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D-*glycero*-D-*gulo*-HEPTONO-1,4-LACTONE AS A PRECURSOR FOR THE SYNTHESIS OF DEOXYHEPTONOLACTONES AND ANHYDRO-HEPTONOLACTONES*

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ABSTRACT

Hydrogenolysis of D-*glycero*-D-*gulo*-heptono-1,4-lactone penta-acetate gave 3-deoxy-D-*gluco*-heptonolactone tetra-acetate, which was converted easily into methyl 3-deoxy-D-*gluco*-heptonate and, thence, into 7-bromo-3,7-dideoxy- and 3,7-dideoxy-D-*gluco*-heptono-1,4-lactone. Reaction of D-*glycero*-D-*gulo*-heptono-1,4-lactone (**4a**) with hydrogen bromide–acetic acid gave 2,7-dibromo-2,7-dideoxy-D-*glycero*-D-*ido*-heptono-1,4-lactone (**5**), hydrogenolysis of which gave 7-bromo-2,7-dideoxy- (**7**), 2,7-dideoxy- (**8**), or 7-bromo-2,3,7-trideoxy-heptono-1,4-lactone (**9**), depending on the conditions. When **5** was heated in water, it gave 2,5:4,7-dianhydro-D-*glycero*-D-*gulo*-heptonic acid. Reaction of **4a** with formic acid in hydrogen fluoride yielded a mixture of 3,6-anhydro-L-*glycero*-D-*gulo*-heptono-1,4-lactone and 3,7-anhydro-D-*glycero*-D-*gulo*-heptono-1,4-lactone. Similar treatment converted **7** and **8** into 3,6-anhydrides.

INTRODUCTION

Aldonolactones have been used as starting materials for the synthesis of deoxy- and dideoxy-aldonolactones and of the corresponding deoxy sugars[1]. Two main types of reaction were used, one of which was the hydrogenolysis of acetylated aldonolactones leading to 3-deoxyaldonolactones[2]. The other reaction involved the treatment of aldonolactones with hydrogen bromide in acetic acid to give bromo-deoxy- or dibromodideoxy-aldonolactones[1,3,4]. These reactions have now been applied to commercially available D-*glycero*-D-*gulo*-heptono-1,4-lactone (**4a**).

RESULTS AND DISCUSSION

Catalytic hydrogenolysis of the penta-acetate (**4b**) of **4a** in the presence of triethylamine gave 90% of the acetylated 3-deoxylactone **1**. The structure was not

*Dedicated to Professor Hans Paulsen.

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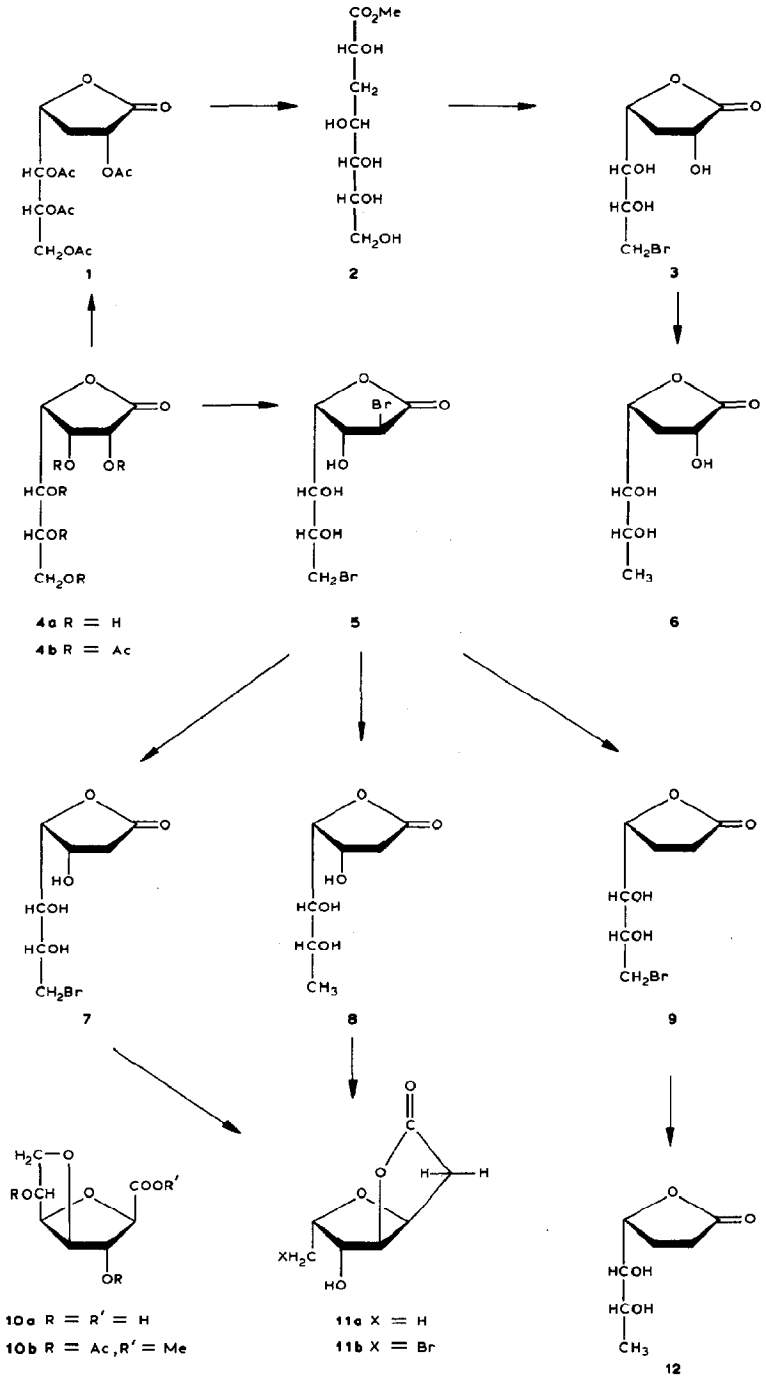

1
2
3
4a R = H
4b R = Ac
5
6
7
8
9
10a R = R′ = H
10b R = Ac, R′ = Me
11a X = H
11b X = Br
12

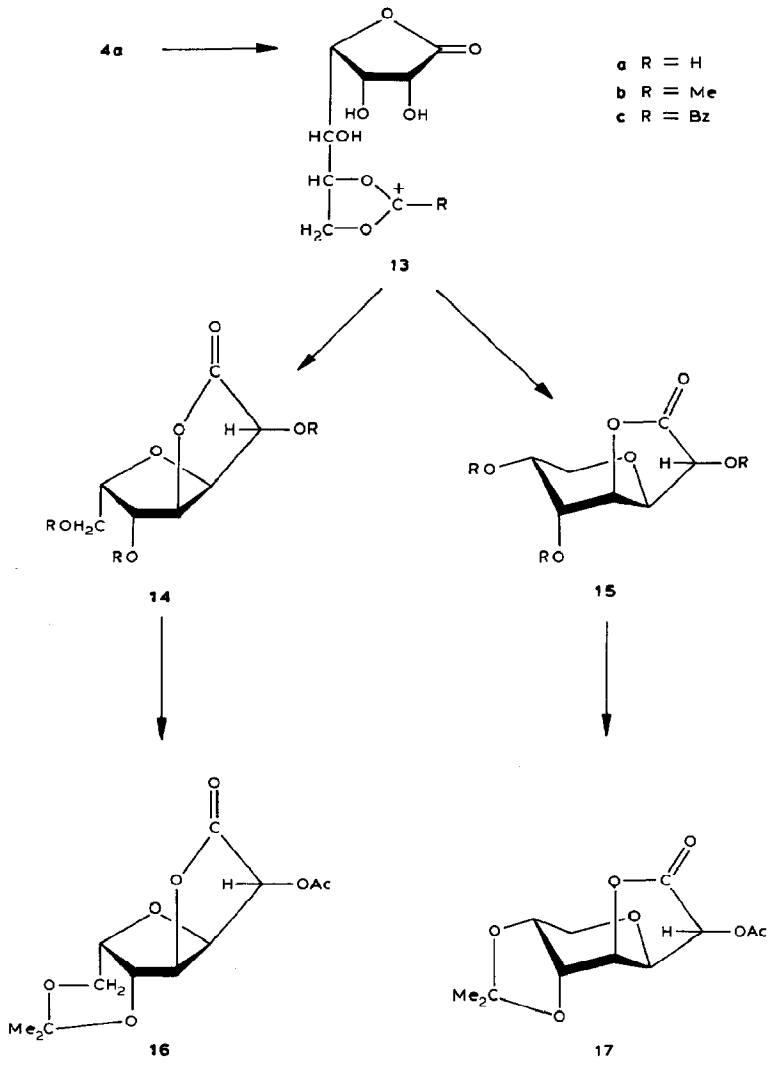
proved rigorously but is in agreement with the n.m.r. spectra; in previous studies of this reaction, AcO-2 was always found to be *cis* to the exocyclic group[2]. The benzoate corresponding to **1** has been prepared by a similar procedure[5]. Zemplén deacetylation of **1** gave 90% of the known[6] methyl 3-deoxy-D-*gluco*-heptonate (**2**). Hence, the latter is readily obtainable in large quantities from **4a**. Treatment of **2** with hydrogen bromide in acetic acid yielded 75% of the 7-bromolactone **3**, hydrogenolysis of which, in the presence of triethylamine, gave the 3,7-dideoxylactone **6**.

By analogy with previous results, treatment of **4a** with hydrogen bromide in acetic acid followed by deacetylation produced a 2,7-dibromolactone assumed to have the D-*glycero*-D-*ido* configuration[1,3,4] (**5**). The yield was only ~45% since two other products were formed also (see below). Crystalline **5** was isolated easily from the reaction mixture and therefore can be prepared readily in rather large quantities. Reduction of **5** with hydrazine hydrate[7] gave 50% of the 7-bromo-2-deoxylactone **7**, whereas hydrogenolysis in the presence of triethylamine gave the 2,7-dideoxylactone **8**. When **5** was hydrogenolysed in ethanol, using no acid acceptor, 56% of the 7-bromo-2,3,7-trideoxylactone[8] **9** was obtained, which was converted into the trideoxylactone **12**.

Treatment of **4a** with hydrogen bromide in acetic acid gave, in addition to the dibromolactone **5**, two other products assumed to be 3,6-anhydro-L-*glycero*-D-*gulo*-heptono-1,4-lactone (**14a**) and 3,7-anhydro-D-*glycero*-D-*gulo*-heptono-1,4-lactone (**15a**). A ^{13}C-n.m.r. spectrum of the crude mixture obtained after the removal of **5** showed **14a** and **15a** to be present in the ratio 2:1. A series of experiments in which **4a** was treated with hydrogen bromide–acetic acid under various conditions indicated that **14a** and **15a** were not formed *via* any bromolactone but were obtained as the only products when **4a** was treated with 1 equiv. of either formic or acetic acid in anhydrous hydrogen fluoride followed by hydrolysis of the ester groups. This indicates that a formoxonium ion (**13a**) or an acetoxonium ion (**13b**) is formed in hydrogen fluoride[9]; attack of HO-3 at C-6 or C-7 subsequently yields **14a** and **15a**, respectively, as partially acetylated or formylated derivatives. The acetoxonium ion **13b** would also be an intermediate in the reaction of **4a** with hydrogen bromide–acetic acid[10] where it can either react with bromide ion at C-7 or cyclise to give **14a** or **15a**.

The structures of **14a** and **15a** were not proved rigorously, but the ^{13}C-n.m.r. spectra of acidic and basic solutions and the ^{1}H-n.m.r. spectra of the tribenzoates **14c** and **15c** accorded with the proposed structures. Furthermore, treatment of a crude mixture of **14a** and **15a** with acetone yielded isopropylidene derivatives, isolated as the 2-acetates **16** and **17**, the ^{13}C-n.m.r. spectra of which clearly showed the presence of six- and five-membered isopropylidene rings. Thus, the resonance of the quaternary carbon of **16** is found at 97.4 p.p.m. and those of the isopropylidene methyl groups (28.4 and 18.7 p.p.m.) are separated by ~10 p.p.m. In **17**, the resonance of the acetal carbon is at lower field (109.5 p.p.m.) and those of the methyl groups (27.5 and 25.5 p.p.m.) are less separated[11].

Treatment of the 2,7-dideoxylactone **8** with hydrogen bromide–acetic acid



gave only small amounts of bromo derivatives, the main product being the 3,6-anhydride **11a**, which was obtained in better yield by treatment of **8** with formic acid in hydrogen fluoride. Hence, **11a** is probably formed in a manner analogous to that of **14** and **15** *via* a 5,6-dioxolanylium ion in which HO-3 attacks C-6. Treatment of the 7-bromo-2-deoxylactone **7** with formic acid in hydrogen fluoride gave the 7-bromo-anhydride **11b**.

When an aqueous solution of the dibromolactone **5** was boiled, it gave the 2,5:4,7-dianhydride **10a**, isolated as the crystalline, acetylated methyl ester **10b** in a yield of 60%. Similar treatment of the 7-bromo-2-deoxylactone **7** gave a mixture of products which was not further studied.

EXPERIMENTAL

General methods. — ^{1}H-N.m.r. spectra (internal Me_4Si) were recorded with a Bruker AM-500 instrument. For solutions in D_2O, the water signal (δ 4.60) was used as internal reference. For ^{13}C-n.m.r. spectra (internal 1,4-dioxane, 67.40 p.p.m.), a Bruker WH-90 instrument was used. Column chromatography was performed on Silica Gel 60 (40–63 μm, Merck, 9385) using the "flash technique"[12]. Melting points are uncorrected.

*2,3,5,6,7-Penta-*O*-acetyl-*D-glycero-D-gulo-*heptono-1,4-lactone* (**4b**). — To a suspension of the heptonolactone **4a** (29.8 mg) in acetic anhydride (200 mL) was added aqueous 60% perchloric acid (1 mL) with cooling and stirring. After 2 h, water (500 mL) was added, the solution was extracted with dichloromethane, and the extract was washed with water, dried, and concentrated. The residue crystallised from ether to give **4b** (57 g, 95%), m.p. 127–129°. Recrystallisation from ethanol gave a product with m.p. 128–129°, $[\alpha]_D^{20}$ −28° (*c* 3.5, chloroform); lit.[13] m.p. 128°, $[\alpha]_D$ −23.8°.

*2,5,6,7-Tetra-*O*-acetyl-3-deoxy-*D-gluco-*heptono-1,4-lactone* (**1**). — To a solution of **4b** (40 g) in ethyl acetate (400 mL) was added triethylamine (50 mL) and 5% Pd/C (1.5 g). The mixture was stirred for 24 h under hydrogen, then filtered through carbon, washed with dilute hydrochloric acid and water, dried, and concentrated. The residue crystallised from ether to give **1** (31 g, 90%), m.p. 97–100°. Recrystallisation from ethanol gave a product with m.p. 101–103°, $[\alpha]_D^{20}$ −8° (*c* 2.4, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.50 ($J_{2,3a}$ 9.1, $J_{2,3b}$ 10 Hz, H-2), 2.76 ($J_{3,3}$ 13.0, $J_{3a,4}$ 6.2 Hz, H-3a), 2.01 ($J_{3b,4}$ 10 Hz, H-3b), 4.71 ($J_{4,5}$ 3.3 Hz, H-4), 5.31 ($J_{5,6}$ 6.7 Hz, H-5), 5.25 ($J_{6,7a}$ 2.8, $J_{6,7b}$ 5.2 Hz, H-6), 4.39 ($J_{7,7}$ 12.4 Hz, H-7a), 4.21 (H-7b), 2.16 (2 OAc), 2.10, 2.06 (OAc).

Anal. Calc. for $C_{15}H_{20}O_{10}$: C, 50.00; H, 5.60. Found: C, 50.21; H, 5.71.

*Methyl 3-deoxy-*D-gluco-*heptonate* (**2**). — To a suspension of **1** (40 g) in methanol (200 mL) was added methanolic M sodium methoxide (5 mL), and the mixture was stirred until a homogeneous solution was formed (~5 min). The mixture was kept overnight at 5°, and the precipitate was collected, washed with methanol and ether, and dried to give **2** (23.3 g, 94%), m.p. 143–145°, which was sufficiently pure for further use. Recrystallisation from methanol gave a product with m.p. 173–175°, $[\alpha]_D^{20}$ +12° (*c* 1.6, water): lit.[6] m.p. 175–176°, $[\alpha]_D^{25}$ +11°. ^{13}C-N.m.r. data (D_2O): 177.6 (C-1), 74.2, 71.9, 68.5, 66.9 (C-2,4,5,6), 63.9 (C-7), 38.3 (C-3), 53.5 p.p.m. (OMe).

*7-Bromo-3,7-dideoxy-*D-gluco-*heptono-1,4-lactone* (**3**). — Compound **2** (10 g) was stirred with a 32% solution (40 mL) of hydrogen bromide in acetic acid for 40 min. Methanol (250 mL) was then added, the solution was kept for 20 h and then concentrated, and water (3 × 50 mL) and toluene (3 × 50 mL) were evaporated from the residue which was crystallised from ethyl acetate–ether to give **3** (11.5 g), m.p. 100°. An additional recrystallisation gave a product (8.4 g, 74%) with m.p. 131–133°, $[\alpha]_D^{20}$ −33° (initial and final) (*c* 2.2, water). ^{13}C-N.m.r. data (D_2O): 179.9

(C-1), 76.9 (C-4), 71.6, 69.9, 68.7 (C-2,5,6), 38.4 (C-3), 32.6 p.p.m. (C-7).

Anal. Calc. for $C_7H_{11}BrO_5$: C, 32.96; H, 4.35; Br, 31.33. Found: C, 32.77; H, 4.28; Br, 30.99.

3,7-Dideoxy-D-gluco-*heptono-1,4-lactone* (**6**). — A solution of **3** (5.0 g) in ethanol (50 mL) containing triethylamine (5 mL) was stirred for 20 h under hydrogen in the presence of 5% Pd/C (300 mg). The mixture was filtered and concentrated, the residue was extracted several times with boiling ethyl acetate, and the combined extracts were concentrated. Column chromatography (acetone) of the residue gave, as the main fraction, **6** (2.0 g, 58%), m.p. 133–134° (from ethanol–ether), $[\alpha]_D^{20}$ −59° (initial and final) (*c* 1.5, water). N.m.r. data (D_2O): ^{13}C, 180.1 (C-1), 77.5 (C-4), 75.6, 68.7, 67.6 (C-2,5,6), 33.1 (C-3), 19.1 p.p.m. (C-7); ^1H, δ 4.60 ($J_{2,3a}$ 7.8, $J_{2,3b}$ 10 Hz, H-2), 2.52 ($J_{3,3}$ 11, $J_{3a,4}$ 5.0 Hz, H-3a), 2.02 ($J_{3b,4}$ 10 Hz, H-3b), 4.6 ($J_{4,5}$ 3.1 Hz, H-4), 3.32 ($J_{5,6}$ 7.1 Hz, H-5), 3.73 ($J_{6,7}$ 6.2 Hz, H-6), 1.13 (H-7).

Anal. Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.94; H, 7.34.

2,7-Dibromo-2,7-dideoxy-D-glycero-D-ido-*heptono-1,4-lactone* (**5**). — A mixture of **4a** (10 g) and a 32% solution of hydrogen bromide in acetic acid (75 mL) was stirred for 1 h, becoming homogeneous after ~30 min. Methanol (300 mL) was then added, and the solution was kept overnight, then concentrated, and co-concentrated with water. The syrupy residue was dissolved in water (400 mL) and extracted with ether (8 × 25 mL), the combined extracts were dried and concentrated, and the residue (11.6 g) was crystallised from ether–pentane to give **5** (7.8 g, 46%), m.p. 145–147°. Recrystallisation from ethyl acetate gave a product with m.p. 146–147°, $[\alpha]_D^{20}$ −38° (*c* 2.1, water). N.m.r. data (D_2O): ^{13}C, 174.6 (C-1), 81.4 (C-4), 75.6 (C-3), 69.6, 69.5 (C-5,6), 45.0 (C-2), 38.0 p.p.m. (C-7); ^1H, δ 4.78 ($J_{2,3}$ 7.7 Hz, H-2), 4.81 ($J_{3,4}$ 6.6 Hz, H-3), 4.91 ($J_{4,5}$ 1.8 Hz, H-4), 3.99 ($J_{5,6}$ 9.0 Hz, H-5), 3.74 ($J_{6,7a}$ 2.7, $J_{6,7b}$ 5.0 Hz, H-6), 3.63 ($J_{7,7}$ 11.0 Hz, H-7a), 3.56 (H-7b).

Anal. Calc. for $C_7H_{10}Br_2O_5$: C, 25.18; H, 3.02; Br, 47.85. Found: C, 25.27; H, 2.98; Br, 47.56.

The aqueous phase from the ether extraction contained a 2:1 mixture of the anhydrides **14a** and **15a** indicated by the ^{13}C-n.m.r. spectrum (see below).

7-Bromo-2,7-dideoxy-D-gluco-*heptono-1,4-lactone* (**7**). — A solution of **5** (5.82 g) in water (60 mL) was cooled in ice and stirred, and aqueous 80% hydrazine hydrate (2.5 mL) was added during ~2 min. After a further few min, bromine was added dropwise until a persistent bromine colour remained. The solution was then concentrated to 20 mL, saturated with sodium chloride, and extracted with ethyl acetate (6 × 20 mL). The combined extracts were dried and concentrated, and the residue (2.6 g) was crystallised from ethyl acetate to give **7** (2.1 g, 50%), m.p. 120–122°. Recrystallisation gave a product with m.p. 123–124°, $[\alpha]_D^{20}$ −31.5° (*c* 1.5, water). ^{13}C-N.m.r. data (D_2O): 180.1 (C-1), 84.0 (C-4), 70.9, 70.6, 69.0 (C-3,5,6), 38.8, 37.8 p.p.m. (C-2,7).

Anal. Calc. for $C_7H_{11}BrO_5$: C, 32.96; H, 4.35; Br, 31.33. Found: C, 33.06; H, 4.35; Br, 31.41.

2,7-Dideoxy-D-gluco-*heptono-1,4-lactone* (**8**). — A solution of **5** (15 g) in ethanol (200 mL) and triethylamine (25 mL) containing 5% Pd/C (750 mg) was stirred under hydrogen for 24 h; ~2 L of hydrogen were consumed. The mixture was then filtered and concentrated, the residue was extracted several times with boiling ethyl acetate, and the combined extracts were concentrated. Column chromatography (acetone) of the residue gave a main fraction (8 g) from which hydrochloric acid was evaporated in order to ensure lactonisation. Evaporation of toluene from the residue and crystallisation from ethyl acetate gave **8** (5.1 g, 64%), m.p. 103–105°. After recrystallisation, the m.p. was 104–106°, $[\alpha]_D^{20}$ −68 → −64° (*c* 0.7, water). N.m.r. data (D_2O): ^{13}C, 179.9 (C-1), 85.4 (C-4), 73.7, 69.0, 67.7 (C-3,5,6), 39.7 (C-2), 18.6 p.p.m. (C-7); ^1H, δ 2.88 ($J_{2,2}$ 18.0, $J_{2a,3}$ 6.3 Hz, H-2a), 2.50 ($J_{2b,3}$ 2.5 Hz, H-2b), 4.57 ($J_{3,4}$ 5 Hz, H-3), 4.51 ($J_{4,5}$ 5 Hz, H-4), 3.81 (H-5,6), 1.11 ($J_{6,7}$ 6.3 Hz, H-7).

Anal. Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.71; H, 6.88.

7-Bromo-2,3,7-trideoxy-D-arabino-*heptono-1,4-lactone* (**9**). — A solution of **5** (10 g) in ethanol (100 mL) was stirred under hydrogen in the presence of 5% Pd/C (500 mg). During ~2 h, 2 mol (~1400 mL) of hydrogen was consumed; stirring overnight caused no additional uptake of hydrogen. The solution was filtered, concentrated, and co-concentrated with water, leaving a residue which consisted of **9** mixed with 20% of **7**. Crystallisation from cold water (15 mL) gave **9** (4.1 g, 60%), m.p. 123–125°. After recrystallisation from ethyl acetate, the product had m.p. 126–127°, $[\alpha]_D^{20}$ −36° (*c* 2.1, water). ^{13}C-N.m.r. data (D_2O): 182.9 (C-1), 81.3 (C-4), 73.4, 70.2 (C-5,6), 38.4 (C-7), 29.4 (C-2), 23.9 p.p.m. (C-3).

Anal. Calc. for $C_7H_{11}BrO_4$: C, 35.17; H, 4.64; Br, 33.43. Found: C, 35.02; H, 4.60; Br, 33.22.

2,3,7-Trideoxy-D-arabino-*heptono-1,4-lactone* (**12**). — A solution of **9** (1.0 g) in ethyl acetate (30 mL) and triethylamine (2.5 mL) was stirred under hydrogen with 5% Pd/C (0.1 g) for 18 h. Filtration, concentration, and crystallisation of the residue from ethyl acetate gave **12** (438 mg, 65%), m.p. 99–102°. Further recrystallisation gave a product with m.p. 103–105°, $[\alpha]_D^{20}$ −66.5° (initial and final) (*c* 1.1, water). N.m.r. data (D_2O): ^{13}C, 183.0 (C-1), 81.9 (C-4), 77.0, 67.8 (C-5,6), 29.4 (C-2), 24.2 (C-3), 19.2 p.p.m. (C-7); ^1H, δ 2.52 ($J_{2,2}$ 0, $J_{2,3a}$ 8, $J_{2,3b}$ 9 Hz, H-2a,2b), 2.23 ($J_{3,3}$ 12.5, $J_{3a,4}$ 7.5 Hz, H-3a), 2.06 ($J_{3b,4}$ 7.0 Hz, H-3b), 4.79 ($J_{4,5}$ 3.0 Hz, H-4), 3.32 ($J_{5,6}$ 7.0 Hz, H-5), 3.70 ($J_{6,7}$ 6.3 Hz, H-6), 1.12 (H-7).

Anal. Calc. for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.47; H, 7.61.

Treatment of D-glycero-D-gulo-*heptono-1,4-lactone* (**4a**) *with formic acid in anhydrous hydrogen fluoride.* — A mixture of **4a** (5 g), formic acid (0.91 mL, 1 mol), and anhydrous hydrogen fluoride (20 mL) was kept for 3 days at 20°. The HF was then evaporated in a stream of air and the residue was co-concentrated with water (3 × 25 mL), leaving a syrup (4.4 g) which contained equal parts of 3,6-anhydro-L-*glycero*-D-*gulo*-heptono-1,4-lactone (**14a**) and 3,7-anhydro-D-*glycero*-D-*gulo*-heptono-1,4-lactone (**15a**). ^{13}C-N.m.r. data (D_2O): **14a**, 178.3 (C-1), 85.8, 83.3, 78.1, 74.2, 69.8 (C-2/6), 60.5 p.p.m. (C-7); **15a**, 178.4 (C-1), 78.5, 72.5, 71.5, 65.9, 64.8, 63.6 (C-2/7).

The same two products were obtained when acetic acid was used instead of formic acid under otherwise identical conditions.

*3,6-Anhydro-2,5,7-tri-*O*-benzoyl-*L-glycero-D-gulo-*heptono-1,4-lactone* (**14c**). — The mixture of **14a** and **15a**, obtained as described above from **4a** (2.5 g), was treated conventionally with benzoyl chloride in pyridine to give a mixture (4.8 g) of the tribenzoates **14c** and **15c**. Crystallisation from ether gave **14c** (1.4 g, 23%), m.p. 155–158°. Recrystallisation gave a product with m.p. 162–163°, $[\alpha]_D^{20}$ −17° (*c* 2.9, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.60 ($J_{2,3}$ 5.7 Hz, H-2), 5.33 ($J_{3,4}$ 4.0 Hz, H-3), 5.24 ($J_{4,5}$ 1.0 Hz, H-4), 5.88 ($J_{5,6}$ 3.5 Hz, H-5), 4.70 ($J_{6,7}$ 6.0 Hz, H-6), 4.58 (H-7a,7b).

Anal. Calc. for $C_{28}H_{22}O_9$: C, 66.93; H, 4.41. Found: C, 67.11; H, 4.38.

Column chromatography (ethyl acetate–hexane) twice of the material in the mother liquor gave almost pure, syrupy 3,7-anhydro-2,5,6-tri-*O*-benzoyl-D-*glycero*-D-*gulo*-heptono-1,4-lactone (**15c**). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.75 ($J_{2,3}$ 4.3 Hz, H-2), 4.91 ($J_{3,4}$ 2.2 Hz, H-3), 4.80 ($J_{4,5}$ 3.8 Hz, H-4), 6.02 ($J_{5,6}$ 3.2, $J_{5,7e}$ ~1 Hz, H-5), 5.57 ($J_{6,7e}$ 5.0, $J_{6,7a}$ 10.0 Hz, H-6), 4.17 ($J_{7,7}$ 11.2 Hz, H-7*a*), 3.96 (H-7*e*).

*2-*O*-Acetyl-3,7-anhydro-5,6-*O*-isopropylidene-*D-glycero-D-gulo-*heptono-1,4-lactone* (**17**). — To a solution of the mixture of **14a** and **15a** [obtained from **4a** (2.5 g)] in acetone (100 mL) were added anhydrous sodium sulfate (10 g) and a few drops of concentrated sulfuric acid. The mixture was kept for 20 h, then filtered, neutralised with solid sodium hydrogencarbonate, filtered, and concentrated. The residue was acetylated conventionally with acetic anhydride in pyridine to give a product (2.3 g) column chromatography (ethyl acetate-pentane 1:2) of which gave, *inter alia,* a fraction (800 mg) that crystallised from ether–pentane to give **17** (500 mg, 15%), m.p. 165–166°, $[\alpha]_D^{20}$ −83° (*c* 1.5, chloroform). N.m.r. data ($CDCl_3$): ^{1}H, δ 5.50 ($J_{2,3}$ 4.8 Hz, H-2), 4.03 ($J_{3,4}$ 2.8 Hz, H-3), 4.19 ($J_{4,5}$ 1.9 Hz, H-4), 4.06 ($J_{5,6}$ 6.0 Hz, H-5), 4.32 ($J_{6,7e}$ 5.8, $J_{6,7a}$ 8.5 Hz, H-6), 3.87 ($J_{7,7}$ 12.2 Hz, H-7*a*), 3.35 (H-7*e*), 2.24 (OAc), 1.50, 1.41 (CMe_2); ^{13}C, 169.8, 169.4 (C=O), 109.5 *C*Me_2), 73.5, 71.0, 70.5, 69.6, 68.3 (C-2/6), 64.5 (C-7), 27.2, 25.5 (*Me*$_2$C), 20.1 p.p.m. (OAc).

Anal. Calc. for $C_{12}H_{16}O_7$: C, 52.94; H, 5.92. Found: C, 53.20; H, 6.15.

A second fraction was re-chromatographed to give almost pure, syrupy 2-*O*-acetyl-3,6-anhydro-5,7-*O*-isopropylidene-L-*glycero*-D-*gulo*-heptono-1,4-lactone (**16**, 600 mg). N.m.r. data ($CDCl_3$): ^{1}H, δ 5.48 ($J_{2,3}$ 5.3 Hz, H-2), 5.11 ($J_{3,4}$ 3.8 Hz, H-3), 4.98 ($J_{4,5}$ ~0.5 Hz, H-4), 4.57 ($J_{5,6}$ 2, $J_{5,7b}$ 0.5 Hz, H-5), 3.96 ($J_{6,7a}$ 2.3, $J_{6,7b}$ 0.5 Hz, H-6), 4.07 ($J_{7,7}$ 13.5 Hz, H-7a), 4.04 (H-7b), 2.26 (OAc), 1.47, 1.39 (CMe_2); ^{13}C, 170.7, 169.2 (C=O), 97.4 (*C*Me_2), 84.1 (C-3), 76.3, 73.1, 72.1, 69.0 (C-2,4,5,6), 59.7 (C-7), 28.4, 18.7 (*CMe*$_2$), 20.0 p.p.m. (OAc).

*3,6-Anhydro-2,7-dideoxy-*L-ido-*heptono-1,4-lactone* (**11a**). — A solution of **8** (1.0 g) in anhydrous hydrogen fluoride (5 mL) and formic acid (0.22 mL, 1 equiv.) was kept for 3 days at 20°. The HF was then evaporated in a stream of air, and the residue was co-concentrated with water (3 × 15 mL) and toluene. The residue was recrystallised from ethyl acetate–hexane to give **11a** (780 mg, 87%), m.p. 137–140°. Recrystallisation from ethyl acetate gave a product with m.p. 140–141°, $[\alpha]_D$ −22°

(final) (*c* 1.7, water). N.m.r. data (D_2O): ^1H, δ 2.90 ($J_{2,2}$ 14, $J_{2a,3}$ 6.9 Hz, H-2a), 2.55 ($J_{2b,3}$ ~0.3 Hz, H-2b), 4.93 ($J_{3,4}$ 5.8 Hz, H-3), 5.0 ($J_{4,5}$ 0.5 Hz, H-4), 4.16 ($J_{5,6}$ 2.7 Hz, H-5), 4.08 ($J_{6,7}$ 6.3 Hz, H-6), 1.13 (H-7); ^{13}C, 179.1 (C-1), 88.4 (C-3), 76.3, 75.7, 73.8 (C-4,5,6), 35.7 (C-2), 12.4 p.p.m. (C-7).

Anal. Calc. for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 53.49; H, 6.57.

When **8** was treated with hydrogen bromide in acetic acid for 20 h, 47% of **11a** was obtained together with small amounts of bromodeoxy compounds.

3,6-Anhydro-7-bromo-2,7-dideoxy-L-ido-*heptono-1,4-lactone* (**11b**). — Treatment of **7** (1 g) with hydrogen fluoride and formic acid, as described above, gave a syrup which was washed through silica gel with ethyl acetate and crystallised from ether–pentane to give **11b** (600 mg, 65%), m.p. 88–90°, $[\alpha]_D^{20}$ −22° (*c* 1.8, chloroform). N.m.r. data: ^1H ($CDCl_3$), δ 2.74 ($J_{2,2}$ 18.8, $J_{2a,3}$ 5.5 Hz, H-2a), 2.69 ($J_{2b,4}$ ~1 Hz, H-2b), 5.03 ($J_{3,4}$ 4.4, $J_{3,5}$ ~1 Hz, H-3), 4.93 ($J_{4,5}$ ~1 Hz, H-4), 4.62 ($J_{5,6}$ 3.1 Hz, H-5), 4.34 ($J_{6,7a}$ 8.4, $J_{6,7b}$ 6.2 Hz, H-6), 3.50 ($J_{7,7}$ 9.3 Hz, H-7a), 3.48 (H-7b); ^{13}C (D_2O), 180.0 (C-1), 89.4 (C-3), 81.9, 78.3, 74.0 (C-4,5,6), 36.7 (C-2), 28.9 (C-7).

Anal. Calc. for $C_7H_9BrO_4$: C, 35.46; H, 3.83, Br, 33.71. Found: C, 35.50; H, 3.80; Br, 33.53.

Methyl 3,6-di-O-*acetyl-2,5:4,7-dianhydro*-D-glycero-D-gulo-*heptonate* (**10b**). — The dibromolactone **5** (5.0 g) was boiled in water (50 mL) for 3 h. Concentration then left a syrup which contained mainly 2,5:4,7-dianhydro-D-*glycero*-D-*gulo*-heptonic acid (**10a**), as inferred from the ^{13}C-n.m.r. data (D_2O): 174.0 (C-1), 87.4, 84.2, 83.7, 78.4, 73.2, 71.6 p.p.m. (C-2/7).

Methanol was evaporated from the syrup, a solution of which in methanol (100 mL) was kept overnight and then concentrated. The residue was acetylated conventionally with acetic anhydride in pyridine, yielding a product (3.8 g) which crystallised from ether–pentane to give **10b** (2.39 g, 59%), m.p. 57–59°. Recrystallisation gave an analytical sample, m.p. 60–61.5°, $[\alpha]_D^{20}$ +48° (*c* 2.1, chloroform). ^1H-N.m.r. data ($CDCl_3$): δ 4.53 ($J_{2,3}$ 2.2 Hz, H-2), 5.50 ($J_{3,4}$ 1.5, $J_{3,5}$ 0.5 Hz, H-3), 4.47 ($J_{4,5}$ 3.3 Hz, H-4), 4.89 ($J_{5,6}$ 4.5 Hz, H-5), 5.14 ($J_{6,7a} = J_{6,7b}$ = 7.5 Hz, H-6), 4.09 ($J_{7,7}$ 8.5 Hz, H-7a), 3.91 (H-7b), 3.79 (OMe), 2.18, 2.11 (OAc).

Anal. Calc. for $C_{12}H_{16}O_8$: C, 50.00; H, 5.59. Found: C, 49.74; H, 5.48.

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