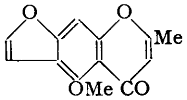
# 965. *Furano-compounds. Part XII.** *Some Analogues of Kellin and Visnagin.*

By G. H. Phillipps, Alexander Robertson, and W. B. Whalley.

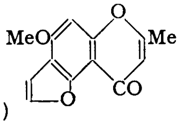
The second possible angular isomeride of visnagin, *allo*visnagin (III), has been obtained from 2 : 4-dihydroxy-6-methoxyacetophenone by the application of standard methods. The preparation of a series of furanochromones and 4-hydroxyfuranocoumarins, related to kellin and visnagin, from 2 : 4- and 4 : 6-diacetylresorcinol is described.

When kellin and related natural furanochromones had been shown to possess valuable coronary vascodilator properties (see, *inter al.*, Anrep, Barsoum, Kenawy, and Misrahy, *Lancet*, 1947, **257**, 557), the synthesis of an extensive series of analogous compounds for pharmacological testing was undertaken in these laboratories. A number of these analogues has since been described (Davies and Norris, *J.*, 1950, 3195; Davies and Deegan, *ibid.*, p. 3202; Davies, McCrea, Norris, and Ramage, *ibid.*, p. 3206) and the present memoir deals only with the synthesis of *allo*visnagin and furanochromones from 2 : 4- and 4 : 6-diacetylresorcinol.

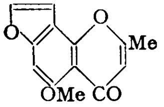
Following the establishment of the structures of visnagin (I) (Späth and Gruber, *Ber.*, 1941, **74**, 1492) and of *iso*visnagin (II) (Part VIII, *J.*, 1948, 2260) the synthesis of the second angular isomeride (III), which we have named *allo*visnagin, was carried out.



(I)

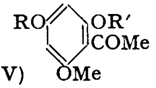


(II)

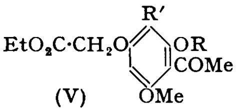


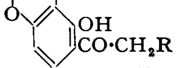
(III)

(IV)



(V)





(VI)

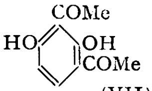
Condensation of 2 : 4-dihydroxy-6-methoxyacetophenone (IV; R = R′ = H) with ethyl bromoacetate in boiling acetone containing potassium carbonate gave ethyl 4-acetyl-3-hydroxy-5-methoxyphenoxyacetate (IV; R = $EtO_2C{\cdot}CH_2$, R′ = H) which on methylation by the methyl iodide–potassium carbonate method yielded ethyl 4-acetyl-3 : 5-dimethoxyphenoxyacetate (V; R = Me, R′ = H), identical with a specimen prepared by the interaction of 4-hydroxy-2 : 6-dimethoxyacetophenone (IV; R = H, R′ = Me) with ethyl bromoacetate in the usual manner, thus confirming the orientation of (V; R = R′ = H). Application of the Gattermann aldehyde synthesis to (V; R = R′ = H) gave a mixture of ethyl 4-acetyl-2-formyl-3-hydroxy-5-methoxyphenoxyacetate (V; R = H, R′ = CHO) and the corresponding acid, unaccompanied by detectable quantities of the isomeric

---

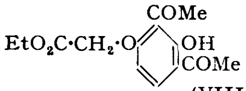
* Part XI, *J.*, 1950, 2381.

6-formyl derivative. The orientation of the phenoxy-ester (V; R = H, R′ = CHO) was confirmed by its preparation, although in poor yield, from 3-formyl-2 : 4-dihydroxy-6-methoxyacetophenone and ethyl bromoacetate by the standard procedure. Prepared by the hydrolysis of its ester (V; R = H, R′ = CHO), 4-acetyl-2-formyl-3-hydroxy-5-methoxyphenoxyacetic acid was converted into 5-acetyl-4-hydroxy-6-methoxycoumarone (VI; R = H) with boiling acetic anhydride and sodium acetate, and on condensation with ethyl acetate and sodium this coumarone gave the diketone (VI; R = COMe) which, on cyclisation with warm acetic acid containing a little hydrochloric acid, furnished 5-methoxy-2-methylfurano(2′ : 3′-7 : 8)chromone, *allo*visnagin (III), characterised by the preparation of the piperonylidene derivative.

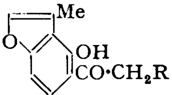
For the remaining syntheses the starting materials, *viz.*, 2 : 4- (VII) and 4 : 6-diacetylresorcinol (XIII) have now been produced conveniently by using boron trifluoride in place of aluminium chloride to effect the Fries rearrangement of resorcinol diacetate. Ethyl 2 : 4-diacetyl-3-hydroxyphenoxyacetate (VIII) was prepared from (VII) and ethyl bromoacetate and converted by the standard method into 5-acetyl-4-hydroxy-3-methylcoumarone (IX; R = H) from which 2 : 4′-dimethylfurano(2′ : 3′-7 : 8)chromone (X) was obtained by way of the diketone (IX; R = COMe). Limaye and Nagarkar (*Rasayanam*, 1943, **1**, 253) have prepared the ketone (IX; R = H) by an independent route but did not comment on its orientation. Of the possible alternative structures (XI) and (XII) for the coumarone (IX; R = H), formula (XI), which would not be expected to give rise to a furanochromone, is excluded because the ketone gives a strong ferric reaction whilst a direct comparison with an authentic specimen of (XII), obtained by the method of Limaye and Sathe (*Rasayanam*, 1936, **1**, 48), showed that the two compounds were not identical. Hence, as expected on general grounds, the product formed by the condensation of (VII) with ethyl bromoacetate has the formula (VIII).



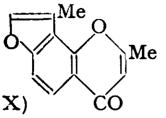
(VII)



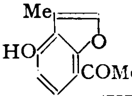
(VIII)



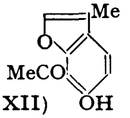
(IX)



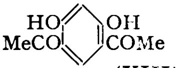
(X)



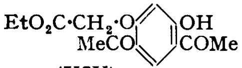
(XI)



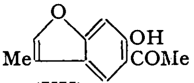
(XII)



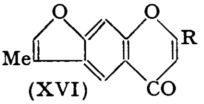
(XIII)



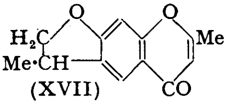
(XIV)



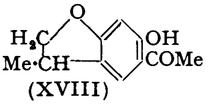
(XV)



(XVI)

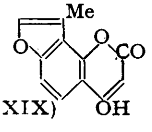


(XVII)

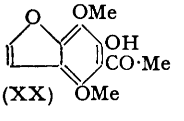


(XVIII)

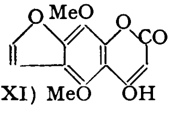
Ethyl 2 : 4-diacetyl-5-hydroxyphenoxyacetate (XIV), of unambiguous orientation, was prepared from 4 : 6-diacetylresorcinol (XIII) and was converted by the standard procedure into 4′-methyl- (XVI; R = H) and 2 : 4′-dimethyl-furano(3′ : 2′-6 : 7)chromone (XVI; R = Me). Similarly the dihydrofuranochromone (XVII) was obtained from the coumaran (XVIII) which was formed by the hydrogenation of (XV).



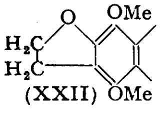
(XIX)



(XX)



(XXI)



(XXII)

By the method of Boyd and Robertson (*J.*, 1948, 174) 5-acetyl-4-hydroxy-3-methylcoumarone (IX; R = H), kellinone (XX), and dihydrokellinone were converted into the respective 4-hydroxyfuranocoumarins (XIX), (XXI), and (XXII), which were characterised by the formation of their respective 4-methyl ethers.

## EXPERIMENTAL

*Ethyl 4-Acetyl-3-hydroxy-5-methoxyphenoxyacetate* (V; R = R′ = H).—A solution of 2 : 4-dihydroxy-6-methoxyacetophenone (4 g.), ethyl bromoacetate (3·7 g.), and acetone (100 ml.), containing potassium carbonate (8 g.), was heated under reflux for 1½ hours. On isolation in the usual manner the *ester* (V; R = R′ = H) (3·8 g.) separated from ethyl alcohol in colourless, long, slender prisms, m. p. 120°, having a red-brown ferric reaction in alcohol (Found: C, 58·2; H, 6·0. $C_{13}H_{16}O_6$ requires C, 58·2; H, 6·0%). Prepared by the pyridine–acetic anhydride method, the *acetate* of this ester separated frqm benzene–light petroleum (b. p. 60—80°) in colourless stout prisms, m. p. 69°, insoluble in cold 2N-sodium hydroxide and having a negative ferric reaction (Found: C, 58·0; H, 5·7. $C_{15}H_{18}O_7$ requires C, 58·0; H, 5·9%).

*Ethyl 4-Acetyl-3 : 5-dimethoxyphenoxyacetate* (V; R = Me, R′ = H).—(*a*) Methylation of the foregoing ketonic ester (0·5 g.) with potassium carbonate (1 g.) and excess of methyl iodide in boiling acetone (30 ml.) for 16 hours gave a quantitative yield of *ethyl 4-acetyl-3 : 5-dimethoxyphenoxyacetate* which formed colourles prisms, m. p. 82°, from aqueous alcohol, having a negative ferric reaction (Found: C, 59·6; H, 6·4. $C_{14}H_{18}O_6$ requires C, 59·6; H, 6·4%).

(*b*) Interaction of 4-hydroxy-2 : 6-dimethoxyacetophenone (Canter, Curd, and Robertson, *J.*, 1931, 1249) (0·5 g.) and ethyl bromoacetate (0·5 g.) in boiling acetone (25 ml.), containing potassium carbonate (2 g.), gave a quantitative yield of the ester (V; R = Me, R′ = H), m. p. and mixed m. p. 82°, after recrystallisation.

*Ethyl 4-Acetyl-2-formyl-3-hydroxy-5-methoxyphenoxyacetate* (V; R = H, R′ = CHO).—A mixture of ethyl 4-acetyl-3-hydroxy-5-methoxyphenoxyacetate (2 g.), chloroform (10 ml.), ether (150 ml.), zinc cyanide (1 g.), and hydrogen cyanide (10 ml.) was saturated with hydrogen chloride at 5° and 48 hours later the colourless crystalline product along with a small quantity of a viscous oil was dissolved in water (200 ml.). This solution was rapidly heated to boiling and on being cooled gave a crystalline solid (1·3 g.) which was separated with the aid of aqueous sodium hydrogen carbonate into *ethyl 4-acetyl-2-formyl-3-hydroxy-5-methoxyphenoxyacetate* (V; R = H, R′ = CHO) (0·7 g.) and the corresponding *acid* (0·6 g.). The ester crystallised from alcohol in almost colourless, long, slender, thin prisms, m. p. 166°, having a red-brown ferric reaction in alcohol (Found: C, 56·9; H, 5·5. $C_{14}H_{16}O_7$ requires C, 56·8; H, 5·4%). The 2 : 4-*dinitrophenylhydrazone* formed rosettes of scarlet needles, m. p. 240° (decomp.), from acetic acid (Found: N, 11·9. $C_{20}H_{20}O_{10}N_4$ requires N, 11·8%). 4-Acetyl-2-formyl-3-hydroxy-5-methoxyphenoxyacetic acid separated from aqueous methanol in almost colourless, slender needles, m. p. 199°, identical with the product obtained by hydrolysis of the ester (V; R = H, R′ = CHO) with 2N-sodium hydroxide on the steam-bath for 10 minutes, and gave a red-brown ferric reaction in alcohol (Found: C, 53·7; H, 4·5. $C_{12}H_{12}O_7$ requires C, 53·7; H, 4·5%).

*5-Acetyl-4-hydroxy-6-methoxycoumarone* (VI; R = H).—A mixture of 4-acetyl-2-formyl-3-hydroxy-5-methoxyphenoxyacetic acid (1 g.), acetic anhydride (15 ml.), and sodium acetate (3g.) was heated under reflux for 30 minutes and the greater part of the acetic anhydride removed in a vacuum. A solution of the residue in water (200 ml.) was neutralised with sodium hydrogen carbonate and extracted with ether, giving the acetate of 5-acetyl-4-hydroxy-6-methoxycoumarone as a colourless oil which was deacetylated with warm 2N-sodium hydroxide (10 ml.) on the steam-bath for 15 minutes. The resulting *5-acetyl-4-hydroxy-6-methoxycoumarone* separated from aqueous methanol in very pale lemon-yellow prisms (0·6 g.), m. p. 85°, unchanged after sublimation at 120°/0·1 mm. (Found: C, 64·2; H, 5·0. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·9%). The coumarone, which did not give a 2 : 4-dinitrophenylhydrazone, was insoluble in 2N-sodium hydrogen carbonate, gave an emerald-green ferric reaction in alcohol, and formed a bright yellow solution in cold concentrated sulphuric acid which became cherry-red on warming.

*5-Methoxy-2-methylfurano(2′ : 3′-7 : 8)chromone* (allo*Visnagin*) (III).—A mixture of the coumarone (VI; R = H) (0·5 g.), ethyl acetate (10 ml.), and powdered sodium (0·7 g.) was heated on the steam-bath for 5 hours with the addition of more ethyl acetate (5 ml.) and sodium (0·3 g.) after 2 hours. After the addition of a little methanol to destroy the excess of sodium, the cooled mixture was diluted with ice-water (50 ml.) and acidified with acetic acid. After the evaporation of the unchanged ethyl acetate in a stream of air the residual solid was crystallised from aqueous methanol, giving *5-acetoacetyl-4-hydroxy-6-methoxycoumarone* in slender colourless needles (0·5 g.), m. p. 114°, which had an olive-brown ferric reaction in alcohol (Found: C, 63·2; H, 4·8. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·9%). A solution of this diketone (0·2 g.) in acetic acid (5 ml.) containing concentrated hydrochloric acid (2 drops) was boiled for 2 minutes, cooled, diluted with water, and extracted with chloroform. Sublimation of the residue left on evaporation of the dried extracts (140°/0·1 mm.) gave a quantitative yield of allo*visnagin* (III) in rosettes of almost colourless stout prisms, m. p. 162° (Found : C, 67·6; H, 4·7. $C_{13}H_{10}O_4$ requires C, 67·8; H, 4·4%). In concentrated sulphuric acid this compound formed a green, faintly fluorescent solution which was unchanged on heating. The *piperonylidene* derivative separated from alcohol in pale yellow needles, m. p. 264° (Found : C, 69·6; H, 4·0. $C_{21}H_{14}O_6$ requires C, 69·6; H, 3·9%).

2 : 4- *and* 4 : 6-*Diacetylresorcinol.*—A solution of resorcinol diacetate (5 g.) in acetic acid (10 ml.) was saturated at room temperature with boron trifluoride, and the resultant syrup heated on the steam-bath for 1 hour, cooled, and treated with water (100 ml.) and then sodium acetate (5 g.). The suspension was boiled until a clear solution was obtained upon the addition of alcohol (50 ml.). The cooled hydrolysate deposited the mixed acetylresorcinols (4 g.) in colourless needles, m. p. 100—130°.

The dried product was extracted with warm light petroleum (b. p. 40—60°) (4 × 100 ml.) and on concentration the combined extracts deposited 2 : 4-diacetylresorcinol (3·1 g.) in colourless needles, m. p. 85°. Crystallised from a mixture of light petroleum (b. p. 60—80°) and chloroform the residue gave 4 : 6-diacetylresorcinol in colourless needles (0·8 g.), m. p. 182° (cf. Baker, *J.*, 1934, 71, 1684). The overall yield was consistent but the proportion of the isomerides varied considerably.

*Ethyl* 2 : 4-*Diacetyl*-3-*hydroxyphenoxyacetate.*—A mixture of 2 : 4-diacetylresorcinol (10 g.), ethyl bromoacetate (6 g.), acetone (300 ml.), and anhydrous potassium carbonate (16 g.) was heated under reflux for 6 hours and the acetone evaporated. Treatment of the residue with water (100 ml.) followed by alcohol (20 ml.) gave a solid which on purification from alcohol furnished ethyl 2 : 4-diacetyl-3-hydroxyphenoxyacetate (VIII) (14 g.) in colourless needles, m. p. 87° (Found : C, 59·8; H, 6·0. Calc. for $C_{14}H_{16}O_6$ : C, 60·0; H, 5·8%) (cf. Limaye and Nagarkar, *loc. cit.*, who give m. p. 75°). Prepared by the pyridine method, the *acetate* separated from light petroleum (b. p. 60—80°) in tiny, colourless, elongated prisms, m. p. 92° (Found : C, 59·1; H, 5·9. $C_{16}H_{18}O_7$ requires C, 59·6; H, 5·6%).

5-*Acetyl*-4-*hydroxy*-3-*methylcoumarone* (IX; R = H).—The ester (VIII) (5 g.) was heated on the steam-bath with 2N-sodium hydroxide (40 ml.) for 15 minutes and on acidification the cooled hydrolysate gave 2 : 4-diacetyl-3-hydroxyphenoxyacetic acid which formed colourless needles (4·2 g.), m. p. 165°, from water (Found : C, 57·1; H, 4·9. Calc. for $C_{12}H_{12}O_6$ : C, 57·1; H, 4·8%) (cf. Limaye and Nagarkar, *loc. cit.*, who give m. p. 168°). Esterified with warm methanol containing a drop of sulphuric acid, this acid yielded the *methyl* ester which formed colourless needles, m. p. 74°, from aqueous methanol (Found : C, 58·8; H, 5·4. $C_{13}H_{14}O_6$ requires C, 58·7; H, 5·3%). Cyclisation of the acid (5 g.) with boiling acetic anhydride (50 ml.), containing sodium acetate (12·5 g.), during 45 minutes gave a dark oil which slowly solidified. Extraction of this solid with light petroleum (b. p. 60—80°) furnished 4-acetoxy-5-acetyl-3-methylcoumarone (4·0 g.), in irregular, colourless prisms, m. p. 109°, having a negative ferric reaction in alcohol (Found : C, 67·3; H, 5·3. Calc. for $C_{13}H_{12}O_4$ : C, 67·2; H, 5·2%) (cf. Limaye and Nagarkar, *loc. cit.*, who give m. p. 108°). The 2 : 4-*dinitrophenylhydrazone* separated from light petroleum–benzene in rosettes of orange needles, m. p. 159° (Found : N, 13·8. $C_{19}H_{16}O_7N_4$ requires N, 13·6%), and in yellow needles, m. p. 152° (Found : N, 13·6%).

Deacetylation of this acetate (5 g.) with 2N-sodium hydroxide (50 ml.) on the steam-bath for 20 minutes gave rise to 5-acetyl-4-hydroxy-3-methylcoumarone (3·6 g.), which formed very pale yellow, elongated, rectangular prisms, m. p. 64°, from dilute alcohol, having a green ferric reaction in alcohol (Found : C, 69·2; H, 5·5. Calc. for $C_{11}H_{10}O_3$ : C, 69·4; H, 5·3%) (cf. Limaye and Nagarkar, *loc. cit.*, who give m. p. 70°). The 2 : 4-*dinitrophenylhydrazone* separated from dioxan in small red needles, m. p. 265—267° (decomp.) (Found : N, 15·3. $C_{17}H_{14}O_6N_4$ requires N, 15·1%).

5-*Acetyl*-4-*hydroxy*-3-*methylcoumaran.*—5-Acetyl-4-hydroxy-3-methylcoumarone (3 g.), dissolved in methanol (100 ml.) was hydrogenated with hydrogen and a palladium–charcoal catalyst (from 1·5 g. of charcoal and 10 ml. of 2% aqueous palladium chloride) during 4 hours and the product purified by distillation, giving 5-*acetyl*-4-*hydroxy*-3-*methylcoumaran* (2·9 g.) as a pale yellow oil, m. p. approx. 20°, b. p. 160°/0·5 mm. (Found : C, 68·6; H, 6·5. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%). The 2 : 4-*dinitrophenylhydrazone* separated from dioxan–ethanol in scarlet, elongated, rectangular prisms, m. p. 268—269° (Found : N, 16·0. $C_{17}H_{16}O_6N_4$ requires N, 15·1%).

2 : 4′-*Dimethylfurano*(2′ : 3′-7 : 8)*chromone* (X).—Prepared in the usual manner from 5-acetyl-4-hydroxy-3-methylcoumarone with ethyl acetate and sodium, 5-*acetoacetyl*-4-*hydroxy*-3-*methylcoumarone* separated from light petroleum (b. p. 60—80°) in yellow rosettes of needles, m. p. 83° (Found : C, 67·5; H, 5·5. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%), and on cyclisation

with boiling acetic acid containing 1% of hydrochloric acid for 20 minutes gave 2 : 4′-dimethylfurano(2′ : 3′-7 : 8)chromone which separated from aqueous alcohol in pale fawn, elongated prisms, m. p. 198° (Found : C, 72·6; H, 5·0. Calc. for $C_{13}H_{10}O_3$ : C, 72·9; H, 4·7%) (cf. Kelkar and Limaye, *Rasayanam*, 1941, **1**, 228). The *piperonylidene* derivative formed compact groups of yellow needles, m. p. 242°, from acetic acid (Found : C, 72·6; H, 4·3. $C_{21}H_{14}O_5$ requires C, 72·8; H, 4·1%).

The condensation of 5-acetyl-4-hydroxy-3-methylcoumarone with ethyl formate under the usual conditions gave a 70% yield of 5-formylacetyl-4-hydroxy-3-methylcoumarone which could not be satisfactorily purified, but which in boiling acetic acid containing 1% of hydrochloric acid cyclised to give *4′-methylfurano*(*2′* : *3′-7* : *8*)*chromone*. This compound formed rosettes of almost colourless prisms, m. p. 140°, from dilute alcohol (Found : C, 72·1; H, 4·0. $C_{12}H_8O_3$ requires C, 72·0; H, 4·0%).

*Ethyl* 2 : *4-Diacetyl-5-hydroxyphenoxyphenoxyacetate* (XIV).—A mixture of 4 : 6-diacetyl resorcinol (2 g.), ethyl bromoacetate (1·8 g.), acetone (30 ml.), and potassium carbonate (3 g.) was heated under reflux for 2 hours. On isolation the crude product was fractionally crystallised from ethanol and then methanol, giving *ethyl* 2 : *4-diacetyl-5-hydroxyphenoxyacetate* (XIV) (1·2 g.) in pale yellow plates, m. p. 134°, which had a red-brown ferric reaction in alcohol (Found : C, 59·7; H, 5·9. $C_{14}H_{16}O_6$ requires C, 60·0; H, 5·7%). 5-Acetyl-2 : 4-biscarbethoxymethoxyacetophenone (0·4 g.), m. p. 130° (Algar, Barry, and Twomey, *Proc. Roy. Irish Acad.*, 1932, **41**, *B*, 8) was obtained from the mother-liquors.

Prepared by the pyridine–acetic anhydride method, the *acetate* of (XIV) separated from light petroleum (b. p. 60—80°) in colourless plates, m. p. 93°, having a negative ferric reaction (Found : C, 59·1; H, 5·8. $C_{16}H_{18}O_7$ requires C, 59·6; H, 5·6%).

*5-Acetyl-6-hydroxy-3-methylcoumarone* (XV).—Hydrolysis of the ester (XIV) (5 g.) with 2N-sodium hydroxide (30 ml.) on the steam-bath for 15 minutes yielded 4 : *6-diacetyl-3-hydroxyphenoxyacetic acid* which separated from aqueous dioxan in small, colourless needles, m. p. 255° (decomp.), having a red ferric reaction (Found : C, 57·3; H, 4·9. $C_{12}H_{12}O_6$ requires C, 57·2; H, 4·8%). The *acetate* formed small, colourless needles, m. p. 275° (decomp.), from aqueous dioxan, and had a negative ferric reaction (Found : C, 57·3; H, 4·9. $C_{14}H_{14}O_7$ requires C, 57·1; H, 4·8%).

A mixture of 2 : 4-diacetyl-5-hydroxyphenoxyacetic acid (2 g.), sodium acetate (5 g.), and acetic anhydride (20 ml.) was heated under reflux for 2 hours and treated with water (100 ml.). Two days later the black crystalline precipitate was dried and extracted with hot light petroleum (b. p. 60—80°), giving *6-acetoxy-5-acetyl-3-methylcoumarone* (1·7 g.) which separated from the concentrated extracts in colourless, squat needles, m. p. 108°, insoluble in 2N-sodium hydroxide and having a negative ferric reaction in alcohol (Found : C, 67·1; H, 5·4. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%). The 2 : *4-dinitrophenylhydrazone* separated from methyl acetate in orange needles, m. p. 221° (Found : N, 13·4. $C_{19}H_{16}O_7N_4$ requires N, 13·6%).

Deacetylation of this acetate (2·3 g.) with 2N-sodium hydroxide (15 ml.) on the steam-bath for 30 minutes furnished *5-acetyl-6-hydroxy-3-methylcoumarone* (XV) (1·7 g.) which crystallised from aqueous alcohol (charcoal) in pale yellow needles, m. p. 132°, having a deep green ferric reaction in alcohol (Found : C, 69·5; H, 5·5. $C_{11}H_{10}O_3$ requires C, 69·4; H, 5·3%). With sulphuric acid it formed a red solution changing to purple. The 2 : *4-dinitrophenylhydrazone* separated from dioxan in red, rectangular prisms, m. p. 285° (decomp.) (Found : N, 15·1. $C_{17}H_{14}O_6N_4$ requires N, 15·1%).

*5-Acetyl-6-hydroxy-3-methylcoumaran* (XVIII).—(*a*) The hydrogenation of 5-acetyl-6-hydroxy-3-methylcoumarone (4 g.), dissolved in methanol (300 ml.), with hydrogen and a palladium–charcoal catalyst (from 2 g. of charcoal and 15 ml. of 2% palladium chloride solution) was complete in 20 minutes. An ethereal solution of the residue left on evaporation of the filtered reaction mixture was washed, dried, and evaporated, leaving a product which, on purification from light petroleum (b. p. 60—80°), gave *5-acetyl-6-hydroxy-3-methylcoumaran* (3·8 g.) in rosettes of almost colourless needles, m. p. 86°, having a red-brown ferric reaction in alcohol (Found : C, 68·9; H, 6·4. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%). The wine-red solution of the coumaran in warm concentrated sulphuric acid had a purple fluorescence. The *acetate* separated from light petroleum (b. p. 60—80°) in colourless needles, m. p. 100° (Found : C, 66·3; H, 6·3. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%), and the 2 : *4-dinitrophenylhydrazone* from dioxan in red needles, m. p. 300° (decomp.) (Found : N, 15·5. $C_{17}H_{16}O_6N_4$ requires N, 15·1%).

(*b*) A stream of boron trifluoride was led into a solution of 6-hydroxy-3-methylcoumaran (2·2 g.) (Foster and Robertson, *J.*, 1948, 2254) in a mixture of acetic acid (8 ml.) and acetic anhydride (20 ml.) on the steam-bath for 15 minutes; yellow crystals of the boron complex began to separate. The mixture was then heated for 30 minutes, cooled, treated successively with alcohol (30 ml.), water (50 ml.), and 2N-sodium hydroxide (10 ml.), and then heated on the steam-bath until the precipitate dissolved. On being cooled the hydrolysate deposited 5-acetyl-6-hydroxy-3-methylcoumaran in colourless needles, m. p. 86°, identical with that prepared by method (*a*).

*4′-Methylfurano*(3′ : 2′-6 : 7)*chromone* (XVI; R = H).—Condensation of 5-acetyl-6-hydroxy-3-methylcoumarone with ethyl formate by means of sodium gave a good yield of the formyl derivative and on cyclisation with boiling alcohol containing a little concentrated hydrochloric acid during 5 minutes this product furnished *4′-methylfurano*(3′ : 2′-6 : 7)*chromone*, forming pale yellow needles, m. p. 136°, from dilute alcohol (Found : C, 72·1; H, 4·2. $C_{12}H_8O_3$ requires C, 72·0; H, 4·0%).

2 : *4′-Dimethylfurano*(3′ : 2′-6 : 7)*chromone* (XVI; R = Me).—After the initial reaction between 5-acetyl-6-hydroxy-3-methylcoumarone (2 g.), ethyl acetate (20 ml.) at 0°, and powdered sodium (2 g.) had subsided, the mixture was heated under reflux for 5 hours, cooled, treated with a little alcohol followed by ice-water (100 ml.), and acidified with dilute acetic acid. Next day the precipitate was collected, dried, and purified from ethyl acetate–light petroleum (b. p. 60—80°), giving 5-*acetoacetyl*-6-*hydroxy*-3-*methylcoumarone* (2 g.) in colourless prisms, m. p. 143—145°, which had a red ferric reaction in alcohol (Found : C, 67·4; H, 5·3. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%). Cyclisation of this diketone in the usual manner gave an almost quantitative yield of the 2 : *4′-dimethylfurano*(3′ : 2′-6 : 7)*chromone* which separated from ethyl acetate–light petroleum (b. p. 60—80°) in colourless needles, m. p. 158° (Found : C, 73·0; H, 4·8. $C_{13}H_{10}O_3$ requires C, 72·9; H, 4·7%). The *piperonylidene* derivative formed pale yellow needles, m. p. 239°, from dilute alcohol (Found : C, 62·6; H, 4·4. $C_{21}H_{14}O_5$ requires C, 72·8; H, 4·1%).

4′ : *5′-Dihydro*-2 : *4′-dimethylfurano*(3′ : 2′-6 : 7)*chromone* (XVII).—Prepared in good yield from 5-acetyl-6-hydroxy-3-methylcoumaran, ethyl acetate, and sodium by the method employed for 5-acetoacetyl-6-hydroxy-3-methylcoumarone. 5-*acetoacetyl*-6-*hydroxy*-3-*methylcoumaran* separated from ethyl acetate–light petroleum (b. p. 60—80°) in almost colourless rectangular prisms, m. p. 106·5°, having an olive-green ferric reaction in alcohol (Found : C, 66·4; H, 5·9. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%). On cyclisation this diketone gave an almost quantitative yield of 4′ : *5′-dihydro*-2 : *4′-dimethylfurano*(3′ : 2′-6 : 7)*chromone* which separated from light petroleum (b. p. 60—80°) in colourless prisms, m. p. 131° (Found : C, 72·1; H, 5·5. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%). The *piperonylidene* derivative formed pale yellow needles, m. p. 188°, from alcohol (Found : C, 72·5; H, 4·6. $C_{21}H_{16}O_5$ requires C, 72·4; H, 4·6%).

4-*Hydroxy*-5 : 8-*dimethoxyfurano*(3′ : 2′-6 : 7)*coumarin* (XXI).—A solution of kellinone (3 g.) in ethyl carbonate (25 ml.) was mixed with powdered sodium (3 g.) at 0° and after the initial reaction had subsided the mixture was heated on the steam-bath for ½ hour. The excess of sodium was destroyed with a little alcohol, the reaction mixture was diluted with ether (50 ml.), and a solution of the precipitate in water was acidified with acetic acid. 24 Hours later the crystalline product was collected and purified from dilute alcohol, giving *ω-carbethoxykellinone* (3·2 g.) in small, yellow, elongated prisms, m. p. 71—72° (Found : C, 58·2; H, 5·4. $C_{15}H_{16}O_7$ requires C, 58·4; H, 5·2%). This compound is insoluble in sodium hydrogen carbonate solution and gives a green ferric reaction in alcohol.

A mixture of this β-keto-ester (2 g.), acetic acid (8 ml.), and concentrated hydrochloric acid (8 ml.) was heated on the steam-bath for 10 minutes and the resulting dark solution was poured into water (100 ml.), thus precipitating 4-*hydroxy*-5 : 8-*dimethoxyfurano*(3′ : 2′-6 : 7)*coumarin* (1·5 g.) which formed pale fawn rectangular prisms, m. p. 200—201°, from dilute acetic acid, readily soluble in 2N-sodium hydrogen carbonate (Found : C, 59·5; H, 3·7. $C_{13}H_{10}O_6$ requires C, 59·5; H, 3·8%).

4′ : 5′-*Dihydro*-4-*hydroxy*-5 : 8-*dimethoxyfurano*(3′ : 2′-6 : 7)*coumarin* (XXII).—Prepared from dihydrokellinone in the foregoing manner, *ω-carbethoxydihydrokellinone* crystallised from aqueous alcohol in yellow, rectangular prisms, m. p. 100—101°, insoluble in 2N-sodium hydrogen carbonate and giving a violet ferric reaction in alcohol (Found : C, 58·0; H, 6·0. $C_{15}H_{18}O_7$ requires C, 58·1; H, 5·8%). Cyclisation of this ester gave 4′ : 5′-*dihydro*-4-*hydroxy*-5 : 8-*dimethoxyfurano*(3′ : 2′-6 : 7)*coumarin* which separated from aqueous acetic acid in colourless, elongated rectangular plates, m. p. 186—187°, readily soluble in 2N-sodium hydrogen carbonate (Found: C, 59·3; H, 4·8. $C_{13}H_{12}O_6$ requires C, 59·1; H, 4·6%). Prepared by diazomethane in chloroform–ether the *methyl ether* separated from aqueous methanol in colourless prisms, m. p. 167—168° (Found : C, 60·4; H, 5·1. $C_{14}H_{14}O_6$ requires C, 60·4; H, 5·1%).

4-*Hydroxy*-4'-*methylfurano*(2' : 3'-7 : 8)*coumarin* (XIX).—Condensation of 5-acetyl-4-hydroxy-3-methylcoumarone and ethyl carbonate with sodium furnished a high yield of 4-*hydroxy*-4'-*methylfurano*(2' : 3'-7 : 8)*coumarin* which separated from aqueous alcohol in very pale yellow, small, irregular prisms, m. p. 256—259° (Found : C, 66·8; H, 3·9. $C_{12}H_8O_4$ requires C, 66·7; H, 3·7%). The *methyl ether* formed pale yellow prisms, m. p. 167—170°, from dilute methanol (Found : C, 68·0; H, 4·8. $C_{13}H_{10}O_4$ requires C, 67·8; H, 4·4%).

The authors thank Messrs. Smith, Kline, and French for a grant in aid of this investigation and Mr. N. B. Dean, B.Sc., of this Department, for the preparation of the phloroglucinol monomethyl ether used in the synthesis of *allo*visnagin.

UNIVERSITY OF LIVERPOOL.

[*Received, July* 29*th*, 1952.]