# 55. 1 : 6-*Diamino* 2 : 3 : 4 : 5-*Dimethylene Mannitol.*

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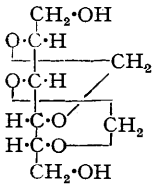
The preparation of 1 : 6-diamino 2 : 3 : 4 : 5-dimethylene mannitol, together with characteristic derivatives, is described. Crystalline salts of the diamine with dibasic acids were obtained. These salts polymerise on heating above their melting points to give polyamides which, however, do not give oriented fibres when cold drawn.

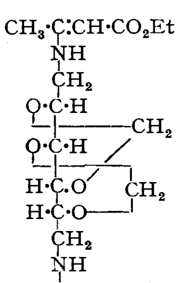
Mannitol was converted into 1 : 6-dichloro mannitol by treatment with fuming hydrochloric acid at 95° under pressure according to the method of Siwoloboff (*Annalen,* 1886, **233**, 368). 1 : 6-*Dichloro dimethylene mannitol* (m. p. 156°) was obtained from 1 : 6-dichloro mannitol either by treatment with 38% formaldehyde solution saturated with hydrogen chloride (Micheel, *Annalen*, 1932, **496**, 77) or by fusion with paraformaldehyde and concentrated sulphuric acid, although the yield by the latter method was inferior.

The description of this compound as 1 : 6-dichloro 2 : 3 : 4 : 5-dimethylene mannitol is justified by its formation from 2 : 3 : 4 : 5-dimethylene mannitol (Haworth and Wiggins, this vol., p. 58), since the structure of this compound was proved by these authors and also by the work of Haskins, Hann, and Hudson (*J. Amer. Chem. Soc.*, 1943, **65**, 67). In addition, the mother-liquors from the recrystallisation of several batches of dichloro dimethylene mannitol yielded a small amount of an isomeric dichloro dimethylene mannitol (m. p. 96°). 1 : 6-Dichloro dimethylene mannitol (m. p. 156°) on treatment with a large excess of methyl-alcoholic ammonia (saturated at 0°) in an autoclave at 150° for 72 hours was converted into crystalline 1 : 6-*diamino* 2 : 3 : 4 : 5-*dimethylene mannitol dihydrochloride*, from which crystalline 1 : 6-*diamino dimethylene mannitol* or its *hydrate* was isolated by treatment with a slight excess of barium hydroxide. The distilled diamine was obtained in 60% of the theoretical yield from dichloro dimethylene mannitol. Secondary and tertiary amino-products were not encountered. Greatly diminished yields resulted if the concentration of dichloro dimethylene mannitol in the methyl-alcoholic ammonia exceeded 3% or if the reaction temperature was very much lower than 150°. Under these conditions extensive and sometimes violent polymerisation often accompanies distillation of the product, and only small amounts of diamino dimethylene mannitol distil. Probably this is caused by the elimination of the elements of hydrogen chloride between some unchanged dichloro dimethylene mannitol and the diamino dimethylene mannitol, with the formation of secondary amino-linkages. 1 : 6-*Diphthalimido dimethylene mannitol* was obtained from 1 : 6-dichloro dimethylene mannitol, although in poor yield, and gave, by means of Ing and Manske's hydrazine method of hydrolysis (J., 1926, 2348), the crystalline 1 : 6-diamino dimethylene mannitol.

The orientation of the methylene groups in these compounds is at present in doubt. The isolation of two isomeric dichloro dimethylene mannitols from the same 1 : 6-dichloro mannitol can only be accounted for by different orientation of the methylene groups. Obviously there are the same three possible structures for dichloro dimethylene mannitol and diamino dimethylene mannitol as for dimethylene mannitol itself (Haworth and Wiggins, *loc. cit.*), since the methylene groups may bridge (*a*) $C_2$ and $C_4$, $C_3$ and $C_5$; (*b*) $C_2$ and $C_3$, $C_4$ and $C_5$; and (*c*) $C_2$ and $C_5$, $C_3$ and $C_4$. We are not yet able to state which of the three possibilities corresponds to each of the isomers actually isolated. The structures (*a*) and (*c*) will possess a rigidity which is not shown by (*b*), since free rotation about the $C_3$–$C_4$ bond is possible in this structure. From the point of view of the formation of linear polymers, a structure of the diamino dimethylene mannitol based on either (*a*) or (*c*) is more favourable, since in these the carbon chain must be extended and rigid, whereas in (*b*), where the methylene groups are attached to adjacent carbon atoms, this is not the case. The formula (I) shows the first of these possibilities, which has some support from the following facts: we have obtained the dimethylenetetrahydroxy-$\Delta^{1:5}$-hexadiene of Micheel (*loc. cit.*) in excellent yield by the action of alcoholic potash or of sodium on 1 : 6-dichloro dimethylene mannitol (m. p. 156°); the difficulty which Micheel (*loc. cit.*) found in cyclising derivatives of dimethylene mannitol to dimethylene cyclitol. A study of models of (I) shows that the methylene groups are so arranged that the addenda on $C_1$ and $C_6$ are relatively far apart.

The 1 : 6-diamino dimethylene mannitol gave a number of well-crystallised derivatives. A Schiff's *base* with salicylaldehyde, a *di*-p-*nitrobenzenesulphonyl* derivative, and also a dipicrate were obtained. 1 : 6-Diamino dimethylene mannitol was also converted by fusion with phthalic anhydride in 50% yield into 1 : 6-diphthalimido dimethylene mannitol, identical with that obtained by the reaction between dichloro dimethylene mannitol and potassium phthalimide. Furthermore, the diamine gave a crystalline *compound*, $C_{20}H_{32}O_8N_2$, on treatment with ethyl acetoacetate in the presence of a trace of hydrogen chloride. This derivative may have the structure represented by (II).


(I.)


(II.)

Crystalline *salts* were also obtained with such dibasic acids as oxalic, adipic, and sebacic acid. Attempts were made to prepare salts of the diamine with the dimethylene glucosaccharic acid and its epimeride dimethylene *l*-idosaccharic acid (Haworth, Jones, Stacey, and Wiggins, this vol., p. 61); the former did not yield a solid compound, but the latter gave a very fine crystalline salt. Tetramethyl glucosaccharic acid also failed to form a crystalline salt with the diamine.

Polymerisation of the crystalline salts was carried out by heating in a vacuum or in sealed tubes in an atmosphere of nitrogen. In every case, however, serious darkening of the product occurred, and, moreover, the fibres which could be drawn from the cooling melt were brittle and did not exhibit the property of "cold drawing" which is characteristic of the Nylon fibres.

The methylene groups in 1 : 6-diamino dimethylene mannitol were exceedingly stable towards acids. Boiling with 5% hydrochloric acid did not effect hydrolysis. Long boiling with 10% hydrochloric acid, however, removed the methylene groups and in this way crystalline 1 : 6-*diamino mannitol dihydrochloride* was obtained.

## EXPERIMENTAL.

1 : 6-*Dichloro Mannitol.*—Mannitol (50 g.) was mixed with 300 c.c. of fuming hydrochloric acid, which was prepared by passing hydrogen chloride into concentrated hydrochloric acid cooled to 0° until it was saturated, and the resulting solution poured into a Pyrex-glass tube of 500 c.c. capacity, and the tube immediately sealed off. Ten such tubes were prepared and placed upright in a large water-bath so that at least the liquid inside the tubes was immersed in the water. The tubes rested on a wire-gauze tray fixed 3" from the bottom of the water-bath. A cover was placed over the tubes and they were heated at 90—95° for 36 hours. When the tubes had cooled, they were opened in the usual way. On rare occasions the end of the tube was blown off during this opening process but never with any great force. The contents of the tubes were poured into a large bolt-head flask, and evaporated to dryness in a vacuum below 50°. The residue, a semi-crystalline mass, was taken up in 800 c.c. of water and evaporated to dryness again; if this was repeated once more, there was very little hydrogen chloride left in the product. The semi-crystalline residue was taken up in 1 l. of water, heated on the boiling water-bath for 5 minutes with charcoal, and filtered hot, the filtrate being evaporated in a vacuum to crystallising point, whereupon the liquid was poured into a conical flask and allowed to crystallise at 0°. The crystals were collected after 24 hours, and washed with a little ice-water and alcohol. Yield, 120 g.; m. p. 174°. The mother-liquors were again saturated at 0° with hydrogen chloride, and the liquid distributed equally amongst ten tubes, each being made up to 300 c.c. with fuming hydrochloric acid. The tubes were sealed and heated under the same conditions as before, and the product isolated in the same way. Yield of crystals, 60 g.; m. p. 174°. Total yield, 180 g.; 30% of the theoretical. In some preparations yields of 40% were obtained.

The residues after these two treatments with hydrochloric acid have not been fully investigated, but give on distillation a liquid which contains some 1 : 4—3 : 6-dianhydromannitol and some 2-chloro dianhydromannitol, and some partly chlorinated monoanhydro-compounds. A full account will be published later.

1 : 6-*Dichloro Dimethylene Mannitol.*—1 : 6-Dichloro mannitol (100 g.) was suspended in 40% formalin solution (250 c.c.), and the mixture cooled in ice. Hydrogen chloride was passed in with constant shaking until a saturated solution was obtained; the dichloro mannitol dissolved, and a precipitate separated together with an oily polymer of formaldehyde. On keeping overnight at 0° crystallisation was complete, and after dilution with water the product was collected and washed with water. Recrystallised from alcohol, it formed large, thick needles (80 g.), m. p. 156°. The mother-liquors from the recrystallisation of several batches were combined, and after separation of a little more 1 : 6-dichloro dimethylene mannitol, m. p. 156°, a very small amount of feathery needles separated, m. p. 96°, $[\alpha]_D$ $-18{\cdot}2°$ (Found : C, 39·4; H, 5·2; Cl, 28·1. $C_8H_{12}O_4Cl_2$ requires C, 39·5; H, 5·0; Cl, 29·2%). This substance was an isomeric *dichloro dimethylene mannitol.*

An alternative method of preparation was tried. Dichloro mannitol (20 g.) was ground with paraformaldehyde (20 g.) and stirred with 13 c.c. of concentrated sulphuric acid. The mixture warmed to about 60° and was stirred occasionally until it cooled again. It was then shaken for 3 hours with 200 c.c. of chloroform, the chloroform poured off, another 200 c.c. added, and the mixture shaken for a further hour. The combined chloroform extracts were washed with dilute aqueous ammonia and with water, dried over anhydrous magnesium sulphate, and evaporated to dryness. The residue was crystallised from alcohol. Yield, 13 g. (60%); m. p. 155—156°

1 : 6-*Diphthalimido Dimethylene Mannitol.*—1 : 6-Dichloro dimethylene mannitol (2 g.) was intimately mixed with potassium phthalimide (4 g.) and heated to 200°; when a few drops of glycerol were added, the mass became semi-liquid (without the addition of glycerol no fusion occurred). Heating was continued for 3 hours at 160—170°. When cold, the mass was extracted twice with boiling water, and the residue dried and recrystallised from chloroform–petrol; m. p. 277°. Yield, 0·7 g. (20%) (Found : C, 61·9; H, 3·9; N, 6·8. $C_{24}H_{20}O_8N_2$ requires C, 61·8; H, 4·2; N, 6·2%).

1 : 6-*Diamino Dimethylene Mannitol from the Diphthalimide Derivative.*—1 : 6-Diphthalimido dimethylene mannitol (0·45 g.), suspended in 25 c.c. of absolute alcohol and boiled with hydrazine hydrate (2 c.c.), dissolved after ¾ hour; after a further ¾ hour the alcohol was removed under diminished pressure. The residue was dissolved in 5 c.c. of water, N-hydrochloric acid added until the solution was acid to Congo-red paper, the mixture heated for 5 minutes at 100°, and the precipitate of phthalhydrazide removed. The filtrate was made alkaline with N-sodium hydroxide and evaporated to dryness. The dry residue was extracted several times with boiling chloroform, and the extracts dried and evaporated. Yield of syrup, which rapidly crystallised on cooling, 0·13 g. This was recrystallised from ethyl acetate–ether; m. p. 48—52°. A mixed m. p. with the diamino dimethylene mannitol obtained by the action of methyl-alcoholic ammonia on 1 : 6-dichloro dimethylene mannitol showed no depression.

1 : 6-*Diamino Dimethylene Mannitol.*—1 : 6-Dichloro dimethylene mannitol (30 g.) was suspended in 1 l. of methyl-alcoholic ammonia (saturated at 0°) and heated in an autoclave at 145—150° for 3 days. The brown solution was evaporated to dryness in a vacuum until all the ammonia had disappeared. Barium hydroxide (40 g.), dissolved in 300 c.c. of hot water, was added, and the mixture heated for 1 hour in a stream of nitrogen. The water was evaporated, and the residue dried at 100° in a vacuum vessel, an atmosphere of nitrogen being present. The residue was extracted 6 times with 250-c.c. portions of chloroform under reflux, and the extracts evaporated to a syrup; this distilled under high vacuum as a yellow oil which crystallised completely. Yield, 15 g. (60%). All the latter operations were conducted in an atmosphere of nitrogen.

1 : 6-*Diamino* 2 : 3 : 4 : 5-*Dimethylene Mannitol Dihydrochloride.*—1 : 6-Diamino dimethylene mannitol (13 g.) (distilled product) was dissolved in water (30 c.c.), and concentrated hydrochloric acid (15 c.c.) added at 0°. Alcohol was then added until a slight turbidity had developed; crystallisation took place rapidly. Yield, 15·5 g. (90%); m. p. 220—224° (decomp.) (Found : C, 34·3; H, 6·3; N, 11·0; Cl, 25·7. $C_8H_{18}O_4N_2Cl_2$ requires C, 34·7; H, 6·5; N, 10·1; Cl, 25·6%).

*Conversion of* 1 : 6-*Diamino Dimethylene Mannitol Dihydrochloride into* 1 : 6-*Diamino Dimethylene Mannitol.*—The dihydrochloride (13 g.) was dissolved in 50 c.c. of water, a solution of 16 g. barium hydroxide in 100 c.c. of hot water added, and the mixture heated at 100° for 1 hour in a stream of nitrogen. Evaporation to dryness and extraction with chloroform (6 times under reflux) gave a light yellow syrup (9 g.) which crystallised to a solid mass on cooling. Recrystallisation was effected from dioxan–ether. Yield, 8 g. (83%); m. p. 48—52°. The product was colourless but very hygroscopic and was apparently a *monohydrate*; $[\alpha]_D^{18°}$ $+67{\cdot}7°$ ($CHCl_3$; *c*, 2·48) (Found : C, 43·8; H, 7·9; N, 12·5; $H_2O$, 6·1. $C_8H_{16}O_4N_2,H_2O$ requires C, 43·2; H, 7·9; N, 12·7; $H_2O$, 8·1%). The anhydrous *diamine*, m. p. 50°, could be obtained by recrystallisation from dry ethyl acetate–ether (Found : C, 47·4; H, 8·1; N, 12·0. $C_8H_{16}O_4N_2$ requires C, 47·1; H, 7·8; N, 13·7%).

1 : 6-*Bis*-N-*salicylideneamino Dimethylene Mannitol.*—1 : 6-Diamino dimethylene mannitol (0·2 g.) was dissolved in a few c.c of water containing a drop of N-sodium hydroxide. Salicylaldehyde (0·23 g.) was added, and the mixture vigorously shaken for an hour. The yellow solid which had separated was collected, washed with water, and recrystallised from alcohol–acetone, forming yellow plates (0·28 g.), m. p. 191—192° (Found : C, 64·1; H, 5·5; N, 6·8. $C_{22}H_{24}O_6N_2$ requires C, 63·8; H, 5·5; N, 6·4%).

*Salts of* 1 : 6-*Diamino Dimethylene Mannitol.*—*Oxalate.* The diamine (0·1 g.) was dissolved in absolute alcohol, and 0·05 g. of oxalic acid, also dissolved in alcohol, added; a fine granular precipitate then separated. An equal volume of water was added, and the alcohol boiled off until a clear solution was obtained. Crystals separated on cooling (0·06 g.), m. p. 280° (decomp.) (Found : C, 41·2; H, 6·3; N, 10·3. $C_8H_{16}O_4N_2,H_2C_2O_4$ requires C, 40·8; H, 6·1; N, 9·5%).

*Dimethylene* l-*idosaccharate.* A solution of the diamine (0·1 g.) in alcohol was added to dimethylene *l*-idosaccharic acid (0·1 g.), also dissolved in alcohol; a granular precipitate separated. This was treated as for the oxalate, feathery needles of the *salt* separating (0·16 g.); it decomposed slowly between 270° and 300° (Found : C, 43·9; H, 6·0; N, 6·2. $C_8H_{16}O_4N_2,C_8H_6O_8$ requires C, 43·8; H, 5·9; N, 6·4%). An attempt to prepare a salt with dimethylene glucosaccharic acid failed to produce any crystals.

*Adipate.* The diamine (0·1 g.) was dissolved in alcohol, and an alcoholic solution of adipic acid (0·07 g.) added; a granular precipitate formed. On being worked up as before, this *adipate* separated in small needles (0·08 g.), m. p. 205° (Found : C, 48·2; H, 7·4; N, 8·5. $C_8H_{16}O_4N_2,C_6H_{10}O_4$ requires C, 48·0; H, 7·4; N, 8·0%).

*Sebacate.* 1 : 6-Diamino dimethylene mannitol (0·1 g.), dissolved in alcohol, was added to sebacic acid (0·1 g.) dissolved in alcohol–water. The mixture was boiled until clear, and alcohol added until the solution was just turbid. Long feathery needles separated (0·12 g.), m. p. (after drying at 100°) 162° (Found : C, 52·8; H, 8·6; N, 6·5. $C_8H_{16}O_4N_2,C_{10}H_{18}O_4$ requires C, 53·1; H, 8·4; N, 6·9%).

*Polymerisation.*—(*a*) 1 : 6-Diamino dimethylene mannitol adipate (0·5 g.) was heated in a vacuum. A fine capillary tube through which nitrogen was passing was immersed in the salt, which was heated a little above its m. p., *i.e.*, at 210—215°. The melt, however, darkened appreciably to a red-brown. After 3 hours the melt on cooling set to a hard resin, and if a glass rod was dipped into the cooling mass, long fibres could be drawn out and wound round a test tube. These light yellow fibres were highly lustrous but brittle. They could not be " cold drawn."

(*b*) The corresponding sebacate was heated in a sealed tube, in which the air had been replaced by nitrogen, immersed in an oil-bath at 170° for 4 hours. The melt thickened appreciably, and after the tube had been cooled and opened, the melt, on warming, could be drawn into light brown fibres; these, however, were brittle and could not be cold drawn. The tube was resealed, and the contents heated again, in an atmosphere of nitrogen at 250° for a further 4 hours. The product, however, darkened still more, became an elastic gel, and resinified on cooling, and fibres could not satisfactorily be drawn from it.

1 : 6-*Bis*-p-*nitrobenzenesulphonamido Dimethylene Mannitol.*—1 : 6-Diamino dimethylene mannitol (0·5 g.) was dissolved in dry pyridine, *p*-nitrobenzenesulphonyl chloride (1 g.) added, and the mixture kept at room temperature for several days. The solution assumed a deep orange colour and crystals separated. When it was poured into ice-water, a solid separated. After being washed with water, this was recrystallised from acetone–water, forming small crystals (1·1 g.), m. p. 249—251° (Found : C, 41·9; H, 3·9; N, 10·1. $C_{20}H_{22}O_{12}N_4S_2$ requires C, 41·8; H, 3·8; N, 9·7%).

*Condensation of* 1 : 6-*Diamino Dimethylene Mannitol with Phthalic Anhydride.*—The diamine (1 g.) was mixed with phthalic anhydride (1·4 g.) and heated at 160° for 2 hours. Some frothing occurred at 130°, and after about ½ hour's heating the melt hardened appreciably. After cooling, the mixture was ground and extracted with boiling chloroform, the extract filtered (charcoal) and evaporated to dryness, and the residue extracted with boiling water. The residual mass was dried, and recrystallised from chloroform–petrol. Yield, 1·1 g. (50%); m. p. 277°, not depressed by the product of reaction between 1 : 6-dichloro dimethylene mannitol and potassium phthalimide.

*Condensation of* 1 : 6-*Diamino Dimethylene Mannitol with Ethyl Acetoacetate.*—The diamine (0·2 g.) was mixed with the ester (3 c.c.), and 1 drop of concentrated hydrochloric acid added. The mixture was shaken occasionally for 12 hours, a little ether added, and the mixture left overnight; the crystals which separated were filtered off and recrystallised from alcohol, forming colourless prisms, m. p. 120°, $[\alpha]_D^{15°}$ +67·2° (*c*, 2·62 in chloroform) (Found : C, 56·6; H, 7·4; N, 6·3. $C_{20}H_{32}O_8N_2$ requires C, 56·1; H, 7·5; N, 6·5%). The *compound* was soluble in chloroform and alcohol but insoluble in water.

1 : 6-*Diamino Mannitol Dihydrochloride.*—(*a*) 1·3 G. of 1 : 6-diamino dimethylene mannitol dihydrochloride were dissolved in 50 c.c. of 5% hydrochloric acid and boiled for 12 hours. Evaporation gave a crystalline mass which, recrystallised from alcohol–water, formed prisms, m. p. 217—220° (decomp.); mixed m. p. with the original material gave no depression (Found : C, 34·4; H, 6·9; N, 10·4. Calc. for $C_8H_{16}O_4N_2$,2HCl : C, 34·7; H, 6·5; N, 10·1%). Therefore no hydrolysis of the methylene groups had taken place under these conditions.

(*b*) The dihydrochloride as in (*a*) (1 g.) was heated with 100 c.c. of 10% hydrochloric acid for 16 hours. Evaporation gave a solid residue, which was recrystallised from alcohol–water. Yield, 0·5 g.; m. p. 238—240° (decomp. at 302—305°) (Found : C, 28·5; H, 7·0; N, 11·6; Cl, 28·5. $C_6H_{16}O_4N_2$,2HCl requires C, 28·4; H, 7·1; N, 11·1; Cl, 28·1%).

*Dimethylenetetrahydroxy*-$\Delta^{1:5}$-*hexadiene.*—This substance was first prepared by Micheel (*loc. cit*) and the following are improvements on his method.

(*a*) 1 : 6-Dichloro dimethylene mannitol (5 g.) was dissolved in 2N-alcoholic potassium hydroxide (100 c.c.) and refluxed for 4 hours. After neutralisation with 2N-hydrochloric acid and separation of the precipitated potassium chloride, the filtrate was evaporated to dryness. Extraction of the residue with ether gave, after removal of the ether, a thin syrup which rapidly crystallised. Recrystallisation from ether–petrol (b. p. 40—60°) gave dimethylenetetrahydroxy-$\Delta^{1:5}$-hexadiene in 91% of the theoretical yield, m. p. 80°.

(*b*) 1 : 6-Dichloro dimethylene mannitol (10 g.) was melted and kept at 160° while sodium wire (2·4 g.) was slowly added. The vigorous reaction which took place initially necessitated the removal of the external source of heat until most of the sodium had been added and the reaction mixture had become solid owing to the separation of sodium chloride. Dry toluene (30 c.c.) was added, and the mixture heated for 2 hours under reflux. The clear, supernatant liquid was decanted, and two further extractions made. The combined toluene extracts were filtered and evaporated, a mobile liquid being obtained which crystallised rapidly on cooling. After recrystallisation from benzene–light petroleum, dimethylenetetrahydroxy-$\Delta^{1:5}$-hexadiene separated, m. p. 80°. Yield, 5·6 g. (85%); $[\alpha]_D^{20°}$ +281·5° ($CHCl_3$). Micheel (*loc. cit.*) gives m. p. 80°, $[\alpha]_D^{20°}$ +280° ($CHCl_3$).

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