

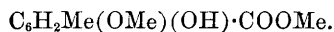
CI.—*Derivatives of β -Resorcylic acid.*

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INTRODUCTORY.

THE following investigation was originally instituted with the object of gaining some insight into the constitution of certain natural colouring matters, but, owing to pressure of other work, it has been laid aside from time to time, and it has thus unfortunately happened that some of the results have been anticipated by others. It seemed desirable, therefore, to lay before the Society an account of such new products as have been obtained, more especially as the results attained did not serve the purpose for which they were originally intended.

The action of methylic iodide on the alkaline sodium salt of β -resorcylic acid does not yield the dimethyl ether of the methylic salt of this acid, $C_6H_3(OMe)_2 \cdot COOMe$, the principal product being a substance having the same composition, namely, $C_{10}H_{12}O_4$, and insoluble in alkalis; it, however, contained only two methoxy-groups, one of which is present in the $COOMe$ group. It appeared, therefore, that the constitution was represented by the formula,



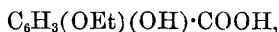
Crystallised from alcohol, it formed prismatic needles, melting at $76-77^\circ$. By hydrolysis, the acid itself, $C_6H_2Me(OMe)(OH) \cdot COOH$,

was obtained; this crystallises in slender needles, melting at 210° , soluble in alkalis, and containing one methoxy-group.

That portion of the product of the methylation of β -resorcylic acid which was soluble in alkalis consisted chiefly of two substances, one of which melted at 210° , and proved to be the acid just mentioned. The other, which was more readily soluble, was found to be the monomethyl ether of β -resorcylic acid, $[\text{COOH} : \text{OH} : \text{OCH}_3 = 1 : 2 : 4]$, previously obtained by Tiemann and Parrisius (*Ber.*, 1885, **13**, 2375). The presence of this substance indicates that the hydroxyl group in β -resorcylic acid which resists methylation is in the ortho-position relatively to the carboxyl group.

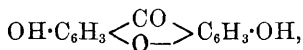
The behaviour of the alkaline sodium salt of β -resorcylic acid towards ethylic iodide is also peculiar, the principal product formed contains but two ethoxy-groups, and has apparently the constitution of a monethylic ether of the ethylic salt of β -resorcylic acid, $\text{C}_6\text{H}_3(\text{OEt})(\text{OH})\cdot\text{COOEt}$. In this case, contrary to what takes place when methylic iodide is used, there is no displacement of a hydrogen of the nucleus by an ethyl group.

By saponification it is converted into the acid,



melting at 153 — 154° . That portion of the product of the ethylation soluble in alkali consisted chiefly of the free acid, m. p. 153 — 154° , there being also present a trace of a substance of lower melting point.

It being important to determine the position of the ethyl group in the above ethyl ether of the acid, its behaviour towards acetic anhydride was studied. It has been shown by W. H. Perkin (*Trans.*, 1883, 35), that when salicylic acid is distilled with acetic anhydride, diphenylene ketone oxide, $\text{C}_6\text{H}_4\langle\text{CO}\rangle\text{C}_6\text{H}_4$, is produced. β -Resorcylic acid under similar conditions yields iso-euxanthone,



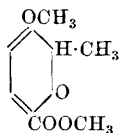
and it appeared evident that if the monethyl ether in a similar way yielded iso-euxanthone diethyl ether, it must have the constitution, $\text{OEt} : \text{OH} : \text{COOH} = 1 : 3 : 4$. On making the experiment such was found to be the case. Iso-euxanthone diethyl ether forms nearly colourless needles, melting at 185° . It is therefore evident that the hydroxyl group in β -resorcylic acid which resists ethylation is the one in the ortho-position relatively to the carboxylic group. It is interesting to notice that these peculiar results are due in this instance to the influence of the carboxyl group, for resorcyaldehyde when methylated behaves normally, giving the dimethyl ether,

$C_6H_3(OMe)_2 \cdot COH$, and diethyl ether (Tiemann and Parrisius, *loc. cit.*). These, when oxidised, yield the corresponding derivatives of the acid, $C_6H_3(OMe)_2 \cdot COOH$, &c., which, as shown above, are not formed by its direct methylation or ethylation. According also to the results of Habermann (*Ber.*, 1877, **10**, 868) resorcinol dimethyl ether, $C_6H_4(OMe)_2$, is readily formed.

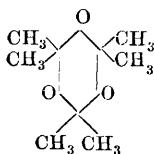
I have also studied the action of methylic iodide on resacetophenone, but unfortunately these results have been anticipated by Gregor (*Monatsh.*, 1894, **15**, 437), and Wechsler (*ibid.*, **15**, 239). With methylic iodide, resacetophenone yields a substance having the constitution, $C_6H_2Me(OMe)(OH) \cdot CO \cdot CH_3$, insoluble in alkalis, the results resembling, therefore, those obtained with β -resorcylic acid. Curiously, however, the action of ethylic iodide gives a normal result, resacetophenone diethyl ether being formed. The distinctive behaviour of these substances on methylation and ethylation is exhibited more clearly by the following table.

β -Resorcylic acid, $C_6H_3(OH)_2 \cdot COOH$, yields
$C_6H_2Me(OMe)(OH) \cdot COOMe$ and $C_6H_2(OEt)(OH) \cdot COOEt$.
Resacetophenone, $C_6H_3(OH)_2 \cdot CO \cdot CH_3$, yields
$C_6H_2Me(OMe)(OH) \cdot CO \cdot CH_3$ and $C_6H_3(OEt)_2 \cdot CO \cdot CH_3$.
Resorcylic aldehyde, $C_6H_3(OH)_2 \cdot COH$, yields
$C_6H_3(OMe)_2 \cdot COH$ and $C_6H_3(OEt)_2 \cdot COH$.
Resorcinol, $C_6H_4(OH)_2$, yields $C_6H_4(OMe)_2$.

It appears probable that the insolubility in cold alkali of the methyl ethers of resorcylic acid and resacetophenone, which apparently contain a free hydroxyl group, is due to the oxygen of the latter having assumed the ketonic form. The constitution of these substances would therefore be thus represented.

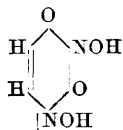


Somewhat analogous to the above is the behaviour of phloroglucinol, which yields a triacetyl derivative, a trioxime, a hexamethyl derivative (Margulies, *Monatsh.*, 1888, **9**, 1046),



and a hexethyl derivative (Herzig, Zeisel, *ibid.*, **9**, 896). Though

resorcinol does not react with hydroxylamine (Baeyer, *Ber.*, 1886, **19**, 163), yet on treatment with nitrous acid it is converted into dinitrosoresorcinol, which can be regarded as diquinoyldioxime,



in that by treatment with hydroxylamine it now reacts with it, yielding diquinoyltetroxime (Kostanecki, *Ber.*, 1889, **22**, 1345).

A preliminary investigation of the action of methylic iodide on the sodium salt of gallacetophenone has been made; the principal product, which forms colourless needles melting at $77-78^{\circ}$, has the constitution of a gallacetophenone dimethyl ether.

The study of the above substance is being continued, and at the same time the action of methylic and ethylic iodides on α -resorcylic acid, cresorcinol-, and quinol-carboxylic acids will be investigated.

An account is also given in this paper of the oximes of gallacetophenone, quinacetophenone, and resacetophenone. Digestion for a short time with acetic anhydride converts them into monacetyl derivatives.

EXPERIMENTAL.

Methylation of β -Resorcylic acid.

β -Resorcylic acid dissolved in a solution of the calculated quantity of sodium methoxide in methylic alcohol was treated with excess of methylic iodide, and the mixture boiled for 50 hours. After removing the unchanged methylic iodide, the product was poured into water, extracted with ether, and the extract, after being washed, first with water, and then with dilute sodium carbonate solution, was dried over calcium chloride and evaporated. The brown, syrupy residue thus obtained deposited crystals on standing; these were drained upon a porous tile and purified by several crystallisations from methylic alcohol.

0.1438 gave 0.3226 CO_2 and 0.0824 H_2O . $\text{C} = 61.18$; $\text{H} = 6.36$.

$\text{C}_{10}\text{H}_{12}\text{O}_4$ requires $\text{C} = 61.22$; $\text{H} = 6.12$ per cent.

It formed a beautiful, colourless mass of long, prismatic needles, melting at $76-77^{\circ}$, readily soluble in hot alcohol, but somewhat sparingly in light petroleum. It is insoluble in cold solutions of the alkali hydroxides. The methoxy-groups present were determined by Zeisel's method.

0.2274 gave 0.5430 AgI . $\text{CH}_3 = 15.24$.

$\text{CH}_3 \cdot \text{C}_6\text{H}_2(\text{OCH}_3)(\text{OH}) \cdot \text{COOCH}_3$ requires $\text{CH}_3 = 15.30$ per cent.

It contained, therefore, but two methoxy-groups, of which one is present in the form of the methylic salt; it must therefore be considered to be a *monomethyl ether of the methylic salt of methyl- β -resorcylic acid*. As discussed in the introduction, its constitution is apparently $\text{OCH}_3 : \text{OH} : \text{COOCH}_3 = 1 : 3 : 4$. In order to obtain the acid from this methylic salt, it was first digested with boiling dilute alkali until a clear solution was obtained; the alkaline solution was then neutralised with acid, and the colourless precipitate collected, washed, and dried. It was purified by crystallisation from alcohol and toluene respectively.

0.1192 gave 0.2590 CO_2 and 0.0614 H_2O . $\text{C} = 59.25$; $\text{H} = 5.72$.
0.1094 gave, by Zeisel's method, 0.1487 AgI . $\text{CH}_3 = 8.67$.

$\text{CH}_3 \cdot \text{C}_6\text{H}_2(\text{OCH}_3)(\text{OH}) \cdot \text{COOH}$ requires $\text{C} = 59.34$; $\text{H} = 5.49$; $\text{CH}_3 = 8.24$ per cent. It was therefore a *monomethyl ether of methyl- β -resorcylic acid*.

Thus obtained, it formed colourless needles, melting at 210° with evolution of gas, this decomposition being evidently due to the splitting off of the carboxyl group, as is the case with β -resorcylic acid itself. The product consisted of a brownish oil, which, after standing for several days, became crystalline, but its examination was deferred until larger quantities could be obtained. It is readily soluble in alcohol, sparingly in water and toluene. With ferric chloride, an aqueous solution of the acid yields a claret-red coloration.

The alkaline washings of the ethereal extract obtained during the isolation of the above methylic salt were neutralised with acid, extracted with ether, and the extract evaporated. The nearly colourless, crystalline residue consisted chiefly of two substances, which were separated by fractional crystallisation from alcohol and dilute alcohol, a somewhat tedious process, the most insoluble product being obtained in colourless needles, melting at 210° , and the second, which had a similar appearance, melting at 151° .

The former, on examination, proved to be the monomethyl ether of methyl- β -resorcylic acid [$\text{OCH}_3 : \text{OH} : \text{COOH} = 1 : 3 : 4$] described above. A Zeisel's determination gave the following result.

0.4302 gave 0.5564 AgI . $\text{CH}_3 = 8.25$.

$\text{CH}_3 \cdot \text{C}_6\text{H}_2(\text{OCH}_3)(\text{OH}) \cdot \text{COOH}$ requires $\text{CH}_3 = 8.24$ per cent.

The second, or more soluble, substance, melting at 151° , was analysed, with the following result.

0.1370 gave 0.2900 CO_2 and 0.0645 H_2O . $\text{C} = 57.73$; $\text{H} = 5.22$.

0.2195 gave, by Zeisel's method, 0.3090 AgI . $\text{CH}_3 = 8.98$.

$\text{OCH}_3 \cdot \text{C}_6\text{H}_3(\text{OH}) \cdot \text{COOH}$ requires $\text{C} = 57.14$; $\text{H} = 4.76$; $\text{CH}_3 = 8.92$ per cent. It was evidently a *monomethyl ether of β -resorcylic acid*. Its properties agreed with those given for the methyl ether [$\text{OCH}_3 : \text{OH} : \text{COOH} = 1 : 3 : 4$] previously obtained by Tiemann and Parrisius (*loc. cit.*) by the methylation of β -resorcylic acid.

The original aqueous liquid remaining after the extraction of the mixed products of the methylation with ether was neutralised with acid, extracted with ether, and the extract evaporated. A dark brown, oily residue remained, from which nothing crystalline separated, even on long standing. It probably consisted of a mixture of methyl ethers of resorcinol, the latter being produced from the decomposition of some of the resorcylic acid in the earlier stages of the reaction.

Ethylation of β -Resorcylic acid.

The method employed in studying the action of ethylic iodide on β -resorcylic acid was similar to that previously described. The product was extracted with ether, the extract washed with dilute sodium carbonate solution, dried, and evaporated. The oily residue thus obtained deposited crystals, on standing, which were drained upon a porous tile and purified by several crystallisations from methylic alcohol.

0.1123 gave 0.2578 CO_2 and 0.0690 H_2O . $\text{C} = 62.60$; $\text{H} = 6.82$.

$\text{OEt} \cdot \text{C}_6\text{H}_3(\text{OH}) \cdot \text{COOEt}$ requires $\text{C} = 62.85$; $\text{H} = 6.66$ per cent.

It was obtained in long, colourless needles, melting at 53° , readily soluble in alcohol; cold alkali solutions dissolve it with difficulty.

In order to convert it into the acid, it was digested with a boiling solution of dilute caustic potash, until a clear solution was formed; this, when acidified, deposited a colourless precipitate, which was collected, washed, and purified by crystallisation from dilute alcohol.

0.1090 gave 0.2372 CO_2 and 0.0562 H_2O . $\text{C} = 59.34$; $\text{H} = 5.72$.

0.1964 gave, by Zeisel's method, 0.2575 AgI . $\text{C}_2\text{H}_5 = 16.17$.

$\text{OEt} \cdot \text{C}_6\text{H}_3(\text{OH}) \cdot \text{COOH}$ requires $\text{C} = 59.34$; $\text{H} = 5.49$; $\text{C}_2\text{H}_5 = 15.93$ per cent.

β -Resorcylic acid monethyl ether forms colourless needles, melting at 153 – 154° , sparingly soluble in water, readily in alcohol. Its aqueous solution gives a claret-red coloration with ferric chloride.

Salicylic acid, when distilled with acetic anhydride, yields diphenylene ketone oxide, $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{CO} \\ \diagup \quad \diagdown \\ \text{O} \end{smallmatrix} \text{C}_6\text{H}_4$, and β -resorcylic acid, by

similar treatment, gives iso-euxanthone, $\text{OH}\cdot\text{C}_6\text{H}_3\langle\text{CO}\rangle\text{C}_6\text{H}_3\cdot\text{OH}$. If the above ethyl ether have the constitution, $\text{OEt}:\text{OH}:\text{COOH} = 1:3:4$, iso-euxanthone diethyl ether should be produced from it by this reaction. In order to determine this point, a small portion of the substance was digested with acetic anhydride in a small retort and the product rapidly distilled. Towards the end of the operation a distillate was obtained, which solidified in the neck of the retort; this was collected, washed with a little alcohol, and recrystallised from the same solvent.

0.1203 gave 0.3150 CO_2 and 0.0574 H_2O . $\text{C} = 71.41$; $\text{H} = 5.30$.

$\text{C}_{17}\text{H}_{10}\text{O}_4$ requires $\text{C} = 71.83$; $\text{H} = 5.63$ per cent.

It appeared as a mass of nearly colourless needles, melting at 185° , moderately soluble in alcohol, but insoluble in alkaline solutions.

Experiment showed that the yield of this diethyl ether from the ethyl ether of β -resorcylic acid is considerably greater than that of iso-euxanthone from β -resorcylic acid itself.

From these results, it is evident that the ethylic salt of the ethyl ether of β -resorcylic acid and the free acid produced by its saponification have respectively the constitution, $\text{OEt}:\text{OH}:\text{COOEt}$ and $\text{OEt}:\text{OH}:\text{COOH} = 1:3:4$.

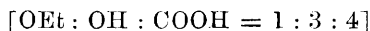
The alkaline washings of the ethereal extract obtained during the isolation of the above ethylic salt, were neutralised with acid, extracted with ether, and the extract evaporated. The nearly colourless, crystalline residue consisted chiefly of a single substance, there being traces present, however, of a second more soluble product. By crystallisation from toluene, the latter was readily removed.

0.1142 gave 0.2493 CO_2 and 0.0590 H_2O . $\text{C} = 59.53$; $\text{H} = 5.74$.

0.1191 „ 0.2577 „ „ 0.0590 „ $\text{C} = 59.01$; $\text{H} = 5.50$.

$\text{OEt}\cdot\text{C}_6\text{H}_3(\text{OH})\cdot\text{COOH}$ requires $\text{C} = 59.34$; $\text{H} = 5.49$ per cent.

It crystallised in colourless needles, melting at 153 – 154° , and is identical with the monethyl ether of β -resorcylic acid



above described. The quantity of the more soluble product accompanying it being small, its examination has been deferred.

Methylresacetophenone Monomethyl Ether.

Experiments were made on the methylation of resacetophenone, but, as stated in the introduction, the results obtained have been anticipated by others. The principal product of the reaction, which

was insoluble in alkalis, crystallised in colourless leaflets, melting at $83-84^{\circ}$.

0.1812 gave 0.4450 CO_2 and 0.1345 H_2O . C = 66.96; H = 7.22.

0.1543 „ 0.3780 „ „ 0.0940 „ C = 66.81; H = 6.76.

$\text{C}_6\text{H}_2\text{Me}(\text{OMe})(\text{OH})\cdot\text{CO}\cdot\text{CH}_3$ requires C = 66.66; H = 6.66 per cent.

It possessed the above constitution, which has been previously assigned to it by G. Gregor (*loc. cit.*).

To investigate the action of bromine on this substance, it was dissolved in six times its weight of carbon bisulphide, and the solution treated gradually with sufficient bromine, dissolved in the same solvent, to form the monobrominated derivative. The action took place readily, and as soon as hydrobromic acid ceased to be evolved, the solution was evaporated, the residue spread upon a porous tile, and purified by several crystallisations from light petroleum.

0.3359 gave 0.2422 AgBr . Br = 30.69 per cent.

$\text{C}_6\text{HBrMe}(\text{OMe})(\text{OH})\cdot\text{CO}\cdot\text{CH}_3$ requires Br = 30.89 per cent.

It forms long, thin, colourless needles, melting at $63-64^{\circ}$, sparingly soluble in light petroleum. It is not attacked, even when digested with boiling alcoholic potash, and from this and other reactions it was shown to contain the bromine in the nucleus, and not in the side chain.

Preliminary experiments have also been carried out on the methylation of gallacetophenone, in a similar manner to those previously described with β -resorcylic acid. The chief product of the action crystallised in colourless needles melting at $77-78^{\circ}$.

0.1133 gave 0.2540 CO_2 and 0.0650 H_2O . C = 61.13; H = 6.37.

$\text{C}_6\text{H}_2(\text{OH})(\text{OCH}_3)_2\cdot\text{CO}\cdot\text{CH}_3$ requires C = 61.22; H = 6.12 per cent.

It has therefore the composition of a dimethyl ether. I desire to reserve to myself the further study of this substance.

Oxime of Gallacetophenone.

Gallacetophenone (4 grans) dissolved in an aqueous solution of potash (14 grams) was treated with a solution of hydroxylamine hydrochloride (4 grams), rise in temperature being avoided. After standing 12 hours, the product was neutralised with acid, extracted with ether, and the extract evaporated; the brown, crystalline residue was purified first by crystallisation from water, and finally from toluene with the aid of animal charcoal.

0.3600 gave 24 c.c. moist nitrogen at 17° , and 743 mm. N = 7.56.

$\text{C}_6\text{H}_2(\text{OH})_3\cdot\text{C}(\text{NOH})\cdot\text{CH}_3$ requires N = 7.65 per cent.

It formed colourless needles, melting at $162-163^{\circ}$, and decomposing slightly above this temperature. Crystallisation of the crude product from water, in which it is sparingly soluble, does not render

it colourless, benzene and toluene being the only useful solvents for this purpose. It dissolves readily in acetic anhydride, on gentle warming, but this solution, when raised to the boiling point, suddenly solidifies if concentrated, owing to the separation of crystals. These were collected, drained upon a porous tile, and purified by crystallisation from acetic acid.

0.1053 gave 0.2068 CO_2 and 0.0505 H_2O . $\text{C} = 53.56$; $\text{H} = 5.32$.

0.1677 „ 8.8 c.c. moist nitrogen at 20° , and 756 mm. $\text{N} = 5.97$.

$\text{C}_{10}\text{H}_{11}\text{NO}_5$ requires $\text{C} = 53.33$; $\text{H} = 4.90$; $\text{N} = 6.22$ per cent.

A determination of the acetic acid yielded by its decomposition with baryta water gave 28.19 per cent., the theory for one acetyl group being 28.09 per cent.; it was therefore a monacetyl derivative. From acetic acid, it crystallises in almost colourless needles, soluble in dilute alkalis. When heated, it commences to darken at 150 – 155° , and melts with rapid decomposition at 165° , gas being evolved, and if some quantity be melted, this action is so violent as to frequently give rise to a slight explosion; on digestion with solvents of high-boiling point, the same decomposition takes place, but more moderately, and it is hoped in this way to study the action.

The *oxime of resacetophenone* has been studied by Wechsler (*loc. cit.*), and, in order to investigate its behaviour with acetic anhydride, a small quantity was prepared; it readily dissolved, on gently warming, and when the solution was boiled for a few seconds and cooled rapidly, crystals separated. These were collected and purified by crystallisation from toluene.

0.1466 gave 7.7 c.c. moist nitrogen at 17° , and 766 mm. $\text{N} = 6.14$.

0.1423 „ 0.2995 CO_2 and 0.0730 H_2O . $\text{C} = 57.40$; $\text{H} = 5.69$.

$\text{C}_{10}\text{H}_{11}\text{NO}_4$ requires $\text{C} = 57.41$; $\text{H} = 5.26$; $\text{N} = 6.6$ per cent.

It was obtained as nearly colourless needles, readily soluble in acetic acid, soluble in alkalis. When heated, it melts and decomposes at 174 – 175° , but this action is not violent, as is the case with the gallacetophenone compound, gas being but gently evolved.

Oxime of Quinacetophenone.

This was prepared in a similar way to the gallacetophenone compound. The product was purified by crystallisation from water and toluene.

0.1894 gave 14.4 c.c. moist nitrogen at 18° , and 767 mm. $\text{N} = 8.86$.

$\text{C}_6\text{H}_3(\text{OH})_2\text{C}(\text{NOH})\cdot\text{CH}_3$ requires $\text{N} = 8.38$ per cent.

It crystallises from toluene in colourless leaflets, melting at 149 – 150° .

When heated with acetic anhydride, it behaves similarly to resaceto-

phenone oxime, a substance, apparently a monacetyl compound, being produced ; this crystallises from benzene in colourless needles, soluble in alkalis, and melting with gentle decomposition at 146—147°.

In concluding this paper, I desire to express my thanks to Mr. W. R. Allen, a former student, for his assistance during the carrying out of a portion of this investigation.

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