

VII.—*The Oxidation of Organic Acids in Presence of Ferrous Iron. Part I.*

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THE oxidation of various organic substances by means of hydrogen dioxide and other agents in presence of small quantities of iron salts, has formed the subject of a considerable number of communications to the Society and elsewhere (compare Fenton, *Chem. News.*, 1876, **33**, 190; 1881, **43**, 110; *Trans.*, 1894, **65**, 899; 1896, **69**, 546; *Proc.*, 1898, **14**, 119; *Brit. Assoc. Reports*, 1895, 1898, 1899; Fenton and Jackson, *Trans.*, 1899, **75**, 1; Cross and Bevan, *Trans.*, 1898, **73**, 463; 1899, **75**, 747; Morrell and Crofts, *Trans.*, 1899, **75**, 786; Martinon, *Bull. Soc. Chim.*, 1885, [ii], **23**, 196).

The present paper deals with a continuation of this investigation, which is being carried out by the authors with a view of arriving at further general conclusions as to the nature of the reaction, the subjects selected for examination being various acids of typical constitution.

Hydrogen dioxide has been employed as the oxidising agent in quantities corresponding to one atom of oxygen, or less, per molecule of acid, and the experiments have been carried out at low temperatures (0° to 15°). Larger proportions of oxygen and higher temperatures will probably give rise to interesting modifications in the results, and these will be studied on a future occasion. The iron, which is always used in the ferrous condition, is generally added as a salt of the acid operated upon, but in some cases ferrous sulphate or acetate is employed.

The following is a brief outline of the method employed in carrying out the initial experiments:

I. The acid (1 mol.) was dissolved in, or in some cases mixed with, a small quantity of water, cooled by ice, and hydrogen dioxide was added in proportion corresponding to about $\frac{1}{4}$ at. of oxygen.

II. The experiment was repeated under exactly similar conditions, but, with the previous addition of ferrous sulphate solution corresponding to $\frac{1}{8}$ at. of iron, the dioxide being added in quantity corresponding to about $\frac{1}{4}$ at. of oxygen in excess of that required to oxidise the iron.

The mixtures were kept in ice and tested for free hydrogen dioxide after five minutes and again after thirty minutes, chromic acid or titanous acid being used for this purpose.

With the following acids, strongly marked indications of free

hydrogen dioxide were shown in both series of experiments even after 30 minutes: *acetic, monochloroacetic, oxalic, malonic, succinic, dibromosuccinic, fumaric, maleic*. Considering the small proportion of dioxide employed, these acids may therefore be considered, at any rate for the present purpose, as inactive towards the reagent.

In the case of *formic, glycollic, lactic, glyceric, tartronic, β -hydroxybutyric, tartaric, malic, saccharic, mucic, pyromucic, acetylenedicarboxylic, acetonedicarboxylic, dihydroxytartaric, dihydroxymaleic, benzoic*, and *picric* acids, however, a rapid (generally almost instantaneous) oxidation takes place in experiment II, that is, in the presence of the ferrous salt, all traces of the dioxide disappearing within five minutes, whereas in experiment I, where iron is absent, strongly marked indications of the dioxide remain after 30 minutes. *Citric* and *β -iodopropionic* acids behave similarly, but the oxidation in presence of iron is less rapid.

Pyruvic acid alone appears to be immediately attacked by hydrogen dioxide, either *with* or *without* the presence of iron.

In the case of nearly all of the above acids which are 'active' towards the reagent, the products appear to be of great interest, new substances being obtained or oxidations effected which are not possible by other means. The systematic study of these changes, although in some cases direct and simple, yet often, in others, presents peculiar difficulties owing to the unstable nature of the products.* It is evident, therefore, that the complete investigation of these products, together with those of several other acids which suggest themselves, will occupy a very considerable time, and it is considered desirable in the present communication to give an account of results which have been obtained up to the present date.

Glycollic Acid.

The pure crystallised acid (1 mol.) was dissolved in water, mixed with a small quantity of ferrous acetate ($\frac{1}{8}$ at. or less of Fe), the mixture cooled by ice, and hydrogen dioxide (1 at. of oxygen) slowly added. On addition of phenylhydrazine acetate (1 mol.), a dark coloured precipitate is immediately formed, which soon turns orange-red and increases considerably in quantity on standing. This precipitate was washed, dried, and purified first by crystallisation from a mixture of ether and light petroleum, and then from a small quantity of hot ethyl acetate (a small quantity of light yellow, insoluble matter remains which appears to be ferrous oxalate). This product crystallises in orange-yellow needles which melt and decompose at

* Compare, for example, the identification and isolation of dihydroxymaleic acid (Trans., 1894, 65, 899 *et seq.*).

137°, and corresponds entirely with the hydrazone of *glyoxylic acid*, $\text{CH}(\text{N}_2\text{H}\cdot\text{C}_6\text{H}_5)\cdot\text{CO}_2\text{H}$, which was prepared by Elbers from calcium glyoxylate (*Annalen*, 1885, **227**, 341).

0.2120 gave 31.7 c.c. nitrogen at 18° and 752 mm. $\text{N} = 17.30$.

$\text{C}_8\text{H}_8\text{O}_2\text{N}_2$ requires $\text{N} = 17.07$ per cent.

The yield of crude hydrazone is nearly equal to the weight of acid used.

Lactic Acid.

When this acid is oxidised in a similar manner, a very considerable evolution of heat occurs, and, in order to obtain the best results, it is necessary to add the oxidising agent very slowly, and to take especial care to keep the mixture cold; it was found advisable also to use only about one-half the calculated quantity of oxygen. The reason that these precautions are necessary is probably to be found in the great instability of the product towards hydrogen dioxide (see pyruvic acid).

On adding phenylhydrazine acetate (1 mol. in proportion to the dioxide employed), a greenish or yellow precipitate of pyruvic acid hydrazone, $\text{CH}_3\cdot\text{C}(\text{N}_2\text{H}\cdot\text{C}_6\text{H}_5)\cdot\text{CO}_2\text{H}$, is obtained, which, when washed with a little cold alcohol and recrystallised from hot alcohol, separates in the form of long, pale yellow, transparent needles, which, when quickly heated, melt at 192°.

0.2102 gave 29.1 c.c. nitrogen at 22° and 758.3 mm. $\text{N} = 16.03$.

$\text{C}_9\text{H}_{10}\text{O}_2\text{N}_2$ requires $\text{N} = 15.73$ per cent.

Tartronic Acid.

This was prepared from dihydroxytartaric acid in the manner previously described by one of the authors (*Trans.*, 1898, **73**, 72). The aqueous solution was mixed with ferrous sulphate ($\frac{1}{4}$ at. Fe) and hydrogen dioxide corresponding to rather less than 1 at. of oxygen slowly added. On the addition of phenylhydrazine hydrochloride (1 mol. in proportion to the oxygen employed) a bulky, brownish-yellow precipitate of mesoxalic acid hydrazone, $\text{C}(\text{CO}_2\text{H})_2\cdot\text{N}_2\text{H}\cdot\text{C}_6\text{H}_5$, was obtained. This, when recrystallised from hot alcohol, was obtained in long, transparent, pale yellow prisms, which melted at 170—171° when quickly heated.* The yield of hydrazone is nearly equal to the weight of acid oxidised.

0.2342 gave 27.5 c.c. nitrogen at 20.5° and 753 mm. $\text{N} = 13.57$.

$\text{C}_9\text{H}_8\text{O}_4\text{N}_2$ requires $\text{N} = 13.46$ per cent.

* Elbers (*loc. cit.*, 355) gives the melting point of this hydrazone as 158—164°, but Clemm (*Ber.*, 1898, **31**, 1451) found that, if quickly heated, it melts at 174°.

The direct oxidation of tartronic to mesoxalic acid has not hitherto been effected, although of course the converse change is well known. It is possible that the process may be found advantageous for the preparation of mesoxalic acid, especially since tartronic acid is so easily obtained by the method above mentioned.

Glyceric Acid.

The pure acid, free from glycerol, was oxidised in the manner above described, the iron being added in the form of ferrous glycerate. The action is immediate, and but little heat is evolved. One mol. of hydrogen dioxide appears to be used up almost quantitatively since, on the addition of any further quantity, but not before, the free dioxide can be detected in the mixture.

The resulting solution, when made alkaline with caustic soda, gives a beautiful *violet* colour, which is much intensified on the addition of ferric chloride. Treated with a mixture of alcohol and ether, the iron is nearly wholly precipitated, and the solution, on evaporation, leaves a thick syrup, which, when made alkaline, gives again the violet colour with ferric chloride. The substance, purified in this way, reduces ammoniacal silver nitrate, very slowly restores the colour to a rosaniline salt bleached by sulphurous acid, and gives precipitates with lead, barium, and silver salts.

On adding phenylhydrazine acetate (1 mol.), a bulky, orange precipitate is at once produced. The yield of crude substance (air-dried) is about equal to the weight of acid oxidised. It was purified by washing with a little cold benzene and recrystallising from hot benzene, from which it separates in aggregates of short prisms which melt at 203—205°. These, on analysis, gave N = 19·5 per cent. The specimen prepared in this way, however, was found to contain a trace of iron, so that for further analysis it was purified by the method mentioned below.

On heating the substance with a strong solution of sodium carbonate, it dissolves to a yellow solution which dyes wool, &c., a bright lemon-yellow colour. Beautiful, yellow glistening plates or needles separate as the solution cools, and these, when dried at 100°, melted at 235—237°.

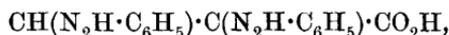
On decomposing this sodium compound with hot dilute hydrochloric acid, the original substance separates as an orange precipitate which, when recrystallised from hot benzene, melts at 207°. Dried at 100° it gave, on analysis, the following results :

0·1201 gave 0·2817 CO₂ and 0·0532 H₂O. C = 63·96 ; H = 4·92.

0·1295 „ 22·5 c.c. nitrogen at 19° and 760 mm. N = 20·37.

C₁₅H₁₄N₄O₂ requires C = 63·82 ; H = 4·96 ; N = 19·85 per cent.

Nastvogel (*Annalen*, 1888, **248**, 85) obtained a substance of this composition by acting upon dibromopyruvic acid (1 mol.) with phenylhydrazine (2 mols.). It formed orange crystals which melted at 201—203°, and its properties exactly corresponded to those of the substance obtained in the present case. The sodium salt was obtained in a similar way, and melted at 231°. From its mode of formation and properties, he assigned to it the formula



and termed it the osazone of glyoxal-carboxylic acid.

Later, W. Will (*Ber.*, 1891, **24**, 400) obtained this osazone in an entirely different way. He treated a solution of collodion-wool in alcoholic ether with a 10 per cent. solution of caustic soda for about 24 hours at 20°, and obtained an acid which had reducing properties, and, with phenylhydrazine acetate, gave an osazone, melting at 205°, identical with the above. Analysis of the calcium, strontium, and other salts of the acid indicated the formula $\text{C}_3\text{H}_4\text{O}_4$ for the latter, so that it must be either hydroxypyruvic acid, $\text{CH}_2(\text{OH})\cdot\text{CO}\cdot\text{CO}_2\text{H}$, or the semi-aldehyde of tartronic acid, $\text{CHO}\cdot\text{CH}(\text{OH})\cdot\text{CO}_2\text{H}$, either of which would, of course, give the osazone in question. From the facts that the acid is not oxidised by bromine, and that it is not altered by heating with lime water or baryta water, Will concluded that it is hydroxypyruvic acid.

By acting upon an alcoholic solution of the osazone with hydrogen chloride, he obtained a substance crystallising in reddish-yellow needles and melting at 149°, which at first was considered to be the ethyl ester, but later (*loc. cit.*, 3831) was shown to be a pyrazolone

derivative, $\text{NHPh}\cdot\text{N}\cdot\text{C}\begin{matrix} \text{CO}\cdot\text{NPh} \\ \text{CH}\cdot\text{N} \end{matrix}$. It is, in fact, identical with the phenylhydrazine ketophenylpyrazolone which Knorr obtained by heating the osazone with acetic anhydride (*Ber.*, 1888, **21**, 1201).

In order further to confirm the identity of the osazone at present under consideration with that of Nastvogel and Will, it was converted into the pyrazolone by the method employed by the latter. The alcoholic solution of the osazone was saturated with dry hydrogen chloride, allowed to stand for some time, evaporated to dryness on a water-bath dissolved in dilute soda solution, filtered, and acidified with dilute sulphuric acid. The precipitated substance, on recrystallisation from alcohol, was obtained in beautiful orange needles melting at 148°.

From these results, it is evident that the oxidation product of glyceric acid may be either (1) the semi-aldehyde of tartronic acid, (2) hydroxypyruvic acid, or (3) the semi-aldehyde of mesoxalic acid. In order to throw further light upon the question, a solution of the oxidised product, prepared from a known weight of glyceric acid, was

mixed with a quantity of bromine corresponding to more than 2 atomic proportions in excess of that required to oxidise the iron present. After standing for 24 hours at the ordinary temperature, with repeated shaking, the free bromine was removed by sulphurous acid, and sodium acetate and phenylhydrazine acetate added. The resulting precipitate was found to be identical in every respect with that originally obtained, and the yield was but little diminished. Further experiments were made, using a considerably larger excess of bromine, and also allowing the mixture to stand for over a fortnight, but in all cases the resulting liquid gave strong evidence of the presence of the original substance, an intense violet colour being obtained on testing the mixture with ferric chloride and alkali after removal of the free bromine. It appears therefore that the substance is incapable of oxidation by bromine, in presence of water, at the ordinary temperature. Heated with bromine on a water-bath for several hours, the substance is slowly oxidised; the resulting product has not been fully examined, but appears to be neither tartronic nor mesoxalic acid.

With excess of freshly precipitated silver oxide, again, very little oxidation results at the ordinary temperature, the mixture, even after standing for some days and subsequent removal of the silver, showing a strong reaction with ferric chloride and giving the same osazone with phenylhydrazine. When heated for some time at about 40° , the oxidation proceeds more quickly, but the product, after removal of silver, appears to be only oxalic acid. A copious precipitate of phenylhydrazine oxalate is obtained on adding the acetate, whereas the hydrochloride gives only a slight precipitate resembling the original osazone.

If the original solution (containing iron) is mixed with a large excess of baryta water, the violet precipitate which is formed remains permanent, even on heating for two or three hours on a water-bath.

These facts afford fairly strong evidence that the oxidation product is not aldehydic, and consequently that the acid under consideration is *hydroxypyruvic acid*. The *absence* of the other two acids in minute quantity is of course not absolutely certain, since small traces of tartronic or mesoxalic acids might not be detected in the products mentioned.

The properties of the substance coincide in fact very closely with those of the acid obtained by Will from collodion. In Will's papers, however, no mention is made of the remarkable colour reaction with ferric chloride, which is certainly the most striking property of the present substance. This colour reaction is very similar to that produced by dihydroxymaleic acid, and the authors were at first inclined to believe that the product might be dihydroxyacrylic acid, $\text{CH}(\text{OH})\text{:C}(\text{OH})\cdot\text{CO}_2\text{H}$, which would be formed from glyceric acid by

removal of two non-hydroxylic hydrogen atoms (compare Proc., 1898, 14, 119). It is of course possible that this may represent the initial reaction and that the product afterwards undergoes tautomeric change, becoming hydroxypyruvic acid.

Malic Acid.

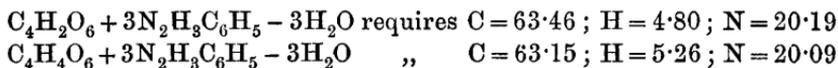
On addition of hydrogen dioxide to a solution of this acid containing a little ferrous salt, the colour of the liquid immediately becomes deep red, much heat is evolved, and carbon dioxide is given off. If, however, the solution is carefully cooled by a freezing mixture and the hydrogen dioxide added very slowly, the action proceeds without any appreciable evolution of gas. In the following experiments, the acid was dissolved in very little water and the required quantity of iron (*ferrum redactum* about $\frac{1}{8}$ at.) dissolved in the liquid.* The hydrogen dioxide was used in quantity representing rather *less* than 1 at. of oxygen.

On adding phenylhydrazine acetate (1 mol. in proportion to the oxygen employed) to the resulting liquid, a very copious, bright, orange-yellow precipitate is formed *immediately*. The yield of this precipitate (air dried) considerably exceeds the weight of acid oxidised. This substance dissolves sparingly in most cold solvents, but fairly easily in hot alcohol, benzene, or chloroform. It may be crystallised from any of these solvents, but the last appears to give the best result. It is thus obtained in brilliant, long, orange-yellow prisms belonging to the prismatic system, and melting at 217—219°.

Distinct specimens prepared on different occasions, and all melting within the above range of temperature, gave the following results on analysis :

I. C = 63·30.	H = 5·17.	N = 20·10.
II. C = 63·35.	H = 5·47.	N = 20·21.
III. C = 62·87.	H = 4·95.	N = 20·07.
IV. C = 63·31.	H = 5·12.	N = 20·26.

Assuming that the product is derived from an acid containing four carbon atoms these numbers correspond best with those required for a derivative of dihydroxytartaric acid or of dihydroxymaleic (or isomeric) acid.



It will be shown in the following communication (p. 81) that this substance is the result of further action of the oxidising agent upon the product which is first formed. It was evident, in fact, that the action

* It is now found, however, that the addition of ferrous sulphate or acetate answers equally well.

of phenylhydrazine does not in this case afford direct evidence as to the nature of the reaction under investigation, and the problem was therefore attacked in a different manner. The experiments which were made resulted in the isolation of *oxalacetic acid*, and from the special interest which attaches to this substance, the authors have thought it advisable to give an account of this part of the investigation in a separate paper.

The following acids have been only superficially examined :

Mucic and *Saccharic Acids*, when oxidised in the above manner, yield products which give brown precipitates with phenylhydrazine acetate, and when made alkaline with caustic soda give deep red-violet colours, which are intensified by the addition of ferric chloride. If the action is analogous to that of tartaric acid, it is evident that these products may be of much interest. They are very unstable, however, and it will doubtless be a matter of some difficulty to isolate them.

Pyromucic Acid turns an intense but transient violet colour, and *picric acid* gives an intense green colour ; both products react with phenylhydrazine.

Acetylenedicarboxylic Acid is immediately attacked in presence of iron—the solution becoming dark brown. The solution now gives an immediate precipitate with phenylhydrazine, which is quite different from the precipitate slowly formed with the original acid.

Acetonedicarboxylic Acid.—This is similarly oxidised when iron is present, the change taking place rather more slowly than in the preceding cases. The product gives an intense purple colour with alkalis, which is intensified on addition of ferric chloride. This colour is quite distinct from that given by the original acid with ferric chloride, which is destroyed by alkalis.

Benzoic Acid is immediately oxidised, the result giving a violet colour with ferric salts, presumably due to the formation of salicylic acid.

It is the intention of the authors to make a complete study of these products, and to extend the observations to a large number of other acids. It is evident that several general conclusions might already be suggested by the foregoing results, but it is considered preferable to defer such considerations until the investigation is completed.

Part of the expenditure which has been incurred in carrying out this research has been defrayed by funds kindly placed at the disposal of one of the authors by the Government Grant Committee of the Royal Society.
