and 3.67 (dd, 1 H, H-5'); ^{13}C ($CDCl_3$): 169.6 (C-1), 81.9 (C-4), 69.9 (C-3), 45.6 (C-2), and 30.1 p.p.m. (C-5).

(*b*) Treatment of 2-bromo-2-deoxy-D-arabinono-1,4-lactone (**12**, 1.3 g) with HBA (12 ml) for 4 days, with work-up as described above, gave a product (1.12 g, 67%; chloroform extract) whose ^{13}C-n.m.r. spectrum showed it to be a mixture of the dibromolactones **11a**, **9**, and **10** in the ratios 10:4:1. An ether extract gave **12** (342 mg, 18%).

Treatment of **11a** *with HBA.* — When **11a** (391 mg) was treated with HBA (5 ml) for 4 days and worked-up as described above, the chloroform extract contained a product (309 mg, 79%) that consisted of **11a** together with a small proportion of unsaturated products, as indicated by the ^{13}C-n.m.r. spectrum. The dibromolactones **9** and **10** were not detected.

*2-Bromo-2-deoxy-*D*-xylose* (**4**). — The bromolactone **2** (2.5 g) was dissolved in water (25 ml), and Amberlite IR-120 (H^+) resin was added[5]. The mixture was cooled in ice and stirred while sodium borohydride (450 mg, 1 mol. equiv.) was added, during 30 min, at such a rate that the pH was kept <6.

After an additional 30 min, the resin was removed and the filtrate was co-concentrated with methanol to remove boric acid. The residue was eluted from a column of silica gel with ethyl acetate to give **2** (310 mg, 12%) and then **4** (1.5 g, 60%); after crystallisation from ethyl acetate, **4** had m.p. 117–118°, $[\alpha]_D^{25}$ +51.5° (equil.; *c* 0.4, water). ^{13}C-N.m.r. data (D_2O): **α4**: 92.7 (C-1), 73.2 (C-3), 70.8 (C-4), 61.4 (C-5), and 53.3 p.p.m. (C-2), $J_{C\text{-}1,H\text{-}1}$ 172 Hz; **β4**: 96.9 (C-1), 76.8 (C-3), 70.3 (C-4), 65.5 (C-5), and 56.0 p.p.m. (C-2), $J_{C\text{-}1,H\text{-}1}$ 164 Hz. The ^1J values show that

both anomers adopt the same conformation[13]. The ^{1}H-n.m.r. spectrum (pyridine-d_5) showed two signals: δ 5.64 (J 3.0 Hz, α anomer) and 5.29 (J 8.0 Hz, β anomer), indicating that each anomer adopts the $^4C_1$ conformation.

Anal. Calc. for $C_5H_9BrO_4$: C, 28.19; H, 4.26; Br, 37.51. Found: C, 28.38; H, 4.32; Br, 37.79.

3,4-Di-O-benzoyl-2-bromo-2-deoxy-D-xylopyranose. — Crude **4**, as described above (from 2.5 g of **2**), was treated with benzoyl chloride (8 ml) in pyridine (15 ml) at 0° for 1 h and at room temperature overnight. Work-up in the usual way gave a mixture (4.7 g, ~75%) of the anomeric tri-*O*-benzoyl-2-bromo-2-deoxy-D-xylopyranoses, as indicated by the ^{1}H-n.m.r. spectrum. The product was stirred with HBA (30 ml) for 2 h, and the mixture was then diluted with dichloromethane, washed with water and aqueous $NaHCO_3$, dried, and concentrated. The residue (4.8 g) consisted of a mixture of the anomeric di-*O*-benzoyl-2-bromo-2-deoxy-D-xylopyranosyl bromides, as indicated by the ^{1}H-n.m.r. spectrum[6]. The product was stirred for 20 h in water (30 ml) and acetone (200 ml) in the presence of silver carbonate (5 g). Filtration and concentration left the title compound (3.2 g, 64%) which, after recrystallisation from ether–pentane, had m.p. 146–147°, $[\alpha]_D^{20}$ −32° (equil.: c 1.4, chloroform); lit.[6] m.p. 145–146°, $[\alpha]_D$ −30.5°.

2-Bromo-2-deoxy-D-arabinose (**13**). — The 2-bromolactone **12** (1.0 g) was reduced with sodium borohydride (500 mg) as described above. A ^{13}C-n.m.r. spectrum of the crude product revealed a mixture of the pyranoses **13**, the lactone **12**, and 2-bromo-2-deoxy-D-arabinitol in the ratios 1:1:0.3. The product (927 mg) was eluted from a column of silica gel[12] with ethyl acetate, to give **12** (320 mg, 32%) and then **13** (280 mg, 28%); after crystallisation from ethyl acetate–pentane, **13** had m.p. 122–124°, $[\alpha]_D^{20}$ −121 → −113° (c 1.1, water); lit.[7] m.p. 125°, $[\alpha]_D^{18}$ −121° (after 5 min). ^{13}C-N.m.r. data: **α13** (D_2O): 97.4 (C-1), 74.2 (C-3), 69.7 (C-4), 67.4 (C-5), and 56.2 p.p.m. (C-2), $J_{C\text{-}1,H\text{-}1}$ 165 Hz; **β13**: 93.3 (C-1), 69.9 and 69.7 (C-3,4), 63.6 (C-5), and 53.2 p.p.m. (C-2), $J_{C\text{-}1,H\text{-}1}$ 174 Hz. The ^1J values indicate that both anomers adopt the same conformation[13]. The ^{1}H-n.m.r. spectrum (pyridine-d_5) showed signals at δ 5.76 (J 3.0 Hz, β anomer) and 5.13 (J 8.0 Hz, α anomer) indicating a $^1C_4$ conformation for each isomer.

3,5-Di-O-benzoyl-2-deoxy-D-threo-pentono-1,4-lactone (**5c**). — A solution of the 2-bromolactone **12** (1.0 g) in ethyl acetate (30 ml) and triethylamine (0.7 ml) was hydrogenolysed for 2.5 h at atmospheric pressure in the presence of 5% palladium-on-carbon (200 mg). The mixture was then filtered and concentrated, leaving syrupy 2-deoxy-D-*threo*-pentono-1,4-lactone[8] (**5a**) containing some triethylamine hydrobromide. ^{13}C-N.m.r. data (D_2O): 180.2 (C-1), 84.4 (C-4), 68.5 (C-3), 60.7 (C-5), and 39.6 p.p.m. (C-2).

The crude product was treated with benzoyl chloride (1.5 ml) in pyridine (5 ml) at room temperature overnight. Work-up in the usual way gave a product (962 mg) that crystallised from ether to give **5c** (660 mg, 41%), m.p. 104–106°. Recrystallisation from ether gave a product with m.p. 104–106°, $[\alpha]_D^{25}$ +19° (c 1.7, ethyl acetate). ^{1}H-N.m.r. data (90 MHz, $CDCl_3$): δ 5.89 (m, 1 H, $J_{3,4}$ 4.6 Hz, H-3), 5.04 (q, 1 H,

$J_{4,5}$ 4.6 Hz, H-4), 4.69 (d, 2 H, H-5), 3.13 (dd, 1 H, $J_{2,2'}$ 18.2, $J_{2,3}$ 6.4 Hz, H-2), and 2.73 (dd, 1 H, $J_{2',3}$ 2.5 Hz, H-2').

Anal. Calc. for $C_{19}H_{16}O_6$: C, 67.05; H, 4.74. Found: C, 66.74; H, 4.82.

2-Deoxy-N-*phenyl*-D-erythro-*pentosylamine*. — To a cooled solution of syrupy 2-deoxy-D-*erythro*-pentono-1,4-lactone[9] (**16a**, from 1.19 g of **12**) in tetrahydrofuran (2 ml) was added a solution of di-isoamylborane [prepared[14] from the borane–dimethyl sulfide complex (2.3 ml) and 2-methyl-2-butene (5.7 ml) in tetrahydrofuran (10 ml)]. The mixture was kept overnight at room temperature and then boiled with water (5 ml) for 1.5 h, extracted with dichloromethane (3 × 50 ml), and concentrated. A ^{13}C-n.m.r. spectrum of the residue revealed a mixture of 2-deoxy-D-*erythro*-pentose and **16a** in the ratio 1.3 : 1. If sufficient borane was used to reduce all of the lactone, a large proportion of 2-deoxy-D-*erythro*-pentitol was formed. The dried product was dissolved in ethanol (5 ml), and freshly distilled aniline (0.57 ml) in ethanol (2 ml) was added. After 4 h at room temperature, the product was collected, washed with ether, and dried, yielding the title anilide (495 mg, 42 %), m.p. 152–156°. Recrystallisation from ethanol gave a product with m.p. 168–170°. A mixture m.p. with an authentic sample (m.p. 164–166°) was 165–167°; lit.[9,15] m.p. 170–173° and 172–173°.

3,5-Di-O-*benzoyl-2-deoxy*-D-erythro-*pentono-1,4-lactone* (**16c**). — Compound **16a** (prepared from 1 g of **12**) was treated with benzoyl chloride in pyridine and worked-up in the usual way. The product was crystallised from dichloromethane–pentane to give **16c** (695 mg, 43%), m.p. 99–100°, $[\alpha]_D^{25}$ +19° (*c* 3.3, ethyl acetate). ^1H-N.m.r. data (90 MHz, $CDCl_3$): δ 5.60 (dq, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 4.93 (dt, 1 H, $J_{4,5}$ 3.5 Hz, H-4), 4.71 (dd, 1 H, $J_{5,5'}$ 14.0 Hz, H-5), 4.53 (dd, 1 H, $J_{4,5'}$ 4.0 Hz, H-5'), 3.18 (dd, 1 H, $J_{2,2'}$ 18.5, $J_{2,3}$ 7.0 Hz, H-2), and 2.75 (dd, 1 H, $J_{2',3}$ 2.4 Hz, H-2').

Anal. Calc. for $C_{19}H_{16}O_6$: C, 67.05; H, 4.74. Found: C, 67.15; H, 4.68.

5-Bromo-2,5-dideoxy-D-threo-*pentono-1,4-lactone* (**6a**). — A mixture of the bromolactone **3a** (1.51 g), ethyl acetate (30 ml), triethylamine (0.8 ml, 1.1 mol. equiv.), and 5% palladium-on-carbon (200 mg) was hydrogenolysed at 1 atmos. In ~30 min, 1 equiv. of hydrogen had been consumed and the rate of uptake then decreased. The mixture was filtered, washed with 4M hydrochloric acid (5 ml), dried, and concentrated, leaving crude **6a** (1.0 g). ^{13}C-N.m.r. spectrum (D_2O): 176.2 (C-1), 83.3 (C-4) 67.3 (C-3), 38.8 (C-2), and 27.2 p.p.m. (C-5). Column chromatography with ethyl acetate–pentane (1 : 1) gave material (679 mg, 72%) having $[\alpha]_D^{25}$ +59° (*c* 2.6, water); lit.[9] $[\alpha]_D$ +54°.

3-O-*Acetyl-5-bromo-2,5-dideoxy*-D-threo-*pentono-1,4-lactone* (**6b**). — (*a*) To the dibromolactone **3a** (1.0 g) in acetic anhydride (10 ml) were added a few drops of 60% aqueous perchloric acid. After 30 min, ice was added and, after hydrolysis of the acetic anhydride, the mixture was extracted with dichloromethane. The extract was washed with water, dried, and concentrated, to give crude 3-*O*-acetyl-2,5-dibromo-2,5-dideoxy-D-xylono-1,4-lactone (**3b**; 1.1 g, 95%).

The product was stirred at room temperature for 20 h in acetone (15 ml) and

trifluoroacetic acid (2 ml) in the presence of sodium iodide (7 g). Chloroform was then added, and the mixture was washed with water, aqueous $NaHCO_3$, and aqueous $Na_2S_2O_3$, dried, and concentrated. The residue (780 mg) was crystallised from ether to give **6b** (449 mg, 52%), m.p. 93–96°. Recrystallisation from dichloromethane–pentane gave a product with m.p. 96–97.5°, $[\alpha]_D^{25}$ −5° (*c* 2.4, ethyl acetate). ^{1}H-N.m.r. data (90 MHz, $CDCl_3$): δ 5.56 (m, 1 H, $J_{3,4}$ 4.5 Hz, H-3), 4.79 (dt, 1 H, $J_{4,5}$ 7.0, $J_{4,5'}$ 7.5 Hz, H-4), 3.4–3.8 (2 H, ABX-system, H-5,5'), 3.00 (dd, 1 H, $J_{2,2'}$ 18.1, $J_{2,3}$ 5.5 Hz, H-2), 2.60 (dd, 1 H, $J_{2',3}$ 1.5 Hz, H-2'), and 2.11 (OAc).

Anal. Calc. for $C_7H_9BrO_4$: C, 35.47; H, 3.83; Br, 33.71. Found: C, 35.52; H, 3.78; Br, 33.46.

(*b*) Crude 2-deoxylactone **5a** (prepared from 2.5 g of **2** as described above) was treated with HBA (20 ml) for 48 h at room temperature. Acetic anhydride (5 ml) was then added and, after 2 h, water and dichloromethane were added. The solution was washed with water, dried, and concentrated, leaving **6b** (1.4 g, 50%), m.p. 91–93° (from ether–pentane). N.m.r. spectroscopy proved its identity with the product described above.

3-O-Acetyl-5-bromo-2,5-dideoxy-D-erythro-*pentono-1,4-lactone* (**15b**, X = Br). — The dibromolactone **11a** (866 mg) was hydrogenolysed in ethyl acetate (10 ml) and triethylamine (0.44 ml) in the presence of 5% palladium-on-carbon (100 mg) until 1 equiv. of hydrogen had been consumed. The mixture was then filtered and concentrated, leaving a syrup that consisted of crude 5-bromo-2,5-dideoxy-D-*erythro*-pentono-1,4-lactone (**15a**, X = Br). ^{13}C-N.m.r. data (D_2O): 174.8 (C-1), 85.3 (C-4), 69.0 (C-3), 37.3 (C-2), and 32.4 p.p.m. (C-5).

The product was acetylated with acetic anhydride (5 ml) and a few drops of 60% aqueous perchloric acid. Work-up in the usual manner gave crude **15b** (X = Br) (450 mg). Purification by p.l.c. (ether–pentane, 1 : 1) gave material (248 mg, 33%), m.p. 61–63°, which, on recrystallisation from ethyl acetate–pentane, yielded **15b** (X = Br), m.p. 63.5–64°. $[\alpha]_D^{25}$ −4° (*c* 3.5, ethyl acetate). ^{1}H-N.m.r. data (90 MHz, $CDCl_3$): δ 5.23 (dt, 1 H, $J_{3,4}$ 2.2 Hz, H-3), 4.73 (dt, 1 H, $J_{4,5}$ 3.2, $J_{4,5'}$ 4.0 Hz, H-4), 3.73 and 3.62 (ABX-system, H-5,5'), 3.11 (dd, 1 H, $J_{2,2'}$ 19.5, $J_{2,3}$ 7.6 Hz, H-2), 2.57 (dd, 1 H, $J_{2',3}$ 2.4 Hz, H-2'), and 2.09 (OAc).

Anal. Calc. for $C_7H_9BrO_4$: C, 35.47; H, 3.83; Br, 33.71. Found: C, 35.53; H, 3.84; Br, 33.49.

3-O-Acetyl-2,5-dideoxy-5-iodo-D-erythro-*pentono-1,4-lactone* (**15b**, X = I). — The dibromolactone **11a** (1.7 g) was acetylated with acetic anhydride and perchloric acid, as described above, to give crude, syrupy 3-*O*-acetyl-2,5-dibromo-2,5-dideoxy-D-arabinono-1,4-lactone (**11b**, 2 g), which was characterised by its ^{1}H-n.m.r. spectrum ($CDCl_3$): δ 5.47 (dd, 1 H, $J_{3,4}$ 3.6 Hz, H-3), 4.70 (m, 1 H, $J_{4,5}$ 5.0 Hz, H-4), 4.51 (d, 1 H, $J_{2,3}$ 4.0 Hz, H-2), 3.76 (d, 2 H, H-5), and 2.16 (OAc).

The product was dissolved in acetone (30 ml) and stirred for 20 h with sodium iodide (15 g) and trifluoroacetic acid (2 ml). Work-up as described above gave material (1.4 g) which was purified by column chromatography with ether. Eluted first was **15b** (X = I) (591 mg, 56%), m.p. 48–51°. Recrystallisation from ether–

pentane gave a product with m.p. 54–55°, $[\alpha]_D^{25}$ −10° (*c* 1.6, ethyl acetate). The product was unstable and a correct micro-analysis could not be obtained. N.m.r. data: ^{1}H (90 MHz, $CDCl_3$): δ 5.16 (dt, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 4.53 (m, 1 H, $J_{4,5}$ 4.5, $J_{4,5'}$ 5.0 Hz, H-4), 3.46 (dd, 1 H, $J_{5,5'}$ 10.5 Hz, H-5), 3.36 (dd, 1 H, H-5'), 3.13 (dd, 1 H, $J_{2,2'}$ 19.0, $J_{2,3}$ 7.8 Hz, H-2), 2.56 (dd, 1 H, $J_{2',3}$ 2.8 Hz, H-2'), and 2.1 (OAc); ^{13}C ($CDCl_3$): 172.4 (C-1), 82.7 (C-4), 73.3 (C-3). 34.8 (C-2), 20.6 (OAc), and 4.8 p.p.m. (C-5).

3,5-Di-O-benzoyl-2-deoxy-L-erythro-*pentono-1,4-lactone* (**7c**). — To a solution of **6a** (345 mg) in water (2 ml) was added M potassium hydroxide (0.2 ml). The solution was kept for 30 min at room temperature and then briefly heated to 80°. Excess of Amberlite IR-120 (H^+) resin was added and the mixture was kept overnight. A ^{13}C-n.m.r. spectrum of the solution obtained after filtering off the resin was identical with that of **16a**.

The solution was then treated with Amberlite IR-4B (HO^-) resin to pH ~4, filtered, and concentrated, leaving syrupy 2-deoxy-L-*erythro*-pentono-1,4-lactone (**7a**; 170 mg, 73%). A cold solution of benzoyl chloride (0.5 ml) in pyridine (2 ml) was added, and the mixture was stirred at 0° for 30 min and then overnight at room temperature. Dichloromethane was added, and the solution was washed with 2M H_2SO_4 and aqueous $NaHCO_3$, dried, and concentrated. Crystallisation of the residue from ether gave **7c** (148 mg, 63%), m.p. 96–97.5°. An additional recrystallisation gave a product with m.p. 98–99°, $[\alpha]_D^{25}$ −19° (*c* 1, ethyl acetate). A ^{1}H-n.m.r. spectrum was identical with that of **16c**.

Anal. Calc. for $C_{19}H_{16}O_6$: C, 67.05; H, 4.74. Found: C, 67.03; H, 4.76.

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