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## XXXIV.—The Oxidation of Mannitol by Nitric Acid. d.-Mannosaccharic Acid.

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According to the text-books on organic chemistry, saccharic acid may be obtained by oxidising mannitol with nitric acid. This statement appears to date as far back as 1860, when Backhaus (*Neu. Rep. Pharm.*, 9, 291, &c.; *Jahresber.*, 1861, 522) announced that he had obtained oxalic and a small quantity of saccharic acid by oxidising mannitol with nitric acid according to the method given by Liebig (*Jahresber.*, 1860) for the oxidation of milk-sugar to tartaric acid.

A close relationship should, therefore, exist between mannitol and saccharic acid, and this conclusion seemed to be further strengthened by the observation that dextrose yields mannitol when reduced with sodium amalgam, but yields saccharic acid when oxidised by nitric acid.

The recent researches of Emil Fischer and his pupils have, however, shown that dextrose on reduction yields mannitol with difficulty, whereas mannose, the stereochemical isomeride of dextrose, passes almost quantitatively into mannitol when treated with sodium This result seemed to indicate that the relationship amalgam. between dextrose and mannitol was not so simple as had been supposed. The close relationship between mannitol and mannose, however, is shown by the ease with which the one can be converted into If mannose be further oxidised with bromine-water, it the other. yields monobasic d.-mannonic acid, which may be oxidised by nitric acid to bibasic d.-mannosaccharic acid, isomeric with ordinary saccharic acid (Wirthle, Dissertation, Erlangen, 1890). The new acid differs markedly from saccharic acid, more especially in that it yields no sparingly soluble acid potassium salt; and passes readily by internal condensation into a crystalline double lactone.

These results made it appear probable that mannitol would not yield saccharic by direct oxidation with nitric acid, but mannosaccharic acid; and at Professor Fischer's suggestion, I have carried out the oxidation with nitric acid of various strengths. Our supposition as to the nature of the reaction was completely realised, mannosaccharic and oxalic acids being the only products which could be identified.

In the first place, in order to ascertain whether saccharic acid was formed by the oxidation of mannitol, 5 grams of mannitol were warmed on the water-bath with 30 grams of nitric acid of sp. gr. 1.15;

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when the reaction had almost ceased, the liquid was evaporated to a syrup, diluted with water, and again evaporated, so as to get rid of excess of nitric and nitrous acids and to destroy any nitro-compounds which might be present. The syrup was then diluted with 30 c.c. of water, exactly neutralised with potassium carbonate, evaporated to a small bulk, and an excess of acetic acid added. No crystallisation occurred even when crystals of acid potassium saccharate were placed in the liquid and allowed to remain there for several days. Saccharic acid cannot, therefore, have been produced in the reaction. A like result was arrived at when experiments were made on a larger scale and with more highly concentrated nitric acid.

The next step was to find out what acid, if any, had been produced in the above operation. With this object, 10 grams of mannitol were oxidised as above described, and the syrup, after having been diluted to 250—300 c.c., was boiled with precipitated chalk until neutral to test-paper. The liquid was filtered, a considerable quantity of calcium oxalate together with unaltered chalk remaining on the filter. The dark-brown filtrate, after being evaporated until a film appeared on its surface, was allowed to cool, when a reddish-brown calcium salt separated. This to the naked eye appeared crystalline, but under the microscope was found to consist of aggregates of most characteristic nodules, bearing an astonishing likeness to a yeast plant. A further quantity of the salt was precipitated on adding alcohol to the mother liquor.

Although this calcium salt is not remarkably insoluble in water, it is somewhat difficult to get into solution, for if put into hot water it melts to a thick oil which remains at the bottom of the liquid, darkens in colour, and then passes into solution very slowly indeed. If, however, the crude calcium salt be ground to a very thin paste with cold water, and then added gradually to a large quantity of boiling water, it dissolves immediately, giving a darkly coloured solution which can be readily decolorised with animal charcoal. On concentrating the solution, the calcium salt separates out on cooling as a cream-coloured powder which under the microscope exhibits the same structure as the crude salt. If the solution is allowed to evaporate spontaneously, the salt separates out in vitreous grains with no welldeveloped faces. These grains have no action on polarised light.

The calcium salt contains water and is efflorescent; after drying at 100°, it gave the following result :---

0.1880 gram gave 0.1035 gram CaSO<sub>4</sub>.

		Calculated for
	Found.	C6H8O8Ca.
Ca	16.19	16.12

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The salt would thus appear to be calcium saccharate or an isomer thereof. That it was not ordinary calcium saccharate was proved by decomposing 1 gram of the salt with an equivalent amount of potassium carbonate, concentrating, and adding acetic acid. No sparingly soluble salt separated out.

A silver salt was prepared from the concentrated solution of the calcium salt. It could not be recrystallised, and rapidly darkened in colour. Upon analysis,

- I. 0.1646 gram gave 0.0978 gram  $CO_2$ , 0.0305 gram  $H_2O$ , and 0.0813 gram Ag.
- II. 0.1691 gram gave 0.1009 gram CO<sub>2</sub>, 0.0378 gram H<sub>2</sub>O, and 0.0835 gram Ag.

	Fo	und.	
			Calculated for
	Ι.	11.	$C_6H_8O_8Ag,H_2O_8$
С	16.20	16.26	16.28
н	2.02	2.48	2.26
Ag	49.39	49.37	48.86

These results could not be regarded as satisfactory, and it was decided to attempt the preparation of the free acid from the calcium salt by decomposition with oxalic acid. In the meantime, the above results were communicated to Professor Emil Fischer, who kindly forwarded a specimen of the lactone of d.-mannosaccharic acid for comparison with the acid which I was about to prepare.

On decomposing the calcium salt with an equivalent quantity of oxalic acid, filtering, and concentrating, a syrup was obtained which refused to crystallise even after long standing. The addition of a crystal of Fischer's lactone, however, immediately caused the syrup to change to a solid mass of crystals These were freed as completely as possible from mother liquor by means of a vacuum filter, washed with ice-cold water, and then recrystallised from hot water. The substance was thus obtained in colourless needles, which, after washing with absolute alcohol, gave the following results on analysis :---

0.1407 gram gave 0.0593 gram  $H_2O$  and 0.1750 gram  $CO_2$ .

		Calculated for
	Found.	$C_{6}H_{10}O_{8}$ .
C	33.91	34.28
Н	4.68	4.76

These results agree with those to be expected from an acid, and not from a lactone; the crystals, however, effloresce, and by drying in a vacuum over sulphuric acid lose 2 mols.  $H_2O$ .

Of the dried substance,

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0.1308 gram gave 0.0393 gram  $H_2O$  and 0.1977 gram  $CO_2$ .

		Calculated for
	Found.	$C_6H_6O_6$ .
C	41.21	41.37
Н	3.33	3.44

The colourless, efflorescent crystals above mentioned would seem to be merely the lactone crystallised with 2 mols.  $H_2O$ , and not the acid itself; for if these crystals are dissolved in water, the solution is absolutely neutral when freshly prepared. After standing, however, for some hours, the solution acquires an acid taste and reddens litmus strongly, showing that the lactone passes into the acid when in solution. The identity of the above lactone with Fischer's d.-mannosaccharolactone appears to be complete. The fact that the latter crystallises in the first instance with 2 mols.  $H_2O$  is, indeed, not mentioned in Wirthle's dissertation, but it is a fact which might well escape notice. The points of resemblance are the following :—

(1.) The two lactones (both dried over sulphuric acid) when placed in capillary tubes, and heated side by side in a sulphuric acid bath, exhibited exactly the same behaviour. At  $170^{\circ}$ , they began to darken, and at  $182^{\circ}$ , both melted with decomposition.

(2.) A small quantity of Fischer's lactone, when boiled with chalk and the filtered solution concentrated, yielded a calcium salt which separated in microscopic spherules, just like those furnished by the calcium salt from mannitol.

(3.) Both reduce Fehling's solution strongly; this, however, is a character shared by many other oxy-acids.

(4) Both are strongly dextrorotatory. Mr. H. E. Schmitz, of St. John's College, has kindly made some experiments upon the optical properties of the lactone. Unfortunately, I had left Cambridge, and was unable to supply him with sufficient material to finish his investigations. Suffice it to say that in a solution, the strength of which was only about 1 per cent., the apparent sp. rot. power  $[\alpha]_D = +167.9^{\circ}$ . That of d.-mannosaccharolactone in 5 per cent. solution =  $+197.1^{\circ}$ . I hope to be enabled to communicate an accurate determination of the rotatory power in a subsequent note.

It remains to discuss the best method for the preparation of the lactone from mannitol. Hitherto the best yield has been obtained as follows :---

• 20 grams of mannitol are placed in a small flask, and covered with 120 grams of nitric acid, sp. gr. 1.15, and the flask slowly warmed in a water-bath, a thermometer being placed inside the flask. When the contents of the flask have obtained a temperature of 75°, the thermometer begins to rise rapidly, showing that an energetic action is begin-

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ning. The flask is now cooled down to  $65^{\circ}$ , and kept between  $65^{\circ}$  and  $70^{\circ}$  until the reaction has nearly ceased; generally 5—6 hours. The temperature is now allowed to rise slowly to  $80^{\circ}$ , and after the reaction has again diminished, the flask is kept at  $90^{\circ}$  for a couple of hours.

If the contents of the flask be now diluted with water, boiled with an excess of chalk, and filtered, a solution will be obtained which, when evaporated to saturation, and poured into five times its volume of alcohol, deposits the whole of the calcium salt as an amorphous, flocculent precipitate. If this is washed by decantation, then well shaken up with water, and the turbid liquid poured into a large volume of boiling water, the salt goes completely into solution. The solution, after being decolorised with animal charcoal, yields the calcium salt as a nearly colourless powder. By this method, 80 grams of mannitol yielded 32 grams of crude calcium salt, and this, after recrystallisation, gave 20 grams of pure salt, that is, 25 per cent. of the mannitol employed.

The acid may, however, be prepared from the crude oxidation product without first preparing the calcium salt; for this purpose, the product of the oxidation is evaporated in an open dish, with constant stirring, until a syrup is produced. This, if slightly diluted and allowed to cool, deposits a large quantity of oxalic acid, which must be filtered off and the mother liquor concentrated. On now adding a crystal of the lactone (prepared from the calcium salt) to the solution, the product will solidify, and can be purified by recrystallisation from water. Sometimes the liquid crystallises of its own accord, but usually refuses obstinately to do so; the addition of alcohol assists the crystallisation.

10 grams of mannitol treated in this manner gave 0.9 gram of pure lactone, but I have little doubt that the process can be modified so as to give a better yield.