

75. *The Anhydrides of Polyhydric Alcohols. Part II. Derivatives of  
1 : 2-5 : 6-Dianhydro Mannitol.*

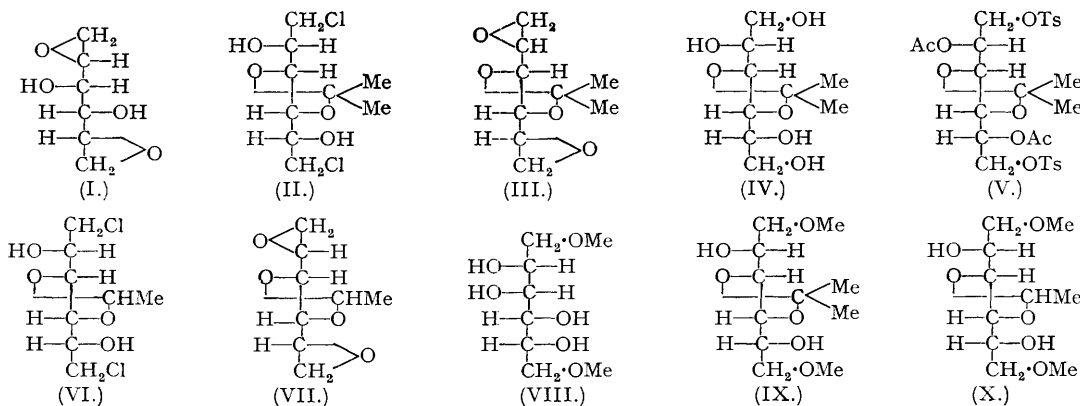
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By the action of cold sodium methoxide on 1 : 6-dichloro 3 : 4-monoacetone mannitol and 1 : 6-dichloro 3 : 4-ethylidene mannitol the *monoacetone* and the *monoethylidene* derivative of 1 : 2-5 : 6-dianhydro mannitol have been obtained. These compounds were extremely reactive and suffered ring fission under mild alkaline or acid conditions.

The constitutions of these compounds have been proved and some products of ring fission have been described.

It is well known that ethylene oxidic ring compounds, as exemplified by ethylene oxide itself, glycidol, or ethylene oxide anhydro bodies of the sugar series, are extremely reactive. Thus in the last class the ethylene oxidic ring can react additively with alkaline reagents such as sodium methoxide, ammonia, or hydrazine (see for example Peat and Wiggins, *J.*, 1938, 1810; Robertson and Whitehead, *J.*, 1940, 319) and with acidic reagents such as halogen acids (cf. Müller, *Ber.*, 1934, 67, 421; Peat and Wiggins, *loc. cit.*; Robertson and Dunlop, *J.*, 1938, 472).

It was envisaged that if difunctional substances of this type could be prepared then they would probably undergo ring scission with other difunctional compounds such as diamines or dibasic acids to give polymeric materials of some value. Such a compound would be 1 : 2-5 : 6-dianhydro mannitol (I) which possesses at each extremity of the molecule an ethylene oxide anhydro ring which would be available for reaction with suitable difunctional compounds. Although it has not yet been found possible to prepare 1 : 2-5 : 6-dianhydro mannitol itself yet two derivatives of this substance, namely 3 : 4-monoacetone and 3 : 4-monoethylidene 1 : 2-5 : 6-dianhydro mannitol, have been obtained and it is with the preparation and proof of the constitution of these compounds that this paper is chiefly concerned.



1 : 6-Dichloro mannitol (Siwoloboff, *Annalen*, 1886, 233, 368; Haworth, Heath, and Wiggins, *J.*, 1944, 155) gives on acetonisation three products consisting of (i) 1 : 6-dichloro monoacetone mannitol obtained in 70% yield, (ii) 1 : 6-dichloro diacetone mannitol (m. p. 100—102°), and (iii) liquid isomeric 1 : 6-dichloro diacetone mannitol. The compounds (ii) and (iii) are new and probably differ in respect of the orientation of their acetone groups, which are probably attached in one case to adjacent carbon atoms and in the other to alternate carbon atoms. The monoacetone derivative (i) was first prepared by Micheel (*Annalen*, 1932, 496, 77) who assigned to it, without proof, the structure 1 : 6-dichloro 3 : 4-monoacetone mannitol (II). In the course of the following argument this contention is proved. On treatment of (II) with sodium methoxide a liquid was obtained, the analytical figures for which showed it to possess two anhydro rings and to be a dianhydro monoacetone mannitol. The anhydro rings in this compound were extremely labile and it underwent ring scission on boiling for a few hours with aqueous sodium hydroxide. In this way a product was obtained which after benzoylation in pyridine solution gave the 1 : 2 : 5 : 6-tetrabenzoyl 3 : 4-monoacetone mannitol of Brigl and Grüner (*Ber.*, 1933, 66, 933). Therefore the acetone group in Micheel's 1 : 6-dichloro monoacetone mannitol and in the dianhydro compound derived from it must certainly be attached to C<sub>3</sub> and C<sub>4</sub>, and the former compound is correctly represented by (II). It is clear therefore that in the dianhydro compound C<sub>1</sub>, C<sub>2</sub>, C<sub>5</sub>, and C<sub>6</sub> must be involved in anhydro ring formation. This being so, since the dianhydro compound is produced by hydrolysis of the halogen atoms attached to C<sub>1</sub> and C<sub>6</sub> each anhydro ring must also involve either C<sub>1</sub> or C<sub>6</sub> and therefore two possible structures for the anhydride are apparent: (a) 1 : 2-5 : 6-dianhydro 3 : 4-monoacetone mannitol, and (b) 1 : 5-2 : 6-dianhydro 3 : 4-monoacetone mannitol. The first structure involves rings of the ethylene oxide type which are characterised by their greater activity, and the second involves rings of the pyran type which are considerably more stable. The actual properties of the dianhydro body strongly suggest (a) as the correct structure. Moreover atomic models show that (a) can exist but that it is impossible to build up structure (b). Therefore the correct structure of the dianhydro compound must be that of 1 : 2-5 : 6-dianhydro 3 : 4-monoacetone mannitol represented by (III).

A second route to the synthesis of 1 : 2-5 : 6-dianhydro 3 : 4-monoacetone mannitol has been worked out and involves the following steps. Mannitol is readily converted into triacetone mannitol by the original method of Fischer (*Ber.*, 1895, 28, 1167) and, on partial hydrolysis with 70% acetic acid, 3 : 4-monoacetone mannitol (IV) is obtained in 80% yield (see Wiggins, this vol., p. 13). Tosylation followed by acetylation gave 1 : 6-ditosyl 2 : 5-diacetyl 3 : 4-monoacetone mannitol (V) which on treatment with four equivalents of sodium methoxide in the cold gave 1 : 2-5 : 6-dianhydro 3 : 4-monoacetone mannitol identical in respect of refractive index, b. p., and optical inactivity with the substance obtained from 1 : 6-dichloro 3 : 4-monoacetone mannitol.

A second derivative of 1 : 2-5 : 6-dianhydro mannitol, namely the 3 : 4-monoethylidene derivative, has been prepared as follows. 1 : 6-Dichloro mannitol on treatment with paraldehyde and a few drops of concentrated

sulphuric acid gave a mixture of three ethylidene derivatives of dichloro mannitol; (a) 1 : 6-dichloro diethylidene mannitol (m. p. 160°); (b) isomeric 1 : 6-dichloro diethylidene mannitol (m. p. 195°); and (c) 1 : 6-dichloro monoethylidene mannitol.

The compound (c) on treatment with two equivalents of sodium methoxide in the cold gave dianhydro monoethylidene mannitol in practically quantitative yield. This dianhydro compound also readily suffers ring fission on boiling with aqueous sodium hydroxide, to yield a crystalline monoethylidene hexitol, which must have retained the configuration of mannitol, since this was isolated on acid hydrolysis. Moreover this monoethylidene mannitol on treatment with lead tetra-acetate according to the procedure of Hockett and McClenahan (*J. Amer. Chem. Soc.*, 1939, **61**, 1667) rapidly consumed two equivalents of oxygen, thus revealing the presence of two glycol groups. The only allocation of the acetaldehyde residue which would account for this fact, and the fact that this substance has been derived from 1 : 6-dichloro mannitol, is to C<sub>3</sub> and C<sub>4</sub>; the compound is therefore 3 : 4-monoethylidene mannitol. It follows that (c) is 1 : 6-dichloro 3 : 4-monoethylidene mannitol (VI). Furthermore the dianhydro body derived from this compound must have the constitution 1 : 2-5 : 6-dianhydro 3 : 4-monoethylidene mannitol (VII) for precisely the same reasons that this type of structure was allocated to the corresponding acetone derivative.

In agreement with the expected properties of ethylene oxide anhydro rings both the monoacetone and monoethylidene derivatives of 1 : 2-5 : 6-dianhydro mannitol readily suffered ring fission with either alkaline or acid reagents. Thus 1 : 2-5 : 6-dianhydro 3 : 4-monoacetone mannitol on treatment with methyl alcoholic sodium methoxide under reflux gave a liquid dimethyl 3 : 4-monoacetone hexitol (A) which by analogy with the results of ring fission with sodium hydroxide must have retained the configuration of mannitol. Moreover, acid hydrolysis gave a crystalline dimethyl mannitol which, on methylenation with paraformaldehyde and concentrated sulphuric acid, gave 1 : 6-dimethyl 2 : 4-3 : 5-dimethylene mannitol identical with the product of methylation of 2 : 4-3 : 5-dimethylene mannitol (Haworth and Wiggins, *J.*, 1944, 58) and which therefore must be 1 : 6-dimethyl mannitol (VIII). The substance (A) is then 1 : 6-dimethyl 3 : 4-monoacetone mannitol (IX).

Similarly 1 : 2-5 : 6-dianhydro 3 : 4-monoethylidene mannitol gave crystalline 1 : 6-dimethyl 3 : 4-monoethylidene mannitol (X) which on acid hydrolysis gives the same 1 : 6-dimethyl mannitol (VIII) as above described. 1 : 2-5 : 6-Dianhydro 3 : 4-monoacetone mannitol on treatment with methyl alcoholic ammonia under pressure gave a liquid diamino monoacetone mannitol which by analogy with the result of the action of sodium methoxide on this anhydride must be 1 : 6-diamino 3 : 4-monoacetone mannitol. Similarly the anhydro rings were opened by means of methylamine, but in this case a resinous material was the only product obtained. On being heated with a diamine, for example, 1 : 6-diamino dimethylene mannitol, the dianhydride reacted extremely vigorously, and rapidly gave an insoluble resin. 1 : 2-5 : 6-Dianhydro 3 : 4-monoacetone mannitol also underwent ring fission with acid reagents, so easily in fact that the anhydro rings opened in preference to the hydrolysis of the acetone residue. Thus after treatment of 1 : 2-5 : 6-dianhydro 3 : 4-monoacetone mannitol with hydrochloric acid in the cold both 1 : 6-dichloro mannitol and 1 : 6-dichloro 3 : 4-monoacetone mannitol (II) were isolated. Similarly, hydriodic acid gave a di-iodo hexitol, proved to be 1 : 6-di-iodo mannitol since on methylenation it gave the 1 : 6-di-iodo 2 : 4-3 : 5-dimethylene mannitol of Micheel (*loc. cit.*). With organic dibasic acids the dianhydride rapidly gave resinous products. Thus on its being heated for about a minute at 150—160° with phthalic acid the mixture rapidly resinified and a hard insoluble light brown resin was obtained. However, the resinous products here described had the disadvantage of thermal instability so that they usually darkened appreciably during the heat treatment.

#### EXPERIMENTAL.

*Acetonisation of 1 : 6-Dichloro Mannitol.*—1 : 6-Dichloro mannitol (100 g.) was suspended in acetone (2.5 l.) containing 0.5% sulphuric acid and the mixture shaken for 24 hours. The acid was then neutralised with anhydrous sodium carbonate and the solution filtered and evaporated, whereupon the residue rapidly crystallised. After recrystallisation from benzene-petrol the product (82 g.) had m. p. 76° identical with that described by Micheel (*loc. cit.*). When no more crystals could be obtained the mother liquors were evaporated and the residual syrup distilled at 130—140° (bath temp.)/0.03 mm. The distillate (21.2 g.) partly crystallised and the crystals were drained on a porous tile. After recrystallisation from chloroform these had m. p. 100—102°,  $[\alpha]_D^{17} + 16.1^\circ$  in chloroform (*c*, 2.237), and were 1 : 6-dichloro diacetone mannitol (Found : C, 48.7; H, 6.5. C<sub>12</sub>H<sub>20</sub>O<sub>4</sub>Cl<sub>2</sub> requires C, 48.2; H, 6.7%). The liquid portion of the distillate was recovered by extraction of the porous tile with chloroform. Evaporation of the solvent gave a liquid (14.4 g.) which distilled at 130—140° (bath temp.)/0.03 mm. and showed  $n_D^{20} 1.4750$ ,  $[\alpha]_D^{17} - 5.4^\circ$  chloroform (*c*, 3.69). This was an isomeric 1 : 6-dichloro diacetone mannitol (Found : C, 48.3; H, 6.7. C<sub>12</sub>H<sub>20</sub>O<sub>4</sub>Cl<sub>2</sub> requires C, 48.2; H, 6.7%).

*1 : 2-5 : 6-Dianhydro 3 : 4-Monoacetone Mannitol.*—1 : 6-Dichloro 3 : 4-monoacetone mannitol (70 g.) was dissolved in chloroform (400 c.c.), and dry methyl alcohol (250 c.c.) containing sodium (14 g.) was added carefully at 0°. Thereafter the solution was allowed to warm up to room temperature and kept thereat for 4 hours. More chloroform was then added, the mixture washed with water, and the chloroform extract dried (MgSO<sub>4</sub>) and evaporated. The liquid product distilled at 80—90° (bath temp.)/0.04 mm. (47 g.; 95% of the theoretical),  $n_D^{16} 1.4560$ ,  $[\alpha]_D$  zero in chloroform (Found : C, 58.2; H, 7.6. C<sub>9</sub>H<sub>14</sub>O<sub>4</sub> requires C, 58.0; H, 7.5%).

*1 : 6-Ditosyl 2 : 5-Diacetyl 3 : 4-Monoacetone Mannitol.*—3 : 4-Monoacetone mannitol (21 g.) was dissolved in dry pyridine (400 c.c.) and tosyl chloride (38.5 g.; 2.05 mols.) carefully added at 0°. The mixture was left to warm to room temperature and kept thereat overnight. Acetic anhydride (80 c.c.) was then added and the mixture kept at room temperature for 48 hours. The solution was poured into water and the resulting mixture extracted with chloroform. The extract was washed successively with dilute sulphuric acid, sodium bicarbonate solution, and water, and was then dried (MgSO<sub>4</sub>) and evaporated to a syrup which partly crystallised on trituration with alcohol. After separation the solid material was recrystallised from chloroform-petrol; the compound then had m. p. 111—113°,  $[\alpha]_D^{17} + 25.2^\circ$  in chloroform (*c*, 2.778), yield 21 g. (Found : C, 52.5; H, 5.2. C<sub>27</sub>H<sub>34</sub>O<sub>12</sub>S<sub>2</sub> requires C, 52.8; H, 5.5%).

*The Action of Cold Sodium Methoxide on 1 : 6-Ditosyl 2 : 5-Diacetyl 3 : 4-Monoacetone Mannitol.*—The material (21 g.) was dissolved in chloroform (200 c.c.) and methyl alcohol, containing 3.6 g. of sodium dissolved in it, carefully added at 0°. The mixture was left to warm to room temperature and kept thereat for 3 hours with occasional shaking. During this period a precipitate of sodium *p*-toluenesulphonate had separated. The mixture was then diluted with chloroform and washed with water, and the chloroform layer was dried (MgSO<sub>4</sub>). After evaporation of solvent a mobile liquid remained which distilled at 75° (bath temp.)/0.02 mm. (5.2 g.; 80% of the theoretical),  $n_D^{18}$  1.4552,  $[\alpha]_D$  zero (in chloroform), and was 1 : 2-5 : 6-dianhydro 3 : 4-monoacetone mannitol (Found : C, 58.1; H, 7.3. Calc. for C<sub>9</sub>H<sub>14</sub>O<sub>4</sub> : C, 58.0; H, 7.5%).

*Action of Sodium Hydroxide on 1 : 2-5 : 6-Dianhydro 3 : 4-Monoacetone Mannitol.*—The material (1.1 g.) was boiled for 12 hours with an aqueous solution of sodium hydroxide (20 c.c. containing 1.5 g.). The alkali was then neutralised with dilute sulphuric acid and the solution evaporated to dryness in the presence of barium carbonate. The residue was extracted with acetone and after evaporation of the extract a thick syrup (1.5 g.) was left which, however, was contaminated with inorganic impurities which prevented crystallisation. A portion (0.4 g.) was benzoylated by treatment at room temperature with benzoyl chloride (1.5 c.c.) in dry pyridine (10 c.c.). After being kept for 24 hours the solution, from which some pyridine hydrochloride had separated, was poured into water and the oily precipitate triturated with water and finally with alcohol when crystallisation occurred. The product was separated and recrystallised from alcohol and had m. p. 121—122° and  $[\alpha]_D$  -1.95° in chloroform (*c*, 7.041). It was 1 : 2 : 5 : 6-tetrabenzoyl 3 : 4-monoacetone mannitol. M. p. in admixture with a specimen prepared from 3 : 4-monoacetone mannitol showed no depression.

*Treatment of 1 : 6-Dichloro Mannitol with Paraldehyde.*—1 : 6-Dichloro mannitol (40 g.) suspended in paraldehyde (350 c.c.) containing concentrated sulphuric acid (1 c.c.) was shaken overnight, after which the solution was diluted with chloroform, washed first with sodium bicarbonate solution and then with water, and dried (MgSO<sub>4</sub>). After evaporating the solution a syrup was obtained which partly crystallised. Crystals (8 g.) were separated and a residual syrup (A) (34 g.) remained. The crystalline material had m. p. 140—150° and was fractionally crystallised with some difficulty; two fractions were separated: (i) recrystallised from alcohol in large thin leaves (3.5 g.), m. p. 159—160°,  $[\alpha]_D$  +89.1° in chloroform (*c*, 3.21), and was 1 : 6-dichloro diethylidene mannitol (Found : C, 44.6; H, 6.0; Cl, 25.3. C<sub>10</sub>H<sub>16</sub>O<sub>4</sub>Cl<sub>2</sub> requires C, 44.2; H, 6.0; Cl, 26.2%); (ii) recrystallised from dilute alcohol, yield 0.3 g., m. p. 195°,  $[\alpha]_D$  -10.8° in chloroform (*c*, 1.48), and was an isomeric 1 : 6-dichloro diethylidene mannitol (Found : C, 44.7; H, 5.6; Cl, 26.0%).

The residual syrup (A) was distilled and collected in two fractions: fraction (1) at 130°/0.03 mm. (7 g.), and fraction 2 at 130—135°/0.03 mm. (26.2 g.). Fraction (1) partly crystallised but only a small amount (0.5 g.) of substance B having a sharp m. p. was obtained. Fraction (2) also partly crystallised and after recrystallisation from ethyl acetate-petrol many times a pure compound (C) (10.5 g.) was obtained, m. p. 92—94°,  $[\alpha]_D^{20}$  +28.7° in chloroform (*c*, 2.23). It was 1 : 6-dichloro 3 : 4-monoethylidene mannitol (Found : C, 39.5; H, 5.7; Cl, 28.4. C<sub>8</sub>H<sub>14</sub>O<sub>4</sub>Cl<sub>2</sub> requires C, 39.5; H, 5.7; Cl, 29.2%). (The mother liquors from the recrystallisation yielded a partly crystalline material from which only small amounts of substances (B) and (C) could be separated.)

1 : 2-5 : 6-Dianhydro 3 : 4-Monoethylidene Mannitol.—1 : 6-Dichloro 3 : 4-monoethylidene mannitol (6 g.) was dissolved in chloroform (75 c.c.), and dry methyl alcohol (35 c.c.) containing 1.35 g. of sodium was added at 0°. The mixture was kept for 4 hours at room temperature with occasional shaking. A precipitate of sodium chloride separated. The mixture was then diluted with water and extracted with chloroform, and the chloroform extract dried (MgSO<sub>4</sub>) and evaporated. The liquid product distilled at 85—90° (bath temp.)/0.04 mm. (3.7 g.; 91% of the theoretical),  $n_D^{15}$  1.4600,  $[\alpha]_D^{17}$  +15.1° in chloroform (*c*, 3.45) (Found : C, 55.8; H, 7.1. C<sub>8</sub>H<sub>12</sub>O<sub>4</sub> requires C, 55.8; H, 7.1%).

*The Action of Sodium Methoxide on 1 : 2-5 : 6-Dianhydro 3 : 4-Monoethylidene Mannitol.*—The material (0.93 g.) was dissolved in methyl alcohol (20 c.c.) containing sodium (1 g.) dissolved in it and the mixture boiled under reflux for 12 hours. Thereafter the solution was extracted with chloroform, and the extract washed with water, dried (MgSO<sub>4</sub>), and evaporated. The syrupy product distilled at 150° (bath temp.)/0.005 mm. as a thick colourless oil (0.6 g.),  $n_D^{18}$  1.4643. On standing at 0° the distillate completely crystallised and, recrystallised from ether-light petroleum, formed needles, m. p. 59—60°,  $[\alpha]_D^{17}$  +33.5° in chloroform (*c*, 2.083). It was 1 : 6-dimethyl 3 : 4-monoethylidene mannitol (Found : C, 51.2; H, 8.6. C<sub>10</sub>H<sub>20</sub>O<sub>6</sub> requires C, 50.8; H, 8.5).

*Hydrolysis of 1 : 6-Dimethyl 3 : 4-Monoethylidene Mannitol.*—1 : 6-Dimethyl monoethylidene mannitol (0.25 g.) was dissolved in *n*-sulphuric acid (15 c.c.) and heated at 100° for 6 hours. The solution was neutralised with barium carbonate, filtered, the barium residues washed with hot water, and the combined filtrates evaporated to dryness under diminished pressure. The residue was extracted with ethyl acetate and the extract evaporated. A crystalline residue remained which after recrystallisation from ethyl acetate (0.2 g.), had m. p. 128—129°, alone or in admixture with 1 : 6-dimethyl mannitol prepared from the corresponding monoacetone derivative (below).

*The Action of Sodium Hydroxide Solution on 1 : 2-5 : 6-Dianhydro 3 : 4-Monoethylidene Mannitol.*—The dianhydride (1.2 g.) was dissolved in water containing sodium hydroxide (1 g.) and the solution boiled over a gauze for 20 hours. It was nearly neutralised with sulphuric acid and evaporated to dryness under diminished pressure. The dried residue was extracted with acetone and the extract evaporated. A crystalline mass remained (0.6 g.); this was recrystallised twice from ethyl acetate-alcohol. 3 : 4-Monoethylidene mannitol thus obtained had m. p. 107—109° and  $[\alpha]_D^{18}$  +37.7° in water (*c*, 1.324) (Found : C, 46.5; H, 7.4. C<sub>8</sub>H<sub>16</sub>O<sub>6</sub> requires C, 46.2; H, 7.7%).

*Acid Hydrolysis of 3 : 4-Monoethylidene Mannitol.*—The material (0.2 g.) was dissolved in 10 c.c. of *n*-sulphuric acid and the mixture heated at 100° for 6 hours. The acid was then neutralised with barium carbonate, the solution filtered, the residue well washed with hot water, and the combined filtrate and washings evaporated to dryness. The residue was extracted with hot alcohol from which crystals (0.1 g.) of mannitol were deposited, m. p. alone or in admixture with an authentic sample 165—166°.

*The Action of Lead Tetra-acetate on 3 : 4-Monoethylidene Mannitol.*—The procedure used was that of Hockett and McClenahan (*loc. cit.*). The reaction of 0.0005 mols. of the material with standard lead tetra-acetate solution proceeded as follows: 0.25 (3 mins.); 0.51 (17 mins.); 0.97 (43 mins.); 1.31 (99 mins.); 1.69 (185 mins.); 1.97 (324 mins.); 2.03 (404 mins.) g.-atoms of oxygen per g.-mol. of monoethylidene mannitol.

*The Action of Sodium Methoxide on 1 : 2-5 : 6-Dianhydro 3 : 4-Monoacetone Mannitol.*—Dianhydro monoacetone mannitol (1 g.) was dissolved in dry methyl alcohol (20 c.c.) and 10% methyl alcoholic sodium methoxide (20 c.c.) added. The mixture was boiled under reflux for 6 hours, the solution extracted with chloroform, and the extract washed with water, dried (MgSO<sub>4</sub>), and evaporated to a syrup. The product distilled at 130—135° (bath temp.)/0.02 mm. as a fairly mobile liquid (0.9 g.) showing  $n_D^{16}$  1.4575 and  $[\alpha]_D^{15}$  +26.0° in chloroform (*c*, 1.308) and was 1 : 6-dimethyl 3 : 4-monoacetone mannitol (Found : C, 53.5; H, 9.0; OMe, 24.0. C<sub>11</sub>H<sub>26</sub>O<sub>6</sub> requires C, 52.8; H, 8.8; OMe, 24.8%).

1 : 6-Dimethyl Mannitol.—1 : 6-Dimethyl 3 : 4-monoacetone mannitol (0.9 g.) was heated with *n*-sulphuric acid (20 c.c.) on a boiling water-bath for 4 hours. The acid was then neutralised with barium carbonate, and the solution filtered and evaporated to dryness. The residue was extracted with hot ethyl acetate and the extract evaporated to small bulk; 1 : 6-dimethyl mannitol then crystallised in small prisms (0.67 g.). It was soluble in water and alcohol, slightly soluble in ethyl acetate, insoluble in chloroform and ether, and had m. p. 127—129°,  $[\alpha]_D^{17}$  +17.0° in chloroform (*c*, 1.644) (Found : C, 46.0; H, 8.7; OMe, 29.8. C<sub>8</sub>H<sub>16</sub>O<sub>6</sub> requires C, 45.7; H, 8.6; OMe, 29.5%).

**1 : 6-Dimethyl 2 : 4-3 : 5-Dimethylene Mannitol.**—1 : 6-Dimethyl mannitol (0.32 g.) was mixed with paraformaldehyde (1 g.) and the mixture stirred with concentrated sulphuric acid (0.5 c.c.) until it had cooled to room temperature when chloroform was added and the mixture shaken overnight. The chloroform extract was decanted, fresh chloroform added, and the mixture shaken for an hour and the extract again separated. The combined extracts were washed with dilute ammonia and with water, dried ( $\text{MgSO}_4$ ), and evaporated. The residue was recrystallised from ether-light petroleum in plates (0.21 g.), m. p. alone or in admixture with an authentic specimen prepared by the method of Haworth and Wiggins (*loc. cit.*), 64—65°.

**Ring Fission of 1 : 2-5 : 6-Dianhydro 3 : 4-Monoacetone Mannitol with Ammonia.**—The dianhydride of mannitol (0.8 g.) was dissolved in methyl alcohol, saturated with ammonia at 0° (70 c.c.), and the solution heated in a sealed tube at 120° for 20 hours. After evaporation of the solvent a thick syrup was left which was 1 : 6-diamino 3 : 4-monoacetone mannitol (Found : C, 49.3; H, 8.6.  $\text{C}_9\text{H}_{20}\text{O}_4\text{N}_2$  requires C, 49.1; H, 9.0%).

The product was a thick colourless liquid soluble in water or alcohol and slightly soluble in ethyl acetate. On attempting to distil the diamine only a very small proportion distilled at 180° (bath temp.)/0.04 mm. and as the heating was continued the residue became thicker and finally set to a glass.

**Treatment of 1 : 2-5 : 6-Dianhydro 3 : 4-Monoacetone Mannitol with 1 : 6-Diamino Dimethylene Mannitol.**—The diamine (0.5 g.) was dissolved in the dianhydride (0.5 g.) and the mixture heated on an oil-bath to 150—160° when a vigorous and exothermic reaction occurred, the reactants darkening appreciably and resinifying in a few seconds. The resin obtained was insoluble in all the usual solvents.

**The Action of Acids on 1 : 2-5 : 6-Dianhydro 3 : 4-Monoacetone Mannitol.**—(a) *Hydrochloric acid.* The dianhydride (1 g.) was dissolved in aqueous acetone (50 : 50) containing 1% hydrochloric acid and the mixture left at room temperature for 3 hours. During this period the rotation changed as follows :  $[\alpha]_D +10.0^\circ$  (5 mins.);  $+38.0^\circ$  (2 hrs.);  $+38.0^\circ$  (3 hrs.). The solution was thereafter neutralised with silver carbonate, filtered, and evaporated to dryness. The residue was partly crystalline and, after separation, the solid material recrystallised from water had m. p. 174° and was 1 : 6-dichloro mannitol. The m. p. was not depressed in admixture with an authentic specimen. The residual syrupy material (0.8 g.) distilled at 135—140° (bath temp.)/0.01 mm. and showed  $n_D^{20} 1.4809$ . Yield, 0.7 g. (Found : Cl, 22.3%). The distillate partly crystallised and, after drying on a porous tile, the solid material recrystallised from benzene had m. p. 86° and was 1 : 6-dichloro 3 : 4-monoacetone mannitol. Yield 0.2 g. There was no depression of m. p. when the product was mixed with authentic 1 : 6-dichloro 3 : 4-monoacetone mannitol.

(b) *Hydriodic acid.* The dianhydride (1 g.) was heated for 3 hours at 100° with 4% hydriodic acid (100 c.c.). The solution was evaporated to half the original volume when a crystalline material (0.32 g.) separated in flat plates. The product, recrystallised from water, formed yellow plates, m. p. 165—167° (decomp.). It was 1 : 6-di-iodo mannitol (Found : C, 18.7; H, 3.4.  $\text{C}_8\text{H}_{12}\text{O}_4\text{I}_2$  requires C, 17.9; H, 3.0%).

**Methylenation of 1 : 6-Di-iodo Mannitol.**—The di-iodo mannitol (0.3 g.) was suspended in 38% formalin (2 c.c.) and the mixture cooled to 0° and saturated with hydrogen chloride. The original material dissolved and 1 : 6-di-iodo dimethylene mannitol separated in crystals which were collected and recrystallised from alcohol. Yield, 0.2 g., m. p. 193° alone or in admixture with an authentic specimen prepared by the method of Micheel (*loc. cit.*) (Found : C, 22.6; H, 3.0. Calc. for  $\text{C}_8\text{H}_{12}\text{O}_4\text{I}_2$  : C, 22.5; H, 2.8%).

**Condensation of 1 : 2-5 : 6-Dianhydro 3 : 4-Monoacetone Mannitol with Dibasic Acids.**—*Phthalic acid.* The mannitol dianhydride (0.5 g.) was mixed with phthalic acid (0.45 g.) and the mixture heated carefully on an oil-bath at 180—200°. The phthalic acid dissolved, the solution rapidly becoming thicker and finally setting to a gel. If the heating is stopped before the gel stage is reached, fibres can be drawn from the cooling melt; they, however, are brittle. The cooled product set to a hard resinous mass, which was only very slightly soluble in organic solvents. The material began to melt at 160° and finally melted at 235°.

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