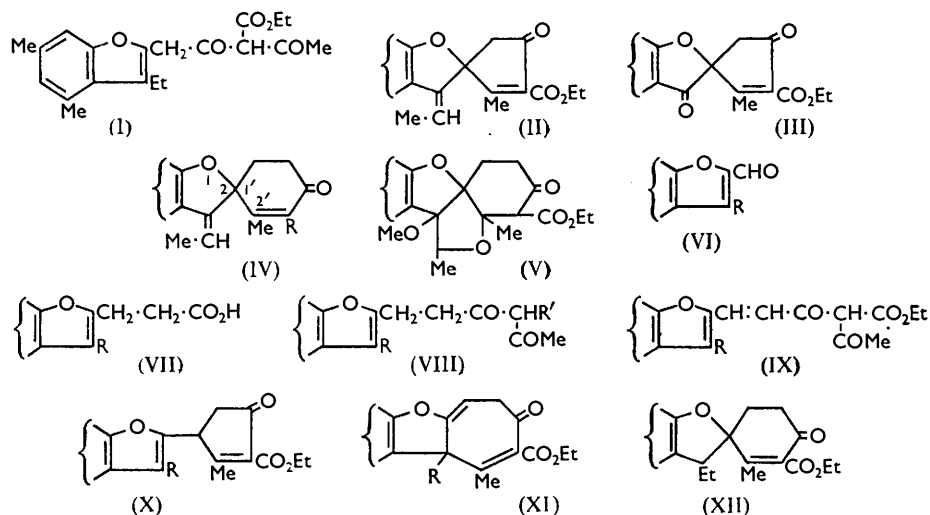


918. *Spirans. Part II.* The Preparation and Ozonolysis of Derivatives of 3-Ethylidenegris-2'-ene. Anomalous Enolisation in β -Oxo-esters.*

By F. M. DEAN, THOMAS FRANCIS, and KAMCHORN MANUNAPICHU.

The cyclisation of appropriately substituted 3-alkylbenzofurans has been extended from the synthesis of *cyclopent-2'-ene-1'-spiro-2-coumarans* to that of 3-alkylidenegris-2'-enes, ozonolysis of which is abnormal and gives derivatives (V) of 2:3:4:4a:6:6a-hexahydro-1H-5:11-dioxadibenzo[*a,d*]-pentalene. The properties of certain β -oxo-esters in this series are interpreted in terms of the non-classical enol $R\cdot CO\cdot\dot{C}:C(OH)\cdot OR$.

PREVIOUSLY,¹ *spirocoumarans* of type (II) were obtained by cyclisation of diketo-esters of type (I) and oxidised by ozone to *spirocoumaranones* (III). In extension, the *gris-2'-ene* (IV) has been similarly synthesised but found to yield with ozone, not the expected grisenone related to griseofulvin,² but the condensed difuranoid β -oxo-ester (V) as an enol of unusual character.



The acrylic acids resulting from interaction of the aldehydes (VI; $R = \text{Me}$ or Et) with malonic acid gave on hydrogenation the β -(benzofuryl)propionic acids (VII; $R = \text{Me}$ or Et), the acid chlorides of which with methoxymagnesium-derivatives of the appropriate acetoacetates or of acetylacetone gave crude diketones (VIII; $R = \text{Me}$ or Et , $R' = \text{CO}_2\text{Me}$, CO_2Et , or Ac), converted by sulphuric acid into *spirocoumarans* of type (IV). Although β -(3:4:6-trimethylbenzofur-2-yl)acrylic acid supplied a crystalline dioxo-ester (IX) with properties typical of β -dicarbonyl compounds, this ester failed to give a spiran as condensation product, presumably because the dienone type of structure which would have resulted is itself labile to acids.³ Because ozonolysis of the ethylidenecoumaran (II) to the coumaranone (III) was essential in the proof¹ of the spiran nature of these compounds but took a different course in the present series, formulæ of types (X) and (XI) could not be rejected by analogy only. However, the infrared absorption spectra of the cyclisation products always possessed bands near 1680 cm^{-1} consistent with the *cyclohexenone*-carbonyl group of structure (IV) but not with the *cyclopentenone*-carbonyl group of (X);

* Part I, *J.*, 1957, 3112 (with the series title, "Spirocyclic Compounds").¹ Dean, Halewood, Mongkolsuk, Robertson, and Whalley, *J.*, 1953, 1250.² Grove, MacMillan, Mulholland, and Rogers, *J.*, 1952, 3977.³ Arkley, Dean, Robertson, and Sidisunthorn, *J.*, 1956, 2322 and references cited therein.

and under conditions in which a furan double bond, as in (X), is invariably resistant, hydrogenation of the cyclisation product (IV; R = CO₂Et) readily gave a dihydro-derivative (XII) retaining this carbonyl absorption. The corresponding ultraviolet spectra (Fig. 1) paralleled those in the established series and showed that the dihydro-derivative lacked an absorption band of λ_{\max} . 242 m μ (log ϵ 4.15), clearly indicating loss of a styrene chromophore of λ_{\max} . 244 m μ (log ϵ 4.1): this evidence eliminated structures of type (XI).

The spiran esters (IV) gave the usual carbonyl derivatives, and one (IV; R = CO₂Et) was hydrolysed with difficulty to the corresponding acid (IV; R = CO₂H), decarboxylation of which was unsatisfactory but gave the grisenone (IV; R = H) with the appropriate

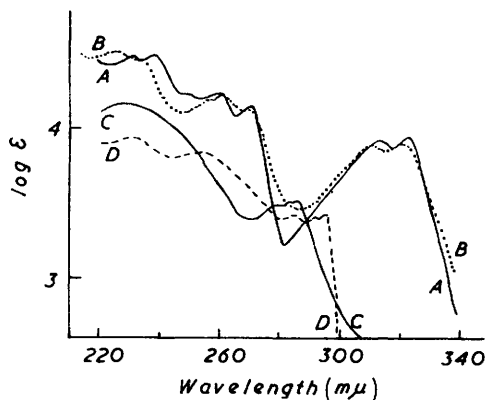
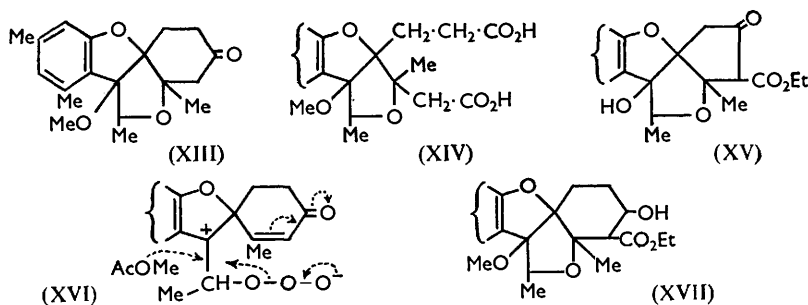


FIG. 1. Ultraviolet spectra of: A, ethyl 3-ethylidene-4:6:2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylate (IV; R = CO₂Et); B, ethyl 4:6:2'-trimethyl-3-methylene-4'-oxocyclopent-2'-ene-1'-spiro-2-coumaran-3'-carboxylate (II); C, dihydro-derivative (XII) of (A); and D, ozonolysis product (V) of (A) (all in alcohol).

spectroscopic properties. The same grisenone (IV; R = H) resulted when its acetyl derivative (IV; R = Ac) was hydrolysed by acid, and also when the diketone obtained by selective deacetylation of triketone (VIII; R = Et, R' = Ac) with sodium methoxide was cyclised with sulphuric acid.

No conditions were found in which ozonolysis of the 3-methylenegrisenone (IV; R = CO₂Et; with =CH₂ for =CHMe) in the usual solvents, or of the 3-ethylidenegrisenones (IV) in carbon tetrachloride, would give volatile aldehydes or tractable residues. In contrast, ozonolysis in methyl acetate (for which ethyl acetate could not be substituted) smoothly converted the 3-ethylidenegrisenone (IV; R = CO₂Et) into a product to which we ascribe structure (V). No peroxidic materials were detected in the reaction mixture.



The ozonolysis product (V) gave analytical data consistent with the uptake of one oxygen atom and the elements of methanol. Since the compound was devoid of hydroxyl absorption near 3 μ , was stable to severe drying, and retained the methoxyl group during degradation, the presence of methoxyl was clearly not due to solvation. The product was obviously a β -oxo-ester because of its solubility in alkali, its intense ferric reaction, and its dual hydrolysis in warm alkali to ketonic (XIII) and acidic (XIV) products. The grisanone

(XIII) had the requisite carbonyl band at 1717 cm^{-1} but was transparent near $3\ \mu$, gave a 2:4-dinitrophenylhydrazone and a positive Zimmermann reaction, possessed an ultraviolet spectrum typical of a simple coumaran (Fig. 2), and was also obtained directly by ozonolysis of the appropriate grisenone (IV; R = H) in methyl acetate. The dibasic acid (XIV) had almost the same ultraviolet spectrum as the ketone (XIII), gave a dimethyl ester with selective absorption at 1742 cm^{-1} (saturated ester) but none near $3\ \mu$, and had pK_a 4.85 (one inflection) typical of propionic acids.

FIG. 2. Ultraviolet spectra of: A, ketone (XIII); B, diacid (XIV); and C, 1:2:3:4:10:11-hexahydro-6:11-dimethyldibenzofuran-2-one³ (all in alcohol).

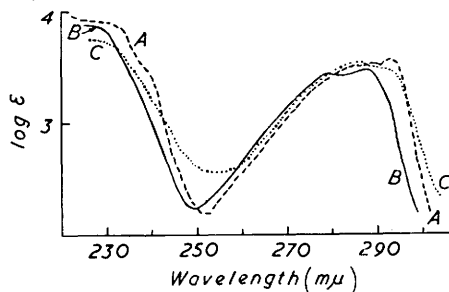
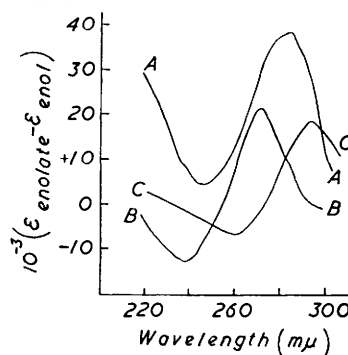


FIG. 3. $\Delta\epsilon$ curves for: A, ozonolysis product (V); B, ethyl acetoacetate; and C, acetylacetone. Spectra were obtained from 10^{-4}M -solutions in neutral alcohol and in 0.01N-alcoholic sodium hydroxide. The data for B and C in neutral alcohol were amended to give values approximating to those for 100% enolisation.



The ultraviolet spectrum of the β -oxo-ester (V) was difficult to dissect into its components, but by subtraction⁴ the spectra in neutral and alkaline alcohol gave a curve characteristic of the enolic system only, comparable to those obtained from typical β -dicarbonyl compounds (Fig. 3).

Because the ozonolysis product (V) has hydrogen at the 3'-position,* either the methoxyl group or the oxygen atom must be placed at the 2'-position, but as the grisenone (IV) does not add methanol (except during ozonolysis) and the methoxyl group survives alkaline and acid fission it is the oxygen atom which is located at the 2'-position since its stability in a position β to carbonyl is then explicable on stereochemical grounds (a similar example is discussed in ref. 3). In conjunction with the relative reactivity of the exocyclic double bond of the grisenone (IV) [compounds of type (XII) resist ozone] and the strain involved in 4-membered rings, these facts lead uniquely to structure (V) for the ozonolysis product.

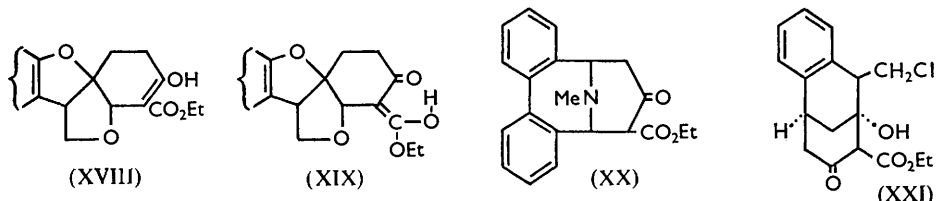
The stability of the benzyl ether system to acids and hydrogenolysis [as in the diacid (XIV)] conforms with a structure (V) because a flat carbonium centre at the 3-position would be highly strained and because access of catalysts to the same site would be considerably hindered. Finally, structure (V) is strongly supported by the oxidation of the authentic *spiropentenone* (II) with osmium tetroxide which gave the β -oxo-ester (XV) instead of a glycol.

That the 2':3'- and the ethylidene double bond are more divergent in the *cyclopentenone* (II) than in the *cyclohexenone* (IV) may account for their different modes of ozonolysis. The ozonolysis could not be simulated by peracids in the presence of methanol, so both double bonds might be involved in ozonolysis as represented in (XVI).

* Grisan numbering (cf. IV).³

⁴ Aulin-Erdtman, *Chem. and Ind.*, 1955, 581.

Compound (V) has physical and chemical properties more easily explained in terms of a non-classical enol of type (XIX) than in terms of a conventional enol of type (XVIII). In the crystalline state or in solution (0.05M in chloroform) the β -oxo-ester (V) has no carbonyl absorption above 1630 cm^{-1} (and no hydroxyl absorption near $3\ \mu$), thus contrasting with the majority of 2-oxocyclohexanecarboxylates which also show frequencies characteristic of the non-enolised ester and carbonyl groups.⁵ Supercooled melts of the β -oxo-ester (V) do have prominent absorption frequencies at 1757 (ester) and 1727 cm^{-1} (C:O), from which it follows that the β -oxo-ester is normally completely enolised. The observed frequency at 1630 cm^{-1} is $\sim 25\text{ cm}^{-1}$ lower than expected for a chelated ester,⁵ but is consistent with a chelated carbonyl group as in (XIX). In general, hydrolysis of 2-oxocycloalkanecarboxylic esters by dilute alkali results chiefly in loss of the ester group and production of the cycloalkanone: instead, the ester (V) is hydrolysed preponderantly to the diacid (XIV), a result which follows from the retention in enol form (XIX) of the carbonyl



group at which attack by hydroxide ion is a prerequisite of this mode of fission. Whereas enols (XVIII) (as opposed to the non-enolised form) react with borohydrides giving hydrogen and a stable complex regenerating the enol with acids (*e.g.*, ethyl β -oxoglutarate⁶), because they no longer possess a carbonyl group which can be attacked by the reagent, the ester (V) is smoothly reduced to the β -hydroxy-ester (XVII), indicating that the ketonic carbonyl group is intact.

Although β -oxo-esters enolise at the carbonyl group because this avoids loss of some carboxyl resonance, the energy difference between enols (XVIII) and (XIX) cannot be very large because these merely represent different ways in which two hydroxyl groups can cross-conjugate with one carbonyl group so that a steric effect might sometimes favour the non-classical enol (XIX). The strain produced by introduction of a double bond into the cyclohexane ring as in (XVIII) is not in itself enough to prevent this type of enolisation, but models suggest that, in conjunction with the constraints applied by the 5-membered rings, introduction of a short and rigid double bond would produce a nearly flat cyclohexene ring. On the other hand, enolisation of type (XIX) permits the 6-membered ring to attain closely the favoured chair conformation* provided that a small angle of twist ($\sim 20^\circ$) between the exocyclic double bonds is allowed. On general grounds⁷ this angle seems small enough to avoid appreciable loss of resonance energy in the chelated system. Further facts consistent with the view that the system resists introduction of an endocyclic double bond (or a similar source of rigidity) are that the β -hydroxy-ester (XVII) is not readily dehydrated, and that the oxime of the β -oxo-ester (V) could not be converted into an isooxazolone.

These considerations can be extended, *e.g.*, to compounds (XX)⁸ and (XXI).⁹ It is significant that these compounds are completely enolised and have no carbonyl absorption above $\sim 1620\text{ cm}^{-1}$, behaviour which we now regard as typical of a non-classical enol.

* That a boat conformation might be preferred in some compounds of this type does not affect the present argument.

⁵ Leonard, Gutowsky, Middleton, and Petersen, *J. Amer. Chem. Soc.*, 1952, **74**, 4070.

⁶ Personal communication from Dr. D. A. H. Taylor.

⁷ Braude, "Determination of Organic Structures by Physical Methods," ed. Braude and Nachod, Academic Press, New York.

⁸ Chapman and Meinwald, *J. Org. Chem.*, 1958, **23**, 162.

⁹ Wenkert and Stevens, *J. Amer. Chem. Soc.*, 1956, **78**, 5627.

Further comment is reserved until determination of the precise stereochemistry of these systems is complete.

EXPERIMENTAL

Ultraviolet spectra were determined for alcohol solutions by means of a Unicam S.P. 500 Spectrophotometer. Infrared spectra were determined on Nujol mulls (unless otherwise stated) by means of Grubb-Parsons and Perkin-Elmer Model 21 double-beam spectrophotometers.

Unless qualified, light petroleum refers to the fraction b. p. 60—80°.

β -(3-Ethyl-4 : 6-dimethylbenzofur-2-yl)propionic Acid (VII; R = Et).—Malonic acid (50 g.) and 3-ethyl-2-formyl-4 : 6-dimethylbenzofuran ¹ (VI; R = Et), kept at 100° in pyridine (150 ml.) containing piperidine (0.5 ml.) for 3 hr. and then cooled, gave β -(3-ethyl-4 : 6-dimethylbenzofur-2-yl)acrylic acid in pale yellow prisms (45 g.) which, when recrystallised from a large volume of dioxan, had m. p. 252° (decomp.), λ_{max} . 245, 330 m μ (log ϵ 3.84, 4.38) (Found: C, 73.3; H, 6.6. C₁₅H₁₆O₃ requires C, 73.7; H, 6.6%), and, in methanolic suspension, gave with ethereal diazomethane the methyl ester forming needles, m. p. 74°, from aqueous methanol (Found: C, 74.1; H, 7.4; OMe, 11.8. C₁₅H₁₆O₂·OMe requires C, 74.4; H, 7.0; OMe, 12.0%). Hydrogenation of this ester (5 g.) in methanol (200 ml.) containing 5% palladium-charcoal (1 g.) furnished methyl β -(3-ethyl-4 : 6-dimethylbenzofur-2-yl)propionate, b. p. 210°/0.2 mm., as needles, m. p. 33° (Found: C, 73.8; H, 7.5; OMe, 12.0. C₁₆H₁₇O₂·OMe requires C, 73.8; H, 7.7; OMe, 11.9%).

Hydrogenation of the acrylic acid was hampered by insolubility of the acid and its sodium salt. The acrylic acid (20 g.) in 0.2N-sodium hydroxide (700 ml.) was hydrogenated at 100°/75 atm. for 6 hr. in the presence of Raney nickel (5 g.). The filtered solution was acidified, liberating β -(3-ethyl-4 : 6-dimethylbenzofur-2-yl)propionic acid which separated from alcohol-light petroleum in needles (18 g.), m. p. 113° (Found: C, 73.6; H, 7.5. C₁₅H₁₆O₃ requires C, 73.2; H, 7.3%), and with diazomethane gave the methyl ester, m. p. and mixed m. p. 33°. Attempts to crystallise the propionic acid from alcohol sometimes gave the ethyl ester, b. p. 158°/1.5 mm. (Found: C, 74.8; H, 8.1. C₁₇H₂₂O₃ requires C, 74.4; H, 8.0%).

β -(3 : 4 : 6-Trimethylbenzofur-2-yl)propionic acid (VII; R = Me).—As described for the 3-ethyl homologue, 2-formyl-3 : 4 : 6-trimethylbenzofuran (VI; R = Me) gave β -(3 : 4 : 6-trimethylbenzofur-2-yl)acrylic acid, pale yellow needles, m. p. 259° (from alcohol), λ_{max} . 247, 255, 335 m μ (log ϵ 3.79, 3.79, 4.49), having carboxyl absorption at 1701 cm.⁻¹ (Found: C, 72.7; H, 6.1. C₁₄H₁₄O₃ requires C, 73.0; H, 6.1%). The methyl ester (prepared by diazomethane) crystallised from methanol in yellow prisms, m. p. 106° (Found: C, 73.5; H, 6.7; OMe, 12.9. C₁₄H₁₃O₂·OMe requires C, 73.7; H, 6.6; OMe, 12.7%). Hydrogenation of this acrylic acid as for the homologue, and purification of the product from aqueous alcohol, furnished β -(3 : 4 : 6-trimethylbenzofur-2-yl)propionic acid, needles, m. p. 131°, λ_{max} . 256, 292 m μ (log ϵ 4.15, 3.39), with carboxyl absorption at 1717 cm.⁻¹ (Found: C, 72.5; H, 7.1. C₁₄H₁₆O₃ requires C, 72.4; H, 6.9%). The methyl ester (prepared by diazomethane) crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 36—37° (Found: C, 73.4; H, 7.6; OMe, 12.8. C₁₄H₁₅O₂·OMe requires C, 73.1; H, 7.4; OMe, 12.6%), also obtainable by hydrogenation (palladium-charcoal) of the above methyl acrylate.

Ethyl 2-Acetyl-3-oxo-5-(3 : 4 : 6-trimethylbenzofur-2-yl)pent-4-enoate (IX).—On treatment with phosphorus pentachloride (2 g.) in chloroform (20 ml.) at room temperature for $\frac{1}{2}$ hr. and then at the b. p. for $\frac{1}{2}$ hr., β -(3 : 4 : 6-trimethylbenzofur-2-yl)acrylic acid (2 g.) gave the acid chloride as an oil which was purified by distillation of the benzene solution and holding of the residue in a vacuum at 50° for $\frac{1}{2}$ hr. Reaction of this oil in ether (100 ml.) with the methoxymagnesium-derivative (dried *in vacuo* at 50° for $\frac{1}{4}$ hr.) of acetoacetic ester (1.15 ml.), also in ether (100 ml.), at the b. p. for 2 hr. gave a sticky complex from which an excess of dilute acetic acid liberated a crude diketone which crystallised from alcohol, giving the *pentenoate* in yellow needles (1.9 g.), m. p. 125°, soluble in dilute aqueous sodium hydroxide, having a red-brown ferric reaction, and giving a red solution in sulphuric acid that became violet when warmed (Found: C, 69.9; H, 6.4; OEt, 13.1. C₁₈H₁₇O₄·OEt requires C, 70.2; H, 6.5; OEt, 12.5%).

Ethyl 3-Ethylidene-4 : 6 : 2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylate (IV; R = CO₂Et).—Prepared as in the previous example the acid chloride from β -(3-ethyl-4 : 6-dimethylbenzofur-2-yl)propionic acid (2 g.) reacted with the methoxymagnesium-derivative of acetoacetic ester (1.15 ml.), giving a crude diketo-ester (VIII; R = Et, R' = CO₂Et) which was partially

purified by extraction of a solution in ether by aqueous sodium hydrogen carbonate and gave a red ferric reaction. Attempts to cyclise this oil with sulphuric acid, polyphosphoric acid, or benzenesulphonic acid were unsuccessful, but when dissolved in sulphuric acid monohydrate (10 ml.) the oil gave after 2 days at -2° a red mass from which the crude cyclisation product was obtained by addition of ice. When isolated with ether, washed with 2N-sodium hydroxide and then water, dried (Na_2SO_4), and recovered by evaporation of the solvent, the product could be crystallised from alcohol or light petroleum, affording *ethyl 3-ethylidene-4:6:2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylate* in faintly yellow needles or prisms (1.2 g.), m. p. 142° (Found: C, 74.4; H, 7.1; OEt, 13.6. $\text{C}_{19}\text{H}_{19}\text{O}_3\cdot\text{OEt}$ requires C, 74.1; H, 7.1; OEt, 13.2%), with infrared absorption at 1681 (unsaturated C=O) and 1721 cm^{-1} (ester). The *dinitrophenylhydrazone* formed red needles, m. p. 233° (decomp.), from alcohol (Found: C, 62.1; H, 5.3; N, 10.7. $\text{C}_{27}\text{H}_{28}\text{O}_7\text{N}_4$ requires C, 62.3; H, 5.4; N, 10.8%), and the *oxime* (best prepared at 80°) formed prisms, m. p. 172° , from benzene-light petroleum (Found: C, 71.0; H, 7.3; N, 4.0; OEt, 12.3. $\text{C}_{19}\text{H}_{20}\text{O}_3\text{N}\cdot\text{OEt}$ requires C, 71.0; H, 7.1; N, 3.9; OEt, 12.7%).

In preliminary experiments hydrolysis of this ethyl oxogrisene-3'-carboxylate with sulphuric acid at various dilutions, with constant-boiling hydrobromic acid or hydrobromic acid in acetic acid, and with hydrochloric acid in acetic acid, gave intractable products. When the ethyl ester (0.5 g.) in boiling alcohol was heated for $\frac{1}{2}$ hr. with 2N-sodium hydroxide (3 ml.), and the sticky product was liberated from the cooled and diluted solution by hydrochloric acid, purification of this product by extraction into ether and thence into aqueous sodium hydrogen carbonate followed by crystallisation from aqueous methanol afforded *3-ethylidene-4:6:2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylic acid hydrate* in yellow plates (0.2 g.), m. p. 174° (Found: C, 69.1; H, 6.5. $\text{C}_{19}\text{H}_{20}\text{O}_4\cdot\text{H}_2\text{O}$ requires C, 69.1; H, 6.7%), with infrared bands at 3400 (OH), 1708 (CO_2H), and 1650 cm^{-1} (conjugated C=O). Crystallisation from alcohol-light petroleum furnished prisms, m. p. 192° . With ethereal diazoethane this acid regenerated the ethyl ester (IV; R = CO_2Et), m. p. and mixed m. p. 142° .

Ethyl 3-Ethyl-4:6:2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylate (XII).—After 1 hr., the foregoing 3-ethylideneoxogrisenecarboxylate (IV; R = CO_2Et) (0.5 g.) in alcohol (200 ml.) containing 5% palladium-charcoal (0.1 g.) no longer absorbed hydrogen. Evaporation of the filtered solution in a vacuum left a glass which crystallised in contact with alcohol and was then recrystallised from light petroleum (charcoal), giving *ethyl 3-ethyl-4:6:2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylate* in plates (0.4 g.), m. p. 106° , with infrared absorption at 1675 (unsaturated C=O) and 1745 cm^{-1} (ester) (Found: C, 73.7; H, 8.0; OEt, 13.3. $\text{C}_{19}\text{H}_{21}\text{O}_3\cdot\text{OEt}$ requires C, 73.7; H, 7.7; OEt, 13.2%). The 2:4-dinitrophenylhydrazone separated from alcohol in red prisms, m. p. 216° (Found: C, 62.2; H, 5.9; N, 10.5; OEt, 8.7. $\text{C}_{25}\text{H}_{25}\text{O}_6\text{N}_4\cdot\text{OEt}$ requires C, 62.1; H, 5.8; N, 10.7; OEt, 8.6%).

Methyl 3-Ethylidene-4:6:2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylate (IV; R = CO_2Me).—Obtained by the same methods as the corresponding ethyl ester above, this *methyl grisene-carboxylate* formed needles (from methanol), m. p. 162° , having infrared absorption bands at 1675 and 1727 cm^{-1} (Found: C, 73.8; H, 6.6; OMe, 9.9. $\text{C}_{19}\text{H}_{19}\text{O}_3\cdot\text{OMe}$ requires C, 73.6; H, 6.8; OMe, 9.5%), and gave the 2:4-dinitrophenylhydrazone as orange needles, m. p. 244° (from methyl acetate) (Found: C, 61.7; H, 5.1; N, 11.0; OMe, 6.4. $\text{C}_{25}\text{H}_{23}\text{O}_6\text{N}_4\cdot\text{OMe}$ requires C, 61.7; H, 5.2; N, 11.1; OMe, 6.2%), and the *oxime* as prisms, m. p. 220° (from benzene) (Found: C, 70.7; H, 6.9; N, 4.2; OMe, 9.1. $\text{C}_{19}\text{H}_{20}\text{O}_3\text{N}\cdot\text{OMe}$ requires C, 70.4; H, 6.8; N, 4.1; OMe, 9.1%).

3'-Acetyl-3-ethylidene-4:6:2'-trimethylgris-2'-en-4'-one (IV; R = Ac).—When the appropriate quantity of the methoxymagnesium-derivative of acetylacetone was used instead of that of acetoacetic ester, β -(3-ethyl-4:6-dimethylbenzofur-2-yl)propionic acid (1 g.) was converted by the standard method into *3'-acetyl-3-ethylidene-4:6:2'-trimethylgris-2'-en-4'-one* which crystallised from aqueous alcohol in plates (0.35 g.), m. p. 167° , λ_{max} 221, 229, 236, 259, 269, 309, 323 μ ($\log \epsilon$ 4.51, 4.55, 4.55, 4.30, 4.21, 3.98, 4.00), having infrared absorption bands at 1681 and 1713 cm^{-1} (*asym-enedione*) (Found: C, 77.1; H, 7.0. $\text{C}_{20}\text{H}_{22}\text{O}_3$ requires C, 77.4; H, 7.1%).

3-Ethylidene-4:6:2'-trimethylgris-2'-en-4'-one (IV; R = H).—(i) A mixture of 3-ethylidene-4:6:2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylic acid (0.4 g.), copper bronze (0.08 g.), and quinoline (4 ml.) was kept at 225° for $\frac{1}{2}$ hr., cooled, diluted with ether, and filtered. Quinoline was removed by means of 2N-hydrochloric acid, and acidic impurities by aqueous sodium hydrogen carbonate, whereafter evaporation of the dried (Na_2SO_4) solution gave an oil which,

when crystallised from light petroleum, gave 3-ethylidene-4 : 6 : 2'-trimethylgris-2'-ene-4'-one in rhombs (0.2 g.), m. p. 106°, λ_{\max} . 228, 235, 256, 263, 266, 306, 314, 317 m μ (log ϵ 4.57, 4.57, 4.25, 4.14, 4.18, 4.00, 4.00, 4.02), ν_{\max} . 1678 cm.⁻¹ (conjugated C=O) (Found: C, 80.6; H, 7.5. C₁₈H₂₀O₂ requires C, 80.7; H, 7.4%). The 2 : 4-dinitrophenylhydrazone separated from ethyl acetate in orange needles, m. p. 250—252° (Found: C, 64.4; H, 5.4; N, 12.2. C₂₄H₂₄O₅N₄ requires C, 64.3; H, 5.4; N, 12.5%).

(ii) When heated for 10 min. at 200°/20 mm. the grisene-3'-carboxylic acid (IV; R = CO₂H) (0.5 g.) decomposed to carbon dioxide and an oil which supplied the grisene, m. p. and mixed m. p. 106°, as in (i) above.

(iii) The neutral fraction of the product resulting from maintaining the acetylgrisene (IV; R = Ac) (0.25 g.) in sulphuric acid monohydrate (3 ml.) at 100° for 3 min. was extracted with boiling light petroleum. The concentrated and cooled extract furnished the grisene in prisms (0.05 g.), m. p. and mixed m. p. 105°.

(iv) The crude triketone (VIII; R = Et, R' = Ac) generated as above from β -(3-ethyl-4 : 6-dimethylbenzofur-2-yl)propionic acid (2.5 g.) was treated in methanol (20 ml.) with sodium methoxide (from 0.17 g. of sodium), also in methanol (10 ml.). 15 Hr. later, acidification by acetic acid and evaporation *in vacuo* furnished a viscous oil [crude diketone (VIII; R = Et, R' = H)] which was cyclised with sulphuric acid monohydrate (5 ml.) at -2° in 1 day. Addition of crushed ice and isolation of the neutral fraction gave the grisene, m. p. 106°, purified and identified as before.

Ethyl 4 : 6 : 2'-Trimethyl-3-methylene-4'-oxo-gris-2'-ene-3'-carboxylate (IV; R = CO₂Et; CH₂= for Me·CH=).—By the method used for the ethylidene analogue, β -(3 : 4 : 6-trimethylbenzofur-2-yl)propionic acid (3 g.) was converted into the 3-methylene-4'-oxogrisene-3'-carboxylate which crystallised from alcohol-light petroleum in needles (2.0 g.), m. p. 141°, ν_{\max} . 1681 and 1730 cm.⁻¹ (Found: C, 73.6; H, 6.8; OEt, 13.7. C₁₈H₁₇O₃·OEt requires C, 73.6; H, 6.8; OEt, 13.8%). The 2 : 4-dinitrophenylhydrazone formed orange needles, m. p. 233°, from ethyl acetate (Found: C, 61.4; H, 5.2; N, 11.1; OEt, 9.0. C₂₄H₂₁O₆N₄·OEt requires C, 61.7; H, 5.2; N, 11.1; OEt, 8.9%).

Ozonolysis of Ethyl 3-Ethylidene-4 : 6 : 2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylate : *Ethyl 2 : 3 : 4 : 4a : 6 : 6a-Hexahydro-6a-methoxy-4a : 6 : 7 : 9-tetramethyl-3-oxo-1H-5 : 11-dioxadibenzo[a,d]pentalene-4-carboxylate* (V).—Ozonised oxygen was passed into a solution of ethyl 3-ethylidene-4 : 6 : 2'-trimethyl-4'-oxogris-2'-ene-3'-carboxylate (0.5 g.) in methyl acetate (60 ml.) at -80° for 20 min. Evaporation of the solvent in a vacuum left a gum which did not affect starch-iodide paper and was not decomposed by water. In subsequent experiments this gum was immediately crystallised from methanol and then light petroleum, giving the *ethyl hexahydro-3-oxo-5 : 11-dioxadibenzo[a,d]pentalene-4-carboxylate* (V) in prisms (0.3 g.), m. p. 136° [Found: On a specimen dried at 120°: C, 67.7; H, 7.2; Alkoxy as OEt, 23.5. On a specimen fused *in vacuo*: C, 67.5; H, 7.3; Alkoxy as OEt, 22.5. C₁₉H₂₀O₄(OEt)·OMe requires C, 68.0; H, 7.3; Alkoxy as OEt, 23.5%]. This compound was soluble in 2N-sodium hydroxide, gave red colours with alcoholic ferric chloride and with sulphuric acid, and gave negative reactions in the Zimmermann and Ehrlich tests. The *oxime* was prepared in boiling alcohol and crystallised from this solvent in needles, m. p. 221° (decomp.) [Found: C, 65.6; H, 7.1; N, 3.7; Alkoxy as OMe, 15.1. C₁₉H₂₁O₄N(OEt)·OMe requires C, 65.5; H, 7.3; N, 3.5; Alkoxy as OMe, 15.3%], and resisted conversion into an *isooxazolone* at all temperatures up to the point of general decomposition.

The mother-liquors from this ozonolysis product contained an oil which was separated by benzene on a silica column into several fractions, none of which yielded pure material, but one of which gave a green colour with nitroprusside in pyridine characteristic of coumaranones.

The ethyl oxogrisene-3'-carboxylate (IV; R = CO₂Et) in carbon tetrachloride gave with ozone a white precipitate which decomposed vigorously near 70°. This solid was decomposed by aqueous alcohol although no pure materials could be isolated and no oxime, 2 : 4-dinitrophenylhydrazone, dimedone derivative, or sodium salt could be prepared.

2 : 3 : 4 : 4a : 6 : 6a-Hexahydro-6a-methoxy-4a : 6 : 7 : 9-tetramethyl-3-oxo-1H-5 : 11-dioxadibenzo[a,d]pentalene (XIII).—Ozonolysis of 3-ethylidene-4 : 6 : 2'-trimethyl-4'-oxogris-2'-ene (IV; R = H) (0.3 g.) in methyl acetate (10 ml.) at -80° for 12 min. gave a gum which was unaffected by water but solidified in contact with methanol and then, when purified from light petroleum, supplied the 5 : 11-dioxadibenzo[a,d]pentalene (XIII) in plates (0.1 g.), m. p. 128°, λ_{\max} . 280, 290 m μ (log ϵ 3.43, 3.47) (Found: C, 72.5; H, 7.8; OMe, 9.1. C₁₈H₂₁O₃·OMe requires C, 72.1;

H, 7.7; OMe, 9.8%). The 2 : 4-dinitrophenylhydrazone crystallised in yellow needles, m. p. 211°, from alcohol-ethyl acetate (Found: C, 60.4; H, 5.8; N, 10.9. $C_{25}H_{28}O_7N_4$ requires C, 60.5; H, 5.7; N, 11.3%).

3a-2'-Carboxyethyl-3-carboxymethyl-1 : 3 : 3a : 8b-tetrahydro-8b-methoxy-1 : 3 : 6 : 8-tetramethyl-2 : 4-dioxacyclopenta[a]indene (XIV).—The above β -oxo-ester (V) (0.85 g.), when kept in 2N-sodium hydroxide (15 ml.) at the b. p. for 1½ hr., gave a cloudy solution from which the neutral oil was extracted into ether. Purification from alcohol-light petroleum then furnished the 5 : 11-dioxadibenzo[a,d]pentalene (XIII) in plates (0.1 g.), m. p. and mixed m. p. 128°, further identified spectroscopically (Found: C, 71.9; H, 7.6; OMe, 9.8%). The solid precipitated by dilute sulphuric acid from the alkaline solution crystallised from aqueous methanol, affording the tetrahydro-2 : 4-dioxacyclopenta[a]indene (XIV) as rhombs, m. p. 198°, λ_{max} . 292 m μ (log ϵ 3.55), with an infrared absorption band at 1715 cm.⁻¹ (CO₂H) [Found: C, 63.2; H, 7.1; OMe, 8.1%; equiv., 183. $C_{17}H_{21}O_2(OMe)(CO_2H)_2$ requires C, 63.5; H, 6.9; OMe, 8.2%; equiv., 189]. After purification by distillation, the dimethyl ester (prepared by diazomethane), b. p. 185° (bath)/0.02 mm., formed needles, m. p. 84° [Found: C, 64.8; H, 7.4; OMe, 22.9. $C_{19}H_{21}O_4(OMe)_3$ requires C, 65.0; H, 7.4; OMe, 22.9%].

This diacid was stable to hydrogenolysis (palladium-charcoal) under a wide variety of conditions.

[With J. C. KNIGHT]. Ethyl 2 : 3 : 4 : 4a : 6 : 6a-Hexahydro-3-hydroxy-6a-methoxy-4a : 6 : 7 : 9-tetramethyl-1H-5 : 11-dioxadibenzo[a,d]pentalene-4-carboxylate (XVII).—The β -oxo-ester (V) (0.225 g.) in ethanol (50 ml.) was reduced by potassium borohydride (0.03 g.) in water (10 ml.). After ½ hr., the solution was acidified (Congo Red) with 2N-sulphuric acid and concentrated. The product was extracted into ether, washed with water, and recovered by evaporation, forming a gum which crystallised from light petroleum, giving the β -hydroxy-ester (XVII) in rhombs, m. p. 114°, λ_{max} . 283, 290, 293 m μ (log ϵ 3.47, 3.50, 3.53), ν_{max} . 3520 (OH) and 1700 cm.⁻¹ (ester) [Found: C, 67.7; H, 7.8; Alkoxy as OMe, 15.9. $C_{19}H_{22}O_4(OEt) \cdot OMe$ requires C, 67.7; H, 7.7; Alkoxy as OMe, 16.6%]. When treated with acetic anhydride and pyridine at 80° for 8 hr. and then at room temperature for 4 days, this alcohol gave the acetate, crystallising from methanol in needles, m. p. 162°, after elution from a silica column by benzene-ether (3 : 2) (Found: C, 66.6; H, 7.5. $C_{24}H_{32}O_7$ requires C, 66.7; H, 7.4%). This acetate had a very strong single band at 1742 cm.⁻¹ (CO₂Et and OAc) and another at 1250 cm.⁻¹ (OAc).

Ethyl 1 : 2 : 3 : 3a : 5 : 5a-Hexahydro-5a-hydroxy-3a : 5 : 6 : 8-tetramethyl-2-oxo-4 : 10-dioxacyclopenta[d]benzo[a]pentalene (XV).—From a solution of ethyl 3-ethylidene-4 : 6 : 2'-trimethylcyclopent-2'-ene-4'-one-1'-spiro-2-benzofuran-3'-carboxylate¹ (II) (0.6 g.) and osmium tetroxide (0.5 g.) in ether (50 ml.) containing pyridine (0.5 ml.) the dark adduct (1.1 g.) separated in 24 hr. The resulting adduct, in 80% methanol (70 ml.) containing charcoal (2 g.), was decomposed by a stream of sulphur dioxide, giving a violet solution which, after filtration, concentration to a small bulk under reduced pressure, and dilution with water, gave a precipitate that was taken up in ether, was washed with water, and recovered as a yellowish oil. This crystallised from aqueous methanol, affording the 4 : 10-dioxacyclopenta[d]benzo[a]pentalenecarboxylate (XV) in needles or plates, m. p. 147–148°, λ_{max} . 208, 226, 278, 288 m μ (log ϵ 4.62, 4.13, 3.48, 3.49), soluble in dilute sodium hydroxide and having an intense red ferric reaction and infrared absorption bands at 3440 and 1650 cm.⁻¹ in the crystalline state and 3440 and 1727 cm.⁻¹ when fused (Found: C, 65.5; H, 6.5; OMe, 11.3. $C_{17}H_{17}O_5 \cdot OEt$ requires C, 65.9; H, 6.4; OMe, 9.0%). The oxime formed clusters of needles, m. p. 200° (decomp.), when purified from benzene-methanol and had an infrared absorption band at 1736 cm.⁻¹ (ester) (Found: N, 3.6. $C_{18}H_{23}O_6N$ requires N, 3.9%).

The analyses were performed by Mr. A. S. Inglis, M.Sc., and his associates in this Department.