## 737. iso*Shekkangenin and the Synthesis of 4-Hydroxycoumarins.*

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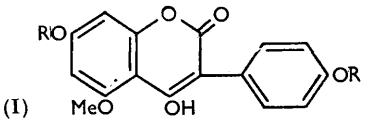
Contrary to the suggestion by Chi *et al.*[1] *iso*shekkangenin is not identical with either 4 : 5 : 4′-trihydroxy-7-methoxy- or 4 : 7 : 4′-trihydroxy-5-methoxy-3-phenylcoumarin. The substitution of methyl chloroformate and potassium carbonate for ethyl carbonate and sodium in an earlier procedure[2] provides a general method for the synthesis of 4-hydroxycoumarins, including polyhydroxy-derivatives.

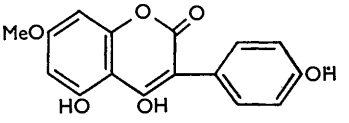
FROM the Chinese drug " shekkan " derived from *Balamacanda chinensis* (Linn) D.C. (identical with *Pardanthus chinensii* Ker Gawl[1]) Marmicke, Schumann, and Liss[3] isolated a glycoside shekkanin, which was shown by Shibata[4] to be identical with tectoridin, giving

[1] Chi, Hsu, Hu, and Wang, *J. Chinese Chem. Soc.*, 1947, **15**, 26.
[2] Boyd and Robertson, *J.*, 1948, 174.
[3] Marmick, Schumann, and Liss, *Arch. Pharm.*, 1937, **275**, 317.
[4] Shibata, *J. Pharm. Soc. Japan*, 1927, No. **543**, 380.

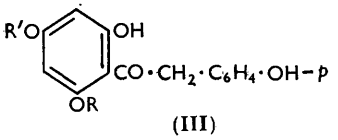
the aglucone tectorigenin. According to Chi, Hsu, Hu, and Wang [1] the variety of this drug obtained from another species of *Iridaceae, Iris wattii* Baker, contains an isomeric glycoside *iso*shekkanin $C_{22}H_{22}O_{11}$ which on hydrolysis gives a hexose and *iso*shekkangenin, $C_{15}H_9O_5$·OMe, m. p. 228°, forming a triacetate, m. p. 184—185°, and a dimethyl ether, m. p. 157°. On hydrolytic fission with 10% alcoholic potassium hydroxide *iso*shekkangenin gave phloroglucinol monomethyl ether and *p*-hydroxyphenylacetic acid. From this the Chinese authors [1] suggested that the aglycone had structure (I; R = H) or a tautomer of it, but did not propose the alternative (II) equally possible on their experimental findings.



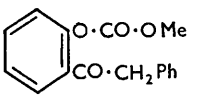

(I)



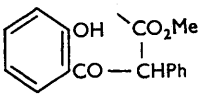

(II)




(III)




(IV)




(V)

The synthesis of the dimethyl ether (I; R = Me), m. p. 243—245°, has been effected by interaction of 2-hydroxy-4 : 6-dimethoxyphenyl 4-methoxybenzyl ketone and ethyl carbonate in the presence of sodium according to an earlier general method [2] but the synthetical compound did not appear to be identical with the dimethyl ether of *iso*shekkangenin. Since alternative orientations are possible for a dimethyl ether of (I; R = H) or (II), synthesis of the compounds (I; R = H) and (II) appeared to be essential.

Application of the ethyl carbonate–sodium method to 2 : 4-dihydroxy-6-methoxyphenyl 4-hydroxybenzyl ketone failed to give a 4-hydroxycoumarin and an investigation of this procedure with polyhydroxy-ketones was undertaken to ascertain its limitations. It was found that with ketones of the type (III), containing two free hydroxyl groups, extremely poor yields of the 4-hydroxycoumarins were obtained and with ketones having three or more free hydroxyl groups the reaction failed completely. In efforts to employ benzyl ethers difficulties arose in attempts to prepare polybenzyloxy-compounds, expecially of phloroglucinol derivatives, but the successful conversion of an impure tri(methoxycarbonyl) derivative of (III; R = Me, R' = H) with sodium into the coumarin (II) in small yield, and the use of carbonyl chloride in the synthesis of 3-acetyl-4-hydroxy-7-methoxycoumarin [5] suggested the use of methyl chloroformate in place of ethyl carbonate. Ultimately it was found that when an *o*-hydroxyacetophenone of the type (III) was heated with methyl (or ethyl) chloroformate and potassium carbonate in boiling acetone good yields of 4-hydroxycoumarins were obtained; further, the reaction was applicable to polyhydroxy-ketones, probably proceeding by way of the intermediates (IV) and (V), involving a Baker–Venkataraman rearrangement; the reaction did not proceed with sodium or pyridine in benzene in place of potassium carbonate–acetone. Comparably with the synthesis of *iso*flavones with ethoxalyl chloride (Baker *et al.*[6]), it was found that the chloroformate reaction required at least $(n + 1)$ mol. of ester where $n$ is the number of hydroxyl groups present in the ketone. The crude product from polyhydroxy-ketones invariably appeared to contain one or more methoxycarbonyl groups which were hydrolysed with dilute alkali. The synthesis of a variety of 4-hydroxycoumarins by this method indicates the scope of the reaction but curiously, though phloropropiophenone gave a satisfactory yield of 4 : 5 : 7-trihydroxy-3-methylcoumarin, phloroacetophenone failed to yield a coumarin.

[5] Badcock, Dean, Robertson, and Whalley, *J.*, 1950, 903.
[6] Baker, Chadderton, Harbourne, and Ollis, *J.*, 1953, 1852.

The 4-hydroxycoumarins (I; R = H) and (II) were prepared from the ketones (III; R = Me, R′ = H and *vice versa*, respectively) but these compounds and their triacetates differ markedly from *iso*shekkangenin and its triacetate. The ketone (III; R = H, R′ = Me) required for the synthesis of the coumarin (II) could not be prepared directly but was obtained by the regulated hydrolytic fission of synthetic 5 : 4′-dihydroxy-7-methoxy*iso*flavone (prunetin).

In examining possible alternative routes to 4-hydroxycoumarins 5 : 7 : 4′-trimethoxy-*iso*flavone was hydrogenated with a palladium–charcoal catalyst, giving 2 : 3-dihydro-5 : 7 : 4′-trimethoxy*iso*flavone but the 2-methylene group could not be oxidised to carbonyl: *e.g.*, with chromic acid the dihydro-compound regenerated the *iso*flavone.

## Experimental

*4-Hydroxy-5 : 7 : 4′-trimethoxy-3-phenylcoumarin.*—A mixture of 2-hydroxy-4 : 6-dimethoxyphenyl 4-methoxybenzyl ketone (2 g.), ethyl carbonate (50 ml.), and powdered sodium (2 g.) was heated on the steam-bath until the reaction subsided. After the addition of a little methanol to decompose unchanged sodium the reddish sodio-derivative was dissolved in water (50 ml.), and the solution extracted with ether (2 × 25 ml.) and then acidified, giving a precipitate (1·2 g.) which on purification from alcohol furnished *4-hydroxy-5 : 7 : 4′-trimethoxy-3-phenylcoumarin*, needles, m. p. 243—245°, readily soluble in acetic acid (Found: C, 65·8; H, 5·1. $C_{18}H_{16}O_6$ requires C, 65·8; H, 4·9%). The *acetate* separated from alcohol in needles, m. p. 177—178° (Found: C, 65·3; H, 4·9. $C_{20}H_{18}O_7$ requires C, 64·9; H, 4·9%).

The same ketone (2 g.) was heated with methyl chloroformate (1 ml.) and potassium carbonate (5 g.) in boiling acetone (50 ml.) for 4·5 hr. and the mixture poured into water (500 ml.). Acidification of this gave the coumarin (1·6 g.) which was washed with water and crystallised from dilute acetic acid, forming needles, m. p. and mixed m. p. 242—245°.

*4 : 7 : 4′-Trihydroxy-5-methoxy-3-phenylcoumarin.*—(*a*) Methyl chloroformate (2·7 ml., 3 mol.) was added dropwise to a cooled and agitated solution of 2 : 4-dihydroxy-6-methoxyphenyl 4-hydroxybenzyl ketone (2·5 g.) in 2·2% aqueous sodium hydroxide (100 ml.; 3 mol. of hydroxide). An hour later, the viscous yellow-brown product was isolated with ether, and the ethereal solution washed with dilute alkali and then water, dried, and evaporated. The residue, which did not crystallise and decomposed on attempted distillation in a high vacuum, was treated in dry benzene (50 ml.) with pulverised sodium (1 g.) and 1 drop of alcohol. This mixture was heated on the steam-bath to complete the reaction and mixed with a little methanol and then water (50 ml.). Acidification of the aqueous layer gave a buff precipitate which on purification from alcohol gave the *4 : 7 : 4′-trihydroxy-5-methoxy-3-phenylcoumarin* in small prisms (0·15 g.), m. p. 316—318°, fairly soluble in alcohol, ethyl acetate, or acetone and insoluble in benzene (Found: C, 63·3; H, 4·2; OMe, 10·3. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0; 1OMe, 10·33%). The *triacetate* formed slender needles, m. p. 200—202°, from alcohol (Found: C, 62·01; H, 4·44. $C_{22}H_{18}O_9$ requires C, 61·97; H, 4·26%).

(*b*) A mixture of ketone (2 g.), methyl chloroformate (2·3 ml.), potassium carbonate (7·5 g.), and acetone (50 ml.) was heated under reflux for 3 hr., poured into water (500 ml.), and acidified with concentrated hydrochloric acid. The solid (1·8 g.) was hydrolysed with warm N-aqueous sodium hydroxide (100 ml.) for 1 hr., cooled, diluted to 200 ml., filtered, and acidified. Crystallised from alcohol, the precipitate gave the coumarin in small prisms (1·4 g.), m. p. and mixed m. p. 317—318°.

*4 : 5 : 4′-Trihydroxy-7-methoxy-3-phenylcoumarin.*—A mixture of 5 : 4′-dihydroxy-7-methoxy-*iso*flavone (1 g.), trisodium phosphate (10 g.), and water (50 ml.) was heated under reflux for 1 hr., cooled, filtered, acidified, and extracted with ether (2 × 25 ml.). The extract was washed with sodium hydrogen carbonate solution, followed by water, dried, and evaporated, leaving *2 : 6-dihydroxy-4-methoxyphenyl 4-hydroxybenzyl ketone* which, on repeated purification from aqueous methanol, formed colourless needles, m. p. 247—249°, with a red-brown ferric reaction in alcohol (Found: C, 65·4; H, 5·2. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·15%). Mixed with *iso*flavone, the compound had m. p. 220—225°. This ketone (0·8 g.) was heated with methyl chloroformate (0·9 ml.) and potassium carbonate (2·5 g.) in boiling acetone (30 ml.) for 3 hr. and the mixture poured into water (250 ml.). The precipitate (0·65 g.) obtained by acidification of this was warmed with N-aqueous sodium hydroxide (50 ml.) for 1 hr., and the cooled mixture diluted with water (50 ml.), filtered, and acidified. Crystallised from dilute

alcohol, the precipitate gave 4 : 5 : 4′-trihydroxy-7-methoxy-3-phenylcoumarin in needles (0·5 g.), m. p. 300—302°, soluble in acetic acid, alcohol, or acetone and having a greenish-blue ferric reaction in alcohol (Found: C, 64·0; H, 4·1. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0%). The *triacetate* formed clusters of needles, m. p. 206—208°, from alcohol (Found: C, 62·2; H, 4·3. $C_{22}H_{18}O_9$ requires C, 62·0; H, 4·3%).

4-*Hydroxy*-5 : 7-*dimethoxy*-3-*phenylcoumarin*.—On acidification the mixture obtained from the reaction of benzyl 2-hydroxy-4 : 6-dimethoxyphenyl ketone (2 g.), diethyl carbonate (50 ml.), and pulverised sodium (2 g.) on the steam-bath gave 4-*hydroxy*-5 : 7-*dimethoxy*-3-*phenylcoumarin* which separated from alcohol in fine needles (1·2 g.), m. p. 204—205° (Found: C, 68·5; H, 4·7; OMe, 19·1. $C_{17}H_{14}O_5$ requires C, 68·45; H, 4·7; 2OMe, 20·8%). The same coumarin (1·4 g.), m. p. and mixed m. p. 203—205°, after purification was obtained from a mixture of the ketone (2 g.), methyl chloroformate (1·1 ml.), and potassium carbonate (2·5 g.) kept in boiling acetone (30 ml.) for 3 hr. The *acetate* separated from alcohol in slender needles, m. p. 168—170° (Found: C, 67·3; H, 4·9. $C_{19}H_{16}O_6$ requires C, 67·05; H, 4·75%).

Boiled with a mixture of hydriodic acid (20 ml.; *d* 1·7), acetic acid (10 ml.), and acetic anhydride (10 ml.), this coumarin (1 g.) gave 4 : 5 : 7-*trihydroxy*-3-*phenylcoumarin* which separated from aqueous alcohol and then ethyl acetate–benzene in prisms, m. p. 278—280°, soluble in aqueous sodium hydrogen carbonate and having a blue-green ferric reaction in alcohol (Found: C, 66·9; H, 4·0. $C_{15}H_{10}O_5$ requires C, 66·7; H, 3·7%). The same coumarin (0·8 g.) was prepared by the methyl chloroformate–potassium carbonate method from benzyl 2 : 4 : 6-trihydroxyphenyl ketone (1 g.), having m. p. and mixed m. p. 278—280° and forming the same *triacetate* which separated from alcohol in needles, m. p. 209—210° (Found: C, 64·0; H, 4·3. $C_{21}H_{16}O_8$ requires C, 63·6; H, 4·3. $C_{21}H_{16}O_8$ requires C, 63·6; H, 4·1%).

4 : 7-*Dihydroxy*-5-*methoxy*-3-*phenylcoumarin*.—The interaction of phloroglucinol monomethyl ether (3 g.), benzyl cyanide (3 g.), and zinc chloride (1 g.) in ether (50 ml.) saturated with hydrogen chloride at 0° followed by hydrolysis of the product gave *benzyl* 2 : 4-*dihydroxy*-6-*methoxyphenyl ketone*, which formed plates (2·1 g.), m. p. 145—146°, from aqueous methanol, having a red-brown ferric reaction (Found: C, 69·8; H, 5·4; OMe, 12·1. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·4; 1OMe, 12·1%). By the ethyl chloroformate–potassium carbonate method and treatment of the product with warm N-aqueous sodium hydroxide this ketone (2 g.) gave 4 : 7-*dihydroxy*-5-*methoxy*-3-*phenylcoumarin* which separated from alcohol in tiny needles (1·8 g.), m. p. 292—293° (Found: C, 67·8; H, 4·3. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·2%), forming a *diacetate*, slender needles, m. p. 224—225° (from alcohol) (Found: C, 64·9; H, 4·4. $C_{20}H_{16}O_7$ requires C, 65·2; H, 4·4%).

4 : 4′-*Dihydroxy*-5 : 7-*dimethoxy*-3-*phenylcoumarin*.—By the sodium–ethyl carbonate (yield, *ca.* 30%) or by the methyl chloroformate–potassium carbonate method (yield, *ca.* 80%), 4-hydroxybenzyl 6-hydroxy-2 : 4-dimethoxyphenyl ketone gave 4 : 4′-*dihydroxy*-5 : 7-*dimethoxy*-3-*phenylcoumarin*, forming needles, m. p. 280—282°, from alcohol (Found: C, 64·9; H, 4·5; OMe, 18·3. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5; 2OMe, 19·7%); its *diacetate* formed needles, m. p. 212—214°, from alcohol (Found: C, 63·6; H, 4·7. $C_{21}H_{18}O_8$ requires C, 63·3; H, 4·55%).

The following 4-hydroxycoumarins were prepared by heating the requisite benzyl *o*-hydroxyphenyl ketone with excess of methyl chloroformate and potassium carbonate in boiling acetone for 3 hr. and subsequent treatment of the product with N-aqueous sodium hydroxide (warm or at room temperature). The end of the reaction was clearly indicated when the mixture became yellow and superheated; the yields varied from 75 to 85%. Coumarins with a free hydroxyl group in the 5-position gave a violet or deep blue-green ferric reaction in alcohol.

4 : 5 : 7 : 4′-*Tetrahydroxy*-3-*phenylcoumarin*, from 4-hydroxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone, in tiny prisms, m. p. 334—336°, from alcohol, identical with a specimen (0·4 g.) prepared by the demethylation of 4-hydroxy-5 : 7 : 4′-trimethoxy-3-phenylcoumarin (1 g.) with hydriodic acid (Found, in anhydrous specimen: C, 63·1; H, 3·5. $C_{15}H_{10}O_6$ requires C, 63·0; H, 3·5%), and giving a *tetra-acetate*, prisms, m. p. 196—198° (from alcohol) (Found: C, 60·5; H, 4·0. $C_{23}H_{18}O_{10}$ requires C, 60·8; H, 4·0%).

4 : 5 : 7-*Trihydroxy*-4′-*methoxy*-3-*phenylcoumarin*, from 4-methoxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone (2 g.), in needles (1·4 g.), m. p. 308—310°, from dilute alcohol (Found: C, 64·1; H, 4·3. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0%), giving a *triacetate* in needles, m. p. 208—210°, from the same solvent (Found: C, 62·1; H, 4·2. $C_{22}H_{18}O_9$ requires C, 62·0; H, 4·3%).

4 : 7-*Dihydroxy*-5 : 4′-*dimethoxy*-3-*phenylcoumarin*, from 2 : 4-dihydroxy-6-methoxyphenyl 4-methoxybenzyl ketone, in long needles, m. p. 258—260°, from alcohol (Found: C, 65·3; H, 4·6. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5%), gave a *diacetate* in rosettes of needles, m. p. 207—209°, from the same solvent (Found: C, 63·5; H, 4·7. $C_{21}H_{18}O_8$ requires C, 63·3; H, 4·55%). The *ketone* was prepared from phloroglucinol monomethyl ether and *p*-methoxybenzyl cyanide (Hoesch reaction), and formed slender needles, m. p. 166—167°, from dilute methanol (charcoal), with a wine-red ferric reaction (Found: C, 66·5; H, 5·7. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%).

4-*Hydroxy*-5 : 7 : 2′-*trimethoxy*-3-*phenylcoumarin*, from 2-methoxybenzyl 2-hydroxy-4 : 6-dimethoxyphenyl ketone, in needles, m. p. 246—248°, from 50% acetic acid (Found: C, 65·7; H, 4·9; OMe, 28·1. $C_{18}H_{16}O_6$ requires C, 65·85; H, 4·9; OMe, 28·3%), gave an *acetate* in needles, m. p. 185—188°, from alcohol (Found: C, 65·3; H, 5·1. $C_{20}H_{18}O_7$ requires C, 64·9; H, 4·9%).

4 : 5 : 7-*Trihydroxy*-2′-*methoxy*-3-*phenylcoumarin*, from 2-methoxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone in needles, m. p. 306—308°, from dilute alcohol (Found: C, 64·1; H, 4·2. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0%), gave a *triacetate* in needles, m. p. 200—201°, from alcohol (Found: C, 62·2; H, 4·3. $C_{22}H_{18}O_9$ requires C, 62·0; H, 4·3%).

4 : 7-*Dihydroxy*-5 : 2′-*dimethoxy*-3-*phenylcoumarin*, from 2 : 4-dihydroxy-6-methoxyphenyl 2-methoxybenzyl ketone, in minute needles, m. p. 264—266°, from ethyl acetate (Found: C, 65·0; H, 4·6. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5%) [*diacetate*, prisms, m. p. 226—227°, from alcohol (Found: C, 63·6; H, 4·7. $C_{21}H_{18}O_8$ requires C, 63·3; H, 4·55%)].

4-*Hydroxy*-5 : 7 : 3′-*trimethoxy*-3-*phenylcoumarin*, from 2-hydroxy-4 : 6-dimethoxyphenyl 3-methoxybenzyl ketone, m. p. 179—180°, from dilute acetic acid (Found: C, 65·8; H, 5·0; OMe, 27·1. $C_{18}H_{16}O_6$ requires C, 65·8; H, 4·9; OMe, 28·35%), furnished an *acetate* in silky needles, m. p. 168—170°, from alcohol (Found: C, 65·3; H, 5·0. $C_{20}H_{18}O_7$ requires C, 64·9; H, 4·9%). Prepared by the Hoesch method from phloroglucinol (4 g.), 3-*methoxybenzyl* 2 : 4 : 6-*trihydroxyphenyl ketone* separated from 90% methanol in cubes (2·6 g.), m. p. 168—169°, with an intense red-brown ferric reaction (Found: C, 66·5; H, 5·2. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·1%). With methyl sulphate (2·2 ml.) and potassium carbonate (10 g.) in boiling acetone (50 ml.) for 3 hr. this ketone (3 g.) gave 2-*hydroxy*-4 : 6-*dimethoxyphenyl* 3-*methoxybenzyl ketone*, forming needles (2·3 g.), m. p. 66—67°, from methanol, with a red-brown ferric reaction (Found: C, 67·7; H, 6·1. $C_{17}H_{18}O_5$ requires C, 67·6; H, 6·0%).

4 : 5 : 7-*Trihydroxy*-3′-*methoxy*-3-*phenylcoumarin*, from 3-methoxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone, in needles, m. p. 296—297°, from dilute alcohol (Found, in anhydrous specimen: C, 64·1; H, 4·2. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0%), gave a *triacetate* in long needles, m. p. 210—212°, from alcohol (Found: C, 62·1; H, 4·3. $C_{22}H_{18}O_9$ requires C, 62·0; H, 4·3%).

Prepared from 2 : 4-dimethoxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone by methyl sulphate–potassium carbonate, 2 : 4-*dimethoxybenzyl* 2-*hydroxy*-4 : 6-*dimethoxyphenyl ketone* formed glistening plates, m. p. 136—137°, from methanol, with a red ferric reaction (Found: C, 64·6; H, 6·1. $C_{18}H_{20}O_6$ requires C, 65·1; H, 6·1%), and gave 4-*hydroxy*-5 : 7 : 2′ : 4′-*tetramethoxy*-3-*phenylcoumarin* in needles, m. p. 210—212°, from alcohol (Found: C, 64·1; H, 5·5; OMe, 34·45. $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·0; 4OMe, 34·6%), forming an *acetate*, silky needles, m. p. 203—205°, from alcohol (Found: C, 62·0; H, 4·9. $C_{21}H_{20}O_8$ requires C, 63·0; H, 5·0%).

2 : 4-*Dihydroxy*-6-*methoxyphenyl* 2 : 4-*dimethoxybenzyl ketone* (Hoesch method) separated from dilute methanol in plates, m. p. 169—171°, with a wine-red ferric reaction (Found: C, 63·8; H, 5·8. $C_{17}H_{18}O_6$ requires C, 64·2; H, 5·7%) and gave 4 : 7-*dihydroxy*-5 : 2′ : 4′-*trimethoxy*-3-*phenylcoumarin* in prisms, m. p. 272—273°, from alcohol (Found: C, 63·1; H, 4·9. $C_{18}H_{16}O_7$ requires C, 62·8; H, 4·7%), which yielded a *diacetate* in needles, m. p. 229—230°, from alcohol (Found: C, 61·8; H, 4·4. $C_{22}H_{20}O_9$ requires C, 61·7; H, 4·7%).

4 : 5 : 7-*Trihydroxy*-2′ : 4′-*dimethoxy*-3-*phenylcoumarin*, from 2 : 4-dimethoxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone, formed needles, m. p. 305—307°, from alcohol (Found: C, 61·5; H, 4·3. $C_{17}H_{14}O_7$ requires C, 61·8; H, 4·3%), giving a *triacetate* in needles, m. p. 223—224°, from the same solvent (Found: C, 60·9; H, 4·1. $C_{23}H_{20}O_{10}$ requires C, 60·5; H, 4·4%).

4-*Hydroxy*-5 : 7 : 3′ : 4′-*tetramethoxy*-3-*phenylcoumarin*.—Prepared from phloroglucinol and 3 : 4-dimethoxybenzyl cyanide, 3 : 4-*dimethoxybenzyl* 2 : 4 : 6-*trihydroxyphenyl ketone* separated from dilute methanol in prisms, m. p. 184—186°, with a deep wine-red ferric reaction (Found:

C, 63·4; H, 5·5. $C_{16}H_{16}O_6$ requires C, 63·2; H, 5·3%), and with methyl sulphate–potassium carbonate gave rise to 3 : 4-*dimethoxybenzyl* 2-*hydroxy*-4 : 6-*dimethoxyphenyl ketone* in needles (80%), m. p. 101—103°, from methanol, with the same ferric reaction (Found: C, 65·4; H, 6·1. $C_{18}H_{20}O_6$ requires C, 65·1; H, 6·1%). This ketone furnished 4-*hydroxy*-5 : 7 : 3′ : 4′-*tetramethoxy*-3-*phenylcoumarin* in long needles, m. p. 200—202°, from alcohol (Found: C, 63·65; H, 5·1; OMe, 32·4. $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·1; 4OMe, 34·6%), giving an *acetate* in prismatic needles, m. p. 184—185°, from alcohol (Found: C, 62·7; H, 5·3. $C_{21}H_{20}O_8$ requires C, 63·0; H, 5·0%).

2 : 4-*Dihydroxy*-6-*methoxyphenyl* 3 : 4-*dimethoxybenzyl ketone* (Hoesch reaction) formed prisms, m. p. 179—180°, from ethyl acetate–benzene, with a wine-red ferric reaction (Found: C, 64·2; H, 5·7. $C_{17}H_{18}O_6$ requires C, 64·2; H, 5·7%) and gave 4 : 7-*dihydroxy*-5 : 3′ : 4′-*trimethoxy*-3-*phenylcoumarin*, needles, m. p. 262—265°, from alcohol (Found: C, 62·6; H, 4·5. $C_{18}H_{16}O_7$ requires C, 62·8; H, 4·7%), forming a *diacetate* in needles, m. p. 238—240°, from alcohol (Found: C, 61·7; H, 4·4. $C_{22}H_{20}O_9$ requires C, 61·7; H, 4·7%).

4 : 5 : 7-*Trihydroxy*-3′ : 4′-*dimethoxy*-3-*phenylcoumarin*, from 3 : 4-dimethoxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone, slender needles, m. p. 298—299°, from dilute alcohol (Found: C, 61·6; H, 4·5. $C_{17}H_{14}O_7$ requires C, 61·8; H, 4·3%), gave a *triacetate*, in long needles, m. p. 218—220°, from the same solvent (Found: C, 60·8; H, 3·7. $C_{23}H_{20}O_{10}$ requires C, 60·5; H, 4·4%).

4-*Hydroxy*-5 : 7-*dimethoxy*-3′ : 4′-*methylenedioxy*-3-*phenylcoumarin*.—From 3 : 4-methylenedioxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone (3 g.) by the methyl sulphate–potassium carbonate method, 2-*hydroxy*-4 : 6-*dimethoxyphenyl* 3 : 4-*methylenedioxybenzyl ketone* formed plates, m. p. 98—99°, from methanol with a brown ferric reaction (Found: C, 64·5; H, 4·9; OMe, 19·6. $C_{17}H_{16}O_6$ requires C, 64·55; H, 5·1; OMe, 19·6%) and gave the *coumarin*, in prismatic needles, m. p. 234—235° (Found: C, 63·0; H, 4·2; 2OMe, 17·9. $C_{18}H_{14}O_7$ requires C, 63·2; H, 4·1. OMe, 18·1%), forming an *acetate* in needles, m. p. 188—189°, from alcohol (Found: C, 62·6; H, 4·3. $C_{20}H_{16}O_8$ requires C, 62·5; H, 4·2%).

2 : 4-*Dihydroxy*-6-*methoxyphenyl* 3 : 4-*methylenedioxybenzyl ketone* (Hoesch method) separated from methanol in long plates, m. p. 143—144°, with a red ferric reaction (Found: C, 63·5; H, 4·7; OMe, 10·5. $C_{15}H_{11}O_5$·OMe requires C, 63·6; H, 4·6; OMe, 10·3%), and gave 4 : 7-*dihydroxy*-5-*methoxy*-3′ : 4′-*methylenedioxy*-3-*phenylcoumarin* in needles, m. p. 281—283°, from alcohol (Found: C, 61·9; H, 3·8. $C_{17}H_{12}O_7$ requires C, 62·2; H, 3·7%), forming a *diacetate*, needles, m. p. 218—220°, from the same solvent (Found: C, 60·9; H 4·2. $C_{21}H_{16}O_9$ requires C, 61·2; H, 3·9%).

4 : 5 : 7-*Trihydroxy*-3′ : 4′-*methylenedioxy*-3-*phenylcoumarin*, from 3 : 4-methylenedioxybenzyl 2 : 4 : 6-trihydroxyphenyl ketone, long needles, m. p. >330°, from alcohol (Found: C, 60·9; H, 3·5. $C_{16}H_{10}O_7$ requires C, 61·15; H, 3·2%), gave a *triacetate* in rosettes of prisms, m. p. 216—218°, from the same solvent (Found: C, 60·3; H, 4·1. $C_{22}H_{16}O_{10}$ requires C, 60·0; H, 3·7%).

4 : 5 : 7-*Trihydroxy*-3-*methylcoumarin*, from phloropropiophenone, small needles, m. p. 288—290°, from dilute alcohol (Found: C, 67·5; H, 3·9. $C_{10}H_8O_5$ requires C, 57·7; H, 3·9%), yielded a *triacetate*, long needles, m. p. 180—182°, from alcohol (Found: C, 57·8; H, 4·3. $C_{16}H_{14}O_8$ requires C, 57·5; H, 4·2%).

2 : 3-*Dihydro*-5 : 7 : 4′-*trimethoxy*isoflavone.—5 : 7 : 4′-Trimethoxy*iso*flavone was prepared from 6-hydroxy-2 : 4-dimethoxyphenyl 4-methoxybenzyl ketone (5 g.) in ethyl formate (80 ml.) at <0° with pulverised sodium (2·5 g.) during 24 hr. On isolation in the usual manner the product was purified by chromatography from benzene on aluminium oxide (eluted with methanol–benzene, 1 : 19) and then by crystallisation from alcohol, forming plates (4·1 g.), m. p. 163—165° (cf. Baker and Robinson [7]).

Hydrogenation of this *iso*flavone (0·5 g.) in methanol (200 ml.) with a palladium–charcoal catalyst (from 0·5 g. of charcoal and 20 ml. of 1% palladium chloride solution) gave 2 : 3-*dihydro*-5 : 7 : 4′-*trimethoxy*isoflavone which separated from aqueous methanol in colourless plates (0·4 g.), m. p. 154—155; admixed with parent *iso*flavone it had m. p. 123—146° (Found: C, 68·6; H, 5·9. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·7%). With chromic acid in acetic acid the dihydro-compound regenerated the parent *iso*flavone, m. p. and mixed m. p. 163—165°.

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[7] Baker and Robinson, *J.*, 1926, 2716.