

4. The Acetone Derivatives of Hexahydric Alcohols. Part I. Triacetone Mannitol and its Conversion into d-Arabinose.

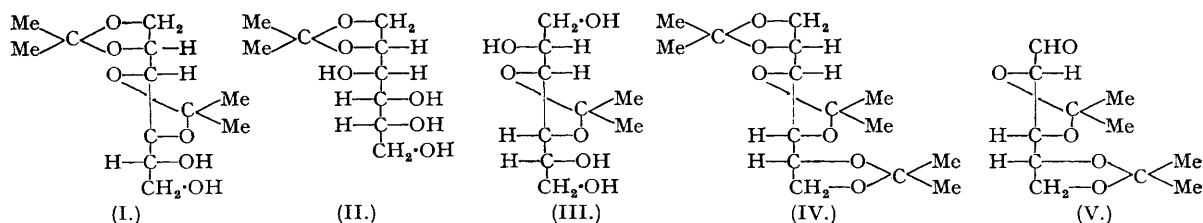
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Evidence is presented for the structure of fully acetonised mannitol as 1 : 2-3 : 4-5 : 6-triacetone mannitol. Its graded hydrolysis yields 3 : 4-monoacetone mannitol and also 1 : 2-3 : 4-diacetone mannitol which is converted through oxidation with lead tetra-acetate into diacetone aldehydo-*d*-arabinose and thence into *d*-arabinose.

TRIACETONE mannitol was first prepared by Fischer (*Ber.*, 1895, **28**, 1167) but it was not until 1914 that a constitution was suggested. Irvine and Patterson (*J.*, 1914, **105**, 898) carried out a graded hydrolysis of triacetone mannitol, and isolated a diacetone and a monoacetone mannitol, the former being designated as the α -form since it was different from the β -diacetone mannitol which Fischer (*loc. cit.*) isolated as a by-product in the acetonisation of mannitol and which was later shown to be 1 : 2-5 : 6-diacetone mannitol (Baer and H. O. L. Fischer, *Helv. Chim. Acta*, 1934, **17**, 622; *J. Biol. Chem.*, 1939, **128**, 463).

Although Irvine and Patterson's structure for triacetone mannitol is now shown to be correct, it was based on no very firm ground. Later workers have sought to correct parts of this earlier work, but the whole position needs clarification and this is attempted in the following argument.

Irvine and Patterson (*loc. cit.*) considered α -diacetone mannitol to be represented by (I) and monoacetone mannitol by (II).



The structure (I) was based on the oxidation of the dimethyl mannitol, obtained by methylation and subsequent hydrolysis of diacetone mannitol, to dimethyl mannonolactone which appeared to be a γ -lactone, although the attachment of the methyl groups at C₅ and C₆ was not rigorously proved. Formula (II) was based on the oxidation of the partly methylated mannitol, obtained by methylation followed by hydrolysis of monoacetone mannitol, to a so-called tetramethyl mannonic acid which would not lactonise. The structure (II) for monoacetone mannitol has now been shown to be incorrect and the experimental results of Irvine and Patterson to have been wrongly interpreted.

That monoacetone mannitol could not be written as (II) was first pointed out by Müller (*Ber.*, 1932, **65**,

1055) who showed that this monoacetone mannitol could be obtained by debenzoylation of 1 : 6-dibenzoyl monoacetone mannitol and that it gave a ditrityl derivative. Therefore, the acetone residue in this monoacetone mannitol could not possibly engage a primary hydroxyl group, and it was suggested that the acetone group was attached to C₃ and C₄. This was proved correct by Brigl and Grüner (*Ber.*, 1933, **66**, 931) who oxidised the tetrabenzoyl mannitol, which Fischer (*Ber.*, 1915, **48**, 266) had prepared from the monoacetone mannitol of Irvine and Patterson, with lead tetra-acetate and obtained dibenzoyl *d*-glyceraldehyde. Further confirmation came from the work of H. O. L. Fischer and Appel (*Helv. Chim. Acta*, 1934, **17**, 1574) who oxidised monoacetone mannitol to acetone dihydroxysuccinic dialdehyde which they subsequently converted into *l*-tartaric acid. From all this evidence there can be no doubt that the monoacetone derivative of mannitol obtained by Irvine and Patterson has the acetone group attached to the hydroxyl groups of C₃ and C₄, (III).

α -Diacetone mannitol has not been studied as extensively and its structure, as 1 : 2-3 : 4-diacetone mannitol, suggested by Irvine and Patterson, rests on no very firm basis. Experiments have now been carried out which prove its constitution more rigidly. The α -diacetone mannitol has been prepared in a yield of 34%, and has been oxidised to diacetone aldehydo-*d*-arabinose. Gatzl and Reichstein (*Helv. Chim. Acta*, 1938, **21**, 914) obtained a similar compound from diacetone arabinose diethyl mercaptal and recorded its having $[\alpha]_D - 34^\circ$ whereas the compound now described had $[\alpha]_D - 14.4^\circ$.

Hydrolysis of the diacetone aldehydo arabinose from diacetone mannitol proceeded smoothly, and *d*-arabinose, identical with an authentic specimen, was obtained. These experiments prove beyond doubt that in α -diacetone mannitol the acetone residues are attached to C₁, C₂, C₃, and C₄, but since, in monoacetone mannitol, the acetone residue is certainly attached to C₃ and C₄ and since the monoacetone compound can be obtained by the further hydrolysis of the diacetone mannitol, it follows that in the latter substance the precise attachment of the acetone residues is to C₁ : C₂ and C₃ : C₄. (Obviously, owing to the symmetrical nature of the mannitol molecule, the acetone residues could equally well be said to be attached to C₅ : C₄ and to C₆ : C₅.) Also, since 1 : 2-3 : 4-diacetone mannitol is produced by partial hydrolysis of triacetone mannitol, the latter compound must be 1 : 2-3 : 4-5 : 6-triacetone mannitol (IV). It follows also that the precise structure of diacetone aldehydo-*d*-arabinose is 2 : 3-4 : 5-diacetone aldehydo-*d*-arabinose (V).

To conform to the normal mode of writing the mannitol molecule, the formulations given in this discussion involve what may seem to be *trans* ketal linkage. Rotation can occur about any of the bonds in the mannitol chain so that *cis* ketal formation is always possible, a fact not realised apparently by Irvine and Patterson (*loc. cit.*) at the time their work was published.

The degradative experiments on diacetone mannitol here described constitute a synthesis of *d*-arabinose from mannitol. An improved method of obtaining 3 : 4-monoacetone mannitol is also described.

EXPERIMENTAL.

1 : 2-3 : 4-Diacetone Mannitol.—Triacetone mannitol (60 g.) (m. p. 69—70°) [prepared in 75% yield by shaking mannitol (80 g.) in acetone (1 l.) with concentrated sulphuric acid (8 c.c.) overnight followed by the usual method of isolation] was dissolved in 70% alcohol (1200 c.c.) containing concentrated hydrochloric acid (4 c.c.) and the solution warmed at 40—45° for 60 minutes. The acid was neutralised with barium carbonate, the filtered solution evaporated to dryness, and the residue extracted with acetone. The acetone extract, on evaporation, gave a residue which was dissolved in a little alcohol and poured into water, when unchanged triacetone mannitol (26.3 g.) was precipitated. Evaporation of the filtrate and extraction of the residue with benzene gave, after cooling the solution, crystals of 3 : 4-monoacetone mannitol (4.5 g.) (m. p. 86—87°). The mother liquors were evaporated and the resulting syrup, after distillation at 135—145° (bath temp.)/0.03 mm., had n_D^{20} 1.4630. It was 1 : 2-3 : 4-diacetone mannitol (10.1 g., 34.5% of the theoretical based on the weight of triacetone mannitol hydrolysed). The distillate crystallised on cooling and was recrystallised from ether-ligroin. It had m. p. 37° (yield 8.9 g.); Irvine and Patterson (*loc. cit.*) give the same m. p.

3 : 4-Monoacetone Mannitol.—Triacetone mannitol (10 g.) was dissolved in 70% acetic acid (200 c.c.) and the solution heated at 40° for 1½ hours. During this period the rotation of the solution changed as follows: $[\alpha]_D + 13.6^\circ$ (initial value); $+ 17.2^\circ$ (½ hour); $+ 18.4^\circ$ (1 hr.); $+ 18.4^\circ$ (1½ hrs.). The solution was evaporated as rapidly as possible at 40—50° under diminished pressure. The residue was extracted with acetone, leaving mannitol (0.7 g.) undissolved. Evaporation of the acetone solution gave a syrup which completely crystallised and which, on being recrystallised from benzene, gave 3 : 4-monoacetone mannitol (6 g.), m. p. 86—87° (80%). Irvine and Patterson (*loc. cit.*) record m. p. 85° for monoacetone mannitol but do not record a yield. Fischer and Appel (*loc. cit.*) record a yield of 45% of the theoretical by hydrolysis with ethanolic hydrogen chloride.

Oxidation of 1 : 2-3 : 4-Diacetone Mannitol with Lead Tetra-acetate.—Diacetone mannitol (3 g.) was dissolved in benzene (40 c.c.) and lead tetra-acetate (6.5 g.), suspended in glacial acetic acid (20 c.c.), added and the mixture allowed to stand at 0° for 24 hours. The mixture was poured into water and extracted with more benzene; the benzene extract was washed with sodium bicarbonate and with water, dried over anhydrous magnesium sulphate and evaporated to a syrup (1.1 g.) which was distilled at 80° (bath temp.)/0.03 mm. The product (0.8 g.) had $[\alpha]_D^{19} - 13.5^\circ$ (c, 1.187), $[\alpha]_D^{17} - 14.4^\circ$ (c, 7.2) in chloroform, n_D^{20} 1.4421. The liquid restored the colour to Schiff's reagent and was diacetone aldehydo arabinose (Found: C, 57.3; H, 7.5. Calc. for C₁₁H₁₈O₅: C, 57.2; H, 7.8%). Gatzl and Reichstein describe diacetone aldehydo-*d*-arabinose as boiling at 84°/0.03 mm. and having $[\alpha]_D - 34^\circ$ in chloroform.

Hydrolysis of Diacetone Aldehydo-*d*-arabinose.—Diacetone aldehydo arabinose (0.54 g.) was heated at 100° for 2 hours with *n*-sulphuric acid (10 c.c.). After neutralisation with barium carbonate, filtration and evaporation, a solid was obtained which on recrystallisation from absolute methanol gave crystals of *d*-arabinose (0.28 g.), m. p. 159°, not depressed by admixture with an authentic specimen. It had $[\alpha]_D^{17} - 140.6^\circ$ (initially) changing to $- 102^\circ$ (after 24 hours) in water (c, 1.338). *d*-Arabinose is described as having m. p. 159—160° and $[\alpha]_D - 105^\circ$ (equilibrium value).