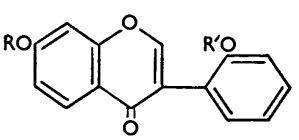
616. 3-*Aroylcoumarones.*

By W. B. Whalley and (in part) G. Lloyd.

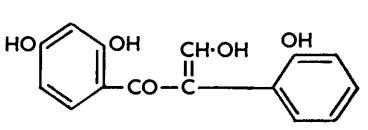
After failure of several methods, application of the rotenonone–rotenononic acid change [1,2] to a selection of chromono(2′ : 3′-3 : 4)coumarins (XI) gave the 3-*o*-hydroxybenzoylcoumarone-2-carboxylic acids (IV) which were converted by way of the ether esters and ether acids into 3-aroylcoumarones (XII; R = H). These substances are very sensitive to acid and are degraded by alkali to formic acid and the appropriate 2′-hydroxy-2-methoxydeoxybenzoins which undergo spontaneous ring closure to 2-phenylcoumarones (VI) during isolation.

The structure of the rotenononic acids is discussed.

The abnormal and rapid resinification of 2′-methoxy*iso*flavones (I; R′ = Me) by the usual acidic demethylating agents was recently reported,[3-7] and the hypothesis was advanced that rearrangement of 2′-hydroxy*iso*flavones (I; R′ = H) by way of intermediates of



(I)



(II)

type (II) to the acid-sensitive 2-unsubstituted 3-aroylcoumarones of type (III) may be responsible for this. The present paper describes the preparation and properties of a number of 3-aroylcoumarones.

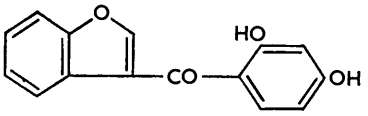
The only known compound of this class appears to be 3-benzoylcoumarone which was prepared by Martynoff [8] from phenylmagnesium bromide and 3-cyanocoumarone. In addition, the generally accepted formula for rotenononic acid (IV) (cf., *inter al.*, Smith and La Forge [9]) contains the 3-aroylcoumarone nucleus.

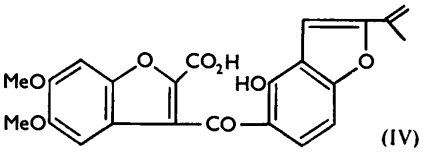
As Martynoff's method was not adaptable to the methoxy-derivatives our initial attempts were from the *iso*flavones (I). Preferential demethylation of 7 : 2′-dimethoxy*iso*flavone (I; R = R′ = Me) with aluminium chloride readily furnished 2′-hydroxy-7-methoxy*iso*flavone (I; R = Me, R′ = H), the orientation of which was established by ethylation to 2′-ethoxy-7-methoxy*iso*flavone (I; R = Me, R′ = Et) which was also synthesised by cyclisation of 2′-ethoxy-2-hydroxy-4-methoxydeoxybenzoin (V; R = Me, R′ = Et, R″ = H) with sodium and ethyl formate. Benzylation of the *iso*flavone (I; R = Me, R′ = H) furnished the ether (I; R = Me, R′ = CH_2Ph) which on mild alkaline degradation gave 2′-benzyloxy-2-hydroxy-4-methoxydeoxybenzoin (V; R = Me, R″ = H, R′ = CH_2Ph). Methylation of this formed 2′-benzyloxy-2 : 4-dimethoxydeoxybenzoin (V; R = R″ = Me, R′ = CH_2Ph) which was expected to give 2′-hydroxy-2 : 4-dimethoxydeoxybenzoin (V; R = R″ = Me, R′ = H) on debenzylation, and this with sodium and ethyl formate should yield the requisite coumarone (XII; R = R″ = H, R′ = Me). However, catalytic debenzylation furnished a compound which had no hydroxyl group and from its method of formation, infrared spectrum, analysis, and general properties could only be 2-(2 : 4-dimethoxyphenyl)coumarone (VI; R = H). Attempts at an

[1] Butenandt and McCartney, *Annalen*, 1932, **494**, 17.
[2] La Forge, *J. Amer. Chem. Soc.*, 1932, **54**, 3377.
[3] Whalley, *ibid.*, 1953, **75**, 1059.
[4] Baker, Chadderton, Harborne, and Ollis, *J.*, 1953, 1853.
[5] Whalley, *J.*, 1953, 3366.
[6] Whalley, *Chem. and Ind.*, 1953, 277.
[7] Baker, Dunstan, Harborne, Ollis, and Winter, *ibid.*, p. 277.
[8] Martynoff, *Bull. Soc. chim. France*, 1952, 1056.
[9] Smith and La Forge, *J. Amer. Chem. Soc.*, 1930, **52**, 1091.

alternative synthesis of this failed since efforts to produce 2 : 4-dimethoxybenzyl alcohol and bromide gave only polymers: the claim by Jacobs and Heidelberger [10] to have synthesised 2 : 4-dimethoxybenzyl alcohol must therefore be accepted with reserve.

Similarly 5 : 7 : 2′-trimethoxy*iso*flavone (VII; R = R′ = Me) was partially demethylated with aluminium chloride to 5 : 2′-dihydroxy-7-methoxy*iso*flavone (VII; R = R′ = H) (cf. Baker *et al.*[4]). This was benzylated, methylated, and then debenzylated, to furnish 2′-hydroxy-5 : 7-dimethoxy*iso*flavone (VII; R = Me, R′ = H). The

(III) 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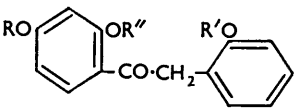
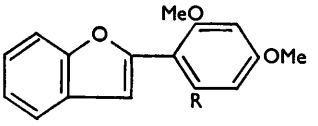
(V) 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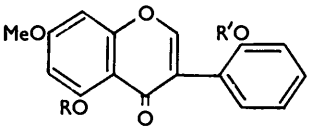
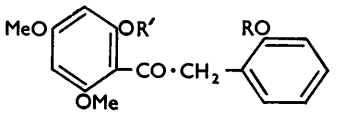
(VII) 


(VIII)

orientation of this *iso*flavone and hence of the cognate derivatives was established by ethylation to 2′-ethoxy-5 : 7-dimethoxy*iso*flavone (VII; R = Me, R′ = Et), which was also prepared by standard methods from 2′-ethoxy-2-hydroxy-4 : 6-dimethoxydeoxybenzoin (VIII; R = Et, R′ = H). Alkali-degradation of 2′-benzyloxy-5 : 7-dimethoxy-*iso*flavone (VII; R = Me, R′ = CH_2Ph) gave 2′-benzyloxy-2-hydroxy-4 : 6-dimethoxydeoxybenzoin (VIII; R = CH_2Ph, R′ = H) which was methylated to 2′-benzyloxy-2 : 4 : 6-trimethoxydeoxybenzoin (VIII; R = CH_2Ph, R′ = Me). Debenzylation of this deoxybenzoin furnished 2-(2 : 4 : 6-trimethoxyphenyl)coumarone (VI; R = OMe) instead of the expected 2′-hydroxy-2 : 4 : 6-trimethoxydeoxybenzoin (VIII; R = H, R′ = Me).

The ready cyclisation of these two 2′-hydroxydeoxybenzoins to 2-phenylcoumarones is in marked contrast to the behaviour of 2 : 2′-dihydroxy-4 : 6-dimethoxy- (VIII; R = R′ = H) and 2 : 2′-dihydroxy-4-methoxy-deoxybenzoin (V; R = Me, R′ = R″ = H) which sublime unchanged and are as stable as the analogous derritol, which must be distilled in the presence of a dehydrating agent to give anhydroderritol,[11,12] formulated as 2-phenylcoumarone (cf. VI). The present work supports this formulation.

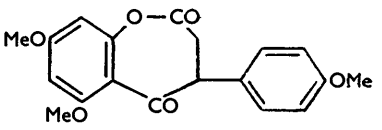
After these failures we investigated the condensation of ethyl bromoacetate with deoxybenzoins (V; R″ = H), to give the phenoxyacetates (cf. XIII; R = Et). However, of the several deoxybenzoins examined only 2-hydroxy-4 : 6 : 2′ : 3′- and -4 : 2′ : 4′ : 6′-tetramethoxydeoxybenzoin furnished the expected esters, which were converted successively by standard procedures into the acids of type (XIII; R = H) and the 3-benzylcoumarones of type (XIV). Attempts to oxidise the methylene group to carbonyl by selenium dioxide or chromium trioxide were unsuccessful, and the usual reagents failed to cyclise the phenoxy-esters to the esters or acids of type (XV; R = Et or H). These anomalous reactions of deoxybenzoins are almost certainly due to the tendency of these substances to react, if not actually to exist, in the enolic form (cf. Badcock, Cavill,

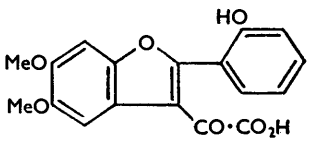
[10] Jacobs and Heidelberger, *J. Biol. Chem.*, 1915, **20**, 678.
[11] Smith and La Forge, *J. Amer. Chem. Soc.*, 1932, **54**, 2997.
[12] Butenandt, *Annalen*, 1928, **464**, 253.

Robertson, and Whalley [13] and Robertson and Whalley [14]). The 2 : 4-dihydroxy-2′ : 4′ : 6′-trimethoxydeoxybenzoin required for this investigation was prepared by Hoesch condensation of resorcinol and 2 : 4 : 6-trimethoxybenzyl cyanide since attempts to prepare 2 : 4 : 6-trimethoxyphenylacetyl chloride by the method of Freudenberg and Harder [15] and by other methods furnished an anomalous product, the nature of which will be reported later.

The only product isolable from the interaction of ethyl bromoacetate and 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin was a small quantity of, probably, 3-(3 : 4-dimethoxybenzyl)-4 : 6-dimethoxycoumarone. 2-Hydroxy-4 : 4′-dimethoxydeoxybenzoin with ethyl bromoacetate furnished only an intractable product, and 2-hydroxy-4 : 6 : 4′-trimethoxydeoxybenzoin gave a low yield of a lactone, devoid of a ferric reaction, and probably having formula (IX).

This approach was consequently also abandoned and attention diverted to the possibility of using the rotenonone–rotenononic acid change [1,2] for the conversion of chromono(2′ : 3′-3 : 4)coumarins (XI), recently made readily available by Baker *et al.*,[16] into analogues of rotenononic acid (IV). Ethoxalyl chloride and 2-hydroxy-4 : 2′-dimethoxydeoxybenzoin

(IX) 



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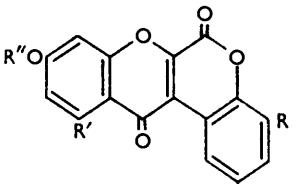
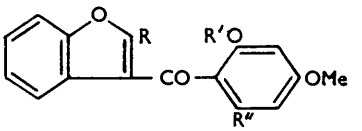
(XI) 



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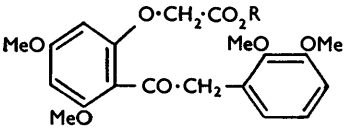
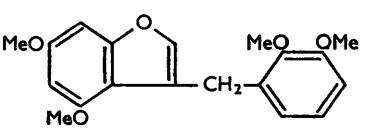
(XIII) 



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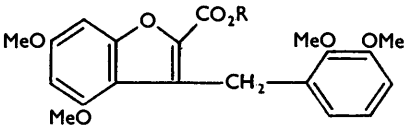
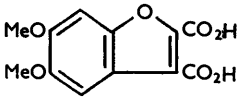
(XV) 



(XVI)

(V; R = R′ = Me, R″ = H) furnished a low yield of 2-ethoxycarbonyl-7 : 2′-dimethoxy-*iso*flavone which was simultaneously partially demethylated and cyclised, to yield 7-methoxychromono(2′ : 3′-3 : 4)coumarin (XI; R″ = Me, R = R′ = H). The action of dilute alkali upon this compound gave 3-(2-hydroxy-4-methoxybenzoyl)coumarone-2-carboxylic acid (XII; R = CO_2H, R′ = R″ = H) and thence its methyl ester which was degraded by alkali to 2-(2 : 4-dimethoxyphenyl)coumarone (VI; R = H).

The readily preparable 5′ : 7′-dihydroxychromono(2′ : 3′-3 : 4)coumarin (XI; R = R″ = H, R′ = OH) [16] was methylated, converted into the acid (XII; R = CO_2H, R′ = H,

[13] Badcock, Cavill, Robertson, and Whalley, *J.*, 1950, 2961.
[14] Robertson and Whalley, *J.*, 1954, 1440.
[15] Freudenberg and Harder, *Annalen*, 1926, **451**, 213.
[16] Baker, Harborne, and Ollis, *J.*, 1953, 1860.

R″ = OMe), and decarboxylated to yield 3-(2 : 4 : 6-trimethoxybenzoyl)coumarone (XII; R = H, R′ = Me, R″ = OMe).

Similarly, 7- and 6-methoxy-3-(2 : 4 : 6-trimethoxybenzoyl)coumarone were prepared from 5′ : 7′ : 8- (XI; R″ = Me, R′ = R″ = OMe) and 5′ : 7′ : 7-trimethoxychromono-(2′ : 3′-3 : 4)coumarin respectively.

The behaviour towards acid and alkali previously adumbrated [3] for these 3-benzoylcoumarones has been fully substantiated by an examination of 3-(2 : 4 : 6-trimethoxybenzoyl)coumarone (XII; R = H, R′ = Me, R″ = OMe) and the 7-methoxy-analogue. Both substances are very sensitive to mineral acids [as are the 2-phenylcoumarones (VI)] and are readily degraded by alkali to formic acid and the appropriate 2′-hydroxy-2-methoxydeoxybenzoins (cf. VIII; R = H, R′ = Me) which on liberation from the alkaline hydrolysate are spontaneously dehydrated to the 2-phenylcoumarones of type (VI).

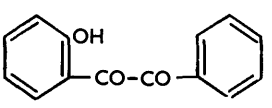
Demethylation of 3-(2 : 4 : 6-trimethoxybenzoyl)coumarone (XII; R = H, R′ = Me, R″ = OMe) under very mild conditions with hydriodic acid furnished 5 : 2′-dihydroxy-7-methoxy*iso*flavone (VII; R = R′ = H) as the only isolable product, whilst aluminium chloride in nitrobenzene gave rise to a small yield of the coumarone (XII; R = R′ = H, R″ = OMe) and much of the *iso*flavone (VII; R = Me, R′ = H). Similarly decarboxylation of the coumarone acid (XII; R = CO_2H, R′ = H, R″ = OMe) in boiling quinoline furnished only a low yield coumarone (XII; R = R′ = H; R″ = OMe) and much of the *iso*flavone (VII; R = Me, R′ = H). The reason for the production of the *iso*flavone in these reactions became clear when it was found that the conversion of 3-*o*-hydroxyaroylcoumarones into *iso*flavones is acid–base-catalysed.

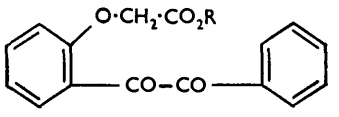
In attempts to effect the thermal decarboxylation of the three carboxylic acids (XII; R = CO_2H, R′ = H), an almost quantitative conversion to the chromono(2′ : 3′-3 : 4)-coumarins (XI) occurred. Whilst rotenononic acid is converted into rotenonone by alkali,[17] acid does not effect this change.[17] There is no report of the effect of heat upon rotenononic acid.

The hydroxyl group in rotenononic acid (IV) is methylated rather more readily than might be expected [2,17] *a priori*. We have observed the same thing for the acid (XII; R = CO_2H, R′ = H, R″ = OMe).

Whilst the acidic transformation products of the chromono(2′ : 3′-3 : 4)coumarins (XI) may be represented as derivatives of 3-aroylcoumarone (cf. XII; R = CO_2H) or of 2-arylcoumarone (cf. X), the general properties of these transformation products and of their cognate derivatives [*inter al.*, the intense ferric reaction of the decarboxylated compounds (XII; R = R′ = H, R″ = OMe), the ease of production of *iso*flavones, and the formation of 2-phenylcoumarones by way of an alkali-soluble intermediate from the decarboxylated acids], clearly substantiate the latter formulation.

The synthesis [18] of arbutic acid (XVI), which is produced together with tubaic acid by hydrogen peroxide oxidation of rotenononic acid, establishes the structure of rotenononic acid as (IV) or of type (X), but does not differentiate between these alternatives. However, the properties of rotenononic acid in conjunction with those of the analogues described in this paper supports the now generally accepted formulæ of type (IV) for these substances (cf. Holton, Parker, and Robertson [18]).

(XVII) 



(XVIII)

During the exploration of other possible routes to 3-aroylcoumarones a number of benzils of type (XVII) were converted into the phenoxy-esters and -acids of type (XVIII) by standard methods. The cyclisation of these acids, which could theoretically give either 3-aroylcoumarones (XII; R = H) or *iso*flavones (cf. I), produced only the latter.

[17] Takei, Miyajima, and Ono, *Ber.*, 1932, **65**, 1048.
[18] Holton, Parker, and Robertson, *J.*, 1949, 2049.

Experimental

Ferric chloride colours refer to reaction in ethanol.

*2'-Hydroxy-7-methoxy*isoflavone (I; R = Me, R' = H).—A solution of aluminium chloride (2 g.) in nitrobenzene (10 ml.) was added to 7 : 2'-dimethoxy*iso*flavone (1 g.) in nitrobenzene (10 ml.), and after 1 hr. on the steam-bath the mixture was decomposed by ice and excess of hydrochloric acid. The product, in ether (100 ml.), was washed with 2N-hydrochloric acid (2 × 20 ml.), water (50 ml.), and 2N-sodium hydroxide (2 × 20 ml.). Acidification of the alkaline extract furnished a crystalline precipitate which was purified from methanol, to give *2'-hydroxy-7-methoxy*isoflavone in prisms (0·7 g.), m. p. 140°, devoid of a ferric reaction (Found: C, 71·4; H, 4·5; OMe, 11·5. $C_{15}H_9O_3$·OMe requires C, 71·6; H, 4·5; OMe, 11·6%). Methylation of this *iso*flavone by methyl sulphate–acetone–potassium carbonate furnished a quantitative yield of 7 : 2'-dimethoxy*iso*flavone, whilst ethylation by the same process gave *2'-ethoxy-7-methoxy*isoflavone in needles, m. p. 121°, from aqueous methanol (Found: C, 72·6; H, 5·3. $C_{18}H_{16}O_4$ requires C, 73·0; H, 5·4%). Hydrolysis of the last *iso*flavone (0·5 g.) with potassium hydroxide (2 g.) in boiling water (10 ml.) and alcohol (10 ml.), during 1½ hr., gave *2'-ethoxy-2-hydroxy-4-methoxybenzoin*, prisms (0·4 g.), m. p. 94°, from methanol (Found: C, 71·2; H, 6·6. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%). This ketone gives an intense red-brown ferric reaction and is most readily purified by sublimation at 150°/0·01 mm. Condensation of resorcinol (8 g.) with *o*-ethoxybenzyl cyanide (5 g.) during 48 hr. by Hoesch's method gave *2'-ethoxy*-2 : 4-*dihydroxydeoxybenzoin*, prisms (from benzene) (1·2 g.), m. p. 148° (Found: C, 70·7; H, 6·3. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%), converted quantitatively by methyl sulphate–acetone–potassium carbonate into 2'-ethoxy-2-hydroxy-4-methoxydeoxybenzoin, identical with the previous specimen, and thence into *2'-ethoxy*-2 : 4-*dimethoxydeoxybenzoin*, plates (from methanol), m. p. 89° (Found: C, 70·9; H, 6·5. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%).

2-*Ethoxy*-4 : *2'-dimethoxydeoxybenzoin*, prepared quantitatively by ethylation of 2-hydroxy-4 : 2'-dimethoxydeoxybenzoin,[5] separated from aqueous methanol in prisms, m. p. 103° (Found: C, 71·7; H, 7·0. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%).

7 : *2'-Dihydroxy*isoflavone (I; R = R' = H).—When a solution of 7 : 2'-dimethoxy*iso*flavone (2 g.) in benzene (25 g.) containing aluminium chloride (2 g.) was heated on the steam-bath for 2 hr., and then decomposed by the addition of ice and hydrochloric acid, crystals separated. Purification from aqueous methanol gave 7 : *2'-dihydroxy*isoflavone, prisms (1·6 g.), m. p. 212°, devoid of a ferric reaction and converted quantitatively into 7 : 2'-dimethoxy*iso*flavone during 2 hr. by methyl sulphate–acetone–potassium carbonate (Found: C, 70·7; H, 4·3. $C_{15}H_{10}O_4$ requires C, 70·9; H, 4·0%).

2 : *2'-Dihydroxy-4-methoxydeoxybenzoin* (V; R = Me, R' = R'' = H).—A solution of 2'-hydroxy-7-methoxy*iso*flavone (2 g.) in water (40 ml.) and potassium hydroxide (4 g.) was heated under reflux for 1 hr., and the solution acidified. The precipitate, crystallised from aqueous methanol, gave 2 : *2'-dihydroxy-4-methoxydeoxybenzoin* as prisms (1·6 g.), m. p. 119°, exhibiting an intense red-brown ferric reaction (Found: C, 69·4; H, 5·7; OMe, 12·3. $C_{14}H_{11}O_3$·OMe requires C, 69·8; H, 5·5; OMe, 12·0%). Methylation of this by methyl sulphate–acetone–potassium carbonate gave a quantitative yield of 2 : 4 : *2'-trimethoxydeoxybenzoin*, prisms (from aqueous alcohol), m. p. 81°, devoid of a ferric reaction in this solvent and identical with the product prepared by the methylation of 2-hydroxy-4 : 2'-dimethoxydeoxybenzoin [Found: C, 71·0; H, 6·7; OMe, 32·6. $C_{14}H_9O(OMe)_3$ requires C, 71·3; H, 6·3; OMe, 32·5%].

Cyclisation of 2 : 2'-dihydroxy-4-methoxydeoxybenzoin (1 g.) with sodium dust (2 g.) and ethyl formate (40 ml.) in the usual way gave only 2'-hydroxy-7-methoxy*iso*flavone (0·6 g.).

2-(2 : 4-*Dimethoxyphenyl*)*coumarone* (VI; R = H).—Interaction of 2'-hydroxy-7-methoxy*iso*flavone (5 g.), benzyl bromide (3·5 g., 1 mol.), and potassium carbonate (30 g.) in boiling acetone (200 ml.) during 2 hr. gave *2'-benzyloxy-7-methoxy*isoflavone, which separated from much methanol in needles (4·0 g.), m. p. 161° [Found: C, 76·7; H, 4·9; OMe, 8·7. $C_{22}H_{15}O_3(OMe)$ requires C, 77·0; H, 5·0; OMe, 8·7%], of which 0·2 g. was debenzylated with acetic acid (5 ml.) and concentrated hydrochloric acid (2 ml.) on the steam-bath during 30 min. to 2'-hydroxy-7-methoxy*iso*flavone (0·1 g.).

A solution of 2'-benzyloxy-7-methoxy*iso*flavone (2 g.) in methanol (30 ml.) and water (10 ml.) containing potassium hydroxide (6 g.) was refluxed during 1½ hr., acidified (Congo-red), and neutralised with 2N-sodium hydrogen carbonate, and the crystalline precipitate was purified

from methanol, to give *2'-benzyloxy-2-hydroxy-4-methoxydeoxybenzoin*, prisms (0·8 g.), m. p. 114°, giving an intense red-brown ferric reaction (Found: C, 75·4; H, 5·7. $C_{22}H_{20}O_4$ requires C, 75·9; H, 5·8%). Methylation of this ketone (3 g.) by methyl sulphate–acetone–potassium carbonate gave *2'-benzyloxy-2 : 4-dimethoxydeoxybenzoin*, prisms (from methanol) (3 g.), m. p. 106°, devoid of a ferric reaction [Found: C, 75·7; H, 6·2; OMe, 17·4. $C_{21}H_{16}O_2(OMe)_2$ requires C, 76·2; H, 6·1; OMe, 17·1%].

Debenzylation of the latter deoxybenzoin (1·5 g.) in acetic acid (50 ml.) containing a catalyst prepared from charcoal (0·7 g.) and palladium chloride (30 ml. of 1% solution) occurred during 45 min. After removal of the solvent under reduced pressure a solution of the residue in ether (100 ml.) was washed with 2N-sodium hydroxide (20 ml.), dried, and evaporated, yielding *2-(2 : 4-dimethoxyphenyl)coumarone* in prisms (0·8 g.), m. p. 53° (from methanol) [Found: C, 75·7; H, 5·7; OMe, 24·8%; *M*, 258. $C_{14}H_8O(OMe)_2$ requires C, 75·6; H, 5·5; OMe, 24·4%; *M*, 254]. Addition of the acetic acid solution after completion of hydrogenolysis to excess of sodium hydrogen carbonate solution, followed by ether-extraction, furnished the same product. Hydrogenolysis did not proceed in methanol.

2'-Benzyloxy-5 : 7-dimethoxyisoflavone (VII; R = Me, R' = CH_2Ph).—A solution of aluminium chloride (4 g.) and 5 : 7 : 2'-trimethoxy*iso*flavone (2 g.) in nitrobenzene (20 ml.) was heated on the steam-bath for 1½ hr., then decomposed with ice and hydrochloric acid, and the product taken up in ether (150 ml.). The ethereal extract was washed with 2N-hydrochloric acid (2 × 50 ml.), water (50 ml.), and 2N-sodium hydroxide (2 × 25 ml.), evaporated, and steam-distilled, to yield a residue of 5'-hydroxy-7 : 2'-dimethoxy*iso*flavone[16] (1 g.). The crystalline precipitate obtained by acidification of the alkaline washings was purified from methanol, giving 5 : 2'-dihydroxy-7-methoxy*iso*flavone (0·8 g.) in needles, m. p. 175°. Baker *et al.*[16] record m. p. 175—177°.

This *iso*flavone (4·5 g.) with benzyl bromide (3·0 g., 1 mol.) and potassium carbonate (10 g.) in boiling acetone (100 ml.) during 4 hr. gave *2'-benzyloxy-5-hydroxy-7-methoxyisoflavone* which separated from methanol in needles (4·0 g.), m. p. 117°, exhibiting an intense violet ferric reaction (Found: C, 73·5; H, 4·6; OMe, 7·5. $C_{22}H_{15}O_4$·OMe requires C, 73·8; H, 4·8; OMe, 8·3%). This *iso*flavone (5 g.) with methyl sulphate–acetone–potassium carbonate furnished *2'-benzyloxy-5 : 7-dimethoxyisoflavone*, prisms (5 g.) (from ethyl acetate), m. p. 171°, devoid of a ferric reaction [Found: C, 73·8; H, 5·3; OMe, 15·7. $C_{22}H_{14}O_3(OMe)_2$ requires C, 74·2; H, 5·3; OMe, 16·0%].

Debenzylation of this *iso*flavone (1 g.) in acetic acid (10 ml.) containing hydrochloric acid (5 ml.) on the steam-bath during 30 min. gave *2'-hydroxy-5 : 7-dimethoxyisoflavone* which separated from aqueous methanol in needles (0·5 g.), m. p. 192°, readily soluble in 2N-sodium hydroxide and devoid of a ferric reaction [Found: C, 68·5; H, 5·1; OMe, 19·8. $C_{15}H_8O_3(OMe)_2$ requires C, 68·5; H, 4·7; OMe, 20·5%].

2'-Ethoxy-5 : 7-dimethoxyisoflavone (VII; R = Me, R' = Et).—(*a*) 2'-Hydroxy-5 : 7-dimethoxy*iso*flavone (1 g.), ethyl iodide, acetone, and potassium carbonate gave *2'-ethoxy-5 : 7-dimethoxyisoflavone*, prisms (from ethyl acetate) (1 g.), m. p. 163° (Found: C, 69·8; H, 5·8. $C_{19}H_{18}O_5$ requires C, 70·0; H, 5·5%).

(*b*) Prepared by the Hoesch method from phloroglucinol (7 g.) and *o*-ethoxybenzyl cyanide during 24 hr., crude 2'-ethoxy-2 : 4 : 6-trihydroxydeoxybenzoin (4 g.) was not readily purified and was methylated directly to *2'-ethoxy-2-hydroxy-4 : 6-dimethoxydeoxybenzoin* which separated from methanol in prisms (2 g.), m. p. 110°, giving an intense violet ferric reaction (Found: C, 68·4; H, 6·4. $C_{18}H_{20}O_5$ requires C, 68·4; H, 6·3%). Cyclisation of this ketone (1·5 g.) with sodium powder (2 g.) and ethyl formate (25 ml.) during 24 hr. at 0° gave *2-hydroxy-2'-ethoxy-5 : 7-dimethoxyisoflavanone*, needles (from methanol) (1 g.), m. p. 184° (decomp.), devoid of a ferric reaction (Found: C, 66·3; H, 6·1. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·9%). When boiled with acetic acid for 15 min. this was converted quantitatively into 2'-ethoxy-5 : 7-dimethoxy*iso*flavone, identical with the product prepared by method (*a*).

2-(2 : 4 : 6-Trimethoxyphenyl)coumarone (VI; R = OMe).—A solution of 2'-benzyloxy-5 : 7-dimethoxy*iso*flavone (2·5 g.) in methanol (30 ml.) and water (10 ml.) containing potassium hydroxide (6 g.) was refluxed during 1½ hr., cooled, and acidified (Congo-red), and the precipitate purified from methanol to furnish *2'-benzyloxy-2-hydroxy-4 : 6-dimethoxydeoxybenzoin*, prisms (2·2 g.), m. p. 117°, giving an intense violet ferric reaction [Found: C, 72·1; H, 6·3; OMe, 16·5. $C_{21}H_{16}O_3(OMe)_2$ requires C, 73·0; H, 5·8; OMe, 16·4%]. This (5 g.) during 20 hr. with methyl sulphate–acetone–potassium carbonate gave *2'-benzyloxy-2 : 4 : 6-trimethoxydeoxybenzoin* as a colourless liquid (5 g.) [Found: OMe, 24·0. $C_{21}H_{15}O_2(OMe)_3$ requires OMe, 23·7%]. Hydrogenolysis of this ketone (1·5 g.) in acetic acid (150 ml.) containing a catalyst prepared from charcoal (0·5 g.) and palladium chloride (40 ml. of 1% solution) was complete in 2 hr., and,

after evaporation of the solvent, 2-(2 : 4 : 6-*trimethoxyphenyl*)*coumarone* separated from methanol in prisms (1 g.), m. p. 105°, insoluble in cold 2N-sodium hydroxide and devoid of a ferric reaction [Found : C, 72·0; H, 6·1; OMe, 32·9%; *M*, 277. $C_{14}H_7O(OMe)_3$ requires C, 71·8; H, 5·7; OMe, 32·8%; *M*, 284]. This hydrogenolysis did not proceed in methanol or ethanol.

4 : 6-*Dimethoxy*-3-(2 : 3-*dimethoxybenzyl*)*coumarone* (XIV).—Interaction of 2-hydroxy-4 : 6 : 2′ : 3′-tetramethoxydeoxybenzoin [5] (5 g.) and excess of ethyl bromoacetate (added as required) in boiling acetone (125 ml.) containing potassium carbonate (10 g.) until a test portion had no ferric reaction in alcohol required 40 hr. After isolation in the usual manner, purification of the semicrystalline product from alcohol–light petroleum (b. p. 60—80°) gave 2-*ethoxycarbonylmethoxy*-4 : 6 : 2′ : 3′-*tetramethoxydeoxybenzoin* in needles (3 g.), m. p. 111°, devoid of a ferric reaction (Found : C, 62·6; H, 6·3. $C_{22}H_{26}O_8$ requires C, 63·2; H, 6·3%). Addition of 20% aqueous alcoholic potassium hydroxide (50 ml.) to the mother-liquors from this crystallisation followed 20 min. later by dilution with water (50 ml.) gave a sticky solid which, purified from acetone, gave 3-(2 : 3-*dimethoxybenzyl*)-4 : 6-*dimethoxycoumarone* in prisms (1 g.), m. p. 115°, devoid of a ferric reaction and insoluble in 2N-sodium hydroxide [Found : C, 69·3; H, 6·1; OMe, 37·7%; *M*, 291. $C_{15}H_8O(OMe)_4$ requires C, 69·5; H, 6·1; OMe, 37·8; *M*, 328].

Hydrolysis of 2-ethoxycarbonylmethoxy-4 : 6 : 2′ : 3′-tetramethoxydeoxybenzoin with an excess of cold 20% alcoholic potassium hydroxide during 20 min. gave quantitatively the *acid*, which separated from aqueous acetone in needles, m. p. 170°, devoid of a ferric reaction [Found : C, 61·5; H, 5·6; OMe, 31·9. $C_{16}H_{10}O_4(OMe)_4$ requires C, 61·5; H, 5·6; OMe, 31·8%]. A mixture of this acid (2 g.), sodium acetate (5 g.), and acetic anhydride (20 ml.) was refluxed for 2½ hr., then poured into water (100 ml.), and 24 hr. later the crystalline precipitate was purified from methanol, to give 3-(2 : 3-dimethoxybenzyl)-4 : 6-dimethoxycoumarone in prisms (1 g.), m. p. 115°, giving a deep green solution in sulphuric acid on the steam-bath [Found : C, 69·7; H, 6·1; OMe, 37·9. Calc. for $C_{15}H_8O(OMe)_4$: C, 69·5; H, 6·1; OMe, 37·8%], identical with the previous specimen.

3-(3 : 4-*Dimethoxybenzyl*)-4 : 6-*dimethoxycoumarone*.—Interaction of 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin (5 g.) with ethyl bromoacetate as above (*ca.* 100 hr.) gave a semi-solid product which, purified from acetone, was 3-(3 : 4-*dimethoxybenzyl*)-4 : 6-*dimethoxycoumarone* (1 g.), tablets, m. p. 118° [Found : C, 69·8; H, 6·2; OMe, 37·8. $C_{15}H_8O(OMe)_4$ requires C, 69·5; H, 6·1; OMe, 37·8%].

2 : 3 : 4 : 5-*Tetrahydro*-6 : 8-*dimethoxy*-4-p-*methoxyphenyl*-2 : 5-*dioxobenz*[b]*oxepin* (IX) *from Ethyl Bromoacetate and* 2-*Hydroxy*-4 : 6 : 4′-*trimethoxydeoxybenzoin*.—This deoxybenzoin (10 g.) with excess of ethyl bromoacetate during 100 hr. in the usual way furnished an oil which on solution in acetone gradually deposited crystals, which separated from acetone (sparingly soluble) in needles (1 g.) of the *lactone*, m. p. 227° (decomp.) [Found : C, 66·4; 5·1; OMe, 27·2%; *M*, 341. $C_{16}H_9O_3(OMe)_3$ requires C, 66·7; H, 5·3; OMe, 27·1%; *M*, 342]. This compound gives a negative ferric reaction and is insoluble in cold 2N-sodium hydroxide, but dissolves readily in the presence of a little alcohol to form a clear solution from which it is precipitated unchanged on acidification but not by dilution with water.

2 : 4 : 6-*Trimethoxybenzyl Cyanide*.—Hydrolysis during 8 hr. of the azlactone [15] (50 g.) of 2 : 4 : 6-trimethoxybenzaldehyde with boiling 10% aqueous sodium hydroxide (500 ml.) furnished 2 : 4 : 6-*trimethoxyphenylpyruvic* acid (35 g.) which separated from benzene in pale yellow leaflets, m. p. 112°, giving a green ferric reaction (Found : C, 56·4; H, 5·8. $C_{12}H_{14}O_6$ requires C, 56·7; H, 5·5%). The *oxime* (10 g.) prepared from this acid (10 g.) in the usual way formed needles, m. p. 177° (decomp.), from aqueous acetic acid (Found : C, 53·8; H, 5·8; N, 5·4. $C_{12}H_{15}O_6N$ requires C, 53·5; H, 5·6; N, 5·2%). Dehydration of this oxime (8 g.) with warm acetic anhydride furnished the *cyanide* (4·5 g.), which separated from methanol in yellow tablets, m. p. 117° (Found : C, 63·5; H, 6·3; N, 6·9. $C_{11}H_{13}O_3N$ requires C, 63·8; H, 6·3; N, 6·8%).

6-*Methoxy*-3-(2 : 4 : 6-*trimethoxybenzyl*)*coumarone*.—A solution of resorcinol (6 g.) and 2 : 4 : 6-trimethoxybenzyl cyanide (3·5 g.) in ether (300 ml.) containing zinc chloride (3 g.) was saturated with hydrogen chloride at 0°. After 48 hr. the product was purified from aqueous methanol, to give 2 : 4-*dihydroxy*-2′ : 4′ : 6′-*trimethoxydeoxybenzoin* (2 g.) in prisms, m. p. 198° (Found : C, 64·0; H, 5·9. $C_{17}H_{18}O_6$ requires C, 64·2; H, 5·7%).

This ketone (2 g.) with methyl iodide–potassium carbonate in boiling acetone during 20 min. gave 2-*hydroxy*-4 : 2′ : 4′ : 6′-*tetramethoxydeoxybenzoin* (2 g.) in prisms, m. p. 156° (from methanol) [Found : C, 64·9; H, 5·9; OMe, 36·9. $C_{14}H_8O_2(OMe)_4$ requires C, 65·1; H, 6·1; OMe, 37·3%], giving an intense red-brown ferric reaction.

Cyclisation of this ketone (1 g.) by sodium–ethyl formate furnished 2-*hydroxy*-7 : 2′ : 4′ : 6′-*tetramethoxy*iso*flavanone* (1 g.), prisms (from methanol), m. p. 196—197° (decomp.), giving a negative ferric reaction (Found : C, 63·3; H, 5·4. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6%).

When heated above the m. p. or boiled with acetic acid for 10 min. the foregoing *iso*flavanone furnished quantitatively 7 : 2′ : 4′ : 6′-*tetramethoxy*iso*flavone*, which separated from methanol in prisms, m. p. 223°, giving a negative ferric reaction (Found : C, 66·3; H, 5·2. $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%).

Interaction of excess of ethyl bromoacetate and 2-hydroxy-4 : 2′ : 4′ : 6′-tetramethoxydeoxybenzoin (4·6 g.) in boiling acetone (100 ml.) containing potassium carbonate (15 g.) during 8 hr. gave 2-*ethoxycarbonylmethoxy*-4 : 2′ : 4′ : 6′-*tetramethoxydeoxybenzoin* (4·5 g.), prisms (from ethanol), m. p. 125°, not giving a ferric reaction (Found : C, 63·4; H, 6·3; $C_{22}H_{26}O_8$ requires C, 63·2; H, 6·3%).

Hydrolysis of this ester (10 g.) with 20% methanolic potassium hydroxide (100 ml.) for 30 min. gave 2-*carboxymethoxy*-4 : 2′ : 4′ : 6′-*tetramethoxydeoxybenzoin*, prisms (100%), m. p. 158° (from benzene–acetone) [Found : C, 62·3; H, 6·0; OMe, 30·4. $C_{16}H_{10}O_4(OMe)_4$ requires C, 61·6; H, 5·6; OMe, 31·8%].

Cyclisation of this ketone (3·6 g.) in boiling acetic anhydride (25 ml.) containing sodium acetate (10 g.) during 3 hr. gave 6-*methoxy*-3-(2 : 4 : 6-*tetramethoxybenzyl*)*coumarone* (2·5 g.), which separated from methanol in needles, m. p. 96° [Found : C, 69·1; H, 6·2; OMe, 37·4. $C_{15}H_8O(OMe)_4$ requires C, 69·5; H, 6·1; OMe, 37·8%].

2 : 3-*Dihydro*-6-*methoxy*-3-(2 : 4 : 6-*trimethoxybenzyl*)*coumarone*.—A solution of the previous coumarone (1 g.) in methanol (100 ml.) containing palladium–charcoal [from palladium chloride (0·25 g.) and charcoal (0·5 g.)] was shaken in hydrogen during 35 min. (uptake, 75 ml., 1 mol.). 2 : 3-*Dihydro*-6-*methoxy*-3-(2 : 4 : 6-*trimethoxybenzyl*)*coumarone*, isolated by distillation as an oil, b. p. 150°/0·01 mm., crystallised from aqueous methanol in needles (0·7 g.), m. p. 58°, insoluble in 2N-sodium hydroxide and devoid of a ferric reaction (Found : C, 69·3; H, 7·2. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7%).

7′-*Methoxychromono*(2′ : 3′-3 : 4)*coumarin* (XI; R = R′ = H, R″ = Me).—(*a*) Cyclisation of 2-hydroxy-4 : 2′-dimethoxydeoxybenzoin [5] (10 g.) with ethoxalyl chloride according to the method of Baker *et al.*,[4] furnished a brown viscous oil which, purified from benzene and then ethanol, gave 2-*ethoxycarbonyl*-2-*hydroxy*-7 : 2′-*dimethoxy*iso*flavanone*, tablets (1—2·5 g.), m. p. 124°, devoid of a ferric reaction (Found : C, 64·2; H, 5·3. $C_{20}H_{20}O_7$ requires C, 64·5; H, 5·4%). When boiled in acetic acid solution during 10 min. this was converted quantitatively into 2-*ethoxycarbonyl*-7 : 2′-*dimethoxy*iso*flavone*, needles (from methanol), m. p. 94° (Found : C, 67·7; H, 5·5. $C_{20}H_{18}O_6$ requires C, 67·8; H, 5·1%).

This ester (2 g.) was refluxed in acetic acid (20 ml.) and hydriodic acid (10 ml.; *d* 1·7) for 30 min., then diluted with water (50 ml.), and the precipitate purified from methanol to give 7′-methoxychromono(2′ : 3′-3 : 4)coumarin, needles (1·5 g.), m. p. 248° (from ethyl acetate) (Found : C, 69·2; H, 3·3; OMe, 10·4. Calc. for $C_{16}H_7O_4{\cdot}OMe$: C, 69·4; H, 3·4; OMe, 10·5%). This substance is insoluble in cold 2N-sodium hydroxide, devoid of a ferric reaction and very sparingly soluble in methanol and alcohol. Seshadri and Veradarajan [19] record m. p. 240—242° for a specimen prepared by an alternative method.

(*b*) The crude product from the reaction of 2 : 4-dihydroxy-2′-methoxydeoxybenzoin (5 g.) and ethoxalyl chloride (8 ml.) in pyridine (50 ml.) was refluxed with hydriodic acid (20 ml.; *d* 1·7) and acetic acid (25 ml.) during 1 hr. Purification from methanol (sparingly soluble) of the product which separated on cooling furnished 7′-*hydroxychromono*(2′ : 3′-3 : 4)*coumarin* (1 g.) in pale buff needles, m. p. >300°, giving no ferric reaction (Found : C, 68·2; H, 3·2. $C_{16}H_8O_5$ requires C, 68·6; H, 2·9%). With methyl sulphate–potassium carbonate–acetone this gave quantitatively 7′-methoxychromono(2′ : 3′-3 : 4)coumarin identical with the product from method (*a*).

3-(2-*Hydroxy*-4-*methoxybenzoyl*)*coumarone*-2-*carboxylic Acid* (XII; R = CO_2H, R′ = R″ = H).—A solution of the previous coumarin (0·5 g.) in 5% aqueous-alcoholic potassium hydroxide (25 ml.) was heated on the steam-bath during 1½ hr., diluted with water (50 ml.), acidified, and 24 hr. later extracted with ether (2 × 50 ml.), and the extract washed with 2N-sodium hydrogen carbonate (2 × 25 ml.). Acidification of this alkaline extract gave a crystalline precipitate which from benzene gave 3-(2-*hydroxy*-4-*methoxybenzoyl*)*coumarone*-2-*carboxylic acid*, prisms (0·2 g.), m. p. 212°, exhibiting an intense red-brown ferric reaction (Found : C, 65·6; H, 4·0; OMe, 9·7. $C_{16}H_9O_5{\cdot}OMe$ requires C, 65·8; H, 3·8; OMe, 10·0%).

[19] Seshadri and Veradarajan, *Proc. Indian Acad. Sci.*, 1953, **37**, *A*, 793.

When heated to *ca.* 250° this acid was converted almost quantitatively into 7′-methoxychromono-(2′ : 3′-3 : 4)coumarin.

This acid (0·1 g.) with methyl sulphate–acetone–potassium carbonate (3 hr.) gave *methyl* 3-(2 : 4-*dimethoxybenzoyl*)*coumarone*-2-*carboxylate* in very pale yellow prisms (0·1 g.), m. p. 146° (from methanol), devoid of a ferric reaction (Found : C, 67·2; H, 5·2. $C_{19}H_{16}O_6$ requires C, 67·1; H, 4·7%).

When a solution of this ester (50 mg.) in methanol (5 ml.) and water (3 ml.) containing potassium hydroxide (0·5 g.) was refluxed for 1 hr., and the product isolated with ether from the acidified solution, 2-(2 : 4-dimethoxyphenyl)coumarone was obtained as prisms (from methanol) (30 mg.), m. p. 53°, identical with the previous specimen.

3-(2-*Hydroxy*-4 : 6-*dimethoxybenzoyl*)*coumarone*-2-*carboxylic Acid* (XII; R = CO_2H, R′ = H, R″ = OMe).—5′ : 7′-Dihydroxychromono(2′ : 3′-3 : 4)coumarin [16] (5 g.) suspended in boiling acetone (250 ml.) containing methyl sulphate (10 g.) and potassium carbonate (30 g.) was refluxed for 24 hr., the hot solution filtered, and the filter-cake treated with hot water (500 ml.). The insoluble residue was collected, washed with more hot water (250 ml.), and crystallised from acetic acid (1500 ml.), to give 5′ : 7′-*dimethoxychromono*(2′ : 3′-3 : 4)*coumarin* in almost colourless needles (4 g.), m. p. 312° [Found : C, 66·5; H, 3·8; OMe, 18·8. $C_{16}H_6O_4(OMe)_2$ requires C, 66·7; H, 3·7; OMe, 19·1%], devoid of a ferric reaction and very sparingly soluble in the usual organic solvents.

This dimethyl ether (1 g.) and 5% aqueous alcoholic potassium hydroxide (40 ml.) were heated on the steam-bath for 90 min., cooled, diluted with water (100 ml.), and acidified; the crystalline precipitate was purified from aqueous methanol, to give 2 : 2′-*dihydroxy*-4 : 6-*dimethoxydeoxybenzoin* in needles (0·8 g.), m. p. 155°, giving an intense red-brown ferric reaction [Found : C, 66·9; H, 5·6; OMe, 21·6. $C_{14}H_{10}O_3(OMe)_2$ requires C, 66·7; H, 5·6; OMe, 21·5%]. Methylation of this deoxybenzoin (0·5 g.) during ½ hr. as usual gave 2-hydroxy-4 : 6 : 2′-trimethoxydeoxybenzoin (0·5 g.), identical with an authentic specimen.[5]

A solution of 5′ : 7′-dimethoxychromono(2′ : 3′-3 : 4)coumarin (1 g.) in 5% alcoholic potassium hydroxide (20 ml.) and water (20 ml.) was heated on the steam-bath for 40 min., diluted with water (100 ml.), acidified, and shaken with ether (150 ml.), and the mixture filtered to remove unchanged starting material (0·2 g.). The ethereal solution was washed with 2N-sodium hydrogen carbonate (2 × 50 ml.), and the crystalline precipitate obtained on acidification of these washings was purified from benzene–acetone, to yield 3-(2-*hydroxy*-4 : 6-*dimethoxybenzoyl*)*coumarone*-2-*carboxylic acid* (0·4 g.) in needles, m. p. 192° [Found : C, 63·6; H, 4·1. OMe, 18·5. $C_{16}H_8O_5(OMe)_2$ requires C, 63·2; H, 4·1; OMe, 18·7%]. This acid is sparingly soluble in benzene, readily soluble in acetone, methanol, and alcohol, exhibits an intense red-brown ferric reaction, gives no derivative with 2 : 4-dinitrophenylhydrazine sulphate, forms a deep orange solution in warm (100°) sulphuric acid, and is unchanged on 45 minutes' boiling in acetic acid containing 5% of hydrochloric acid.

3-(2 : 4 : 6-*Trimethoxybenzoyl*)*coumarone* (XII; R = H, R′ = Me, R″ = OMe).—(*a*) Methylation during 4 hr. of the foregoing acid (1 g.) as usual gave *methyl* 3-(2 : 4 : 6-*trimethoxybenzoyl*)*coumarone*-2-*carboxylate* in needles (1 g.), m. p. 128° (from aqueous methanol) [Found : C, 65·0; H, 5·0; OMe, 33·4. $C_{16}H_6O_3(OMe)_4$ requires C, 64·9; H, 4·9; OMe, 33·5%].

When a solution of this ester (0·7 g.) in methanol (10 ml.) and water (10 ml.) containing potassium hydroxide (1·5 g.) was refluxed for 90 min., cooled, and acidified, isolation with ether furnished 2-(2 : 4 : 6-trimethoxyphenyl)coumarone (0·5 g.), identical with a previous specimen.

A solution of methyl 3-(2 : 4 : 6-trimethoxybenzoyl)coumarone-2-carboxylate (5 g.) in warm methanol (150 ml.) containing 2N-sodium hydroxide (5 ml.) was kept for 1½ hr., then diluted with water (300 ml.), and the clear solution acidified (Congo-red). Purification of the precipitate from aqueous acetone gave 3-(2 : 4 : 6-*trimethoxybenzoyl*)*coumarone*-2-*carboxylic acid* (4·5 g.) in yellow tablets, m. p. 224° (decomp.), devoid of a ferric reaction [Found : C, 64·5; H, 4·6; OMe, 26·0. $C_{16}H_7O_4(OMe)_3$ requires C, 64·1; H, 4·5; OMe, 26·1%].

A mixture of this acid (2 g.), copper bronze (0·7 g.) and quinoline (12 ml.) was rapidly heated to the b. p., cooled, diluted with ether (200 ml.), washed with hydrochloric acid until free from quinoline, then with 2N-sodium hydrogen carbonate (1 × 50 ml.), dried, and evaporated, to furnish 3-(2 : 4 : 6-*trimethoxybenzoyl*)*coumarone* which separated from methanol (moderately soluble) in prisms (1·3 g.), m. p. 134°, devoid of a ferric reaction and dissolving in sulphuric acid to a bright yellow solution, unchanged by heating in the steam-bath [Found : C, 69·8; H, 5·2; OMe, 29·1. $C_{15}H_7O_2(OMe)_3$ requires C, 69·2; H, 5·1; OMe, 29·7%]. The *oxime* separated from aqueous methanol in needles, m. p. 190° (Found : C, 66·1; H, 5·2; N, 4·2. $C_{18}H_{17}O_5N$ requires C, 66·1; H, 5·2; N, 4·3%). When boiled for 2 hr. with methanol (10 ml.)

and water (5 ml.) containing potassium hydroxide (2 g.), this benzofuran (0·5 g.) gave 2-(2 : 4 : 6-trimethoxyphenyl)coumarone (0·4 g.) identical with the previous specimen. In the absence of methanol formic acid was detected in the hydrolysate and identified as the *NN'*-diphenylformamidine.[20]

(*b*) A mixture of 3-(2-hydroxy-4 : 6-dimethoxybenzoyl)coumarone-2-carboxylic acid (1 g.), copper bronze (0·3 g.), and quinoline (10 ml.) was boiled for 3 min., cooled, diluted with ether (150 ml.), washed with hydrochloric acid till free from base, then with 2N-sodium hydrogen carbonate, dried, and evaporated, to yield a dark brown gum (0·8 g.). Extraction with boiling light petroleum (b. p. 60—80°) (5 × 25 ml.) followed by concentration to 15 ml. furnished crystals (0·25 g.) which, purified from methanol, gave 3-(2-*hydroxy*-4 : 6-*dimethoxybenzoyl*)-*coumarone* in yellow prisms (0·2 g.), m. p. 133° [Found: C, 68·5; H, 4·8; OMe, 19·8. $C_{15}H_8O_3(OMe)_2$ requires C, 68·4; H, 4·7; OMe, 20·8%]. This substance is slowly soluble in 2N-sodium hydroxide, and exhibits an intense red-brown ferric reaction. Methylation as usual gave quantitatively 3-(2 : 4 : 6-trimethoxybenzoyl)coumarone identical with that prepared by route (*a*), and when heated in acetic acid solution on the steam-bath during 1 hr. it was transformed quantitatively into 2'-hydroxy-5 : 7-dimethoxy*iso*flavone. Purification of the brown, residual gum from methanol gave 2'-hydroxy-5 : 7-dimethoxy*iso*flavone (0·3 g.) identical with an authentic specimen and converted by methylation into 5 : 7 : 2'-trimethoxy*iso*flavone.

Demethylation of 3-(2 : 4 : 6-*Trimethoxybenzoyl*)*coumarone*.—(*a*) When a solution of this coumarone (0·3 g.) in acetic acid (from 3 ml. of anhydride) and hydriodic acid (10 ml.; *d* 1·7) was refluxed for 20 min., dilution of the dark solution yielded a flocculent intractable red precipitate (0·25 g.).

(*b*) A solution of this coumarone (0·5 g.) in acetic acid (10 ml.) and hydriodic acid (2 ml.; *d* 1·7) was heated on the steam-bath for 1 hr., then diluted with water (50 ml.), and the red precipitate purified from methanol, to furnish 5 : 2'-dihydroxy-7-methoxy*iso*flavone (0·2 g.), identical with an authentic specimen and converted quantitatively into 5 : 7 : 2'-trimethoxy-*iso*flavone.

(*c*) A solution of the coumarone (0·5 g.) in nitrobenzene (10 ml.) containing aluminium chloride (0·7 g.) was heated on the steam-bath and the mixture decomposed by ice 1 hr. later. Isolated by ether, the product was purified from methanol, to furnish (i) 2'-hydroxy-5 : 7-dimethoxy*iso*flavone (0·25 g.) and (ii) 3-(2-hydroxy-4 : 6-dimethoxybenzoyl)coumarone (50 mg.).

5' : 7' : 8-*Trimethoxychromono*(2' : 3'-3 : 4)*coumarin* (XI; R = R' = OMe, R'' = Me).—Prepared from 2 : 4 : 6-trihydroxy-2' : 3'-dimethoxydeoxybenzoin [5] (10 g.) and ethoxalyl chloride according to the method of Baker *et al.*,[16] the crude semisolid product was heated under reflux for 1 hr. with acetic acid (100 ml.) and hydriodic acid (50 ml.; *d* 1·7). The product separated from the boiling solution and was purified from a very large volume of acetic acid, to give 5' : 8-*dihydroxy*-7'-*methoxychromono*(2' : 3'-3 : 4)*coumarin* in yellow needles (7 g.), m. p. >300°, exhibiting an intense red-brown ferric reaction and very sparingly soluble in the usual organic solvents (Found: C, 62·2; H, 3·2; OMe, 9·5. $C_{16}H_7O_6$·OMe requires C, 62·6; H, 3·1; OMe, 9·5%). Methylation of this coumarin (5 g.) as usual for 24 hr., followed by isolation as described for the analogue, furnished 5' : 7' : 8-*trimethoxychromono*(2' : 3'-3 : 4)-*coumarin* which separated from a large volume of acetic acid in pale yellow needles (4 g.), m. p. 299°, devoid of a ferric reaction in alcohol and sparingly soluble in the usual organic solvents [Found: C, 64·3; H, 4·0; OMe, 26·3. $C_{16}H_5O_4(OMe)_3$ requires C, 64·4; H, 4·0; OMe, 26·3%].

7-*Methoxy*-3-(2 : 4 : 6-*trimethoxybenzoyl*)*coumarone*.—Alkali degradation of this coumarin (1 g.) in the conditions used for the other phloroglucinol analogue furnished unchanged material (0·1 g.) and 3-(2-*hydroxy*-4 : 6-*dimethoxybenzoyl*)-7-*methoxycoumarone*-2-*carboxylic acid* which separated from aqueous acetic acid in needles (0·4 g.), m. p. 213° (decomp.), giving an intense red-brown ferric reaction [Found: C, 61·5; H, 4·3; OMe, 24·9. $C_{16}H_7O_5(OMe)_3$ requires C, 61·3; H, 4·3; OMe, 25·0%]. When heated to 250° for 5 min. this acid was converted almost quantitatively into 5' : 7' : 8-trimethoxychromono(2' : 3'-3 : 4)coumarin.

Methylation of this acid (2·5 g.) as usual for 4 hr. gave *methyl* 7-*methoxy*-3-(2 : 4 : 6-*trimethoxybenzoyl*)*coumarone*-2-*carboxylate*, prisms (2·5 g.), m. p. 144° (from aqueous methanol) [Found: C, 62·9; H, 5·1; OMe, 39·0. $C_{16}H_5O_3(OMe)_5$ requires C, 63·0; H, 5·0; OMe, 38·8%]. This ester is devoid of a ferric reaction and on hydrolysis gave quantitatively the *acid*, yellow prisms (from aqueous acetone), m. p. 209° [Found: C, 62·3; H, 4·7; OMe, 32·1. $C_{16}H_6O_4(OMe)_4$ requires C, 62·1; H, 4·7; OMe, 31·9%], (2 g. of which were decarboxylated in quinoline (10 ml.) containing copper bronze (0·5 g.) to 7-*methoxy*-3-(2 : 4 : 6-*trimethoxybenzoyl*)*coumarone*,

[20] Whalley, *J.*, 1948, 1014.

prisms (1·2 g.), m. p. 201° (from acetone) [Found : C, 67·0; H, 5·2; OMe, 35·4. $C_{15}H_6O_2(OMe)_4$ requires C, 66·7; H, 5·3; OMe, 36·2%]. This substance (0·2 g.) is resinified completely when refluxed with acetic acid (3 ml.) and hydriodic acid (5 ml.; *d* 1·7) for 20 min., is only moderately soluble in alcohol and acetone, and dissolves in hydrochloric acid to a deep yellow solution, unchanged on the steam-bath.

When this coumarone (0·5 g.) was heated under reflux for 3 hr. with methanol (20 ml.) and water (5 ml.) containing potassium hydroxide (5 g.), isolation with ether from the acidified hydrolysate gave *7-methoxy-2-(2 : 4 : 6-trimethoxyphenyl)coumarone* which separated from methanol in needles (0·3 g.), m. p. 135°, devoid of a ferric reaction and insoluble in 2N-sodium hydroxide [Found : C, 68·4; H, 5·7; OMe, 38·7. $C_{14}H_6O(OMe)_4$ requires C, 68·8; H, 5·7; OMe, 38·1%].

6-Methoxy-3-(2 : 4 : 6-trimethoxybenzoyl)coumarone.—When the crude product from the reaction of 2 : 4 : 6-trihydroxy-2′ : 4′-dimethoxydeoxybenzoin [5] (10 g.) and ethoxalyl chloride (20 ml.) in pyridine (50 ml.) was refluxed for 1 hr. with hydriodic acid (25 ml.; *d* 1·7) and acetic acid (50 ml.) orange-yellow crystals (4 g.) separated. The coumarin was methylated without further purification, as usual, to furnish *5′ : 7′ : 7-trimethoxychromono(2′ : 3′-3 : 4)coumarin* (4 g.), yellow needles, m. p. 292° (from acetic acid; moderately soluble) [Found : C, 64·0; H, 4·5; OMe, 24·9. $C_{16}H_5O_4(OMe)_3$ requires C, 64·4; H, 3·9; OMe, 26·3%].

When the compound (1 g.) was treated with alkali as described for the phloroglucinol analogues the resultant *3-(2-hydroxy-4 : 6-dimethoxybenzoyl)-6-methoxycoumarone-2-carboxylic acid* was obtained (from aqueous acetic acid) in needles (0·3—0·5 g.), m. p. 204° with rapid re-solidification and reversion to the parent chromonocoumarin [Found : C, 60·7; H, 4·6; OMe, 23·8. $C_{16}H_7O_5(OMe)_3$ requires C, 61·3; H, 4·3; OMe, 25·0%]. This acid exhibits an intense red-brown ferric reaction.

Methylation of this acid (4 g.) as usual gave *methyl 3-(2 : 4 : 6-trimethoxybenzoyl)-6-methoxycoumarone-2-carboxylate* (4 g.) in needles, m. p. 150° (from methanol; moderately soluble) [Found : C, 62·4; H, 5·3; OMe, 38·8. $C_{16}H_5O_3(OMe)_5$ requires C, 63·0; H, 5·0; OMe, 38·8%], hydrolysed (2·5 g.) in methanol (50 ml.) with 2N-sodium hydroxide (5 ml.) quantitatively at room temperature (20 min.) to *6-methoxy-3-(2 : 4 : 6-trimethoxybenzoyl)coumarone-2-carboxylic acid*, yellow needles (from aqueous acetone), m. p. 215° [Found : C, 62·9; H, 5·3; OMe, 32·2. $C_{16}H_6O_4(OMe)_4$ requires C, 62·2; H, 4·7; OMe, 32·1%].

Decarboxylation of this acid (1·7 g.) with copper-bronze (0·3 g.) in quinoline (15 ml.), as previously described, gave *6-methoxy-3-(2 : 4 : 6-trimethoxybenzoyl)coumarone* (1·2 g.), needles (from methanol), m. p. 151° [Found : C, 66·7; H, 5·5; OMe, 36·3. $C_{15}H_6O_2(OMe)_4$ requires C, 66·7; H, 5·3; OMe, 36·3%]. This gives no ferric reaction and is rapidly resinified by warm dilute mineral acids.

2′-Methoxyisoflavone.—A solution of 2-hydroxy-2′-methoxybenzil [21] (8 g.) and ethyl bromoacetate (5 g., 1·1 mol.) in acetone (100 ml.) containing potassium carbonate (15 g.) was refluxed until a test portion gave no ferric reaction (8 hr.). After isolation, *2-ethoxycarbonylmethoxy-2′-methoxybenzil* (8 g.) separated from aqueous ethanol in prisms, m. p. 79°, not giving a ferric reaction (Found : C, 66·4; H, 5·3. $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%).

Hydrolysis of this ester occurred rapidly at room temperature with 2N-aqueous-alcoholic sodium hydroxide to furnish almost quantitatively *2′-methoxy-2-methoxycarbonylbenzil* which separated from benzene in needles, m. p. 149° (Found : C, 65·0; H, 4·6; OMe, 10·2. $C_{16}H_{11}O_5$·OMe requires C, 65·0; H, 4·6; OMe, 10·0%).

Cyclisation of this acid (6 g.) in boiling acetic anhydride (30 ml.) containing sodium acetate (20 g.) during 1½ hr. gave *2′-methoxyisoflavone* (3·5 g.), prisms (from methanol; sparingly soluble), m. p. 184° (Found : C, 75·9; H, 5·2; OMe, 12·6. $C_{15}H_9O_2$·OMe requires C, 76·2; H, 4·8; OMe, 12·3%).

Hydrolysis of this compound (0·5 g.) with boiling methanol (10 ml.) and water (5 ml.) containing potassium hydroxide (2 g.) during 1½ hr. gave almost quantitatively *2-hydroxy-2′-methoxydeoxybenzoin*, m. p. 64° [from light petroleum (b. p. 40—60°)], giving an intense violet ferric reaction (Found : C, 74·5; H, 5·8. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%).

Cyclisation of this ketone by sodium–ethyl formate gave quantitatively the unstable 2-hydroxy-2′-methoxy*iso*flavanone which was rapidly converted, in the presence of a trace of acid, into 2′-methoxy*iso*flavone.

7 : 2′ : 4′-Trimethoxyisoflavone.—A solution of 2 : 2′ : 4 : 4′-tetrahydroxybenzil [22] (4·7 g.) and dimethyl sulphate (6·5 g., 3 mol.) in boiling acetone (100 ml.) containing potassium carbonate

[21] Schönberg and Kraemer, *Ber.*, 1922, **55**, 1185.
[22] Schraufstätter, *Chem. Ber.*, 1948, **81**, 240.

(15 g.) was refluxed for 6 hr. After isolation the crude product was dissolved in alcohol, most of the 2 : 2′ : 4 : 4′-tetramethoxybenzil (2·1 g.) separating. After evaporation of the mother-liquors the residue was dissolved in ether and washed with 2N-sodium hydroxide (2 × 50 ml.), the extract acidified, and the precipitate purified from methanol, to give 2-*hydroxy*-2′ : 4 : 4′-*trimethoxybenzil* (1·2 g.) in pale yellow needles, m. p. 110°, giving an intense red-brown ferric reaction [Found : C, 64·5; H, 5·2; OMe, 29·1. $C_{14}H_7O_3(OMe)_3$ requires C, 64·6; H, 5·1; OMe, 29·4%].

Condensation of this benzil (3 g.) with ethyl bromoacetate in the usual manner gave 2-*ethoxycarbonylmethoxy*-2′ : 4 : 4′-*trimethoxybenzil* (3 g.), plates, m. p. 102° (Found : C, 62·6; H, 5·6. $C_{21}H_{22}O_8$ requires C, 62·7; H, 5·5%), hydrolysed (2·5 g.) to the *acid* (2·2 g.), needles, m. p. 195° (from acetone) [Found : C, 61·0; H, 4·9; OMe, 24·7. $C_{16}H_9O_5(OMe)_3$ requires C, 61·0; H, 4·8; OMe, 24·8%].

Cyclisation of this acid (2 g.) with sodium acetate (5 g.) and boiling acetic anhydride (15 ml.) during 45 min. gave 7 : 2′ : 4′-trimethoxy*iso*flavone (1 g.) identical with an authentic specimen.[14]

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