121. *The Chemistry of Fungi. Part II. Derivatives of 3 : 4-Dimethoxyphenol.*

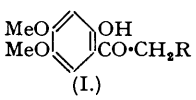
By G. H. Jones, J. B. D. Mackenzie, Alexander Robertson, and W. B. Whalley.

The syntheses of a number of coumarone, coumarin, and chromone derivatives from 3 : 4-dimethoxyphenol required as reference compounds in the course of studies on the degradation of methyl *O*-dimethylcitromycetin and of *O*-dimethylcitromycin are described. The alkaline hydrolysis product $C_{12}H_{12}O_5$ from methyl *O*-dimethylcitromycetin (Hetherington and Raistrick, *loc. cit.*) is not identical with either 5 : 6-dimethoxy-2-acetylcoumaran-3-one (V), 4-hydroxy-6 : 7-dimethoxy-3-methylcoumarin (VII, R = Me), or 3-hydroxy-6 : 7-dimethoxy-2-methylchromone (VIII, R = Me; R_1 = OH).

In the course of an analytical investigation on the structure of citromycetin in progress in these laboratories a number of degradation products have been isolated from *O*-dimethylcitromycin and methyl *O*-dimethylcitromycetin (Hetherington and Raistrick, *Phil. Trans.*, 1931, *B*, **220**, 209), which contain the 3 : 4-dimethoxyphenol nucleus and in which the third oxygen atom of the latter residue is present in an ether system. The synthetical work described in the present communication was undertaken in the course of the definition of these derivatives.

(A) *Coumarone Derivatives.*—Prepared from 3 : 4-dimethoxyphenol by the method of Hoesch, 2-hydroxy-4 : 5-dimethoxyacetophenone (I, R = H) was converted into the *3-methylcoumarone* (III, R = H) by way of the *phenoxyacetic acid* (II, R = H). By Gattermann's aldehyde synthesis the *2-formylcoumarone* (III, R = CHO) was obtained from (III, R = H), and the application of the Hoesch reaction to (III, R = H) furnished the corresponding *2-acetylcoumarone* (III, R = Ac). The orientations of the aldehyde (III, R = CHO) and of the ketone (III, R = Ac) follow from that of analogous compounds prepared by the same methods (*J.*, 1938, 306; 1939, 92 and 1594; and unpublished work).

Formed from 3 : 4-dimethoxyphenol and chloromethyl cyanide by the Hoesch reaction, the *ω-chloro-ketone* (I, R = Cl) gave 5 : 6-*dimethoxycoumaran-3-one* on treatment with sodium acetate in boiling alcohol, whilst on being boiled in benzene containing potassium carbonate the *acetate* of (I, R = Cl) yielded 5 : 6-*dimethoxy-2-acetylcoumaran-3-one* (V). This convenient general procedure for the synthesis of 2-acetylcoumaran-3-ones type (V) was first described by von Auwers (*Ber.*, 1910, **43**, 2000) who suggested that the reaction probably proceeded by way of the intermediate diketone type (IV) which loses hydrogen chloride to give type (V). In view of the closely analogous formation of *o*-hydroxy-ω-acetylacetophenones from *o*-acetoxyacetophenones observed by Baker (*J.*, 1933, 1381; 1940, 1370), it is now clear that von Auwers's explanation is the correct one.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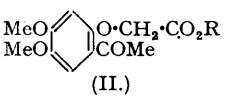
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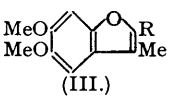
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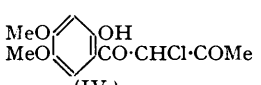
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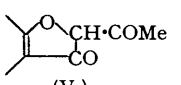
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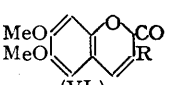

(VI.)

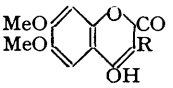
(B) *Coumarin Derivatives.*—The easy condensation of 2-hydroxy-4 : 5-dimethoxybenzaldehyde with ethyl acetoacetate in the presence of piperidine furnished the *3-acetylcoumarin* (VI, R = Ac) in good yield. With aceturic acid under standard conditions the same aldehyde yielded 4-(*2'-acetoxy-4'* : *5'-dimethoxybenzylidene*)-*2-methyloxazolone* which on hydrolysis gave *3-hydroxy-6* : *7-dimethoxycoumarin* (VI, R = OH).

Attempts to utilise the older methods of synthesis to prepare *4-hydroxy-6* : *7-dimethoxycoumarin* (VII, R = H) gave unsatisfactory results. Thus the condensation of cyanoacetic acid with 3 : 4-dimethoxyphenol by the method of Hoesch gave the expected *ketimine*, but hydrolysis of this product was troublesome and meagre yields of the required 4-hydroxycoumarin (VII, R = H) were obtained from it. Similarly, the interaction of 2-acetoxy-4 : 5-dimethoxybenzoyl chloride with ethyl sodio-malonate resulted in the formation of ethyl 4-hydroxy-6 : 7-dimethoxycoumarin-3-carboxylate (VII, R = CO_2Et), but hydrolysis of this ester, which was accompanied by decarboxylation of the resulting acid, furnished only small amounts of (VII, R = H). Subsequently, when the general method of Boyd and Robertson for the synthesis of 4-hydroxycoumarins (*J.*, 1948, 174) had been established, the compounds

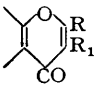
(VII, R = H), (VII, R = Me), and (VII, R = Et) were prepared by this procedure from the requisite ketones (I, R = H), (I, R = Me), and (I, R = Et) in good yield.

(C) *Chromone and Chromanone Derivatives.*—The condensation of ethyl formate with the ketone (I, R = H) at about −10° furnished an excellent yield of the *formyl* derivative (I, R = CHO) which on cyclisation yielded 6 : 7-*dimethoxychromone* (VIII, R = H; R_1 = H). Similarly, 6 : 7-*dimethoxy*-2-*methylchromone* (VIII, R = Me; R_1 = H) was obtained from (I, R = H) by way of the *diketone* (I, R = Ac), whilst vigorous acetylation of (I, R = H) gave the 3-*acetylchromone* (VIII, R = Me; R_1 = Ac), from which the chromone (VIII, R = Me; R_1 = H) was obtained by removal of the *C*-acetyl group under standard conditions. 3-*Hydroxy*-6 : 7-*dimethoxy*-2-*methylchromone* (VIII, R = Me; R_1 = OH) was synthesised from two intermediates. Vigorous acetylation of ω-chloro-2-hydroxy-4 : 5-dimethoxyacetophenone (I, R = Cl) with sodium acetate and acetic anhydride gave 3-*acetoxy*-6 : 7-*dimethoxy*-2-*methylchromone* (VIII, R = Me; R_1 = AcO), a reaction which clearly proceeds by way of the ω-acetoxy-ketone (I, R = AcO). Deacetylation of (VIII, R = Me; R_1 = AcO) furnished the required chromonol. The second intermediate, the *ketone* (I, R = Ph·CO_2), was prepared by condensation of benzoyloxymethyl cyanide and 3 : 4-dimethoxyphenol according to the method of Hoesch. On vigorous acetylation with excess of acetic anhydride and sodium acetate the ketone (I, R = Ph·CO_2) underwent cyclisation, and simultaneously the benzoyl group was replaced by acetyl, giving the 3-acetoxychromone (VIII, R = Me; R_1 = AcO) which on deacetylation yielded the chromonol (VIII, R = Me; R_1 = OH).

For the synthesis of compounds of the type (VII, R = Ac) the method employed by Anschütz (*Annalen*, 1906, **346**, 286) for the preparation of 4-hydroxy-3-acetylcoumarin, the parent member of this series—*viz.*, the interaction of an *o*-acetoxybenzoyl chloride with excess of ethyl sodio-acetoacetate in boiling ether—appears to have been the only procedure so far described. When 2-acetoxy-3 : 4-dimethoxybenzoyl chloride was employed in this reaction only a small amount of a condensation product *P*, m. p. 250°, having the empirical formula, $C_{13}H_{12}O_6$, of the expected coumarin (VII, R = Ac), was obtained, and consequently we investigated other possible routes to this type of compound. It was found that, whilst the condensation of the diketone (I, R = Ac) with ethyl carbonate by means of sodium gave only a poor yield of substance *P*, the interaction of the disodio-derivative of the diketone (I, R = Ac) with carbonyl chloride in a benzene–toluene medium provided a more satisfactory yield of the substance *P* in a relatively pure condition. Clearly the synthetical procedures employed could give rise to either the 3-acetylcoumarin (VII, R = Ac) or the chromone-3-carboxylic acid (VIII, R = Me; R_1 = CO_2H), *e.g.*, the intermediate (IX) formed in the Anschütz procedure could cyclise to give either (VII, R = Ac) or (VIII, R = Me; R_1 = CO_2H), and on account of the strongly acidic properties exhibited by 4-hydroxycoumarins it is not easy to distinguish between the two types of compound.



(VII.)



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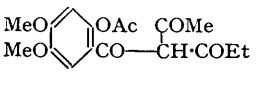

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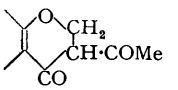

(X.)

In the course of a detailed examination of *P* it was found that, like the authentic 4-hydroxycoumarins synthesised in the course of the present investigation, the substance was acidic, dissolving readily in aqueous sodium hydroxide or sodium carbonate and, more slowly, in aqueous sodium hydrogen carbonate. With ethereal diazomethane, *P* furnished mainly a resinous product together with traces of alkali-insoluble crystalline material. Hydrolytic fission of *P* with boiling aqueous sodium hydroxide gave acetone, acetic acid, the ketone (I, R = H), and 2-hydroxy-4 : 5-dimethoxybenzoic acid, which are the decomposition products expected from both the coumarin (VII, R = Ac) and the chromone (VIII, R = Me; R_1 = CO_2H). In addition, a small amount of 4-hydroxy-6 : 7-dimethoxycoumarin was obtained. On the other hand, compound *P* did not react with 2 : 4-dinitrophenylhydrazine whereas 3-acetyl-, 3-acetyl-6-methyl-, and 7-methoxy-3-acetyl-4-hydroxycoumarin have been found to form 2 : 4-dinitrophenylhydrazones readily (private communication from Mr. G. G. Badcock of this laboratory). The substance *P* reacts smoothly with piperonal in the presence of alcoholic sodium ethoxide to give a typical yellow *styryl* derivative, a reaction characteristic of 2-methylchromones, and, although 4-hydroxy-3-acetylcoumarins could presumably condense with a reactive aldehyde under similar conditions, this reaction has not been found to take place under the conditions employed (*loc. cit.*). Attempts to establish the presence of a carboxyl

group by submitting *P* to decarboxylation procedures were unsuccessful. Under these conditions the compound underwent deep-seated decomposition, and the expected 6 : 7-dimethoxy-2-methylchromone (VIII, R = Me; R_1 = H) was not obtained. From the fact that *P* readily forms a styryl derivative but does not appear to contain a reactive carbonyl group we are of the opinion that it is clearly 6 : 7-*dimethoxy*-2-*methylchromone*-3-*carboxylic acid* (VIII, R = Me; R_1 = CO_2H) and not the expected isomeric coumarin. The synthesis of this group of compounds and of the isomeric coumarins type (VII, R = Ac) is being further investigated; in the course of numerous experiments on the condensation of the diketone (I, R = Ac) with ethyl carbonate by means of sodium a mixed product was obtained in two experiments which gave a small amount of a 2 : 4-dinitrophenylhydrazone, indicating the presence of (VII, R = Ac) in the reaction mixture.

In connection with the allocation of the chromone structure (VIII, R = Me; R_1 = CO_2H) to *P* it may be noted that the isolation of small amounts of (VII, R = H) from the alkaline hydrolysate of *P* might seem to support the coumarin structure (VII, R = Ac). The formation of (VII, R = H) can, however, be reconciled with the chromone structure and clearly takes place by the opening of the chromone ring and subsequent loss of a *C*-acetyl group, thus giving 2-hydroxy-4 : 5-dimethoxybenzoylacetic acid which on acidification of the alkaline solution readily undergoes cyclisation with the formation of 4-hydroxy-6 : 7-dimethoxycoumarin (VII, R = H).

In the course of experiments on the condensation of the diketone (I, R = Ac) and ethyl orthoformate by means of acetic anhydride it was found that when the reaction was carried out at 160° with 2 mols. of ester and 1·5 moles of anhydride the only product isolated was 6 : 7-*dimethoxy*-3-*acetylchromone* (VIII, R = H; R_1 = Ac), in which the presence of a reactive carbonyl group was demonstrated by the formation of a 2 : 4-*dinitrophenylhydrazone*. In experiments with a lower proportion of ester and a higher proportion of anhydride, *e.g.*, with 1 mol. of ester and 2 mols. of anhydride at 150°, the orthoformic ester did not take part in the reaction and the only product obtained was 6 : 7-dimethoxy-3-acetyl-2-methylchromone (VIII, R = Me; R_1 = Ac). The exact conditions determining the course of these condensations have not been elucidated, but further work on this topic is in progress.

The condensation of 6 : 7-dimethoxychroman-4-one with ethyl acetate by means of sodium methoxide or of the sodio-derivative of the chromanone with acetyl chloride gave rise to 6 : 7-*dimethoxy*-3-*acetylchroman*-4-*one* (X).

In their studies on the degradation of methyl *O*-dimethylcitromycetin, Hetherington and Raistrick (*loc. cit.*) obtained a compound $C_{12}H_{12}O_5$ as a product of alkaline hydrolysis which they suggested might be either the chromonol (VIII, R = Me; R_1 = OH) or the 4-hydroxycoumarin (VII, R = Me) (formulated in the enolic form). Direct comparison has shown that this degradation product is not identical with the chromonol (cf. Healey and Robinson, *J.*, 1934, 1625), the 4-hydroxycoumarin, or the isomeric 2-acetylcoumaranone (V).

Experimental.

2-*Hydroxy*-4 : 5-*dimethoxyacetophenone* (I, R = H).—Condensation of 3 : 4-dimethoxyphenol (5 g.) with methyl cyanide (5 ml.) by means of zinc chloride (5 g.) and excess of hydrogen chloride in the course of 24 hours and subsequent hydrolysis of the resulting ketimine with water (150 ml.) on the steam-bath for ½ hour gave the ketone (I, R = H) as a brown solid. This substance was purified by distillation in a vacuum, b. p. 125°/0·004 mm., and then formed colourless prisms (3 g.), m. p. 112°, from methanol, soluble in benzene, warm ethyl acetate, or ether, and giving a deep blue ferric reaction in alcohol which changes to green on the addition of water (Found : C, 61·5; H, 6·3. Calc. for $C_{10}H_{12}O_4$: C, 61·2; H, 6·1%). The compound forms a 2 : 4-*dinitrophenylhydrazone* which separates from ethyl acetate in scarlet needles, m. p. 228° (decomp.) (Found : C, 51·2; H, 4·4; N, 14·8. $C_{16}H_{16}O_7N_4$ requires C, 51·1; H, 4·3; N, 14·9%) (cf. Smith and Haller, *J. Amer. Chem. Soc.*, 1934, **56**, 237).

5 : 6-*Dimethoxy*-3-*methylcoumarone* (III, R = H).—Interaction of the foregoing ketone (5 g.) and ethyl bromoacetate (5 g.) in boiling acetone (50 ml.) containing potassium carbonate during 12 hours with subsequent filtration and evaporation of the acetone liquors gave *ethyl* 4 : 5-*dimethoxy*-2-*acetylphenoxyacetate* (II, R = Et) which crystallised from aqueous acetone in hexagonal prisms (7 g.), m. p. 132—133°, soluble in acetone, alcohol, or benzene (Found : C, 59·4; H, 6·5. $C_{14}H_{18}O_6$ requires C, 59·6; H, 6·4%). Hydrolysis of this ester (5 g.) with a solution of potassium hydroxide (5 g.) in alcohol (40 ml.) and water (60 ml.) on the steam-bath followed by evaporation of the greater part of the alcohol in a vacuum and acidification of the residue with dilute hydrochloric acid furnished 4 : 5-dimethoxy-2-acetylphenoxyacetic acid (II, R = H), forming colourless prisms (4·3 g.), m. p. 209°, from aqueous alcohol. A mixture of this acid (4 g.), sodium acetate (10 g.), and acetic anhydride (30 ml.) was kept at 160° for ½ hour and then poured into water (200 ml.). After the anhydride had decomposed the product was collected, washed with aqueous sodium hydrogen carbonate and then water, dried, and distilled in a vacuum. Recrystallisation of the distillate, b. p. 125°/0·004 mm., from 80% acetic acid gave the *coumarone* (III, R = H) in colourless plates (2·8 g.), m. p. 99°, exhibiting a green sulphuric acid reaction

which when the mixture was warmed became pink and then red (Found : C, 68·6; H, 6·5. $C_{11}H_{12}O_3$ requires C, 68·8; H, 6·3%). This substance is readily soluble in the usual organic solvents except light petroleum and cold ether.

2-*Formyl*-5 : 6-*dimethoxy*-3-*methylcoumarone* (III, R = CHO).—A solution of the foregoing coumarone (4 g.) in ether (100 ml.), containing hydrogen cyanide (10 ml.), was saturated with hydrogen chloride in the course of 4 hours, and next day the light green aldimine was collected, well washed with ether, and dissolved in water (100 ml.). This strongly acid solution was rendered only faintly acid to Congo-red by addition of aqueous sodium hydrogen carbonate and then heated on the steam-bath for 20 minutes. Next day the resulting *aldehyde* was collected and crystallised from aqueous alcohol, forming rhombic plates (4 g.), m. p. 119° (Found : C, 65·5; H, 5·4. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·5%). With sulphuric acid this compound gave an orange coloration which when the mixture was warmed became deep red and finally green. The *oxime* separated from dilute alcohol in plates, m. p. 184—185° (Found : N, 5·7. $C_{12}H_{13}O_4N$ requires N, 6·0%).

5 : 6-*Dimethoxy*-2-*acetyl*-3-*methylcoumarone* (III, R = Ac).—Condensation of 5 : 6-dimethoxy-3-methylcoumarone (2 g.) with methyl cyanide (2 ml.) by means of zinc chloride (2 g.) and excess of hydrogen chloride in ether (100 ml.) during 24 hours followed by hydrolysis of an aqueous solution of the resulting ketimine (100 ml.) which had been almost neutralised by the addition of aqueous sodium hydrogen carbonate, on the steam-bath for ½ hour, gave rise to a solid from which the *ketone* was isolated by repeated extraction with boiling light petroleum (b. p. 40—60°) and evaporation of the combined extracts. Crystallised from aqueous alcohol, the compound formed colourless rod-like prisms (1·5 g.), m. p. 127°, having a yellow sulphuric acid reaction which became deep red when the mixture was warmed (Found : C, 66·4; H, 5·7. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%).

ω-Chloro-2-*hydroxy*-4 : 5-*dimethoxyacetophenone* (I, R = Cl).—Condensation of 3 : 4-dimethoxyphenol (10 g.) and chloromethyl cyanide (5·4 ml.) was effected in ether (250 ml.) with zinc chloride (12 g.) and excess of hydrogen chloride in the course of 24 hours. After having been well washed with ether to remove hydrogen chloride the resulting ketimine was hydrolysed with water (250 ml.) on the steam-bath for 20 minutes, giving the *chloro-ketone* as a light brown solid which separated from alcohol in pale straw-coloured prisms (7 g.), m. p. 154—155°, and gave a green coloration with alcoholic ferric chloride (Found : C, 51·9; H, 5·0; Cl, 15·7. $C_{10}H_{11}O_4Cl$ requires C, 52·1; H, 4·8; Cl, 15·4%). The 2 : 4-*dinitrophenylhydrazone* formed thick crimson prisms, m. p. 210° (decomp.), from alcohol (Found : N, 13·7. $C_{16}H_{15}O_7N_4Cl$ requires N, 13·6%).

This ketone could not be acetylated by the pyridine method or by means of acetyl chloride on the sodium salt, but, on being boiled with excess of commercial acetyl chloride for 30 minutes with subsequent decomposition of the unchanged chloride with ice–water, it gave an almost quantitative yield of the *acetate* which separated from alcohol in colourless needles, m. p. 141°, having a negative ferric reaction (Found : Cl, 13·0. $C_{12}H_{13}O_5Cl$ requires Cl, 13·0%). The use of commercial acetyl chloride readily furnished the acetate, but absolute acetyl chloride did not affect acetylation. The presence of hydrogen chloride in the reaction mixture appeared to be essential for success.

5 : 6-*Dimethoxy*-2-*acetylcoumaran*-3-*one* (V).—A solution of the foregoing acetate (1·4 g.) in benzene containing potassium carbonate (6 g.) was refluxed for 8 hours, and next day the mixed potassium salts were collected, washed with ether, and dissolved in water. Acidification of the resulting reddish solution with dilute sulphuric acid gave a precipitate of the *coumaranone* (0·5 g.) which, on recrystallisation from alcohol, formed pale yellow prisms, m. p. 181°, having a red-brown ferric reaction (Found : C, 60·9; H, 5·2. $C_{13}H_{12}O_5$ requires C, 61·0; H, 5·1%). A solution of this compound (0·5 g.) in 2N-sodium hydroxide (10 ml.) was vigorously agitated with benzoyl chloride (0·5 ml.), and the *benzoate* of the enolic form, 3-hydroxy-5 : 6-dimethoxy-2-acetylcoumarone, separated as a crystalline mass. Recrystallised from alcohol, this derivative formed colourless needles, m. p. 162°, having a negative ferric reaction in alcohol and insoluble in aqueous sodium hydroxide (Found : C, 67·1; H, 4·7. $C_{19}H_{16}O_6$ requires C, 67·1; H, 4·7%).

When ω-chloro-2-hydroxy-4 : 5-dimethoxyacetophenone (1 g.) was refluxed in alcohol (20 ml.) containing sodium acetate (1 g.) for 20 minutes, an almost theoretical yield of 5 : 6-*dimethoxycoumaran*-3-*one* was obtained, which formed pale cream coloured needles, m. p. 169°, from alcohol, sparingly soluble in the usual organic solvents except hot alcohol or ethyl acetate (Found : C, 61·7; H, 5·0. $C_{10}H_{10}O_4$ requires C, 61·9; H, 5·2%). The interaction of the coumaranone (0·3 g.) and piperonal (0·5 g.) in a mixture of alcohol (5 ml.) and 10% aqueous sodium hydroxide (2 ml.) on the steam-bath for ½ hour gave the *piperonylidene* derivative, which separated from acetic acid in yellow needles (0·5 g.), m. p. 260° (Found : C, 66·3; H, 4·0. $C_{18}H_{14}O_6$ requires C, 66·3; H, 4·3%).

6 : 7-*Dimethoxydihydrocoumarin*.—On being kept at 180° for 8 hours, a mixture of 2-acetoxy-4 : 5-dimethoxybenzaldehyde (5·5 g.), sodium acetate (5·5 g.), and acetic anhydride (5 ml.) gave *O*-dimethylæsculetin which, on being purified by sublimation at 170°/1 mm., and then by crystallisation from alcohol, formed needles (2·5 g.), m. p. 144°, identical with a specimen (5 g.) prepared by the methylation of æsculetin (5 g.) from natural sources by the methyl iodide–potassium carbonate method (cf. Tiemann and Will, *Ber.*, 1882, **15**, 2075).

A solution of the di-sodium derivative of 2-hydroxy-4 : 5-dimethoxycinnamic acid was prepared by agitating a mixture of *O*-dimethylæsculetin (1 g.), warm alcohol (20 ml.), and 25% aqueous sodium hydroxide (2 ml.) until a test sample did not show an opalescence on being diluted with water. After the addition of water (50 ml.) this salt was hydrogenated *in situ* with hydrogen and a palladium–charcoal catalyst (from 1 g. of charcoal and 0·1 g. of palladium chloride), the catalyst was removed, dilute hydrochloric acid (sufficient to neutralise the aqueous sodium hydroxide originally used) was then added, and the aqueous liquor evaporated at 40°/14 mm. A hot extract of the residue in ethyl acetate–light petroleum (b. p. 60—80°) on cooling deposited β-2-*hydroxy*-4 : 5-*dimethoxyphenylpropionic acid* in slender prisms (0·6 g.), m. p. 100°, changing to 118° after having been dried in a vacuum at room temperature, readily soluble in ether, alcohol, or aqueous sodium hydrogen carbonate (Found : C, 58·2; H, 6·2. $C_{11}H_{14}O_5$ requires C, 58·4; H, 6·2%). This compound was converted into the *dihydrocoumarin* by being

kept at 150° until the vigorous evolution of water had subsided. The product was purified by sublimation at 0·1 mm. and then by crystallisation from light petroleum (b. p. 60—80°), forming rosettes of colourless needles (0·7 g.), m. p. 79°, readily soluble in alcohol, benzene, or ethyl acetate (Found : C, 63·2; H, 6·0. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

6 : 7-*Dimethoxy*-3-*acetylcoumarin* (VI, R = Ac).—To a mixture of 2-hydroxy-4 : 5-dimethoxybenzaldehyde (2 g.) and excess of ethyl acetoacetate, piperidine (0·5 ml.) was added with cooling to keep the temperature of the mixture below room temperature. 24 Hours later the resulting 3-*acetylcoumarin* was isolated and crystallised from ethyl acetate, forming golden prisms, m. p. 234°, which have a negative ferric reaction in alcohol (Found : C, 62·6; H, 4·8. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·8%). The 2 : 4-*dinitrophenylhydrazone* separated from alcohol, chloroform, or dioxan in brownish-red, felted needles, m. p. 280° (decomp.) (Found : N, 13·1. $C_{19}H_{16}O_8N_4$ requires N, 13·1%).

3-*Hydroxy*-6 : 7-*dimethoxycoumarin* (VI, R = OH).—A mixture of 2-acetoxy-4 : 5-dimethoxybenzaldehyde (1 g.), aceturic acid (1 g.), sodium acetate (1 g.), and acetic anhydride (5 ml.) was heated on the steam-bath for 1½ hours, cooled, and treated with water. Next day the *azlactone* was isolated and purified from ethyl acetate, forming bright yellow needles (0·6 g.), m. p. 181° (Found : N, 4·2. $C_{15}H_{15}O_6N$ requires N, 4·6%). Hydrolysis of this compound (1 g.) with boiling 2N-hydrochloric acid (25 ml.) for 3 hours gave 3-*hydroxy*-6 : 7-*dimethoxycoumarin*, which separated from the cooled hydrolysate and on isolation was purified by crystallisation from alcohol, forming colourless elongated prisms (0·4 g.), m. p. 220°, giving a green ferric reaction in alcohol (Found : C, 59·6; H, 4·3. $C_{11}H_{10}O_5$ requires C, 59·5; H, 4·1%).

Methylation of this coumarin (0·75 g.) in methanol (10 ml.) with excess of ethereal diazomethane gave the *methyl ether* (0·7 g.), which separated from methanol in rosettes of colourless needles, m. p. 146°, insoluble in aqueous sodium carbonate and having a negative ferric reaction (Found : C, 60·8; H, 4·9. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%).

4-*Hydroxy*-6 : 7-*dimethoxycoumarin* (VII, R = H).—(*a*) A mixture of 2-hydroxy-4 : 5-dimethoxyacetophenone (1 g.), ethyl carbonate (20 ml.), and powdered sodium (0·35 g.) was heated on the steam-bath with occasional shaking for ½ hour, the cooled mixture was diluted with ether (200 ml.), and the resulting granular precipitate of the sodium salt of 4-*hydroxy*-6 : 7-*dimethoxycoumarin* was collected, drained, and dissolved in water (100 ml.). Acidification of this solution with hydrochloric acid gave colourless prisms (0·9 g.), m. p. 278 (decomp.), from alcohol, having a very pale brown ferric reaction darkening slightly on warming (Found : C, 59·2; H, 4·4. $C_{11}H_{10}O_5$ requires C, 59·5; H, 4·5%). This coumarin, which is moderately soluble in acetone and sparingly soluble in ethyl acetate or chloroform, is readily soluble in aqueous sodium hydrogen carbonate with the evolution of carbon dioxide.

(*b*) When a mixture of 3 : 4-dimethoxyphenol (5 g.), cyanoacetic acid (3 g.), anhydrous zinc chloride (10 g.), and ether (50 ml.) was slowly saturated with hydrogen chloride a dark oil gradually separated. Next day excess of ether was added, the solvent decanted, and the residual oil well washed with fresh solvent. On being kept, a solution of this product in water (200 ml.) slowly deposited the *ketimine* in needles, m. p. 238°, after purification from alcohol (Found : N, 6·7. $C_{11}H_{11}O_4N$ requires N, 6·3%). When a mixture of this compound (1 g.) and 50% sulphuric acid (10 g.) was heated on the steam-bath for 2·5 hours and then diluted with an equal volume of water a precipitate of the crude coumarin slowly separated. Repeated crystallisation from acetone (charcoal) gave the compound as colourless prisms, m. p. and mixed m. p. 278° (decomp.) (Found : C, 58·8; H, 4·4%).

When the ketimine (0·5 g.) was subjected to hydrolysis with 10% aqueous sodium hydroxide (15 ml.) on the steam-bath until the evolution of ammonia had ceased (1·5 hours) and the hydrolysate acidified with hydrochloric acid and cooled, a small yield of crude 4-hydroxycoumarin gradually separated, m. p. 278°, after purification.

Acetylation of 4-hydroxy-6 : 7-dimethoxycoumarin (1 g.) with pyridine (2 ml.) and acetic anhydride (5 ml.) at 100° for ½ hour gave the *acetate* which formed straw-coloured needles, m. p. 242°, from ethyl acetate (Found : C, 58·8; H, 4·5. $C_{13}H_{12}O_6$ requires C, 59·1; H, 4·5%).

Methylation of 4-hydroxy-6 : 7-dimethoxycoumarin (0·5 g.), dissolved in chloroform (10 ml.), with an excess of ethereal diazomethane gave 4 : 6 : 7-*trimethoxycoumarin* (0·5 g.) which formed rosettes of colourless needles, m. p. 202°, from aqueous alcohol, insoluble in aqueous sodium carbonate (Found : C, 61·0; H, 5·2. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%). Methylation of the compound by the methyl iodide–potassium carbonate method yielded the same methyl ether, m. p. and mixed m. p. 202°.

Ethyl 4-*Hydroxy*-6 : 7-*dimethoxycoumarin*-3-*carboxylate* (VII, R = CO_2Et).—2-Acetoxy-4 : 5-dimethoxybenzoic acid (Head and Robertson, *J.*, 1931, 32) (4·8 g.) was suspended in cooled anhydrous chloroform (50 ml.) and converted into the acid chloride by gradual addition of phosphorus pentachloride (4·2 g.), and, after completion of the reaction, the solvent and phosphorus oxychloride were removed in a vacuum. To remove the remaining traces of phosphorus oxychloride more chloroform (25 ml.) was added to the residue and the evaporation process repeated. Finally, to ensure complete removal of remaining traces of phosphorus oxychloride and solvent, the product was kept in a vacuum at 100° for 10 minutes. On cooling, the unstable acid chloride was obtained as a yellowish solid and was sufficiently pure for the next stage.

Ethyl sodio-malonate was prepared from the ester (7·7 g.) and powdered sodium (1·1 g.) in ether (45 ml.), and the foregoing acid chloride (from 4 g. of acid) introduced. The mixture was then refluxed for 16 hours, the solid was collected and dissolved in water, unchanged ester was removed by means of ether, and the aqueous liquor was acidified (Congo-red) with concentrated hydrochloric acid. Crystallised from 95% alcohol, the resulting *ethyl* 4-*hydroxy*-6 : 7-*dimethoxycoumarin*-3-*carboxylate* formed colourless needles (3·5 g.), m. p. 240°, readily soluble in acetone or chloroform and in aqueous sodium hydrogen carbonate (Found : C, 57·4; H, 4·7. $C_{14}H_{14}O_7$ requires C, 57·1; H, 4·8%). On methylation with ethereal diazomethane this compound was quantitatively converted into the *methyl ether* which separated from aqueous alcohol in long needles, m. p. 130°, insoluble in aqueous sodium hydrogen carbonate (Found : C, 58·2; H, 5·3. $C_{15}H_{16}O_7$ requires C, 58·4; H, 5·2%).

Attempts to convert this ester into 4-hydroxy-6 : 7-dimethoxycoumarin by means of warm sulphuric acid were unsuccessful, but, when the ester was heated with a little 10% aqueous sodium hydroxide on the steam-bath for 10 minutes and the cooled mixture acidified, a small yield of the required crude substance was obtained. Crystallised from alcohol this material gave 4-hydroxy-6 : 7-dimethoxycoumarin, m. p. and mixed m. p. 278° (decomp.), identical with an authentic specimen.

4-Hydroxy-6 : 7-dimethoxy-3-methylcoumarin (VII, R = Me).—The condensation of 3 : 4-dimethoxyphenol (5 g.) with ethyl cyanide (2·4 g.) by means of zinc chloride (10 g.) gave an oily product which on being isolated was washed with ether and dissolved in water (200 ml.). The solution was almost neutralised (faintly acid to Congo-red) by the addition of sodium hydrogen carbonate, and then heated on the steam-bath for 45 minutes. *2-Hydroxy-4 : 5-dimethoxypropiophenone* separated from the cooled mixture and on isolation crystallised from methanol in almost colourless needles (1·1 g.), m. p. 125°, having a dark green ferric reaction in alcohol (Found : C, 62·5; H, 6·4. $C_{11}H_{14}O_4$ requires C, 62·6; H, 6·7%). The 2 : 4-*dinitrophenylhydrazone* formed crimson needles, m. p. 231° (decomp.) from ethyl acetate (Found : N, 14·7. $C_{17}H_{18}O_7N_4$ requires N, 14·4%).

Interaction of this ketone (0·5 g.) with ethyl carbonate (70 ml.) in the presence of powdered sodium (0·5 g.) on the steam-bath for 1·5 hours gave rise to the sodio-derivative of the *4-hydroxy-6 : 7-dimethoxy-3-methylcoumarin* which was precipitated by the addition of excess of ether, collected and decomposed with dilute hydrochloric acid. On isolation this coumarin separated from alcohol in colourless prisms, m. p. 273°, having a negative ferric reaction in alcohol and being readily soluble in aqueous sodium hydrogen carbonate (Found : C, 61·0; H, 5·1. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%).

Methylation of 4-hydroxy-6 : 7-dimethoxy-3-methylcoumarin (0·25 g.), dissolved in a little chloroform, with an excess of ethereal diazomethane gave the *methyl ether* which formed silky needles, m. p. 150°, from aqueous methanol (Found : C, 62·5; H, 5·8. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%).

4-Hydroxy-6 : 7-dimethoxy-3-ethylcoumarin (VII, R = Et).—By means of *n*-propyl cyanide in place of ethyl cyanide, 2-hydroxy-4 : 5-dimethoxy-*n*-butyrophenone was prepared according to the method employed for the analogous propiophenone. The crude ketone, which contained quantities of a dark oily tar, became semi-solid in course of 14 days, and after having been drained on tile, was repeatedly crystallised from dilute alcohol, forming colourless needles (0·35 g.), m. p. 81°, which gave a blue-green ferric reaction in alcohol. The condensation of this substance (0·25 g.) with ethyl carbonate (7 ml.) by means of sodium (0·3 g.) followed by the isolation of the product in the usual manner gave *4-hydroxy-6 : 7-dimethoxy-3-ethylcoumarin* (VII, R = Et) which formed colourless needles, m. p. 262°, from alcohol, having a negative ferric reaction and readily soluble in aqueous sodium hydrogen carbonate (Found : C, 62·6; H, 5·6. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%).

6 : 7-Dimethoxychromone (VIII, R = R_1 = H).—A solution of 2-hydroxy-4 : 5-dimethoxyacetophenone (1·8 g.) in ethyl formate (10 ml.), cooled to −10°, was mixed with pulverised sodium (0·6 g.), and the mixture kept at this temperature for 2 hours and then at room temperature for 24 hours. After addition of methanol (2 ml.) to destroy traces of unchanged sodium followed by ice–water (20 ml.), the mixture was acidified with acetic acid and the excess of ethyl formate removed by a current of air. Crystallisation of the resulting solid from water gave the *formyl-ketone* in colourless needles (1·7 g.), m. p. 159°, readily soluble in alcohol or benzene and having a green ferric reaction in alcohol (Found : C, 58·8; H, 5·1. $C_{11}H_{12}O_5$ requires C, 58·9; H, 5·4%). When a mixture of this ketone (1 g.), alcohol (10 ml.), and concentrated hydrochloric acid (6 drops) was boiled for 1 minute and cooled, *6 : 7-dimethoxychromone* separated, and on crystallisation from carbon tetrachloride formed pale yellow prisms (0·7 g.), m. p. 163°, soluble in benzene or ethyl acetate and sparingly soluble in alcohol (Found : C, 63·9; H, 4·8. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·9%).

6 : 7-Dimethoxy-2-methylchromone (VIII, R = Me, R_1 = H).—Interaction of 2-hydroxy-4 : 5-dimethoxyacetophenone (1·5 g.) and ethyl acetate (15 ml.) was effected with sodium methoxide (from 0·5 g. of sodium) on the steam-bath for 5 hours. The cooled mixture was treated with ice–water, and acidified with acetic acid, and next day *2-hydroxy-4 : 5-dimethoxybenzoylacetone* (I, R = Ac) was collected and crystallised from light petroleum (b. p. 80—100°), forming slender yellow prisms, and then from dilute alcohol, being finally obtained in colourless needles (1·2 g.), m. p. 109°, having a green ferric reaction in alcohol (Found : C, 60·3; H, 5·9. $C_{13}H_{14}O_5$ requires C, 60·5; H, 5·9%). This compound, which is readily soluble in the usual organic solvents except light petroleum, distilled unchanged in a high vacuum, b. p. 130°/0·01 mm.

Cyclisation of the diketone (1 g.) in boiling alcohol (10 c.c.) containing 6 drops of concentrated hydrochloric acid gave 6 : 7-dimethoxy-2-methylchromone, which on isolation with ether separated from light petroleum (b. p. 80—100°) in colourless prisms (0·7 g.), m. p. 149°, readily soluble in alcohol, ether, or benzene (Found : C, 65·7; H, 5·3. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·5%). Interaction of this chromone (0·5 g.) with piperonal (0·4 g.) in alcohol containing sodium ethoxide (from 0·3 g. of sodium) on the steam-bath for ½ hour furnished *6 : 7-dimethoxy-2-(3′ : 4′-methylenedioxystyryl)chromone* which separated from alcohol in yellow rhombic prisms (0·5 g.), m. p. 212° (Found : C, 68·0; H, 4·4. $C_{20}H_{16}O_6$ requires C, 68·2; H, 4·5%).

6 : 7-Dimethoxy-3-acetyl-2-methylchromone (VIII, R = Me; R_1 = Ac).—A mixture of 2-hydroxy-4 : 5-dimethoxyacetophenone (2 g.), sodium acetate (2·6 g.), and acetic anhydride (16 ml.) was kept at 180° (oil-bath) for 12 hours, cooled, and mixed with water (100 ml.). Crystallisation of the product from aqueous alcohol gave the *3-acetyl-chromone* in colourless prisms (1·5 g.), m. p. 193° (Found : C, 64·2; H, 5·3. $C_{14}H_{14}O_5$ requires C, 64·1; H, 5·3%). The 2 : 4-*dinitrophenylhydrazone* formed crimson needles, m. p. 240°, from alcohol (Found : N, 12·9. $C_{20}H_{18}O_8N_4$ requires N, 12·7%).

When 6 : 7-dimethoxy-3-acetyl-2-methylchromone (1 g.) was boiled for 8 hours with 2N-aqueous sodium carbonate (100 ml.) and the cooled mixture acidified with hydrochloric acid, a pale brown solid was obtained which appeared to be a mixture of 6 : 7-dimethoxy-2-methylchromone and the parent 2-hydroxy-4 : 5-dimethoxy-ω-acetylacetophenone. A solution of this material in a little alcohol containing 2 drops of concentrated hydrochloric acid was refluxed for 2 minutes, the solvent evaporated, and the residue crystallised from light petroleum (b. p. 60—80°), giving 6 : 7-dimethoxy-2-methyl-

chromone in colourless prisms (0·5 g.), which on repeated purification had m. p. 149°, identical with an authentic specimen.

6 : 7-*Dimethoxy*-3-*acetylchromone* (VIII, R = H; R_1 = Ac).—A mixture of 2-hydroxy-4 : 5-dimethoxybenzoylacetone (I, R = Ac) (1 g.), ethyl orthoformate (1·25 g., 2 mols.), and acetic anhydride (0·5 g., 1·5 mols.) was kept at 160° for 45 minutes, cooled, and treated with water (50 ml.). Next day the solid was collected and crystallised from alcohol, giving 6 : 7-*dimethoxy*-3-*acetylchromone* in colourless needles (0·5 g.) which on recrystallisation had m. p. 166°, sparingly soluble in benzene, moderately soluble in ethyl acetate, and insoluble in light petroleum or aqueous sodium hydroxide (Found : C, 62·7; H, 4·7. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·8%). The 2 : 4-*dinitrophenylhydrazone* separated from glacial acetic acid in orange needles, m. p. 261 (Found : N, 12·9. $C_{19}H_{16}O_8N_4$ requires N, 13·1%).

When a mixture of the diketone (1 g.), ethyl orthoformate (0·6 g., 1 mol.), and acetic anhydride (0·7 g., 2 mols.) was kept at 150° for an hour and then treated with water the product was obtained in light brown needles (0·5 g.). Recrystallised from light petroleum (b. p. 80—100°) and then from dilute alcohol, this product gave 6 : 7-dimethoxy-3-acetyl-2-methylchromone in colourless needles, m. p. 193°, undepressed on admixture with an authentic specimen (Found : C, 64·2; H, 5·3%).

2-*Hydroxy*-ω-*benzoyloxy*-4 : 5-*dimethoxyacetophenone* (I, R = Ph·CO_2) (*with* F. M. Dean).—A solution of 3 : 4-dimethoxyphenol (10 g.) and benzoyloxymethyl cyanide (Aloy and Rabaut, *Bull. Soc. chim.*, 1913, **13**, 457) (7·8 g.) in ether (120 ml.) kept at 0° was saturated with hydrogen chloride, and next day the green crystalline mass was isolated, well washed with ether, and heated with water (100 ml.) on the steam-bath for 1 hour. 24 Hours later the oily layer was separated, and on being mixed with a little methanol gave the crystalline *ketone* which then formed colourless prisms (3·4 g.), m. p. 128°, from the same solvent, readily soluble in 2N-sodium hydroxide, and giving a green ferric reaction in alcohol (Found : C, 64·1; H, 4·6. $C_{17}H_{16}O_6$ requires C, 64·6; H, 5·1%). The 2 : 4-*dinitrophenylhydrazone* formed reddish-brown needles from alcohol or ethyl acetate, m. p. 206° (decomp.) (Found : C, 55·4; H, 3·9; N, 11·4. $C_{23}H_{20}O_9N_4$ requires C, 55·6; H, 4·0; N, 11·3%).

Acetylation of the ketone (1 g.) with acetic anhydride (1 ml.) and pyridine (5 ml.) on the steam-bath for 10 minutes gave the *acetate* which separated from 90% ethanol in long needles having a negative ferric reaction, m. p. 128° (Found : C, 64·1; H, 5·3. $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·0%). A mixture of this derivative and the parent ketone melted at 106—116°.

Evaporation of the alcoholic liquors from the above ketone left a small amount of a second product which formed colourless needles, m. p. 93°, insoluble in 2N-sodium hydroxide and having a negative ferric reaction (Found : C, 61·8; H, 5·4%).

3-*Hydroxy*-6 : 7-*dimethoxy*-2-*methylchromone* (VIII, R = Me; R_1 = OH).—(*a*) A mixture of ω-chloro-2-hydroxy-4 : 5-dimethoxyacetophenone (5 g.), sodium acetate (5 g.), and acetic anhydride (10 g.) was kept at 180° for 5 hours, and the excess of anhydride decomposed with water. The aqueous liquor was decanted from the tarry product which, after having been dried, was repeatedly extracted with boiling light petroleum (b. p. 80—100°). The oily brown solid obtained on evaporation of the light petroleum extracts was purified by crystallisation from ethyl acetate–light petroleum (b. p. 80—100°), giving 3-*acetoxy*-6 : 7-*dimethoxy*-2-*methylchromone* in cream coloured prisms (1 g.), m. p. 185°, soluble in ethyl acetate and sparingly soluble in alcohol (Found : C, 60·6; H, 4·9. $C_{14}H_{14}O_6$ requires C, 60·4; H, 5·0%). This compound was deacetylated by being dissolved in a little concentrated sulphuric acid, and the solution added to excess of water. Thus precipitated, 3-*hydroxy*-6 : 7-*dimethoxy*-2-*methylchromone* (VIII, R = Me, R_1 = OH) formed colourless needles (0·5 g.), m. p. 238° (slight decomp.), from alcohol (charcoal), which did not react with 2 : 4-dinitrophenylhydrazine and gave a mauve ferric reaction in alcohol (Found : C, 60·9; H, 5·0. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%).

(*b*) A mixture of the acetate of the 2-hydroxy-ω-benzoyloxy-4 : 5-dimethoxyacetophenone (2 g.), sodium acetate (2 g.), and acetic anhydride (5 ml.) was kept at 180° (oil-bath) for 24 hours, cooled, and treated with water (100 ml.). Next day the solid product (1·8 g.) was isolated and extracted several times with hot alcohol, and the combined extracts were evaporated, leaving 3-acetoxy-6 : 7-dimethoxy-2-methylchromone which, on recrystallisation from 90% alcohol or ethyl acetate–ligroin, formed almost colourless prisms, m. p. 185—186°, undepressed on admixture with a specimen prepared by method (*a*) (Found : C, 60·8; H, 5·2%). The foregoing experiment was repeated, but after the addition of water the mixture was kept for a month, and on isolation by the same method the product consisted of the 3-hydroxy-chromone which, on recrystallisation from alcohol and then ethyl acetate, had m. p. 238° and was identical with a specimen prepared by method (*a*) (Found : C, 61·0; H, 5·6%).

6 : 7-*Dimethoxy*-2-*methylchromone*-3-*carboxylic Acid* (VIII, R = Me; R_1 = CO_2H).—(*a*) A suspension of ethyl sodio-acetoacetate (from 5·0 g. of ester, 2 mols.) in ether (100 ml.) was added to a solution of freshly prepared 2-acetoxy-4 : 5-dimethoxybenzoyl chloride (2·5 g., 1 mol.) in ether (25 ml.), and after the reaction had ceased (8 hours, with occasional agitation) the mixture was refluxed for 8 hours, the yellow-brown solid was collected, washed with ether, and dissolved in water, and the solution was acidified with dilute hydrochloric acid. Next day the precipitate was collected and crystallised from alcohol, giving the *chromone*-3-*carboxylic acid* in colourless needles (1·4 g.), m. p. 247° (Found : C, 59·1; H, 4·5. $C_{13}H_{12}O_6$ requires C, 59·2; H, 4·5%). This compound is sparingly soluble in ether, hot alcohol, ethyl acetate, or benzene, soluble in chloroform, and slowly dissolves in aqueous sodium hydrogen carbonate. It did not react with 2 : 4-dinitrophenylhydrazine and did not give a coloration with alcoholic ferric chloride.

(*b*) A mixture of 2-hydroxy-4 : 5-dimethoxybenzoylacetone (I, R = Ac) (1 g.), pulverised sodium (0·3 g.), and ethyl carbonate (10 ml.) was kept at room temperature and occasionally agitated during 48 hours. Ether (200 ml.) was added to the mixture followed by ice–water (20 ml.), and the aqueous layer separated and immediately acidified with dilute hydrochloric acid, giving a precipitate of the chromone-3-carboxylic acid (0·2 g.) which on purification from alcohol was obtained in colourless needles, m. p. 250°, undepressed on admixture with specimen, m. p. 247°, prepared by method (*a*).

(*c*) When alcoholic sodium ethoxide (from 0·25 g. of sodium and 15 ml. of alcohol) was added to a solution of 2-hydroxy-4 : 5-dimethoxybenzoylacetone (1 g.) in alcohol (5 ml.), the disodio-derivative of

the diketone began to separate. One hour later the solid product was collected, washed with a little alcohol, suspended in anhydrous benzene, and gradually treated with a 10% solution of carbonyl chloride in toluene (10 ml.). On the addition of each portion of the carbonyl chloride solution to the mixture a bright orange colour developed which was allowed to fade before the addition of the next portion. The mixture finally became orange-red, and, after having been kept at room temperature for 16 hours, the pink solid was collected, washed with water, dried, and crystallised from alcohol, giving the chromone-3-carboxylic acid in colourless needles (0·6 g.), m. p. 250°, identical with specimens prepared by methods (*a*) and (*b*).

A mixture of the chromone (0·1 g.), sodium ethoxide (from 0·03 g. of sodium), piperonal (0·07 g.), and alcohol (10 ml.) was heated on the water-bath for 15 minutes, and the resulting deep yellow solution cooled and acidified with dilute hydrochloric acid. The solid was collected, washed, and crystallised from acetic acid, giving the *styryl* derivative in yellow needles, m. p. 305° (Found : C, 63·4; H, 3·8. $C_{21}H_{16}O_8$ requires C, 63·6; H, 4·0%).

Hydrolysis of 6 : 7-*Dimethoxy*-2-*methylchromone*-3-*carboxylic Acid.*—A solution of this compound (0·5 g.) in 2N-sodium hydroxide (25 ml.) was heated on the steam-bath for 15 minutes, and the cooled mixture acidified with dilute sulphuric acid and filtered to remove traces of unchanged material. Two-thirds of the solution was treated with excess of aqueous 2 : 4-dinitrophenylhydrazine sulphate, and next day the precipitate was collected, washed, and dried. This product was extracted with warm benzene, and the solution was chromatographed on a column of aluminium oxide, the chromatogram was developed with fresh solvent, and the lowest zone containing the 2 : 4-dinitrophenylhydrazone of acetone was washed through the column. On isolation this compound had m. p. 126°, after having been recrystallised from methyl alcohol, and was identical with an authentic specimen. The next zone on the chromatogram was washed through with chloroform, and on evaporation of the solvent the 2 : 4-dinitrophenylhydrazone of 2-hydroxy-4 : 5-dimethoxyacetophenone was obtained, which formed scarlet needles, m. p. 228° (decomp.), undepressed on admixture with an authentic specimen.

The residue insoluble in warm benzene was recrystallised from ethyl acetate, giving a small amount of 4-hydroxy-6 : 7-dimethoxycoumarin (*ca.* 5 mg.) in colourless prisms, m. p. and mixed m. p. 278° (decomp.), identical with an authentic specimen.

The aqueous filtrate from the crude mixture of dinitrophenylhydrazones was distilled, the acidic distillate was neutralised with aqueous sodium hydroxide, the resulting liquor was evaporated to dryness, and the residue (30 mg.) was boiled with aniline (0·5 g.) containing aniline hydrochloride (0·2 g.) for 15 minutes. The mixture was treated with excess of dilute hydrochloric acid and then extracted several times with ether, the combined extracts were washed once with a little dilute hydrochloric acid, dried, and evaporated, and a solution of the residue in an excess of benzene was poured through a short column (5 cm.) of aluminium oxide. Evaporation of the benzene liquor left acetanilide, m. p. and mixed m. p. 112°, after recrystallisation.

The remaining one-third portion of the crude acidified hydrolysate was extracted several times with chloroform, and the combined chloroform liquors were then extracted twice with aqueous sodium hydrogen carbonate. After acidification of the sodium hydrogen carbonate extracts with hydrochloric acid, 2-hydroxy-4 : 5-dimethoxybenzoic acid was isolated with the aid of chloroform. Crystallised from a small amount of the same solvent, the acid was obtained in colourless prisms, m. p. 214° (decomp.), having an intense blue ferric reaction in alcohol, identical with an authentic specimen (Head and Robertson, *loc. cit.*).

6 : 7-*Dimethoxy*-3-*acetylchroman*-4-*one* (X).—Sodium methoxide (from 0·15 g. of sodium) was added to 6 : 7-dimethoxychroman-4-one (0·5 g.) (Robertson *et al.*, *J.*, 1936, 1832) in ethyl acetate (10 ml.) kept at −10° and the mixture kept at this temperature for 4 hours and then at −5° for 24 hours. After the addition of ice, the mixture was acidified with dilute hydrochloric acid, and next day the solid was collected, triturated with a little boiling alcohol, and then crystallised from chloroform–light petroleum, giving the *acetyl* derivative in colourless squat prisms (0·25 g.), m. p. 249°, which had a green ferric reaction in alcohol (Found : C, 62·4; H, 5·6. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%). This compound, which is insoluble in the usual organic solvents (cold) except cold chloroform, gives a product with 2 : 4-dinitrophenylhydrazine forming crimson needles, m. p. 163°, from alcohol, which decomposes on further purification from this solvent.

Evaporation of the alcoholic solution from the crude product left unchanged chromanone (0·2 g.).

The same product was obtained when ether was employed as a solvent for the reaction and a molecular proportion of ethyl acetate used.

Similarly, interaction of 6 : 7-dimethoxychroman-4-one (0·5 g.) with pulverised sodium (0·05 g.) in ether (20 ml.) at −5° for 24 hours followed by the addition of acetyl chloride (0·2 g.) gave after 24 hours at −5° a mixture of unchanged chromanone (0·3 g.) and the 3-acetyl derivative (0·1 g.), m. p. and mixed m. p. 249°, after purification.

The authors are indebted to Messrs. Imperial Chemical Industries Limited for a grant in aid of this investigation.

UNIVERSITY OF LIVERPOOL. [*Received, May 18th,* 1948.]