XVIII.—*Derivatives of β -Resorcylic Acid and of Protocatechuic Acid.*

By WILLIAM HENRY PERKIN, jun., and EMANUEL SCHIESS.

DURING the course of a long series of researches on the constitution of brazilin and hæmatoxylin, it was found necessary, for the purposes of comparison, to prepare and investigate several new derivatives of resorcinol and catechol, and in this paper we give a brief account of some of the compounds which were thus prepared.

Dimethylresorcylic Acid, $(\text{MeO})_2\text{C}_6\text{H}_3\cdot\text{CO}_2\text{H}$, and its *Methyl and Ethyl Esters*.

Methyl dimethyl- β -resorcylicate, $(\text{MeO})_2\text{C}_6\text{H}_3\cdot\text{CO}_2\text{Me}$, is readily obtained when β -resorcylic acid is treated with caustic potash and methyl sulphate in aqueous solution. It is thus seen that the hydroxyl group in β -resorcylic acid, which is in the *o*-position with respect to the carbonyl group, may be methylated by means of aqueous caustic potash and methyl sulphate, whereas, as is well known, the hydroxyl group in the above position in this and other similar compounds is hardly attacked by the usual treatment with alcoholic potash and methyl iodide.

β -Resorcylic acid (30 grams) is dissolved in 240 grams of 10 per

cent. aqueous caustic soda, and then methyl sulphate (65 grams) added in small quantities at a time. After each addition, the bottle containing the mixture is vigorously shaken on the machine and cooled, if necessary, no further quantity being added until the last portion has been completely decomposed. Care is also taken, by adding small quantities of strong caustic soda solution from time to time, that the liquid is always strongly alkaline. The oil which separates is extracted with ether, the ethereal solution washed with dilute aqueous caustic soda, dried over calcium chloride, and evaporated, and the residual oil fractionated under reduced pressure, when almost the whole distils at 160—162° (13 mm.). The boiling point of this oil under the ordinary pressure was observed to be 294—296°.

0.2261 gave 0.4978 CO₂ and 0.1126 H₂O. C = 60.9 ; H = 6.1.

C₁₀H₁₂O₄ requires C = 61.2 ; H = 6.1 per cent.

The yield of methyl dimethyl- β -resorcyate (which does not appear to have been previously prepared) varies considerably, but is usually 30—40 per cent. of the theoretical. As, however, by acidifying the alkaline liquids, quantities of methyl- and dimethyl- β -resorcylic acids may be precipitated and used in a subsequent operation, the total yield from a given quantity of β -resorcylic acid is actually much greater than this. When the above methyl ester is boiled with alcoholic potash for a few minutes and the solution, after evaporating with water, acidified with hydrochloric acid, dimethyl- β -resorcylic acid separates at once, and after recrystallising melts at 108°.

Ethyl Dimethyl- β -resorcyate, (MeO)₂C₆H₃·CO₂Et.

This ester was prepared by boiling dimethyl- β -resorcylic acid with alcohol and sulphuric acid for about 6 hours, and then adding water and extracting with ether. After washing with sodium carbonate, drying over calcium chloride, and distilling off the ether, an oil was obtained which distilled constantly at 170° under 13 mm. pressure.

0.1337 gave 0.3080 CO₂ and 0.0826 H₂O. C = 62.8 ; H = 6.9.

C₁₁H₁₄O₄ requires C = 62.9 ; H = 6.7 per cent.

2 : 4-Dimethoxybenzoylacetophenone, (MeO)₂C₆H₃·CO·CH₂·CO·C₆H₅.

This substance is produced by the condensation of ethyl β -resorcyate and acetophenone in the presence of sodium, and in our first experiments, which were carried out under ordinary conditions (see, for example, Kostanecki, Różycki, and Tambor, *Ber.*, 1900, 33, 3413), great difficulty was experienced in isolating more than traces of the crystalline product of the reaction. On using, however, conditions

similar to those recommended by the Farbwerke vorm. Meister, Lucius, and Brüning (*Ber.*, 1890, **23**, *Ref.* 40; see also Bülow and Riess, *ibid.*, 1902, **35**, 3902), we were able to obtain an excellent yield of 2:4-dimethoxybenzoylacetophenone. Ethyl dimethyl- β -resorcylate (21 grams) is dissolved in dry ether, mixed with acetophenone (12 grams) and treated with finely divided sodium (2.5 grams).^{*} Any rise of temperature is prevented by placing the flask in ice-water, the reaction is promoted by repeated shaking, and after two hours the flask is allowed to remain overnight at the ordinary temperature. The sodium gradually passes into solution and the sodium compound separates as a crystalline powder, the whole ultimately becoming a semi-solid mass. In order to isolate the dimethoxybenzoylacetophenone, the product is made slightly acid by the addition of dilute acetic acid, extracted with ether, the ethereal solution washed with dilute sodium carbonate solution and well agitated on the machine with aqueous copper acetate until no further separation of the green copper derivative takes place. This is collected at the pump, washed with water and alcohol, and purified by recrystallisation from benzene, from which the copper derivative of 2:4-dimethoxybenzoylacetophenone separates in slender, green needles containing one molecule of benzene of crystallisation.[†]

0.2335 gave 0.0259 CuO. Cu = 8.6.

$C_{34}H_{30}O_8Cu$, C_6H_6 requires Cu = 8.4 per cent.

After drying at 110° until constant, the following complete analysis was made:

0.1803 gave 0.4277 CO₂, 0.0778 H₂O, and 0.0226 CuO.

C = 64.7; H = 4.8; Cu = 10.0.

$C_{34}H_{30}O_8Cu$ requires C = 64.9; H = 4.8; Cu = 10.0 per cent.

The pure copper compound was then mixed with excess of dilute hydrochloric acid and the diketone extracted with ether, the ethereal solution was washed with water until free from copper, dried over calcium chloride, and evaporated, when an oil was obtained which rapidly solidified. The substance was further purified by recrystallisation from alcohol, from which it separates in plates.

0.1501 gave 0.3948 CO₂ and 0.0779 H₂O. C = 71.7; H = 5.8.

$C_{17}H_{16}O_4$ requires C = 71.8; H = 5.7 per cent.

2:4-Dimethoxybenzoylacetophenone melts at 55° and is readily soluble

^{*} This condition is best obtained by melting the sodium under boiling toluene and then shaking vigorously.

[†] It is noteworthy that the copper derivative of 3:5-dimethoxybenzoylacetophenone also crystallises with one molecule of benzene (Bülow and Riess, *loc. cit.*).

in benzene, ether, and chloroform, more sparingly in alcohol and light petroleum. Its solution in alcohol gives with ferric chloride an intense reddish-brown coloration.

2 : 4-Dimethoxycinnamic Acid, $(\text{MeO})_2\text{C}_6\text{H}_3\cdot\text{CH}:\text{CH}\cdot\text{CO}_2\text{H}$.

This acid was first obtained from umbelliferone by Will and Tiemann (*Ber.*, 1882, 15, 2080 ; 1883, 16, 2116) in two forms— α - and β -—which melt at 138° and 184° respectively, and obviously represent the *cis*- and *trans*-modifications of the acid. Since it was probable that we should require considerable quantities of this acid, a number of experiments were made with the object of preparing the substance synthetically, with the result that two methods were devised by which it may be readily obtained in quantity from dimethyl- β -resorcyraldehyde.

Method I. Preparation of 2 : 4-Dimethoxycinnamic Acid from Dimethyl- β -resorcyraldehyde by the Action of Sodium Acetate and Acetic Anhydride.

Dimethyl- β -resorcyraldehyde (10 grams) is intimately mixed with anhydrous sodium acetate (10 grams) and heated with acetic anhydride (30 grams) in a reflux apparatus for 20 hours in an oil-bath at 170° . The brown mass is diluted with water and the excess of acetic acid removed by distillation in steam, the residue is then made alkaline by adding sodium carbonate, and allowed to remain until quite cold. The unchanged aldehyde which separates is filtered off, the filtrate acidified with hydrochloric acid, and the very sparingly soluble dimethoxycinnamic acid, which separates at once, collected and purified by recrystallisation from acetic acid. The acid thus obtained is the β -modification and melts at 186° .

0.1420 gave 0.3317 CO_2 and 0.0780 H_2O . $\text{C} = 63.7$; $\text{H} = 6.1$.

$\text{C}_{11}\text{H}_{12}\text{O}_4$ requires $\text{C} = 63.5$; $\text{H} = 5.8$ per cent.

Method II. Preparation of Ethyl 2 : 4-Dimethoxycinnamate, $(\text{MeO})_2\text{C}_6\text{H}_3\cdot\text{CH}:\text{CH}\cdot\text{CO}_2\text{Et}$, by the Condensation of Dimethyl- β -resorcyraldehyde with Ethyl Acetate in the presence of Sodium.

This ethyl ester was first prepared by the esterification of the acid with alcohol and sulphuric acid, and was thus obtained as a crystalline solid which melted at 61° and distilled at 210 — 212° under 13 mm. pressure. Subsequently it was discovered that it can be obtained directly, and in a yield of at least 80 per cent. of the theoretical amount, by

β -RESORCYLIC ACID AND OF PROTOCATECHUIC ACID. 163

the general method devised by Claisen (*Ber.*, 1890, 23, 977), and which appears to be not nearly so well known as it deserves to be. Dimethyl- β -resorcylaldehyde (16.6 grams) is dissolved in 30 grams of ethyl acetate (which has been carefully freed from water and alcohol) and then finely divided sodium (2.5 grams, see foot-note, p. 161) added all at once. The sodium begins to act immediately, and, after two hours in ice-water, the mixture is left overnight at the ordinary temperature, when all the sodium will have disappeared. The dark brown liquid is acidified with dilute acetic acid, extracted with ether, the ethereal solution well washed, dried over calcium chloride, and evaporated, when an oil is obtained which rapidly solidifies. In purifying this substance, it is best to distil the product first under reduced pressure, when almost the whole passes over at 208—212° (13 mm.), leaving only a small quantity of resinous matter in the retort. The distillate, which solidifies at once, is pure enough for most experiments, but for analysis the substance was recrystallised from light petroleum, from which it separated in slender needles melting at 61°.

0.1518 gave 0.3668 CO₂ and 0.0941 H₂O. C=65.9; H=6.9.

C₁₃H₁₆O₄ requires C=66.1; H=6.8 per cent.

Ethyl 2:4-dimethoxycinnamate is readily soluble in alcohol, ether, or benzene, but sparingly so in cold light petroleum. Attempts were made to convert this ester into ethyl dimethoxyphenyl- $\alpha\beta$ -dibromopropionate by the action of bromine, but, so far, these have not been successful. When bromine is added to the chloroform solution of the ester, dark decomposition products are formed, and hydrogen bromide is evolved even at 0°. Possibly under different conditions, a method of avoiding this decomposition and substitution may be found, and further experiments with this end in view are in progress.

3:4-Dimethoxycinnamic Acid, (MeO)₂C₆H₃·CH:CH·CO₂H.

The methyl ester of this acid is formed when 3:4-dihydroxycinnamic acid (caffeic acid) or either of its two isomeric 3- and 4-monomethyl derivatives, (MeO)(OH)C₆H₃·CH:CH·CO₂H, called respectively ferulic and isoferulic acids, is heated with methyl iodide and caustic potash in methyl alcoholic solution (Tiemann and Nagai, *Ber.*, 1878, 11, 652; Tiemann and Will, *ibid.*, 1881, 14, 959).

The melting point of the methyl ester is given as 64°, and that of the free acid as 180—181°. Although 2:4-dimethoxycinnamic acid (see p. 162) exists in two well-defined stereoisomeric forms, the 3:4-dimethoxy-acid has, so far, only been obtained in the one modification. In our experiments on the synthesis of 3:4-dimethoxycinnamic acid, we employed in the first instance an exactly similar

process to that described in the case of the 2:4-dimethoxy-acid, that is, we heated a mixture of 3:4-dimethoxybenzaldehyde (dimethylcatecholaldehyde) and sodium acetate with acetic anhydride. The yield of acid obtained was upwards of 50 per cent. of the aldehyde employed, and a good deal of the latter was recovered unchanged. 3:4-Dimethoxycinnamic acid melts at 180° and crystallises from acetic acid in needles; it is very sparingly soluble in water.

0.1439 gave 0.3358 CO_2 and 0.0739 H_2O . $\text{C} = 63.6$; $\text{H} = 5.7$.

$\text{C}_{11}\text{H}_{12}\text{O}_4$ requires $\text{C} = 63.5$; $\text{H} = 5.8$ per cent.

Ethyl 3:4-Dimethoxycinnamate, $(\text{MeO})_2\text{C}_6\text{H}_3\cdot\text{CH}:\text{CH}\cdot\text{CO}_2\text{Et}$.

When 3:4-dimethoxybenzaldehyde is condensed with ethyl acetate under the conditions described in the case of the preparation of the ethyl salt of the 2:4-dimethoxy-acid (p. 162) and the product purified by fractionation, ethyl 3:4-dimethoxycinnamate is readily obtained pure and in a yield of 85 per cent. of that theoretically possible. It crystallises from light petroleum in plates, melts at 59° , and distils at $196\text{--}197^{\circ}$ under 13 mm. pressure.

0.1507 gave 0.3642 CO_2 and 0.0936 H_2O . $\text{C} = 65.9$; $\text{H} = 6.9$.

$\text{C}_{13}\text{H}_{16}\text{O}_4$ requires $\text{C} = 66.1$; $\text{H} = 6.8$ per cent.

It dissolves readily in alcohol, benzene, or chloroform, but is sparingly soluble in light petroleum.

Ethyl 3:4-Dimethoxyphenyl- $\alpha\beta$ -dibromopropionate,
 $(\text{MeO})_2\text{C}_6\text{H}_3\cdot\text{CHBr}\cdot\text{CHBr}\cdot\text{CO}_2\text{Et},$
and 3:4-Dimethoxyphenylpropionic Acid,
 $(\text{MeO})_2\text{C}_6\text{H}_3\cdot\text{C}:\text{C}\cdot\text{CO}_2\text{H}.$

In its behaviour towards bromine, ethyl 3:4-dimethoxycinnamate shows much greater stability than the corresponding 2:4-dimethoxy-compound (p. 163), and this enabled us to prepare, without much difficulty, considerable quantities of the dibromo-additive product in a pure condition. Ethyl 3:4-dimethoxycinnamate (23.6 grams) is dissolved in chloroform (40 grams), the solution cooled with ice-water, and then 16 grams of bromine, dissolved in 30 grams of chloroform, gradually added. When the colour of the bromine has disappeared, the chloroform is removed at as low a temperature as possible, by distillation under reduced pressure, and the oily residue then solidifies to a hard, yellow, crystalline cake. After triturating with cold light petroleum and filtering at the pump, the substance is then crystallised from the same solvent.

0.2218 gave 0.2092 AgBr. Br = 40.2.

$C_{13}H_{16}O_4Br_2$ requires Br = 40.4 per cent.

Ethyl 3:4-dimethoxyphenyl- $\alpha\beta$ -dibromopropionate crystallises from light petroleum in colourless needles and melts at 110—111°; it is readily soluble in alcohol, ether, benzene, chloroform, or hot light petroleum, but sparingly so in the latter solvent in the cold.

3:4-Dimethoxyphenylpropionic acid is readily obtained when ethyl 3:4-dimethoxyphenyl- $\alpha\beta$ -dibromopropionate (1 mol.) is digested for 8 hours with a large excess of alcoholic potash (6 mols.). The product is evaporated on the water-bath to remove the bulk of the alcohol, the residue dissolved in water, and neutralised with hydrochloric acid. After filtering from a small quantity of dark resinous matter which usually separates, the clear solution is acidified, when the new acid is precipitated in white flocks. It is collected at the pump, washed thoroughly with water, dried on porous porcelain, and purified by recrystallisation from benzene.

0.1426 gave 0.3338 CO_2 and 0.0694 H_2O . C = 63.9; H = 5.0.

$C_{11}H_{10}O_4$ requires C = 64.1; H = 4.8 per cent.

3:4-Dimethoxyphenylpropionic acid melts at 149° with decomposition and is readily soluble in alcohol, but sparingly so in cold benzene or chloroform; it dissolves very sparingly in hot water and is almost insoluble in the cold; it crystallises best from benzene, from which it separates in colourless, microscopic needles.

THE OWENS COLLEGE,
MANCHESTER.