

264. Anhydrides of Polyhydric Alcohols. Part VII.

1 : 4-3 : 6-Dianhydro-d- and -l-iditol.

By L. F. WIGGINS.

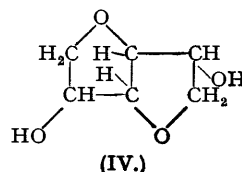
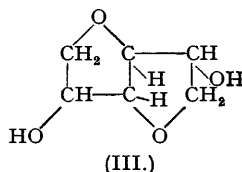
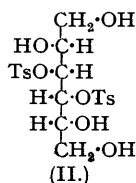
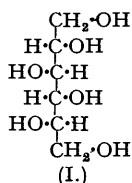
l-Iditol readily undergoes anhydride formation on being heated in the presence of hydrochloric acid, giving 1 : 4-3 : 6-dianhydro-*l*-iditol the structure of which is proved by a constitutional synthesis of its enantiomorph.

THE action of acidic reagents on both mannitol and sorbitol gives rise to the dianhydrides of these polyhydric alcohols by internal loss of two molecules of water. Dianhydromannitol, first obtained by Fauconier (*Compt. rend.*, 1882, **95**, 991), was shown to possess the constitution of 1 : 4-3 : 6-dianhydromannitol by Wiggins in Part I of this series (*J.*, 1945, 4) and by Hockett, Fletcher, Sheffield, Goepf, and Soltzberg (*J. Amer. Chem. Soc.*, 1946, **68**, 930). Dianhydrosorbitol, prepared in a similar way to its mannitol analogue, was shown by synthetical methods (Wiggins and Montgomery, *Nature*, 1946, **157**, 372; *J.*, 1946, 390) also to have the 1 : 4-3 : 6-ring structure. Hockett, Fletcher, Sheffield, and Goepf (*J. Amer. Chem. Soc.*, 1946, **68**, 927) have arrived at the same conclusions by different methods.

l-Iditol (I) also undergoes a similar dehydration on being heated in the presence of acids and gives a dianhydride, in the form of a *hemihydrate* which, like the corresponding compounds of mannitol and sorbitol, is stable to treatment with sodium methoxide at 120° under pressure. The *bismethanesulphonyl* and the *dibenzoyl* derivative were readily obtained from it.

By analogy with the dianhydrides of mannitol and sorbitol it would be expected that this compound would also have the hydrofuranol type of ring structure shown in (III). After the completion of this work, Fletcher and Goepf (*J. Amer. Chem. Soc.*, 1945, **67**, 1042; 1946, **68**, 939) reported that 1 : 4-3 : 6-dianhydrosorbitol and dianhydromannitol on dehydrogenation with Raney nickel followed by hydrogenation are both partly converted into dianhydroiditol, and on the assumption that the rings are stable under these conditions, have declared the establishment of the 1 : 4-3 : 6-ring structure for all three hexitol dianhydrides. The present paper is concerned with a proof of constitution of the dianhydroiditol along quite different lines. A preliminary note of this appeared in *Nature* (1946, **157**, 372).

If mannitol could be tosylated at C₃ and C₄ to give 3 : 4-ditosyl mannitol (II), this compound on removal of the tosyl groups with sodium methoxide could form only two dianhydrides, (a) 1 : 3-4 : 6-dianhydrohexitol, and (b) 1 : 4-3 : 6-dianhydrohexitol. Moreover, since it is established in the sugar series that, when hydrolytic removal of tosyl groups is accompanied by anhydro-ring formation, Walden inversion always accompanies the hydrolysis (see Peat, *Ann. Reports*, 1939, **36**, 258), it follows that both (a) and (b) would have the configuration of *β*-iditol.



A suitable derivative substituted at C₃ and C₄ with tosyl residues is 3 : 4-ditosyl 1 : 2-5 : 6-diacetone mannitol (Brigl and Gruner, *Ber.*, 1934, **67**, 1969). This compound, on partial hydrolysis

followed by acetylation, gave liquid 3 : 4-ditosyl 1 : 2 : 5 : 6-tetra-acetyl mannitol which on treatment with sodium methoxide gave a crystalline dianhydrohexitol which gave crystalline bis-methanesulphonyl and dibenzoyl derivatives. These had the same melting points as and specific rotation equal, but opposite in sign, to the corresponding derivatives obtained from the product of the anhydrodisidation of *l*-iditol. Therefore the two sets of compounds are enantiomorphous, and dianhydro-*d*-iditol and bismethanesulphonyl and dibenzoyl dianhydro-*d*-iditol must have been obtained from mannitol.

The precise constitution of dianhydroiditol is limited to the possibilities (a) and (b) above. Since (a) involves four-membered rings which are extremely unlikely of formation when five-membered rings are possible, and since in (a) the two free hydroxyl groups would approach near enough to be joined in acetal formation by a benzylidene residue, and because dianhydroiditol does not form such a derivative, structure (b) must be regarded as the correct one. Dianhydro-*d*-iditol is formulated by (III), a representation differing from that of 1 : 4-3 : 6-dianhydro-*d*-mannitol (IV) only in the orientation of the two rings.

EXPERIMENTAL.

1-Iditol.—This was prepared from *l*-sorbose by catalytic hydrogenation and separated from the accompanying *l*-sorbitol by fractional crystallisation of the acetyl derivatives (Jones and Wiggins, *J.*, 1944, 363).

Action of Hydrochloric Acid on 1-Iditol.—Crystalline *l*-iditol (5 g.) was boiled under reflux for 50 hours with fuming hydrochloric acid (50 c.c.). The dark brown solution was evaporated to a syrup which was distilled at 150—155° (bath temp.)/0.05 mm. The distillate (3.1 g.) crystallised completely on cooling. It recrystallised in prisms from ethyl acetate (2.3 g.), m. p. 43—45°, $[\alpha]_D^{17} + 18.4^\circ$ (*c.* 2.389 in water), and was 1 : 4-3 : 6-dianhydro-*l*-iditol hemihydrate (Found: C, 46.7, 46.1; H, 7.0, 7.3. $C_6H_{10}O_4 \cdot \frac{1}{2}H_2O$ requires C, 46.5; H, 7.1%).

Treatment of Dianhydro-*l*-iditol with Sodium Methoxide.—The dianhydroiditol (1.7 g.) was heated in a sealed tube with 5% methyl-alcoholic sodium methoxide at 120° for 24 hours. Thereafter, the solution was diluted with water, neutralised with sulphuric acid, and evaporated to dryness, and the residue was extracted with ethyl acetate. The extract was evaporated and the syrupy product distilled at 160°/0.02 mm. The distillate, which completely crystallised, was unchanged 1 : 4-3 : 6-dianhydro-*l*-iditol (1.55 g.); it recrystallised from ethyl acetate as the hemihydrate, m. p. 43—45° alone or in admixture with the starting material.

Attempted Condensation of Dianhydro-*l*-iditol with Benzaldehyde.—The dianhydride (0.55 g.) was shaken with freshly distilled benzaldehyde (10 c.c.) and zinc chloride (0.5 g.) for 48 hours. The resulting suspension was poured into water-ligroin which completely dissolved it. Sodium carbonate (0.5 g.), dissolved in water, was added and the mixture distilled under reduced pressure, with addition of water until all the benzaldehyde was removed. After being evaporated to dryness the residue was extracted with ethyl acetate, and the extract evaporated. From ethyl acetate there crystallised unchanged dianhydro-*l*-iditol hemihydrate (0.4 g.), m. p. 43—45° alone or in admixture with the starting material.

2 : 5-Bismethanesulphonyl 1 : 4-3 : 6-Dianhydro-*l*-iditol.—The dianhydride (0.2 g.), dissolved in dry pyridine (5 c.c.), was treated with methanesulphonyl chloride (0.4 g.) at room temperature. The mixture was kept for 24 hours and then poured into ice-water. The crystalline precipitate was collected; the compound recrystallised from alcohol in long needles, m. p. 155—156°, $[\alpha]_D^{17} + 41.9^\circ$ (*c.* 1.145 in acetone) (Found: C, 32.2; H, 4.9. $C_8H_{14}O_8S_2$ requires C, 31.8; H, 4.6%).

2 : 5-Dibenzoyl Dianhydro-*l*-iditol.—The dianhydride (0.1 g.) was dissolved in 5*N*-sodium hydroxide (3 c.c.), and benzoyl chloride (0.3 g. added). After vigorous shaking for $\frac{1}{2}$ hour, the solid which had separated was collected and washed with water; the compound recrystallised from alcohol in plates (0.13 g.), m. p. 110—111°, $[\alpha]_D^{15} + 139.1^\circ$ (*c.* 1.04 in chloroform) (Found: C, 67.7; H, 4.9. $C_{20}H_{18}O_6$ requires C, 67.8; H, 5.1%).

3 : 4-Ditosyl Tetra-acetyl Mannitol.—3 : 4-Ditosyl 1 : 2-5 : 6-diacetone mannitol (10 g.) (prepared by the method of Brigl and Gruner, *loc. cit.*) was hydrolysed by heating it for 3 hours at 70° with 70% acetic acid (100 c.c.). The acetic acid was removed under reduced pressure. The resulting syrup was acetylated by boiling with acetic anhydride (26 c.c.) and sodium acetate (10 g.). The mixture was poured into water and the product neutralised with sodium bicarbonate and extracted with chloroform. The extract was dried ($MgSO_4$) and evaporated. The compound was a syrup (7.5 g.) which could not be induced to crystallise; $[\alpha]_D^{15} - 0.8^\circ$ (*c.* 10.23 in chloroform) (Found: S, 9.6. $C_{28}H_{34}O_{14}S_2$ requires S, 9.7%).

Treatment of 3 : 4-Ditosyl Tetra-acetyl Mannitol with Sodium Methoxide.—The syrup (7.5 g.) was dissolved in chloroform (100 c.c.), and sodium methoxide (4 g.), dissolved in dry methyl alcohol (40 c.c.), added at 0°. The mixture was allowed to warm up to room temperature and to remain thereat for 4 hours. The mixture was extracted with water and separated from the chloroform layer. The aqueous extract was neutralised with *N*-sulphuric acid and the solution evaporated to dryness. The residue was extracted with ethyl acetate, and on evaporation of this solvent a syrup (0.9 g.) was obtained. This distilled at 160° (bath temp.)/0.08 mm. and showed $n_D^{20} 1.4925$, $[\alpha]_D^{18} - 16.7^\circ$ (*c.* 5.27 in water) (Found: C, 48.8; H, 6.8. $C_6H_{10}O_4$ requires C, 49.3; H, 6.8%). The product crystallised but it was not possible to recrystallise it.

2 : 5-Dibenzoyl 1 : 4-3 : 6-Dianhydro-*d*-iditol.—The above distillate (0.8 g.) was dissolved in 5*N*-sodium hydroxide; benzoyl chloride (2 c.c.) was added, and the mixture shaken vigorously for $\frac{1}{2}$ hour. The dibenzoyl derivative was collected, washed with water, and recrystallised from alcohol. Yield, 0.94 g.; m. p. 110—111°; $[\alpha]_D^{15} - 138.6^\circ$ (*c.* 3.475 in chloroform) (Found: C, 68.0; H, 5.2. $C_{20}H_{18}O_6$ requires C, 67.8; H, 5.1%).

2 : 5-Bismethanesulphonyl 1 : 4-3 : 6-Dianhydro-d-*iditol*.—Dianhydro-*d*-*iditol* (0.3 g.) was dissolved in dry pyridine (6 c.c.) and methanesulphonyl chloride (0.8 g.) added at 0°. The mixture was kept at room temperature for 74 hours and was then poured into ice-water, and the solid which had separated was collected and washed with water; the *compound* recrystallised from alcohol in the form of needles. Yield, 0.25 g.; m. p. 156°; $[\alpha]_D^{25} - 41.2^\circ$ (*c.* 1.41 in acetone) (Found: C, 32.1; H, 4.3. $C_8H_{14}O_8S_2$ requires C, 31.8; H, 4.6%).

Fletcher and Goepf (*loc. cit.*) give, for anhydrous dianhydro-*l*-*iditol*, m. p. 63.7—64.5°, $[\alpha]_D + 20.8^\circ$ (in water), and for the dibenzoate, m. p. 111—111.3°, $[\alpha]_D + 141.9^\circ$ (in chloroform).

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THE A. E. HILLS LABORATORIES,
THE UNIVERSITY, EDGBASTON, BIRMINGHAM, 15.

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