XXX.—*Some Oxidation Products of the Hydroxybenzoic Acids. Part II.*

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In the previous communication (Trans., 1905, **87**, 1412), it was shown that ellagic acid is formed when gallic acid dissolved in a mixture of acetic and sulphuric acids is oxidised by means of potassium persulphate. Experiments carried out in a similar way with protocatechuic, *p*-hydroxybenzoic, and *m*-hydroxybenzoic acids gave only minute traces of oxidation products insoluble in water, but, on the other hand, when concentrated sulphuric acid was employed as the solvent, moderate yields of interesting compounds were produced, which in constitution bear a simple relationship to ellagic acid. The present paper deals with a description of the oxidation products which are obtained from gallic acid itself when dissolved in both dilute and concentrated sulphuric acid, and which have been already referred to in a preliminary note (*loc. cit.*, p. 429).

Experimental.

The Oxidation of Gallic Acid in the Presence of Dilute Sulphuric Acid.

Twenty grams of finely-powdered gallic acid were treated with 160 c.c. of 96 per cent. sulphuric acid, 66 c.c. of water added, and the hot solution thus obtained was cooled to 50° and maintained at this temperature during the gradual addition of 40 grams of potassium persulphate. The resulting deep brown liquid, from which minute crystals of an oxidation product had separated, was poured into water, causing the deposition of a pale brown precipitate, which was collected and washed with water. The dry substance weighed 15·1 grams, and this yield, it was subsequently ascertained, was not materially affected by a slight variation of the temperature or the dilution of the sulphuric acid employed in the reaction. This compound, which closely resembled ellagic acid, and at first appeared to consist of this colouring matter, was purified by crystallisation from pyridine, which is probably the only solvent suitable for this purpose. It was soon noted, however, that its solubility in this respect was somewhat less than that of ellagic acid, and a fractional crystallisation was accordingly resorted to, as it was only likely from previous results (*loc. cit.*) that some quantity of the latter substance might be present. Thus obtained, the pure compound consisted of small, pale yellow, prismatic needles, which contain pyridine, and this was partially removed by means of hot alcohol, and the final traces by drying at 160°.

Found, C = 53·08; H = 2·22. $C_{14}H_6O_9$ requires C = 52·82; H = 1·89 per cent.

It does not melt below 360°, and, like ellagic acid, is almost insoluble in the usual solvents, but it is distinguished from this colouring matter by its somewhat yellower appearance and by the fact that its solution in dilute alkali has a well-marked green tint. With nitric acid containing nitrous acid and subsequent dilution, it gives a blood-red coloration (Griessmayer reaction) which has long been considered as characteristic of ellagic acid. By distillation with zinc dust, a small quantity of a hydrocarbon was obtained; this, after crystallisation from alcohol, formed colourless leaflets, melting at 109°, and evidently consisted of *fluorene*. This compound, for which the name "*flavellagic acid*" is suggested, dyes mordanted woollen cloth in shades somewhat resembling, but stronger than, those produced by ellagic acid. The following results were obtained:

Chromium.	Aluminium.	Tin.	Iron.
Yellowish-olive	Pale greenish-yellow	Pale yellow	Dark olive-brown

Acetylflavellagic acid is prepared by digesting the substance with a large excess of boiling acetic anhydride for some hours, or more readily in the presence of two or three drops of sulphuric acid. On cooling, a colourless, crystalline precipitate separates, which is purified by recrystallisation from acetic anhydride.

Found, C = 54·24, 54·29; H = 3·28, 3·26. $C_{14}HO_9(C_2H_3O)_5$ requires C = 54·54; H = 3·03 per cent.

It formed glistening needles melting at 317—319°, very sparingly soluble in the usual solvents.

Acetyl determinations were carried out by the indirect method, employing 25 c.c. of acetic acid, 3 c.c. of sulphuric acid, and 0·6 gram (approximately) of substance.

Found, $C_{14}H_6O_9$ = 59·68, 59·78. $C_{14}HO_9(C_2H_3O)_5$ requires $C_{14}H_6O_9$ = 60·22 per cent.

It was therefore a *penta*-acetyl compound.

Obtained in this manner, the regenerated flavellagic acid is a pale yellow, microcrystalline powder, but if the acetyl compound (1 gram approximately) is dissolved by digestion with 12 c.c. of pyridine, the solution treated with 15 c.c. of acetic acid, and 12 c.c. of hydrochloric acid is then gradually added to the boiling liquid, the colouring matter is deposited in the form of long, glistening, hair-like needles.

Benzoylflavellagic acid may be produced by treating the substance with a large excess of benzoic anhydride at 200—210° until a clear solution is formed, and subsequently digesting at 170—180° for three hours. The product is poured into alcohol, and the precipitate which separates on standing is collected and purified by crystallisation from nitrobenzene with the aid of animal charcoal.

Found, C = 70·20; H = 3·44. $C_{14}HO_9(C_7H_5O)_5$ requires C = 70·16; H = 3·10 per cent.

It forms prismatic needles melting at 287—289°.

A molecular weight determination was carried out by the cryoscopic method, employing naphthalene as a solvent.

0·5190 in 14·19 naphthalene gave $\Delta t - 0{\cdot}3125°$. M.W. = 819.
$C_{49}H_{26}O_{14}$ requires M.W. = 838.

These results therefore indicate that flavellagic acid has the formula $C_{14}H_6O_9$.

Action of Boiling Potassium Hydroxide Solution.

Twelve grams of flavellagic acid dissolved in 60 c.c. of boiling 50 per cent. aqueous potassium hydroxide were digested at the boiling point until the solution possessed a pale brown colour and a drop of the liquid on exposure to air developed a bluish-violet tint. The product was treated with twice its volume of water and at once neutralised with dilute sulphuric acid, causing the formation of a clear solution, which on standing became semi-solid owing to the separation of almost colourless needles. These were collected, and when dry weighed 8·71 grams (72·5 per cent.), but in some operations, owing to the difficulty in determining the end of this reaction, as little as 5·5 grams (45·8 per cent.) could be obtained.

This compound is best purified by conversion into its acetyl derivative, which after recrystallisation is hydrolysed by acid. In the dry condition it is somewhat sparingly soluble in alcohol, but in the moist, freshly-precipitated state it dissolves much more readily, and it is possible by treating such a solution with animal charcoal and subsequently evaporating to obtain a fairly pure product. Air-dried, it contains 1 molecule of water of crystallisation, which is slowly removed by heating at 160°.

Found, $H_2O = 5{\cdot}63$. $C_{13}H_8O_8,H_2O$ requires $H_2O = 5{\cdot}80$ per cent.

The anhydrous substance thus obtained is exceedingly hygroscopic, and on standing in air soon reassumes its original weight. Owing to this behaviour, the analyses of the product dried at 160° (A) were not very satisfactory, and in order to corroborate these an air-dried sample (B) was also examined.

A. Found, C = 53·03; H = 3·03. $C_{13}H_8O_8$ requires C = 53·42; H = 2·74 per cent.

B. Found, C = 50·32; H = 3·39. $C_{13}H_8O_8,H_2O$ requires C = 50·32; H = 3·22 per cent.

This compound, to which the formula $C_{13}H_8O_8$ was therefore assigned, forms almost colourless needles, which on exposure to light become somewhat greyer in appearance. When heated, it does not melt below 300°, and probably not below 360°, but this could not be satisfactorily determined owing to the discoloration of the tube at this temperature. It is sparingly soluble in most solvents with the exception of pyridine, in which it readily dissolves, but attempted purification in this manner did not give a satisfactory result. Solutions of the alkaline hydroxides dissolve it with a dull orange-yellow tint, and these on dilution with water and exposure to air develop a strong bluish-violet coloration. With alcoholic lead acetate, it gives an orange-yellow precipitate which rapidly passes to olive-green, with alcoholic ferric chloride a bluish-green coloration, and its solution in sulphuric acid is orange-yellow. Nitric acid dissolves it with an orange-red coloration, which on dilution with water becomes redder, but is devoid of the blood-like tint produced in this manner from both ellagic and flavellagic acids. It dyes mordanted calico rather feebly, but with mordanted woollen cloth the following somewhat better results were obtained.

Chromium.	Aluminium.	Tin.	Iron.
Brown	Pale brownish-yellow	Pale yellow	Brownish-purple

This substance was acetylated by a three hours' digestion with boiling acetic anhydride. The solution was concentrated, and the crystalline product, which separated out on cooling, was collected and recrystallised from the same solvent, employing animal charcoal.

Found, C = 55·09; H = 3·85. $C_{13}H_2O_8(C_2H_3O)_6$ requires C = 55·15; H = 3·67 per cent.

Thus obtained, it forms colourless, prismatic needles melting at 232—234°, somewhat sparingly soluble in the usual solvents.

The determination of the acetyl groups in this substance was, as will be seen later, a matter of considerable importance with regard to the constitution of flavellagic acid, and analyses were therefore carried out both by the direct and indirect methods. In the former case, the ethyl acetate method was adopted, and in the latter the finely-powdered acetyl derivative (1 gram approximately in 20 c.c. of acetic acid) was hydrolysed by the gradual addition of 10 c.c. of hydrochloric acid. The digestion was continued for at least fifteen minutes after the reaction had apparently terminated, for, owing to the insoluble nature of the original compound, special care was necessary in case some portion remained unattacked.

Found, acetic acid = 67·01, 65·30, 66·12, 67·30. $C_{13}H_2O_8(C_2H_3O)_6$ requires $C_2H_4O_2 = 66{\cdot}17$ per cent.

Found, $C_{13}H_8O_8 = 53{\cdot}43$. $C_{13}H_2O_8(C_2H_3O)_6$ requires $C_{13}H_8O_8 = 53{\cdot}67$ per cent.

Found, $C_{13}H_8O_8,H_2O = 56{\cdot}64$, 56·93. $C_{13}H_2O_8(C_2H_3O)_6$ requires $C_{13}H_8O_8,H_2O = 56{\cdot}98$ per cent.

These results indicate that the substance $C_{13}H_8O_8$ contains six hydroxyl groups.

For the purpose of a molecular weight determination, a *benzoyl* derivative was prepared by treating the substance (1 gram) dissolved in pyridine (15 grams) with benzoyl chloride (11·5 grams). The new compound was readily isolated by the usual methods and was purified by crystallisation from a mixture of benzene and alcohol. It formed colourless prisms melting at 261—263°, and when heated with benzoic anhydride at 170° for two hours suffered no change.

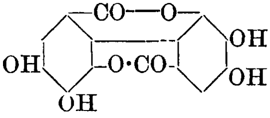
0·6877 in 14·21 of naphthalene gave $\Delta t - 0{\cdot}38°$. M.W. = 892. $C_{55}H_{32}O_{14}$ requires M.W. = 916.

It thus appeared certain that the formula assigned to the substance $C_{13}H_8O_8$ is correct.

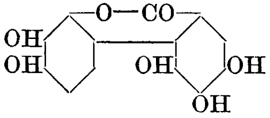
To obtain, if possible, some further insight into its constitution, it was heated with ten times its weight of potassium hydroxide at 220—240° for twenty minutes. The product of the fusion, on solution in water and neutralisation with acid, yielded to ether a mixture of compounds, some quantity of which consisted of unattacked substance. That portion which was soluble in water contained *gallic acid* (found, C = 49·89; H = 3·91 per cent.), which was identified by the usual tests, and on evaporating the mother liquors obtained during the isolation of this compound a semi-crystalline but very soluble residue remained, the nature of which could unfortunately not be ascertained. The presence of a small quantity of pyrogallol derived from the gallic acid was to be anticipated, but there were indications that it did not constitute the main bulk of this product.

Summary of Results.

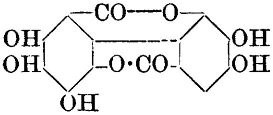
In considering the constitution of flavellagic acid, one cannot help observing that not only its composition, $C_{14}H_6O_9$, but its general reactions, notably the Griessmayer coloration and the production of fluorene from it by means of zinc dust, indicate a close relationship to ellagic acid. The analogy between these colouring matters is also strikingly brought out by their behaviour towards boiling potassium hydroxide solution, for whereas in this manner ellagic acid gives pentahydroxydiphenylmethylolid, $C_{13}H_8O_7$, from flavellagic acid the similar compound $C_{13}H_8O_8$ is thus formed. These facts, together with the other results described above, can only be interpreted to mean that *flavellagic acid* is *hydroxyellagic acid*, and the substance $C_{13}H_8O_8$ a *hexahydroxydiphenylmethylolid*, and constitutions (*loc. cit.*) similar to those previously assigned to ellagic acid and its decomposition product are accordingly suggested for these compounds.



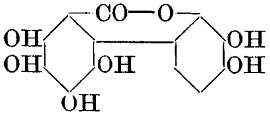
Ellagic acid.



Pentahydroxydiphenylmethylolid.



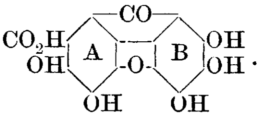
Flavellagic acid.



Hexahydroxydiphenylmethylolid.

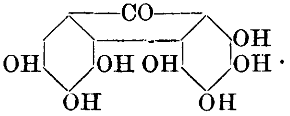
Such a formula for flavellagic acid indicates that during the reaction, either before or after the diphenyl condensation, a fourth hydroxyl is introduced into one of the pyrogallol nuclei, a type of oxidation which, as is well known, is frequently effected by this method. The production, for instance, of catellagic acid from *p*-hydroxybenzoic acid, described in the former communication, may be cited as an illustration of the case in point (*loc. cit.*).

In the earlier stages of the work, and having regard to the fact that flavellagic acid differs from gallic acid by possessing a well-marked yellow tint, it appeared just possible that the former colouring matter was constituted as follows :



this being apparently the only other possible formula for this substance.

Apart from those changes occurring during the formation of such a substance from gallic acid in the presence of concentrated sulphuric acid due to oxidation, and which have been discussed above, the elimination of a carboxyl group and its subsequent reintroduction in another portion of the molecule are points which, although necessary for an explanation of this formula, do not appear to be very likely to occur. Again, if this were the case, the substance $C_{13}H_8O_8$ must of necessity contain seven hydroxyls, whereas according to the analytical methods employed the presence of only six such groups could be detected.



An examination of the more soluble fractions obtained during the fractional crystallisation of the crude flavellagic acid from pyridine indicated that these occasionally contained a minute trace of *ellagic acid.* It was noted, for instance, on exhausting the crude dry hexahydroxydiphenylmethylolid, obtained by the action of boiling potassium hydroxide solution on these residues, that a trace of a readily soluble substance could be isolated. This, which when pure crystallised in long, hair-like needles, had the properties of *pentahydroxydiphenylmethylolid,* the characteristic decomposition product of ellagic acid.

Oxidation of Gallic Acid in the Presence of 96 *per cent. Sulphuric Acid.*

When gallic acid (10 grams) dissolved in 50 c.c. of 96 per cent. sulphuric acid is treated with 20 grams of potassium persulphate at 50°, the features of the oxidation are of a similar nature to those occurring when a more dilute acid is employed. The mixture, on treatment with water, deposits a pale brown, crystalline powder, which after washing and drying weighs on the average 6·6 grams. In certain cases, the product of the experiment when poured into much water gave at first a clear liquid, from which, on standing, crystals somewhat slowly separated, but this peculiar effect appears to be due to some accidental circumstance not as yet ascertained, and recent attempts to reproduce it have, curiously enough, been unsuccessful. Owing to the sparing solubility of this compound in the usual solvents, it was at first purified by means of its acetyl derivative, which after recrystallisation was hydrolysed by acid. The product thus obtained formed groups of microscopic needles of a very pale yellow colour resembling ellagic acid in appearance, and was soluble in alkaline solutions with a greenish-yellow tint. With nitric acid, it gave the Griessmayer reaction, and when distilled with zinc dust gave a small quantity of a hydrocarbon which was found to consist of *fluorene.* Again, its dyeing properties were almost identical with those yielded by ellagic acid, so that in many respects there was a close resemblance between these substances. The analytical numbers (found, C = 54·08, 53·55; H = 2·36, 2·48 per cent.) obtained with distinct preparations did not, however, accord with one another so closely as was to be desired, and, again, could not be made to harmonise with any simple formula. The *acetyl* derivative, prepared by boiling with acetic anhydride or more rapidly in the presence of sulphuric acid, separated as very minute needles, but these on recrystallisation from the same solvent assumed a peculiar gelatinous appearance, and were in this condition difficult to manipulate. This product melted at 224—226°, gave on analysis C = 55·04 ; H = 3·20, and on examination by the indirect method of acetyl determination gave 64·22 and 64·06 per cent. of regenerated colouring matter. These numbers suggested as possible that this compound might consist of an anhydride of flavellagic acid, $(C_{14}H_6O_9)_2—H_2O$, but this was negatived by the failure to obtain such a substance from flavellagic acid by means of sulphuric acid. Large quantities of the oxidation product were now fused with potassium hydroxide at 210—220° in the usual manner, and the fused product, after solution with water, was neutralised with acid. On cooling, some quantity of a crystalline precipitate (*A*) separated, which was removed by filtration and the filtrate extracted with ether. The residue obtained by the evaporation of this extract was digested with boiling water, in which a portion dissolved, and the clear solution was allowed to stand for twelve hours. A quantity of fine hair-like needles (*B*) had then separated, which were collected and purified by crystallisation from dilute alcohol.

Found, C = 56·31 ; H = 3·12. $C_{13}H_8O_7$ requires C = 56·52 ; H = 2·89 per cent.

The *acetyl* derivative of this substance melted at 224—226°, and by the ethyl acetate method gave acetic acid = 62·45 per cent. ; again, the benzoyl compound (found, C = 72·39 ; H = 3·87 per cent.) melted at 258—259°, so that it was evident that this compound was identical with the *pentahydroxydiphenylmethylolid* previously obtained from ellagic acid. The aqueous mother liquors arising from the purification of this substance (*B*) contained among other products some quantity of *gallic acid*, which was identified by means of its acetyl derivative (m. p. 172—174°).

The more sparingly soluble substance (*A*), present in but small amount, on solution in alkali and exposure to air yielded a bluish-violet-coloured liquid, and appeared likely to consist of the *hexahydroxydiphenylmethylolid* previously described in this paper. To ascertain if this was correct, the purified product was acetylated and the acetyl derivative isolated by the former method.

Found, C = 55·17 ; H = 3·94. $C_{13}H_2O_8(C_2H_3O)_6$ requires C = 55·15 ; H = 3·67 per cent.

It melted at 232—234°, and no doubt as to its identity could therefore exist. More recent experiments have shown that by digesting the gallic acid oxidation product with boiling 50 per cent. potassium hydroxide solution, the same compounds are obtained, so that the use of alkali at so high a temperature as that given above is not necessary.

The formation in this manner of two substances respectively obtainable by the action of alkali on ellagic and flavellagic acids suggested that the oxidation of gallic acid by the method employed had yielded a mixture of the latter substances. Knowing that flavellagic acid is less soluble than ellagic acid in pyridine, a repeated fractional crystallisation from this solvent was carried out, but without effecting the desired separation, and as the acetyl derivative in various solvents did not give a better result, it appeared at one time that the product in question was after all a distinct substance. An interesting point was, however, subsequently obtained in support of the mixture theory, for it was found that in the presence of a small quantity of flavellagic acid, ellagic acid gave an ill-defined, semi-gelatinous acetyl compound, corresponding in appearance with that given by the oxidation product itself. The difficulty was eventually surmounted by a study of the benzoyl derivative.

The crude product of the oxidation was heated at 210° with a large excess of benzoic anhydride until a clear liquid resulted, and the temperature was then kept at 190° for three hours. The hot solution was cautiously treated with a few drops of alcohol, causing the almost immediate separation of a colourless crystalline precipitate, which was collected on a warm funnel by means of the pump and washed with hot benzoic anhydride containing a trace of alcohol. It was again dissolved in benzoic anhydride at about 200°, reprecipitated as before, collected, and finally purified by crystallisation from nitrobenzene.

Found, $C=70{\cdot}37$; $H=3{\cdot}29$. $C_{14}H_2O_8(C_7H_5O)_4$ requires $C=70{\cdot}19$; $H=3{\cdot}06$ per cent.

This substance consisted of prismatic needles melting at 332—333°, and had therefore the composition of a *tetrabenzoylellagic acid.* Such a compound has been prepared by Goldschmidt and Jahoda (*Monatsh.*, 1892, **13**, 51), but as they do not give a melting point, a sample was prepared and found to be identical with the product isolated as above (found, $C=70{\cdot}19$; $H=3{\cdot}21$ per cent.). This compound, it was incidentally noted, is prepared more readily by the agency of benzoic anhydride than by means of benzoyl chloride, which was the reagent employed by the above authors.

It was now interesting to obtain, if possible, ellagic acid itself from the benzoyl compound, and for this purpose a modification of the indirect acetyl method described in a former paper (Trans., 1905, **87**, 107) was employed; 0·65 gram of the finely-powdered substance suspended in 25 c.c. of acetic acid was treated with 8 c.c. of sulphuric acid and digested at the boiling temperature for three hours. The colourless benzoyl derivative had then disappeared, and was replaced by a pale greenish-yellow deposit consisting of fine needles. The mixture was diluted with half its volume of water and the crystals collected and weighed (0·2682 gram).

Found, $C_{14}H_6O_8 = 41·26$. Theory requires $C_{14}H_6O_8 = 42·06$ per cent.

That this product was indeed ellagic acid was determined by analysis:

Found, $C = 55·55$; $H = 2·29$. $C_{14}H_6O_8$ requires $C = 55·62$; $H = 1·98$ per cent.;

and also by an examination of its acetyl compound, which melted at 343—346°.

Experiments were now carried out in order to isolate the more soluble compound produced during the benzoylation, and which was by far the minor constituent of the mixture. The alcoholic benzoic anhydride mother liquors obtained as above described were treated with some quantity of alcohol, and the crystalline deposit which separated on standing was collected and freed from a small quantity of benzoylellagic acid still present by fractionally precipitating its solution in benzoic anhydride with alcohol. The more soluble product was finally crystallised from a mixture of nitrobenzene and alcohol.

Found, $C = 70·21$; $H = 3·50$. $C_{14}HO_9(C_7H_5O)_5$ requires $C = 70·16$; $H = 3·10$ per cent.

This substance consisted of prismatic needles melting at 287—289°, and was identical with the *benzoylflavellagic acid* previously described.

A portion of this substance was now hydrolysed with sulphuric acid according to the method employed for benzoylellagic acid.

Found, $C_{14}H_6O_9 = 37·13$. Theory requires $C_{14}H_6O_9 = 37·94$ per cent.

An analysis gave:

Found, $C = 52·85$; $H = 2·21$. $C_{14}H_6O_9$ requires $C = 52·82$; $H = 1·89$ per cent.

It dissolved in alkaline solutions with the greenish-yellow tint characteristic of *flavellagic acid*, and as its acetyl derivative melted at 317—319° there could be no doubt as to its identity with this substance.

The product of the oxidation of gallic acid in the presence of 96 per cent. sulphuric acid is therefore a mixture of ellagic and flavellagic acids. It was not possible to determine the exact proportion of each which was present, but it was ascertained that the former colouring matter is without doubt the main substance produced by this reaction. Again, it has been observed that, due probably to some slight variation in the conditions of the experiment, the quantities of these two constituents also vary somewhat in distinct preparations, and on at least one occasion, owing to some cause which unfortunately could not be accounted for, a product which consisted almost entirely of ellagic acid was found to have been formed. As, however, the necessary features of the reaction have now been explained, it was not worth while to devote more time to this point. If gallic acid is oxidised in the presence of 100 per cent. sulphuric acid, the yield is somewhat poorer than when the ordinary commercial acid is employed, and the crude substance does not appear to differ in any marked manner from that described above.

The molecular weight of ellagic acid, although most probably represented as $C_{14}H_6O_8$, has not been determined by cryoscopic methods, and experiments were carried out in the hope that benzoylellagic acid would be sufficiently soluble in naphthalene for this purpose. It was observed, however, that a trace of this substance crystallised out at or about the freezing point of the mixture.

0·3057 in 15·13 naphthalene gave $\Delta t - 0{\cdot}1525$. M.W = 927.

$C_{42}H_{22}O_{12}$ requires M.W = 718.

There can be little doubt, however, that, although this result is not satisfactory enough to indicate a definite formula, ellagic acid must be represented as C_{14} rather than C_{21} or C_{28}, which is practically all the information that is necessary. If this was not the case, it is obvious that under the imperfect conditions of the experiment a much higher number would have been obtained.

An investigation is in progress with the view of obtaining some insight into the constitution of ellagitannic acid, a substance of much importance in the tanning industry, and from which the natural ellagic acid appears to be almost entirely derived.

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