261. *The Chemistry of Extractives from Hardwoods. Part XXXV.* The Constitution of Maesopsin (2-Benzyl-2,4,6,4′-tetrahydroxycoumaranone) and of its Alkali Fusion Products.*

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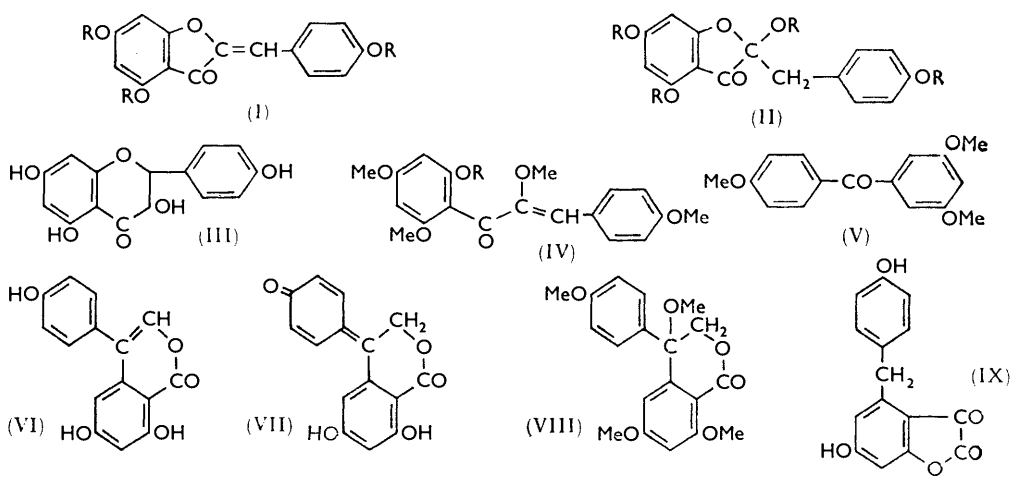
Maesopsin, $C_{15}H_{12}O_6$, earlier obtained from the heartwood of *Maesopsis eminii* [1] has now been identified as 2-benzyl-2,4,6,4′-tetrahydroxycoumaranone. With alkali at 130° it forms a yellow derivative, $C_{15}H_{10}O_5$, further degraded at 200° to 3,5,4′-trihydroxydiphenylmethane. The mechanism suggested for the transformation of the original phloroglucinol-containing compound into a derivative of resorcinol indicates the nature of the yellow intermediate for which a structure has now been agreed.

SUCCESSIVE extractions of the African timber musizi (*Maesopsis eminii*) have given two new crystalline phenols. The first, musizin, deep yellow and removed with boiling light petroleum, proved to be 2-acetyl-1,8-dihydroxy-3-methylnaphthalene.[1] The second, termed maesopsin, was isolated in amounts of 0·7—1·7% by continuous treatment with hot acetone.

Maesopsin, $C_{15}H_{12}O_6$, is colourless and can be crystallised by concentrating ethereal extracts of its aqueous solutions. It has phenolic properties but failed to give flavonoid colour reactions with magnesium–hydrochloric acid or sodium amalgam–ethanol. With boiling 5% sulphuric acid in acetic acid a yellow anhydro-compound, $C_{15}H_{10}O_5$, was formed. The belief that this might be a trihydroxyaurone, suggested by the appearance of anisic acid as an oxidation product of maesopsin tetramethyl ether (*q.v.*), led to a comparison of its ultraviolet absorption with those of typical aurones whence it was seen to be coincident with that of the 4,6,4′-trihydroxy-derivative (I; R = H).[2] Repetition of its synthesis from 4,6-dihydroxycoumaranone and *p*-hydroxybenzaldehyde enabled the identity of this anhydro-derivative to be confirmed.[2,3] Of the two structures theoretically



derivable from (I; R = H) by hydration of the double bond, (II; R = H) was preferred since it belongs to the well-established group of hydrated aurones of which naturally occurring

* Part XXXIV, Housely, King, King, and Taylor, *J.*, 1962, 5095.

[1] Covell, King, and Morgan, *J.*, 1961, 702.
[2] Geissman and Harborne, *J. Amer. Chem. Soc.*, 1956, **78**, 832.
[3] Geissman and Harborne, *J. Amer. Chem. Soc.*, 1955, **77**, 4622.

examples are already known in 2-benzyl-2,6,3′,4′-tetrahydroxycoumaranone and its 4′-methyl ether from *Schinopsis spp.*,[4] and in the 2,4,6,3′,4′-pentahydroxy-compound from *Alphitonia excelsa*.[5] Moreover, benzyl-2-hydroxycoumaranones may be obtained from dihydroflavonols by brief treatment with hot alkali in the absence of oxygen,[6] and the 2-benzyl-2,4,6,4′-tetrahydroxycoumaranone prepared in this way from dihydrokæmpferol (III) was indistinguishable from maesopsin, thus unambiguously establishing its construction.

Both tetra- and penta-methyl ethers are obtained from maesopsin with methyl sulphate–potassium carbonate. Oxidation with permanganate gives anisic acid with both derivatives but more readily with the pentamethyl compound. The two ethers may also be distinguished by their ultraviolet absorption, the tetramethyl compound resembling maesopsin, with a peak at 293 mμ, while the pentamethyl ether exhibits a bathochromic shift to 328 mμ. From these observations it may be inferred that the former is the normal maesopsin ether (II; R = Me), ring-opening of which gives the pentamethyl derivative (IV; R = Me). In confirmation, the action of sulphuric acid in acetic acid on the two ethers gave a trimethoxyaurone (I; R = Me) from the tetramethoxy-compound whereas no new product was obtained from the pentamethyl ether.

2-Benzyl-2,4,6,4′-tetramethoxycoumaranone (II; R = Me) is already known as one of the cyclisation products of 2′-hydroxy-α,4,4′,6′-tetramethoxychalcone (IV; R = H),[7] and a sample prepared by this method was identical with the tetramethyl ether originating from maesopsin. Moreover, further methylation of the chalcone gave the maesopsin pentamethyl ether, which therefore confirms the structure (IV; R = Me) already attributed to it. The other product of the above cyclisation, 2-benzyl-2-hydroxy-4,6,4′-trimethoxycoumaranone was independently prepared by the action of alkali on dihydrokæmpferol 5,7,4′-trimethyl ether with rigid exclusion of air to avoid oxidation to kæmpferol trimethyl ether.[8]

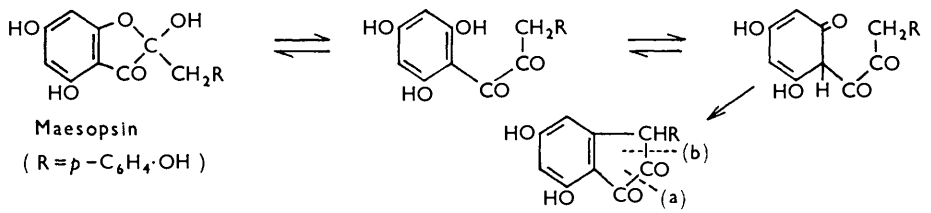
The fusion of maesopsin with sodium hydroxide–potassium hydroxide at 130° produced a crystalline golden-yellow product, $C_{15}H_{10}O_5$, and further degradation with alkali at 200° led to a colourless compound, $C_{13}H_{12}O_3$. The latter formed a trimethyl ether from which, on oxidation with chromic acid, impure anisic acid was obtained. Oxidation of the trimethyl compound with permanganate gave a trimethoxybenzophenone, an unexpected result indicative of a profound structural change during the alkali fusion. The final fusion product must therefore be a 4-hydroxydiphenylmethane with two additional hydroxyl groups in the other aromatic ring. A positive vanillin test suggested that they were present as a resorcinol nucleus. By synthesis two of the three possible isomers for the derived trimethoxybenzophenone were obtained, namely the hitherto unknown 2,6,4′-trimethoxybenzophenone which was different from that originating from maesopsin, and secondly, 3,5,4′-trimethoxybenzophenone (V) which was identical with it, although the melting point differed from that previously recorded.[9] Accordingly the colourless product from alkali degradation was identified as 3,5,4′-trihydroxydiphenylmethane.

The yellow phenolic compound, $C_{15}H_{10}O_5$, formed in the milder alkali fusion gave only syrupy products with diazomethane, but on short treatment with dimethyl sulphate–potassium carbonate a crystalline yellow monomethyl ether, $C_{16}H_{12}O_5$, was isolated and after prolonged reaction a colourless crystalline tetramethyl ether, $C_{19}H_{20}O_6$. The tetramethyl ether was hydrolysed by dilute alkali to an acidic trimethyl ether from which the tetramethyl compound was recovered on treatment with diazomethane. The tetramethyl derivative was resistant to oxidation by potassium permanganate whereas the trimethyl

[4] King, White, and Hughes, *J.*, 1961, 3234.
[5] Birch, Ritchie, and Speake, *J.*, 1960, 3593.
[6] Gowan, Philbin, and Wheeler, "The Chemistry of the Vegetable Tannins," Society of Leather Trades' Chemists, Croydon, 1956, p. 133.
[7] Tominaga, *J. Pharm. Soc. Japan*, 1953, **73**, 1179.
[8] Tominaga, *J. Pharm. Soc. Japan*, 1953, **73**, 1175.
[9] Mauthner, *J. prakt. Chem.*, 1913, [2], **87**, 406.

ether was readily oxidised to a carboxytrimethoxybenzophenone together with a small quantity of anisic acid. Decarboxylation of the main product by heating with copper in quinoline produced 3,5,4'-trimethoxybenzophenone (V), thus demonstrating that the diphenylmethane skeleton was also present in the yellow alkali-fusion product. The formation of anisic acid in the permanganate oxidation which is the exclusive product also of chromic acid oxidation, indicates that the carboxyl group lost as a result of pyrolysis is attached to the other, resorcinol, nucleus.

The infrared spectrum (Nujol mull) of the yellow alkali-fusion product has strong bands at 1694 and 1820 cm.$^{-1}$, the former being characteristic of an aromatic ester or lactone carbonyl group with an adjacent hydroxyl group. This assignment appeared to be further supported by the yellow ferric reaction (in absolute ethanol) of the yellow alkali-fusion product, while the trihydroxydiphenylmethane obtained by further degradation gave no colour with this reagent. In view of these observations, formula (VI), a trihydroxy-4-phenylisocoumarin, was initially proposed for the yellow fusion product, later modified to embrace the tautomer (VII).[10] These structures originated from the following mechanism devised to explain the transformation of the original phloroglucinol-containing hydrated aurone into a derivative of resorcinol:



Ring fission of the indanedione at position (a) would then lead to structures (VI) or (VII) simply by lactonisation of the resulting aldehydocarboxylic acid in its enol form.

The colour of the yellow fusion product, though stable in dioxan, is fugitive in ethanol, a difference reflected in the ultraviolet spectra of the respective solutions. This colour change in alcohol (compare fuchsone [11]) was attributed to carbinol ether formation through addition of the solvent to the quinonoid system of (VII). The insolubility of the tetramethyl ether in cold alkali, its stability to permanganate, and the formation of an acidic trimethyl ether under hydrolysis conditions were also interpreted as evidence of carbinol base formation in these derivatives and hence of the quinonoid nature of the fusion product. Nuclear magnetic resonance measurements on the fusion product (in acetone), which revealed a band at 5·86 τ characteristic of the system $-O\cdot CH_2\cdot C{=}C-$, also appeared at first to support the quinonoid formulation (VII). On the other hand, the infrared spectrum does not readily accommodate this structure in that the 1820 cm.$^{-1}$ band is outside the range of the normal quinonoid carbonyl absorption. Moreover, the characteristic band at 5·86 τ of the fusion product is also observed in the tetramethyl ether, thus indicating that the environment of the methylene group is identical in both compounds, and this condition is not satisfied by the structures (VII) and (VIII).

An alternative structure avoiding these difficulties may be derived if, contrary to the earlier supposition, the indanedione ring, behaving as a β-diketone vinylogue, is severed at position (b). A benzoylformic acid is thereby obtained which can undergo an alternative cyclisation with the adjacent phenolic group. The yellow fusion product is thus represented as a coumaran-2,3-dione (IX).* This leads to a trimethoxy methyl ester structure

* This structure was suggested by Dr. F. M. Dean, University of Liverpool, to whom the authors express their acknowledgment.

[10] Janes, King, and Morgan, *Chem. and Ind.*, 1961, 346.

[11] Orndorff, Gibbs, McNulty, and Shapiro, *J. Amer. Chem. Soc.*, 1927, **49**, 1545; Beynon and Bowden, *J.*, 1957, 4247.

for the so-called tetramethyl ether, a formulation which readily explains its hydrolysis to the acidic trimethyl ether and regeneration therefrom by diazomethane. Fading of the yellow alcoholic solutions is in agreement with the behaviour of coumarandiones which readily undergo alcoholysis to the corresponding hydroxy-esters. The absorption at 5·86 τ shown by the fusion product and its ethers can now be assigned to the diphenylmethane methylene group although the methylene absorption of diphenylmethane (in carbon disulphide) has the rather different value of 6·27 τ.

When coumaran-2,3-dione was prepared by the method of Huntress and Hearon [12] the product was found to have strong infrared bands at 1720 and 1807 cm.$^{-1}$ (with a weak band at 1842 cm.$^{-1}$) thus confirming the structure of the yellow fusion product as 6-hydroxy-4-*p*-hydroxybenzylcoumaran-2,3-dione (IX).

The ready conversion of dihydrokæmpferol into maesopsin under alkaline conditions suggests that the former should also undergo these reactions on fusion with alkali, and this was verified experimentally in the formation of the yellow fusion product from the dihydroflavonol in similar yield. However, the transformation does not appear to have been encountered before in the recorded alkali degradation of dihydroflavonols, *i.e.*, of alpinone,[13] ampelopsin,[14] and dihydrokæmpferol,[15] each having given smaller fragments expected from direct scission of the C_6–C_3–C_6 units. The conversion of maesopsin into the yellow product could not be effected in aqueous sodium hydroxide in concentrations up to 30%, maesopsin being recovered unchanged, but with 60% aqueous sodium hydroxide the yellow product was obtained in 50% yield. This is in contrast to the behaviour of dihydroflavonols and 2-benzyl-2-hydroxycoumaranones having methylated phenolic groups which undergo a benzilic acid rearrangement to the corresponding 3-benzylidenecoumaran-2-ones.[6,16,17]

Nuclear Magnetic Resonance Spectra.—The following measurements are due to Dr. R. L. Erskine and Dr. S. A. Knight of The British Petroleum Company Limited, Sunbury Research Centre, Middlesex, to whom the authors are indebted for helpful discussion.

Alkali fusion product		Monomethyl ether		Tetramethyl ether		
τ	Relative intensity	τ	Relative intensity	τ	Relative intensity	Assignment
2·76 2·97/*J*/8·6 c.p.s. 3·17 δ 14·3 3·38	4	2·75 2·96/*J*/8·5 c.p.s. 3·17 δ 14·6 3·38	4	2·77 2·98/*J*/8·4 c.p.s. 3·15 δ 12·3 3·35	4	AB pattern. Coupled pairs of aromatic-type hydrogen atoms
3·47	2	3·33	1			Phenolic hydrogen
				3·42 3·47/*J*/ 3·52~2·3 c.p.s. 3·59	2	AB pattern. Pair of *meta*-coupled aromatic hydrogen atoms
5·86	2	5·87	2	5·86	2	Hydrogen atoms on carbon adjacent to O or O–CO·R
		6·07	3	6·15 6·19	9 3	OMe hydrogen atoms

Experimental

Melting points are uncorrected, and solvent evaporations were carried out under reduced pressure.

Maesopsin (II; R = H).—The comminuted wood of *Maesopsis eminii* (2·5 kg.), after extraction by boiling light petroleum to remove the fraction containing musizin,[1] was extracted for 18

[12] Huntress and Hearon, *J. Amer. Chem. Soc.*, 1941, **63**, 2762.
[13] Kimura and Hosi, *J. Pharm. Soc. Japan*, 1937, **57**, 147.
[14] Kotake and Kubota, *Annalen*, 1940, **544**, 253.
[15] Hillis, *Austral. J. Sci. Res.*, 1952, *A*5, 379.
[16] Hergert, Coad, and Logan, *J. Org. Chem.*, 1956, **21**, 304; Eneback and Gripenberg, *ibid.*, 1957, **22**, 220.
[17] Molho and Chadensen, *Bull. Soc. chim. France*, 1959, 453.

hr. with boiling acetone. The solution obtained was evaporated to a brown syrup (120 g.) which was leached with boiling water. The cooled aqueous solution was decanted and extracted by ether, and the evaporated ethereal extracts afforded crude maesopsin as a pale brown crystalline solid (67·5 g.). Purification was effected by redissolution in hot water, extraction with ether, and concentration of the ethereal solution which deposited colourless crystals of *maesopsin*, m. p. 218—220° (decomp.), $[\alpha]_D \pm 0°$ (*c*, 1 in ethanol) [Found: C, 62·3; H, 4·3%; *M* (Menzies Wright), 260. $C_{15}H_{12}O_6$ requires C, 62·5; H, 4·2%; *M*, 288], $\nu_{max.}$ (mull) 1670 cm.$^{-1}$; $\lambda_{max.}$ (ethanol) 211, 290 mμ (log ε 4·38, 4·28). Maesopsin gives a purple-brown colour with ferric chloride, and a red colour with vanillin–hydrochloric acid, but no colours were produced in the magnesium–hydrochloric acid, zinc–hydrochloric acid, or sodium amalgam–ethanol tests. Chromatography on paper (Whatman No. 4) in butanol–acetic acid–water (4 : 1 : 5), propan-2-ol–water (22 : 78), and ethyl acetate saturated with water, gave R_F values 0·88, 0·72, and 0·93, respectively; ferric chloride or diazotised sulphanilic acid sprays were used.

(+)-Dihydrokæmpferol (0·5 g.) was added to boiling aqueous 2N-sodium hydroxide (50 ml.) under a current of nitrogen, and boiling was continued for 5 min. The solution was rapidly cooled, acidified, filtered, and extracted with ether. Concentration of the ethereal solution afforded maesopsin (0·35 g.), m. p. 218—220° (decomp.), with infrared spectrum identical with that of the natural product.

4,6,4′-Trihydroxyaurone (I; R = H).—A solution of maesopsin (1 g.) in acetic acid (45 ml.) containing concentrated sulphuric acid (2·2 g.) was boiled for 1 hr. Sodium acetate (3 g.) was then added to the bright red solution which was concentrated to low bulk and diluted with water, leaving a yellow solid (0·7 g.). This was collected in ether and recrystallised from aqueous ethanol as needles of 4,6,4′-trihydroxyaurone, m. p. above 300° (vac.) (lit.[2] 295—300°, decomp.) (Found: C, 66·4; H, 3·7. Calc. for $C_{15}H_{10}O_5$: C, 66·7; H, 3·7%), $\lambda_{max.}$ 392 mμ (log ε 4·43), $\lambda_{min.}$ 279 mμ (log ε 3·28), $\lambda_{infl.}$ 245, 340 mμ (log ε 3·95, 4·15) in agreement with recorded values.[2]

The trihydroxyaurone was synthesised by Geissman and Harborne's method [3] by condensation of 4,6-dihydroxycoumaranone (15 g.) [18] and *p*-hydroxybenzaldehyde (1·1 g.) in acetic acid (50 ml.) in the presence of concentrated hydrochloric acid (2 ml.) at room temperature. The product, m. p. above 300°, obtained after recrystallisation from aqueous ethanol, gave an infrared spectrum identical with that of the trihydroxyaurone derived from maesopsin.

Methylation of Maesopsin.—A mixture of maesopsin (6 g.), dimethyl sulphate (15 ml.), anhydrous potassium carbonate (30 g.), and acetone (250 ml.) was boiled under reflux with stirring for 5 hr. The filtered acetone solution was evaporated to low volume and diluted with water, and aqueous ammonia added. The precipitated gum was crystallised from methanol (15 ml.) to give a mixture of colourless crystals which were recrystallised from methanol with slow cooling. Two distinct forms, needles and cubes, were deposited and these were separated by hand. Recrystallisation of each form independently gave cubes of maesopsin tetramethyl ether (II; R = Me) (3·2 g.), m. p. 130—131° [Found: C, 66·5; H, 5·8; OMe, 36·2%; *M* (Rast), 345. Calc. for $C_{19}H_{20}O_6$: C, 66·3; H, 5·9; OMe, 36·0%; *M*, 344], $\nu_{max.}$ (in CCl_4) 1710 cm.$^{-1}$, $\lambda_{max.}$ (in ethanol) 213, 293 mμ (log ε 4·42, 4·28), and needles of *α,4,2′,4′,6′-pentamethoxychalcone* (IV; R = Me) (1·1 g.), m. p. 134—135° (Found: C, 66·8; H, 6·2; OMe, 43·0. $C_{20}H_{22}O_6$ requires C, 67·0; H, 6·2; OMe, 43·3%), $\lambda_{max.}$ (in ethanol) 328 mμ (log ε 4·46). Rapid recrystallisation of maesopsin tetramethyl ether from methanol sometimes produced a form with m. p. 118—119°.

A solution of maesopsin tetramethyl ether (0·3 g.) and hydroxylamine hydrochloride (1·5 g.) in pyridine (10 ml.) was boiled under reflux for 18 hr.,[19] and then poured into water. Recrystallisation of the precipitated solid from ethanol gave blades of the *oxime* (0·2 g.), m. p. 201—202° (Found: C, 63·1; H, 5·85; N, 4·1; OMe, 33·9. $C_{19}H_{21}NO_6$ requires C, 63·5; H, 5·85; N, 3·9; OMe, 34·5%).

Oxidation of the Methyl Ethers.—The pentamethoxychalcone (IV; R = Me) (0·3 g.) in acetone (50 ml.) was shaken with potassium permanganate (0·3 g.) at room temperature for 20 hr. The precipitate was collected, suspended in water, and treated with a stream of sulphur dioxide, leaving a colourless solid in suspension. Recrystallisation from water gave needles of anisic acid (0·05 g.), m. p. and mixed m. p. 183—184°. Similar treatment of the tetramethyl ether gave the starting compound.

A suspension of maesopsin tetramethyl ether (II; R = Me) (0·5 g.) and potassium permanganate (4 g.) in aqueous 2N-sodium hydroxide (100 ml.) was boiled for 30 min., cooled, and

[18] Shriner and Grosser, *J. Amer. Chem. Soc.*, 1942, **64**, 382.
[19] Campbell, McCallum, and Mackenzie, *J.*, 1957, 1922.

extracted with ether, which removed unchanged starting compound (0·23 g.). The acidified aqueous layer afforded anisic acid (0·03 g.), m. p. and mixed m. p. 181°.

4,6,4′-*Trimethoxyaurone* (I; R = Me).—Treatment of maesopsin tetramethyl ether (1 g.) with sulphuric acid in acetic acid (30 ml., 5% w/v) as described above for maesopsin, afforded 4,6,4′-trimethoxyaurone (0·65 g.) as yellow needles, m. p. 171—172° (from methanol) (lit.[20] 167°) (Found: C, 69·3; H, 5·2. Calc. for $C_{18}H_{16}O_5$: C, 69·2; H, 5·2%), $\nu_{max.}$ (in $CHCl_3$) 1685, 1642 cm.$^{-1}$; $\lambda_{max.}$ 392 mμ (log ε 4·43), $\lambda_{min.}$ 279 mμ (log ε 3·32), $\lambda_{infl.}$ 224, 245, 340 mμ (log ε 4·04, 3·94, 4·15).

Methylation of synthetic 4,6,4′-trihydroxyaurone with dimethyl sulphate and potassium carbonate in acetone gave an identical sample of 4,6,4′-trimethoxyaurone, m. p. and mixed m. p. 171—172°.

Synthesis of the Methyl Ethers.—A solution of 2-hydroxy-ω,4,6-trimethoxyacetophenone (2 g.) [21] and anisaldehyde (2·5 g.) in ethanol (24 ml.) and aqueous 2N-sodium hydroxide (40 ml.) was kept at room temperature overnight.[22] Saturation of the solution with carbon dioxide then precipitated a solid, which recrystallised from aqueous alcohol as needles of 2′-hydroxy-α,4,4′,6′-tetramethoxychalcone (2·9 g.), m. p. 120—121° (lit.[22] 121°).

A solution of the chalcone (1·5 g.) in 90% ethanol (250 ml.) containing concentrated hydrochloric acid (9 ml.) was boiled under reflux for 4·25 hr.,[7] then concentrated to remove most of the ethanol. Water was added and the mixture obtained was extracted with ether. The ethereal solution was shaken with 10% sodium hydroxide and then evaporated giving 2,4,6-trimethoxy-2-4′-methoxybenzylcoumaranone (II; R = Me) (0·17 g.), m. p. 130° (lit.[7] 127°) undepressed by maesopsin tetramethyl ether. The acidified aqueous layer precipitated crystals which crystallised from benzene–light petroleum as 2-hydroxy-4,6-dimethoxy-2-4′-methoxybenzylcoumaranone (0·52 g.), m. p. 144—145° (lit.[7] 158—159°) (Found: C, 65·2; H, 5·5. Calc. for $C_{18}H_{18}O_6$: C, 65·5; H, 5·5%). Repeated recrystallisation did not raise the melting point.

By boiling dihydrokæmpferol 5,7,4′-trimethyl ether (2 g.) with 5% potassium hydroxide in ethanol (50 ml.) under nitrogen for 5 min. an identical sample (1·6 g.), m. p. and mixed m. p. 145°, was obtained.

Methylation of the above chalcone with dimethyl sulphate and potassium carbonate in acetone gave α,4,2′,4′,6′-pentamethoxychalcone (IV; R = Me) (0·24 g.), m. p. 134° undepressed by the sample from the methylation of maesopsin.

6-*Hydroxy*-4-p-*hydroxybenzylcoumaran*-2,3-*dione* (IX).—A mixture of maesopsin (2 g.), potassium hydroxide (4 g.), sodium hydroxide (4 g.), and water (2 ml.) was heated under nitrogen at 130° for 10 min. Water was added to the cooled melt and then concentrated hydrochloric acid (caution) so that the mixture boiled vigorously during the addition. The precipitated orange solid (0·95 g.) was filtered from the hot solution and recrystallised from hot water as golden-yellow needles of 6-*hydroxy*-4-p-*hydroxybenzylcoumaran*-2,3-*dione*, m. p. 244—245° (Found: C, 66·4; H, 3·8. $C_{15}H_{10}O_5$ requires C, 66·7; H, 3·7%), $\nu_{max.}$ (mull) 1694, 1820 cm.$^{-1}$, $\lambda_{max.}$ 288 mμ (log ε 4·06), $\lambda_{infl.}$ 315 mμ (log ε 3·94). The compound gave a yellow colour with ferric chloride in alcohol, and a purple-brown colour with aqueous alcoholic ferric chloride. The same product was obtained in 43% yield by fusion of dihydrokæmpferol under the same conditions and in 50% yield by boiling a mixture of maesopsin (1 g.), sodium hydroxide (15 g.), and water (25 ml.) for 1 hr. In the latter experiment, when the amount of sodium hydroxide was halved only impure maesopsin was isolated.

Methylation of 6-*Hydroxy*-4-p-*hydroxybenzylcoumaran*-2,3-*dione*.—The alkali-fusion product (1·5 g.), potassium carbonate (7 g.), dimethyl sulphate (3 ml.), and acetone (100 ml.) were boiled and stirred for 1·5 hr. The insoluble part was filtered off and dissolved in water, and the solution was acidified and extracted with ether. The evaporated extract afforded yellow needles of the *monomethyl ether* (1·1 g.), m. p. 180—181° (from benzene–methanol) (Found: C, 67·1; H, 4·25; OMe, 11·3. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·25; OMe, 10·9%), $\nu_{max.}$ (mull) 1801, 1700 cm.$^{-1}$. The compound reacted to ferric chloride as the parent phenol.

A mixture of the alkali-fusion product (2·5 g.), dimethyl sulphate (10 ml.), potassium carbonate (25 g.), and acetone (150 ml.) was boiled with stirring for 18 hr., and then filtered. The evaporated filtrate and acetone washings were treated with aqueous ammonia and the resultant suspension was extracted into ether. Evaporation of the ether afforded a syrup which

[20] Geissman and Fukushima, *J. Amer. Chem. Soc.*, 1948, **70**, 1686.
[21] Herzig and Hofmann, *Ber.*, 1909, **42**, 155.
[22] Kimura, *J. Pharm. Soc. Japan*, 1938, **58**, 415.

was leached out with boiling light petroleum (b. p. 80—100°). From the petroleum solution there were obtained prisms of *methyl* 4,6-*dimethoxy*-2-4′-*methoxybenzylbenzoylformate* (2·1 g.), m. p. 77—78° (from methanol) (Found: C, 66·6; H, 6·0; OMe, 35·1. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·9; OMe, 36·0%), $\nu_{max.}$ (in CCl_4) 1735, 1681 cm.$^{-1}$; $\lambda_{max.}$ (in ethanol) 284 mμ (log ε 4·03). The tetramethyl compound did not form an oxime under normal conditions [23] (unchanged starting compound being recovered) or under the forcing conditions [19] described above. Attempted oxidation of the tetramethyl derivative by potassium permanganate in boiling acetone or 10% acetic acid in acetone afforded starting compound, m. p. and mixed m. p. 71°, in almost quantitative yield.

Hydrolysis of Methyl 4,6-*Dimethoxy*-2-4′-*methoxybenzylbenzoylformate*.—The ester (0·3 g.) in 10% aqueous sodium hydroxide (20 ml.) was boiled until the solid dissolved (5 min.) and the cooled solution was then acidified. The product, extracted by ether, gave 4,6-*dimethoxy*-2-4′-*methoxybenzylbenzoylformic acid*, m. p. 90—91° (from benzene–light petroleum) (Found: C, 65·5; H, 5·6; OMe, 27·2. $C_{18}H_{18}O_6$ requires C, 65·5; H, 5·5; OMe, 28·2%). Methylation of this acid with an excess of diazomethane in ether gave the methyl ester, m. p. and mixed m. p. 77—78°.

Oxidation of 4,6-*Dimethoxy*-2-4′-*methoxybenzylbenzoylformic Acid*.—Potassium permanganate (2·4 g.) was added to a solution of the acid (0·6 g.) in acetone (150 ml.) which was boiled for 45 min. The precipitated solid was suspended in water and saturated with sulphur dioxide. The residual undissolved solid (0·2 g.) yielded needles of 2-*carboxy*-3,5,4′-*trimethoxybenzophenone* m. p. 197—198° (from aqueous methanol) (Found: C, 64·3; H, 5·1. $C_{17}H_{16}O_6$ requires C, 64·6; H, 5·1%), $\lambda_{max.}$ 261, 290 mμ (log ε 4·15, 4·13). Extraction of the aqueous solution by ether gave a semicrystalline solid which was chromatographed on silica in benzene. Elution by ether–benzene (1 : 4) gave anisic acid (0·1 g.), m. p. and mixed m. p. 180°. Anisic acid was the sole product of oxidation by chromic acid in acetic acid at 40°.

The action of an excess of ethereal diazomethane on the carboxytrimethoxybenzophenone afforded the *methyl ester*, m. p. 128° (Found: C, 65·5; H, 5·3. $C_{18}H_{18}O_6$ requires C, 65·5; H, 5·5%), as needles from aqueous ethanol.

A mixture of the carboxytrimethoxybenzophenone (150 mg.) and copper powder (50 mg.) in freshly distilled quinoline (2·5 ml.) was boiled under reflux for 15 min. Ether (50 ml.) was then added and the solution was filtered, washed with aqueous acid and aqueous alkali, and evaporated to a solid which was chromatographed on alumina in benzene. Elution by benzene–ether (4 : 1) afforded the known 3,5,4′-trimethoxybenzophenone (V) (32 mg.), m. p. and mixed m. p. 88—89°.

3,5,4′-*Trihydroxydiphenylmethane*.—A mixture of maesopsin (2 g.), potassium hydroxide (4 g.), sodium hydroxide (4 g.), and water (2 ml.) was heated under nitrogen at 200° for 30 min. The cooled melt was dissolved in water and acidified with hydrochloric acid to give a solution which was extracted with ether. The ethereal solution was washed with aqueous sodium hydrogen carbonate and evaporated to a solid which recrystallised from water (charcoal) as prisms of 3,5,4′-*trihydroxydiphenylmethane* (0·69 g.), m. p. 192—193° (Found: C, 72·3; H, 5·7. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%), $\lambda_{max.}$ 278 mμ (log ε 3·54). The compound did not give a colour with ferric chloride, but gave a red colour with vanillin and hydrochloric acid. Fusion of the yellow fusion product (IX) with alkali under the above conditions gave the trihydroxydiphenylmethane, m. p. and mixed m. p. 192—193°.

Boiling acetic anhydride and pyridine afforded needles (from aqueous methanol) of the *triacetate*, m. p. 89° [Found: C, 66·8; H, 5·2%; *M* (Rast), 329. $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%; *M*, 318]. With dimethyl sulphate and potassium carbonate in boiling acetone, after 2 hr., prisms (from methanol) of a *trimethyl ether*, m. p. 65° (Found: C, 74·5; H, 6·9. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%), were obtained.

3,5,4′-*Trimethoxybenzophenone* (V).—Potassium permanganate (1·8 g.) was added in four portions during 2 hr. to a solution of 3,5,4′-trimethoxydiphenylmethane (0·45 g.) in boiling acetone. After boiling for a further 1 hr., the mixture was cooled and filtered and the filtrate evaporated to a residue which was chromatographed on alumina in benzene solution Elution with benzene afforded unchanged starting compound (0·18 g.), m. p. and mixed m. p. 64°, and elution with ether–benzene (1 : 4) gave a solid (0·13 g.) which recrystallised from methanol or light petroleum as needles of 3,5,4′-trimethoxybenzophenone, m. p. 88—89° undepressed by a

[23] Linstead and Weedon, "A Guide to Qualitative Organic Chemical Analysis," Butterworths, London, 1956, p. 27.

synthetic sample (Found: C, 70·8; H, 6·0. Calc. for $C_{16}H_{16}O_4$: C, 70·6; H, 5·9%), $\lambda_{max.}$ 224, 291 mμ (log ε 4·40, 4·30).

Synthesis of 3,5,4′- *and* 2,6,4′-*Trimethoxybenzophenone.*—A mixture of 3,5-dimethoxybenzoyl chloride (1·2 g.),[9] anisole (0·7 g.), powdered aluminium chloride (1 g.), and carbon disulphide (20 ml.) was boiled for 30 min. Trituration of the precipitated solid with 10% sodium hydroxide gave a suspension which was extracted with ether. The product from the evaporated extract was filtered through a short column of alumina in benzene solution, and the eluted solid recrystallised from light petroleum as needles of 3,5,4′-trimethoxybenzophenone (0·47 g.), m. p. 88—89° (lit.[9] 97—98°). Repeated recrystallisation and sublimation did not raise the melting point.

A solution of 2,6-dimethoxybenzoic acid (7·2 g.) [24] in thionyl chloride (7·5 ml.) was warmed until effervescence ceased, and then diluted with light petroleum, precipitating crystals of the acid chloride (5 g.), m. p. 68°. This acid chloride (5 g.), anisole (4 ml.), and aluminium chloride (5 g.) in carbon disulphide (30 ml.), by essentially the same procedure, gave 2,6,4′-*trimethoxybenzophenone* (4 g.), m. p. 110—111° (Found: C, 70·8; H, 6·0. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%), as needles from methanol.

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[24] *Org. Synth.*, Coll. Vol. III, p. 293; Cartwright, Jones, and Marmion, *J.*, 1952, 3499.