607. *Spirocyclic Compounds. Part I. The Preparation of Compounds Related to* 3 : 2′-*Dioxogrisan.*

By F. M. DEAN and KAMCHORN MANUNAPICHU.

Alkylations of coumaran-3-ones generally lead to 2 : 2-disubstituted products some of which can be converted into spirocyclic compounds related to griseofulvin. Cyclisation was achieved only by acid-catalysed cyclodehydration; it led to 4 : 6 : 4′-trimethyl- (XXXII; Me for OMe) and 4 : 6-dimethoxy-4′-methyl-3 : 2′-dioxogris-3′-en (XXXII). The latter compound was oriented by the production of 2-hydroxy-4 : 6-dimethoxybenzoic acid when the corresponding diol suffered periodate oxidation, which could include oxidation of hydrogen at the 2-position of a coumaran-3-one. This type of oxidation has been realised in simple coumaranones and compared with the autoxidations of 2-alkyl- and 2-acetyl-coumaran-3-ones.

ATTEMPTS to synthesise spirocyclic systems similar to those of griseofulvin [1] (I) and the derivative (II) of usnolic acid [2] from coumaranones of type (IV) have led to spirocyclic diketones of type (III).

Addition of vinyl cyanide to 4 : 6-dimethoxycoumaran-3-one (IV; R = OMe) led only to the dicyanide (V; R = OMe), which had the appropriate absorption bands at 2257 ($C{\vdots}N$) and 1698 cm.$^{-1}$ (coumaranone $C{:}O$), and the same ultraviolet absorption as the parent dimethoxycoumaranone. In contrast, no reaction with allyl cyanide could be realised in spite of reports by Michael and Ross [3] and Bruson.[4] Similarly, the dicyanide (V; R = Me) was easily prepared from 4 : 6-dimethylcoumaran-3-one (IV; R = Me) and appeared to be suitable for cyclisation to a derivative of *cyclo*hexanone by the technique of Ziegler, Eberle, and Ohlinger.[5] This dicyanide, however, resisted cyclisation by lithium ethylanilide, and was therefore hydrolysed to the dibasic acid (VI; R = Me, R′ = H); the acid, however, was not cyclised by acetic anhydride, nor did its ester (VI; R = R′ = Me) undergo the Dieckmann reaction. Attention was therefore directed to 2-acylcoumaran-3-ones in which but one incoming substituent could be accommodated at the 2-position.

The glyoxylic ester (VII) formed from the coumaranone (IV; R = Me) and ethyl

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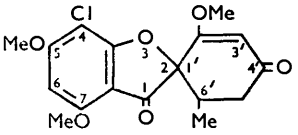
[1] Grove, MacMillan, Mulholland, and Rogers, *J.*, 1952, 3977.
[2] Dean, Halewood, Mongkolsuk, Robertson, and Whalley, *J.*, 1953, 1250.
[3] Michael and Ross, *J. Amer. Chem. Soc.*, 1931, **53**, 1150.
[4] Bruson, *ibid.*, 1942, **64**, 2457.
[5] Ziegler, Eberle, and Ohlinger, *Annalen*, 1933, **504**, 94.

oxalate did not give the desired β-keto-ester when heated with powdered glass. Whilst 2-acetyl-4 : 6-dimethylcoumaran-3-one (VIII) was readily accessible by Claisen condensation of the coumaranone (IV; R = Me), this reaction failed to produce the dimethoxy-derivative (X), possibly because electronic interaction between the carbonyl group and the methoxyl groups of the coumaranone (IV; R = OMe) interferes with activation of the 2-position. However, the required acetylcoumaranone (X) was prepared by base-catalysed rearrangement of the enol acetate (IX) [obtained by acetylation of the coumaranone (IV; R = MeO)] or by simultaneous rearrangement and cyclisation[6] of 2-acetoxy-ω-chloro-4 : 6-dimethoxyacetophenone (XI) induced by sodium acetate.



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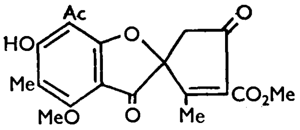

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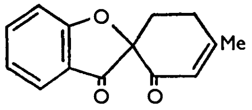

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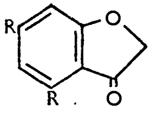

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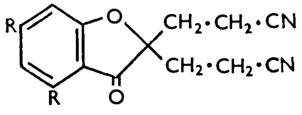

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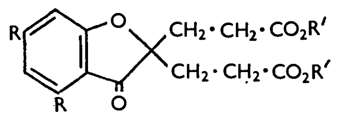

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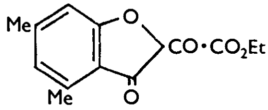

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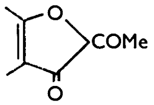

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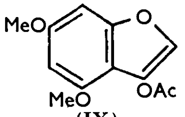

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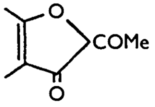

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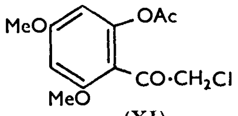

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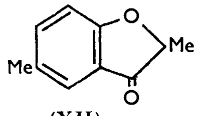

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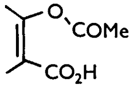

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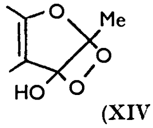

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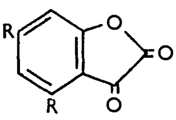

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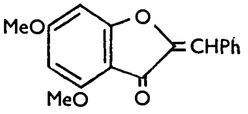

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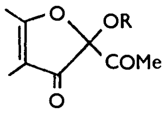

(XVII)

Alkylation and addition reactions of the 2-acetylcoumaranones (VIII) and (X) were complicated by attack by air. Autoxidation of simple coumaranones was examined by von Auwers,[7] who regarded (for example) the production of the acetate (XIII) from the 2-methylcoumaranone (XII) as evidence for an intermediate of structure (XIV). When aerated, however, both 2-acetylcoumaranones (VIII) and (X) lost their acetyl groups to give the coumaran-2 : 3-diones (XV; R = Me or OMe) in which the link between $C_{(2)}$ and $C_{(3)}$ is intact. The dione (XV; R = Me) was characterised by its smooth conversion into 2-hydroxy-4 : 6-dimethylbenzoic acid in alkaline hydrogen peroxide, whilst the dione (XV; R = MeO) was identified with an authentic specimen prepared by ozonolysis of the benzylidenecoumaranone[8] (XVI). Autoxidations of this kind are now usually

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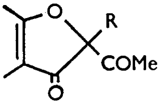
[6] Philbin, O'Sullivan, and Wheeler, *J.*, 1955, 860.

[7] von Auwers, *Ber.*, 1910, **43**, 2192.

[8] Dumont and Tambor, *Ber.*, 1910, **43**, 1969.

considered[9] to involve hydroperoxides of type (XVII; R = OH) and it was therefore of interest that 2-acetyl-4 : 6-dimethoxycoumaran-3-one (X) gave, not only the dione (XV; R = OMe), but also the alcohol (XVII; R = H). The last compound had infrared bands (Nujol) at 3310 and 3270 (OH), 1724 (acetyl C:O), and 1686 cm.$^{-1}$ (coumaranone C:O lowered by hydrogen bonding), and ultraviolet absorption close to that of 4 : 6-dimethoxycoumaran-3-one; enolisable hydrogen was absent since, unlike its parent, it gave no immediate ferric reaction. In confirmation of structure (XVII; R = H) the derived acetate was also produced by reaction between the 2-acetylcoumaranone (X) and lead tetra-acetate. Autoxidation was not observed with any 2 : 2-disubstituted coumaran-3-one.

Alkylation of 2-acetylcoumaran-3-ones might give *C*-alkyl compounds of type (XVIII), and *O*-alkyl compounds of types (XIX) and (XX), distinguishable by spectroscopic and chemical properties. Compounds (XVIII) had the same ultraviolet absorption spectrum as the parent coumaran-3-ones, whereas compounds (XIX) had spectra similar to those of 2-acetylbenzofurans. Unfortunately, no model compound of type (XX) was available, but on general grounds its ultraviolet absorption was expected to differ from that of types (XVIII) or (XIX). In the infrared region, compounds with the grouping (XVIII) showed the expected dual absorption at (approximately) 1720 and 1698 cm.$^{-1}$, whilst those with the grouping (XIX) had but one band near 1670 cm.$^{-1}$, similar to that of an αβ-unsaturated ketone. Conjugated ketones of type (XX) are usually considered[10] to absorb below 1640 cm.$^{-1}$ so that it was somewhat surprising to find that 2-benzylidene-4 : 6-dimethoxycoumaran-3-one had carbonyl absorption similar to that at 1698 cm.$^{-1}$ of simple coumaran-3-ones: double-bond absorption occurred at 1661 cm.$^{-1}$. As an additional criterion, therefore, emphasis was placed on carbonyl derivatives, because coumaran-3-ones are well known[11] for their unreactivity in this respect, whereas compounds with groupings (XVIII) and (XIX) gave monosemicarbazones and other derivatives without difficulty in virtue of their acetyl groups. In the event, compounds of types (XVIII) and (XIX) were formed, but compounds of type (XX) were not.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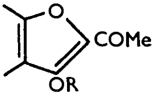
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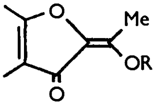
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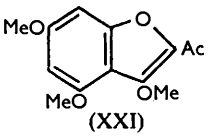
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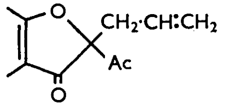
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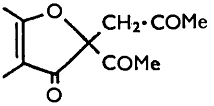
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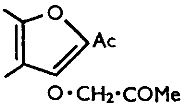
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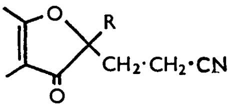
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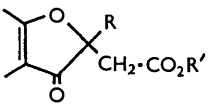
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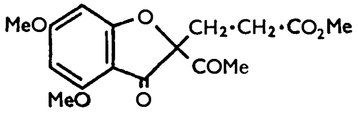
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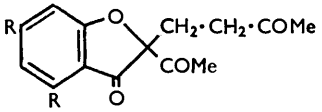
(XXVIII)

Methylation of 2-acetyl-4 : 6-dimethoxycoumaran-3-one (X) with methyl sulphate and aqueous alkali gave a product assigned structure (XXI) by means of the criteria discussed above. In contrast, there was no reaction between the dry sodium salt of the acetylcoumaranone (X) and methyl iodide, whilst with allyl bromide incursion of

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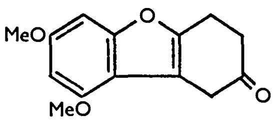
[9] Hawkins, *Quart. Rev.*, 1950, **4**, 251.
[10] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1954.
[11] (*a*) Mulholland, *J.*, 1952, 3995; (*b*) Grove, MacMillan, Mulholland, and Rogers, *J.*, 1952, 3949.

C-alkylation resulted in the diketone (XXII). With chloroacetone, *O*- and *C*-alkylation were concurrent, the products being the triketone (XXIII) and the benzofuran (XXIV). Cyanoethylation of 2-acetyl-4 : 6-dimethoxycoumaran-3-one (X) gave the dioxocyanide (XXV; R = Ac), hydrolysis of which supplied the monoadduct (XXV; R = H) not available directly from 4 : 6-dimethoxycoumaran-3-one (X). The cyanide band of (XXV; R = H) at 2257 cm.$^{-1}$ was abnormally weak: similarly, the acetyl derivative (XXV; R = Ac) and even the dicyanide (V; R = MeO) had very weak cyanide bands; in spite of the greater distance between the interacting groups, this is probably related to the " cyanide quenching " noted [12] in the acetates of cyanohydrins. 2-Acetyl-4 : 6-dimethylcoumaran-3-one (VIII) by cyanoethylation and hydrolysis led to the cyanide (XXV; R = H, Me for OMe). Obtained from the appropriate acetylcoumaranone (VIII) and ethyl bromoacetate, the ester (XXVI; R = Ac; R′ = Et) also lost its acetyl group when hydrolysed and furnished the acid (XXVI; R = R′ = H), whilst the ester (XXVII) and the triketones (XXVIII; R = Me or OMe) were available by reaction of the requisite coumaranones (VIII) and (X) with methyl acrylate and methyl vinyl ketone respectively.

Of the many possibilities for ring-closure of these compounds to *spiro*coumaranones, those needing basic reagents were discounted partly because of earlier failures and partly for fear of reversed Michael additions and of loss of the 2-acetyl groups. Indeed, no definite product was formed by sodium methoxide from the ketonic esters (XXVI; R = Ac, R′ = Et) and (XXVII) and, in basic media, the triketone (XXVIII; R = OMe) lost its acetyl group and cyclised (with rearrangement of the double-bond produced) to the benzofuran (XXIX) (cf. Henecka [13]). On the other hand, two types of compound appeared to be suitable for acid-induced cyclodehydration. Of these, (XXIII) would lead to compounds in the usnolic acid group, and (XXVIII) to compounds in the griseofulvin group. The latter has now been examined.



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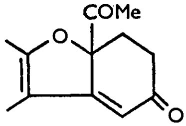
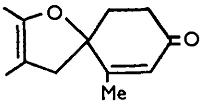


(XXX)



(XXXI)

Ring-closure could give products of the types (XXX), (XXXI), and (XXXII). The cyclised materials from the triketone (XXVIII; R = Me or OMe) had spectra showing that extended conjugated systems and isolated acetyl groups as in (XXX) were absent: further, the dimethoxy-product resembled griseofulvin (I) spectroscopically. Thus structure (XXXI) or (XXXII) was indicated, but differentiation between them was less easy. It had been found by Grove *et al.*[1] that, in the griseofulvin series, a 4′-carbonyl group [grisan numbering: see (I)] gave normal ketone reactions whereas a 2′-carbonyl group was unreactive. Although the dehydration product from (XXVIII; R = OMe) readily formed a 2 : 4-dinitrophenylhydrazone and resisted acid hydrolysis, structure (XXXI) was invalid because chromic acid did not give a quinone and because controlled oxidation conclusively favoured structure (XXXII): the product from (XXVIII; R = Me) is presumed to be constituted similarly.

A diol was obtained by oxidation with zinc permanganate or (less satisfactorily) osmium tetroxide. Had this diol possessed structure (XXXIII), periodate must have produced from it the acid related to (XXVII). Now the triketone (XXVIII; R = OMe), the dicyanide (V; R = OMe), and the dehydration product of (XXVIII; R = OMe) were stable to periodate under the conditions used, so no further degradation of the acid (XXVII;

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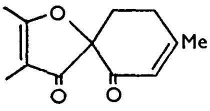
[12] Kitson and Griffith, *Analyt. Chem.*, 1952, **24**, 334.
[13] Henecka, *Chem. Ber.*, 1948, **81**, 197.

CO_2H for CO_2Me) was to be expected. However, periodate oxidation of the diol caused degradation to 2-hydroxy-4 : 6-dimethoxybenzoic acid (XXXVII) as the sole crystalline product (a non-volatile water-soluble ketone which unfortunately escaped characterisation is now thought to have been lævulic acid or an equivalent). Thus the diol has structure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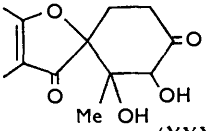
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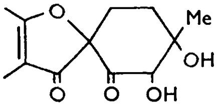
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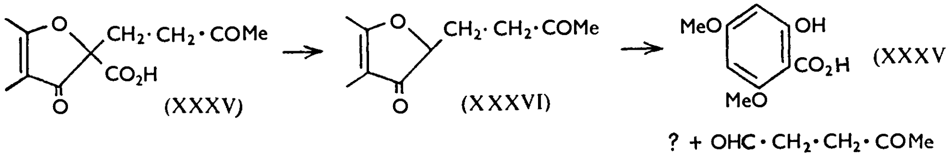
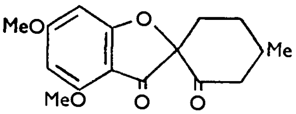

(XXXV) (XXXVI) (XXXVII)

(XXXIV), and its oxidation involves the steps (XXXV) and (XXXVI). Periodates are able to oxidise coumaran-3-ones with at least one hydrogen atom in the 2-position : 6-methoxycoumaran-3-one gave 2-hydroxy-4-methoxybenzoic acid, and 2-acetyl-4 : 6-dimethoxycoumaran-3-one (X) gave 4 : 6-dimethoxycoumaran-2 : 3-dione (XV; R = MeO) (cf. Wolfrom and Bobbitt [14]), thus paralleling aerial oxidation.

Hydrogenation of the grisen (XXXII) over palladium–charcoal furnished the grisan (XXXVIII) which unlike the derivative from griseofulvin [11a] readily supplied a semicarbazone, but as a β-diketone underwent alkaline hydrolysis in conditions in which 3 : 4′-dioxogrisans are stable : the hydrolysis product was extremely difficult to purify, but was essentially the expected acid (XXXIX). These conclusions were confirmed by the details kindly communicated to us by Dr. J. MacMillan and Dr. P. J. Suter who obtained the 3 : 4′-dioxogrisan (XL) by degradation of dechlorogriseofulvin (see following paper).

Hydrogenation of the *spiro*coumaranone (XXXII) on Raney nickel supplied two alcohols (XLI) both of which were oxidised to the ketone (XXXVIII) and so differed only in the configuration of the hydroxyl group. Spectra of the alcohols and the ketone were typical of coumaran-3-ones, confirming their spirocyclic structure since the derivatives of (XXX) must have had widely different properties. Finally, the alcohols (XLI) have been oriented tentatively. One, m. p. 163—165°, had an absorption band at 1698 cm.$^{-1}$; the other, m. p. 159—160°, at 1692 cm.$^{-1}$ (in solution). This bathochromic shift, typical [15] of non-conjugated hydrogen-bonding in hydroxy-ketones and also shown by the ketol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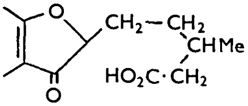
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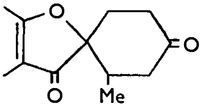
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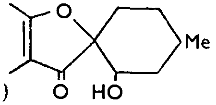
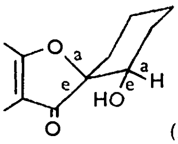

(XLI)


(XLII)

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[14] Wolfrom and Bobbitt, *J. Amer. Chem. Soc.*, 1956, **78**, 2489.

[15] Rasmussen, Tunnicliff, and Brattain, *ibid.*, 1949, **71**, 1068.

(XVII; R = H), is taken as indicating proximity of the two groups, as in (XLI). In agreement, this isomer is the more soluble in benzene and somewhat the lower-melting. If the *cyclo*hexane has the usual chair form, the coumaranone-carbonyl group must be attached by an equatorial bond to avoid severe crowding. Then, for hydrogen-bonding, the hydroxyl group must be in this isomer, as in (XLII). No evidence regarding the disposition of the methyl group is to hand.

EXPERIMENTAL

Unless qualified, "light petroleum" refers to the fraction of b. p. 60—80°, and infrared spectra were determined in Nujol mulls by means of a Grubb-Parsons double-beam spectrophotometer. Ultraviolet spectra were determined for $\sim 10^{-3}$M-solutions in alcohol.

4 : 6-Dimethylcoumaran-3-one (IV; R = Me) had $\lambda_{\text{max.}}$ 262, 328 mμ (log ε 4·09, 3·70) and carbonyl absorption at 1701 cm.$^{-1}$.

4 : 6-Dimethoxycoumaran-3-one (IV; R = OMe) had $\lambda_{\text{max.}}$ 283, 315 mμ (log ε 4·33, 3·73) and carbonyl absorption at 1698 cm.$^{-1}$.

2 : 2-*Di-2′-cyanoethyl*-4 : 6-*dimethylcoumaran*-3-*one* (V; R = Me).—After addition of Triton B (2·5 ml.) to a stirred solution of 4 : 6-dimethylcoumaran-3-one (4·9 g.) in freshly purified dioxan (14 ml.), introduction of vinyl cyanide (7 ml.) was regulated to avoid a rise in temperature beyond 45°. 4 hr. later, the mixture was acidified with dilute hydrochloric acid and diluted to 250 ml. to precipitate the product as a red mass which, when washed with water and crystallised from 95% alcohol, gave the *dicyanide* (V; R = Me) in rhombic prisms (6·5 g.), m. p. 96—97° (Found: C, 71·3; H, 6·0; N, 10·5. $C_{16}H_{16}O_2N_2$ requires C, 71·6; H, 6·0; N, 10·4%). This was unaffected by lithium ethylanilide in ether during 4 hr. Using 1 equiv. of vinyl cyanide (0·6 g.) and 4 : 6-dimethylcoumaran-3-one (2 g.) also gave the dicyanide (1 g.), m. p. and mixed m. p. 97°, and unchanged coumaranone (0·7 g.).

2 : 2-*Di*-2′-*carboxyethyl*-4 : 6-*dimethylcoumaran*-3-*one* (VI; R = Me, R′ = H).—When ammonia was no longer evolved from a mixture of the dicyanide (V; R = Me) (2 g.) and 2N-aqueous sodium hydroxide (25 ml.) at the b. p. (40 hr.), the solution was cooled, washed with ether, and acidified with dilute sulphuric acid. The precipitated *acid* formed needles (2·1 g.), m. p. 176—178°, from aqueous methanol (Found: C, 62·6; H, 6·1. $C_{16}H_{18}O_6$ requires C, 62·7; H, 5·9%). It was recovered by extraction with aqueous sodium hydrogen carbonate of the mass formed when it was heated with acetic anhydride for 4 hr., then freed from reagent, and heated at 230° for 10 min.

With ethereal diazomethane, this acid (2 g.) gave the *dimethyl ester* (VI; R = R′ = Me), needles (from dilute methanol) (1·9 g.), m. p. 104—105° [Found: C, 64·3; H, 6·7; OMe, 18·7. $C_{16}H_{16}O_4(OMe)_2$ requires C, 64·7; H, 6·6; OMe, 18·6%]. This ester (1 g.), in boiling benzene (25 ml.) containing powdered sodium (0·07 g.) and a drop of methanol, was unchanged after 6 hr. apart from slight hydrolysis to the acid, m. p. and mixed m. p. 177°.

2 : 2-*Di*-2′-*cyanoethyl*-4 : 6-*dimethoxycoumaran*-3-*one* (V; R = OMe).—4 : 6-Dimethoxycoumaran-3-one (2 g.) and vinyl cyanide (8 ml.) interacted in the presence of Triton B (1 ml.) as described for the 4 : 6-dimethyl analogue. The *dicyanide* crystallised from methanol in needles (2·5 g.), m. p. 154—155° [Found: C, 63·8; H, 5·6; N, 9·4; OMe, 17·4. $C_{14}H_{10}O_2N_2(OMe)_2$ requires C, 64·0; H, 5·4; N, 9·3; OMe, 20·7%].

Ethyl 4 : 6-*Dimethyl*-3-*oxocoumaran*-2-*glyoxylate* (VII).—A solution of ethyl oxalate (4 g.) and 4 : 6-dimethylcoumaran-3-one (5 g.) in ether (100 ml.) was added gradually to a suspension of sodium ethoxide from sodium (0·7 g.) and magnesium-dried alcohol also in ether. After a further ½ hr. at room temperature, the insoluble sodium salt was collected, washed with ether, and decomposed by ice-cold dilute sulphuric acid to liberate a product which, purified from alcohol, gave the *glyoxylate* in yellow needles (4 g.), m. p. 113°, having a brown ferric reaction in alcohol and subliming unchanged when heated with powdered glass and iron filings under reduced pressure at 160° (Found: C, 63·9; H, 5·5; OEt, 15·5. $C_{12}H_9O_4{\cdot}OEt$ requires C, 64·1; H, 5·4; OEt, 17·2%).

2-*Acetyl*-4 : 6-*dimethylcoumaran*-3-*one* (VIII).—To a suspension of powdered sodium (1·5 g.) in boiling ether (50 ml.), magnesium-dried alcohol (3·8 ml.) was added during 1 hr. After a further 4 hr. at the b. p., the stirred mixture was treated with ethyl acetate (25 ml.) added in one portion, and then 4 : 6-dimethylcoumaran-3-one (10 g.) in ether (200 ml.) was added during

15 min. : ½ hr. later the precipitated sodium salt was collected and dissolved in water. When this solution was reddish, it was clarified with charcoal before liberation of the product by dilute sulphuric acid at 0°. When crystallised from alcohol, the precipitate supplied the acetylcoumaranone (VIII) in needles (11·0 g.), m. p. 83°, with a green ferric reaction. Because of its instability in air, this compound gave erratic analytical results but its derivatives were comparatively stable. The *semicarbazone* separated from alcohol in faintly yellow needles, m. p. 206° (Found: C, 59·7; H, 5·8; N, 16·2. $C_{13}H_{15}O_3N_3$ requires C, 59·8; H, 5·8; N, 16·1%), and the 2 : 4-*dinitrophenylhydrazone* from dioxan in scarlet needles, m. p. 224—226° (decomp.) (Found: C, 55·9; H, 4·2; N, 14·6. $C_{18}H_{16}O_6N_4$ requires C, 56·3; H, 4·2; N, 14·6%).

2-*Acetyl*-4 : 6-*dimethoxycoumaran*-3-*one* (X).—(i) 4 : 6-Dimethoxycoumaran-3-one (2 g.) and sodium acetate (0·8 g.) in refluxing acetic anhydride (17 ml.) gave in ½ hr. a product, which when isolated by addition of crushed ice and purified from light petroleum (b. p. 40—60°) supplied 3-*acetoxy*-4 : 6-*dimethoxybenzofuran* (IX) as rhombs (1·5 g.), m. p. 71—72°, $\lambda_{max.}$ 256 mμ (log ε 4·15) (Found: C, 61·2; H, 5·0. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%). Isomerised by potassium carbonate (5 g.) in boiling benzene (20 ml.) during 5 hr., this acetate (3 g.) gave a potassium salt from an aqueous solution of which 2N-sulphuric acid freed 2-*acetyl*-4 : 6-*dimethoxycoumaran*-3-*one* (X) separating from alcohol in needles (0·9 g.), m. p. 110°, with a green ferric reaction [Found: C, 61·1; H, 5·2; OMe, 26·6. $C_{10}H_6O_3(OMe)_2$ requires C, 61·0; H, 5·1; OMe, 26·3%]. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethylene glycol dimethyl ether in dark red-brown needles, m. p. 219—220° (Found: C, 51·9; H, 4·0; N, 13·3. $C_{18}H_{16}O_8N_4$ requires C, 51·9; H, 3·9; N, 13·5%).

(ii) Interaction of chloromethyl cyanide (5·4 ml.) and phloroglucinol dimethyl ether (10 g.) in ether (250 ml.) saturated with hydrogen chloride at 0° and containing zinc chloride (5 g.) gave in one day an aldimine hydrochloride which was hydrolysed in ½ hr. by boiling water and then, when fractionally crystallised from alcohol, supplied (as the less soluble component) ω-chloro-2-hydroxy-4 : 6-dimethoxyacetophenone (5 g.), m. p. 149°, undepressed by a sample prepared according to directions of Freudenberg, Fikentscher, and Harder.[16] The *acetate* (XI) formed plates, m. p. 86—87°, devoid of a ferric reaction, from benzene–light petroleum (Found: C, 52·9; H, 4·8; Cl, 12·9. $C_{12}H_{13}O_5Cl$ requires C, 52·8; H, 4·8; Cl, 13·0%). The more soluble product from the Hoesch reaction was purified from a small volume of alcohol and gave ω-*chloro*-4-*hydroxy*-2 : 6-*dimethoxyacetophenone* as rhombs (4·5 g.), m. p. 188° (Found: C, 52·2; H, 4·8; Cl, 15·3. $C_{10}H_{11}O_4Cl$ requires C, 52·1; H, 4·8; Cl, 15·4%), with a negative ferric reaction, and forming an *acetate* which crystallised from light petroleum in needles, m. p. 86° (Found: C, 53·1; H, 4·9; Cl, 12·8. $C_{12}H_{13}O_5Cl$ requires C, 52·8; H, 4·8; Cl, 13·0%).

The potassium salts obtained when the acetate (XI) (14·7 g.) was heated with potassium carbonate (68 g.) in boiling benzene (225 ml.) for 5 hr. were washed with ether and then with a small volume of water which removed much of the residual potassium carbonate. The remaining salts were treated in water with charcoal, whereafter acidification of the filtrate with 2N-sulphuric acid precipitated 2-acetyl-4 : 6-dimethoxycoumaran-3-one (X) (8·7 g.) identical with material from (i) above.

4 : 6-*Dimethoxycoumaran*-2 : 3-*dione* (XV; R = OMe).—During 1 hr. a stream of ozonised oxygen was passed through 2-benzylidene-4 : 6-dimethoxycoumaran-3-one [8] (1 g.) in ethyl acetate (25 ml.) at 0°. The residue from evaporation of the solvent was digested with water producing a solid that, when washed with aqueous sodium hydrogen carbonate and then with a little alcohol, was purified from ethyl acetate, giving 4 : 6-*dimethoxycoumaran*-2 : 3-*dione* (XV; R = OMe) in yellow needles (0·5 g.), m. p. 198—200°, having a reddish ferric reaction in alcohol [Found: C, 57·7; H, 3·8; OMe, 30·3. $C_8H_2O_3(OMe)_2$ requires C, 57·7; H, 3·9; OMe, 29·8%].

2-*Acetoxy*-2-*acetyl*-4 : 6-*dimethoxycoumaran*-3-*one* (XVII; R = Ac).—2 hr. after dropwise addition of a solution of lead tetra-acetate (0·9 g.) in the minimum of acetic acid to 2-acetyl-4 : 6-dimethoxycoumaran-3-one (0·5 g.), in acetic acid at 10°, removal of the solvent under reduced pressure left an oil which crystallised when its ethereal solution was allowed to evaporate. Purification of the solid from benzene–light petroleum (charcoal) supplied 2-*acetoxy*-2-*acetyl*-4 : 6-*dimethoxycoumaran*-3-*one* (XVII; R = Ac) in prisms (0·3 g.), m. p. 162—163° [Found: C, 57·0; H, 4·9; OAc, 29·0. $C_{10}H_8O_3(OAc)_2$ requires C, 57·1; H, 4·8; OAc, 29·3%].

Autoxidation of 2-*Acetyl*-4 : 6-*dimethoxycoumaran*-3-*one*.—A solution of this coumaranone in

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[16] Freudenberg, Fikentscher, and Harder, *Annalen*, 1925, **441**, 168.

benzene or light petroleum soon gave a positive reaction with the starch–iodide reagent when kept in air. After 3 days (or 6 hr. when air was bubbled through the solution) the green ferric reaction given by the original material could no longer be detected, and partial crystallisation had occurred. Recrystallised from ethyl acetate, the product furnished 4 : 6-dimethoxycoumaran-2 : 3-dione in yellow needles, m. p. and mixed m. p. 196°. On evaporation the mother-liquors yielded colourless needles which, when separated by hand from the accompanying dione, crystallised from benzene–light petroleum giving 2-*acetyl*-2-*hydroxy*-4 : 6-*dimethoxycoumaran*-3-*one* (XVII; R = H) in needles, m. p. 170—176° (decomp.) [Found: C, 57·0; H, 4·8; OMe, 23·8%; *M* (micro-Rast), 244. $C_{10}H_6O_4(OMe)_2$ requires C, 57·1; H, 4·8; OMe, 24·6%; *M*, 252]. When kept with ferric chloride, an alcoholic solution of this substance developed a red-brown colour. It had ultraviolet absorption max. at 293, 325 mμ (log ε 4·31, 3·70), and infrared absorption at 3310 and 3270 (hydrogen-bonded OH), 1724 (aliphatic C:O), and 1686 cm.$^{-1}$ (coumaranone C:O with hydrogen bonding). With acetic anhydride containing a trace of sulphuric acid, this alcohol gave the acetate (XVII; R = Ac), m. p. and mixed m. p. 162—163°.

Autoxidation of 2-*Acetyl*-4 : 6-*dimethylcoumaran*-3-*one*.—After a few hours in contact with air, a solution of 2-acetyl-4 : 6-dimethylcoumaran-3-one in light petroleum (b. p. 40—60°) lost its green ferric reaction and liberated iodine from iodides. Removal of the solvent and crystallisation of the residue from light petroleum furnished 4 : 6-dimethylcoumaran-2 : 3-dione in yellow needles, m. p. 145° (Fries [17] gives m. p. 145°) (Found: C, 68·6; H, 4·7. Calc. for $C_{10}H_8O_3$: C, 68·2; H, 4·6%). From a solution of this dione in 2N-aqueous sodium hydroxide which had been treated for a few minutes with 1% hydrogen peroxide at 0°, acidification liberated 2-hydroxy-4 : 6-dimethylbenzoic acid, m. p. and mixed m. p. 168°.

2-*Acetyl*-3 : 4 : 6-*trimethoxybenzofuran* (XXI).—Methyl sulphate was added in small portions and with agitation to 2-acetyl-4 : 6-dimethoxycoumaran-3-one (1 g.) dissolved in alcohol (15 ml.) containing 2N-sodium hydroxide (10 ml.), further quantities of base being added intermittently. When the mixture remained clear in the presence of an excess of alkali, it was diluted with water until precipitation was complete. Purified from light petroleum, the deposit gave 2-*acetyl*-3 : 4 : 6-*trimethoxybenzofuran* (XXI) in needles (0·5 g.), m. p. 133°, $\lambda_{max.}$ 248, 328 mμ (log ε 4·19, 4·35) [Found: C, 62·6; H, 5·7; OMe, 37·0. $C_{10}H_5O_2(OMe)_3$ requires C, 62·4; H, 5·6; OMe, 37·2%]. The *semicarbazone* separated from methanol in needles, m. p. 234° [Found: C, 55·0; H, 5·6; N, 14·0; OMe, 30·1. $C_{11}H_8O_2N_3(OMe)_3$ requires C, 54·7; H, 5·6; N, 13·7; OMe, 30·3%]; the 2 : 4-*dinitrophenylhydrazone* crystallised from benzene in red needles, m. p. 236° [Found: 53·7; H, 4·2; N, 13·1; OMe, 20·7. $C_{16}H_9O_5N_4(OMe)_3$ requires C, 53·0; H, 4·2; N, 13·0; OMe, 21·6%].

2-*Acetyl*-2-*allyl*-4 : 6-*dimethoxycoumaran*-3-*one* (XXII).—For this and similar alkylations the sodium salt of 2-acetyl-4 : 6-dimethoxycoumaran-3-one was prepared by addition of the requisite amount of alcoholic sodium ethoxide to a solution of the β-diketone in warm alcohol and then separated in a finely divided state suitable for desiccation at 100° before use.

The sodium salt (2 g.) of 2-acetyl-4 : 6-dimethoxycoumaran-3-one was heated under reflux with allyl bromide (10 ml.) for 3 hr. After distillation of the excess of allyl bromide, the residue was washed with a little water and then crystallised from alcohol in needles (1·8 g.), m. p. 119—120°, $\lambda_{max.}$ 288, 325 mμ (log ε 4·31, 3·69) [Found: C, 65·3; H, 6·1; OMe, 23·4. $C_{13}H_{10}O_3(OMe)_2$ requires C, 65·2; H, 5·8; OMe, 22·5%], CO bands at 1698 and at 1718 cm.$^{-1}$ (weak). The 2 : 4-*dinitrophenylhydrazone* formed orange rhombs, m. p. 190°, from alcohol [Found: N, 12·2; OMe, 13·7. $C_{19}H_{14}O_6N_4(OMe)_2$ requires N, 12·3; OMe, 13·6%], and the *semicarbazone* crystallised from dilute alcohol in needles, m. p. 226—227° [Found: N, 12·7; OMe, 18·6. $C_{14}H_{13}O_3N_3(OMe)_2$ requires N, 12·6; OMe, 18·6%].

2-*Acetonyl*-2-*acetyl*-4 : 6-*dimethoxycoumaran*-3-*one* (XXIII).—Isolated with ether, the product obtained by addition of water to a mixture of the sodium salt (2 g.) of 2-acetyl-4 : 6-dimethoxycoumaran-3-one and chloroacetone (8 ml.) which had been kept at 120° for 3 hr. was treated at 100° *in vacuo* to remove the excess of chloroacetone. The liquid residue was taken up in ether and kept at 0° until partial crystallisation occurred, after which evaporation of the filtrate and trituration of the viscous residue with a little methanol gave further quantities of solid which were combined with the original crystalline precipitate (combined yield, 1·5 g.). Aided by hand picking, fractional crystallisation of the solid from methanol gave two products.

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[17] Fries, *Annalen*, 1925, **442**, 262.

2-*Acetonyl*-2-*acetyl*-4 : 6-*dimethoxycoumaran*-3-*one* (XXIII) formed plates, m. p. 157°, $\lambda_{max.}$ 288, 325 mμ (log ε 4·35, 3·72) [Found : C, 61·7; H, 5·7; OMe, 21·4. $C_{13}H_{10}O_4(OMe)_2$ requires C, 61·6; H, 5·5; OMe, 21·2%], and showed one broad band at 1701 cm.$^{-1}$ attributed to unresolved carbonyl peaks; the 3-*acetonyloxy*-2-*acetyl*-4 : 6-*dimethoxybenzofuran* (XXIV) formed needles, m. p. 116—117°, $\lambda_{max.}$ 248, 328 mμ (log ε 4·20, 4·32) (Found : C, 61·3; H, 5·5; OMe, 21·1), the infrared spectrum of which had one peak at 1736 cm.$^{-1}$ (aliphatic C:O with an electronegative α-substituent) and a second at 1661 cm.$^{-1}$ (C:O of 2-acetylbenzofuran).

2-2′-*Cyanoethyl*-4 : 6-*dimethoxycoumaran*-3-*one* (XXV; R = H).—Vinyl cyanide (10 ml.) was added gradually and with stirring to 2-acetyl-4 : 6-dimethoxycoumaran-3-one (6 g.) in dioxan (40 ml.) containing Triton B (2·5 ml.). After 3 hr., the product resulting from acidification and dilution was washed with a little ether and purified from dilute alcohol, giving the 2-2′-*cyanoethylcoumaran*-3-*one* (XXV; R = Ac) in needles (5·5 g.), m. p. 140°, with a negative ferric reaction [Found : C, 62·0; H, 5·4; N, 4·8; OMe, 21·7. $C_{13}H_9O_3N(OMe)_2$ requires C, 62·3; H, 5·2; N, 4·8; OMe, 21·4%], infrared bands at 2257 (C⋮N), 1715 (COMe), and 1704 cm.$^{-1}$ (coumaranone C:O). The 2 : 4-*dinitrophenylhydrazone* separated from alcohol in orange-yellow needles, m. p. 195° [Found : C, 53·4; H, 4·3; N, 15·1; OMe, 13·7. $C_{19}H_{13}O_6N_5(OMe)_2$ requires C, 53·7; H, 4·1; N, 14·9; OMe, 13·2%], and the *semicarbazone* in rhombs, m. p. 234°, from aqueous alcohol [Found: N, 16·1; OMe, 18·0. $C_{14}H_{12}O_3N_4(OMe)_2$ requires N, 16·2; OMe, 17·9%].

This coumaranone (0·5 g.) was heated under reflux with water (30 ml.) and sulphuric acid (5 ml.) for 1 hr. Isolated by decantation, the residue was washed with aqueous sodium hydrogen carbonate and crystallised from dilute alcohol or benzene–light petroleum, giving 2-2′-*cyanoethyl*-4 : 6-*dimethoxycoumaran*-3-*one* (XXV; R = H) in prisms (0·3 g.), m. p. 123°, which did not give the usual carbonyl derivatives [Found : C, 63·0; H, 5·5; N, 5·7; OMe, 24·5. $C_{11}H_7O_2N(OMe)_2$ requires C, 63·2; H, 5·3; N, 5·7; OMe, 25·1%] and had infrared peaks at 2249 (C⋮N) and 1698 cm.$^{-1}$ (coumaranone C:O).

2-2′-*Cyanoethyl*-4 : 6-*dimethylcoumaran*-3-*one* (XXV; R = H, Me for OMe).—Vinyl cyanide (4 ml.) and 2-acetyl-4 : 6-dimethylcoumaran-3-one (2 g.) in dioxan (6 ml.) containing Triton B (2 ml.), gave, as above (4 hr.) a product, isolated with ether, which distilled at 60—70°/0·001 mm. and then solidified in contact with 2N-aqueous sodium hydroxide. Recrystallisation from alcohol gave the 2-*cyanoethylcoumaranone* in needles (1·0 g.), m. p. 108°, devoid of carbonyl activity (Found : C, 72·5; H, 5·8; N, 6·4. $C_{13}H_{13}O_2N$ requires C, 72·5; H, 6·1; N, 6·5%).

Ethyl 2-*Acetyl*-4 : 6-*dimethyl*-3-*oxocoumaran*-2-*ylacetate* (XXVI; R = Ac, R′ = Et).—The sodium salt (4·4 g.) of 2-acetyl-4 : 6-dimethylcoumaran-3-one was kept with ethyl bromoacetate (5 ml.) at 145° for 3 hr. Water (25 ml.) was added and the product, isolated with ether, was heated on the steam-bath *in vacuo* to remove volatile material. Distillation of the residue supplied a fraction, b. p. 148—152°/0·05 mm., which was devoid of a ferric reaction and, when further purified by chromatography from benzene on a column of " acid " aluminium oxide followed by re-distillation, gave the *ethyl ester* as a pale yellow viscous oil, b. p. 150°/0·05 mm., $\lambda_{max.}$ 267, 328 mμ (log ε 4·13, 3·68) (Found : C, 66·2; H, 6·1; OEt, 15·7. $C_{14}H_{13}O_4{\cdot}OEt$ requires C, 66·2; H, 6·2; OEt, 15·5%), having infrared peaks at 1761 (ester) and 1718 cm.$^{-1}$ (unresolved carbonyl bands). From alcohol, the *semicarbazone* was obtained as plates, m. p. 214° (Found: C, 58·8; H, 6·0; N, 12·2; OEt, 13·9. $C_{15}H_{16}O_4N_3{\cdot}OEt$ requires C, 58·8; H, 6·1; N, 12·1; OEt, 13·0%).

Hydrolysed by 20% hydrochloric acid (120 ml.) at the b. p. for 1 hr., the ester (1 g.) gave the acid (XXVI; R = R′ = H), isolated with ether and sodium hydrogen carbonate solution, and crystallising from dilute alcohol in needles (0·6 g.), m. p. 139° (Found : C, 65·5; H, 5·7. $C_{12}H_{12}O_4$ requires C, 65·4; H, 5·5%).

Methyl β-(2-*Acetyl*-4 : 6-*dimethoxy*-3-*oxocoumaran*-2-*yl*)*propionate* (XXVII).—Triton B (1·5 ml.), 2-acetyl-4 : 6-dimethoxycoumaran-3-one (3 g.) and methyl acrylate (6 ml.) in dioxan (18 ml.) (5 hr.) led, as above, to a solid that, purified from light petroleum, gave the *propionate* (XXVII) in needles (2·8 g.), m. p. 92°, having a negative ferric reaction and $\lambda_{max.}$ 288, 325 mμ (log ε 4·33, 3·69) [Found : C, 59·5; H, 5·8; OMe, 28·9. $C_{13}H_9O_4(OMe)_3$ requires C, 59·6; H, 5·6; OMe, 28·9%] : the infrared spectrum possessed the expected peaks at 1748 (ester) and 1706 cm.$^{-1}$ (unresolved C:O absorptions). The 2 : 4-*dinitrophenylhydrazone* separated from alcohol in needles, m. p. 166° [Found : C, 52·7; H, 4·5; N, 11·0; OMe, 18·6. $C_{19}H_{13}O_7N_4(OMe)_3$ requires C, 52·6; H, 4·4; N, 11·2; OMe, 18·5%]; the *semicarbazone* formed prisms, m. p. 214—216°, from alcohol [Found : N, 10·8; OMe, 24·6. $C_{14}H_{12}O_4N_3(OMe)_3$ requires N, 11·1; OMe, 24·6%].

*2-Acetyl-2-3′-oxo-*n*-butyl-4 : 6-dimethylcoumaran-3-one* (XXVIII; R = Me).—The dropwise addition of aqueous methyl vinyl ketone (azeotropic mixture; 6 ml.) to a stirred solution of 2-acetyl-4 : 6-dimethylcoumaran-3-one (6·2 g.) and Triton B (1·5 ml.) in dioxan (20 ml.) was conducted under nitrogen. 4 hr. later, the mixture was acidified with dilute hydrochloric acid and poured into water (400 ml.). In ethereal solution, the product was washed with aqueous sodium hydrogen carbonate and then with water, dried ($MgSO_4$), and distilled. The fraction (7·6 g.), b. p. 135—139°/0·1 mm., was purified from benzene on aluminium oxide and then, when redistilled, gave the *2-3′-oxo-*n*-butylcoumaranone* (XXVIII; R = Me) as a yellowish oil, b. p. 136—138°/0·1 mm., $\lambda_{max.}$ 275, 340 mμ (log ε 4·10, 3·60) (Found : C, 70·2; H, 6·3. $C_{16}H_{18}O_4$ requires C, 70·1; H, 6·6%). In the carbonyl stretching region, this triketone had but one very broad band at 1701 cm.$^{-1}$.

4 : 6 : *4′-Trimethylgris-3′-en-3 : 2′-dione* (XXXII; Me for OMe).—(i) Sulphuric acid (2·5 ml.) was cautiously added to the foregoing oxo-*n*-butylcoumaranone (0·8 g.) at 0°. Two days later, addition of iced water precipitated a product which, after being separated by decantation and ground with dilute alcohol, crystallised from alcohol yielding the *grisendione* as rhombs (0·4 g.), m. p. 139°, $\lambda_{max.}$ 248, 260, 330 mμ (log ε 4·27, 4·26, 3·68) (Found : C, 75·2; H, 6·3. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%). The infrared spectrum included peaks at 1701 (coumaranone C:O) and 1669 cm.$^{-1}$ (αβ-unsaturated C:O). From alcohol the 2 : *4-dinitrophenylhydrazone* formed orange-red needles, m. p. 188° (Found : C, 60·5; H, 4·7; N, 12·6. $C_{22}H_{20}O_6N_4$ requires C, 60·5; H, 4·6; N, 12·8%).

(ii) When the 2-3′-oxo-*n*-butylcoumaranone (1·5 g.) was slowly distilled at 20 mm. from a pad of glass wool the distillate partially solidified. The solid crystallised from alcohol, giving the grisendione (XXXII; Me for OMe) in rhombs (0·4 g.), m. p. 139°, not depressed on admixture with a specimen from (i).

*2-Acetyl-2-3′-oxo-*n*-butyl-4 : 6-dimethoxycoumaran-3-one* (XXVIII; R = OMe).—During 10 min. aqueous methyl vinyl ketone (azeotropic mixture; 5 ml.) was added dropwise and with agitation to 2-acetyl-4 : 6-dimethoxycoumaran-3-one (5 g.) in dioxan (30 ml.) containing Triton B (2 ml.). 4·5 hr. later, the acidified (hydrochloric acid) mixture was poured into water (300 ml.). Next day, the deposit was washed with a little ether and then purified from benzene–light petroleum giving the *2-3′-oxo-*n*-butylcoumaranone* (XXVIII; R = OMe) in rhombs (5·4 g.), m. p. 117°, $\lambda_{max.}$ 288, 325 mμ (log ε 4·34, 3·69), which gave no colour with ferric chloride [Found : C, 62·7; H, 5·9; OMe, 20·1. $C_{14}H_{12}O_4(OMe)_2$ requires C, 62·7; H, 5·9; OMe, 20·3%]. In the infrared region, this compound had very broad unresolved carbonyl absorption at 1698 cm.$^{-1}$.

1 : 2 : 3 : *4-Tetrahydro-5 : 7-dimethoxy-3-oxodibenzofuran* (XXIX).—The foregoing oxo-*n*-butylcoumaranone (0·5 g.) was boiled with 2N-aqueous sodium hydroxide (25 ml.) under nitrogen for 1 hr.; the large lumps which formed were occasionally pulverised before the reaction was allowed to continue. When cold, the solid was washed with water and then with a little alcohol; recrystallisation from alcohol furnished the *dibenzofuran* (XXIX) in needles (0·3 g.), m. p. 168—170°, $\lambda_{max.}$ 257 mμ (log ε 4·20) [Found : C, 67·8; H, 5·7; OMe, 25·5. $C_{12}H_8O_2(OMe)_2$ requires C, 68·3; H, 5·7; OMe, 25·5%]. Orange needles, m. p. 232°, were obtained when the 2 : *4-dinitrophenylhydrazone* crystallised from benzene [Found : C, 56·2; H, 4·4; N, 13·1; OMe, 14·5. $C_{18}H_{12}O_5N_4(OMe)_2$ requires C, 56·3; H, 4·3; N, 13·1; OMe, 14·6%].

4 : *6-Dimethoxy-4′-methylgris-3′-en-3 : 2′-dione* (XXXII).—Cyclisation of 2-acetyl-2-3′-oxobutyl-4 : 6-dimethoxycoumaran-3-one (6·7 g.) was effected with sulphuric acid (27 ml.) as for the dimethyl analogue. The product was purified from alcohol, giving the *dimethoxygrisendione* in rhombs (4·2 g.), m. p. 178°, $\lambda_{max.}$ 223, 240, 287, 325 (log ε 4·36, 4·21, 4·32, 3·61) [Found : C, 66·4; H, 5·6; OMe, 21·4; *C*-Me, 5·0%; *M* (micro-Rast), 299. $C_{14}H_{10}O_3(OMe)_2$ requires C, 66·7; H, 5·6; OMe, 21·5; *C*-Me, 5·2%; *M*, 288]. The infrared spectrum was devoid of hydroxyl absorption but possessed carbonyl peaks at 1698 and 1669 cm.$^{-1}$. This compound reacted rapidly with bromine water and with neutral permanganate but did not affect Fehling's solution or ferric chloride in alcohol. It was insoluble in cold 3N-aqueous sodium hydroxide and was recovered when boiled with 20% sulphuric acid for 2 hr. The 2 : *4-dinitrophenylhydrazone* crystallised from benzene–light petroleum in orange needles, m. p. 222—225° [Found : C, 56·3; H, 4·3; N, 11·9; OMe, 12·6. $C_{20}H_{14}O_6N_4(OMe)_2$ requires C, 56·4; H, 4·3; N, 12·0; OMe, 13·2%].

2'-Hydroxy-4 : 6-dimethoxy-4'-methylgrisan-3-one (α- *and* β-*forms*) (XLI).—The above dimethoxygrisendione (1 g.) in ethyl acetate (250 ml.) or alcohol (250 ml.) was shaken with Raney nickel (1·5 g.) in hydrogen under ordinary conditions. The initial rapid absorption stopped after 15 min., when 2 mols. had been taken up, whereafter removal of the catalyst and the solvent left a residue which at first dissolved in benzene (5 ml.) but then partly separated again. The precipitate was washed with benzene and recrystallised from the same solvent, giving the α-*hydroxygrisanone* (XLI) in needles (0·5 g.), m. p. 163—165°, unaffected by recrystallisation from alcohol [Found: C, 65·8; H, 6·9; OMe, 21·1. $C_{14}H_{14}O_3(OMe)_2$ requires C, 65·7; H, 6·9; OMe, 21·2%]. This isomeride had $\lambda_{max.}$ 283, 325 mμ (log ε 4·34, 3·64) and infrared bands at 3430 (OH) and 1698 cm.$^{-1}$ (coumaranone C:O).

From the benzene mother-liquors, light petroleum precipitated the isomeric β-*hydroxygrisanone* (XLI) which, when purified from benzene–light petroleum and then from light petroleum (b. p. 80—100°), formed plates (0·3 g.), m. p. 159—160°, markedly depressed by admixture with the α-isomeride (Found: C, 65·8; H, 6·9; OMe, 21·2%). This alcohol had $\lambda_{max.}$ 283, 315 mμ (log ε 4·33, 3·70) and infrared bands in Nujol at 3430 (OH) and 1681 cm.$^{-1}$ (hydrogen-bonded coumaranone C:O) or in $CHCl_3$ at 3600 and 3425 (OH) and 1692 cm.$^{-1}$ (hydrogen-bonded coumaranone C:O).

4 : *6-Dimethoxy-4'-methylgrisan-3 : 2'-dione* (XXXVIII).—(i) A solution of chromic oxide (0·3 g.) in acetic acid (3 ml.) and water (0·8 ml.) was gradually added to the α-hydroxygrisanone (0·32 g.) in warm acetic acid (7·5 ml.). 1 hr. later, the *grisandione* was precipitated by dilution and, when purified from alcohol, formed rhombs (0·15 g.), m. p. 186—187°, $\lambda_{max.}$ 285, 320 mμ (log ε 4·31, 3·71) [Found: C, 66·5; H, 6·2; OMe, 21·6. $C_{14}H_{12}O_3(OMe)_2$ requires C, 66·2; H, 6·3; OMe, 21·4%]. The infrared spectrum possessed peaks at 1724 (*cyclo*hexanone C:O) and 1698 cm.$^{-1}$ (coumaranone C:O).

(ii) The same diketone, m. p. and mixed m. p. 186—187°, resulted in similar yield when the β-hydroxygrisanone was oxidised by the same method.

(iii) 4 : 6-Dimethoxy-4'-methylgris-3'-en-3 : 2'-dione (1·0 g.) in alcohol (150 ml.) was shaken under hydrogen with 2% palladium–charcoal (0·5 g.). The rapid uptake of hydrogen ceased after the absorption of 1 mol. (*ca.* 80 ml.). The *grisandione* (XXXVIII) was isolated in the usual way and formed prisms (0·7 g.), m. p. and mixed m. p. 187°. The *semicarbazone* formed prisms, m. p. 264° (decomp.), from aqueous methanol (Found: C, 58·9; H, 6·3; N, 11·8. $C_{17}H_{21}O_5N_3$ requires C, 58·8; H, 6·1; N, 12·1%). The 2 : 4-dinitrophenylhydrazone decomposed when attempts were made to crystallise it.

Hydrolysis of 4 : *6-Dimethoxy-4'-methylgrisan-3 : 2'-dione.*—The dione (200 mg.) in methanol (8 ml.) was kept at 80° with N-aqueous sodium hydroxide (5 ml.) under nitrogen for ¼ hr., giving a solution which was concentrated to 4 ml. *in vacuo*, cooled, and acidified with dilute hydrochloric acid. The gummy precipitate slowly became granular and when crystallised from acetone–light petroleum formed needles, m. p. *ca.* 140° (110 mg.), and prisms, m. p. *ca.* 114° (53 mg.), which were separated by hand. Neither product could be satisfactorily recrystallised, but neither reacted with 2 : 4-dinitrophenylhydrazine sulphate or gave a ferric reaction. The needles, m. p. 140°, were soluble in aqueous sodium hydrogen carbonate and are considered to be impure acid (XXXIX) (Found: C, 61·3; H, 6·4%; equiv., 299. Calc. for $C_{15}H_{19}O_4{\cdot}CO_2H$: C, 62·3; H, 6·5%; equiv., 308). This material had $\lambda_{max.}$ 283, $\lambda_{infl.}$ 312 mμ (log ε 4·29, 3·73). The prisms were not soluble in sodium hydrogen carbonate solutions but dissolved in aqueous sodium hydroxide (Found: C, 60·9; H, 6·4%).

3' : *4'-Dihydroxy-4 : 6-dimethoxy-4'-methylgrisan-3 : 2'-dione* (XXXIV).—(i) The mixture obtained by the gradual addition of zinc permanganate (1·2 g.) in water (150 ml.) to the dimethoxydioxogrisen (XXXII) (1·2 g.) in acetone (80 ml.) was kept for 2·5 hr. before filtration and leaching of the residue with acetone. When evaporated, the combined acetone filtrates yielded a crude solid which was washed with aqueous sodium hydrogen carbonate (15 ml.) and then fractionally crystallised from alcohol, giving unchanged dione (0·2 g.), m. p. and mixed m. p. 178°, as the less soluble component, and, as the more soluble component, the *diol* (XXXIV) crystallising from dilute alcohol or benzene in needles (0·5 g.), m. p. 198—201° [Found: C, 59·9; H, 5·7; OMe, 17·5; active H (Zerewitinov), 0·60. $C_{14}H_{10}O_3(OH)_2(OMe)_2$ requires C, 59·6; H, 5·6; OMe, 19·3; active H, 0·62%]. The infrared spectrum had peaks at 3430 (OH), 1712 (*cyclo*hexanone C:O), and 1686 cm.$^{-1}$ (coumaranone C:O).

(ii) Interaction of the dimethoxydione (XXXII) (0·5 g.) in pyridine (5 ml.) with ethereal osmium tetroxide (0·5 g.) was complete in 12 hr. The product was taken up in hot methanol

(5 ml.) through which sulphur dioxide was being bubbled and the solution was clarified by use of a short column of alumina. The eluate was evaporated, leaving a dark residue which, after several recrystallisations (charcoal) from dilute alcohol, gave the diol (XXXIV) (0·05 g.), m. p. and mixed m. p. 198—201°.

Periodate Oxidations.—(i) 6-Methoxycoumaran-3-one (1·6 g.) in 50% acetic acid (10 ml.) was kept under nitrogen with sodium paraperiodate (7·2 g.) in the same solvent (40 ml.). After a few hr. in darkness the mixture had become brown and iodic acid had separated. Next day the solution was decanted and diluted with ether (200 ml.). After having been washed with water (5 × 15 ml.), the ethereal solution was extracted with small quantities of 2N-sodium hydroxide, and the earlier extracts, which were reddish and nearly neutral, were rejected. Further treatment with alkali produced striking colour changes to green and dark red: when no further change occurred the ether contained almost no neutral material. Acidification of the extracts furnished a dark mass which was dried and purified on a silica column from a chloroform solution. The earlier eluates contained a brownish acidic solid which was purified by reprecipitation from its solution in aqueous sodium hydrogen carbonate and then crystallised from water (charcoal), giving 2-hydroxy-4-methoxybenzoic acid in needles (118 mg.), m. p. and mixed m. p. 159°, having an intense purple ferric reaction.

(ii) When 2-acetyl-4 : 6-dimethoxycoumaran-3-one (1·2 g.) was dissolved in 50% acetic acid (20 ml.) and kept under nitrogen with sodium paraperiodate (4·1 g.) in the same solvent (30 ml.), a yellow colour developed rapidly. 2 hr. later, the decanted solution was mixed with equal volumes of ether and water, and the ethereal layer was freed from acetic acid by means of sodium hydrogen carbonate. When evaporated, the ethereal solution gave a gum which was chromatographed on a silica column from a benzene solution. Evaporation of the earlier eluates furnished a yellowish mass which, purified from ethyl acetate, gave 4 : 6-dimethoxycoumaran-3-one in needles, m. p. and mixed m. p. 198—200°.

(iii) No change could be detected when 2 : 2-di-2′-cyanoethyl-4 : 6-dimethoxycoumaran-3-one (V; R = MeO), 2-acetyl-2-3′-oxo-*n*-butyl-4 : 6-dimethoxycoumaran-3-one (XVIII), or 4 : 6-dimethoxy-4′-methylgris-3′-en-3 : 2′-dione (XXXII) was kept for 3 days in 50% acetic acid with an excess of sodium paraperiodiate as described in (i) and (ii).

(iv) Dissolved in acetic acid (2 ml.), the diol (XXXIV) (200 mg.) was treated with sodium paraperiodate (350 mg.) in 50% acetic acid (3 ml.). Next day, the diluted solution was extracted with ether, evaporation of which then gave a semisolid mass almost entirely soluble in aqueous sodium hydrogen carbonate. Regained by acidification and purified from aqueous alcohol (charcoal), this material gave 2-hydroxy-4 : 6-dimethoxybenzoic acid in needles (60 mg.), m. p. and mixed m. p. 145°.

With 2 : 4-dinitrophenylhydrazine sulphate, the ether-extracted aqueous solution gave a copious light yellow precipitate which later resinified, but the agent responsible was not volatile in a current of air and appeared to decompose when attempts were made to isolate it by exhaustive extraction with ether.

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