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Note

1,3:4,6-Di-*O*-benzylidene-D-mannitol

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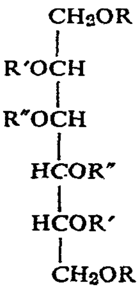
During an investigation of products resulting from the acid-catalyzed condensation of bromoacetaldehyde diethyl acetal and D-mannitol[1], 2,5-di-*O*-methyl-D-mannitol (**1**) (or its peracetate **2**) was needed for structural confirmation. The procedures for preparing this dimethylhexitol required either the preparation of three intermediates[2] (five steps in all) or the graded hydrolysis of 1,3:2,5:4,6-tri-*O*-ethylidene-D-mannitol[3], entailing a laborious separation of tri-, di-, mono-*O*-acetals, and free D-mannitol, methylation, and hydrolysis. As either procedure was lengthy and difficult, a simpler method was sought.

Acid-catalyzed condensation of aldehydes with D-mannitol usually yields a 1,3:2,5:4,6-tri-*O*-alkylidene-D-mannitol[3-5]. From the experimental conditions reported in the literature it appeared that product insolubility favored tricyclic acetal formation. Since the last ring to be formed is a seven-membered ring, reaction in a homogeneous medium might favor formation of the dicyclic acetal with six-membered rings. This was shown when D-mannitol was treated with benzaldehyde in acidified methyl sulfoxide to give a di-*O*-benzylidene-D-mannitol **3**. Proof that this product was a di-*O*-acetal was obtained by treatment with excess methanesulfonyl chloride in pyridine to give a di-*O*-methanesulfonate **4**, and by methylation with barium oxide–methyl iodide in *N*,*N*-dimethylformamide (Kuhn's procedure) to give a di-*O*-methyl ether **5**. Evidence for a 1,3:4,6-di-*O*-acetal structure was established by acid hydrolysis of compound **5** to give **1**, which was not isolated but directly converted into its tetra-*O*-acetyl ester **2**.



$$\begin{array}{r} CH_2OR \\ | \\ R'OCH \\ | \\ R''OCH \\ | \\ HCOR'' \\ | \\ HCOR' \\ | \\ CH_2OR \end{array}$$

1 $R = R'' = H,\ R' = Me$

2 $R = R'' = Ac,\ R' = Me$

3 $R+R'' = PhCH,\ R' = H$

4 $R+R'' = PhCH,\ R' = MeSO_2$

5 $R+R'' = PhCH,\ R' = Me$

EXPERIMENTAL

T.l.c. was performed on Silica Gel G* with air-equilibrated plates of 0.25-mm thickness and the solvent systems as specified. The spots were detected by spraying with 5% ethanolic sulfuric acid and heating until charred. U.v. spectra were measured with a Cary Model 14 spectrophotometer. I.r. spectra were determined with a Perkin–Elmer Model 621 spectrophotometer. N.m.r. spectra were obtained with a Varian Model HA-100 spectrometer. Chemical shifts were compared against internal tetramethylsilane. Melting points were determined on a Mel-Temp or a Mettler FP-1 apparatus. Analytical samples were dried in a 1–10 mm vacuum in presence of sodium hydroxide and sulfuric acid for 24–36 h.

*1,3:4,6-Di-O-benzylidene-*D*-mannitol* (3). — After D-mannitol (20 g) was dissolved in a mixture of benzaldehyde (40 ml) and methyl sulfoxide (200 ml), conc. sulfuric acid (10 ml) was added dropwise (requiring *ca.* 20 min) during which time the mixture warmed. After being kept 24 h at room temperature, the mixture was poured onto an ice–water slush (3 l). An oil separated which slowly turned solid as the ice melted. This solid was separated by filtration and washed with hexane (200 ml); it was then covered with water (4–6 l) and heated to boiling. Sodium carbonate was added to maintain the pH at 7–8 (paper). A small amount of solid remained insoluble at the boiling point and was removed by filtration; it melted at 214–216° and is probably a tri-*O*-benzylidene-D-mannitol[6]. On cooling, the filtrate slowly deposited crystals, which were separated by filtration to yield 4.96 g (12%) of 3, m.p. 146–149°; $[\alpha]_D^{23}$ $-7°$ (*c* 1.063, acetone); λ_{max}^{KBr} 730 cm^{-1} (phenyl); λ_{max} in 95% ethanol, 256 nm (ε 435); R_F 0.21 (1:1 carbon tetrachloride–ethyl acetate); n.m.r.: δ 5.56 (benzyl CH), ratio of aromatic to benzyl to aliphatic protons 9.9:1.9:10.0 (theory 10:2:10).

Anal. Calc. for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19. Found: C, 67.32; H, 6.17.

*1,3:4,6-Di-O-benzylidene-2,5-di-O-methylsulfonyl-*D*-mannitol* (4). — Methanesulfonyl chloride (0.3 ml) was added to a cooled pyridine solution (2 ml) containing 3 (275 mg). After being kept for 64 h at 0–5°, the reaction mixture was worked up in the usual manner. The resulting solid was recrystallized from acetone–water to give **4**, 330 mg (83%), m.p. 187–189° (decomp.); $[\alpha]_D^{22}$ $-30°$ (*c* 0.416, acetone); λ_{max}^{KBr} 1370, 1340, 1185, 1175 (SO_3), and 700 cm^{-1} (phenyl); λ_{max} in 95% ethanol, 256 nm (ε 440); R_F 0.57 (1:1 carbon tetrachloride–ethyl acetate); n.m.r.: δ 5.50 (benzyl CH), 2.96 (CH_3), ratio of aromatic to benzyl to aliphatic to methyl protons 5.2:1.0:4.2:3.0 (theory 5:1:4:3).

Anal. Calc. for $C_{22}H_{26}O_{10}S_2$: C, 51.35; H, 5.09; S, 12.46. Found: C, 51.48; H, 5.16; S, 12.38.

*1,3:4,6-Di-O-benzylidene-2,5-di-O-methyl-*D*-mannitol* (5). — A mixture of *N,N*-dimethylformamide (20 ml), methyl iodide (5 ml), barium oxide (5 g), and 3 (790 mg) was stirred vigorously for 3 days at room temperature, diluted with chloroform (25 ml), and filtered. The solid remaining on the funnel was washed with chloro-

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* The mention of firm names or trade products does not imply that they are endorsed or recommended by the Department of Agriculture over other firms or similar produts not mentioned.

form, and the washings were combined with the filtrate. After being washed with water, the organic layer was dried and concentrated to give impure **5** (802 mg), m.p. 140–146°. Recrystallization from 95% ethanol (20 ml) gave matted needles of pure **5** (710 mg, 83%), m.p. 144–145.5°; $[\alpha]_D^{23}$ −22° (*c* 0.842, acetone); ν_{max}^{KBr} 2830 (OMe), and 730 cm^{-1} (phenyl); λ_{max}, in 95% ethanol, 256 nm (ε 420); R_F 0.75 (2:1 carbon tetrachloride–ethyl acetate); n.m.r.: δ 5.61 (benzyl CH), 3.46 (OMe), ratio of aromatic to benzyl to aliphatic to methoxyl protons 10.0:2.0:8.6:5.7 (theory 10:2:8:6).

Anal. Calc. for $C_{22}H_{26}O_6$: C, 68.37; H, 6.78. Found: C, 68.72; H, 6.95.

*1,3,4,6-Tetra-O-acetyl-2,5-di-O-methyl-*D*-mannitol* (**2**). — A suspension of **5** (533 mg) in 70% acetic acid (50 ml) was warmed until dissolution. The solution was kept for 16 h at room temperature, and concentrated in vacuum to a syrup. This syrup, acetic anhydride (10 ml), and anhydrous sodium acetate (1 g) were heated for 2 h at 100°, cooled to room temperature, and added to vigorously stirred ice (150 ml). After the ice melted, the solution was extracted with three 20-ml portions of chloroform. The extracts were washed with 100-ml portions of water, 10% sodium hydrogen carbonate, and water, dried, and concentrated to a thick oil. A solution of this oil in hot ethanol (10 ml) deposited crystalline **2** on cooling, 272 mg (52%), m.p. 107–108.8°; $[\alpha]_D^{24}$ +42° (*c* 0.224, methanol); ν_{max}^{KBr} 2840 (OMe), 1745, and 1735 cm^{-1} (ester); R_F 0.48 (1:1 carbon tetrachloride–ethyl acetate); n.m.r.: δ 3.38 (OMe), 2.09, and 2.06 (OAc). (Lit.[3]: m.p. 107–108°, $[\alpha]_D^{23}$ +39.5°).

Anal. Calc. for $C_{16}H_{26}O_{10}$: C, 50.79; H, 6.92. Found: C, 51.00, H, 6.84.

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