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Note

A new synthesis of 1-deoxy-D-psicose and 1-deoxy-D-tagatose

ISIDORO IZQUIERDO CUBERO* AND DIEGO GARCIA POZA
Department of Organic Chemistry, University of Granada, Granada (Spain)
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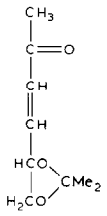
As a part of our work on the use of enulose derivatives, obtained from *aldehydo* sugars either by the Knoevenagel–Doebner reaction[1] or by the Wittig reaction[2], as starting products for the synthesis of hexuloses[1], 1-deoxyhexuloses[1,3], and branched-chain deoxyhexuloses[4], the title compounds were required. 1-Deoxy-D-tagatose[5] and 1-deoxy-D-psicose[6,7] have been synthesised by the diazoketone method and the L isomer of the latter compound has been reported[8]. We now describe a new synthesis route for the title compounds.

Hydroxylation of (*Z*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-enulose (**1**) with osmium tetraoxide gave 1-deoxy-5,6-*O*-isopropylidene-D-*lyxo*-hexulose (**2**) and 1-deoxy-5,6-*O*-isopropylidene-D-*ribo*-hexulose (**3**), which were isolated by column chromatography.



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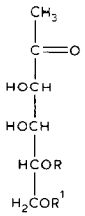
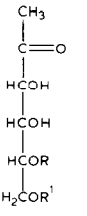
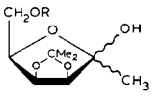


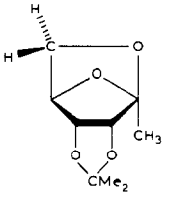
2 R, R^1 = >CMe$_2$
4 R = R^1 = H



3 R, R^1 = >CMe$_2$
5 R = R^1 = H



6 R = H
7 R = Ac



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The structure of **2** was determined as follows. Hydrolysis of **2** afforded a compound with physical constants (see Experimental) very close to those reported[5] for 1-deoxy-D-tagatose (**4**), and acetonation yielded a product identified as 1-deoxy-3,4-*O*-isopropylidene-D-tagatose (**6**). Thus, **6** had i.r. absorption for hydroxyl and two ^{1}H-n.m.r. resonances which disappeared on addition of D_2O. Acetylation of **6**

*To whom correspondence should be addressed.

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gave a monoacetate (**7**) in agreement with the presence of a primary and a tertiary alcohol group, and the downfield shift of the signal for H-6,6′ in **7** indicated that the acetyl group was located at position 6. The ^{1}H-n.m.r. spectrum of **6** indicated the presence of an isopropylidene group, and the ^{13}C-n.m.r. spectrum (off-resonance) contained two singlets at low field associated[9] with the acetal carbon atom of the 3,4-*O*-isopropylidene group and C-2.

The anomeric configuration of **6** remains unknown, but is likely to be β, since an α configuration would involve all the bulky groups being on the same face of the furanoid ring. The formation of **6** accords with the results of acetonation of D-lyxose[10], where a compound analogous to **6** was obtained.

Hydrolysis of **3** gave a product with chromatographic and optical properties similar to those reported for 1-deoxy-D-psicose (**5**). Acetonation of **3** gave a product whose optical and spectroscopic data were identical to those reported[11] for 2,6-anhydro-1-deoxy-3,4-*O*-isopropylidene-β-D-psicofuranose (**8**).

EXPERIMENTAL

General methods. — Melting points were determined with a Reichter hot-plate microscope and are uncorrected. Solutions in organic solvents were concentrated under diminished pressure after drying over $MgSO_4$. ^{1}H-N.m.r. (80 MHz) and ^{13}C-n.m.r. (20 MHz) spectra (broad band and off-resonance) were recorded with a Bruker WP-80 SY spectrometer for solutions in $CDCl_3$ (internal Me_4Si). I.r. spectra were recorded with a Pye Unicam SP 1000 Spectrophotometer. Optical rotations were measured for solutions in $CHCl_3$ (1-dm tube), using a Perkin–Elmer 141 polarimeter. 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 solvent *A* (1-butanol–ethanol–water, 4:1:5; upper layer) or *B* (1-butanol–ethanol–water, 28:7:13), and detection with silver nitrate[12].

*Hydroxylation of (Z)-1,3,4-trideoxy-5,6-O-isopropylidene-*D-glycero-*hex-3-enulose* (**1**). — To a solution of **1**[2] (2 g, 11.8 mmol) in methanol–water (1:1, 25 mL) was added a solution of potassium chlorate (735 mg, 6 mmol) in the same solvent (25 mL). The mixture was acidified (pH 5) with acetic acid (0.5 mL), and then aqueous 1% osmium tetraoxide (6 mL) was added. The mixture was left at room temperature overnight; t.l.c. (ether) then revealed that **1** had disappeared, and that two products (R_F 0.34 and 0.28) were present. The mixture was neutralised (anhydrous $NaHCO_3$) and concentrated. The residue was extracted with ethyl acetate (3 × 30 mL), the extract was concentrated, and the residue was subjected to column chromatography (ether–hexane, 3:1). Eluted first was syrupy 1-deoxy-5,6-*O*-isopropylidene-D-*lyxo*-hexulose (**2**; 966 mg, 40%), $[\alpha]_D$ +71° (*c* 0.9); ν_{max}^{film} 3370 (OH), 1715 (ketone, C=O), 1370 (CMe_2), 1210, 1150, 1055, and 840 cm^{-1} (dioxolane ring). N.m.r. data: ^{1}H, δ 4.32 (ddd, 1 H, $J_{4,5}$ 4, $J_{5,6}$ 8, $J_{5,6'}$ 6 Hz, H-5), 4.12 (dd, 1 H, $J_{3,4}$ 8, $J_{HO,3}$ 5 Hz, H-3), 4.10 (t, 1 H, $J_{6,6'}$ 8 Hz, H-6), 3.88

(dd, 1 H, H-6'), 3.57 (d, 1 H, HO-3), 3.48 (ddd, 1 H, H-4), 2.81 (d, 1 H, $J_{HO,4}$ 6 Hz, HO-4), 2.40 (s, 3 H, 3 H-1), 1.48 and 1.40 (2 s, 6 H, CMe_2).

Eluted second was 1-deoxy-5,6-*O*-isopropylidene-D-*ribo*-hexulose (**3**; 750 mg, 31%), m.p. 59–61° (from hexane), $[\alpha]_D$ −52.5° (*c* 1); ν_{max}^{KBr} 3360 (OH), 1751 (ketone, C=O), 1380 and 1370 (CMe_2), 1205, 1150, 1055, and 845 cm^{-1} (dioxolane ring). ^{1}H-N.m.r. data: δ 4.35–3.75 (m, 5 H, H-3,4,5,6,6'), 3.87 (d, 1 H, $J_{HO,3}$ 5 Hz, HO-3), 2.88 (d, 1 H, $J_{HO,4}$ 7 Hz, HO-4), 2.30 (s, 3 H, 3 H-1), 1.40 and 1.30 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.56; H, 7.97.

*1-Deoxy-*D*-tagatose* (**4**). — A suspension of **2** (212 mg, 1 mmol) in aqueous 50% acetic acid (5 mL) was left at room temperature overnight. T.l.c. (ether–hexane, 1:1) then showed that **2** had disappeared and that a non-mobile substance was present. The mixture was concentrated and the remaining acetic acid was removed by codistillation with water to afford 4 (165 mg, 97%) that was homogeneous by p.c. (R_F 0.40, solvent *A*); m.p. 128–130°, $[\alpha]_D$ −14.3° (*c* 1.7, water) {lit.[5] R_F 0.40, m.p. 121–123°, $[\alpha]_D$ −14° (*c* 2, water)}; ν_{max}^{KBr} 3460, 3340, and 3200 (OH), 1205, 1100, 1075, 1030, 900, 850, 765, and 705 cm^{-1}.

Anal. Calc. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 43.90; H, 7.52.

*1-Deoxy-*D*-psicose* (**5**). — Hydrolysis of **3** (200 mg, 1 mmol), as described for **2**, yielded syrupy **5** (155 mg, 96.4%) that was homogeneous by p.c. (R_F 0.43, solvent *B*); $[\alpha]_D$ +2.3° (*c* 1.3, water) {lit.[6] $[\alpha]_D$ +1.5° (*c* 5, water); lit.[7] $[\alpha]_D$ −0.1° (*c* 0.9, water); lit.[8], for the L isomer, $[\alpha]_D$ −0.25° (*c* 2.5, water)}.

Acetonation of **2**. — A solution of **2** (609 mg, 3 mmol) in dry acetone (30 mL) and conc. sulfuric acid (0.15 mL) was stirred at room temperature with anhydrous copper sulfate (3 g) for 24 h. T.l.c. (ether) then revealed a complex mixture, in which the substance with R_F 0.42 was in highest concentration. The mixture was stirred for a further 36 h (after which no appreciable difference was observed) and then neutralised (K_2CO_3), filtered, and concentrated. The residue was subjected to column chromatography (ether–hexane, 1:1 → 1:2) to give 1-deoxy-3,4-*O*-isopropylidene-D-tagatofuranose (**6**; 58 mg, 9.5%), m.p. 123–125° (from chloroform), $[\alpha]_D$ +16° (*c* 1.24), R_F 0.42 (ether); ν_{max}^{KBr} 3360 and 3200 (OH), 1380 (CMe_2), 1210, 1160, 1110, 1070, 910, and 860 cm^{-1}. N.m.r. data (acetone-d_6): ^{1}H, δ 4.80 (dd, 1 H, $J_{3,4}$ 6, $J_{4,5}$ 4 Hz, H-4), 4.36 (d, 1 H, H-3), 4.10 (ddd, 1 H, $J_{5,6}$ 6, $J_{5,6'}$ 5 Hz, H-5), 3.83–3.60 (m, 2 H, H-6 and HO-6), 3.43 (dd, 1 H, $J_{6,6'}$ 7 Hz, H-6'), 2.78 (d, 1 H, HO-2), 1.40 (s, 3 H, 3 H-1), 1.38 and 1.27 (2 s, 6 H, CMe_2); ^{13}C, δ 112.82 (s, 1,3-dioxolane acetal C), 105.25 (s, C-2), 85.76 (d, C-5), 81.16 (d, C-4), 79.07 (d, C-3), 61.22 (t, C-6), 26.08 and 24.75 (2 q, CMe_2), and 22.38 (q, C-1).

Anal. Calc. for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.52; H, 7.48.

When acetonation was carried out on compound **4** (257 mg, 1.6 mmol) under the above conditions, only compound **6** could be isolated.

Conventional treatment of **6** (40 mg, 0.19 mmol) with pyridine (1 mL) and acetic anhydride (0.5 mL) gave, after column chromatography (ether–hexane, 1:1), the 6-acetate **7** (21 mg, 43.5%), m.p. 78–79°, $[\alpha]_D$ +26.3° (*c* 0.8), R_F 0.50 (ether–

hexane, 3:1); ν_{max}^{KBr} 3220 (OH), 1720 (acetate, C=O), 1390 (CMe_2), 1265 (acetate, C-O), 1220, 1205, 1160, 1100, 1065, 1025, 905, and 860 cm^{-1}. ^{1}H-N.m.r. data: δ 4.85 (dd, 1 H, $J_{3,4}$ 6, $J_{4,5}$ 2 Hz, H-4), 4.47 (d, 1 H, H-3), 4.60–4.10 (m, 3 H, H-5,6,6'), 2.40 (s, 1 H, HO-2), 2.08 (s, 3 H, Ac), 1.56 (s, 3 H, 3 H-1), 1.48 and 1.34 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 54.26; H, 6.88.

Acetonation of **3**. — A solution of **3** (455 mg, 2.23 mmol) in dry acetone (15 mL) and conc. sulfuric acid (0.1 mL) was stirred with powdered, anhydrous copper sulfate (2 g) for 24 h. T.l.c. (ether–hexane, 3:1) then revealed the presence of a complex mixture, with the component having R_F 0.52 in highest concentration. The stirring was continued for a further 48 h. Treatment of the mixture as above gave a residue that was subjected to column chromatography (ether–hexane, 1:1), to afford 2,6-anhydro-1-deoxy-3,4-*O*-isopropylidene-β-D-psicofuranose (**8**; 240 mg, 58%), m.p. 105–106° (from hexane), $[\alpha]_D$ −78.1° (*c* 1.1) {lit.[11] m.p. 108–111°, $[\alpha]_D$ −78.9° (*c* 1)}, R_F 0.52 (ether–hexane, 3:1); ν_{max}^{KBr} 1400, 1380 and 1370 (CMe_2), 1260, 1205, 1170, 1150, 1080, 1060, 990, 865, 850, 830, and 820 cm^{-1}. N.m.r. data: ^{1}H, δ 4.61 (d, 1 H, $J_{4,5} = J_{5,6endo} = 0$, $J_{5,6exo}$ 4 Hz, H-5), 4.41 (d, 1 H, $J_{3,4}$ 5 Hz, H-4), 4.13 (d, 1 H, H-3), 3.58 (dd, 1 H, $J_{6endo,6exo}$ 7 Hz, H-6*exo*), 3.38 (d, 1 H, H-6*endo*), 1.62 (s, 3 H, 3 H-1), 1.48 and 1.30 (2 s, 6 H, CMe_2); ^{13}C, δ 112.13 (s, 1,3-dioxolane acetal C), 107.30 (s, C-2), 82.84 (d, C-5), 80.86 (d, C-4), 78.18 (d, C-3), 64.43 (t, C-6), 26.17 and 25.58 (2 q, CMe_2), and 13.92 (q, C-1).

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.73; H, 7.41.

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