CLXIX.—*Studies on Certain Aliphatic Hydroxy-acids.*

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DURING a course of investigations on the oxidation of organic compounds in presence of iron as catalyst, a considerable number of new substances have been brought to light, and several relationships of interest have been observed, especially amongst the hydroxy-acids of the three-carbon and four-carbon series (Trans., 1904, **65**, 899; 1895, **67**, 48, 744; 1896, **69**, 546; 1897, **71**, 375; 1898, **73**, 71; 1900, **77**, 77; 1902, **81**, 426; 1905, **87**, 804; etc.).

These investigations are being continued by the present authors, and an account is here given of some of the results which have recently been obtained.

Oxalacetic Acid and its Relationship to Dihydroxymaleic Acid.

It has been shown by Fenton and Jones (*loc. cit.*, 1900, **77**, 77) that, by the oxidation of malic acid by hydrogen dioxide in presence of ferrous iron, oxalacetic acid is obtained. The acid is isolated from the reaction mixture by addition of concentrated sulphuric acid and extraction with ether; when prepared in this manner, the product melts at 180—184°. Wohl and Oesterlin (*Ber.*, 1901, **34**, 1139) afterwards showed that by action of pyridine on diacetyltartaric anhydride and decomposition of the resulting compound with dilute acids, an acid of the composition and properties of oxalacetic acid is obtained, which, however, melts at 152°. Later it was found that this product when dissolved in sulphuric acid (30 per cent.) and extracted with ether is converted into the modification melting at 184°. From measurements of molecular refraction, and from the behaviour of the acids towards ferric chloride, potassium permanganate, etc., Wohl concludes that both acids are enolic, the difference between them being ascribed to geometrical isomerism. If this is admitted, it is evident from the melting points, mode of transformation, and anhydride formation, that the acids melting at 184° and 152° are hydroxyfumaric and hydroxymaleic acids respectively.

The constitution of dihydroxymaleic acid was inferred (Trans., 1905, **87**, 804) from the readiness with which anhydride formation occurs and from the fact that an acid, apparently isomeric, is produced from it by action of fuming hydrobromic acid. This configuration was not insisted on, however, since the mode of formation from *d*-tartaric acid, and the production of racemic acid by action of hydriodic acid, would be more easily explained if the acid is regarded as dihydroxyfumaric acid.*

Some light is thrown on these problems by the recent observations of the present authors, since they find that the modification of "oxalacetic acid" of higher melting point can be directly transformed into "dihydroxymaleic acid."

* It has been suggested that the initial form of the acid, obtained in aqueous solution, may be trihydroxysuccinic acid or the keto-acid, $\text{CO}_2\text{H}\cdot\text{CH}(\text{OH})\cdot\text{CO}\cdot\text{CO}_2\text{H}$ (compare Nef, *Annalen*, 1910, **376**, 116), and that this form is changed by the concentrated sulphuric acid used in the preparation. Recent experiments show, however, that the usual form, crystallising in diamond-shaped plates, is obtained, without the use of sulphuric acid, by evaporation of the original solution in a vacuum.

When oxalacetic acid (m. p. 180—184°) is dissolved in a cold solution of sodium hydroxide in slight excess, and bromine is gradually added in one molecular proportion, the solution being maintained alkaline, the resulting solution gives an intense violet colour with ferric chloride; addition of dilute sulphuric acid changes this to a transient green. If the solution is just acidified with acetic acid and barium acetate is added, a bulky, white precipitate is obtained, which, when decomposed with dilute sulphuric acid, yields again the same colour reactions with ferric salts.

This barium salt when dried in a vacuum desiccator and afterwards at 100° gave the following result on analysis:

0.2906 gave 0.2399 BaSO₄. Ba=48.53.

C₄H₂O₆Ba (barium dihydroxymaleate) requires Ba=48.40 per cent.

If the original solution, after addition of bromine, is acidified with sulphuric acid and extracted with ether, a residue is obtained on evaporation of the ethereal solution which, when dissolved in warm water, gives, on cooling, the characteristic diamond-shaped plates of dihydroxymaleic acid. A similar result is obtained by decomposing the dried barium salt with dilute sulphuric acid. From this result it would appear that, if "the spatial relations of the original molecule persist in the new product," the geometrical configuration of the "oxalacetic" acid of higher melting point must be the same as that of "dihydroxymaleic acid." Presumably, therefore, the result must be regarded as evidence in favour of ascribing the fumaroid configuration to the latter acid. The result, however, might be accounted for in other ways; thus, Wohl considers that the normal salts of oxalacetic acid have the keto-form, and that when these are decomposed with dilute acids the less stable maleinoid form first arises, in accordance with Ostwald's rule. In the present case, therefore, the keto-form of oxalacetic acid may give the corresponding form of "dihydroxymaleic acid," and this on acidification may undergo a similar transformation to the maleinoid form.

Bromo-oxalacetic Anhydride or Bromohydroxymaleic Anhydride.

The oxidation of oxalacetic acid to dihydroxymaleic acid referred to in the last section may be effected in two stages, the free acid being brominated in water, ether, alcohol, etc., as solvent, and the product then acted on by alkali hydroxides. The initial stage appears to be of considerable interest, and the product has, after some difficulty, been isolated in the form of its anhydride.

When oxalacetic acid is dissolved in ether and bromine is slowly added, the colour of the bromine is instantly discharged until nearly the calculated quantity (1 mol.) has been added. If the resulting

solution is now rapidly distilled, under diminished pressure, to remove the ether and hydrogen bromide, a syrup remains which sometimes partly sets to a buttery, crystalline mass. This product again gives the intense violet colour when treated with alkali hydroxide and ferric chloride. The product is, however, remarkably unstable; if it is kept overnight in a vacuum desiccator, a considerable quantity of hydrogen bromide is liberated, and crystals of oxalacetic acid (m. p. 180—184°) separate. About half the original acid can be actually recovered in this way. The mother liquor from these crystals now no longer gives the violet colour with ferric salts and alkali; but sodium hydroxide or carbonate produces a white precipitate and phenylhydrazine an orange precipitate, which, after crystallisation from alcohol, melts at 203°.

A possible explanation of this remarkable change is that the initial product is bromohydroxyfumaric acid; that the group $\cdot\text{C}(\text{OH})\cdot\text{CBr}\cdot$ is unstable, and that the two molecules of the acid resolve themselves into oxalacetic and dihydroxytartaric acids, hydrogen bromide being evolved:

Since, however, water would be necessary to complete this change, it may be assumed that the anhydride of dihydroxytartaric acid is produced instead of the acid.

Regarding the matter from this point of view, it appeared probable that acetylation of the hydroxy-group in bromohydroxyfumaric acid might yield a product of greater stability, and it was found that if the product obtained as described above (by bromination and distilling off the ether) is immediately heated with acetyl chloride or acetic anhydride, its colour-giving property remains much more permanent. Proceeding in this way, however, it was found impossible to obtain any crystalline compound, so that the experiment was modified as follows:

The oxalacetic acid was dissolved in hot glacial acetic acid, the solution cooled, and the calculated quantity of bromine run in. Excess of acetyl chloride was then added, and the mixture kept boiling in a reflux apparatus for about fifteen minutes. The solvent was then distilled off under greatly diminished pressure, and the residual syrup left in a vacuum desiccator over sulphuric acid and potassium hydroxide. After remaining for a day or two, large, semi-transparent prisms separated; these were drained, pressed, and recrystallised from dry ether. The crystals so obtained melt at 114—116°. They dissolve readily in water, and the solution gives at once the characteristic intense violet colour with ferric chloride

in presence of alkali hydroxide. With ferric chloride alone an intense red colour is obtained.

Analysis shows that this product is not an acetyl derivative, as was at first expected, but an anhydride of bromo-oxalacetic acid:

0.2019 gave 0.1833 CO₂ and 0.0144 H₂O. C=24.8; H=0.79.

0.2796 „ 0.2704 AgBr. Br=41.2.

C₄H₃O₄Br requires C=24.8; H=0.52; Br=41.4 per cent.

The product is therefore either

When oxalacetic acid itself is treated under similar conditions, without bromination, with acetic acid and acetyl chloride, a crystalline product results, which, when recrystallised from ether, melts at 88—89°. (Found, C=45.5; H=2.7. C₆H₄O₅ requires C=46.1; H=2.5 per cent.)

This compound is evidently identical with the acetoxymaleic anhydride:

(m. p. 89—91°), which Michael obtained by the action of acetic anhydride on acetylenedicarboxylic acid (*Ber.*, 1895, **28**, 2511).

From these observations it would appear, regarding oxalacetic acid as the hydroxy-form, that the initial bromination prevents acetylation. This circumstance might be ascribed either to the steric hindrance of the bromine atom or to a tautomeric change to the keto-form during one of the operations involved.

The bromine in this compound is extremely reactive, and a further study of its reactions will probably be of much interest.

Isomeric Esters of Dihydroxymaleic Acid.

The ethyl and methyl esters of dihydroxymaleic acid are readily obtained by the usual method. The alcoholic solution of the acid is saturated, or nearly saturated, with hydrogen chloride, and the mixture allowed to remain. The methyl ester separates to a large extent after a few hours. In the case of the ethyl ester the liquid is distilled to small volume under diminished pressure, when the residual liquid sets, on cooling, to a crystalline mass.

It was previously shown that each of these esters exists in two modifications having distinct crystalline forms, but the differences were not further investigated. The two forms of the ethyl ester have now been more closely studied, with the following results: The crystalline mass obtained in the preparation, described above, is well drained, pressed, and allowed to dry in the air. It is then

digested with ether. One portion dissolves immediately, and crystallises from this solution in long, silky needles (form A). The portion remaining is only very sparingly soluble in ether; it is washed repeatedly with ether, and is then found to consist of short, rod-like prisms (form B). In other organic solvents, also, the (A) form has a much greater solubility. Both forms give the same result on analysis:

(A) 0.1605 gave 0.2752 CO_2 and 0.0822 H_2O . $\text{C}=46.7$; $\text{H}=5.69$.

(B) 0.1251 „ 0.2113 CO_2 „ 0.0660 H_2O . $\text{C}=47.0$; $\text{H}=5.4$.

$\text{C}_8\text{H}_{12}\text{O}_6$ requires $\text{C}=47.05$; $\text{H}=5.88$ per cent.

(A) melts at 68° , (B) at $126-128^\circ$.

Further points of difference are the following:

(1) Alcoholic ferric chloride gives a dark but transient green colour with an alcoholic solution of (A); no colour with (B).

(2) Alkali hydroxides give at once a lemon-yellow colour with (A) and no colour with (B).

(3) Phenylhydrazine reacts slowly with both forms when they are heated with the reagent in alcoholic solution, but with (A) the change is much more rapid. The product eventually obtained is, as previously shown, the pyrazolone derivative which Anschütz and Parlato prepared from ethyl dihydroxytartrate (dioxysuccinate). It crystallises in orange needles melting at 154° (Trans., 1905, **87**, 810).

(4) When the (A) form is mixed with acetyl chloride it dissolves immediately, and after boiling in a reflux apparatus for a short time and removal of the excess of solvent, yields a crystalline mass. This product (ethyl diacetoxymaleate,

dissolves unchanged in boiling water, and separates on cooling in fine needles, which melt at 68° :

0.1502 gave 0.2731 CO_2 and 0.0737 H_2O . $\text{C}=49.6$; $\text{H}=5.4$.

$\text{C}_{12}\text{H}_{16}\text{O}_8$ requires $\text{C}=50.0$; $\text{H}=5.5$ per cent.

The form (B) when boiled for an hour or more with considerable excess of acetyl chloride is scarcely affected. The greater part remains insoluble, and the small quantity which passes into solution leaves, on evaporation, only a syrup, which does not crystallise even on keeping in a desiccator.

The experiment was then repeated with acetic anhydride in place of acetyl chloride. In this the (B) ester dissolves at once on warming. After heating on a water-bath for half an hour, and distilling off the solvent under diminished pressure, the residue set to a mass of long needles. This product was found to have all the properties of the (A) ester, and gave the same result on analysis. It was

subsequently found that the (A) ester is not altered by treatment with acetic anhydride in similar circumstances.

The effect of heating the (B) ester with acetic anhydride is therefore merely its conversion into the (A) form.

(5) In a previous communication (*loc. cit.*) it has been stated that the ethyl ester of dihydroxymaleic acid undergoes a remarkable change when kept in a desiccator over sulphuric acid or phosphoric oxide in presence of air. In these circumstances it becomes partly or entirely converted into a yellow liquid after about twelve hours; this change is attended at first with a slight increase in weight, after which the weight regularly diminishes, the loss continuing for some weeks. When kept in the atmosphere at the ordinary temperature the ester is quite stable, and remains unaltered for months. These experiments were made with the initial product obtained in the preparation of the ester, or with the same recrystallised from ether, and the fact of the existence of two forms was not then recognised. It is now found that it is only the (A) form that undergoes this change. The (B) form remains quite unaltered when kept in the desiccator, in presence of air, at any rate, for some weeks. This difference in the behaviour of the two forms is most striking, and it may perhaps afford evidence with regard to the character of the isomerism.

The nature of the change which takes place when the (A) ester undergoes liquefaction in this way was at first not easy to understand. It is now found, however, that the resulting liquid product when dissolved in alcohol reacts at once with phenylhydrazine, and yields the pyrazolone derivative melting at 154° , which has been referred to above. Presumably, therefore, the change consists in the oxidation and dehydration of ethyl dihydroxymaleate to ethyl dioxosuccinate:

$\text{CO}_2\text{Et}\cdot\text{C}(\text{OH})\cdot\text{C}(\text{OH})\cdot\text{CO}_2\text{Et} + \text{O} = \text{CO}_2\text{Et}\cdot\text{CO}\cdot\text{CO}\cdot\text{CO}_2\text{Et} + \text{H}_2\text{O}$,
a supposition which would also account for the yellow colour of the product. Even if this simple explanation is the true one, it is somewhat remarkable that the dehydration is essential.

(6) A dilute aqueous solution of potassium permanganate is instantly decolorised when added to a solution of (A) in acetone, whereas a solution of (B) in the same solvent is only slowly affected at first; the colour in the latter case persists for a minute or so.

In addition to the behaviour of the two esters towards the reagents mentioned, there are many other points of difference which are being further studied. The isomerism in this case appears to be of particular interest because of the very sharp differences in properties and the persistence of the two forms.

In attempting to account for these remarkable differences, the

very commonly occurring problem is encountered of deciding whether the phenomenon is one of keto-enolic isomerism or of geometrical isomerism. The same problem presents itself in oxalacetic acid, and appears, as above mentioned, to have been successfully solved by Wohl, although differences of opinion may still exist with regard to his conclusions.

In the present case the authors are inclined to attribute the difference to keto-enolic isomerism, which would easily account for most of the facts, such as the behaviour towards ferric chloride, acetyl chloride, potassium permanganate, and phenylhydrazine. The alternative hypothesis is, however, by no means excluded, and would afford perhaps a more simple explanation of the peculiar behaviour of the (A) ester when dehydrated in presence of oxygen.

Aldehydoglyceric Acid.

It was found by Fenton and Jones (Trans., 1900, 77, 73) that when glyceric acid is oxidised by hydrogen dioxide in presence of ferrous iron, a product is obtained which gives an intense bluish-violet colour with ferric salts in presence of alkali, and which when acted on by phenylhydrazine yields the osazone,

which Nastvogel first obtained from dibromopyruvic acid. This product is of much interest, owing to its relationship with the acid which Will obtained by action of alkalis on collodion wool. The present authors have therefore made a further study of this product, and have succeeded in obtaining it in the crystalline state, although only in small quantities, and not entirely free from admixed solvents.

After oxidation of glyceric acid in the manner previously described, the mixture is treated with calcium carbonate in order to remove small quantities of oxalic acid (which are usually formed in the reaction unless special care is taken), and lead acetate is then added in excess. A bulky, yellow precipitate is thus produced, which, when well washed and decomposed by hydrogen sulphide (avoiding excess), gives a solution having the properties referred to above. The conditions of dilution, etc., chosen are such as to preclude the possibility of the separation of lead glycerate, should any of this acid remain unoxidised.

For analysis, this lead salt was well washed with water, alcohol, and ether, and then dried at 100°:

0.4185 gave 0.3873 PbSO_4 . $\text{Pb} = 63.4$.

$(\text{C}_3\text{H}_3\text{O}_4)_2\text{Pb}\cdot\text{PbO}\cdot\text{H}_2\text{O}$ requires $\text{Pb} = 63.3$ per cent.

The calcium salt was obtained by neutralising the purified solution

of the acid with calcium carbonate and precipitating by alcohol. This, when dried in a desiccator, gave the following numbers :

0.2374 gave 0.1124 CaSO_4 . $\text{Ca} = 13.9$.

$(\text{C}_3\text{H}_3\text{O}_4)_2\text{Ca} \cdot 2\text{H}_2\text{O}$ requires $\text{Ca} = 14.2$ per cent.

With the same salt dried at 100° :

0.1928 gave 0.1105 CaSO_4 . $\text{Ca} = 15.3$.

$(\text{C}_3\text{H}_3\text{O}_4)_2\text{Ca} \cdot \text{H}_2\text{O}$ requires $\text{Ca} = 15.1$ per cent.

If the lead salt, thoroughly washed with water, alcohol, and ether, is covered with dry acetone and carefully decomposed by hydrogen sulphide, and the resulting solution is kept in a vacuum desiccator, a syrup is left. This, when dissolved in ether and mixed with light petroleum until a turbidity is produced, yields after a day or two white crystals, which firmly adhere to the sides of the flask. These crystals are extremely hygroscopic, and there is considerable difficulty in separating them completely from the mother liquor. When dissolved in water they give the characteristic colour with ferric chloride and alkali. (In this case the colour is somewhat slowly developed, a property which is also observed when a solution of the acid prepared from the lead salt in aqueous solution is kept.)

For analysis, the crystals were dissolved off the sides of the flask with ether, and the solution kept in a vacuum desiccator. The result evidently indicates that the product retains traces of the solvent :

0.2155 gave 0.2785 CO_2 and 0.0785 H_2O . $\text{C} = 35.2$; $\text{H} = 4.0$.

$\text{C}_3\text{H}_4\text{O}_4$ requires $\text{C} = 34.6$; $\text{H} = 3.8$ per cent.

From the properties mentioned and from the analyses, it follows that the acid under consideration is either hydroxypyruvic acid, $\text{CH}_2(\text{OH}) \cdot \text{CO} \cdot \text{CO}_2\text{H}$, tartronic semialdehyde, $\text{CHO} \cdot \text{CH}(\text{OH}) \cdot \text{CO}_2\text{H}$, or the tautomeric dihydroxyacrylic acid, $\text{CH}(\text{OH}) : \text{C}(\text{OH}) \cdot \text{CO}_2\text{H}$.

Will (*Ber.*, 1891, **24**, 400) regarded the acid obtained from collodion wool as hydroxypyruvic acid, because of its stability towards bromine and towards alkalis. He stated, however, that the acid is feebly laevorotatory. Since no asymmetric carbon atom is present in hydroxypyruvic acid, it was obvious that further investigation was necessary. Aberson afterwards (*Zeitsch. physikal. Chem.*, 1899, **31**, 17) drew the conclusion that the optical activity is due to impurity, and found that the acid when acted on by hydrocyanic acid, and the product hydrolysed with barium hydroxide, gave rise to glyceric acid. Hence it would appear that the acid is hydroxypyruvic acid, the glyceric acid being the result of decomposition of the "isotartaric" acid,

first produced.

An entirely different conclusion was subsequently arrived at by Neuberg and Silbermann (*Zeitsch. physiol. Chem.*, 1905, **44**, 134). They state that the acid is lævorotatory, and that by action of potassium cyanide they obtain *l*-tartaric acid. By reduction of the original acid with sodium amalgam, *l*-glyceric acid was obtained. For these reasons they assign the formula $\text{CHO}\cdot\text{CH}(\text{OH})\cdot\text{CO}_2\text{H}$ to the acid, and name it "aldehydoglyceric" acid.

In view of these contradictory statements, it appeared that additional evidence was desirable, and it seemed probable that the properties of the acid obtained from glyceric acid by oxidation might throw light on the question. The latter acid is sharply distinguished from Will's acid by the colour reaction with ferric chloride; also by the fact that it is destroyed by heating on a water-bath, a process employed during the preparation of Will's acid.

The acid was obtained in aqueous solution by oxidation of glyceric acid, precipitation as lead salt, and decomposition with hydrogen sulphide. A solution of potassium cyanide, somewhat in excess, was added, and the mixture allowed to remain for about ten days in a closed vessel. The dark-coloured liquid so obtained was treated with a quantity of *N*-sulphuric acid equivalent to the potassium cyanide employed, and heated for about half-an-hour. Barium hydroxide was then added in calculated quantity, the filtered solution concentrated, and precipitated with lead acetate. The precipitate obtained in this way was washed and decomposed under water with hydrogen sulphide, avoiding excess. Ammonia in slight excess was added to the solution, and then calcium chloride; the resulting calcium glycerate, $(\text{C}_3\text{H}_5\text{O}_4)_2\text{Ca}\cdot 2\text{H}_2\text{O}$, was purified by dissolving in hot water and precipitating with alcohol. (Found, $\text{Ca}=14\cdot 2$. Calc., $\text{Ca}=14\cdot 0$ per cent.)

This result, so far as it goes, points to the hydroxypyruvic acid formula for the acid obtained by oxidation of glyceric acid, and consequently would appear to add confirmation to the results of Neuberg and Silbermann. The question of tautomeric change has, however, to be considered, and from the character of the ferric chloride reaction (which closely resembles that of dihydroxymaleic acid) it seems most probable that the product is originally present, principally, at any rate, as dihydroxyacrylic acid.

Action of Semicarbazide.—When this product of oxidation of glyceric acid is mixed with a solution of semicarbazide hydrochloride, white crystals appear after some time, which, after recrystallisation from acetic acid, melt at 221° , and appear to consist of the semicarbazide salt of the semicarbazone,

0.1423 gave 0.1310 CO_2 and 0.060 H_2O . $\text{C}=25.1$; $\text{H}=4.68$.

0.1201 „ 36.8 c.c. N_2 at 15° and 740 mm. $\text{N}=35.5$.

$\text{C}_5\text{H}_{12}\text{O}_5\text{N}_6$ requires $\text{C}=25.4$; $\text{H}=5.07$; $\text{N}=35.6$ per cent.

It is interesting to observe that a compound identical in every respect with the foregoing is obtained when dihydroxymaleic acid in aqueous solution is mixed with semicarbazide hydrochloride and allowed to remain. This result affords further evidence in support of the view previously expressed (Trans., 1905, **87**, 806) that the loss of carbon dioxide from dihydroxymaleic acid probably takes place in two stages, the products being dihydroxyacrylic acid (or its tautomeric form) and glycollaldehyde respectively.

Condensations with Carbamide.

It was shown by the present authors (Trans., 1909, **95**, 1329) that dihydroxymaleic acid when heated alone with carbamide gives rise to a crystalline compound having the molecular formula $\text{C}_3\text{H}_4\text{ON}_2$, which, in most of its properties, closely resembles Marckwald's iminazolone (glyoxalone). Since, however, there appeared to be certain important points of difference, the term "*isoiminazolone*" was provisionally adopted.

In addition to this compound, the condensation of carbamide with dihydroxymaleic acid gives rise to a considerable number of other products, some of which appear to be of particular interest.

When the acid (1 mol.) is heated with carbamide (2 mols.) and excess of phosphorus pentachloride, a product is obtained which, after treatment with excess of barium hydroxide, gives a very intense murexide reaction when evaporated with hydrochloric acid containing nitric acid. This product can be partly separated by cupric acetate, a yellowish-brown precipitate being formed, from which it can be recovered by hydrogen sulphide. In these and other of its properties, the product appears to show a remarkable resemblance to xanthine, the formation of which could be accounted for in accordance with the simple relation :

although isomeric rearrangement would, of course, have to be assumed.

So far, it has not been found possible to obtain this product in a sufficiently pure state for analysis, and many other methods have been attempted for effecting the condensation without the use of phosphorus haloids. The ethyl esters, or the diacetyl-anhydride, when simply melted with carbamide, yield products which give the murexide reaction, but the quantity is very small.

When the ethyl ester (1 mol.) and carbamide (2 mols.) are melted

together, dry hydrogen chloride passed into the mixture, and the temperature kept at about 140° for an hour, a yellow solid is obtained, which when boiled with excess of sodium hydroxide partly dissolves. If the less soluble portion is dissolved in hot hydrochloric acid and allowed to cool slowly, a mass of colourless, silky needles separates. For analysis they were dried in a vacuum desiccator:

0.1681 gave 0.2105 CO_2 and 0.0381 H_2O . $\text{C}=34.15$; $\text{H}=2.51$.

0.1631 „ 22 c.c. N_2 at 15° and 754 mm. $\text{N}=16.0$.

$\text{C}_5\text{H}_4\text{O}_5\text{N}_2$ requires $\text{C}=34.8$; $\text{H}=2.32$; $\text{N}=16.27$ per cent.

From these numbers and from the mode of formation it would appear that the substance is *glyoxalone-4:5-dicarboxylic acid*,

This product does not give the murexide reaction. The part more soluble in sodium hydroxide yields another crystalline substance, which has not yet been examined; it gives the murexide reaction, but not very strongly.

The experiment was then varied by dissolving dihydroxymaleic acid in alcohol, adding excess of carbamide, and saturating the mixture with hydrogen chloride. On allowing to remain for some time and evaporation of the solvent, a crystalline product was obtained, which melted at $258-259^{\circ}$, and consisted of *ethyl glyoxalone-4:5-dicarboxylate*:

0.2070 gave 26.9 c.c. N_2 at 16° and 754 mm. $\text{N}=12.1$.

$\text{C}_9\text{H}_{12}\text{O}_5\text{N}_2$ requires $\text{N}=12.3$ per cent.

The behaviour of dihydroxytartaric acid under similar conditions is of interest in comparison with this result; thus, a solution of free dihydroxytartaric acid with excess of carbamide in alcohol, when saturated with hydrogen chloride, yields a crystalline product melting at 245° .

Found: $\text{C}=42.1$; $\text{H}=4.85$; $\text{N}=19.6$.

$\text{C}_{10}\text{H}_{14}\text{O}_6\text{N}_4$ requires $\text{C}=41.9$; $\text{H}=4.89$; $\text{N}=19.6$ per cent.

This product is evidently identical with the compound which Anschütz and Geldermann obtained from carbamide and ethyl dioxosuccinate (*Annalen*, 1891, **261**, 129), and which, presumably, may be regarded as ethyl glycolurildicarboxylate,

By saponification of this product with sodium hydroxide, acidification with hydrochloric acid, and extraction with alcohol, the free acid was obtained as a crystalline product melting at $195-200^{\circ}$. (Found, $\text{N}=24.1$. $\text{C}_6\text{H}_6\text{O}_6\text{N}_4$ requires $\text{N}=24.3$ per cent.)

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It has previously been shown (*loc. cit.*) that dihydroxymaleic acid when oxidised by mercuric chloride and acted on by carbamide yields glycoluril.

It may be mentioned here that dihydroxytartaric acid when mixed with carbamide in alcoholic solution yields a well crystallised urea salt, which when heated to 100° for a short time decomposes, giving carbamide and a sparingly soluble, crystalline product, which melts at 218° , and is easily identified as hydantoin. (Found, $N=28.15$. $C_3H_4O_2N_2$ requires $N=28.0$ per cent.) The change appears to be practically quantitative, and may be represented as :

The relationships of some of the principal compounds described in the foregoing and other communications, and the transformations which have, so far, been actually accomplished, will be seen at a glance from the subjoined table :

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