LXXXII.—*Further Studies on Dihydroxymaleic Acid.*

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THE mode of formation, constitution, properties and relationships of dihydroxymaleic acid have been discussed in several previous communications to the Society and elsewhere (Trans., 1894, **65**, 899 ; 1895, **67**, 48 and 774 ; 1896, **69**, 546 ; 1897, **71**, 375 ; 1898, **73**, 71 ; 1902, **81**, 426 ; Proc., 1898, 14, 119 ; *Proc. Camb. Phil. Soc.*, 1901, **11**, 109 ; 1902, **11**, 358, &c.), and in the present paper an account is given

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of some of the principal investigations which have since been carried out in connection with the subject.

This acid proves to be of importance not only in consequence of the scientific interest attaching to its constitution and peculiar mode of formation, but also because it serves as the starting point for the preparation, by direct and simple transformations, of many compounds which can otherwise only be obtained with considerable difficulty or not at all.

In the communications above referred to it was shown that the acid results from the oxidation of tartaric acid in presence of ferrous iron ; it is thus obtained in the form of lustrous, diamond-shaped plates which have the formula $C_4H_4O_6 \cdot 2H_2O$. It is a dibasic acid, as evidenced by the composition of its salts and esters ; the presence also of two alcoholic hydroxyl groups is shown by the action of acetic anhydride and of acetyl and benzoyl chlorides. In constitution it must therefore be represented as either dihydroxymaleic or dihydroxyfumaric acid, $CO_2H \cdot C(OH) : C(OH) \cdot CO_2H$. The former configuration is to be preferred in consequence of the readiness with which anhydride formation takes place, and the action of hydrobromic acid transforms it into an isomeric modification which has probably therefore the fumaroid form ; it cannot be said, however, that these respective configurations are finally established (compare Proc., *loc. cit.*).

Fuming hydriodic acid reduces it ultimately to succinic acid, racemic acid having been isolated as an intermediate stage. When oxidised by bromine under certain conditions, it is converted almost quantitatively to dihydroxytartaric acid ; this action was shown to be reversible and, under different conditions, bromine is liberated when hydrogen bromide acts on dihydroxytartaric acid with the production of the lactonic acid of dihydroxyfumaric acid. By heating an aqueous solution of dihydroxytartaric acid, tartronic acid is obtained in a pure condition.

Oxidation by means of ferric salts converts dihydroxymaleic acid into the semialdehyde of mesoxalic acid, and it was pointed out that the latter product also results when tartaric acid is oxidised by chlorine in presence of iron.

An aqueous solution of dihydroxymaleic acid, when heated to about $50-60^\circ$, gives off carbon dioxide and yields glycollic aldehyde ; by distillation of the resulting solution under reduced pressure, the latter compound is obtained in a crystalline condition.

The methyl and ethyl esters are crystalline solids, and it was shown that the former exists in two modifications ; later investigation indicates that the ethyl ester behaves similarly, but the two forms have not yet been completely examined.

Notwithstanding the conclusive evidence above referred to in

support of the dihydroxy-formula for this acid, it is not improbable, as was previously suggested (Trans., 1896, 69, 547), that the compound may, under certain conditions, assume the tautomeric keto-form,

and in some of the later observations it will be noticed that the latter constitution suggests the more rational interpretation of the changes involved.

Condensation with Ammonia. Synthesis of Pyrazinedicarboxylic Acid.

When the ammonium or the sodium salt of dihydroxymaleic acid is mixed with an excess of strong aqueous ammonia and the mixture is allowed to stand for some days at the ordinary temperature, the salt slowly dissolves, and the solution acquires a bright yellow colour. This change is greatly accelerated if the mixture is warmed on a water-bath at about 50—60°, and appears under these conditions to be completed in about half an hour. After removal of the excess of ammonia by evaporation or by distillation under reduced pressure, the addition of an acid causes the evolution of much carbon dioxide together with the separation of a brown, crystalline precipitate consisting of small, transparent prisms. These are very sparingly soluble in boiling water, alcohol, or other solvents, but dissolve easily in alkalis. They dissolve also in concentrated sulphuric acid, and separate out on dilution with water. By repeated recrystallisation from boiling aqueous alcohol or by solution in dilute alkalis and reprecipitation with acids, the crystals become practically colourless. The yield of this product is not large, but it appears to be increased if a current of air is drawn through the mixture during the preparation; in this case also the resulting crystals are less discoloured.

The aqueous solution of this substance is acid towards indicators and effervesces with sodium carbonate; with ferrous sulphate, it develops a beautiful violet colour, which is discharged by mineral acids or by alkalis. Ferric salts, on the other hand, produce no colour. Silver, lead, barium, and calcium salts give white precipitates from which the acid can be regenerated in the usual ways; the calcium salt separates from hot solutions in prisms. The solid acid, when heated, begins to decompose, and partly vaporises between 250° and 300° without melting.

Analysis of the purified crystals when dried in a vacuum desiccator gave the following results:

0.1529 gave 0.2397 CO_2 and 0.0372 H_2O . C = 42.75; H = 2.70.

0.2861 „ 40.6 c.c. nitrogen at 18° and 748 mm. N = 16.43.

$\text{C}_3\text{H}_2\text{NO}_2$ requires C = 42.85; H = 2.38; N = 16.66 per cent.

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0.1291 of the air-dried crystals, when kept in a vacuum desiccator until the weight was constant, lost $\text{H}_2\text{O} = 0.0226$; $\text{H}_2\text{O} = 17.50$.

$\text{C}_3\text{H}_2\text{NO}_2, \text{H}_2\text{O}$ requires $\text{H}_2\text{O} = 17.64$ per cent.

0.3322 of the vacuum-dried crystals, when dissolved in standard caustic soda and titrated with standard sulphuric acid, required 7.1 c.c. of caustic soda solution containing 22.386 NaOH per litre. An acid having the formula $(\text{C}_3\text{H}_2\text{NO}_2)_n$, if n -basic, would require 7.06 c.c.

From the above results, it is evident that the composition and properties of this acid correspond in every respect with those of the pyrazine-2:5-dicarboxylic acid, $\text{C}_4\text{H}_2\text{N}_2(\text{CO}_2\text{H})_2, 2\text{H}_2\text{O}$, which was first obtained by Stoehr (*Ber.*, 1891, **24**, 4105) by the oxidation of dimethylpyrazine with potassium permanganate.

The same acid was prepared by Wolff (*Ber.*, 1893, **26**, 721) in the following way. β -Hydroxy-(or β -bromo-)lævulic acid condenses with ammonia to give tetramethylpyrazine, $2\text{C}_5\text{H}_8\text{O}_4 + 2\text{NH}_3 = \text{C}_4\text{N}_2(\text{CH}_3)_4 + 2\text{CO}_2 + 4\text{H}_2\text{O} + \text{H}_2$, and by oxidation of the latter with potassium permanganate the somewhat unstable tetracarboxylic acid, $\text{C}_4\text{N}_2(\text{CO}_2\text{H})_4$, is obtained. The dipotassium salt of this, when heated with water to about 200° , yields the dicarboxylic acid, together with pyrazine and other products.

The identity of the product obtained in the present instance with this dicarboxylic acid is further confirmed by its behaviour when heated. The vacuum-dried substance, when heated in a small distilling flask to about 280 — 300° , gave a white, solid sublimate, together with a volatile liquid which solidified in the neck of the flask to a crystalline mass. These crystals melted at 55° , had the characteristic heliotrope odour of pyrazine, and their aqueous solution gave, with mercuric chloride, a white precipitate.

In the condensation of hydroxylævulic acid with ammonia, as in the formation of dimethylpyrazine from aminoacetone by heat (Gabriel and Pinkus, *Ber.*, 1893, **26**, 2205) and of pyrazine from aminoacetaldehyde or aminoacetal (Wolff, *loc. cit.*, 1830), it will be observed that the changes involved imply the loss of two atoms of hydrogen; for this reason, the addition of oxidising agents, such as mercuric chloride, improves the yield. In the present case, the condensation is of the same type, $2\text{C}_4\text{H}_4\text{O}_6 + 2\text{NH}_3 = \text{C}_4\text{H}_2\text{N}_2(\text{CO}_2\text{H})_2 + 4\text{H}_2\text{O} + 2\text{CO}_2 + \text{H}_2$, but it has not so far been found advantageous to employ oxidising agents other than air, since the addition of metallic salts, such as mercuric chloride, leads to undesirable complications.

With regard to the mechanism of the change, there are, of course, several possible explanations. If carbon dioxide is eliminated in the first stage, the initial product may be tartronic semialdehyde,

hydroxypyruvic acid, $\text{CH}_2(\text{OH})\cdot\text{CO}\cdot\text{CO}_2\text{H}$, or dihydroxyacrylic acid, $\text{CH}(\text{OH})\cdot\text{C}(\text{OH})\cdot\text{CO}_2\text{H}$; condensation of any of these acids with ammonia would evidently take place in a manner similar to that in which Wolff (*loc. cit.*) represents the formation of pyrazine from aminoacetaldehyde. From tartronic semialdehyde, for example, the changes might be as follows

On the other hand, the initial product may be a tetracarboxylic acid which, by oxidation and loss of carbon dioxide, gives the dicarboxylic acid in question:

A change of an entirely different character takes place when the ethyl or methyl ester of dihydroxymaleic acid is treated with aqueous ammonia.

In this case the liquid assumes a deep orange-red colour, and a white precipitate separates which proves to be *oxamide*. The solution contains ammonium oxamate together with another substance which has not yet been obtained sufficiently pure for analysis. It is evident, therefore, that disruption occurs, under these conditions, at the double linkage.

Action of Hydrazines.

It was previously shown (Trans., 1896, 69, 548) that dihydroxymaleic acid reacts with phenylhydrazine only to produce a *salt*, $\text{C}_4\text{H}_4\text{O}_6\cdot 2\text{N}_2\text{H}_3\cdot\text{C}_6\text{H}_5$, a brilliant silver-white, crystalline substance which, when heated for some time with phenylhydrazine acetate solution, becomes orange-yellow, loses carbon dioxide, and is converted into Nastvogel's osazone of glyoxalcarboxylic acid:

this crystallises in needles or prisms which melt at 222—224° (compare Trans., 1901, 79, 100, and 1902, 81, 430).

When the salt is boiled with water alone, it behaves similarly, but in this case the osazone remains principally dissolved as a colloidal solution, from which it immediately separates on the addition of a drop of acetic acid.*

Other hydrazines are now found to behave with dihydroxymaleic acid in a similar way; hydrazine hydrate, for example, gives a white precipitate consisting of long needles or prisms, which has the composition $C_4H_4O_6 \cdot 2N_2H_4$. Analysis gave N = 26.55 per cent., theory requiring 26.41 per cent.

Phenylbenzylhydrazine likewise gives a white, flocculent precipitate which, when washed with alcohol and dried in a vacuum desiccator, melts at 128—130°, and gives, on analysis, N = 10.57 per cent., $C_4H_4O_6 \cdot 2N_2H_2BzPh$ requiring 10.29 per cent. When this salt is heated with water to boiling for about an hour, it becomes converted into a gummy mass, which, when treated with hot alcohol, only partially dissolves. The residue, after treatment with alcohol, was recrystallised first from hot benzene and then from a mixture of toluene and absolute alcohol; in this way, it was obtained in the form of nearly colourless prisms which are aggregated together, and which, when exposed to the air, gradually turn pink at the edges. These crystals, after drying at 100°, melted at 197°.

0.1590 gave 0.4680 CO_2 and 0.0905 H_2O . C = 80.27; H = 6.32.

0.1445 „ 17.27 c.c. nitrogen at 19.5° and 731 mm. N = 13.46.

$C_{28}H_{26}N_4$ requires C = 80.38; H = 6.22; N = 13.39 per cent.

This product is therefore evidently the phenylbenzyllosazone of glyoxal,† $\begin{matrix} CH:N_2BzPh \\ | \\ CH:N_2BzPh \end{matrix}$, which was first obtained by Ruff and Ollendorff from the products resulting when galactonic and lactobionic acids are oxidised in presence of iron; it was also obtained by the same authors directly from glyoxal (*Ber.*, 1900, 23, 1806).

When glycollic aldehyde is heated for some time on a water-bath with an alcoholic solution of phenylbenzylhydrazine, a product is obtained which is in all respects the same as the osazone here described. It is evident that in this case the $CH_2 \cdot OH$ group becomes oxidised, that is to say, that an osazone is formed from a sugar of the aldose type

* When the phenylhydrazine salt is heated with dry pyridine the product consists principally of the phenylosazone of glyoxal.

† Strictly speaking, this is of course a *dihydrazone* of glyoxal or an *osazone* of glycollic aldehyde, but the above name is employed in accordance with common usage.

by the action of a secondary aromatic hydrazine (compare Ofner, *Ber.*, 1904, **37**, 3362).

It was previously stated that methyl and ethyl dihydroxymaleates give no reaction with phenylhydrazine; this is true as regards the initial result, but it is now found that on prolonged heating a change does slowly take place. When, for example, the ethyl ester is heated on a water-bath with phenylhydrazine acetate in either alcoholic or acetic acid solution for about an hour and is then allowed to stand for some time, an orange-coloured precipitate slowly separates. This, after being washed with cold alcohol and recrystallised from hot alcohol or glacial acetic acid, is obtained in the form of brilliant orange-coloured prisms which melt sharply at 154°. On analysis, these gave C = 63.57, H = 4.79 per cent., the formula $C_{18}H_{16}O_3N_4$ requiring C = 64.28, H = 4.76. The properties of this compound correspond in every way with those of the product which Wislicenus and Scheidt (*Ber.*, 1891, **24**, 4210) obtained by the action of phenylhydrazine on the ethyl ester of ethoxoxaloacetic acid, and which they designate as the ethyl ester of phenylhydrazonketophenylpyrazolonecarboxylic acid,

The same compound was obtained by Anschütz and Parlato by the action of phenylhydrazine on the ethyl ester of dioxosuccinic acid (*Ber.*, 1892, **25**, 1979), and it results also from either of the three isomeric osazones of ethyl dioxosuccinate when they are heated with glacial acetic acid (Anschütz and Pauly, *Ber.*, 1895, **28**, 66).

When ethyl dihydroxymaleate is heated with an excess of phenylhydrazine in alcoholic solution, there is also formed after a time a bright scarlet substance, which is nearly insoluble in boiling alcohol and which melts at 256—259°. This is evidently the compound first noticed by Peny, which arises from the action of phenylhydrazine on either the ethyl or propyl esters of dioxosuccinic acid (*loc. cit.*, 67).

It appears therefore that the final products obtained by the continued action of phenylhydrazine on the esters of dihydroxymaleic acid are the same as those which result from dioxosuccinic esters,

that is, the esters obtained from dihydroxytartaric acid.

The above results are most easily interpreted if it is supposed that dihydroxymaleic acid assumes the tautomeric form

and that the CHOH group is oxidised by phenylhydrazine in the usual way.

Preparation of the Acid (compare Trans., 1894, **65**, 901).

A cold, nearly saturated solution of tartaric acid, containing a small proportion of iron in the ferrous condition, is surrounded by a freezing mixture, and a previously cooled solution of hydrogen peroxide (20 volume or stronger) is very slowly added, in small portions at a time, with constant stirring, until the mixture assumes a nearly permanent black tint.

No separation of the acid occurs from this mixture even on long standing, unless a dehydrating agent is added. Nordhausen sulphuric acid was found to be the most suitable agent for this purpose; it has, of course, to be introduced with the greatest care in order to prevent rise of temperature, and is best dropped from a long funnel below the surface of the liquid. After persistent stirring, the crystals of dihydroxymaleic acid begin to separate in a few minutes and continue to deposit for several days when the mixture is kept at about 0°.

The yield of the product is always small as compared with the amount of tartaric acid employed: this is partly due to the unstable nature of the acid and to the fact that a considerable portion remains in solution after crystallisation ceases; but the principal cause is to be found in the circumstance that the product itself is very readily oxidised by hydrogen peroxide in presence of iron (compare Fenton and Ryffel, Trans., 1902, **81**, 434), and the oxidising agent only preferentially attacks the tartaric acid when the latter is in large excess. For this reason, it is never advantageous to employ more than about one-tenth of the calculated quantity of hydrogen peroxide.

Many experiments have been undertaken with the object of improving the yield, but so far only with partial success. The substitution of orthophosphoric acid (sp. gr. 1·7) for Nordhausen sulphuric acid as a dehydrating agent is found to be an advantage in many respects; the yield certainly appears to be better and the reagent may be added with greater boldness and with less danger of a rise in temperature, but it is important to make sure of the absence of impurities, such as sodium or calcium salts, which would contaminate the product.

When anhydrous sodium sulphate is used in place of the above-named dehydrating agents, the product which separates proves to be the *acid sodium* salt; the yield of this is very much greater, in proportion to theory, than that of the free acid when acid dehydrators are used, and for certain purposes the manufacture of this salt is therefore to be preferred.

Acid Sodium Salt.

If to the mixture obtained by oxidation of tartaric acid in the manner above described a strong solution of a sodium salt is added, a bulky, crystalline precipitate soon separates, which consists of long, lustrous needles or prisms; addition of the sodium salt in the solid state gives a similar result. This product is less soluble than sodium hydrogen tartrate, and it is advisable, if the solid salt is used, so to adjust the final concentration of the mixture (by previous trial with a small portion of the original solution) that no separation of the acid tartrate is likely to occur.

This product, dried in the air, was analysed with the following results:

- I. 0.5086 gave 0.1736 Na_2SO_4 . Na = 11.05.
 II. 0.3107 „ 0.1072 Na_2SO_4 . Na = 11.19.
 $\text{NaHC}_4\text{H}_2\text{O}_6 \cdot 2\text{H}_2\text{O}$ requires Na = 11.16 per cent.

The aqueous solution of this salt has a strongly acid reaction, and when titrated with caustic soda, using phenolphthalein as indicator, the following numbers were obtained:

III. 1.0953 grams required 8.7 c.c. soda solution, containing 14.13 grams Na per litre, theory requiring 8.6 c.c.

This salt is more stable than the free acid and may be recrystallised from hot water with but little loss; when, however, the aqueous solution is heated for some time, or when it is boiled, carbon dioxide is evolved and a white precipitate separates; the solution remaining gives the reactions of glycollic aldehyde, and the white precipitate proves to be the normal salt of dihydroxymaleic acid. 0.1855 gave 0.1344 Na_2SO_4 . Na = 23.47. $\text{Na}_2\text{C}_4\text{H}_2\text{O}_6$ requiring Na = 23.95 per cent.

It is evident, therefore, that the acid salt breaks up into normal salt and free acid, the latter then yielding glycollic aldehyde and carbon dioxide.

When this acid salt is covered with acetic acid and treated with bromine in slight excess, it is, like the free acid, oxidised to the state of dihydroxytartrate, the change being approximately quantitative:—

2.9 grams of acid sodium dihydroxymaleate, when oxidised by bromine and the product neutralised with sodium carbonate, gave 3.7 grams of sodium dihydroxytartrate (air-dried), the theoretical amount being 3.81.

Oxidation with Mercuric Oxide. Preparation of Mesoxalic Acid.

When dihydroxymaleic acid is shaken with cold water and the calculated quantity of freshly precipitated mercuric oxide, it is gradually oxidised to dihydroxytartaric acid with separation of metallic mercury. Further, when an aqueous solution of dihydroxytartaric acid is heated at about 50—60° with mercuric oxide in calculated quantity, carbon dioxide is evolved and the solution contains mesoxalic acid. The solution so obtained is free from mercury, but is liable to contain some oxalic acid, especially if the temperature is not carefully regulated. The operation may, of course, be performed in a single stage from dihydroxymaleic acid, using two molecules of mercuric oxide for one molecule of the acid.

For the purpose of obtaining pure mesoxalic acid, however, it is found preferable to start with dihydroxytartaric acid, prepared in the manner previously described (Trans., 1898, 73, 72), and to employ an excess of mercuric oxide.

In this case, mesoxalic acid is converted into a sparingly soluble mercury salt, and by decomposing this with hydrogen sulphide, avoiding excess, the acid is obtained free from oxalic acid. On evaporation of the resulting solution in a vacuum desiccator over sulphuric acid, deliquescent crystals of mesoxalic acid remain, which are practically pure without recrystallisation, the product melting at about 110—115°.

On addition of phenylhydrazine hydrochloride or acetate to the aqueous solution, the pale yellow needles of mesoxalic acid phenylhydrazone begin, after a few minutes, to separate in the cold. These, after being well washed and dried in a vacuum desiccator, melted at 170—171° (compare Trans., 1902, 81, 433).

0.1498 gave 17.5 c.c. nitrogen at 18° and 759 mm. $N = 13.73$.

$C_9H_8O_4N_2$ requires $N = 13.46$ per cent.

It would appear that this reaction affords one of the most simple methods for the preparation of mesoxalic acid, and the yield is good; from one gram of dihydroxytartaric acid, 1.1 grams of mesoxalic acid hydrazone were obtained, the theoretical yield being about 1.2 grams.

Formation of Mesoxalic Semialdehyde.

It was shown in a former communication (Fenton and Ryffel, Trans., 1902, 81, 434) that when dihydroxymaleic acid reacts with ferric salts in aqueous solution at about 40°, carbon dioxide is liberated, and the resulting solution contains the semialdehyde of mesoxalic acid, $CHO \cdot CO \cdot CO_2H$. This product was identified by (a) the immediate

formation of Nastvogel's osazone when the solution is mixed with phenylhydrazine acetate, (b) the oxidation to mesoxalic acid by means of alkaline cupric hydroxide, and (c) the production of Söderbaum's dioximinopropionic acid by the action of hydroxylamine.

An objection to this mode of preparation of the semialdehyde is the difficulty of removing the large amount of ferrous salt which is produced in the reaction. Later investigation has shown that mercuric chloride may advantageously be employed as oxidising agent and that the mercury is, in this case, entirely separated as calomel, according to the relation

The mercuric chloride is dissolved in hot water and the solution kept at about 60—70°; the calculated quantity of crystallised dihydroxymaleic acid is added in small portions at a time, and the mixture is then allowed to stand for an hour or two. The resulting solution, if the proportions have been accurately adjusted, is now practically free from mercury, any traces which may remain being removed by cautious addition of hydrogen sulphide. The solution gives all the reactions of mesoxalic semialdehyde, and it may be obtained free from the admixed hydrochloric acid by careful addition of the calculated quantity of silver carbonate; the product, however, appears to be much more stable in presence of free hydrochloric acid, and in this condition it may be preserved for some time with but little change. It may be evaporated to the consistence of a syrup in a vacuum desiccator, over solid caustic potash and sulphuric acid, and even rapid evaporation on a water-bath does not altogether destroy it; but when the solution is boiled for some time or is repeatedly evaporated it loses carbon dioxide yielding glyoxal. These changes can be easily followed by examination of the osazones resulting from the addition of phenylhydrazine.

Mesoxalic semialdehyde is not destroyed by neutralisation with sodium carbonate in the cold; boiling with sodium carbonate, however, changes it to tartronic acid (see below).

Since the aldehyde-hydrate of mesoxalic semialdehyde,

might be tautomeric with the missing trihydroxyacrylic acid,

it appeared to be possible that the substance should, under certain conditions, condense with urea to give uric acid, and several experiments are being made in this direction. When the aqueous solution of the semialdehyde is mixed with urea and allowed to stand for several hours, a crystalline substance slowly separates; the change is

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accelerated when hydrochloric acid is present, and it takes place in a few minutes if the mixture is heated on a water-bath.

This crystalline product is very sparingly soluble in boiling water, but dissolves easily in alkalis; it dissolves also in cold concentrated mineral acids, and separates again in the crystalline form when the solutions are diluted with water. The crystals consist either of needles, prisms, or octahedra according to the conditions under which they are separated; they are at first somewhat discoloured, but by repeated recrystallisation become quite colourless.

When heated, the substance decomposes without melting, giving off hydrogen cyanide, ammonia, and a white sublimate. So far many of the properties resemble uric acid, but when evaporated with nitric acid the white or yellow residue obtained gives only a brownish-orange colour on addition of ammonia. If strong nitric acid is used in this experiment and the residue, after evaporation, is treated with caustic potash or soda, a faint bluish-violet colour is produced, and this, on the addition of a drop of sodium hypochlorite, changes to an intense purple coloration.

Analysis of the crystals, dried at 100° , furnished the following results:

0.1133 gave 0.1378 CO_2 and 0.0435 H_2O . $\text{C} = 33.17$; $\text{H} = 4.26$.

0.0859 „ 28.9 c.c. nitrogen at 19° and 755 mm. $\text{N} = 39.19$.

$(\text{C}_2\text{H}_3\text{ON}_2)$ requires $\text{C} = 33.80$; $\text{H} = 4.22$; $\text{N} = 39.43$ per cent.

From the above results it is evident that the product is *glycoluril*,

or “acetylene-urea,” which was first obtained by Reineck (*Annalen*, 1864, **131**, 119) by the reduction of allantoin with sodium amalgam; Schiff obtained the same substance later (*Annalen*, 1877, **189**, 157) by the condensation of urea with glyoxal, and the products derived from these two sources were at first thought to be different. Widmann, however (*Ber.*, 1886, **19**, 2477), carefully compared the properties of the products and showed that they were identical.

The properties of glycoluril, as described by these authors, coincide entirely with those of the substance at present under consideration, but the remarkable colour reaction given by alkaline hypochlorites in the manner above-mentioned appears to have been entirely overlooked.

The formation of glycoluril in the present case may, of course, arise from the action of urea on glyoxal, supposing that the latter is first

formed by decomposition of the mesoxalic semialdehyde. But since the product is obtained in considerable yield under conditions in which mesoxalic semialdehyde is stable, it appears more probable that the initial product is glycolurilcarboxylic acid, $C_4H_5N_4O_2 \cdot CO_2H$ (isomeric with pseudo-uric acid), which then loses carbon dioxide to give glycoluril.

By modification of the conditions, it is yet hoped that it may be possible to isolate this glycolurilcarboxylic acid, or perhaps, by isomeric change, to obtain pseudo-uric or uric acids. If the carbamide salt of dihydroxymaleic acid is oxidised with mercuric chloride under similar conditions to those above-mentioned, the product is a dark brown, very sparingly soluble substance, which differs from glycoluril in that it dissolves in strong nitric acid to an intense crimson-red solution. This product has yet to be identified.

Relation of Mesoxalic Semialdehyde to Tartronic Acid.—It was pointed out above that a solution of mesoxalic semialdehyde is fairly stable in acid solution, and that when decomposition does take place, by continued heating or evaporation, the products are, mainly at any rate, glyoxal and carbon dioxide. In presence of alkalis, however, the semialdehyde is quickly changed on heating, the product in this case being tartronic acid.

This change was illustrated in the following manner. A solution of the semialdehyde was divided into two parts, and one part was made alkaline with sodium carbonate in the cold, acidified with acetic acid, and precipitated with lead acetate. The resulting white precipitate was then well washed, suspended in water, and decomposed with hydrogen sulphide, avoiding excess; on adding phenylhydrazine acetate to the solution so obtained, the bright orange precipitate of Nastvogel's osazone was obtained, the semialdehyde having undergone little if any change. The other part of the original solution was treated exactly in the same manner, except that after addition of sodium carbonate the alkaline solution was heated on a water-bath at $90-100^\circ$ for about 15 minutes. In this case, the solution, after acidification with acetic acid, no longer reacted with phenylhydrazine acetate, and the acid solution resulting after decomposition of the lead salt with hydrogen sulphide, when evaporated to small bulk and allowed to stand, set to a mass of transparent crystals. These were recognised by all their properties to be tartronic acid. After drying at 100° , they melted at $158-159^\circ$ (compare Trans., 1898, 73, 74), and without recrystallisation furnished the following result on analysis:

0.1995 gave 0.2142 CO_2 and 0.0599 H_2O . C = 29.28; H = 3.33.

$C_3H_4O_5$ requires C = 30.00; H = 3.33 per cent.

The yield of tartronic acid, calculated from the weight of dihydroxy-

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maleic acid originally taken, amounted to about 60 per cent. of that required by theory; bearing in mind, however, the unavoidable loss involved in the several operations, there is little doubt that the actual yield is much greater than this. This change, like that of glyoxal to glycollic acid, is an illustration of the great readiness with which the group $-\text{CO}\cdot\text{CHO}$ is transformed, in presence of alkalis, to $-\text{CH}(\text{OH})\cdot\text{CO}_2\text{H}$.

The facts here recorded have an interesting bearing on the mode of decomposition of dihydroxytartaric acid when its aqueous solution is heated (*loc. cit.*, p. 73). The products are in this case only tartronic acid and carbon dioxide. Addition of hydrochloric acid appears only to have the effect of making the dihydroxytartaric acid more stable; such a mixture may be evaporated on a water-bath almost to dryness without complete destruction of the dihydroxy-acid, but the decomposition products are here again only tartronic acid and carbon dioxide.

No mesoxalic semialdehyde or glyoxal has been detected at any stage of this decomposition, and this fact would appear to exclude the very plausible hypothesis that mesoxalic semialdehyde is the initial product, for under exactly similar conditions mesoxalic semialdehyde would either remain undecomposed or would yield glyoxal. It is evident, therefore, that the generally accepted formula for dihydroxytartaric acid does not convey a clear indication of this decomposition.

With the *salts* of dihydroxytartaric acid, however, the case is different, since, in reference to the experiments here mentioned, the formation of a tartronate would, according to the above hypothesis, be expected, the mesoxalic semialdehyde first formed being changed to tartronic acid in presence of the resulting alkali.

Formation of Glycollic Aldehyde.

Dihydroxymaleic acid, when heated with water to about $50-60^\circ$, rapidly loses carbon dioxide and is converted nearly quantitatively to glycollic aldehyde (Trans., 1895, 67, 774). The dry acid undergoes no change when heated to this temperature—or even at $90-100^\circ$ —nor does it decompose when heated under boiling benzene or chloroform. The addition of a few drops of water, however, to the hot mixture causes an immediate evolution of carbon dioxide. The hypothesis previously suggested to account for these facts (*loc. cit.*, 777) was that combination with water first takes place to produce trihydroxy-succinic acid, and that this then loses two molecules of carbon dioxide, giving glycollic aldehyde hydrate.

It had recently been observed, however, that the perfectly dry acid, $\text{C}_4\text{H}_4\text{O}_6$, decomposes completely and smoothly when heated with dry

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pyridine to 50—60°. After distilling off the pyridine under reduced pressure, crystals of glycollic aldehyde appear in the neck of the flask and may be purified from any adhering pyridine by washing with ether.

This fact therefore appears to show that the decomposition is rather to be ascribed to the instability of the negative ion, $C_2(OH)_2(CO_2)_2$, and is therefore conditioned by the ionising capacity of the solvent employed.

When alcohol is used as solvent, decomposition takes place only very slowly on long boiling. The product in this case is different from glycollic aldehyde, and its nature has yet to be determined.

Attempts are being made so to arrange the conditions under which decomposition is effected that only one molecule of carbon dioxide is lost from one molecule of the acid—a change which does occur when simultaneous oxidation takes place—and if this could be accomplished the result should be, as before mentioned, either dihydroxyacrylic acid, tartronic semialdehyde, or hydroxypyruvic acid.

Many other interesting properties of dihydroxymaleic and dihydroxytartaric acids and their derivatives are still under investigation, and it is hoped that the results will shortly be ready for publication.

From the accounts given in this and in former communications, it will be evident that, starting with dihydroxymaleic acid, it is easy to prepare, in either one or two simple operations, any of the following compounds—*dihydroxytartaric acid*, *tartronic acid*, *mesoxalic acid*, *glycollic aldehyde*, *mesoxalic semialdehyde* *glyoxal*, *pyrazinedicarboxylic acid*. In view of these and many other applications, it is hoped that chemical manufacturers may see their way to prepare and supply dihydroxymaleic acid as a commercial article.

In conclusion, the author desires to acknowledge the very valuable assistance which he has received during a considerable portion of these later researches from the co-operation of Mr. J. H. Ryffel, M.A., of Peterhouse, Cambridge, and Guy's Hospital, and to place on record his high appreciation of Mr. Ryffel's scientific enthusiasm and analytical skill.

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