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Note

A new synthesis of 1-deoxy-3-*C*-methyl-D-psicose*

ISIDORO IZQUIERDO CUBERO**, MARIA D. PORTAL OLEA, AND DIEGO GARCIA POZA
Department of Organic Chemistry, University of Granada, Granada (Spain)
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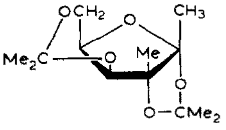
Although 1-deoxy-3-*C*-methyl-D-psicose has been reported[2], few of its derivatives are known. We have been interested in the synthesis of such sugars as part of our work on the Knoevenagel–Doebner reaction between *aldehydo*-sugars and β-keto acids[1,3] for the synthesis of branched-chain sugars.

Partial hydrolysis of 1-deoxy-2,3:4,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-sorbofuranose[1] (**1**) gave the 2,3-*O*-isopropylidene derivative **2**. The formation of **2** was in agreement with the finding[4] that a 1,3-dioxolane ring *cis*-fused to a furanoid ring is more stable than a *cis*-fused 1,3-dioxane ring.



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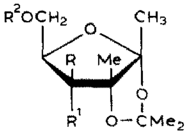

2 R = OH, $R^1 = R^2 = H$
3 R = OH, $R^1 = H, R^2 = Bz$
4 R = R^1 = —O—, $R^2 = Bz$
5 R = H, $R^1 = OH, R^2 = Bz$
6 R = $R^2 = H, R^1 = OH$

Selective benzoylation of **2** afforded 6-*O*-benzoyl-1-deoxy-2,3-*O*-isopropylidene-3-*C*-methyl-α-D-sorbofuranose (**3**), but more than 1 mol of the acylating agent was required because of the formation of benzoylpyridine. Oxidation of **3** with ruthenium tetraoxide[5] gave 6-*O*-benzoyl-1-deoxy-2,3-*O*-isopropylidene-3-*C*-methyl-α-D-*erythro*-2,4-hexodiulo-2,5-furanose (**4**), which was reduced by sodium borohydride to afford only one compound that had chromatographic, optical, and spectroscopic properties different from those of **3**, reflecting a change in the configuration at C-4. The product was 6-*O*-benzoyl-1-deoxy-2,3-*O*-

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*Branched-chain Sugars, Part X. For Part IX, see ref. 1.
**To whom correspondence should be addressed.

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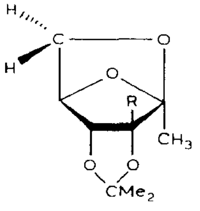
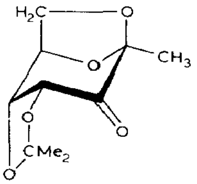


8 R = Me
9 R = H



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isopropylidene-3-*C*-methyl-α-D-psicofuranose (**5**). The high stereoselectivity in the reduction of **4** accorded with that reported[6] for similar compounds and is explained by the preferential attack of the reagent at the β-face of the carbonyl group because of steric hindrance of the α-face by the *endo*-methyl group of the 1,3-dioxolane ring.

Debenzoylation of **4** with methanolic sodium methoxide gave 1-deoxy-2,3-*O*-isopropylidene-3-*C*-methyl-α-D-psicofuranose (**6**), which was hydrolysed to 1-deoxy-3-*C*-methyl-D-psicose (**7**).

The structure of **7** was confirmed by acetonation with acetone–conc. sulfuric acid–anhydrous copper sulfate, which gave 2,6-anhydro-1-deoxy-3,4-isopropylidene-3-*C*-methyl-β-D-psicofuranose (**8**), identified on the basis of analytical and spectroscopic data. The formation of **8** accords with the results for the acetalation of D-ribose[7], where a compound with analogous structure was obtained. On the other hand, the multiplicities of the signals for H-4,5,6_{en},6_{ex} in **8** were the same as those reported for 2,6-anhydro-1-deoxy-3,4-*O*-isopropylidene-β-D-psicofuranose[8] (**9**), produced by photochemical decarbonylation of 2,7-anhydro-1-deoxy-4,5-*O*-isopropylidene-β-D-*ribo*-2,3-heptodiulo-2,6-pyranose (**10**). Thus, the signal for H-4 in **8** was a singlet, whereas in **9** it was a doublet due to coupling with H-3. Similarly, H-5 and H-6_{en} appeared as doublets and H-6_{ex} as a double doublet in both **8** and **9**, reflecting *geminal* coupling between H-6_{en} and H-6_{ex}, and the absence of coupling between H-5 and H-6_{en}. Examination of a molecular model of **8** and **9** explained the above results. Thus, the dihedral angle formed by H-5 with H-4 and H-6_{en} is ~90°, and, according to the Karplus equation[9], negligible values of the coupling constants are to be expected.

EXPERIMENTAL

General methods. — Melting points were determined with a Reichter hotplate microscope and are uncorrected. Solutions in organic solvents were concentrated under diminished pressure after drying over $MgSO_4$. ^{1}H- (80 MHz) and ^{13}C-n.m.r. (20 MHz) spectra 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 on solutions in $CHCl_3$ (1-dm tube) with 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 1-butanol–ethanol–water (28:7:13), and detection with silver nitrate[10].

*1-Deoxy-2,3-O-isopropylidene-3-C-methyl-α-*D*-sorbofuranose* (**2**). — A suspension of **1**[1] (2 g, 7.75 mmol) in 1:1 aqueous acetic acid (10 mL) was heated at ~100° for 30 min. T.l.c. (ether) then showed that **1** had disappeared, and that a new compound, R_F 0.48, was present. The mixture was concentrated and 1:1 benzene–ethanol (2 × 100 mL) was distilled from the residue, which was then subjected to column chromatography (hexane–ether, 1:5) to afford syrupy **2** (1.5 g, 89%), $[\alpha]_D$ −6°, $[\alpha]_{365}$ −26° (*c* 1.2); ν_{max}^{film} 3410 (OH), 1375 (CMe_2), 1230, 1170, 1120, 1020, and 850 cm^{-1} (1,3-dioxolane ring). N.m.r. data: ^1H, δ 4.40–4.23 and 4.23–3.90 (2 m, 6 H, H-4,5,6,6′ and HO-4,6), 1.55 (s, 3 H, 3 H-1), and 1.44 (s, 9 H, Me-3 and CMe_2); ^{13}C, δ 114.34 (s, C-2), 109.98 (s, 1,3-dioxolane acetal C), 91.22 (s, C-3), 79.16 (d, C-5), 78.34 (d, C-4), 61.33 (t, C-6), 29.53 and 28.19 (2 q, CMe_2), 22.42 (q, C-1), and 17.43 (q, Me-3).

The above assignments were based on the reported[11] data for isopropylidene derivatives of sugars.

*6-O-Benzoyl-1-deoxy-2,3-O-isopropylidene-3-C-methyl-α-*D*-sorbofuranose* (**3**). — To an ice-cold and stirred solution of **2** (0.9 g, 4.1 mmol) in dry pyridine (10 mL) was slowly added benzoyl chloride (0.6 g, 4.27 mmol), and the mixture was left at room temperature overnight. T.l.c. (hexane–ether, 1:3) then revealed **2** together with a new compound, R_F 0.68. More benzoyl chloride (0.65 g, 4.6 mmol) was added, and the mixture was left until **2** had disappeared. Work-up of the mixture as usual then gave a residue, column chromatography (hexane–ether, 1:5) of which yielded **3** contaminated with benzoylpyridine. Further column chromatography (hexane–ether, 2:1 → 1:2) afforded pure **3** as a syrup (1.229 g, 92.5%), $[\alpha]_D$ +3°, $[\alpha]_{365}$ −5° (*c* 1); ν_{max}^{film} 3470 (OH), 1730 (benzoate C=O), 1605 and 1590 (benzoate), 1450, 1375 (CMe_2), 1275 (benzoate C-O), 1230, 1170, 1120, 1000, 850 (1,3-dioxolane ring), and 700 cm^{-1} (aromatic). N.m.r. data: ^1H, δ 8.17–7.97 and 7.65–7.35 (2 m, 5 H, Ph), 4.81 (dd, 1 H, $J_{5,6}$ 6. $J_{6,6'}$ 9 Hz, H-6), 4.55 (o, 1 H, H-5), 4.32 (dd, 1 H, $J_{5,6'}$ 4 Hz, H-6′), 3.95 (dd, 1 H, $J_{HO,4}$ 4, $J_{4,5}$ 2 Hz, H-4), 3.30 (d, 1 H, HO-4), 1.55 (s, 3 H, 3 H-1), 1.50 and 1.45 (2 s, 9 H, relative intensity 1:2, Me-3 and CMe_2); ^{13}C, δ 167.36 (s, benzoyl C=O), 133.40 (d, 1 C-*para,* PhCO), 129.91 (d, 2 C-*ortho,* PhCO), 129.61 (s, C-*ipso,* PhCO), 128.45 (d, 2 C-*meta,* PhCO), 114.35 (s, C-2), 110.11 (s, 1,3-dioxolane acetal C), 90.81 (s, C-3), 77.77 (d, C-5), 77.25 (d, C-4), 62.63 (t, C-6), 29.60 and 28.26 (2 q, CMe_2), 22.42 (q, C-1), and 17.65 (q, Me-3).

*6-O-Benzoyl-1-deoxy-2,3-O-isopropylidene-3-C-methyl-α-*D-erythro*-2,4-hexodiulo-2,5-furanose* (**4**). — To a stirred mixture of **3** (1.129 g, 3.5 mmol) in chloroform (20 mL), ruthenium dioxide (150 mg), and saturated aqueous sodium hydrogencarbonate (10 mL) was added aqueous 5% sodium periodate (25 mL) dropwise during 3 h. T.l.c. (hexane–ether, 1:3) then showed that **3** had disappeared and that a new compound, R_F 0.81, was present. 2-Propanol (0.5 mL) was added, the organic phase was separated, and the aqueous phase was extracted with chloroform (2 × 20 mL). Concentration of the combined chloroform solutions gave a residue that was purified by column chromatography (hexane–ether, 2:1) to afford pure **4** as a syrup (788 mg, 70.2%), $[\alpha]_D$ +85° (c 1.3); ν_{max}^{film} 1780 (ketone C=O), 1730 (benzoate C=O), 1605 and 1585 (benzoate), 1400, 1380 (CMe$_2$), 1270 (benzoate C-O), 1230, 1125, 1060, 1000, 915, 850 (1,3-dioxolane ring), and 700 cm^{-1} (aromatic). N.m.r. data: ^{1}H, δ 8.17–7.87 and 7.60–7.37 (2 m, 5 H, Ph), 4.75 (dd, 1 H, $J_{5,6}$ 3, $J_{6,6'}$ 12 Hz, H-6), 4.70 (dd, 1 H, H-5), 4.45 (dd, 1 H, $J_{5,6'}$ 4 Hz, H-6'), 1.55 (s, 3 H, 3 H-1), 1.44 and 1.33 (2 s, 9 H, relative intensity 2:1, Me-3 and CMe$_2$); ^{13}C, δ 210.47 (s, C-4), 165.88 (s, benzoate C=O), 133.23 (d, 1 C-*para,* PhCO), 129.73 (s, C-*ipso,* PhCO), 129.60 (d, 2 C-*ortho,* PhCO), 128.50 (d, 2 C-*meta,* PhCO), 112.11 (s, C-2), 111.42 (s, 1,3-dioxolane acetal C), 82.23 (s, C-3), 77.07 (d, C-5), 62.80 (t, C-6), 29.19 and 28.02 (2 q, CMe$_2$), 22.06 (q, C-1), and 15.15 (q, Me-3).

6-O-Benzoyl-1-deoxy-2,3-O-isopropylidene-3-C-methyl-α-D-psicofuranose (**5**). — To a stirred solution of **4** (688 mg, 2.15 mmol) in anhydrous methanol (15 mL) was added sodium borohydride (100 mg) portionwise, and the mixture was left at room temperature overnight. T.l.c. (hexane–ether, 1:3) then revealed a new compound, R_F 0.54. The mixture was neutralised by dropwise addition of acetic acid and concentrated, and the semicrystalline mass was extracted with chloroform (3 × 20 mL). Concentration of the combined extracts followed by column chromatography (hexane–ether, 1:1) of the residue yielded pure, syrupy **5** (600 mg, 86.7%), $[\alpha]_D$ +9°, $[\alpha]_{365}$ +19° (c 1.1); ν_{max}^{film} 3470 (OH), 1730 (benzoate C=O), 1600 and 1585 (benzoate), 1450, 1380 (CMe$_2$), 1270 (benzoate C-O), 1230, 1130, 1060, 1000, 850 (1,3-dioxolane ring), and 700 cm^{-1} (aromatic). N.m.r. data: ^{1}H, δ 8.17–7.97 and 7.65–7.35 (2 m, 5 H, Ph), 4.70 (dd, 1 H, $J_{5,6}$ 3, $J_{6,6'}$ 12 Hz, H-6), 4.38 (dd, 1 H, $J_{5,6'}$ 5 Hz, H-6'), 4.03 (o, 1 H, $J_{4,5}$ 9 Hz, H-5), 3.59 (bt, 1 H, $J_{HO,4}$ 8 Hz, H-4), 2.40 (bd, 1 H, HO-4), 1.55 (s, 3 H, 3 H-1), 1.51 and 1.45 (2 s, 9 H, relative intensity 1:2, Me-3 and CMe$_2$); ^{13}C, δ 166.43 (s, benzoate C=O), 133.05 (d, 1 C-*para,* PhCO), 130.08 (s, C-*ipso,* PhCO), 129.73 (d, 2 C-*ortho,* PhCO), 128.39 (d, 2 C-*meta,* PhCO), 113.07 (s, C-2), 110.75 (s, 1,3-dioxolane acetal C), 87.16 (s, C-3), 78.47 (d, C-5), 77.31 (d, C-4), 63.91 (t, C-6), 29.37 and 28.08 (2 q, CMe$_2$), 22.84 (q, C-1), and 20.16 (q, Me-3).

1-Deoxy-2,3-O-isopropylidene-3-C-methyl-α-D-psicofuranose (**6**). — To a solution of **5** (490 mg, 1.5 mmol) in anhydrous methanol (15 mL) was added methanolic M sodium methoxide (2 mL), and the mixture was kept at room temperature overnight. T.l.c. (ether) then showed that **5** had disappeared and that a new compound, R_F 0.33, had been formed. The mixture was neutralised by stirring with Amberlite IR-120 (H$^+$) resin (4 g). The resin was collected and washed with methanol, and the combined filtrate and washings were concentrated. The residue was subjected to column chromatography (ether) to afford **6** (310 mg, 93.5%) as a syrup that crystallised on storage; m.p. 88–89° (from hexane), $[\alpha]_D$ +12°, $[\alpha]_{365}$

+27° (*c* 1.4); $\nu_{\text{max}}^{\text{film}}$ 3450 (OH), 1380 (CMe_2), 1230, 1140, 1060, 1000, 960, 915, and 850 cm^{-1} (1,3-dixolane ring). N.m.r. data: ^1H, δ 4.35–4.00 (m, 5 H, H-4,5,6,6′ and HO-6), 2.39 (d, 1 H, $J_{HO,4}$ 10 Hz, HO-4), 1.52 (s, 3 H, 3 H-1), 1.50, 1.45, and 1.31 (3 s, 9 H, Me-3 and CMe_2); ^{13}C, δ 112.96 (s, C-2), 110.57 (s, 1,3-dioxolane acetal C), 97.50 (s, C-3), 80.62 (d, C-5), 76.02 (d, C-4), 61.24 (t, C-6), 29.42 and 28.02 (2 q, CMe_2), 22.72 (q, C-1), and 20.04 (q, Me-3).

Anal. Calc. for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.09; H, 8.65.

*1-Deoxy-3-C-methyl-*D*-psicose* (**7**). — A suspension of **6** (254 mg, 1.17 mmol) in 0.5M sulfuric acid (10 mL) was heated under reflux for 45 min. T.l.c. (ether) then showed that **6** had disappeared and a non-mobile substance was present. The mixture was cooled and neutralised with Lewatid MP69 (HCO_3^-) resin (4 g), the resin was collected and washed with water, and the combined filtrate and washings were concentrated. The residue was subjected to chromatography (1-butanol–ethanol–water, 28:7:13) on a column of microcrystalline cellulose to give **7** (134 mg, 64.6%) as a syrup that was homogeneous by p.c. (R_F 0.54); $[\alpha]_D$ −12.5° (*c* 1.5, methanol).

*2,6-Anhydro-1-deoxy-3,4-O-isopropylidene-3-C-methyl-β-*D*-psicofuranose* (**8**). — A solution of **7** (134 mg, 0.75 mmol) in dry acetone (10 mL) and conc. sulfuric acid (0.02 mL) was stirred with powdered, anhydrous copper sulfate (1 g) for 30 min. T.l.c. (hexane–ether, 1:1) then revealed a new compound, R_F 0.66. The mixture was kept at room temperature overnight, neutralised (K_2CO_3), filtered, and concentraed, and the residue was subjected to column chromatography (hexane–ether, 1:1) to yield **8** (94 mg, 62%), m.p. 53–54° (from hexane), $[\alpha]_D$ −52° (*c* 1.23); $\nu_{\text{max}}^{\text{KBr}}$ 1380 and 1370 (CMe_2), 1250, 1110, 1085, 1050, 1000, 988, 862, 845 (1,3-dioxolane ring), and 825 cm^{-1}. N.m.r. data: ^1H, δ 4.50 (d, 1 H, $J_{5,6ex}$ 4 Hz, H-5), 4.02 (s, 1 H, H-4), 3.58 (dd, 1 H, $J_{6en,6ex}$ 7 Hz, H-6*ex*), 3.33 (d, 1 H, H-6*en*), 1.52 (s, 3 H, 3 H-1), 1.45, 1.40, and 1.38 (3 s, 9 H, Me-3 and CMe_2); ^{13}C, δ 112.38 (s, C-2), 109.23 (s, 1,3-dioxolane acetal C), 89.77 (s, C-3), 86.22 (d, C-5), 78.53 (d, C-4), 63.79 (t, C-6), 27.91 and 27.14 (2 q, CMe_2), 19.75 (q, C-1), and 12.29 (q, Me-3).

Anal. Calc. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.06. Found: C, 60.11; H, 8.18.

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