XLII.—*Mesoxalic Semi-Aldehyde.*

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Chlorine and bromine have, as is well known, very little action on an aqueous solution of tartaric acid at the the ordinary temperature; it is found, however, that in presence of ferrous iron the action is considerably accelerated. If the solution be saturated with chlorine, the yellow colour which is first produced soon disappears on standing, and after some hours the odour of chlorine is no longer perceptible. On addition of phenylhydrazine acetate or hydrochloride to the solution so obtained, a bright orange-yellow precipitate is produced.

In order to study the nature of this reaction, the following method was adopted. Ordinary *d*-tartaric acid was dissolved in five to ten times its weight of water and mixed with a small quantity of freshly prepared ferrous tartrate (obtained by dissolving 'ferrum redactum' in a solution of the acid). A slow current of chlorine was then passed into the mixture until saturation appeared complete. After standing overnight, or until the odour of chlorine had disappeared, it was again saturated with the gas, and this treatment repeated until a sufficient quantity of the product had been formed, the progress of the change being ascertained by the phenylhydrazine reaction. The liquid was then concentrated to a small bulk by distillation under very reduced pressure at about 50°, and was then allowed to stand, preferably in a vacuum desiccator, until most of the unaltered tartaric acid had crystallised out. The mother liquor from these crystals remains as a thick syrup which refuses to crystallise. The product is very stable at the ordinary temperature and keeps remarkably well without apparent change, but boiling changes its character, the product then giving a small quantity of a highly crystalline, brownish precipitate when tested with phenylhydrazine.

Bromine, or hypochlorite, produces an effect similar to that of chlorine, and a very simple method of demonstrating the change is to add a small quantity of sodium hypochlorite to potassium hydrogen tartrate suspended in water and mixed with a little ferrous salt. After allowing the mixture to stand a short time and removing any excess of chlorine, if necessary, by a current of air or by sulphurous acid, the liquid gives an abundant orange-yellow precipitate with phenylhydrazine salts.

The proportion of iron used is (as in various similiar oxidation processes previously described by one of the authors) not a matter of importance; the merest traces have a marked effect. In these experiments, about 1/5000 to 1/1000 part of iron to 1 part of acid was employed.

In the present case, a certain amount of action can be detected in absence of iron, but the process is then very slow and the yield poor.

The syrupy product obtained in the manner described above still contains tartaric acid, and in order to investigate its nature the action of various reagents was studied.

Action of Phenylhydrazine.

A dilute solution of the product gives the above described orange-yellow precipitate almost immediately in the cold with either the acetate or hydrochloride of phenylhydrazine. The precipitation is accelerated by heating and is complete in half-an-hour or less. After washing with water and drying in the air, the precipitate dissolves easily in alcohol and sparingly in hot benzene or chloroform. From the latter solvent, it separates on cooling in masses of brilliant orange-golden needles or prisms. These, when quickly heated, melt usually at 218° after the first crystallisation and on further recrystallisation once or twice from the same solvent, melt constantly at 222—224°. Analysis of the product dried at 100° gave the following result:

0·1181 gave 20·1 c.c. nitrogen at 18° and 749 mm. N = 19·74 per cent.

It dissolves in boiling sodium carbonate solution, and, on cooling, a beautifully crystalline sodium salt is deposited, the aqueous solution of which dyes silk, wool, &c., a bright lemon-yellow colour. Heated with acetic anhydride, it yields a substance which crystallises from alcohol in brilliant orange-red needles which melt at 150°.

The composition and properties of the product coincide in every way exactly with those of one which has previously been described in various former communications (Fenton and Jones, Trans., 1900, **77**, 77, and 1901, **79**, 91).

It was first obtained by the further oxidation of malic acid in presence of iron, secondly by oxidation of oxalacetic acid under similar conditions, and thirdly by heating the phenylhydrazine salt of dihydroxymaleic acid with excess of phenylhydrazine for some time on a water-bath. (The same result is also produced by heating the salt with water alone.) Analysis of the compound prepared in these ways gave C = 63·2, H = 5·1, N = 20·1 per cent. as a mean of several concordant experiments. The nature of the compound was the subject of much investigation, since it so closely resembled the osazone of hydroxypyruvic acid, first obtained by Nastvogel from dibromopyruvic acid (*Annalen*, 1888, **248**, 85), and subsequently by Will from collodion-wool (*Ber.*, 1891, **24**, 400 and 3831). The same osazone was afterwards obtained by the action of phenylhydrazine on the product of oxidation of glyceric acid in presence of iron (Fenton and Jones, Trans., 1900, **77**, 72). There remained, however, the very considerable discrepancy in the *melting point*. The osazone of hydroxypyruvic acid melted at 201—203° (Nastvogel), 205° (Will), and 207° (Fenton and Jones); whereas the product at present under discussion melts at 222—224°.*

In consequence of this difference, and in view of the fact that the present product of higher melting point was always obtained from

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* Friedel and Combes (*Bull. Soc. Chim.*, 1890, [iii], **3**, 770) state that by adding phenylhydrazine to the product of electrolysis of tartaric acid, they obtained the osazone of glyoxal, melting at 160°, and the osazone of glyoxalcarboxylic acid, melting at 218°. They give, however, no details, analyses, or further information whatever.

acids containing 4 carbon atoms in the molecule, other possible explanations as to its nature were suggested (Fenton and Jones, Trans., 1901, **79**, 98). It might, for example, be the hydrazide-dihydrazone of dioxosuccinic acid, and this idea was apparently supported by the fact that when heated with acetic anhydride it gives notable quantities of carbon dioxide and aniline in addition to the phenylhydrazine-ketophenylpyrazolone of Knorr. This result might, however, be otherwise explained, and the question still remained open whether the product of higher melting point is a derivative of a 3 or 4 carbon acid. The calculated composition shows very little difference, Nastvogel's osazone, $C_{15}H_{14}O_2N_4$, requiring C 63·82, H 4·96, N 19·85 per cent., and the 4 carbon derivative above suggested, $C_{22}H_{20}O_3N_6$, requiring C 63·46, H 4·80, N 20·19 per cent.

By a numerical coincidence, the same close similarity of composition exists between the corresponding derivatives of various other hydrazines (nitrophenyl-, bromophenyl-, tolyl-hydrazine, &c.), so that it is evident that the question cannot be settled by analysis of any of these derivatives. It appeared probable, however, that a careful comparison of the properties of derivatives of these substituted hydrazines obtained from dibromopyruvic acid with those from the tartaric acid oxidation product now under discussion should give more definite information as to the question, and the following experiments were therefore made with this object.

(1) The product obtained from tartaric acid by action of chlorine, described above, was mixed with excess of p-*bromophenylhydrazine* dissolved in acetic acid. The resulting orange-coloured precipitate was washed, dried in the air, and recrystallised twice from a mixture of absolute alcohol and benzene. The long, bright orange-coloured needles so obtained melted at 245—246°.

Dibromopyruvic acid (1 mol.) was then dissolved in water and mixed with a solution of *p*-bromophenylhydrazine hydrochloride (2 mols.) and the mixture allowed to stand 3 to 4 hours at the ordinary temperature. An orange precipitate exactly similar to that last mentioned was obtained, and this, when recrystallised in a similar way, melted precisely at the same temperature, 245—246°.

(2) The tartaric acid product was mixed with an excess of p-*tolylhydrazine* hydrochloride in aqueous solution. An orange-red precipitate soon appeared, and after 3 or 4 hours was filtered off, washed, dried, and recrystallised from hot benzene. The orange-coloured needles so obtained, when slowly heated, began to soften at 188° and melted completely at 194—195°. Nastvogel (*loc. cit.*), by the action of *p*-tolylhydrazine hydrochloride on dibromopyruvic acid, obtained golden needles which melted at 186—188°.

(3) These results pointed so strongly to the identity of the products from the two different sources that it appeared desirable to prepare the *phenylhydrazine* derivative from dibromopyruvic acid exactly according to Nastvogel's directions, and to compare it with the osazone from the tartaric acid product.

The melting point of this osazone from tartaric acid, oxalacetic acid, malic acid, and dihydroxymaleic acid has been determined a very large number of times, and the results from all these different sources are remarkably concordant; it may, in fact, be taken as established that the melting point is 222—224°.

The specimens from all these sources have, for analysis, been recrystallised from *chloroform* and the melting points determined by the quick-heating method. But even slow heating does not lower the melting point more than 3° or 4°.

With regard to Nastvogel's osazone, this author does not mention how the melting point was determined, but Will determined it by the quick-heating method. But in all the methods by which this osazone has hitherto been obtained (that is, from dibromopyruvic acid, collodion-wool, and glyceric acid) the product was purified by crystallisation from *benzene*.

Nastvogel's experiment was therefore carefully repeated:—3·5 grams of phenylhydrazine hydrochloride were dissolved in water and a solution of 3 grams of dibromopyruvic acid was added, the mixture being kept cold. A bright orange precipitate began to separate almost at once, and after 3½ hours was collected, washed, dried in the air, and recrystallised three times from hot *chloroform*. The resulting product resembled in every respect the osazone from tartaric acid, &c., and melted at 222—224°.

It is therefore evident that this is the true melting point of the osazone, and it is remarkable that so many observers have obtained the lower value, the explanation being, apparently, that chloroform is the more appropriate solvent for its purification.

The above facts practically remove all doubt as to the identity of Nastvogel's osazone with that at present under discussion. Further evidence of this was obtained in the following way. The highly concentrated syrup from the oxidation product of tartaric acid was dissolved in absolute alcohol, saturated with dry hydrogen chloride, allowed to stand overnight, and distilled to small bulk under diminished pressure and the product again treated in a similar manner. It was then poured into cold water, extracted with ether, and dried over calcium chloride. After distilling off the ether, the liquid contains some ethyl tartrate and the products are difficult to separate, but on adding phenylhydrazine acetate and diluting with water a lemon-yellow precipitate slowly separates. This, when recrystallised, first from alcohol and then from benzene and a little light petroleum, was obtained in yellow, transparent plates which melted at 229—231°. This substance dissolves easily in hot alcohol or benzene, but is nearly insoluble in alkalis.

0·1889 gave 29·8 c.c. nitrogen at 19° and 751 mm. N = 18·28.

$C_{17}H_{18}O_2N_4$ requires N = 18·06 per cent.

This product is evidently identical with that which Will obtained by the action of ethyl iodide on the osazone from collodion-wool, and is, in fact, the ethyl ester of this osazone:

$$CH(N_2HPh)\cdot C(N_2HPh)\cdot CO_2Et.$$

The osazone, $CH(N_2HPh)\cdot C(N_2HPh)\cdot CO_2H$, may obviously be derived from (1) hydroxypyruvic acid, (2) the semi-aldehyde of tartronic acid, or (3) the semi-aldehyde of mesoxalic acid. The product which Will obtained from collodion-wool is considered by him to be hydroxypyruvic acid from analysis of its metallic salts and from the fact that it is not oxidised by bromine.

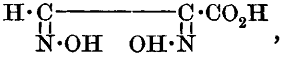
The substance obtained by Fenton and Jones by oxidation of glyceric acid in presence of iron is in many respects similar, but it gives an intense violet colour with ferric salts in presence of alkalis, a property which presumably is not possessed by Will's product, since no mention is made of it. The glyceric acid product, if it is not hydroxypyruvic acid, may possibly be the tautomeric dihydroxyacrylic acid,

$$CH(OH){:}C(OH)\cdot CO_2H.$$

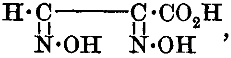
The oxidation product from tartaric acid at present under discussion might, so far, be any of the above-named acids. It gives, however, when its formation is complete (see below), no colour with ferric salts in presence of alkali. It might conceivably be dichloropyruvic acid, but this is excluded by the fact that if the solution be precipitated with barium acetate, the well-washed barium salt obtained contains no chlorine, and on decomposition with dilute sulphuric acid gives, with phenylhydrazine, the same osazone as before.

Action of Hydroxylamine.

If the substance under discussion is the semi-aldehyde of mesoxalic acid, it would be expected that the action of excess of hydroxylamine should give the dioxime, $CH(NOH)\cdot C(NOH)\cdot CO_2H$, or dioximidopropionic acid. This oxime was obtained by Söderbaum (*Ber.*, 1892, **25**, 904) by the action of hydroxylamine on dibromopyruvic acid, and was shown to exist in two forms. The 'primary' acid,



$$\begin{array}{ccc} H\cdot C & \text{———} & C\cdot CO_2H \\ \| & & \| \\ N\cdot OH & & OH\cdot N \end{array},$$

melts at 141—143°, and the 'secondary' acid,  $\underset{\overset{\|}{N\cdot OH}}{H\cdot C}\text{———}\underset{\overset{\|}{N\cdot OH}}{C\cdot CO_2H}$, at about 172°.

If the primary acid is dissolved in the least possible quantity of ammonia, well cooled by ice, and acidified with hydrochloric acid, it is transformed into the secondary acid. Both forms give a blood-red colour with ferric chloride, and with ferrous sulphate and a little caustic soda they give an intense, but unstable, violet colour. Cupric acetate gives an olive-green precipitate.

The present tartaric acid oxidation product was concentrated as before and freed as much as possible from unaltered tartaric acid; it was then dissolved in water, mixed with excess of an aqueous solution of hydroxylamine hydrochloride, and neutralised, or nearly so, by the gradual addition of solid sodium carbonate, the mixture being cooled by ice. The solution turns dark red or violet, and on standing deposits a white sodium salt. It was allowed to stand for a few hours at 0° and then for about 24 hours at the ordinary temperature. The mixture was filtered with the aid of suction, the solid sodium salt treated with excess of dilute sulphuric acid, and extracted several times with ether. The ethereal solution was distilled to a small bulk and allowed to stand in a vacuum desiccator, when it solidified to a reddish mass. This was dissolved in the least possible quantity of ammonia, well cooled by ice, and acidified with strong hydrochloric acid.

After standing a short time, a mass of long, colourless needles separated; these were purified by redissolving in ammonia and acidifying with dilute sulphuric acid under similar conditions.

The resulting product, dried in a vacuum desiccator, when slowly heated melted at 178—180°. It is somewhat sparingly soluble in cold water and the aqueous solution behaves with ferric chloride, ferrous sulphate, and cupric acetate exactly as above described with Söderbaum's acid.

The vacuum-dried product gave the following results on analysis:

I. 0·1571 gave 0·1551 CO_2 and 0·0454 H_2O. $C = 26·92$; $H = 3·21$.
II. 0·1064 ,, 18·8 c.c. nitrogen at 18° and 767 mm. $N = 20·98$.
$C_3H_4O_4N_2$ requires $C = 27·27$; $H = 3·03$; $N = 21·21$ per cent.

Oxidation to Mesoxalic Acid.

The action of hydroxylamine and of phenylhydrazine practically settles the question as to the nature of the product under discussion, that it is the semi-aldehyde of mesoxalic acid. It was considered, however, that it would be satisfactory to prove the matter conclusively by oxidation of the aldehyde to mesoxalic acid.

Bromine or chlorine did not appear to be suitable agents for this purpose, owing to the presence of unaltered tartaric acid in the substance to be operated on, so that cupric oxide was selected as the most appropriate. A solution of the tartaric acid oxidation product was made alkaline with soda and mixed with excess of freshly precipitated cupric hydroxide. On warming to about 60°, a rapid reduction took place, and when this appeared to be complete the mixture was filtered, the liquid acidified with hydrochloric acid, and the copper removed by hydrogen sulphide, excess of the latter being avoided. Addition of phenylhydrazine, as acetate or hydrochloride, to this solution gave a yellow colour, and after standing a short time, a pale yellow precipitate consisting of masses of fine needles. These, when recrystallised from hot alcohol, melted at 171—172° and corresponded in properties exactly with the hydrazone of mesoxalic acid (compare Elbers, *Annalen*, 1885, **227**, 341; Clemm, *Ber*, 1898, **31**, 1451; Fenton and Jones, Trans., 1900, **77**, 71).

For analysis, the substance was prepared from the pure product described below and phenylhydrazine hydrochloride. Thus obtained, it was quite pure without recrystallisation. After being well washed with water and alcohol and dried in a vacuum desiccator, two distinct specimens, prepared on different occasions, melted at 173—174° and gave on analysis the following results:

I. 0·2243 gave 25·5 c.c. nitrogen at 14° and 765 mm. N = 13·65.
II. 0·1910 „ 22·2 „ „ 17° „ 759 mm. N = 13·70.
$C_9H_8O_4N_2$ requires N = 13·46 per cent.

Clemm gives the melting point of mesoxalic hydrazone as 174°.

Mode of Formation.

Theoretically there are, of course, several ways in which the semi-aldehyde of mesoxalic acid might result from tartaric acid by oxidation, and experiments were made with the object of ascertaining which of these is more probable. The simple removal of one mol. of carbon dioxide from ‘anhydrous’ *dihydroxytartaric* acid or dioxosuccinic acid would at once afford a direct explanation,

$$CO_2H\cdot CO\cdot CO\cdot CO_2H = CO_2H\cdot CO\cdot CHO + CO_2,$$

but as yet it has not been found possible to prepare the substance from dihydroxytartaric acid; heating the acid alone, with acid and with iron salts all gave negative or unsatisfactory results. It was observed, on the other hand, that in preparing the product by the action of chlorine on tartaric acid in presence of iron in the manner above described, the liquid in the first instance always gives a notable reaction for *dihydroxymaleic* acid when tested with ferric chloride and alkalis (compare Fenton, *Chem. News*, 1876, **33**, 190; 1881, **43**, 110), but after the completion of the process, by further action of chlorine and subsequent distillation, this property no longer appears. The initial change which takes place may therefore consist in the formation of dihydroxymaleic acid, and this, by futher oxidation and loss of carbon dioxide, may give rise to mesoxalic semi-aldehyde,

$$C_4H_4O_6 + O = C_3H_2O_4 + H_2O + CO_2.$$

In order to test the latter hypothesis, pure dihydroxymaleic acid was subjected to oxidation under various conditions. It was previously shown that this acid is oxidised almost quantitatively by bromine at the ordinary temperature to dihydroxytartaric acid (Trans., 1894, **67**, 48), and in trying modifications of the process it was often observed that the presence of iron—the agent which was essential for the formation of dihydroxymaleic acid from tartaric acid—had a deleterious effect. In view of this fact, it seemed not improbable that, in the process at present under discussion, the ferric salt produced may be the active agent in the oxidation of dihydroxymaleic acid to mesoxalic semi-aldehyde. This supposition is entirely borne out by experiment, and the oxidation is found to take place almost quantitatively when carried out in the following way.

Crystallised dihydroxymaleic acid, $C_4H_4O_6,2H_2O$, is covered with water or *dilute* alcohol and a solution of ferric chloride or sulphate gradually added. Each drop of the ferric salt produces an intense violet-black coloration which quickly disappears, with a considerable rise of temperature. The temperature of the mixture is allowed to rise to about 40°, being aided by warming if necessary, and the addition of the ferric salt is continued until a further quantity no longer produces the coloration mentioned. This point is reached when the substances are present very nearly in the ratio of $C_4H_4O_6 : 2Fe$.

The iron is entirely reduced to the ferrous state, and the end-point may easily be demonstrated by the usual indicators. A brisk evolution of carbon dioxide occurs during the process, and the change may be expressed by the equation:

$$C_4H_4O_6 + Fe_2(SO_4)_3 = C_3H_2O_4 + 2FeSO_4 + H_2SO_4 + CO_2.$$

The reaction appears to take place only with ferric salts of strong acid radicles and in presence of water; if ferric acetate be used in aqueous solution, or if alcoholic ferric chloride be added to alcoholic solution of dihydroxymaleic acid, the dark violet colour produced remains quite persistent, at any rate for several hours.

In order to obtain the product free from iron, it is best to employ ferric sulphate as oxidising agent, and, after concentration in a vacuum desiccator, to precipitate the ferrous salt by alcohol and ether, the free sulphuric acid being neutralised by the calculated amount of sodium carbonate or baryta water. By repeating the concentration and treatment with alcohol and ether, and removing the latter in a vacuum desiccator, a syrup practically free from iron is left, which gives all the reactions described above for the tartaric acid oxidation product. Phenylhydrazine acetate or hydrochloride gives the above-described osazone melting at 222—224°; hydroxylamine gives the dioxime identical in every way with that obtained from the tartaric acid product, and oxidation with alkaline cupric hydroxide gives a large yield of mesoxalic acid.

In order to avoid the large quantity of iron salts present in the above method, a very small quantity of a ferric salt may be employed, and, as soon as reduction is complete, the resulting ferrous salt may be re-oxidised by hydrogen dioxide, the addition of the latter being continued until the change is completed. This method appears to give good results except that a small quantity of dihydroxytartaric acid may be formed at the same time, so that the use of a ferric salt only as oxidising agent is the most reliable.

The behaviour of ferric iron in the reaction here described is of much interest in throwing light upon certain processes of oxidation in presence of iron where a ferric salt has been employed (compare Fenton, Trans., 1900, **77**, 1296). In these cases, there is little doubt that a ferrous salt is first produced, possibly only in minute quantity, and that this determines the oxidation in the usual manner; ferric salt appears to encourage the breaking down of the resulting product with evolution of carbon dioxide.

The isolation of mesoxalic semi-aldehyde as above described leaves now only four out of the eleven possible oxidation products of glycerol which have not been obtained; mesoxalic dialdehyde being known only in the form of oxime, and tartronic semi-aldehyde and dialdehyde, and hydroxypyruvic aldehyde being unknown.

Many interesting results may be expected from a further study of this aldehyde-acid; its aldehyde hydrate may be regarded as tautomeric with the hitherto missing trihydroxyacrylic acid, which is of much interest owing to its relationship to uric acid.

A considerable part of the expenses incurred in carrying out this investigation has been defrayed by funds kindly supplied by the Government Grant Committee of the Royal Society.