Note

1,2-Anhydro-6-*O*-methanesulphonyl-D-mannitol

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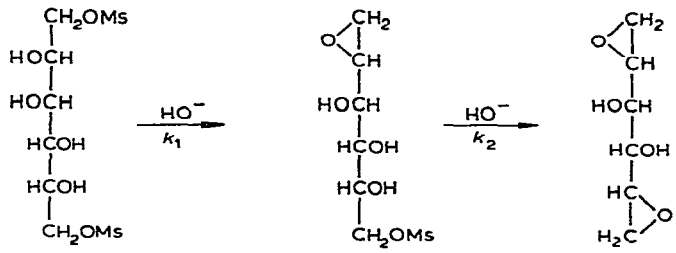
The action of hydroxide ion on 1,6-di-*O*-methanesulphonyl-D-mannitol (**1**) involves two consecutive, irreversible, first-order reactions **1** → **2** → **3**.



1 **2** **3**

1,2:5,6-Dianhydro-D-mannitol (**3**) was recently prepared[1] by the treatment of **1** with 90% of the theoretical amount of alkali at pH ~8. For the intermediate 1,2-anhydro-6-*O*-methanesulphonyl-D-mannitol (**2**) to be isolated, the ratio of k_2/k_1 must be less than unity. Using the method of Swain[2], the average values of k_1 and k_2 deduced from the hydrolysis curve of **1** (determined at pH 7.5) are 3.07 and 2.20 h^{-1}, respectively. The concentration of the intermediate **2** reaches a maximum, the position of which depends on the relative value of the rate constants. Calculation[3] shows that the maximal concentration of **2** is 43% and that this is attained when 35% of the theoretical amount of alkali has been added. It proved possible to obtain 41% of **2** by careful control of pH. It is important to use anhydrous magnesium sulphate as dehydrating agent during the isolation, because the more basic sodium carbonate caused formation of the diepoxide **3**.

The epoxide **2** contained 91% of the theoretical amount of oxirane oxygen (determined by iodide assay), which strongly implies the presence of a terminal epoxide and not a less-strained, five- or six-membered ring. This figure compares favourably with that[1] (93.5%) for **3**. Non-terminal epoxides show a much lower figure in the assay, *e. g.*, 74% for 2,3:4,5-dianhydro-L-iditol[4].

Compound **2** was an effective antitumour agent. It underwent considerable decomposition when stored as the solid and was best kept under ethyl acetate until

required. Aqueous solutions of **2** were also unstable. The biological properties of this compound will be reported in detail elsewhere.

EXPERIMENTAL

A stirred suspension of **1**[5] (1.33 g; 4 mmoles) in water (5 ml) at 35–40° was titrated with M sodium hydroxide (2.80 ml, 35% of theoretical) at a rate which maintained neutrality to phenolphthalein. The solution was then added dropwise to a stirred suspension of anhydrous magnesium sulphate (20 g) in ethyl acetate (100 ml). The filtered solution was evaporated under reduced pressure at 30° to ~15 ml, whereupon unreacted **1** crystallised. After 1 h at room temperature, the solution was filtered, dried ($MgSO_4$), and left at 0° overnight. The initial crop of crystals was unreacted **1**, after which the epoxide **2** separated; t.l.c. (cellulose, butyl alcohol–water, 86:14; detection with sodium iodide–acetone–phenolphthalein) **3** R_F 0.5, **2** R_F 0.3 (pink spots).

Recrystallisation from ethyl acetate gave **2** (400 mg, 41%) as white prisms, m.p. 80–81° (corr.), $[\alpha]_D^{32}$ +67.5° (*c* 1, water) (Found: C, 34.8, H, 5.9; S, 13.2. $C_7H_{14}O_7S$ calc.: C, 34.7; H, 5.8; S, 13.2%).

The n.m.r. data (D_2O, with *tert*-butyl alcohol as internal reference) were consistent with the structure assigned and contained the following signals: δ 1.7–1.8 multiplet, H-1,1′), 2.02 (singlet, OSO_2Me), 2.05 (multiplet, H-2), 2.27 (singlet, 3 *OH*), ~2.55 (multiplet, H-3,4,5)

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