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SYNTHESIS OF 1-DEOXY-3-*C*-METHYL-D-FRUCTOSE AND 1-DEOXY-3-*C*-METHYL-D-SORBOSE*

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ABSTRACT

Hydroxylation of *trans*-1,3,4-trideoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-*glycero*-hex-3-enulose with osmium tetraoxide gave a mixture of 1-deoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-*arabino*- and -D-*xylo*-hexulose that was partially resolved by acetonation to give 1-deoxy-2,3:4,5-di-*O*-isopropylidene-3-*C*-methyl-β-D-fructopyranose (**4**), 1-deoxy-3,4:5,6-di-*O*-isopropylidene-3-*C*-methyl-*keto*-D-fructose (**5**), and 1-deoxy-2,3:4,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-sorbofuranose (**6**). Treatment of a mixture of **4** and **5** with sodium borohydride gave, after column chromatography, **4** and 1-deoxy-3,4:5,6-di-*O*-isopropylidene-3-*C*-methyl-D-*manno*- and -D-*gluco*-hexitol. Deuterated derivatives corresponding to **4**–**6** were obtained when isopropylidenation was carried out with acetone-d_6. Deacetonation of **4** and **5** yielded 1-deoxy-3-*C*-methyl-D-fructose, and **6** similarly afforded 1-deoxy-3-*C*-methyl-D-sorbose.

INTRODUCTION

We have applied[1] the Knoevenagel–Doebner reaction between *aldehydo* sugars and β-keto acids to the synthesis of 1-deoxyhexuloses and hexuloses, and have extended the method[2] to the synthesis of saccharinic acids. We now report the synthesis of 1-deoxy-3-*C*-methylketohexoses having the D-*fructo* and D-*sorbo* configurations.

Few syntheses of branched-chain deoxyhexuloses have been reported. Thus, 1-[3] and 6-deoxy-3-*C*-methyl-D-psicose[4] and some derivatives of 1,3-dideoxy-3-*C*-methyl-D-*ribo*- and -D-*lyxo*-hexulose[5] have been described.

RESULTS AND DISCUSSION

Hydroxylation with osmium tetraoxide of *trans*-1,3,4-trideoxy-5,6-*O*-iso-

*Branched-chain Sugars. Part VIII. For Part VII, see ref. 2.
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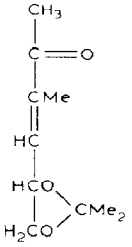
propylidene-3-*C*-methyl-D-*glycero*-hex-3-enulose (**1**) gave a mixture that could not be fractionated by chromatography, and which had i.r. absorptions for hydroxyl and carbonyl but no ^{1}H-n.m.r. resonance for vinylic protons. The hydroxylation of **1** was assumed to have proceeded by way of cyclic intermediates that gave 1-deoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-*arabino*- (**2**) and -D-*xylo*-hexulose (**3**) having the *threo*-configuration at C-3,4. The other ^{1}H-n.m.r. data were consistent with these structures.



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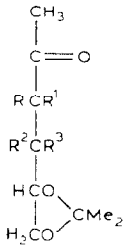
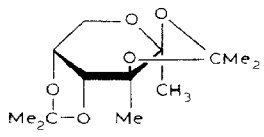


2 R = R^3 = OH, R^1 = Me, R^2 = H

3 R = Me, R^1 = R^2 = OH, R^3 = H

Acetonation[1] of the mixture of **2** and **3** and column chromatography of the products gave, as the material with higher mobility, a ~2:1 mixture of 1-deoxy-2,3:4,5-di-*O*-isopropylidene-3-*C*-methyl-*β*-D-fructopyranose (**4**) and 1-deoxy-3,4:5,6-di-*O*-isopropylidene-3-*C*-methyl-*keto*-D-fructose (**5**) based on the ^{1}H-n.m.r. data. The product of lower mobility was 1-deoxy-2,3:4,6-di-*O*-isopropylidene-3-*C*-methyl-*α*-D-sorbofuranose (**6**). It follows from the 4,6-*O*-isopropylidene-D-hexulofuranose structure of **6** (see below) that HO-4,5 are D-*threo* and, assuming that *cis*-hydroxylation of **1** occurred, that the full configuration is D-*xylo*. It also follows that **4** and **5**, which are shown below to have the same configuration at C-3,4,5, are D-*arabino* derivatives.



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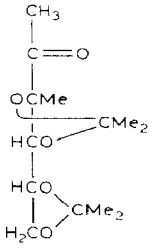

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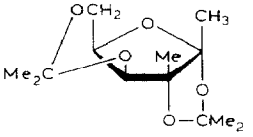


6

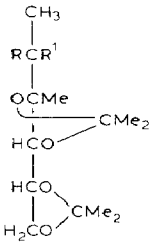
The structure of **6** was established as follows. The i.r. spectrum of **6** indicated the absence of hydroxyl or carbonyl groups, and the ^{1}H-n.m.r. spectrum contained resonances for H-4,5,6 which appeared in a narrow range of chemical shifts in close

agreement with data reported for the analogous di-*O*-isopropylidene derivatives of 1-deoxy-L-[6] and -D-sorbose[6] for which α-furanose structures have been assigned. The ^{13}C-n.m.r. spectrum of **6** was particularly informative. The chemical shift of the signal for the anomeric carbon (C-2) was shifted downfield (~9 p.p.m.) from the position normal for a furanoid ring[7], which must be due to the α-effect of the attached methyl group (C-1). The presence of the 2,3- and 4,6-*O*-isopropylidene groups in **6** was indicated by the resonances having multiplicities and chemical shifts (see Experimental) corresponding to the acetal carbons of a 1,3-dioxolane and a 1,3-dioxane ring[8] and confirmed by the $\Delta\delta$ values (1.6 and 10 p.p.m., respectively) for the *gem*-dimethyl groups present in such rings, which accorded with those previously reported[8]. The small upfield and downfield shifts of the signals for the acetal and the *gem*-dimethyl carbon atoms of the 2,3-*O*-isopropylidene group must reflect the effect[8] of the substituents at C-2 and C-3. The signals for C-3 and C-6 were assigned on the basis of their multiplicities, whereas those of C-4 and C-5, both having the same multiplicity, were assigned on the basis that the signal of the carbon atom linked to the furanoid-ring oxygen generally appears at lower field[7,9]. Finally, the assignments of the resonances of C-1 and Me-3 could be made by comparison of the ^{13}C-n.m.r. spectrum of **6** with that of the analogue prepared using acetone-d_6 in which all the methyl signals had disappeared except those at δ 22.18 and 16.94; the former had a lower intensity due to deuterium exchange at C-1 during the treatment of **10** with deuterium oxide prior to its reaction with acetone-d_6. In addition, the fragmentation pattern shown by the mass spectrum of **6** was also in agreement with the data reported[10] for analogous di-*O*-isopropylidene hexuloses.

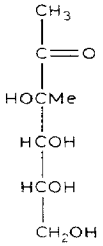
Since only a small amount of pure **4** could be obtained on chromatography of the mixture of **4** and **5**, an alternative approach was used. When the mixture was treated with sodium borohydride, **4** could be obtained in higher yield and was found to have no i.r. absorption for hydroxyl or carbonyl so that a cyclic structure was indicated. The ^{1}H-n.m.r. spectrum demonstrated that **4** was pyranoid in character, the resonances for H-4,5,6,6′ being similar to those reported for the di-*O*-isopropylidene derivatives of 1-deoxy-β-D-fructopyranose[6] and 2-*C*-methyl-β-D-arabinopyranose[1]; there was long-range coupling between H-4 and H-6,6′. The ^{13}C-n.m.r. spectrum of **4** contained signals for acetal carbon atoms indicative[8] of two 1,3-dioxolane rings *cis*-fused to a pyranoid ring, and the chemical shifts were in good agreement with those of the signals for the corresponding carbon atoms in 1,2:4,5-di-*O*-isopropylidene-2-*C*-methyl-β-D-arabinopyranose[1] (see Experimental). The signal of the anomeric carbon atom (C-2) in **4** was shifted downfield by ~4 p.p.m., compared with that in the latter compound, due to the α-effect of the methyl group (C-1). The signals of C-3 and C-6 were assigned on the basis of multiplicities, whereas those of C-5 and C-4 were assigned as the doublets of higher and lower chemical shift, respectively, on the basis of the data previously reported[11] for compounds of similar structure. There were six signals for Me groups in the methyl region; those at low field were assigned to the *gem*-dimethyl groups of the

1,3-dioxolane ring[8] at the 2,3-position, the next two to the *gem*-dimethyl groups of the 1,3-dioxolane ring at the 4,5-position[8], and the others to Me-3 and C-1. The last two assignments were made on the basis of the ^{13}C-n.m.r. data for the analogue of **4** prepared from acetone-d_6 (see above).

Column chromatography of the products obtained by borohydride reduction of the mixture of **4** and **5** gave, in addition to **4**, 1-deoxy-3,4:5,6-di-*O*-isopropylidene-3-*C*-methyl-D-*manno*- (**7**) and -D-*gluco*-hexitol (**8**), which were identified on the basis of analytical and spectroscopic data (see Experimental) and assuming that no isomerisation of the acetal groups occurred during the reduction. The absolute configurations at C-3,4,5 in **7** and **8** were determined by the transformation of these compounds into **5** (see below), whereas the configurations at C-2 were established by the application of Horeau's method[12]. Thus, **7** and **8** gave a dextrorotatory and levorotatory acid, respectively, indicating[12] the 2*R* and 2*S* configuration for **7** and **8**.



7 R = OH, R' = H
8 R = H, R' = OH



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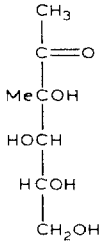

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Oxidation of a mixture of **7** and **8** with Jones' reagent[13] and ruthenium tetraoxide[14] gave **5**, which showed i.r. absorption for carbonyl. The presence in **5** of two *O*-isopropylidene groups of the 1,3-dioxolane type was demonstrated by the ^{13}C-n.m.r. spectrum; in addition, the presence of the methylketonic and terminal dioxolane groups was revealed by the ions with *m/z* 215 and 101 in the mass spectrum[10]. The configuration of **5** was determined by isomerisation of **4** and **6** under the conditions used in the acetonation of **2** and **3** where **4**, but not **6**, gave a mixture of **4** and **5** (~4:1 ratio).

Acid hydrolysis of a mixture of **4** and **5** gave 1-deoxy-3-*C*-methyl-D-fructose (**9**); likewise, **6** gave 1-deoxy-3-*C*-methyl-D-sorbose (**10**).

EXPERIMENTAL

General methods. — Melting points were determined with a Reichter hotplate microscope and are uncorrected. Solutions were concentrated under diminished pressure after drying over $MgSO_4$. ^{1}H-N.m.r. spectra were recorded with

a Perkin–Elmer R20-B or Bruker WP-80 SY spectrometer for solutions in $CDCl_3$ (internal Me_4Si). I.r. spectra were recorded with a Pye Unicam SP 1000 instrument, and mass spectra with a Hewlett–Packard 5930A instrument. Optical rotations were measured for solutions in $CHCl_3$ (1-dm tube) with a Perkin–Elmer 141 polarimeter. T.l.c. was performed on Silica Gel (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[15].

Hydroxylation of trans-*1,3,4-trideoxy-5,6-O-isopropylidene-3-C-methyl*-D-glycero-*hex-3-enulose* (**1**). — To a solution of **1**[5] (3.6 g, 20 mmol) in ethanol–water (1:1, 50 mL) was added a solution of potassium chlorate (1 g, 8 mmol) in the same solvent (50 mL). The mixture was acidified to pH ~4 with aqueous 50% acetic acid, and then aqueous 0.25% osmium tetraoxide (15 mL) was added. After 15 min, t.l.c. (ether–hexane, 2:1) revealed a product with R_F 0.20. The mixture was stored at room temperature for 24 h, when t.l.c. revealed that **1** had disappeared. The mixture was neutralised (K_2CO_3) and concentrated, and the residue was extracted with ethyl acetate. Concentration of the extracts gave a residue that was subjected to column chromatography (ether–hexane, 5:1), to yield a mixture (3.1 g, 84.4%) of 1-deoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-*arabino*- (**2**) and -D-*xylo*-hexulose (**3**) having $[\alpha]_D$ +13°, $[\alpha]_{365}$ +49° (*c* 1.1); ν_{max}^{film} 3440 (OH), 1715 (C=O, ketone), 1380 and 1375 (CMe_2), 1155, 1055, and 850 cm^{-1} (dioxolane ring). ^{1}H-N.m.r. data (60 MHz): δ 4.50–3.50 (m, 4 H, H-4,5,6,6′), 4.19 (bs, 1 H, HO-3), 3.06 (bm, 1 H, HO-4), 2.30 (s, 3 H, MeCO), 1.43 and 1.38 (2 s, relative intensity 1:2, 9 H, CMe_2 and Me-3).

Anal. Calc. for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 54.79; H, 8.26.

Acetonation of the mixture of **2** *and* **3**. — A solution of the mixture (0.4 g) in dry acetone (20 mL) and conc. sulfuric acid (0.2 mL) was stirred with powdered, anhydrous copper sulfate (5 g). After 1 h, t.l.c. (ether–hexane, 1:3) revealed two components (R_F 0.35 and 0.24). The mixture was stirred for a further 18 h, neutralised (K_2CO_3), filtered, and concentrated, to give a residue that was subjected to column chromatography (ether–hexane, 1:5) to give, first, 189 mg of a ~2:1 (based on ^{1}H-n.m.r. data) mixture of two compounds subsequently shown to be 1-deoxy-2,3:4,5-di-*O*-isopropylidene-3-*C*-methyl-β-D-fructopyranose (**4**) and 1-deoxy-3,4:5,6-di-*O*-isopropylidene-3-*C*-methyl-D-*arabino*-hexulose (**5**).

Rechromatography (ether–hexane, 1:7) of the mixture gave **4** (19 mg), m.p. 39.5–40.5° (from hexane), $[\alpha]_D$ +12° (*c* 1.5), R_F 0.47 (ether–hexane, 1:1); ν_{max}^{film} 1380 and 1375 (CMe_2), 1245, 1210, 1125, 1095, 1030, 990, 935, 880, and 745 cm^{-1}. N.m.r. data: ^{1}H (80 MHz), δ 4.30–4.20 (m, 2 H, H-4,5), 4.00 (octet, 1 H, $J_{4,6}$ 1, $J_{5,6}$ 2.5, $J_{6,6'}$ 13 Hz, H-6), 3.63 (sextet, 1 H, $J_{4,6'} = J_{5,6'} = 1.5$ Hz, H-6′), 1.49, 1.46, 1.45, and 1.33 (4 s, 18 H, 2 CMe_2, Me-3, and H-1,1,1); ^{13}C, δ 108.46 (s, acetal C of 4,5-*O*-isopropylidene group), 107.69 (s, acetal C of 2,3-*O*-isopropylidene group), 105.60 (s, C-2), 79.33 (s, C-3), 76.00 (d, C-5), 71.53 (d, C-4), 62.16 (t, C-6), 29.81 and 28.07 (2 q, CMe_2 of 2,3-*O*-isopropylidene group), 26.50 and 24.80 (2 q, CMe_2

of 4,5-*O*-isopropylidene group), 23.75 (q, C-1), and 23.06 (q, Me-3) [^{13}C-n.m.r. data for 1,2:4,5-di-*O*-isopropylidene-2-*C*-methyl-β-D-arabinopyranose[1]: δ 109.80 (s, acetal C of 4,5-*O*-isopropylidene group), 108.53 (s, acetal C of 1,2-*O*-isopropylidene group), 101.59 (d, C-1), 78.34 (s, C-2), 74.74 (d, C-4), 71.05 (d, C-3), 61.22 (t, C-5), 29.71 and 28.13 (2 q, C*Me*$_2$ of 1,2-*O*-isopropylidene group), 26.72 and 24.81 (2 q, C*Me*$_2$ of 4,5-*O*-isopropylidene group), and 23.64 (q, Me-2)]. Mass spectrum: *m/z* 258 (M^+), 243 (M^+ − Me), 185 (M^+ − Me − Me_2CO), 183 (M^+ − Me − AcOH), 157 (M^+ − Me_2CO − CO), 143, 142, 128 ($C_7H_{12}O_2^+$), 125 (M^+ − Me − Me_2CO − AcOH), 113 ($C_7H_{12}O_2^+$ − Me), 101 ($C_5H_9O_2^+$), 99, 97 ($C_6H_9O^+$), 83 ($C_5H_7O^+$), 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_{13}H_{22}O_5$: C, 60.44; H, 8.59. Found: C, 60.33; H, 8.78.

The second product isolated from the initial chromatography was 1-deoxy-2,3:4,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-sorbofuranose (**6**, 150 mg), m.p. 54.5–55° (from hexane), $[\alpha]_D$ −1.3° $[\alpha]_{365}$ −16° (*c* 1.24), R_F 0.34 (ether–hexane, 1:2); ν_{max}^{KBr} 1380 and 1375 (CMe_2), 1240, 1225, 1055, 1000, 925, 860, 840, 809, and 755 cm^{-1}. N.m.r. data: ^{1}H (80 MHz), δ 4.14–3.90 (m, 4 H, H-4,5,6,6'), 1.54 (s, 3 H, H-1,1,1), 1.43, 1.42, 1.40, and 1.37 (4 s, 12 H, 2 CMe_2), and 1.34 (s, 3 H, Me-3); ^{13}C, δ 114.67 (s, C-2), 109.80 (s, acetal C of 2,3-*O*-isopropylidene group), 97.20 (s, acetal C of 4,6-*O*-isopropylidene group), 90.90 (s, C-3), 75.19 (d, C-5), 70.52 (d, C-4), 61.00 (t, C-6), 29.67 and 28.07 (2 q, C*Me*$_2$ of 2,3-*O*-isopropylidene group), 28.88 and 18.89 (2 q, C*Me*$_2$ of 4,6-*O*-isopropylidene group), 22.18 (q, C-1), and 16.94 (q, Me-3). Mass spectrum: *m/z* 258 (M^+), 243 (M^+ − Me), 185 (M^+ − Me − Me_2CO), 183 (M^+ − Me − AcOH), 157 ($C_8H_{13}O_3^+$), 143, 128 ($C_7H_{12}O_2^+$), 127, 125 (M^+ − Me − Me_2CO − AcOH), 115, 114, 113 ($C_6H_9O_2^+$), 101 ($C_5H_9O_2^+$), 99, 83, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Anal. Calc. for $C_{13}H_{22}O_5$: C, 60.44; H, 8.59. Found: C, 60.37; C, 8.49.

Borohydride reduction of **4** *and* **5**. — To a stirred solution of a mixture of **4** and **5** (~7:3, 0.4 g) in anhydrous methanol (5 mL) was added, portionwise, sodium borohydride (100 mg). The mixture was left at room temperature for 3 h, when t.l.c. (ether–hexane, 1:2) revealed three components, R_F 0.47, 0.30, and 0.24. The excess of hydride was decomposed as the mixture was neutralised with acetic acid, concentrated, and extracted with chloroform (3 × 10 mL). The combined extracts were filtered and concentrated, and the residue was subjected to column chromatography (ether–hexane, 1:7 → 1:4) to yield, first, **4** (200 mg). Fractions that contained the compound with R_F 0.30 were combined and concentrated to give syrupy 1-deoxy-3,4:5,6-di-*O*-isopropylidene-3-*C*-methyl-D-*manno*-hexitol (**7**, 22 mg), $[\alpha]_D$ −3°, $[\alpha]_{436}$ −6° (*c* 1.6); ν_{max}^{film} 3460 (OH), 1365 (CMe_2), 1210, 1060, and 835 cm^{-1} (dioxolane ring). ^{1}H-N.m.r. data (80 MHz): δ 4.30–3.90 and 3.85–3.50 (2 m, 6 H, H-2,4,5,6,6' and HO-2), 1.46, 1.41, 1.36, and 1.31 (4 s, 12 H, 2 CMe_2), 1.21 (d, 3 H, $J_{1,2}$ 7 Hz, H-1,1,1), and 1.19 (s, 3 H, Me-3). ^{1}H-N.m.r. exchange with D_2O: 3.69 (q, 1 H, H-2). Mass spectrum: *m/z* 245 (M^+ − Me), 216 (M^+ − C_2H_4O), 215 (M^+ − C_2H_5O), 187 (M^+ − Me − Me_2CO), 157 (M^+ − $C_5H_9O_2$), 145, 127

(M^+ − Me − Me_2CO − AcOH), 109, 101 ($C_5H_9O_2^+$), 99, 85, 83, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Eluted third was syrupy 1-deoxy-3,4:5,6-di-*O*-isopropylidene-3-*C*-methyl-D-*gluco*-hexitol (**8**, 38 mg), $[\alpha]_D$ −1.8°, $[\alpha]_{436}$ −2.8° (*c* 2.5), R_F 0.24 (ether–hexane, 1:2); ν_{max}^{film} 3480 (OH), 1375 (CMe_2), 1210, 1070, and 840 cm^{-1} (dioxolane ring). ^{1}H-N.m.r. data (80 MHz): δ 4.30–3.90 (m, 4 H, H-4,5,6,6'), 3.75 (m, 1 H, H-2), 2.28 (d, 1 H, $J_{2,OH}$ 9 Hz, HO-2), 1.43 and 1.38 (2 s, 12 H, 2 CMe_2), 1.23 (s, 3 H, Me-3), and 1.23 (d, 3 H, $J_{1,2}$ 7 Hz, H-1,1,1). Mass spectrum: *m/z* 245 (M^+ − Me), 215 (M^+ − C_2H_5O), 187 (M^+ − Me − Me_2CO), 157 (M^+ − $C_5H_9O_2$), 141, 127 (M^+ − Me − Me_2CO − AcOH), 109, 101 ($C_5H_9O_2^+$), 99, 85, 84, 83, 72, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

Configurational assignment at C-2 in **7** *and* **8**. — A solution of **7** (17.18 mg, 0.066 mmol) and (±)-α-phenylbutyric anhydride (61.47 mg, 0.198 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 (53.9 mg), $[\alpha]_{436}$ +2° (*c* 3.6).

The reaction of **8** (20.42 mg, 0.079 mmol) and the anhydride (80.61 mg, 0.26 mmol) gave α-phenylbutyric acid (76.6 mg), $[\alpha]_{436}$ −2° (*c* 5).

Synthesis of **5**. — (*a*) To a cooled solution of a mixture of **7** and **8** (30 mg) in acetone (4 mL) was added, dropwise, a solution of chromic oxide in aqueous sulfuric acid (Jones' reagent[13]) until a faint orange colour remained. After 30 min, methanol (0.5 mL) was added, and the mixture was filtered, diluted with water (10 mL), and extracted with dichloromethane. Concentration of the extract and column chromatography (ether–hexane, 2:7) of the residue gave syrupy **5** (12 mg), $[\alpha]_D$ +14°, $[\alpha]_{436}$ +33° (*c* 1), R_F 0.45 (ether–hexane, 1:2); ν_{max}^{film} 1725 (C=O, ketone), 1380 and 1375 (CMe_2), 1210, 1050, and 835 cm^{-1} (dioxolane ring). ^{1}H-N.m.r. data (80 MHz): δ 4.25–3.95 (m, 4 H, H-4,5,6,6'), 2.28 (s, 3 H, H-1,1,1), 1.45, 1.40, 1.38, and 1.35 (4 s, 15 H, intensity ratio 1:1:2:2, 2 CMe_2 and Me-3); ^{13}C, δ 208.99 (s, C-2), 109.74 (s, acetal C of 5,6-*O*-isopropylidene group), 109.62 (s, acetal C of 3,4-*O*-isopropylidene group), 87.09 (s, C-3), 79.27 (d, C-4), 73.97 (d, C-5), 67.57 (t, C-6), 28.36 and 26.67 (2 q, C*Me*$_2$ of 3,4-*O*-isopropylidene group), 26.15 and 25.39 (2 q, C*Me*$_2$ of 5,6-*O*-isopropylidene group), 24.72 (q, C-1), and 18.87 (q, Me-3). Mass spectrum: *m/z* 243 (M^+ − Me), 215 (M^+ − Me − CO or M^+ − MeCO), 183 (M^+ − Me − AcOH), 157 (M^+ − $C_5H_9O_2$), 143, 125 (M^+ − Me − AcOH − Me_2CO), 113, 101 ($C_5H_9O_2^+$), 99, 97, 85, 83, 72, 59 (Me_2COH^+), and 43 (Ac^+, base peak).

(*b*) To a vigorously stirred solution of **7** and **8** (300 mg) in chloroform (15 mL) were added saturated aqueous sodium hydrogencarbonate (10 mL) and ruthenium dioxide (100 mg). Aqueous 5% sodium periodate (10 mL) was then added dropwise at room temperature until the starting product had disappeared

(t.l.c.) and no further reduction of the tetraoxide occurred. The residual tetraoxide was reduced with propan-2-ol (0.5 mL), the organic phase was separated, and the aqueous phase was extracted with chloroform (3 × 10 mL). The combined extracts were concentrated to give an oil that was subjected to column chromatography (ether–hexane, 1:3) to afford **5** (280 mg).

Isomerisation of **4** *and* **6**. — To a stirred solution of **4** (40 mg, 0.16 mmol) in dry acetone (1 mL) were added powdered, anhydrous copper sulfate (200 mg) and conc. sulfuric acid (0.01 mL). The mixture was stirred at room temperature for 3 h, neutralised (K_2CO_3), filtered, and concentrated, and the residue was subjected to column chroamtography to yield a mixture of **4** and **5** (4:1, from the ^{1}H-n.m.r. spectrum).

The above treatment had no effect on **6** (40 mg, 0.16 mmol).

*1-Deoxy-3-*C*-methyl-*D*-fructose* (**9**). — A suspension of a mixture of **4** and **5** (1.2 g) in aqueous 1% sulfuric acid was kept at ~100° until the starting products disappeared (t.l.c.). The mixture was cooled and neutralised with Lewatid MP69 (HCO_3^-) resin, and the resin was collected and washed with water. The combined filtrate and washings were treated with activated charcoal, filtered, and concentrated, and the colourless syrupy residue was subjected to column chromatography on microcrystalline cellulose (Merck), using aqueous 90% ethanol, to give **9** as a syrup (712 mg, 81%), $[\alpha]_D$ +20° (*c* 2, water), which was homogeneous by p.c. (R_F 0.56).

*1-Deoxy-3-*C*-methyl-*D*-sorbose* (**10**). — Application of the above method to **6** (2.5 g) gave syrupy **10** (1.23 g, 71%), $[\alpha]_D$ +0.62°, $[\alpha]_{436}$ −1.2° (*c* 1.6, water), with R_F 0.56.

1-Deoxy-2,3:4,5-[$^2H_{12}$]*di-*O*-isopropylidene-3-*C*-methyl-β-*D*-*[*1,1,1-*$^2H_3$]*fructopyranose and 1-deoxy-2,3:4,6-*[$^2H_{12}$]*di-*O*-isopropylidene-3-*C*-methyl-α-*D*-*[*1,1-*$^2H_2$]*-sorbofuranose*. — A solution of a mixture of **9** and **10** (90 mg), obtained by hydrolysis of **2** and **3** (130 mg), in D_2O (0.3 mL) was left for 3 days at room temperature and then concentrated, and the residue was stored overnight *in vacuo* over phosphorus pentaoxide. The residue was acetonated as described above, but using acetone-d_6, to yield, on column chromatography, first a mixture (45 mg) of the cyclic and acyclic derivatives of fructose (~7:3, ^{1}H-n.m.r. data), from which the title fructose derivative (23 mg) could be isolated as a syrup after treatment with $NaBH_4$ (see above); $[\alpha]_D$ +12° (*c* 1.8); ν_{max}^{film} 2210 (C-D), 1220, 1095, 1075, 1030, 980, 860, and 750 cm^{-1}. ^{1}H-N.m.r. data (80 MHz): δ 4.30–4.20 (m, 2 H, H-4,5), 4.00 (octet, 1 H, $J_{4,6}$ 1, $J_{5,6}$ 2.5, $J_{6,6'}$ 13 Hz, H-6), 3.63 (sextet, 1 H, $J_{4,6'} = J_{5,6'} = 1.5$ Hz, H-6'), and 1.49 (s, 3 H, Me-3); ^{13}C, δ 108.41 (s, acetal C of 4,5-*O*-isopropylidene group), 107.65 (s, acetal C of 2,3-*O*-isopropylidene group), 105.61 (s, C-2), 79.36 (s, C-3), 76.03 (d, C-5), 71.61 (d, C-4), 62.22 (t, C-6), and 23.08 (q, Me-3).

Eluted second was the sorbose derivative (61 mg), m.p. 53–54° (from hexane), $[\alpha]_D$ −1.1°, $[\alpha]_{365}$ −14.5° (*c* 1.4); ν_{max}^{KBr} 2210 (C-D), 1240, 1120, 1040, 940, 855, and 775 cm^{-1}. N.m.r. data: ^{1}H (80 MHz), δ 4.15–3.90 (m, 4 H, H-4,5,6,6'),

1.54 (s, 1 H, H-1), and 1.34 (s, 3 H, Me-3); ^{13}C, δ 114.70 (s, C-2), 109.73 (s, acetal C of 2,3-*O*-isopropylidene group), 97.15 (s, acetal C of 4,6-*O*-isopropylidene group), 90.90 (s, C-3), 75.23 (d, C-5), 70.55 (d, C-4), 61.08 (t, C-6), 22.24 (q, C-1, lower intensity), and 16.96 (q, Me-3).

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