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SYNTHESIS OF 3,4-ANHYDRO-1-DEOXYHEXULOSE DERIVATIVES

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ABSTRACT

Epoxidation of *trans*- and *cis*-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-enulose (**2**) by alkaline hydrogen peroxide gave a mixture of 3,4-anhydro-1-deoxy-5,6-*O*-isopropylidene-D-*arabino*- and -D-*xylo*-hexulose that was resolved by chromatography. Epoxidation of **2** with 3-chloroperbenzoic acid gave (1*S*)-1-acetoxy-1,2-anhydro-3,4-*O*-isopropylidene-D-erythrose hydrate and (1*R*)-1-acetoxy-1,2-anhydro-3,4-*O*-isopropylidene-D-threose hydrate. Reduction of **2** followed by epoxidation and oxidation gave the corresponding epoxides with the D-*ribo* and D-*lyxo* configurations. Structures and configurations of the above compounds were established on the basis of their analytical and spectroscopic data, and by chemical transformations.

INTRODUCTION

Sugar epoxides are important synthesis intermediates because of their susceptibility to attack by nucleophiles to yield modified sugars. Epoxides of aldofuranoses, aldopyranoses[1], and glycitols[2] have been studied extensively and we now report on epoxides of ketoses derived from hex-3-enuloses obtained from *aldehydo* sugars by Knoevenagel–Doebner[3] or Wittig reactions[4].

Epoxides can be prepared by the reaction of peracids with unsaturated compounds[5], but the application of these reagents to α,β-unsaturated ketones results in Baeyer–Villiger rearrangements[6]. However, epoxidation of such compounds can be achieved by alkaline hydrogen peroxide[7].

RESULTS AND DISCUSSION

When the epoxidation of *trans*- (**1**) and *cis*-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-enulose (**2**) by alkaline hydrogen peroxide was monitored

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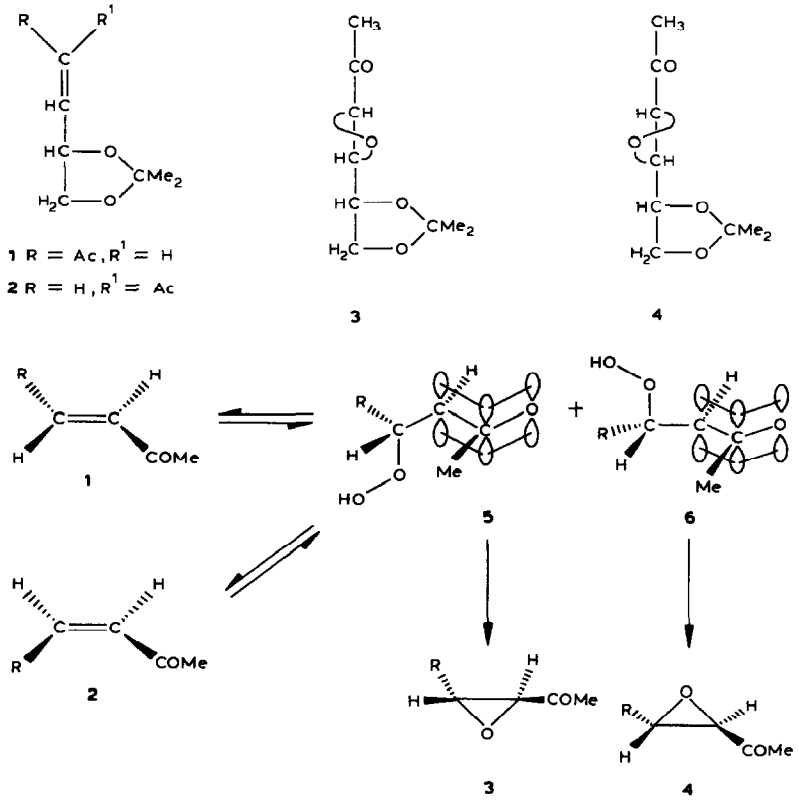
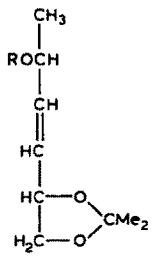


by g.l.c., the rapid formation of two products in the ratios 2:1 and 1:3, respectively, occurred. These products were separated by column chromatography and identified as 3,4-anhydro-1-deoxy-5,6-*O*-isopropylidene-D-*arabino*- (**3**) and -D-*xylo*-hexulose (**4**) on the basis of spectroscopic data (see Experimental).

The configurations assigned to **3** and **4** were tentatively based initially on the mechanism and stereochemistry of the epoxidation reaction[8,9], where a high stereoselectivity is usually found. Thus, attack of the hydroperoxide ion at C-4 of **1** and **2** would give the intermediates **5** and **6**, where the enolate anions would be more stable if they were not eclipsed with a large β-substituent in the transition states[9].

The *trans* relationship of the substituents attached to the oxirane rings in **3** and **4** was established as follows. Reduction of **1** with sodium borohydride yielded a compound identified as *trans*-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*threo*-hex-3-enitol (**7**) which was epoxidised with 3-chloroperbenzoic acid, and the product was oxidised with ruthenium tetraoxide to yield **3** and **4**. This reaction sequence ensured that the substituents attached to the oxirane ring in **3** and **4** were *trans*. Application of the above procedure to the *cis*-isomer **2** yielded the related epoxides with D-*ribo* (**9**) and D-*lyxo* (**10**) configurations.



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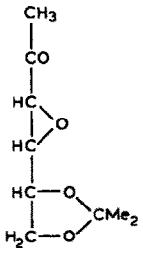
8 R = Ac



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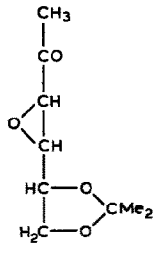

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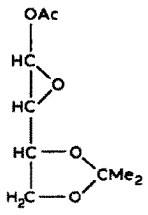

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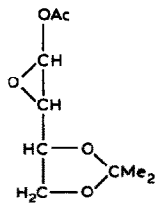

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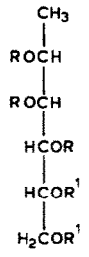
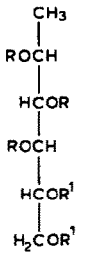
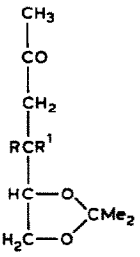


13 R = H,R¹,R¹ = >CMe₂
15 R = R¹ = Ac
16 R = R¹ = H



14 R = H,R¹,R¹ = >CMe₂



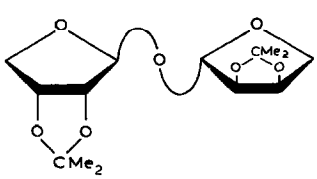
17 R = H,R¹ = OH
18 R = OH,R¹ = H

Epoxidation of **2** with 3-chloroperbenzoic acid gave two epoxides (**11** and **12**) that were different from **3** and **4**. Spectroscopic data showed **11** and **12** to be the products of a Baeyer–Villiger rearrangement[10]. Thus, they had i.r. absorption at 1765 cm^{-1} for ester carbonyl group, and the chemical shifts of the signals for H-1 (δ 5.66 and 5.58 for **11** and **12**, respectively) were in agreement with those of acetalic protons.

The configuration at C-2 of **7** was demonstrated by application of Horeau's method[11] for secondary chiral alcohols, and by the following chemical transformations. Hydroxylation of **7** with osmium tetraoxide gave a mixture of 1-deoxy-5,6-*O*-isopropylidene-D-hexitols (**13** and **14**) that could not be resolved. Removal of the isopropylidene group, followed by acetylation, yielded a mixture of penta-acetates from which 2,3,4,5,6-penta-*O*-acetyl-1-deoxy-D-mannitol[12] (**15**) was isolated. The ^{1}H-n.m.r. spectrum of **15** provided evidence for the assigned configuration[13] and deacetylation gave a product with an $[\alpha]_D$ value close to that reported[12] for 1-deoxy-D-mannitol (**16**).

The mixture of reduction products of **2** could not be resolved.

The configurations of **3** and **4** were established as follows. Reduction of **3** with zinc dust[14] gave exclusively a β-hydroxyketone, the optical and spectroscopic data for which were analogous to those reported[3] for 1,3-dideoxy-5,6-*O*-isopropylidene-D-*erythro*-hexulose (**17**). Hence, the product of reduction of **4** must be 1,3-di-



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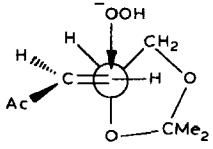

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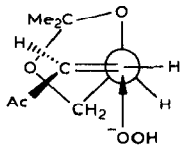

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deoxy-5,6-*O*-isopropylidene-D-*threo*-hexulose (**18**). The configurations of **9** and **10** were established in the same manner.

The configurations of the substituents attached to the oxirane rings in **11** and **12** are probably *cis*, since the $J_{1,2}$ values are similar to those reported[15] for *cis*-hydrogens on oxirane rings. Thus, there was no change in configuration at the double bond during the Baeyer–Villiger rearrangement.

The configuration of **11**, and therefore that of **12**, was established as follows. Hydrolysis of **11** gave D-erythrose, since acetonation followed by column chromatography gave two compounds and that of lower mobility was identified as 2,3-*O*-isopropylidene-β-D-erythrofuranose[16]. The compound of higher mobility was identified as 2,3-*O*-isopropylidene-β-D-erythrofuranosyl 2,3-*O*-isopropylidene-β-D-erythrofuranoside (**19**). Thus, it had no i.r. absorption for hydroxyl and its mass spectrum contained a peak at *m/z* 287 (M^+ − Me), indicating a molecular weight of 302. The ^{1}H-n.m.r. spectrum of **19** indicated that the hydrogen atoms of the two furanose rings were similar and hence only one set of signals was produced. The configuration at C-1 and C-1′ was β, since the zero $J_{1,2}$ value indicated H-1,2 to be *trans*.

The stereoselectivity found in the epoxidation of **1** accorded with that reported[17] for conjugated addition to γ-alkoxyl-α,β-unsaturated carbonyl compounds, where an Ahn–Felkin-type[18] transition state occurred. Thus, attack by hydroperoxide ion on the β-carbon takes place *anti* to the polar, allylic alkoxyl substituent in the most stable conformation (**20**) of **1**, giving preferentially the D-*arabino* epoxide (**3**), whereas the less-stable conformation (**21**) gives the D-*xylo* isomer (**4**).

The epoxidation of **2** does not follow the Ahn–Felkin rule, suggesting that other factors may be involved.

EXPERIMENTAL

General methods. — Solutions were dried over $MgSO_4$ before concentration under diminished pressure. ^{1}H-N.m.r. spectra (200 and 80 MHz, internal Me_4Si) were recorded by Bruker WP-200 SY and WP-80 CW spectrometers for solutions in $CDCl_3$, i.r. spectra with a Perkin–Elmer 782 instrument, and mass spectra with a Hewlett–Packard 5930A Mass Spectrometer and a Hewlett–Packard 5970 M.S.D. Optical rotations were measured for solutions in chloroform (1-dm tube) with a Perkin–Elmer 141 polarimeter. G.l.c. was performed at 210° on a Perkin–Elmer

8310 Gas Chromatograph equipped with a flame-ionisation detector and a steel column (4 m × 0.25 in. i.d.) packed with 10% of SP 2330 on Chromosorb W (100–120 mesh). The N_2 flow rate was 40 mL/min, the injection port temperature was 280°, and the zone-detector temperature was 280°. T.l.c. was performed on Silica Gel G (Merck), with detection by charring with sulfuric acid. Column chromatography was performed on silica gel (Merck, 7734). Descending p.c. was performed on Whatman No. 1 paper with 1-butanol–ethanol–water (28:7:13) and detection with silver nitrate[19].

Epoxidation of trans-*1,3,4-trideoxy-5,6-*O-*isopropylidene-*D-glycero-*hex-3-enulose* (**1**). — To a cooled (ice–water) and stirred solution of **1**[3] (3.4 g, 20 mmol) in methanol (25 mL) and aqueous 30% hydrogen peroxide (6 mL) was added 6M sodium hydroxide (2 mL) dropwise, at such rate that the temperature was maintained at 10–15°. After 30 min, g.l.c. revealed that **1** (*T* 3.35 min) had disappeared and that 3,4-anhydro-1-deoxy-5,6-*O*-isopropylidene-D-*arabino*- (**3**, *T* 5.29 min, 62.3%) and -D-*xylo*-hexulose (**4**, *T* 6.18 min, 36.2%) were present. The mixture was saturated with sodium chloride and extracted with ether (3 × 25 mL), and the combined extracts were concentrated. Column chromatography (ether–hexane, 1:6) of part (2 g) of the residue (3 g) yielded, first, **3** (930 mg), isolated as colourless mobile oil, $[\alpha]_D$ −16° (*c* 1.4); ν_{max}^{film} 2993, 2941, and 2892 (C-H), 1716 (ketone C=O), 1380 and 1375 (CMe_2), 1252, 1219, 1068, 878, and 845 cm^{-1} (oxirane and 1,3-dioxolane ring). N.m.r. data: δ 4.15 (dd, 1 H, $J_{5,6}$ 5.5, $J_{6,6'}$ 7.5 Hz, H-6), 3.99 (q, 1 H, $J_{5,6'} = J_{4,5}$ = 5.5 Hz, H-5), 3.92 (dd, 1 H, H-6'), 3.39 (d, 1 H, $J_{3,4}$ 2 Hz, H-3), 3.21 (dd, 1 H, H-4), 2.13 (s, 3 H, H-1,1,1), 1.47 and 1.37 (2 s, 6 H, CMe_2). Mass spectrum: *m/z* 171 (M^+ − Me), 113 (M^+ − Me − Me_2CO), 111 (M^+ − Me − AcOH), 101 ($C_5H_9O_2^+$), 85 (M^+ − $C_5H_9O_2$), 83, 73, 72, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.57. Found: C, 58.37; H, 7.62.

Eluted second was **4** (350 mg), isolated as a colourless mobile oil, $[\alpha]_D$ +11° (*c* 1.3); ν_{max}^{film} 2995, 2941, and 2890 (C-H), 1715 (ketone C=O), 1375 and 1371 (CMe_2), 1250, 1220, 1070, and 845 cm^{-1} (oxirane and 1,3-dioxolane ring). N.m.r. data: δ 4.14 (dd, 1 H, $J_{5,6}$ 6.5, $J_{6,6'}$ 10 Hz, H-6), 4.10 (dd, 1 H, $J_{5,6'}$ 1.5 Hz, H-6'), 3.89 (o, 1 H, $J_{4,5}$ 4.5 Hz, H-5), 3.43 (d, 1 H, $J_{3,4}$ 2 Hz, H-3), 3.20 (dd, 1 H, H-4), 2.10 (s, 3 H, H-1,1,1), 1.45 and 1.37 (2 s, 6 H, CMe_2). Mass spectrum: *m/z* 171 (M^+ − Me), 113 (M^+ − Me − Me_2CO), 111 (M^+ − Me − AcOH), 101 ($C_5H_9O_2^+$), 85 (M^+ − $C_5H_9O_2$), 83, 75, 73, 72, 61, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.57. Found: C, 58.62; H, 7.41.

Epoxidation of cis-*1,3,4-trideoxy-5,6-*O-*isopropylidene-*D-glycero-*hex-3-enulose* (**2**). — *(a) By alkaline hydrogen peroxide.* Compound **2**[3]* (3.4 g, 20 mmol) was epoxidised as described above. After 1 h, g.l.c. revealed the absence of **2** (*T* 3.12 min) and the presence of **3** (24%) and **4** (74%).

*The yield of **2** was improved (→43%) by using methanol as solvent.

(b) With 3-chloroperbenzoic acid. To a stirred solution of **2** (1.7 g, 10 mmol) in dichloromethane (50 mL) at room temperature was added 3-chloroperbenzoic acid (Merck) (3.4 g, 17 mmol). T.l.c. (ether–hexane, 3:2) then revealed the presence of **2** together with two new compounds (R_F 0.74 and 0.65). After 10 days, **2** was still present. The precipitated 3-chlorobenzoic acid was removed, and the filtrate was washed with aqueous 10% sodium sulfite (until negative to starch–iodide paper), aqueous 5% potassium carbonate, and saturated aqueous sodium chloride, and then concentrated. Column chromatography (ether–hexane, 1:5) of the residue yielded, first, **2** (960 mg). Eluted second was (1*S*)-1-acetoxy-1,2-anhydro-3,4-*O*-isopropylidene-D-erythrose hydrate (**11**, 300 mg), isolated as a colourless mobile oil, $[\alpha]_D$ −83° (*c* 2.5), *T* 4.66 min; ν_{max}^{film} 2995, 2940, and 2880 (C-H), 1765 (ester C=O), 1375 and 1371 (CMe_2), 1255 (ester C-O), 1215, 1070, 1045, and 845 cm^{-1} (oxirane and 1,3-dioxolane ring). N.m.r. data: δ 5.66 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 4.22–4.02 (m, 3 H, H-3,4,4'), 3.12–3.02 (m, 1 H, H-2), 2.18 (s, 3 H, Ac), 1.49 and 1.40 (2 s, 6 H, CMe_2). Mass spectrum: *m/z* 188 (M^+ − 1 − Me), 187 (M^+ − Me), 129 (M^+ − Me − Me_2CO), 127 (M^+ − Me − AcOH), 103, 101 (M^+ − $C_5H_9O_2$ and $C_5H_9O_2^+$), 99, 85, 73, 72, 71, 61, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_9H_{14}O_5$: C, 53.45; H, 6.97. Found: C, 52.98; H, 6.87.

Eluted third was (1*R*)-1-acetoxy-1,2-anhydro-3,4-*O*-isopropylidene-D-threose hydrate (**12**, 50 mg), isolated as a colourless mobile oil, $[\alpha]_D$ +48° (*c* 1.25), *T* 7.28 min; ν_{max}^{film} 2995, 2940, and 2880 (C-H), 1765 (ester C=O), 1385 and 1375 (CMe_2), 1250 (ester C-O), 1215, 1070, and 845 cm^{-1} (oxirane and 1,3-dioxolane ring). N.m.r. data: δ 5.58 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 4.19–4.04 (m, 2 H, H-4,4'), 3.82 (o, 1 H, $J_{2,3}$ 7.5, $J_{3,4}$ 12, $J_{3,4'}$ 3 Hz, H-3), 3.10 (dd, 1 H, H-2), 2.13 (s, 3 H, Ac), 1.50 and 1.40 (2 s, 6 H, CMe_2). Mass spectrum: *m/z* 188 (M^+ + 1 − Me), 187 (M^+ − Me), 127 (M^+ − Me − AcOH), 103, 101 (M^+ − $C_5H_9O_2$ and $C_5H_9O_2^+$), 99, 85, 73, 72, 61, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_9H_{14}O_5$: C, 53.45; H, 6.97. Found: C, 53.92; H, 6.75.

Reduction of **1** *with sodium borohydride.* — To a cooled (ice–water) and stirred solution of **1** (3.5 g, 20.6 mmol) in methanol (40 mL) was added sodium borohydride (0.5 g). The mixture was kept at room temperature overnight when t.l.c. (ether–hexane, 3:2) revealed a compound of lower mobility (R_F 0.57). The mixture was neutralised with acetic acid, concentrated, and extracted with dichloromethane (50 mL). The extract was washed with water, dried, and concentrated. Column chromatography (ether–hexane, 3:2) of a part of the syrupy residue (2.8 g) afforded *trans*-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*threo*-hex-3-enitol (**7**), $[\alpha]_D$ +28° (*c* 1.4); ν_{max}^{film} 3397 (OH), 2990, 2939, and 2882 (C-H), 1681 and 1643 (C=C), 1380 and 1375 (CMe_2), 1259, 1219, 1157, 1061, and 865 (1,3-dioxolane ring), and 976 cm^{-1} (H-C=C-H). N.m.r. data (80 MHz): δ 6.95 (dd, 1 H, $J_{2,3}$ 4, $J_{3,4}$ 14 Hz, H-3), 6.65 (dd, 1 H, $J_{4,5}$ 6 Hz, H-4), 4.67–4.20 (2 m, 2 H, H-2,5), 4.12 (dd, 1 H, $J_{5,6}$ 6, $J_{6,6'}$ 8 Hz, H-6), 3.60 (t, 1 H, $J_{5,6'}$ 8 Hz, H-6'), 1.80 (bs, 1 H, HO-2), 1.43 and 1.40 (2 s, 6 H, CMe_2), and 1.28 (d, 3 H, $J_{1,2}$ 7 Hz, H-1,1,1).

Anal. Calc. for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.38; H, 9.35.

Acetylation of **7** in the usual manner gave *trans*-2-*O*-acetyl-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*threo*-hex-3-enitol (**8**) as a mobile oil, $[\alpha]_D$ +23° (*c* 2); ν_{max}^{film} 2989, 2940, and 2878 (C-H), 1741 (acetate C=O), 1373 (CMe_2), 1241 (acetate C-O), 1167, 1062, and 863 cm^{-1} (1,3-dioxolane ring). N.m.r. data (80 MHz): δ 6.95–6.52 (m, 2 H, H-3,4), 6.37 (m, 1 H, H-2), 4.47 (dt, 1 H, $J_{4,5} = J_{5,6} = 6$, $J_{5,6'}$ 8 Hz, H-5), 4.06 (dd, 1 H, $J_{6,6'}$ 8 Hz, H-6), 3.55 (t, 1 H, H-6'), 2.00 (s, 3 H, Ac), 1.40 and 1.35 (2 s, 6 H, CMe_2), and 1.29 (d, 3 H, $J_{1,2}$ 6.5 Hz, H-1,1,1). Mass spectrum: *m/z* 199 (M^+ – Me), 156 (M^+ – Me – Me_2CO), 154 (M^+ – Me – AcOH), 113 (M^+ – $C_5H_9O_2$), 101 ($C_5H_9O_2^+$), 97, 85, 83, 81, 79, 73, 69, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.46. Found: C, 61.70; H, 8.09.

Configurational assignment at C-2 in **7**. — *(a) By Horeau's method.* A solution of **7** (67 mg, 0.4 mmol) and (±)-α-phenylbutyric anhydride (246 mg, 0.8 mmol) in dry pyridine (1 mL) was kept for 15 h at room temperature. Water (3 mL) was added, and the mixture was stored for 6 h, neutralised to phenolphthalein with M sodium hydroxide, and extracted with ether (3 × 15 mL). The aqueous phase was acidified with conc. hydrochloric acid and extracted again with benzene (5 × 20 mL), and the combined extracts were concentrated to give α-phenylbutyric acid (182 mg), $[\alpha]_D$ +2° (*c* 12.2).

(b) By hydroxylation. To a solution of **7** (1.16 g, 6.7 mmol) in methanol–water (1:1, 10 mL) was added a solution of potassium chlorate (0.4 g, 3.4 mmol) in the same solvent (10 mL). The mixture was acidified (pH ~3) with acetic acid (0.5 mL) and then aqueous 1% osmium tetraoxide (4 mL) was added. The mixture was left at room temperature for 40 h. T.l.c. (ether) then revealed the absence of **7** and the presence of a product of lower mobility. The mixture was neutralised (K_2CO_3) and concentrated, the residue was extracted with ethyl acetate, and the extract was concentrated. Column chromatography (ether–hexane, 5:1) of the residue gave a mixture (550 mg) of 1-deoxy-5,6-*O*-isopropylidene-D-mannitol (**13**) and -D-iditol (**14**). N.m.r. data (80 MHz): δ 4.50–3.00 (m, 9 H, H-2,3,4,5,6,6' and HO-2,3,4), 1.43, 1.36, 1.40, and 1.35 (4 s, 6 H, the later pair of higher intensity, CMe_2), 1.26 and 1.22 (2 d, 3 H, the former of higher intensity, H-1,1,1).

A solution of the mixture (550 mg) in aqueous 10% acetic acid (10 mL) was heated at 70° for 1 h. T.l.c. (ethyl acetate) then showed the presence of a product of low mobility. The solution was concentrated and the residue (380 mg) was acetylated in the usual manner. Column chromatography (benzene→benzene–ethanol, 40:1), of the resulting mixture gave syrupy 2,3,4,5,6-penta-*O*-acetyl-1-deoxy-D-mannitol (**15**, 250 mg), $[\alpha]_D$ +22° (*c* 1); ν_{max}^{film} 2992 (C-H), 1749 (acetate C=O), 1373, 1223 (acetate C-O), 1066, and 1033 cm^{-1}. N.m.r. data (80 MHz): δ 5.36 (dd, 1 H, $J_{3,4}$ 2, $J_{4,5}$ 9 Hz, H-4), 5.15 (dd, 1 H, $J_{2,3}$ 9 Hz, H-3), 5.00 (m, 1 H, H-5), 4.84 (o, 1 H, $J_{1,2}$ 6.5 Hz, H-2), 4.12–4.00 (m, 2 H, H-6,6'), 2.02, 2.00, 1.96, and 1.95 (4 s, 15 H, relative intensity 2:1:1:1, 5 Ac), and 1.11 (d, 3 H, H-1,1,1).

Anal. Calc. for $C_{16}H_{24}O_{10}$: C, 51.05; H, 6.43. Found: C, 51.48; H, 6.57.

Deacetylation of **15** (250 mg) with methanolic sodium methoxide gave 1-

deoxy-D-mannitol (**16**, 42 mg) as a syrup that was homogeneous by p.c. (R_F 0.43), $[\alpha]_D$ −9° (*c* 1, water); lit.[12] $[\alpha]_D$ −10° (*c* 1, water).

Synthesis of **3** *and* **4**. — Compound **7** (2.53 g, 14.7 mmol) was epoxidised with 3-chloroperbenzoic acid (Merck) (11 g, 54.2 mmol) in dichloromethane (80 mL) for 6 h at room temperature. T.l.c. (ether–hexane, 3:2) then revealed the absence of **7**. Work-up of the mixture as described above, with column chromatography of the residue, gave three fractions (total weight, 1.37 g) which ^{1}H-n.m.r. spectroscopy indicated to be mixtures of 3,4-anhydro-1-deoxy-5,6-*O*-isopropylidene-D-mannitol and -D-iditol.

To a stirred mixture of the mixture (610 mg), chloroform (10 mL), ruthenium dioxide (150 mg), and saturated aqueous sodium hydrogen carbonate (10 mL) was added aqueous 5% sodium periodate (15 mL) dropwise during 1 h. The mixture was left at room temperature overnight when g.l.c. revealed **3** (41.6%) and **4** (27.3%).

Reduction of **3**. — To a stirred solution of **3** (282 mg, 1.5 mmol) in methanol (15 mL) were added aqueous 10% ammonium chloride (10 mL) and zinc dust (3 g). After 30 min, t.l.c. (ether–hexane, 3:2) showed that **3** had disappeared and that a compound with the same mobility (R_F 0.32) as 1,3-dideoxy-5,6-*O*-isopropylidene-D-*erythro*-hexulose (**17**) was present. The mixture was filtered through a Celite pad, neutralised with conc. hydrochloric acid, concentrated, and extracted with ether. Concentration of the extract and column chromatography (ether–hexane, 1:2) of the residue yielded **17** (165 mg, 60%), $[\alpha]_D$ −28° (*c* 1.2) {lit.[3] $[\alpha]_D$ −21.52° (*c* 5)}; ν_{max}^{film} 3464 (OH), 2992, 2940, and 2904 (C-H), 1716 (ketone C=O), 1373 (CMe_2), 1260, 1216, 1159, 1069, and 862 cm^{-1} (1,3-dioxolane ring). N.m.r. data: δ 4.18–4.02 (m, 1 H, H-5), 4.02–3.90 (m, 3 H, H-4,6,6'), 3.28 (d, 1 H, $J_{OH,4}$ 2.5 Hz, HO-4), 2.86 (dd, 1 H, $J_{3,4}$ 2, $J_{3,3'}$ 18 Hz, H-3), 2.61 (dd, 1 H, $J_{3',4}$ 8 Hz, H-3'), 2.22 (s, 3 H, H-1,1,1), 1.51 and 1.46 (2 s, 6 H, CMe_2). Mass spectrum: *m/z* 173 (M^+ − Me), 170 (M^+ − H_2O), 155, 130 (M^+ − Me − Ac), 127 (M^+ − H_2O − Ac), 115 (M^+ − Me − Me_2CO), 113 (M^+ − Me − AcOH), 101 ($C_5H_9O_2^+$), 95, 87 (M^+ − $C_5H_9O_2$), 85, 83, 73, 72, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_9H_{16}O_4$: C, 57.41; H, 8.57. Found: C, 57.30; H, 8.59.

Reduction of **4**. — Compound **4** (220 mg, 1.18 mmol) was treated as above. After 2 h, t.l.c. (ether–hexane, 3:2) revealed that **4** had disappeared and that a new compound (R_F 0.26) was present. Work-up of the reaction mixture, as described above, yielded 1,3-dideoxy-5,6-*O*-isopropylidene-D-*threo*-hexulose (**18**; 150 mg, 68%) as a colourless mobile oil, $[\alpha]_D$ +26° (*c* 1.3); ν_{max}^{film} 3475 (OH), 2991, 2939, and 2902 (C-H), 1716 (ketone C=O), 1373 (CMe_2), 1262, 1215, 1159, 1069, and 856 cm^{-1} (1,3-dioxolane ring). N.m.r. data: δ 4.16–3.92 (m, 3 H, H-4,5,6), 3.85 (dd, 1 H, $J_{5,6'}$ 6, $J_{6,6'}$ 8 Hz, H-6'), 2.89 (d, 1 H, $J_{HO,4}$ 4.75 Hz, HO-4), 2.72 (dd, 1 H, $J_{3,4}$ 8, $J_{3,3'}$ 17 Hz, H-3), 2.58 (dd, 1 H, $J_{3',4}$ 3.75 Hz, H-3'), 2.22 (s, 3 H, H-1,1,1), 1.48 and 1.38 (2 s, 6 H, CMe_2). Mass spectrum: *m/z* 174 (M^+ + 1 − Me), 173 (M^+ − Me), 170 (M^+ − H_2O), 130 (M^+ − Me − Ac), 127 (M^+ − H_2O − Ac), 115 (M^+ − Me − Me_2CO), 113 (M^+ − Me − AcOH), 101 ($C_5H_9O_2^+$), 95, 87 (M^+ − $C_5H_9O_2$), 85, 83, 73, 71, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_9H_{16}O_4$: C, 57.41; H, 8.57. Found: C, 57.82; H, 8.60.

Synthesis of **9** *and* **10**. — Compound **2** (1.02 g, 6 mmol) was reduced in methanol (10 mL) with sodium borohydride (0.3 g) as described above, to give a mixture (0.88 g), unresolvable by column chromatography (ether–hexane, 3:2), of *cis*-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*threo*- and -D-*erythro*-hex-3-enitol.

The foregoing mixture (710 mg) was epoxidised with 3-chloroperbenzoic acid (Merck) (1.2 g, 5.9 mmol) in dichloromethane (20 mL) for 5 days at room temperature. Work-up of the reaction mixture, as described above, was followed by column chromatography (ether–hexane, 1:1) of the product (480 mg) and oxidation in chloroform (15 mL) with ruthenium dioxide (130 mg), saturated aqueous sodium hydrogen carbonate (10 mL), and aqueous 5% sodium periodate (20 mL). After 2 h, g.l.c. revealed the presence of 3,4-anhydro-1-deoxy-5,6-*O*-isopropylidene-D-*ribo* (**9**; *T* 4.77 min, 45%) and -D-*lyxo*-hexulose (**10**; *T* 6.30 min, 38.7%). 2-Propanol (0.5 mL) was added; after 20 min, the organic phase was separated and the aqueous phase extracted with chloroform (3 × 10 mL). Concentration of the combined extracts and column chromatography (ether–hexane, 1:5) of the residue yielded, first, **9** (130 mg) as a colourless mobile oil, $[\alpha]_D$ −10° (*c* 1.1); ν_{max}^{film} 2992, 2942, and 2880 (C-H), 1730 (ketone C=O), 1383 and 1384 (CMe_2), 1257, 1224, 1067, 864, and 842 cm^{-1} (oxirane and 1,3-dioxolane ring). N.m.r. data (80 MHz): δ 4.27–3.80 (m, 3 H, H-5,6,6'), 3.72 (d, 1 H, $J_{3,4}$ 4.5 Hz, H-3), 3.23 (dd, 1 H, $J_{4,5}$ 7.5 Hz, H-4), 2.30 (s, 3 H, H-1,1,1), 1.45 and 1.28 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.57. Found: C, 57.59; H, 7.15.

The second product (**10**, 160 mg) was a colourless mobile oil which had $[\alpha]_D$ −42° (*c* 1.3); ν_{max}^{film} 2992, 2942, and 2885 (C-H), 1730 (ketone C=O), 1383 and 1374 (CMe_2), 1258, 1215, 1066, 981, and 846 cm^{-1} (oxirane and 1,3-dioxolane ring). N.m.r. data (80 MHz): δ 4.12–3.62 (m, 3 H, H-5,6,6'), 3.55 (d, 1 H, $J_{3,4}$ 4.7 Hz, H-3), 3.26 (m, 1 H, H-4), 2.27 (s, 3 H, H-1,1,1), 1.45 and 1.33 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.57. Found: C, 58.23; H, 7.82.

Reduction of **10**. — Compound **10** (135 mg, 0.7 mmol) was reduced in methanol (5 mL) with aqueous 20% ammonium chloride (2.5 mL) and zinc dust (1 g). After 7 h, t.l.c. (ether–hexane, 3:2) revealed that **10** had disappeared and that a compound with a mobility the same as that of **18** was present. The i.r. and ^{1}H-n.m.r. spectra of the isolated reduction product were identical to those of **18**.

Hydrolysis of **11**. — A suspension of **11** (100 mg, 0.5 mmol) in aqueous 10% acetic acid was heated at 70° for 10 min; t.l.c. (ethyl acetate) then showed that **11** had disappeared and that a product (R_F 0.16) was present. The solution was concentrated and column chromatography (ethyl acetate) of the residue yielded erythrose (30 mg, 60%) that was homogeneous by p.c. (R_F 0.45).

The foregoing product (20 mg) was treated with dry acetone (4 mL), anhydrous copper sulfate (0.5 g), and conc. sulfuric acid (0.05 mL) for 1 day, and the reaction mixture was worked-up in the usual manner. Column chromatography (ether–hexane, 1:2) of the product afforded, first, 2,3-*O*-isopropylidene-β-D-erythrofuranosyl 2,3-*O*-isopropylidene-β-D-erythrofuranoside (**19**, 8.7 mg), m.p.

110–112°, $[\alpha]_D$ −150° (*c* 0.6); ν_{max}^{KBr} 2996, 2981, 2953, and 2887 (C-H), 1383 and 1378 (CMe_2), 1274, 1201, 1105, 1075, 983, and 854 cm^{-1} (1,3-dioxolane ring). N.m.r. data (80 MHz): ^1H δ 5.29 (s, 2 H, H-1,1'), 4.79 (dd, 2 H, $J_{2,3} = J_{2',3'} = 6$, $J_{3,4ex} = J_{3',4'ex} = 3$ Hz, H-3,3'), 4.04 (d, 2 H, $J_{4en,4ex} = J_{4'en,4'ex} = 10$ Hz, H-4*en*,4'*en*), 3.84 (dd, 2 H, H-4*ex*,4'*ex*), 1.45 and 1.30 (2 s, 12 H, 2 CMe_2); ^{13}C δ 112.54 (2 CMe_2), 102.41 (C-1,1'), 84.99 (C-2,2'), 80.04 (C-3,3'), 72.23 (C-4,4'), 26.33 and 24.99 (2 CMe_2). Mass spectrum: *m/z* 287 (M^+ − Me), 159 (M^+ − $C_7H_{11}O_3$), 143 ($C_7H_{11}O_3^+$), 101 (base peak), 85, 59 (Me_2COH^+), 57, 45, and 43 (Ac^+).

Anal. Calc. for $C_{14}H_{22}O_7$: C, 55.61; H, 7.33. Found: C, 54.92; H, 7.38.

Eluted second was a syrupy compound (8.4 mg) which had $[\alpha]_D$ −62° (*c* 0.5 methanol); lit.[16] m.p. 32.5–34.5°, $[\alpha]_D$ −77.6° → −76.2° in 3 h (*c* 7, methanol), for 2,3-*O*-isopropylidene-β-D-erythrofuranose.

A stirred solution of 2,3-*O*-isopropylidene-β-D-erythrofuranose (225 mg, 1.4 mmol) in dry acetone (6 mL) was treated with anhydrous copper sulfate (0.5 g) and conc. sulfuric acid (0.1 mL) for 2 h. T.l.c. (ether–hexane, 3:2) then revealed starting material together with **19**. Work-up of the reaction mixture, with column chromatography of the product, afforded **19** (50 mg), m.p. 110–112°, $[\alpha]_D$ −150° (*c* 0.6).

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