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Note

Ditosylation of 3,4-di-*O*-*p*-tolylsulfonyl-D-mannitol. Isolation of 1,3,4,6-tetra-*O*-*p*-tolylsulfonyl-D-mannitol and of 1,5-anhydro-3,4,6-tri-*O*-*p*-tolylsulfonyl-D-mannitol*

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From the reaction of 3,4-di-*O*-*p*-tolylsulfonyl-D-mannitol with two equivalents of *p*-toluenesulfonyl chloride in anhydrous pyridine at 0° both 1,3,4,6-tetra-*O*-*p*-tolylsulfonyl-D-mannitol (**1**, 21%) and 1,5-anhydro-3,4,6-tri-*O*-*p*-tolylsulfonyl-D-mannitol (**2**, 21%) were isolated. Compound **2** was produced by an internal nucleophilic substitution and its formation in this reaction is in agreement with the isolation of 1,4- and 1,5-anhydro-ring derivatives from similar reactions[1,2].

The structures of compound **1** and **2**, as well as those of their acetyl derivatives (**3** and **4**) were determined by ^{1}H-n.m.r. spectroscopy and they agree well with analytical data.

The proton-n.m.r. spectra of compounds **1** and **3** showed the characteristic pattern exhibited by open chain D-mannitol derivatives having symmetrical substitution along the chain[3]. In fact, besides the signals for methyl and aromatic protons of the substituent groups, compounds **1** and **3** showed three groups of proton signals, namely, those arising from H-1,6,1′,6′, H-2,5, and H-3,4; the values of the chemical shifts and of the coupling constants for these proton signals are those expected for an open-chain structure.

In contrast, the ^{1}H-n.m.r. spectra of compounds **2** and **4** are in good agreement with a 1,5-anhydro-D-mannitol structure. The n.m.r. spectrum of **2** showed two proton signals at low field, that must be assigned to H-4 and H-3, on the basis of their coupling constant they bear a *trans*-diaxial relationship. Furthermore the large value of the coupling constant of another two downfield proton signals is characteristic[1,4] of a geminal pair of protons in axial and equatorial dispositions at C-1. The ^{1}H-n.m.r. spectrum of the acetylated derivative **4** is even more clear, and all signals (except H-5) are amenable to the first-order approach, the spectrum shows a new proton signal at low field, which must be assigned to a proton (H-2) bonded

*The Sulfonyl Derivatives of Alditols, Part III. For Part II, see ref. 1.

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to the carbon atom that bears the acetoxyl group The pattern of this n m r spectrum resembles that of 2,6-di-*O*-acetyl-1 5-anhydro-3,4-di-*O*-*p*-tolylsulfonyl-D-mannitol both in chemical shifts and coupling constants[1], with minor variations arising from replacement of an acetyl group by a tosyl group at O-6

EXPERIMENTAL

General methods — Melting points were measured with an Electrothermal melting-point apparatus, and are uncorrected Optical rotations were measured with a Hilger and Watts polarimeter Evaporations were performed *in vacuo*, the bath temperature being kept below 45° Column chromatography was performed on silica gel Merck 60 The homogeneity of compounds was verified by ascending t.l c on glass plates coated with 250-μm layers of silica gel HF_{254} (Merck) with solvents (v/v) *A*, 1 1 petroleum ether–ethyl acetate, and *B*, 5 4 petroleum ether–ethyl acetate Proton-n m r spectra were recorded and integrated with a XL-100 Varian spectrometer Tetramethylsilane was used as the internal reference. and the concentration of the sample was 6–8% Coupling constants were measured on 250- and 500-Hz sweep-width spectra. except those of compound **2**, which were taken from a 1000 Hz sweep-width spectrum Chemical shifts are given on the δ scale, relative to internal Me_4Si

1,5-Anhydro-3,4,6-tri-O-p-*tolylsulfonyl*-D-*mannitol* (**2**) — To a stirred, ice–water-cooled solution of 3,4-di-*O*-*p*-tolylsulfonyl-D-mannitol[5] (4 9 g, 10 mmol) in anhydrous pyridine (10 mL) was added a solution of *p*-toluenesulfonyl chloride (4 0 g, 21 mmol) in anhydrous pyridine (12 mL), dropwise, during 1 h The mixture was stirred for 30 h more at room temperature Most of the pyridine was then evaporated off and the residual syrup poured into water (200 mL), and the mixture was extracted with chloroform (100 mL) The chloroform layer was extracted successively with cold 0 25M sulfuric acid, 5% aqueous sodium hydrogencarbonate, and finally with water Chloroform was evaporated off and the residual syrup (5 4 g) was chromatographed on a column of silica gel (380 g) with solvent *A*, and 20-mL fractions were collected

Evaporation of fractions 55–70 yielded a syrup that crystallized from ethanol, giving 0 13 g (2 1%) of compound **2**, m p 179–180° A sample recrystallized from the same solvent had m p 180–181°, $[\alpha]_D^{24}$ +39.5° (*c* 1 44, chloroform), ^{1}H-n m r (pyridine-d_5) δ 2 20 (s 6 H, -CH_3 of tosyl), 2 25 (s, 3 H, CH_3 of tosyl), 3 66 (broad s, 1 H, $J_{1a\,1e}$ 12 Hz, H-1a), 4 05 (dd, 1 H, $J_{1e\,2}$ 3 0 Hz, H-1e), 4 06 (m, 1 H, H-5), 4 4 (dd, 1 H, $J_{5\,6}$ 7, $J_{6\,6}$ 11 Hz, H-6'). 4 50 (broad s, 1 H, H-2), 4 7 (H-6, partly overlapped with HDO signal), 5 1 (dd, 1 H, $J_{3,4}$ 9, $J_{2\,3}$ 3 Hz, H-3), 5 5 (t, 1 H, $J_{4\,5}$ 9 Hz, H-4), 7 18 (m, aromatic), and 7 93 (m, aromatic)

Anal. Calc for $C_{27}H_{30}O_{11}S_3$ C. 51 74. H, 4 82. S, 15 35 Found C, 51 72, H. 4 70. S, 15 15

2-O-*Acetyl-1,5-anhydro-3,4,6-tri*-O-p-*tolylsulfonyl*-D-*mannitol* (**4**) — Compound **2** was acetylated with acetic anhydride and pyridine, affording **4** as a solid

that crystallized from 95% ethanol, m p 97–99° A sample recrystallized from the same solvent had m p 99–100°, $[\alpha]_D^{22}$ −22 4° (c 1 85, chloroform), ^{1}H-n m r (chloroform-*d*) δ 2 0 (s, 3 H, OAc), 2 45 (s, 9 H, CH_3 of tosyl), 3 39 (broad d, 1 H, $J_{1a,1e}$ 13 2 Hz, H-1a), 3 58 (m, 1 H, H-5), 3 90 (dd, 1 H, $J_{1e,2}$ 2 7 Hz, H-1e), 4 01 (dd 1 H, $J_{6,6}$ 11 0, $J_{5,6}$ 6 7 Hz, H-6′), 4 41 (dd, 1 H, $J_{5,6}$ 2 2 Hz, H-6), 4 56 (dd, 1 H, $J_{3,4}$ 9 0, $J_{2,3}$ 3 2 Hz, H-3), 4 78 (t, 1 H, $J_{4,5}$ 8 7 Hz, H-4), 5 04 (broad s, 1 H H-2) 7 30 (m, 6 H, aromatic), and 7 70 (m. 6 H aromatic)

Anal Calc for $C_{29}H_{32}O_{12}S_3$ C, 52 08 H, 4 82, S, 14 38 Found C, 51 90, H, 4 84, S 14 07

1,3,4,6-Tetra-O-p-*tolylsulfonyl*-D-*mannitol* (**1**) — Fractions 40–50 were collected and evaporated, giving 2 60 g of a syrup that showed two spots running very close in t l c This syrup could not be purified by preparative t l c neither could it be crystallized

A portion of this syrup (2 0 g) was chromatographed on a column of silica gel (350 g) with solvent *A* Evaporation of fractions 40–55 yielded a syrup (1 5 g) that still showed a small second spot in t l c A portion of this syrup (0 50 g) was chromatographed again on silica gel (70 g) with solvent *B*. 15-mL fractions were collected Fractions 16–18 yielded 430 mg (21%) of **1** as a chromatographically pure syrup, $[\alpha]_D^{24}$ +50 5° (c 2 06, chloroform) ^{1}H-n m r (chloroform-*d*) δ 2 25 (2 H, OH removed by interchange with D_2O), 2 46 (s 12 H, CH_3 of tosyl), 3 6–4 3 (m, 4 H, H-1 1′,6 6′), 4 20 (m, 2 H, spacing 9 0 Hz, H-2,5), 4 95 (m, 2 H, $J_{2,3} = J_{4,5} = 9$ 0 Hz, H-3,4), 7 30 (m 8 H, aromatic), and 7 74 (m, 8 H, aromatic)

Anal Calc for $C_{34}H_{38}O_{14}S_4$ C 51 11, H, 4 79, S, 16 05 Found C, 50 68 H 4 96, S, 15 47

2,5-Di-O-*acetyl-1,3,4 6-tetra*-O-p-*tolylsulfonyl*-D-*mannitol* (**3**) — Compound **1** (100 mg) was acetylated with acetic anhydride and pyridine, affording **3** as a solid that crystallized from 75% ethanol, m p 116–117° (108 mg) A sample recrystallized from the same solvent had m p 116–117° $[\alpha]_D^{22}$ +14 1° (c 1 81, chloroform), ^{1}H-n m r (chloroform-*d*) δ 1 97 (s, 6 H, CH_3 of acetyl) 2 43 (s, 12 H, CH_3 of tosyl) 3 82 (AB type q, 2 H, $J_{1,2} = J_{6,5} = 4$ 0, $J_{1',1} = J_{6,6} = 12$ 0 Hz, H-1′,6′), 4 33 (AB type q, 2 H, $J_{1,2} = J_{5,6} = 2$ 5 Hz, H-1,6) 4 94 (m, 2 H, H-2 5), 5 16 (d, 2 H, $J_{4,5} = J_{2,3} = 6$ 5 Hz, H-3 4), 7 26 (m, 8 H, aromatic), and 7 70 (m, 8 H, aromatic)

Anal Calc for $C_{38}H_{42}O_{16}S_4$ C, 51 68 H 4 80, S, 14 52 Found C 51 81, H, 4 86, S, 15 03

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