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Note

Convenient syntheses of 1,2-anhydro-3,4:5,6-di-*O*-isopropylidene-D-glucitol and -D-mannitol*

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The title 1,2-anhydro-alditols **1** and **2** were required to confirm a structural assignment during current[1,2] synthetic studies. Compound **1** is claimed[3] to result from the condensation of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose (**3**) with dimethylsulfoxonium methylide, and **2** has been obtained[4] from 1,2:3,4-di-*O*-isopropylidene-D-mannitol (**4**), *via* 6-tosylation. The precursors **3**[1] and **4**[5] are not readily available.

Convenient syntheses of **1** and **2** from D-glucono-1,5-lactone are now described. These compounds are potentially useful intermediates for the synthesis of 1-substituted alditols[4,6] and chain-extended deoxy derivatives[7] by reaction with appropriate nucleophiles or carbanions.

The preparation of the methyl ester **5** in high yield from D-glucono-1,5-lactone has been described[1]; **5** was characterised as the tosylate **6**. Metal-hydride reduction of **5** gave the known diol **7** hydrate[4]. Treatment of anhydrous compound **7** with 1.1 equiv. of toluene-*p*-sulfonyl chloride yielded the crystalline 1-tosylate **8**, which was characterised as the *p*-nitrobenzoate **9**. Detosylation of **8** with methanolic sodium methoxide yielded the epoxide **1**. Treatment of the crude product of monotosylation of **7** in a like manner gave **1** (56.5% from D-glucono-1,5-lactone[1]), thereby constituting a practical synthesis of this epoxide.

Reduction of the ester **6** with sodium borohydride yielded the 2-tosylate **10**, which was characterised as the acetate **11**. Detosylation of **10** with methanolic sodium methoxide yielded the epoxide **2**. Similar treatment of crude **10** gave **2** (75.5%).

The $[\alpha]_D$ value (−16.0°) of **1** was not in agreement with the published[3] value (+4°). The claimed[3] stereospecificity of this route must be questioned. An earlier study[8] showed that the reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde under similar conditions gave a 68:32 mixture of the corresponding *erythro* and *threo* epoxides.

The specificity of the route described here is without contention.

*The Chemistry of D-Gluconic Acid, Part III. For Part II, see ref. 2.

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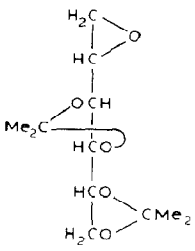

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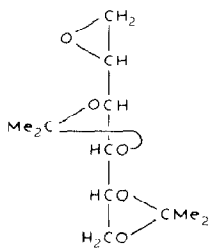

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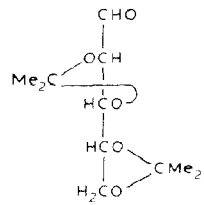

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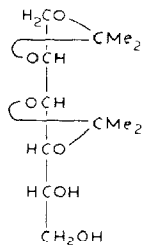

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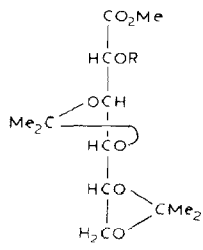
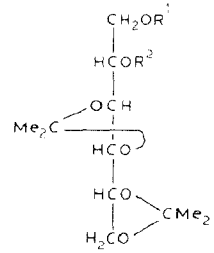
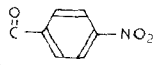


5 R = H
6 R = Ts



7 $R^1 = R^2 = H$
8 R^1 = Ts, R^2 = H
9 R^1 = Ts, R^2 = 
10 R^1 = H, R^2 = Ts
11 R^1 = Ac, R^2 = Ts

EXPERIMENTAL

Optical rotations were determined with a Perkin–Elmer Model 241 automatic polarimeter on 1% solutions in chloroform. T.l.c. was performed (Kieselgel 60, Merck) with light petroleum–ethyl acetate (3:1) and detection by charring with 0.1M $K_2Cr_2O_7$ in M sulfuric acid. ^{1}H-N.m.r. spectra were recorded with a Varian EM 2940 (90 MHz) spectrometer on solutions in $CDCl_3$ (internal Me_4Si).

3,4:5,6-Di-O-isopropylidene-1-O-p-tolylsulfonyl-D-glucitol (**8**). — The diol hydrate **7**[1] (4.7 g) was dehydrated by the distillation *in vacuo* of several portions (10 mL) of dry pyridine therefrom, and to a solution in dry pyridine (20 mL) at −18° was added tosyl chloride (3.54 g) portionwise with stirring during 30 min. The mixture was stored overnight at −18°, treated with ice–water (2 mL) and, after 5 min, poured into ice–water (200 mL). The mixture was extracted with dichloromethane (2 × 130 mL), and the combined extracts were washed successively with 2M hydrochloric acid, saturated aqueous sodium hydrogencarbonate, and water, dried (Na_2SO_4), and concentrated *in vacuo*. Crystallisation and recrystallisation of the product from hexane–isopropyl ether gave **8** (3.49 g, 50%), m.p. 65.5–68°, $[\alpha]_D^{20}$ ~0°. ^{1}H-N.m.r. data: δ 7.82–7.35 (q_{AB} 4 H, aromatic H), 4.17–3.82 (m, 8 H, backbone H), 2.43 (s, 3 H, tosyl Me), 2.2 (s, 1 H, OH), 1.38 (s, 6 H, CMe_2), 1.33 (s, 6 H, CMe_2).

Anal. Calc. for $C_{19}H_{28}O_8S$: C, 54.79; H, 6.78. Found: C, 54.90; H, 6.78.

3,4:5,6-Di-O-isopropylidene-2-O-p-nitrobenzoyl-1-O-p-tolylsulfonyl-D-glucitol (**9**). — A stirred solution of **8** (242 mg) in pyridine (5 mL) at −18° was treated with *p*-nitrobenzoyl chloride (150 mg). The mixture was allowed to attain room temperature slowly, then set aside for 3 days. The crude product (251 mg), obtained after conventional work-up, was recrystallised from ethanol to give **9** (201 mg, 61%), m.p. 113–121.5°, $[\alpha]_D^{20}$ ~0°. ^{1}H-N.m.r. data: δ 8.30–8.15 (q_{AB}, 4 H, aromatic H), 7.75–7.25 (q_{AB}, 4 H, aromatic H), 5.6 (m, 1 H, H-2), 4.47–3.4 (m, 7 H, backbone H), 2.38 (s, 3 H, tosyl Me), 1.37 (s, 12 H, 2 CMe_2).

Anal. Calc. for $C_{26}H_{31}NO_{11}S$: C, 55.21; H, 5.52; N, 2.48. Found: C, 55.39; H, 5.54; N, 2.47.

3,4:5,6-Di-O-isopropylidene-2-O-p-tolylsulfonyl-D-glucitol (**10**). — A stirred solution of **6**[1] (4.44 g) in methanol (50 mL) and water (2 mL) was treated portionwise during 15 min with sodium borohydride (1.51 g). The mixture was stirred for a further 2.5 h, then poured into ice–water (500 mL) to give an oil which crystallised on storage. Recrystallisation of the dried, crude product (3.38 g, 81%) from light petroleum–isopropyl ether gave **10** (2.14 g, 61.4%), m.p. 97.5–105°, $[\alpha]_D^{20}$ +29°. ^{1}H-N.m.r. data: δ 7.83–7.32 (q_{AB}, 4 H, aromatic H), 4.92 (1, 1 H, H-2), 4.27–3.75 (m, 7 H, backbone H), 2.42 (s, 3 H, tosyl Me), 2.40 (s, 1 H, OH), 1.45, 1.33, 1.30, 1.23 (4 s, each 3 H, 2 CMe_2).

Anal. Calc. for $C_{19}H_{28}O_8S$: C, 54.79; H, 6.78. Found: C, 54.62; H, 6.81.

1-O-Acetyl-3,4:5,6-di-O-isopropylidene-2-O-p-tolylsulfonyl-D-glucitol (**11**). — Acetylation of **10** (314 mg) with pyridine–acetic anhydride in the usual manner gave **11** (222 mg, 65%), m.p. 69–73° (from ethanol–water), $[\alpha]_D^{20}$ −5.7°. ^{1}H-N.m.r. data: δ 7.8–7.3 (q_{AB}, 4 H, aromatic H), 5.0 (m, 1 H, H-2), 4.33–3.73 (m, 7 H, backbone H), 2.42 (s, 3 H, tosyl Me), 1.97 (s, 3 H, Ac), 1.45 (s, 3 H, CMe_2), 1.33 (s, 6 H, CMe_2), 1.27 (s, 3 H, CMe_2).

Anal. Calc. for $C_{21}H_{30}O_9S$: C, 55.01; H, 6.59. Found: C, 55.34; H, 6.68.

1,2-Anhydro-3,4:5,6-di-O-isopropylidene-D-glucitol (**1**). — A stirred solution of **8** (1.49 g, 3.59 mmol) in chloroform (10 mL) was treated with methanolic sodium methoxide (10 mL, from 0.15 g, 6.7 mmol of sodium). A white precipitate formed immediately. The mixture was stirred at room temperature for 15 min, and then treated with dichloromethane (50 mL) and water (50 mL). The aqueous layer was extracted with dichloromethane (50 mL), and the organic solutions were washed with water (20 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The essentially pure (t.l.c.) residue (0.875 g) was distilled *in vacuo* to give **1** (0.795 g, 91%), b.p. 65°/0.3 mbar, $[\alpha]_D^{20}$ −16°. ^{1}H-N.m.r. data: δ 4.17–3.77 (m, 5 H, backbone H), 3.07 (m, 1 H, epoxide CH), 2.75 (d, 2 H, *J* 4 Hz, epoxide CH_2). 1.38 and 1.35 (2 s, each 6 H, CMe_2).

Anal. Calc. for $C_{12}H_{20}O_5$: C, 59.0; H, 8.25. Found: C, 58.9; H, 8.2.

In another experiment, crude oily **8** (3.425 g, see above) was treated in a like manner and the product was distilled *in vacuo* to give **1** (1.535 g, 79%), $[\alpha]_D^{20}$ −15°.

1,2-Anhydro-3,4:5,6-di-O-isopropylidene-D-mannitol (**2**). — Methanolic sodium methoxide from sodium (0.176 g, 7.67 mmol) and methanol (13 mL) was

added to a stirred solution of **10** (2.453 g, 5.9 mmol) in chloroform (13 mL). After 4 h, t.l.c. indicated a single product. The mixture was treated with dichloromethane (50 mL) and water (50 mL), and worked-up as described above to give **2** (1.43 g, 99%), b.p. 70°/0.3 mbar, $[\alpha]_D^{20}$ +9.1°, n^{21} 1.4504; lit.[4] b.p. 100–110°/0.05 mbar, $[\alpha]_D^{20}$ +12.4°, n^{20} 1.4468. ^{1}H-N.m.r. data: δ 4.22–3.71 (m, 5 H, backbone H), 3.2 (q, 1 H, *J* 4 Hz, epoxide CH), 2.81 (d, 2 H, *J* 4 Hz, epoxide CH_2), 1.40 (s, 6 H, CMe_2), 1.33 (s, 6 H, CMe_2).

Anal. Calc. for $C_{12}H_{20}O_5$: C, 59.0; H, 8.25. Found: C, 59.0; H, 8.3.

Treatment of crude **10** (3.02 g) in an identical manner, followed by chromatography (light petroleum–ethyl acetate, 3:1) of the product (1.75 g) on silica gel, gave **2** (1.34 g, 75.5%), $[\alpha]_D^{20}$ +8.8°.

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