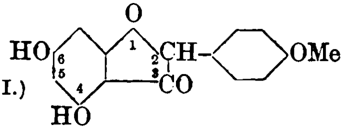
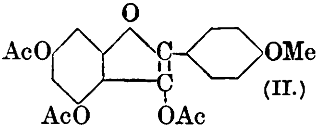
# CXXVI.—2-*Arylcoumaranones.*

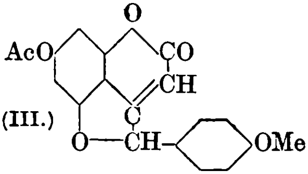
By WILSON BAKER.

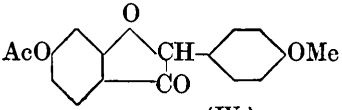
AMONGST the methods available for the preparation of coumaranones are those in which a cyanohydrin or α-monohalogeno-nitrile is condensed with polyhydric phenols under the conditions of the Hoesch synthesis (Sonn, *Ber.*, 1917, **50**, 1262; Slater and Stephen, J., 1920, **117**, 309; Sonn and Falkenheim, *Ber.*, 1922, **55**, 2975; Klarmann, *J. Amer. Chem. Soc.*, 1926, **48**, 2366). Some years ago it was desired to synthesise 4 : 6-*dihydroxy*-2-p-*methoxyphenylcoumaranone* (I), since it appeared probable at one time that such a compound occurred naturally, and it was suggested to the author by Professor R. Robinson that such arylcoumaranones might be synthesised from the readily accessible *O*-benzoyl derivatives of aromatic aldehydes (Francis and Davis, J., 1909, **95**, 1404) by means of the Hoesch reaction. This expectation has been realised, but the yields are very poor and the products difficult to isolate except as acetyl derivatives. Further, the acetylation often takes an abnormal course. The use of aromatic aldehyde cyanohydrins themselves is prohibited owing to the ease with which they undergo condensation to derivatives of 1 : 4-diazines when treated with hydrogen chloride in ethereal solution (Minovici, *Ber.*, 1899, **32**, 2206; Japp and Knox, J., 1905, 87, 701; for mechanism of the reaction see Ingham, J., 1927, 694).


(I.)


(II.)

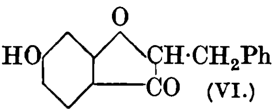
The interaction of *O*-benzoylanisaldehydecyanohydrin and phloroglucinol in ethereal solution with hydrogen chloride in presence of zinc chloride gave a solid ketimine, which after complete hydrolysis with concentrated hydrochloric acid yielded finally the coumaranone (I). Acetylation of the crude coumaranone with acetic anhydride and a trace of pyridine yielded 3 : 4 : 6-*triacetoxy*-2-p-*methoxyphenylcoumarone* (II) and *anhydro-5-hydroxy-7-acetoxy-4-α-hydroxy*-p-*methoxybenzylcoumarin* (III), which were separated by physical means. The constitution assigned to (III) is based on the facts that, unlike (I) and (II), it does not reduce Fehling's solution, and that its alcoholic solution has a violet fluorescence.


(III.)


(IV.)

The analogous condensation of *O*-benzoylanisaldehydecyanohydrin and resorcinol gave, after complete hydrolysis, a product which could be obtained crystalline only after acetylation with acetic anhydride. This again proved to be a mixture, which was separated into 6-*acetoxy*-2-p-*methoxyphenylcoumaranone* (IV), and a compound of high molecular weight which did not reduce Fehling's solution and is tentatively regarded as 3-*keto*-6 : 3′ : 6′-*triacetoxy*-2 : 2′-*di*-p-*methoxyphenyl*-2 : 3′-*dicoumaranyl*.


(V.)


(VI.)

The condensation of *O*-benzoylbenzaldehydecyanohydrin with resorcinol yielded finally after acetylation 2 : 4-*diacetoxy*-O-*acetylbenzoin* (V), the ring in this case not having closed.

2-Arylcoumaranones of the type (I) could doubtless be prepared most readily by the condensation of α-bromophenylacetonitriles with polyhydric phenols, and with this in mind α-bromo-β-phenylpropionitrile was condensed with resorcinol under the conditions of the Hoesch reaction. Acid hydrolysis of the product gave a good yield of *6-hydroxy-2-benzylcoumaranone* (VI), which on acetylation yielded 3 : *6-diacetoxy-2-benzylcoumarone.* It is obvious that the condensation might proceed in a number of ways to give a compound $C_{15}H_{12}O_3$, which might be either (VI), 2 : 4-dihydroxyphenyl styryl ketone, 7-hydroxyflavanone, 7-hydroxy-4-phenyl-3 : 4-dihydrocoumarin (compare Fischer and Nouri, *Ber.*, 1917, **50**, 611), or 7-hydroxy-3-benzyl*iso*coumaranone. The physical properties of the reaction product are not in agreement with those of 2 : 4-dihydroxyphenyl styryl ketone (Ellison, J., 1927, 1720), and of the other possibilities only (VI) could give a diacetyl derivative.

Klarmann (*loc. cit.*) has condensed α-bromo-*n*-butyronitrile with phloroglucinol by the Hoesch reaction and obtained a product which he describes as 4 : 6-dihydroxy-2-ethylcoumaranone. Although this reaction is exactly analogous to the case described above, and might lead to any of five isomeric products, no proof of the constitution of the substance was given; yet by analogy with the present case there can be little doubt that the compound isolated was actually the coumaranone.

The condensation of glycollonitrile with resorcinol has been described by Slater and Stephen (*loc. cit.*), who state that the reaction yields 6-hydroxycoumaranone. Karrer and Biedermann, however (*Helv. Chim. Acta*, 1927, **10**, 441), find that the only product is ω-hydroxyresacetophenone (fisetol). Full experimental details are not given by Slater and Stephen, but as the result of a number of experiments the author confirms the result of Karrer and Biedermann, and has further been unable to convert ω-hydroxyresacetophenone into 6-hydroxycoumaranone by heating with various strengths of hydrochloric or sulphuric acid with or without the addition of zinc chloride—conditions which were probably used by Slater and Stephen in hydrolysing the ketimine.

## EXPERIMENTAL.

*Condensation of* O-*Benzoylanisaldehydecyanohydrin with Phloroglucinol.*—(a) A solution of the cyanohydrin (30 g.; Francis and Davis, *loc. cit.*) and phloroglucinol (14·2 g.) in anhydrous ether (300 c.c.) was saturated with hydrogen chloride at room temperature. After 48 hours the solid ketimine was collected, washed with ether, and hydrolysed by heating with concentrated hydrochloric acid for 4 hours. The product was freed from benzoic acid by washing with sodium bicarbonate solution and was finally dissolved in alcohol (charcoal), and the solution concentrated to a small bulk. After several weeks the crystals which had separated from the viscous fluid were isolated by pressing the product between plates of porous earthenware, and were then recrystallised from a very small volume of alcohol, being obtained in microscopic, almost colourless plates, m. p. 216—217° (Found: C, 66·2; H, 4·6. $C_{15}H_{12}O_5$ requires C, 66·1; H, 4·4%). 4 : *6-Dihydroxy-2-*p*-methoxyphenylcoumaranone* (I) gives a brownish-violet coloration with ferric chloride in alcoholic solution, and its solution in concentrated sulphuric acid is purplish-pink. It readily reduces Fehling's solution.

(b) A solution of the cyanohydrin (20 g.) and phloroglucinol (10 g.) in ether (200 c.c.) was saturated with hydrogen chloride, first at room temperature and then, after the addition of powdered anhydrous zinc chloride, at 0°. After 48 hours at 0°, water was added, and the ketimine hydrolysed by heating on the water-bath for 2 hours. The solid product was collected, heated for 1 hour in dilute sodium hydroxide solution, and reprecipitated by carbon dioxide. It was again collected, dried on porous earthenware, and acetylated by boiling with acetic anhydride and a trace of pyridine for 3 hours. The acetylated material was isolated by the addition of water and was obtained as light-brown crystals by recrystallisation from acetic acid (charcoal), in which it was sparingly soluble (yield, 7 g.). Three further crystallisations from acetic acid yielded a colourless product, which consisted of a mixture of compact prisms (A) and slender needles (B). An almost complete separation of the two substances was effected by stirring the mixture with alcohol, allowing the compact prisms to settle, and pouring off the alcohol while most of the thin needles were still suspended. The process was repeated several times, and finally both substances were separately crystallised from large volumes of alcohol.

Substance (A) separates from its hot alcoholic solution, which has a violet fluorescence, in thin, almost rectangular plates, m. p. 181—182° (Found: C, 67·4; H, 4·1. $C_{19}H_{14}O_6$ requires C, 67·4; H, 4·1%). *Anhydro-5-hydroxy-7-acetoxy-4-α-hydroxy-*p*-methoxybenzylcoumarin* (III) gives a colourless solution in concentrated sulphuric acid, and does not reduce Fehling's solution.

Substance (B) separates from warm alcohol in very thin, prismatic needles, m. p. 174—175° (Found: C, 63·3; H, 4·6. $C_{21}H_{18}O_8$ requires C, 63·3; H, 4·5%). 3 : 4 : *6-Triacetoxy-2-*p*-methoxyphenylcoumarone* (II) gives a non-fluorescent solution in alcohol; the solution in concentrated sulphuric acid is a strawberry-red, which turns deep reddish-violet on standing. It readily reduces Fehling's solution.

*Condensation of* O*-Benzoylanisaldehydecyanohydrin with Resorcinol.*—The condensation, and complete hydrolysis of the product, were carried out as in the case of the corresponding reaction with phloroglucinol (method b). The non-crystalline phenolic substance was acetylated by boiling with acetic anhydride for 6 hours, and the solid isolated by the addition of water was crystallised from acetic acid (charcoal) and then from alcohol, in the latter case the crystals being collected from the still warm solution. A further crystallisation from ethyl acetate gave small colourless needles, m. p. 217° (Found: C, 67·3; H, 5·2; *M*, by Rast's method, 646. $C_{36}H_{30}O_{11}$ requires C, 67·7; H, 4·7%; *M*, 638). This substance gives a colourless non-fluorescent solution in alcohol; in concentrated sulphuric acid an orange solution is obtained, which slowly turns more pink. Prolonged hydrolysis with aqueous-alcoholic potassium hydroxide yields no benzoic acid, and the substance does not reduce Fehling's solution. It is most probably 3-*keto*-6 : 3′ : 6′-*triacetoxy*-2 : 2′-*di*-p-*methoxyphenyl*-2 : 3′-*dicoumaranyl*.

The alcoholic mother-liquor from the crystallisation of the foregoing compound deposited minute slender needles, m. p. about 135°. This second substance was obtained, after two recrystallisations from alcohol, in colourless prismatic needles, m. p. 139° (Found: C, 68·4; H, 4·8. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7%). 6-*Acetoxy*-2-p-*methoxyphenylcoumaranone* (IV) readily reduces Fehling's solution and gives a colourless solution in concentrated sulphuric acid.

*Condensation of* O-*Benzoylbenzaldehydecyanohydrin and Resorcinol.*—A solution of the cyanohydrin (20 g.) and resorcinol (20 g.) in ether (150 c.c.) was saturated with hydrogen chloride at 0°, and powdered anhydrous zinc chloride added. After 24 hours water was added and the whole heated on the water-bath for 2 hours. The semi-solid product was dissolved in sodium hydroxide solution, reprecipitated with carbon dioxide, collected, and acetylated by boiling with acetic anhydride. The acetyl derivative isolated by the addition of water crystallised from alcohol in colourless prismatic needles, m. p. 158° (Found: C, 65·1; H, 4·5. $C_{20}H_{18}O_7$ requires C, 64·9; H, 4·8%). 2 : 4-*Diacetoxy*-O-*acetylbenzoin* (V) readily reduces Fehling's solution and gives a pale yellow colour in concentrated sulphuric acid.

*Condensation of* α-*Bromo*-β-*phenylpropionitrile and Resorcinol.*—A solution of α-bromo-β-phenylpropionitrile (10 g.; Baker and Lapworth, J., 1924, **125**, 2333) and resorcinol (10 g.) in ether (100 c.c.) was saturated with hydrogen chloride at 0°, after the addition of a little powdered zinc chloride. After 48 hours water was added and the ketimine hydrolysed by heating on the water-bath for 1 hour. The solid ketone was collected and dissolved in dilute aqueous sodium hydroxide, and the solution shaken with chloroform. The alkaline layer was acidified; the solid obtained crystallised from chloroform (charcoal) in colourless, thick, diamond-shaped plates, m. p. 161°

(Found in material dried at 140° : C, 74·7 ; H, 5·3. $C_{15}H_{12}O_3$ requires C, 75·0 ; H, 5·0%). 6-*Hydroxy-2-benzylcoumaranone* (VI) gives no coloration with ferric chloride in alcohol, and does not reduce Fehling's solution. Its solution in concentrated sulphuric acid is pale-yellow.

The diacetyl derivative was prepared by boiling the parent substance (2 g.) with acetic anhydride (20 c.c.) and anhydrous sodium acetate (2 g.) for 3 hours. 3 : 6-*Diacetoxy-2-benzylcoumarone*, isolated by the addition of water, crystallised from methyl alcohol (charcoal) in colourless prismatic needles, m. p. 76° (Found : C, 70·5 ; H, 4·9. $C_{19}H_{16}O_5$ requires C, 70·4 ; H, 5·0%. A monoacetyl derivative, $C_{17}H_{14}O_4$, requires C, 72·3 ; H, 5·0%).

THE DYSON PERRINS LABORATORY,
OXFORD.

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