76. *The Anhydrides of Polyhydric Alcohols. Part III. Derivatives of 5 : 6-Anhydro Mannitol and Sorbitol.*

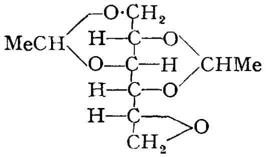
By L. F. Wiggins.

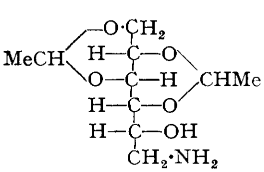
5 : 6-Anhydro 1 : 3-2 : 4-diethylidene sorbitol and 5 : 6-*anhydro* 1 : 2-3 : 4-*diacetone mannitol* have been prepared. These anhydro bodies readily suffer ring fission through the agency of ammonia giving rise to 6-*amino* 1 : 3-2 : 4-*diethylidene sorbitol* and 6-*amino* 1 : 2-3 : 4-*diacetone mannitol.*

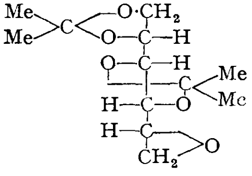
We have recently been interested in amino-derivatives of the polyhydric alcohols sorbitol and mannitol derived from sucrose, and a diamine, 1 : 6-diamino 2 : 4-3 : 5-dimethylene mannitol, has been described (Haworth, Heath, and Wiggins, *J.*, 1944, 155). Two new amino-compounds have now been obtained from intermediate ethylene oxide anhydro derivatives of mannitol and sorbitol, namely 5 : 6-anhydro 1 : 3-2 : 4-diethylidene sorbitol and 5 : 6-*anhydro* 1 : 2-3 : 4-*diacetone mannitol.*

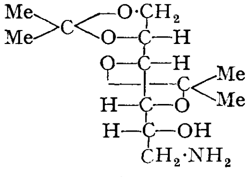
Selective tosylation followed by acetylation of 1 : 3-2 : 4-diethylidene sorbitol gave a compound which is designated as 6-*tosyl* 5-*acetyl* 1 : 3-2 : 4-*diethylidene sorbitol* for the following reasons. It is generally recognised that primary hydroxyl groups react faster than secondary hydroxyl groups with tosyl chloride. For example, tosylation of 1 : 2-monoacetone glucose gives 6-tosyl 1 : 2-monoacetone glucose (Ohle and Dickhauser, *Ber.*, 1925, **58**, 2593), and tosylation of 1 : 2-monoacetone xylose gives 5-tosyl 1 : 2-monoacetone xylose (Levene and Raymond, *J. Biol. Chem.*, 1933, **102**, 317). Moreover, 6-tosyl 5-acetyl 1 : 3-2 : 4-diethylidene sorbitol reacts readily with sodium iodide in acetone solution giving an 80% yield of sodium *p*-toluenesulphonate, although the iodo compound produced could not be obtained crystalline. However, the preference of the tosyl group for the hydroxyl group on C_6 was not complete since some 5 : 6-ditosyl 1 : 3-2 : 4-diethylidene sorbitol * was sometimes obtained as well Detosylation of 6-tosyl 5-acetyl diethylidene sorbitol with sodium methoxide led to the formation of 5 : 6-anhydro 1 : 3-2 : 4-diethylidene sorbitol,* an analogue of that most reactive compound of the sugar series, 5 : 6-anhydro 1 : 2-monoacetone glucofuranose (Ohle and v. Vargha, *Ber.*, 1929, **62**, 2440). The only other ethylene oxide anhydro compounds of the hexahydric alcohols are 5 : 6-anhydro 1-tosyl 2 : 4-benzylidene sorbitol (v. Vargha, *Ber.*, 1935, **68**, 1377) and the dianhydro compounds of mannitol described in Part II (preceding paper).

The orientation of the ethylidene residues in diethylidene sorbitol, by analogy with the corresponding dimethylene (Ness, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 665; Bourne and Wiggins, *J.*, 1944, 517) and dibenzylidene compounds (Hann and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 493) and from the results of the oxidation experiments of Gatzi and Reichstein (*Helv. Chim. Acta*, 1938, **21**, 186), are probably attached to C_1 : C_3 and C_2 : C_4, and 5 : 6-anhydro diethylidene sorbitol may be written as (I).


(I.)


(II.)


(III.)


(IV.)

Ring fission of the 5 : 6-anhydro diethylidene sorbitol with methyl alcoholic ammonia gave a well crystallised amine which can be described as *6-amino* 1 : 3-2 : *4-diethylidene sorbitol* (II), since an ethylene oxide anhydro ring which involves a primary carbon atom opens in such a way that the entering anion becomes attached to that carbon atom. For example, ring scission of 5 : 6-anhydro 1 : 2-monoacetone glucose with various reagents, including ammonia, invariably gives derivatives of monoacetone glucose substituted in the 6-position (Ohle and Mertens, *Ber.*, 1935, **68**, 2176; Ohle and Euler, *Ber.*, 1936, **69**, 1022; Ohle, Euler, and Malerczyk, *Ber.*, 1936, **69**, 1636).

A similar series of reactions has been carried out with a derivative of mannitol and a new amino derivative of this polyhydric alcohol isolated.

It is known that triacetone mannitol (Fischer, *Ber.*, 1895, **28**, 1167) can be partially hydrolysed to 1 : 2-3 : 4-diacetone mannitol (Irvine and Patterson, *J.*, 1914, 898; Wiggins, this vol., p. 13). This compound, on selective tosylation followed by acetylation, gives *6-tosyl 5-acetyl* 1 : 2-3 : *4-diacetone mannitol.* That the tosyl group is indeed attached to the 6-position of the mannitol molecule follows from the fact that the compound reacts with sodium iodide in acetone with formation of sodium *p*-toluenesulphonate in 90% yield.

On treatment of 6-tosyl 5-acetyl 1 : 2-3 : 4-diacetone mannitol with sodium methoxide at room temperature, liquid 5 : *6-anhydro* 1 : 2-3 : *4-diacetone mannitol* (III) was formed. As with the sorbitol anhydride described above, ring fission of this compound was readily effected by methyl alcoholic ammonia giving 6-amino 1 : 2-3 : 4-diacetone mannitol (IV), isolated as a *monohydrate.* The amino group is considered to be attached to the 6-position of the mannitol molecule, for the same reasons as were given for the structure of 6-amino diethylidene sorbitol; the terminal position of the amino-group in (IV) is more rigorously proved by the fact that hydrolytic removal of the acetone residues gave 1-amino mannitol, which, isolated as its oxalic acid salt, was identical with a specimen of 1-amino mannitol oxalate prepared from mannose oxime provided by Dr. R. L. Heath.

EXPERIMENTAL.

Tosylation of 1 : 3-2 : *4-Diethylidene Sorbitol.*—Diethylidene sorbitol (8·4 g.) prepared by the method of Appel (*J.*, 1935, 425) was dissolved in dry pyridine (50 c.c.) and the solution cooled to 0°; tosyl chloride (7·5 g.) was added over the period of 1 hour. The mixture was left to warm to room temperature slowly and to remain thereat for 24 hours. Acetic anhydride (12 c.c.) was then added and the mixture set aside for a further 24 hours. On being poured into ice-water a semi-solid mass was precipitated. This mixture was extracted into chloroform and the chloroform solution was washed successively with 5% sulphuric acid, dilute sodium bicarbonate solution, and water, and then dried ($MgSO_4$). The chloroform was removed under diminished pressure, leaving a crystalline mass (14·5 g.). This, recrystallised from ethyl alcohol, gave *6-tosyl 5-acetyl* 1 : 3-2 : *4-diethylidene sorbitol* (10·5 g.), m. p. 140°, $[\alpha]_D^{17^\circ} + 6{\cdot}0^\circ$ in chloroform (*c*, 1·664) (Found : C, 53·0; H, 6·2. $C_{19}H_{20}O_9S$ requires C, 53·0; H, 6·0%). The products of some preparations were found to melt at 128—131°. These products were contaminated with 5 : 6-ditosyl diethylidene sorbitol which could be isolated by fractional crystallisation or after removal of the monotosyl compound by its conversion into 5 : 6-anhydro diethylidene sorbitol (below), m. p. 173°, $[\alpha]_D - 12{\cdot}6^\circ$ in chloroform (*c*, 2·065) (Found : C, 53·7; H, 5·7. Calc. for $C_{24}H_{30}S_2O_{10}$: C, 53·1; H, 5·6%).

Treatment of 6-Tosyl 5-Acetyl 1 : 3-2 : *4-Diethylidene Sorbitol with Sodium Methoxide.*—6-Tosyl 5-acetyl diethylidene sorbitol (10 g.) was dissolved in chloroform (100 c.c.); methyl alcohol (20 c.c.), containing sodium (1 · 2 g.), was added and the mixture shaken for 15 minutes at room temperature. Water and chloroform were added, and the chloroform layer separated, washed with water, and dried ($MgSO_4$). After the chloroform had been removed a syrup remained which rapidly crystallised. Recrystallised from ethyl acetate–light petroleum, 5 : 6-anhydro 1 : 3-2 : 4-diethylidene sorbitol formed long rods, m. p. 136°, $[\alpha]_D^{17^\circ} - 7{\cdot}3^\circ$ in chloroform (*c*, 1·23). Yield, 2·5 g. (Found : C, 55·6; H, 7·4. Calc. for $C_{10}H_{16}O_5$: C, 55·6; H, 7·4%).

Treatment of 6-Tosyl 5-Acetyl 1 : 3-2 : *4-Diethylidene Sorbitol with Sodium Iodide in Acetone.*—The material (1 g.) was dissolved in dry acetone (30 c.c.) containing dry sodium iodide (1 g.) in solution. The solution was heated in a

---

* Since this work was completed, these compounds have been described by v. Vargha and Puskas (*Ber.*, 1943, **76**, 879) and W. L. Sullivan (*J. Amer. Chem. Soc.*, 1945, **67**, 387).

sealed tube at 100—110° for 5 hours, when crystals of sodium *p*-toluenesulphonate separated and after cooling these were filtered off. Yield, 0·36 g. (80% of the theoretical).

The filtrate was evaporated to dryness and extracted with chloroform, and the extract was washed with sodium thiosulphate solution and with water, dried ($MgSO_4$), and evaporated to a syrup. This contained iodine but could not be induced to crystallise.

6-*Amino* 1 : 3-2 : 4-*Diethylidene Sorbitol.*—5 : 6-Anhydro diethylidene sorbitol (2·7 g.) was heated at 115° for 24 hours under pressure with methyl alcoholic ammonia (80 c.c.; saturated at 0°). The solution was thereafter evaporated under diminished pressure, and the residue recrystallised from ethyl acetate. It was 6-*amino* 1 : 3-2 : 4-*diethylidene sorbitol*, m. p. 156—157°, $[\alpha]_D^{17°}$ + 4·3° in chloroform (*c*, 1·38). Yield, 2·1 g. (Found : C, 51·5; H, 8·0; N, 6·6. $C_{10}H_{19}O_5N$ requires C, 51·5; H, 8·1; N, 6·0%).

6-*Tosyl* 5-*Acetyl Diacetone Mannitol.*—1 : 2-3 : 4-Diacetone mannitol (10 g.) (this vol., p. 13) was dissolved in dry pyridine (100 c.c.) and tosyl chloride (10 g.) added at 0°, and the mixture allowed to stand for 48 hours at room temperature. Acetic anhydride (20 c.c.) was then added, and the solution was left for 72 hours, poured into water, left for several hours more, and then extracted with chloroform. The extract was washed successively with 5% sulphuric acid, sodium bicarbonate solution, and water, and was then dried ($MgSO_4$). Evaporation of the solvent gave a crystalline residue which was recrystallised from methyl alcohol and was 6-*tosyl* 5-*acetyl* 1 : 2-3 : 4-*diacetone mannitol*, m. p. 106°, $[\alpha]_D^{20°}$ + 15·4° in chloroform (*c*, 2·08). Yield, 5·2 g. (Found : C, 55·8; H, 6·6. $C_{21}H_{30}O_9S$ requires C, 55·0; H, 6·5%).

Treatment of 6-*Tosyl* 5-*Acetyl* 1 : 2-3 : 4-*Diacetone Mannitol with Sodium Iodide in Acetone.*—The material (1 g.) together with dry sodium iodide (1 g.) was heated in dry acetone (30 c.c.) in a sealed tube at 105—110° for 2½ hours. Crystals of sodium *p*-toluenesulphonate separated and, after cooling, were collected and washed with a little dry acetone. Yield, 0·41 g. (90% of the theoretical). The filtrate was evaporated to dryness and taken up in a chloroform–water mixture. The chloroform layer was separated, washed first with dilute sodium thiosulphate solution and finally with water, and dried ($MgSO_4$). Evaporation of the chloroform left a syrup which contained iodine but which would not crystallise.

5 : 6-*Anhydro* 1 : 2-3 : 4-*Diacetone Mannitol.*—6-Tosyl 5-acetyl diacetone mannitol (5·2 g.) was dissolved in chloroform, and methyl alcohol containing sodium (0·6 g.) was added. The mixture was left, with occasional shaking, for 3 hours at room temperature, and was then diluted with water and extracted with chloroform. The chloroform extract was washed with water, dried ($MgSO_4$), and evaporated. The *compound* was a liquid which distilled at 100—110°/0·04 mm. (bath temp.), $n_D^{20°}$ 1·4468, $[\alpha]_D^{20°}$ + 12·4° in chloroform (*c*, 1·603). Yield, 2·4 g. (Found : C, 58·5; H, 8·2. $C_{12}H_{20}O_5$ requires C, 59·0; H, 8·2%).

6-*Amino* 1 : 2-3 : 4-*Diacetone Mannitol.*—5 : 6-Anhydro diacetone mannitol (2·2 g.) was heated for 24 hours at 120° in a sealed tube with methyl alcoholic ammonia (80 c.c.; saturated at 0°). The solution was evaporated to dryness and the resulting syrup crystallised by trituration with ether. The material recrystallised from methyl alcohol–benzene–light petroleum in fine needles, m. p. 152°, $[\alpha]_D^{20°}$ + 14·8° in chloroform (*c*, 1·356). Yield, 1·5 g. The substance was 6-amino 1 : 2-3 : 4-diacetone mannitol crystallising as a *monohydrate* (Found : C, 52·1; H, 8·9; N, 4·7. $C_{12}H_{23}O_5N,H_2O$ requires C, 51·6; H, 8·9; N, 5·0%).

1-*Amino Mannitol Oxalate.*—6-Amino diacetone mannitol (0·8 g.) was heated for 4 hours at 100° with 50% aqueous acetone (100 c.c.) containing 2% hydrochloric acid. Thereafter the solution was made neutral by shaking with silver carbonate, filtered with charcoal, the precipitate washed with water, and the filtrate evaporated. A colourless syrup was obtained which, on treatment with the theoretical amount of oxalic acid dissolved in a small amount of water, gave on evaporation a crystalline residue of 1-amino mannitol oxalate which recrystallised from methyl alcohol in small prisms, m. p. 183°. Mixed m. p. with 1-amino mannitol oxalate (prepared from mannose oxime by Dr. R. L. Heath) showed no depression. Yield, 0·35 g.

A. E. Hills Laboratories, The University, Edgbaston, Birmingham.

[*Received, November* 16*th*, 1945.]