## 626. *Furanochromones. Part IV. Synthesis of 2-Methylfurano-(3′ : 2′-6 : 7)chromone and Derivatives thereof.**

By J. S. H. Davies, P. A. McCrea, W. L. Norris, and G. R. Ramage.

5-Acetyl-6-hydroxycoumaran (IV) has been obtained from 6-hydroxycoumaran (III; R = H) by means of acetonitrile or acetyl chloride, and by rearrangement of 6-acetoxycoumaran; on dehydrogenation it gave the coumarone (VI). By extension of the acetyl side-chain to the aldehydo-ketone, β-diketone, or diketo-ester grouping, followed by completion of the γ-pyrone ring, 2-methylfurano(3′ : 2′-6 : 7)chromone (VIII) and the 4′ : 5′-dihydro-compounds (VII; R = H, Me, Et, Pr$^n$, and $CO_2Et$) have been prepared.

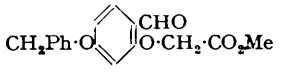
Preparation of kellin, visnagin, and other methoxyfuranochromones or their 4′ : 5′-dihydro-derivatives has been described in Parts I, II, and III of this series (*J.*, 1949, S30; 1950, 3195, 3202). The present communication deals with the preparation of furanochromones unsubstituted in positions 5 and 8. Preliminary attempts to introduce the acetyl group into the coumarone derivatives (II; R = H or benzyl) by the Hoesch or Friedel–Crafts reactions did not appear promising, and in the attempted Fries rearrangement with aluminium chloride and nitrobenzene the acetate (II; R = Ac) gave the hydroxy-ester (II; R = H). However, 6-hydroxycoumaran (III; R = H) readily gave the 5-acetyl derivative (IV) by any of the above methods, and the latter was then dehydrogenated to the required coumarone (VI). The preparation of 6-hydroxycoumaran from 6-hydroxycoumaran-3-one by successive oximation, reduction, and

* Patents pending.

de-amination to 6-hydroxycoumarone, and catalytic reduction of the latter has already been described (Sonn and Patschke, *Ber.*, 1925, **58**, 96; Späth, Manjunath, Pailer, and Jois, *Ber.*, 1936, **69**, 1087). Recently, in a communication which appeared after the relevant part of our work had been completed, Foster, Robertson, and Bushra (*J.*, 1948, 2254) described its preparation from 4-benzyloxy-2-hydroxybenzaldehyde along lines similar to those now described. Methyl 6-hydroxycoumarone-2-carboxylate (II; R = H) has previously been prepared by Reichstein, Oppenauer, Grüssner, Hirt, Rhyner, and Glatthaar (*Helv. Chim. Acta*, 1935, **18**, 816). Their method for preparing 4-benzyloxy-2-hydroxybenzaldehyde has been improved by treating resorcylaldehyde with benzyl bromide or iodide (from benzyl chloride and sodium iodide) in acetone in presence of potassium carbonate. The procedure of Reichstein for the remaining stages of the preparation of (II; R = H) was replaced by a modification of the method of Robertson and his co-workers (*J.*, 1938, 306), whereby 4-benzyloxy-2-hydroxybenzaldehyde was treated with methyl bromoacetate to give methyl 5-benzyloxy-2-formylphenoxyacetate (I). For cyclising this product to methyl 6-benzyloxycoumarone-2-carboxylate (II; R = $C_7H_7$), magnesium methoxide proved more effective than sodium methoxide and furnished the cyclised ester in 77% yield whereas with sodium methoxide the yield was 44%, the product being accompanied by 5-benzyloxy-2-formylphenoxyacetic acid and 6-benzyloxycoumarone-2-carboxylic acid. Catalytic hydrogenolysis of methyl 6-benzyloxycoumarone-2-carboxylate yielded methyl 6-hydroxycoumarone-2-carboxylate, which with acetyl chloride gave the *O*-acetate. 5-Benzyloxy-2-formylphenoxyacetic acid was cyclised and decarboxylated by heating it with acetic anhydride and sodium acetate. The resulting 6-benzyloxycoumarone was catalytically reduced in methanol solution: with an active palladium catalyst, two moles of hydrogen were absorbed to give 6-hydroxycoumaran (III; R = H); larger-scale reductions proceeded at atmospheric pressure with more difficulty, and 6-benzyloxycoumaran (III; R = $C_7H_7$) was obtained, indicating preferential reduction of the furan ring.

6-Hydroxycoumaran, however, is more conveniently prepared by the catalytic reduction of 6-hydroxycoumaran-3-one with Raney nickel at ordinary pressure and temperature or, on a larger scale, at 70° and 10 atms., but better still, as its acetate, by the catalytic reduction of 3 : 6-diacetoxycoumarone (see below). Some success in reducing the coumaranone was achieved by the modified Wolff–Kishner procedure of Huang-Minlon (*J. Amer. Chem. Soc.*, 1946, **68**, 2487), but Clemmensen reduction and Raney alloy in alkaline solution (Papa, Schwenk, and Whitman, *J. Org. Chem.*, 1942, **7**, 587) gave only resins.

Two methods have been employed for preparing 6-hydroxycoumaran-3-one; first, the Hoesch reaction with resorcinol and chloroacetonitrile as described by Sonn (*Ber.*, 1917, **50**, 1262; cf. Horning and Reisner, *J. Amer. Chem. Soc.*, 1948 **70**, 3619) which, on a 0·4-molar scale, gave a yield of about 70%; and secondly, the Friedel–Crafts reaction in nitrobenzene using the more readily available chloroacetyl chloride, which gave about 83% yield (cf. Arima and Okamoto, *Chem. Abstr.*, 1932, **26**, 139).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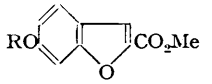
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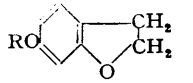
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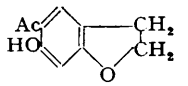
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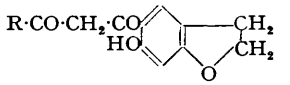
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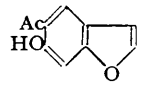
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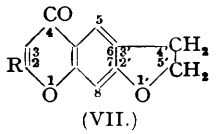
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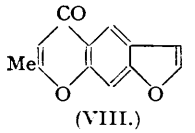
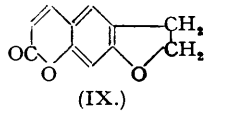

(VIII.)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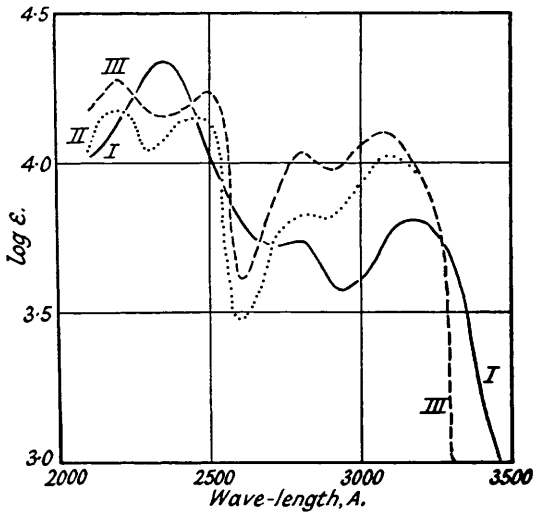
There is some confusion in the literature concerning the acetylation of 6-hydroxycoumaran-3-one; thus Sonn (*Ber.* 1917, **50**, 1262) has described the preparation of two products by the action of acetic anhydride; one m. p. 157—159°, was formulated as 3 : 6-diacetoxycoumarone, the other, m. p. 79°, as 6-acetoxycoumaran-3-one. The latter product, m. p. 77—78°, has also been prepared by the action of acetyl chloride on 6-hydroxycoumaran-3-one in ethyl acetate by Horning and Reisner (*loc. cit.*), who accepted Sonn's formulation.

In a re-examination of the acetylation process under varied conditions, only one product that having m. p. 81°, could be isolated when using Sonn's procedure. In the presence of a drop of sulphuric acid, however, both 6-hydroxycoumaran-3-one and the compound, m. p. 81°, gave a product, m. p. 165°, which is assumed to be identical with Sonn's product, m. p. 157—159°. On the other hand, when dissolved in aqueous sodium hydroxide, 6-hydroxycoumaran-3-one with acetic anhydride gave a product, m. p. 126°.

On the basis of analytical data and the volume of hydrogen absorbed on catalytic hydrogenation, the product, m. p. 81°, is regarded as 3 : 6-diacetoxycoumarone; that, m. p. 126°, as 6-acetoxycoumaran-3-one, both of which on hydrogenation yield 6-acetoxycoumaran whilst the product, m. p. 165°, gave a 2 : 4-dinitrophenylhydrazone consistent with its formulation as a diacetoxyacetylcoumarone. The compound, m. p. 165°, is, therefore, regarded as 3 : 6-diacetoxy-2-acetylcoumarone, in view of the known reactivity of position 2 in the coumarone ring. It is to be noted that the analogous 5-ethyl-6-hydroxycoumaran-3-one gave 3 : 6-diacetoxy-5-ethylcoumarone with acetyl chloride in ethyl acetate.

*Absorption spectra of furanochromones.*




*I.* (————) 2-*Methylfurano*(3′ : 2′-6 : 7)*chromone* (VIII).
*II.* (.....) 4′ : 5′-*Dihydrofurano*(3′ : 2′-6 : 7)*chromone* (VII; R = H).
*III.* (------) 4′ : 5′-*Dihydro*-2-*methylfurano*(3′ : 2′-6 : 7)*chromone* (VII; R = Me).

With acetyl chloride and aluminium chloride in carbon tetrachloride, 6-hydroxycoumaran gave a mixture of products, from which 5-acetyl-6-hydroxycoumaran (IV) was obtained in low yield; on the other hand, with acetonitrile in the Hoesch reaction, the yield was 76%, but a higher yield (90—96%) was obtained when 6-acetoxycoumaran was submitted to the Fries rearrangement using a boron trifluoride–acetic acid complex as catalyst, the yield falling to 68% when aluminium chloride in nitrobenzene was used. The orientation of the acetyl group was based on analogy with the product of formylation of 6-hydroxycoumaran by the modified Gattermann reaction with zinc cyanide; this product must be 5-formyl-6-hydroxycoumaran, since when heated with acetic anhydride and sodium acetate, with iodine as catalyst, it gave dihydropsoralene, identical with the product obtained by the Pechmann reaction as employed by Späth, Manjunath, Pailer, and Jois (*loc. cit.*). That the acetyl group was also in the 5-position was confirmed by the identity of the ethyl-6-hydroxycoumaran, prepared by Clemmensen reduction, and with 5-ethyl-6-hydroxycoumaran obtained from 4-ethylresorcinol *via* 5-ethyl-6-hydroxycoumaran-3-one.

5-Acetyl-6-hydroxycoumaran was condensed with ethyl formate, ethyl acetate, ethyl propionate, ethyl butyrate, and ethyl oxalate in presence of powdered sodium or sodium methoxide to give the corresponding aldehydo-ketone, β-diketone, or diketo-ester (V; R = H, Me, Et, $Pr^n$, and $CO_2Et$). Cyclisation to (VII) could be brought about with ethanolic hydrochloric acid or ethanolic sulphuric acid, but in some cases a pink product was obtained from which the colour was not easily removed, and acetic acid containing hydrochloric acid (cf. Heilbron, Hey, and Lowe, *J.*, 1934, 1311) was more satisfactory.

By subliming 4′ : 5′-dihydro-2-methylfurano(3′ : 2′-6 : 7)chromone (VII; R = Me) twice in a vacuum through a column of supported palladium–norite (30%), it was dehydrogenated to 2-methylfurano(3′ : 2′-6 : 7)chromone (VIII). In a similar manner with palladium–charcoal (10%), 5-acetyl-6-hydroxycoumaran, which was more readily dehydrogenated, gave 5-acetyl-6-hydroxycoumarone (VI). This with ethyl acetate and sodium formed 6-hydroxy-5-β-keto-butyrylcoumarone, which on cyclisation gave the above 2-methylfuranochromone.

The ultra-violet absorption curves of 2-methylfurano(3′ : 2′-6 : 7)chromone (VIII), its 4′ : 5′-dihydro-derivative (VII; R = Me), and 4′ : 5′-dihydrofurano(3′ : 2′-6 : 7)chromone (VII; R = H) are annexed. Dr. F. B. Strauss has supplied the following comments on the curves given here and in Parts II and III.

" The unsubstituted 4′ : 5′-dihydrofurano(3′ : 2′-6 : 7)chromone has an absorption maximum at 3100 A. and another band of lower intensity near 2800 A. The introduction of the 2-methyl group causes a slight shift of the main band towards shorter wave-length. With introduction of methoxy-groups into the benzene ring, this main band becomes broader or merges with the smaller band, the maximum varying between 2970 and 3050 A. Such a simplification of the spectrum is peculiar to the effect of substitution by hydroxy- or alkoxy-groups on the more resolved spectra of benzenoid systems.

" In the angular structures, 4′ : 5′-dihydro-7-methoxy-2-methylfurano(2′ : 3′-5 : 6)chromone and 4′ : 5′-dihydro-5-methoxy-2-methylfurano(2′ : 3′-7 : 8)chromone, the intensity of the 3100-A. band is reduced relative to the 2800-A. band in the former and increased in the latter.

" The replacement of the dihydrofuran ring by the furan ring as in 5 : 8-dimethoxy-2-methylfurano(3′ : 2′-6 : 7)chromone (kellin), 8-methoxy-2-methylfurano(3′ : 2′-6 : 7)chromone, and 2-methylfurano(3′ : 2′-6 : 7)chromone causes displacement of the 3100-A. band of the 4′ : 5′-dihydro-isomers towards longer wave-lengths by 100 to 300 A., which conforms to the known effect of the addition of one conjugated linkage to a conjugated system. In the present case, the magnitude of this effect depends on the number of substituents in the original dihydro-compound; it amounts to 100 A. for the unmethoxylated compounds [cf. 2-methylfurano(3′ : 2′-6 : 7)chromone and its 4′ : 5′-dihydro-derivative], to 140 A. for the monomethoxy-compounds [cf. 8-methoxy-2-methyfurano(3′ : 2′-6 : 7)chromone and its 4′ : 5′-dihydro-derivative] and to 350 A. for the 5 : 8-dimethoxy-compounds."

## Experimental.

(Carbon and hydrogen analyses and ultra-violet absorption curves are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.)

*4-Benzyloxy-2-hydroxybenzaldehyde.*—Anhydrous sodium iodide (36 g.) was dissolved in acetone (150 c.c.), benzyl chloride (28 g.) added, and the solvent gently refluxed for 30 minutes. The precipitated sodium chloride was filtered off, and the filtrate slowly added to a stirred, ice-cooled mixture of resorcylaldehyde (27·6 g.), anhydrous potassium carbonate (40 g.), and acetone (50 c.c.). After 3 hours, the stirred mixture was heated under a reflux for 4 hours before distilling off the solvent. Water and an excess of dilute hydrochloric acid were added, and the product extracted with ether. Most of the ether was removed before adding aqueous sodium hydroxide (200 c.c.; 2N.), the resulting sodium salt was filtered off, washed with water and ether, and decomposed with dilute hydrochloric acid, and the product extracted with ether. Fractionation of the residue after removal of the solvent gave 4-benzyloxy-2-hydroxybenzaldehyde (23 g., 50%) as an oil, b. p. 165—175°/1 mm., which immediately solidified; after this fraction the temperature rose rapidly above 200°.

The method was equally satisfactory with benzyl bromide, and purification through the sodium salt was not essential for the following preparation.

*Methyl 5-Benzyloxy-2-formylphenoxyacetate* (I).—A mixture of 4-benzyloxy-2-hydroxybenzaldehyde (30 g.), anhydrous potassium carbonate (30 g.), and acetone (300 c.c.) was stirred during the addition of methyl bromoacetate (20 g.) before being heated under a reflux for 1 hour. Most of the acetone was distilled off, excess of water added, and the product filtered off, washed with water, dried, and crystallised from methanol or benzene. *Methyl 5-benzyloxy-2-formylphenoxyacetate* (31 g., 78%) was obtained as pale yellow needles, m. p. 128° (Found: C, 68·1; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%).

*5-Benzyloxy-2-formylphenoxyacetic Acid.*—The above methyl ester (5 g.) in aqueous sodium hydroxide (100 c.c.; 2N.) was boiled under a reflux for 30 minutes. On cooling, a highly crystalline sodium salt separated, which was filtered off and acidified with aqueous hydrochloric acid. 5-Benzyloxy-2-formylphenoxyacetic acid (3·5 g., 73%) crystallised from aqueous ethanol in prisms, m. p. 147—148° (Found: C, 66·8; H, 4·9. Calc. for $C_{16}H_{14}O_5$: C, 67·1; H, 4·9%).

On a larger scale, hydrolysis was carried out in aqueous methanol or ethanol, but, with increasing alcohol concentration, hydrolysis was accompanied by cyclodehydration.

*Methyl 6-Benzyloxycoumarone-2-carboxylate* (II; R = $C_7H_7$).—(*a*) Methyl 5-benzyloxy-2-formylphenoxyacetate (10 g.) was added to sodium methoxide (from 0·8 g. of sodium and 100 c.c. of anhydrous methanol) and rapidly passed into solution on boiling under reflux. After 10 minutes' heating, the solution was cooled and *methyl 6-benzyloxycoumarone-2-carboxylate* (4·1 g., 44%) crystallised readily.

Recrystallised from methanol, the ester had m. p. 112° (Found: C, 72·2; H, 5·0. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%).

(*b*) Magnesium (5 g.) was caused to react with dry methanol (150 c.c.), methyl 5-benzyloxy-2-formylphenoxyacetate (10 g.) added, and the mixture heated on the water-bath under reflux for 2 hours. After being cooled and diluted with ether, the solution was poured into excess of aqueous hydrochloric acid (2N.). The ethereal extract was shaken with aqueous sodium hydrogen carbonate and dried and the solvent distilled off. The residue on crystallisation from methanol gave the ester (7·2 g., 77%) identical with the above.

The large excess of magnesium was necessary for maintaining the yield.

*Methyl 6-Hydroxycoumarone-2-carboxylate* (II; R = H).—Methyl 6-benzyloxycoumarone-2-carboxylate (10 g.) in methanol (150 c.c.) was shaken with hydrogen at atmospheric temperature and pressure in the presence of palladium–charcoal (5 g., 10%). Absorption proceeded smoothly to completion; the catalyst was filtered off, and the solvent distilled under reduced pressure. The residue immediately solidified, and methyl 6-hydroxycoumarone-2-carboxylate, crystallised from toluene, had m. p. 174°. The *acetyl* derivative was prepared by short refluxing with acetyl chloride, and after crystallisation from methanol had m. p. 128° (Found: C, 61·7; H, 4·3. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%).

6-*Benzyloxycoumarone*.—A mixture of 5-benzyloxy-2-formylphenoxyacetic acid (26 g.), anhydrous sodium acetate (70 g.), and acetic anhydride (250 c.c.) was gently boiled in an oil-bath under a reflux with occasional shaking for 1 hour. The cooled mixture was poured into water (500 c.c.), the product extracted with ether (or chloroform), and the extract shaken with water, followed by small additions of aqueous ammonia. The solid ammonium salt which separated was filtered off and acidified. On crystallisation from acetic acid, the product gave 6-benzyloxycoumarone-2-carboxylic acid. The last portion of ammonia gave a gummy product (discarded), and the clear ethereal extract was dried ($Na_2SO_4$). After removal of the solvent, the residue on fractionation gave 6-benzyloxycoumarone (15 g., 74%) as an oil, b. p. 150°/1 mm., which rapidly crystallised when seeded. The product was purified by crystallisation from methanol, followed by sublimation in a vacuum for analysis, and then had m. p. 36° (Found: C, 79·8; H, 5·4. Calc. for $C_{15}H_{12}O_2$: C, 80·4; H, 5·4%).

6-*Hydroxycoumaran-3-one*.—Chloroacetyl chloride (28·25 g.) was added dropwise during 1½ hours to a stirred mixture of resorcinol (22 g.), aluminium chloride (33·3 g.), and nitrobenzene (250 c.c.), the temperature being kept at 50—55° during the addition and for a further 15 minutes. The cooled solution was poured into an excess of ice and dilute hydrochloric acid and set aside overnight. The organic layer was separated and extracted with aqueous sodium hydroxide (300 c.c.; N.), and the alkaline extract acidified with concentrated hydrochloric acid to give 6-hydroxycoumaran-3-one (20·3 g.), m. p. 234—238° (decomp.). The aqueous layer gave a further quantity [4·7 g.; m. p. 238—240° (decomp.)] on ether-extraction followed by alkaline extraction of the ethereal solution and acidification, thus furnishing a total yield of 83%. A similar yield was obtained by adding the aluminium chloride in nitrobenzene to the other reactants in the same solvent. A portion, crystallised from a large volume of ethanol, formed golden yellow plates, m. p. 245° (decomp.).

*Acetyl derivative*. 6-Hydroxycoumaran-3-one (7·5 g.) was dissolved in a solution of sodium hydroxide (3·0 g.) in water (40 c.c.). Crushed ice (40 g.), then acetic anhydride (6·4 g.) were added, and the mixture was shaken vigorously for 5 minutes. The yellow precipitate formed was filtered off and washed with water. Crystallisation from ethanol gave 6-*acetoxycoumaran-3-one* (7·5 g., 78%) as pale yellow crystals, m. p. 125—126°. The crystals were sublimed at 110°/0·5 mm. for analysis (Found: C, 62·3; H, 4·1; Ac, 22·7. $C_{10}H_8O_4$ requires C, 62·5; H, 4·2; Ac, 22·4%).

3 : 6-*Diacetoxycoumarone*.—6-Hydroxycoumaran-3-one (60 g.) was suspended in acetic anhydride (150 c.c.). Pyridine (30 c.c.) was added with stirring and cooling. After 24 hours at room-temperature the mixture was stirred into water (1500 c.c.). The solid was filtered off, dried at 60° and distilled in a vacuum. The fraction boiling below 150°/0·2 mm. was collected and crystallised from aqueous methanol (220 c.c., 75%) yielding 3 : 6-*diacetoxycoumarone* (70 g., 75%), m. p. 81° (Found: C, 61·6; H, 4·6; Ac, 37·0. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3; Ac, 36·8%).

3 : 6-*Diacetoxy-2-acetylcoumarone*.—6-Hydroxycoumaran-3-one (10 g.) was boiled for 1 hour under a reflux with acetic anhydride (50 c.c.) containing 1 drop of concentrated sulphuric acid. The dark brown solution was cooled, and water (250 c.c.) added to decompose the excess of acetic anhydride. The black crystalline solid obtained was collected, washed, dried, and then sublimed at 150°/0·2 mm. The sublimate crystallised from ethyl acetate to give 3 : 6-*diacetoxy-2-acetylcoumarone* as colourless prisms (7·5 g., 41%), m. p. 165° [Found: C, 60·8; H, 4·4; Ac, 46·9 (alkaline hydrolysis). $C_{14}H_{12}O_6$ requires C, 60·9; H, 4·35; Ac, 46·75%]. Acid hydrolysis (Freudenberg) gave variable results for Ac.

The 2 : 4-*dinitrophenylhydrazone*, m. p. 213° (decomp.), was prepared in glacial acetic acid (Found: C, 52·7; H, 3·6; N, 11·8. $C_{20}H_{16}O_9N_4$ requires C, 52·7; H, 3·5; N, 12·3%).

6-*Hydroxycoumaran* (III; R = H).—(*a*) 6-Benzyloxycoumarone (5 g.) in methanol (50 c.c.) containing palladium–charcoal (4 g.; 10%) was shaken in hydrogen at room temperature and pressure. One mol. proportion of hydrogen was steadily absorbed, thereafter absorption proceeded slowly. After removal of the catalyst, 6-*benzyloxycoumaran* (III; R = $C_7H_7$), m. p. 59°, crystallised from the methanol on cooling (Found: C, 79·3; H, 6·2. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%). The reduction was completed by shaking the methanol solution with hydrogen and more freshly prepared catalyst (5 g.; 10%). After filtration, removal of the methanol by distillation and fractionation of the residue, 6-hydroxycoumaran distilled as a viscous oil, b. p. 128°/2 mm., which readily crystallised on cooling and then had m. p. 55°. It was not necessary to purify the product further by crystallisation since it gave good yields in the Hoesch and the Gattermann reaction. Späth and his co-workers (*loc. cit.*) describe crystallisation from ether–light petroleum, and the product as having m. p. 61°.

Further preparations were carried out at 40° with an initial hydrogen pressure of 8 atms., and the reduction proceeded to completion without difficulty.

(*b*) A mixture of 6-hydroxycoumaran-3-one (110 g.), methanol (500 c.c.), and freshly prepared Raney nickel catalyst (about 75 c.c.) was stirred in a hydrogen atmosphere at 70° and an initial pressure of 10 atms. After about 15 hours, the absorption reached the equivalent of 2 molecules and was still proceeding relatively slowly. The catalyst was filtered off, the methanol distilled from the filtrate, and the residue immediately fractionated, giving crude 6-hydroxycoumaran (85 g.), b. p. 120—145°/2 mm., which did not crystallise except on long storage. Purification was effected through the sodium salt (with 400 c.c. of 2N-sodium hydroxide), the alkaline solution extracted with ether, and then acidified and again extracted with ether. Fractional distillation gave 6-hydroxycoumaran (70 g., 70%), b. p. 128°/2 mm., which at once crystallised completely when seeded.

(*c*) 6-Hydroxycoumaran-3-one (15 g.) was suspended in ethanol (75 c.c.). Hydrazine hydrate (10 c.c.; 90%) was added, and the mixture boiled under a reflux for 1 hour. At first a clear solution was formed, and then a crystalline precipitate separated. The mixture was evaporated to dryness in a vacuum, and a solution of potassium hydroxide (15 g.) in diethylene glycol (100 c.c.) was added to the residue. The mixture was distilled with stirring until the internal temperature reached 185—190°. This temperature was maintained until no more nitrogen was evolved (about 1½ hours). After cooling, the reaction mixture was poured into dilute hydrochloric acid (*ca.* 400 c.c.) containing sufficient acid to make the final mixture acid to Congo-red paper. The mixture was extracted with ether, and the ether extract dried ($Na_2SO_4$) and distilled. The fraction, b. p. 110—120°/0·75 mm. (7·5 g., 55%), was collected and consisted of relatively pure 6-hydroxycoumaran.

6-*Acetoxycoumaran.*—(a) *From* 6-*acetoxycoumaran*-3-*one*. The acetoxycoumaranone (1·92 g.) in glacial acetic acid (20 c.c.) was shaken at ordinary pressure with palladium–barium sulphate (0·5 g.; 5%; *Org. Synth.*, **26**, 77) in an atmosphere of hydrogen at 65°. Absorption of hydrogen ceased after 70 minutes when 95% of the theoretical 2 moles of hydrogen had been absorbed. After removal of the catalyst, the filtrate was evaporated in a vacuum to small bulk; the addition of water (25 c.c.) gave a crystalline precipitate of 6-acetoxycoumaran (1·6 g., 90%), m. p. 72—73°.

(b) *From* 3 : 6-*diacetoxycoumarone*. The diacetoxycoumarone (2·34 g.) in glacial acetic acid (7 c.c.) was hydrogenated as above using palladium–barium sulphate (0·3 g.; 5%). Absorption of hydrogen ceased after 90 minutes when 99% of the theoretical quantity had been absorbed. Addition of water (25 c.c.) to the filtered and evaporated solution gave 6-acetoxycoumaran as a crystalline precipitate (1·71 g., 96%), m. p. 73—74°. The products obtained by methods (a) and (b) were each identical with that obtained by acetylating 6-hydroxycoumaran.

5-*Acetyl*-6-*hydroxycoumaran* (IV).—(*a*) Hydrogen chloride was rapidly passed into a stirred, ice-cooled mixture of 6-hydroxycoumaran (70 g.), powdered fused zinc chloride (140 g.), acetonitrile (40 g.), and anhydrous ether (500 c.c.). The rate of stirring was increased as a solid product crystallised, and hydrogen chloride was slowly passed in for a further 4 hours. After being kept for 15 hours, the ether was decanted, and the solid decomposed with ice-water (200 g.). The imine hydrochloride rapidly crystallised and was filtered off, washed with a little ether, and decomposed by boiling it gently under a reflux for 1 hour with aqueous sulphuric acid (200 c.c.; 2N.). After cooling, the product was extracted with benzene, and the solvent distilled from the dried extract. The residue rapidly solidified, and crystallisation from methanol gave 5-*acetyl*-6-*hydroxycoumaran* (70 g., 76%) as fine needles, m. p. 107—108° (Found: C, 66·8; H, 5·5. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·7%).

(*b*) Aluminium chloride (5·5 g.) was added in 4 portions to 6-acetoxycoumaran (6 g.) dissolved in dry nitrobenzene (30 c.c.), the temperature rising to 45°. The reaction mixture was heated at 60° for ½ hour and poured into excess of ice and dilute hydrochloric acid. The whole was extracted with ether, and the ethereal layer was washed with dilute hydrochloric acid, then water, and extracted with dilute aqueous sodium hydroxide. Acidification of the alkaline extract with dilute sulphuric acid furnished 5-acetyl-6-hydroxycoumaran (5·2 g.), m. p. 104—105°, and one crystallisation from ethanol gave the pure product (4·1 g., 68%), m. p. and mixed m. p. 107—108°; the 2 : 4-*dinitrophenylhydrazone* formed scarlet needles (from glacial acetic acid), m. p. 293° (decomp.) (Found: C, 53·6; H, 3·9; N, 15·5. $C_{16}H_{14}O_6N_4$ requires C, 53·6; H, 3·9; N, 15·6%).

(*c*) Boron trifluoride–acetic acid complex, $BF_3,2CH_3{\cdot}CO_2H$ (28·2 g.), was added to 6-acetoxycoumaran (17·8 g.), contained in a 500-c.c. flask, and the mixture stirred and heated to 70° for 30 minutes, care being taken to exclude moisture. Dissolution was complete after about 2 minutes, and after about 5 minutes the boron trifluoride complex of 5-acetyl-6-hydroxycourmaran began to crystallise. After the 30 minutes, the mixture was cooled, aqueous sodium hydroxide (400 c.c.; 2N.) was added, and the mixture heated on the steam-bath until dissolution was complete (*ca.* 1½ hours). The cooled, alkaline solution was filtered, and the filtrate made acid to Congo-red paper with hydrochloric acid (15%). The fawn-coloured precipitate was filtered off, washed well with hot water, and dried at 80°. The yield of 5-acetyl-6-hydroxycoumaran, m. p. 106—107°, was 17·0 g. (96%).

5-*Ethyl*-6-*hydroxycoumaran*-3-*one*.—A mixture of 4-ethylresorcinol (13·5 g.), chloroacetonitrile (7·55 g.), and fused powdered zinc chloride (8 g.) in ether (100 c.c.) was cooled in ice, and hydrogen chloride passed in for 7 hours. A solid began to separate in 2 hours; the reaction mixture was set aside overnight, and ice (150 g.) added. After 1 hour's heating on a water-bath, the intermediate 5-*ethyl*-ω-*chlororesacetophenone* (20 g.) was collected. A portion, crystallised from benzene, formed cream-coloured, feathery needles, m. p. 161—161·5° (Found: Cl, 16·7. $C_{10}H_{11}O_3Cl$ requires Cl, 16·5%). The remainder (18·9 g.) was boiled for 1 hour under a reflux with sodium acetate (15 g.) and ethanol (120 c.c.). Approximately half the solvent was distilled off, and water (100 c.c.) was added to the residue to precipitate 5-*ethyl*-6-*hydroxycoumaran*-3-*one* (12·8 g.). This formed golden-yellow plates, m. p. 191—192°, from methanol (Found: C, 67·3; H, 5·9. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·7%).

3 : 6-*Diacetoxy-5-ethylcoumarone*.—A mixture of 5-ethyl-6-hydroxycoumaran-3-one (18·8 g.), acetyl chloride (32 c.c.), and dry ethyl acetate (80 c.c.) was boiled under a reflux for 3 hours. Fractionation, finally at 1 mm., gave 3 : 6-*diacetoxy-5-ethylcoumarone* (15·2 g., 55%) as a yellow oil, which rapidly solidified and crystallised from methanol as colourless prisms, m. p. 69—70° (Found : C, 64·0; H, 5·5; Ac, 31·5. $C_{14}H_{14}O_5$ requires C, 64·1; H, 5·4; Ac, 32·8%).

5-*Ethyl*-6-*hydroxycoumaran*.—(*a*) 5-Acetyl-6-hydroxycoumaran (5 g.), amalgamated zinc (20 g.), water (15 c.c.), and concentrated hydrochloric acid (15 c.c.) were boiled under reflux for 5 hours, more acid (1·5 c.c.) being added at intervals. The product (4·9 g.) was isolated by ether and crystallised from light petroleum–benzene (2 : 1 by vol.) as colourless prisms, m. p. 96·5—97·5°, undepressed on admixture with 5-ethyl-6-hydroxycoumaran described below.

(*b*) 3 : 6-Diacetoxy-5-ethylcoumarone (10 g.) in glacial acetic acid (50 c.c.) was reduced at 40—50°/1 atm. in presence of palladium–charcoal (10 g.; 10%). After the absorption of two moles of hydrogen, the filtered solution was added to water (300 c.c.) and neutralised with solid sodium hydrogen carbonate, and the product isolated with ether. 6-Acetoxy-5-ethylcoumaran (6·35 g.) was obtained as a pale yellow oil, which readily solidified and formed colourless, elongated prisms, m. p. 30°, from well-chilled ethanol. The crude acetate (2·5 g.) was boiled with a solution of sodium hydroxide (1·75 g.) in water (20 c.c.) for 20 minutes, and the solution extracted with ether and acidified. 5-*Ethyl*-6-*hydroxycoumaran* (2·1 g.) was isolated by ether as a pale yellow oil, which readily solidified, and from light petroleum–benzene (2 : 1 by vol.) formed colourless prisms, m. p. 96·5—97·5° (Found : C, 73·0; H, 7·6. $C_{10}H_{12}O_2$ requires C, 73·2; H, 7·3%).

(*c*) The hydrogenation of 5-ethyl-6-hydroxycoumaran-3-one (1·78 g.) in methanol solution in presence of Raney nickel (*ca.* 7 c.c.) was not complete after 24 hours at 40°/1 atm. However, 5-ethyl-6-hydroxycoumaran, identical with the material obtained in (*a*) and (*b*), could be separated from unchanged coumaranone by means of light petroleum–benzene (2 : 1 by vol.).

5-*Formyl*-6-*hydroxycoumaran*.—Hydrogen chloride was passed into a stirred, ice-cooled mixture of 6-hydroxycoumaran (5 g.), dry zinc cyanide (7 g.), and anhydrous ether (100 c.c.) until completely saturated. After 15 hours, the ether was decanted, and the residue decomposed by boiling it under a reflux with water (50 c.c.). After cooling, extraction with ether, and removal of the solvent, 5-formyl-6-hydroxycoumaran (5 g., 83%) was crystallised from methanol, forming needles, m. p. 108° (Found : C, 65·7; H, 4·7. Calc. for $C_9H_8O_3$ : C, 65·9; H, 4·9%).

*Dihydropsoralene* (IX).—5-Formyl-6-hydroxycoumaran (2 g.) was heated under a reflux for 5 hours with acetic anhydride (5 c.c.) and anhydrous sodium acetate (5 g.) with iodine as catalyst (cf. Yanagisawa and Kondo, *Chem. Abstr.*, 1922, **16**, 922). After treatment with water, the resulting solid was filtered off and stirred with cold aqueous sodium hydroxide (5 c.c.; N.). The resulting dihydropsoralene was filtered off and crystallised from methanol in colourless prisms, m. p. 204°, not depressed on admixture with the product prepared from 6-hydroxycoumaran by the method of Spāth and co-workers.

6-*Hydroxy*-5-*β*-*ketobutyrylcoumaran* (V; R = Me).—(*a*) 5-Acetyl-6-hydroxycoumaran (20 g.) in dry ethyl acetate (250 c.c.) was added with ice-cooling to powdered sodium (8 g.) just covered with anhydrous ether. After the initial reaction had subsided, the mixture was allowed to warm and then heated for 2 hours on the water-bath. The solvent was distilled off under reduced pressure, and ice-water (200 g.) and aqueous acetic acid (from 20 c.c. of glacial acetic acid) added with cooling and shaking. A crystalline product rapidly separated, and some light petroleum (b. p. 40—60°) was added before filtration. The solid was washed with water and a little aqueous methanol before being crystallised from ethanol (200 c.c.). 6-*Hydroxy*-5-*β*-*ketobutyrylcoumaran* (15 g., 61%) crystallised as prisms (free from needles of unchanged 5-acetyl compound) and had m. p. 143° (Found : C, 65·2; H, 5·5. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·5%).

(*b*) 5-Acetyl-6-hydroxycoumaran (5 g.) and sodium methoxide (6·0 g.) in pure dry ethyl acetate (60 c.c.) were boiled gently under a reflux for 3 hours on the water-bath with occasional shaking. The diketone (3·1 g., 50%) formed compact prisms, m. p. 143°, from alcohol. The yields were not as consistent as with sodium in route (*a*).

5-*Formylacetyl*-6-*hydroxycoumaran* (V; R = CHO), 6-*Hydroxy*-5-*β*-*ketovalerylcoumaran* (V; R = Et) *and* 6-*Hydroxy*-5-*β*-*ketohexanoylcoumaran* (V; R = Pr$^n$).—A solution of 5-acetyl-6-hydroxycoumaran (5 g.) in ethyl formate (50 c.c.) was added dropwise to powdered sodium (3 g.) covered with a little ether. A vigorous reaction ensued which was moderated by ice-cooling. After ½ hour, the solvents were distilled off in a vacuum, and ice and dilute acetic acid added carefully to the residue. The solid (5·5 g.) was filtered off and dried. Crystallised from ethanol (150 c.c.), 5-*formylacetyl*-6-*hydroxycoumaran* (4·6 g.) formed colourless prisms, m. p. 167° (Found : C, 64·3; H, 5·0. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·9%).

5-Acetyl-6-hydroxycoumaran (9 g.), sodium (4·6 g.), and ethyl propionate or ethyl *n*-butyrate (60 c.c. in each case) gave, respectively, 6-*hydroxy*-5-*β*-*ketovalerylcoumaran* (7·3 g., 62%), prisms, m. p. 123°, from methanol (Found : C, 66·9; H, 5·7. $C_{13}H_{14}O_4$ requires C, 66·7; H, 5·9%) and 6-*hydroxy*-5-*β*-*ketohexanoylcoumaran* (5·7 g., 45%), prisms, m. p. 119°, from methanol (Found : C, 68·4; H, 6·5. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5%).

4′ : 5′-*Dihydro*-2-*methylfurano*(3′ : 2′-6 : 7)*chromone* (VII; R = Me).—6-Hydroxy-5-*β*-ketobutyrylcoumaran (10 g.), glacial acetic acid (40 c.c.), and concentrated hydrochloric acid (1 c.c.) were heated gently under a reflux for 15 minutes, and the solvent then distilled off under reduced pressure. The solid residue crystallised from ethanol to give 4′ : 5′-*dihydro*-2-*methylfurano*(3′ : 2′-6 : 7)*chromone* as colourless prisms (8·3 g., 90%), m. p. 166° (Found : C, 71·2; H, 5·0. $C_{12}H_{10}O_3$ requires C, 71·3; H, 5·0%).

4′ : 5′-*Dihydrofurano*(3′ : 2′-6 : 7)*chromone* (VII; R = H), 4′ : 5′-*Dihydro*-2-*ethylfurano*(3′ : 2′-6 : 7)-*chromone* (VII; R = Et), *and* 4′ : 5′-*Dihydro*-2-n-*propylfurano*(3′ : 2′-6 : 7)*chromone* (VII; R = Pr$^n$).—5-Formylacetyl-6-hydroxycoumaran (3 g.) in glacial acetic acid (40 c.c.) containing 2 drops of

concentrated hydrochloric acid was boiled under a reflux for 10 minutes. The solution was diluted with hot water (100 c.c.), and the brown precipitate (2·2 g.), m. p. 183—185°, collected. Crystallisation from ethanol (charcoal) gave 4′ : 5′-*dihydrofurano*(3′ : 2′-6 : 7)*chromone* (1·5 g.) as colourless, prismatic needles, m. p. 184—185° (Found : C, 69·9; H, 4·5. $C_{11}H_8O_3$ requires C, 70·2; H, 4·3%). In a similar manner, 6-hydroxy-5-β-ketovalerylcoumaran (6·3 g.) gave 4′ : 5′-*dihydro*-2-*ethylfurano*(3′ : 2′-6 : 7)*chromone* (4·3 g., 74%), prisms m. p. 124—125°, from methanol (Found : C, 72·3; H, 5·6. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%), and 6-hydroxy-5-β-ketohexanoylcoumaran (5 g.) gave 4′ : 5′-*dihydro*-2-n-*propylfurano*-(3′ : 2′-6 : 7)*chromone* (2·5 g., 54%), needles, m. p. 103°, from ethanol (Found : C, 73·0; H, 6·0. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%).

5-*Acetyl*-6-*hydroxycoumarone* (VI).—5-Acetyl-6-hydroxycoumaran (2 g.) was sublimed at 100°/$10^{-4}$ mm. through a 30-cm. column of palladium catalyst (0·8 g.) on glass wool (1·5 g.) maintained at 150°, and the product collected on a cold finger. The vaporisation and dehydrogenation were accompanied by a marked increase in the pressure from about $10^{-4}$ to $10^{-3}$ mm., but after about 5 hours the original pressure became restored, and the product (1·8 g.) was then removed. Even when the sublimation was carried out slowly under most favourable conditions, the product was not readily purified by crystallisation. It was better to repeat the sublimation with fresh catalyst. 5-*Acetyl*-6-*hydroxycoumarone* crystallised from methanol in pale yellow needles, m. p. 96° (Found : C, 68·2; H, 4·8. $C_{10}H_8O_3$ requires C, 68·2; H, 4·6%).

Satisfactory results have been obtained with palladium–charcoal (10%), but palladium on norite (30%) prepared as described by Linstead and Thomas (*J.*, 1940, 1127) was the most effective catalyst employed.

6-*Hydroxy*-5-β-*ketobutyrylcoumarone*.—The above conditions for the preparation of 6-hydroxy-5-β-ketobutyrylcoumaran were followed with 5-acetyl-6-hydroxycoumarone (2·0 g.) and gave the 5-β-*ketobutyryl* compound (1·7 g., 68%), which crystallised from methanol as colourless prisms, m. p. 136—137° (Found : C, 66·0; H, 4·85. $C_{12}H_{10}O_4$ requires C, 66·0; H, 4·6%).

2-*Methylfurano*(3′ : 2′-6 : 7)*chromone* (VIII).—(*a*) 6-Hydroxy-5-β-ketobutyrylcoumarone was cyclised readily by ethanolic sulphuric acid (10% by weight) boiling gently under reflux, and the 2-*methylfuranochromone* was isolated by cooling, addition of water, and filtration; crystallisation from ethanol gave colourless needles, m. p. 186° (Found : C, 71·9; H, 4·1. $C_{12}H_8O_3$ requires C, 72·0; H, 4·0%). The acetic–hydrochloric acid procedure was equally satisfactory.

(*b*) 4′ : 5′-Dihydro-2-methylfurano(3′ : 2′-6 : 7)chromone (1 g.) was dehydrogenated by subliming it twice through palladium–norite (30%) as above. The methylfuranochromone (0·8 g.) crystallised from methanol and was identical with the product obtained by the method described in (*a*).

4′ : 5′-*Dihydrofurano*(3′ : 2′-6 : 7)*chromone*-2-*carboxylic Acid* (VII; R = $CO_2H$).—Following the general procedure adopted above, 5-acetyl-6-hydroxycoumaran was condensed with ethyl oxalate (excess) and powdered sodium in ether (the ether being carefully distilled until the reaction commenced), to give the *diketo*-ester (V; R = $CO_2Et$), m. p. 145° after crystallisation from ethanol (Found : C, 60·2; H, 5·0. $C_{14}H_{14}O_6$ requires C, 60·4; H, 5·0%). The product (2·0 g.) was boiled in a mixture of acetic acid (12 c.c.) and hydrochloric acid (2·5 c.c.) for 1½ hours, and 4′ : 5′-*dihydrofurano*(3′ : 2′-6 : 7)*chromone*-2-*carboxylic acid* (1·44 g., 86%) separated as a crystalline precipitate, which crystallised as small colourless crystals, m. p. 283° (decomp.), from a large volume of acetic acid (Found : C, 62·1; H, 3·7. $C_{12}H_8O_5$ requires C, 62·1; H, 3·45%). When the chromone-carboxylic acid was heated a little above its m. p. until effervescence ceased, it was converted into 4′ : 5′-dihydrofurano(3′ : 2′-6 : 7)-chromone, identical with the product prepared above by cyclising 5-formylacetyl-6-hydroxycoumaran.

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