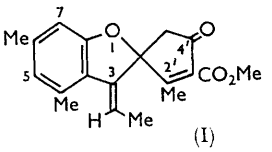
59. *Spirans. Part III.* The Structure and Stereochemistry of the Ozonolysis Products of 3-Alkylidenegris-2′-en-4′-ones.*

By F. M. Dean, D. S. Deorha, J. C. Knight, and Thomas Francis.

Oxidation of 3-alkylidenegris-2′-en-4′-ones (related to griseofulvin) by osmium tetroxide gives products which can be converted into the compounds previously obtained from abnormal ozonolyses of the same grisens. The structures (as IV) assigned to the ozonolysis products have thereby been confirmed: related studies have clarified the chief stereochemical features of these compounds, together with the nature of an unusual base-catalysed epimerisation which occurs in this series.

Improvements in the methods of synthesis of starting materials required in these and cognate studies are discussed.

In the usnolic acid series, spirans (I) are attacked by ozone in the expected fashion to give coumaranones (II), but in the grisan series ozonolysis (in methyl acetate) of spirans (III) gives anomalous results, the products having been assigned structures of type (IV). It is now shown that alcohols of general structures (VI) and (VII) can be prepared in both series by oxidising the appropriate spirans with osmium tetroxide. On the one hand, the alcohols can be methylated to products previously obtained by ozonolysis, thus confirming their structures, and on the other hand they possess a reactive centre (the hydroxyl group) useful in defining the stereochemistry of the tetracycles.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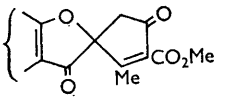
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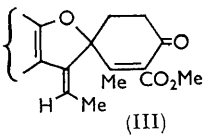
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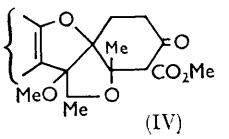
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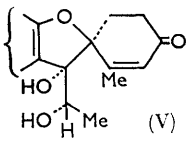
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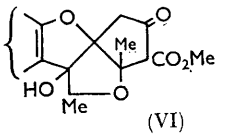
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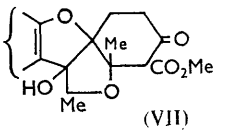
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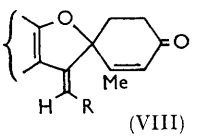
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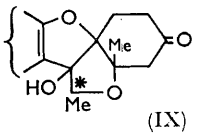
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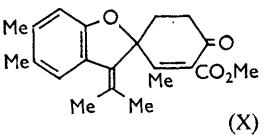

(X)

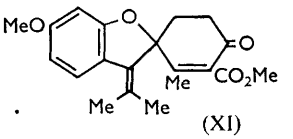
That the addition of osmium tetroxide to spirans of types (I) and (III) occurs, as expected, at the exocyclic double bonds appears from the fact that the adducts retain the spectroscopic characteristics of cyclohexenones. Reduction of the adducts by sulphur dioxide or by hydrogenation led, not to glycols [as (V)], but to isomers inert to periodates and having the more obvious properties of β-oxo-esters. Thus oxidation of the cyclopentenone ester (I) gave the tetracyclic alcohol (VI), and of the ring-homologue (III), gave an analogous alcohol (VII). While the chemical properties and ultraviolet absorption data for the alcohol (VII) were satisfactorily similar to those of the corresponding ozonolysis product (IV), correlations of infrared spectra were obscured by the avidity with which this alcohol (VII) retains methanol and ethanol, the solvents best suited to its preparation and purification. The ethanol could not be removed from the solvated methyl ester (VII) without destroying the crystalline form; and the ethanol solvate of the corresponding ethyl ester behaved similarly. Fortunately the methanol solvate of the ester (VII) could be converted into the solvent-free compound without loss of crystallinity, and the product,

* Part II, *J.*, 1958, 4551.

whether examined in mulls or in solution, did not exhibit infrared carbonyl absorption characteristic of the non-enolic tautomer though it developed this when examined as a supercooled melt. This completed the analogy with the behaviour of the ozonolysis product (IV).

Oxidation of the grisen (VIII; R = Me) by osmium tetroxide furnished the tetracyclic saturated ketone (IX) which had $\nu_{max.}$ 3440 (OH) and 1720 cm.$^{-1}$ (C:O) and formed a 2,4-dinitrophenylhydrazone with $\lambda_{max.}$ 361 mμ (log ε 4·39). This ketone did not form stable solvates and when methylated in nearly neutral media (silver oxide and methyl iodide in dimethylformamide) supplied an ether identical with that obtained previously by ozonolysis of a ketone (III; H for CO_2Me). The suggested structures for the ozonolysis products are therefore confirmed, and it follows that the stereochemistry of these tetracyclic compounds is the same whichever method of oxidation is employed.

Theoretically, spirans such as (I) and (III) can also exist as the geometrical isomers, models showing, however, that in these isomers the methyl groups at the 4-position and on the exocyclic double-bond collide severely. This is clearly responsible for the fact that the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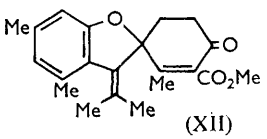
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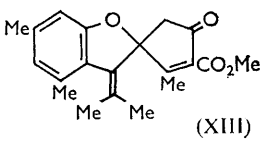
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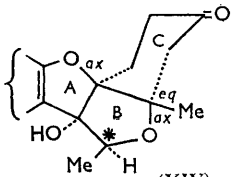
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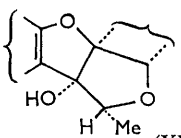
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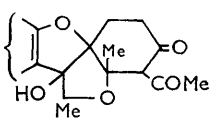
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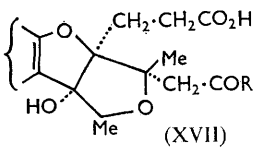
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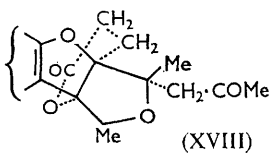
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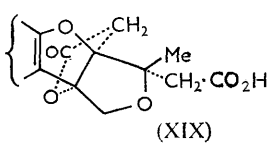
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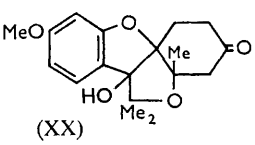
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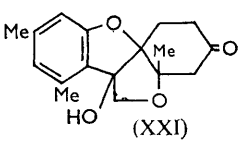
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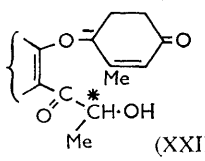
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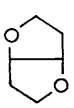

(XXIV)

spirans [I, III, VIII (R = H or Me), X, XI] may be made in good yield by the cyclisation of diketones such as (XXX), whereas spirans (XII) and (XIII), in which collision of methyl groups is unavoidable, cannot be made by this method.

Osmium tetroxide, being a bulky reagent, normally adds to the less hindered side of an ethylene; so the grisen (VIII; R = Me) can be assumed to afford a glycol (V), the dotted bonds lying towards the rear of the plane of the benzene ring. Axial attack by the (secondary) hydroxyl group occurring at the cyclohexenone double bond would accord with accepted views and result in a tetracycle (IX) of configuration (XIV) having the cyclohexanone ring in a favourable conformation, that is, with the phenoxide oxygen atom in the axial position. [In (XIV), the dotted lines refer to the conformation about ring B, the letters *ax* and *eq* to the conformation about the cyclohexanone ring.] It follows that both the A/B and the B/C ring-fusions are *cis*.

To show that the A/B ring-fusion is indeed *cis*, the tetracyclic ester (VI) and also the tetracyclic ketone (XVI), obtained from osmium tetroxide and the ketone (III; COMe for CO_2Me), were hydrolysed by alkali. The latter hydrolysis gave a ketonic acid which, though it had properties consistent with structure (XVII; R = Me), did not crystallise and was therefore converted by heat into the ketonic δ-lactone (XVIII) with $\nu_{max.}$ 1761 * and 1706 cm.$^{-1}$. The ester (VI) supplied what seemed to be a dibasic acid but this could not be fully characterised because it so easily changed into the γ-lactonic acid (XIX), the methyl ester of which had $\nu_{max.}$ 1786 and 1738 cm.$^{-1}$. Both lactones had unexpectedly high lactonic carbonyl frequencies, but it seemed that neither could have been formed at all had the A/B ring-fusion been *trans*. Further work invalidated this simple argument.

The osmium tetroxide oxidation product (IX) isomerised in warm alkali and, as the corresponding methyl ether (IX; OMe for OH) was unaffected, the hydroxyl group must be essential to this change. The new isomer gave a different methyl ether isomeric with the ozonolysis product (IV; H for CO_2Me), and was so closely similar to the original alcohol in both chemical and spectroscopic properties that the change was thought to be stereochemical rather than structural in origin. This view was substantiated and the centre involved shown to be that starred in (IX) by the fact that neither compound (XX) nor (XXI) [obtained from the appropriate grisens (XI; H for CO_2Me) and (VIII; R = H) by the use of osmium tetroxide] was affected by alkali even in very vigorous conditions. Bases would of course induce β-elimination in (XIV), so that the tetracycles would revert to the glycols [as (V)], but in itself this provides no explanation of the above results. In the glycol (V), however, the presence of the tertiary alcohol group (but not, of course, of a methoxyl group) allows a reversed aldol condensation generating—if only momentarily—an intermediate (XXII) in which the starred centre is optically sensitive, so that when the rings close again the more stable of the two structures (XIV) and (XV) would be favoured. The benzene ring eclipses the methyl group at the atom starred in (XIV) but the resulting repulsion is absent from the epimer (XV), so that with (XV) as the structure of the new isomer all the facts can be satisfactorily explained.

The above discussion destroys the chemical evidence adduced for the A/B *cis*-fusion, because the changes involved would allow an initial A/B *trans*-fused system to take up the *cis*-fused arrangement. Fortunately, there is considerable evidence that *cis*-fused tetrahydrofuran rings are nearly strain-free whereas *trans*-fused rings are strained. For example, lignans of type (XXIII) are invariably *cis*-fused, all attempts to prepare the corresponding *trans*-fused systems having failed.[1] The same considerations apply to the skeleton (XXIV), though there is a single instance of *trans*-fusion here.[2] In the present case, one tetrahydrofuran ring is modified by inclusion of a benzenoid double bond, models showing clearly that the strain in the *trans*-fused system is thereby greatly increased while the *cis*-fused system is not much affected. For these reaons it is very probable that, had compounds (XX) and (XXI) had A/B *trans*-fusion, treatment with alkali would have allowed them to attain the more stable A/B *cis*-fusion. As neither compound was affected by alkali even in forcing conditions, they must have been *cis*-fused in the first place. Consequently, expressions such as (XIV) may still be regarded as correct descriptions of the stereochemistry in the tetracyclic compounds.

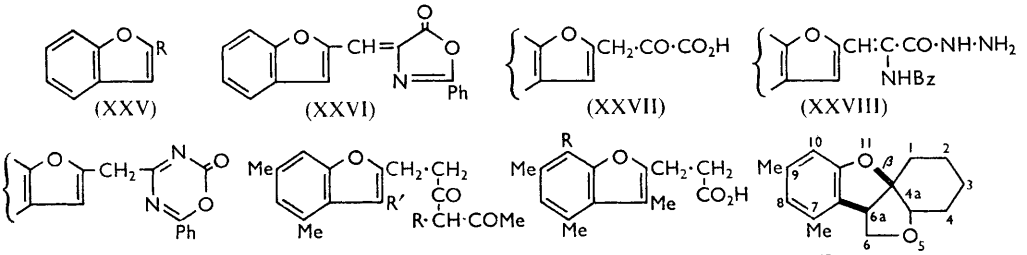
As before, the acids of type (XXV; R = $CH_2{\cdot}CO_2H$ or $CH_2{\cdot}CH_2{\cdot}CO_2H$) required for these and related studies were made from benzofurans (XXV; R = H) which were first converted into the aldehydes (XXV; R = CHO). The Gattermann reaction and the

* A Referee pointed out that this value is higher than those for most strain-free δ-lactones. We consider that the environment of the lactone ring is responsible for this because (XIX), undoubtedly a γ-lactone, also has an unusually high absorption frequency (1786 cm.$^{-1}$) compared with other members of its class. In the absence of suitable authentic model compounds, the matter cannot be pursued further at present.

[1] Hearon and MacGregor, *Chem. Rev.*, 1955, **55**, 959; Freudenberg and Fischer, *Chem. Ber.*, 1956, **89**, 1230; Beroza and Schechter, *J. Amer. Chem. Soc.*, 1956, **78**, 1242.

[2] Owen and Peto, *J.*, 1955, 2382; Ali and Owen, *J.*, 1958, 1074.

method [1] explored by Bisagni, Buu-Hoï, and Royer [3] were both used for this conversion and found to give comparable yields. The latter being much the more convenient, it is now preferred (see next section). 2-Benzofurylacetic acids (XXV; R = $CH_2 \cdot CO_2H$) were previously made from the aldehydes (XXV; R = CHO) by hydrolysis of the derived azlactones (XXVI) to the pyruvic acids (XXVII) and oxidation. This method has been compared with that introduced by Jennings.[4] In this, the azlactones (XXVI) are converted into the hydrazides (XXVIII) which, treated with nitrous acid and heated, form oxadiazines (XXIX) that furnish the furylacetic acids when hydrolysed. Again the two methods gave comparable yields, but that of Jennings was much the more expeditious in spite of the greater number of steps involved (see next section).



None of the methods described in Part II supplied acceptable yields of grisens of type (VIII). To remedy this, the acids (XXV; R = $CH_2 \cdot CO_2H$ or $CH_2 \cdot CH_2 \cdot CO_2H$), as their acid chlorides, were condensed with t-butyl acetoacetate to give dioxo-esters, *e.g.*, (XXX; R = CO_2Bu^t) which were easily transformed by toluene-*p*-sulphonic acid in hot toluene into crystalline diketones, *e.g.*, (XXX; R = H), the reaction being readily followed by the evolution of carbon dioxide. Cyclisation of the diketones then gave the desired grisens in good yield. Attempts to contract this sequence into one step by treating the ester (XXX; R = CO_2Bu^t) itself with sulphuric acid led chiefly to the acid (XXXI; R = Bu^t). The same compound was produced when the propionic acid (XXXI; R = H) was warmed with sulphuric acid and t-butyl alcohol, and is assigned the orientation written because steric hindrance would prevent entry of a t-butyl substituent between two methyl groups.

We have adopted the Editor's suggestions that, for the purpose of systematic nomenclature, the Ring Index method be applied and rings B and C of the tetracyclic spirans be regarded as contained in the plane of the paper, with the bond to the phenoxide oxygen atom rising from this plane and given the arbitrary stereochemical designation β as in (XXXII). Thus compound (XIV) is named 2,3,4,4a,6,6a-hexahydro-6aα-hydroxy-4aβ,6β,7,9-tetramethyl-3-oxo-1*H*-5,11-dioxadibenzo[*a*,*d*]pentalene; compound (VI) is named methyl 1,2,3,3a,5,5a-hexahydro-5a-hydroxy-3a,5,6,8-tetramethyl-2-oxo-4,10-dioxabenzo[*a*]cyclopenta[*d*]pentalene; and compound (XVII; R = OH) is named 3aα-2′-carboxyethyl-3α-carboxymethyl-8bα-hydroxy-1,3,3a,8b-tetrahydro-1,3β,6,8-tetramethyl-2,4-dioxacyclopenta[*a*]indene.

Experimental

2-*Hydroxy*-4,5-*dimethylisobutyrophenone*.—3,4-Dimethylphenyl isobutyrate (60 g.), kept with aluminium chloride (60 g.) at 130° for 5 hr., formed an orange complex which was decomposed with ice and hydrochloric acid. The product, isolated with ether, was purified by distillation, giving the *isobutyrophenone*, b. p. 150°/20 mm., with a purple ferric reaction (Found: C, 74·8; H, 8·3. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%). The *oxime* separated from benzene in prisms, m. p. 136° (Found: N, 6·9. $C_{12}H_{17}NO_2$ requires N, 6·8%).

[3] Bisagni, Buu-Hoï, and Royer, *J.*, 1955, 3688.
[4] Jennings, *J.*, 1957, 1512.

2-Isobutyryl-3,5-dimethylphenoxyacetic Acid.—A mixture of 2-hydroxy-4,6-dimethylisobutyrophenone [5] (100 g.), potassium carbonate (85 g.), ethyl bromoacetate (96 g.), and acetone (500 ml.) was kept at the b. p. for 20 hr. Evaporation of the hot filtrate left an oil which solidified and, when purified from light petroleum (b. p. 40—60°), supplied *ethyl 2-isobutyryl-3,5-dimethylphenoxyacetate* in needles (140 g.), m. p. 67° (Found: C, 68·8; H, 7·9. $C_{16}H_{22}O_4$ requires C, 69·0; H, 8·0%). This ester (70 g.) was heated with sodium hydroxide (40 g.) in alcohol (200 ml.) and water (200 ml.) until it all dissolved (about 1 hr.). After the cooled solution had been made up to 2 l. with water, addition of concentrated hydrochloric acid liberated the *phenoxyacetic acid* which separated from benzene–light petroleum in needles (60 g.), m. p. 138° (Found: C, 67·3; H, 7·2. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%).

2-Isobutyryl-5-methoxyphenoxyacetic Acid.—2-Hydroxy-4-methoxyisobutyrophenone [6] (97 g.) was etherified by ethyl bromoacetate as in the foregoing experiment. The oily phenoxyacetate was not purified but was hydrolysed at once to the *phenoxyacetic acid* which separated from benzene in rods (112 g.), m. p. 108° (Found: C, 61·6; H, 6·5; OMe, 12·2. $C_{12}H_{13}O_4 \cdot OMe$ requires C, 61·9; H, 6·4; OMe, 12·3%).

2-Isobutyryl-4,5-dimethylphenoxyacetic Acid.—Prepared from 2-hydroxy-4,5-dimethylisobutyrophenone by the method described above, this *dimethylphenoxyacetic acid* crystallised from benzene in rhombs, m. p. 118° (Found: C, 67·2; H, 7·2. $C_{14}H_{18}O_4$ requires C, 66·9; H, 7·3%).

2-Isobutyryl-4-methylphenoxyacetic Acid.—Obtained by the same method as the above phenoxy-acids, *2-isobutyryl-4-methylphenoxyacetic acid* formed needles, m. p. 106°, when purified from light petroleum (b. p. 40—60°) (Found: C, 65·9; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

4-Chloro-3,5-dimethyl-2-propionylphenoxyacetic Acid.—Interaction of 3-chloro-6-hydroxy-2,4-dimethylpropiophenone [7] and ethyl bromoacetate by the usual method gave *ethyl 4-chloro-3,5-dimethyl-2-propionylphenoxyacetate* which crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 60° (Found: C, 60·4; H, 6·6. $C_{15}H_{19}O_4Cl$ requires C, 60·3; H, 6·4%). Alkaline hydrolysis supplied the *phenoxyacetic acid* which crystallised from benzene in needles, m. p. 162° (Found: C, 57·4; H, 5·7. $C_{13}H_{15}O_4Cl$ requires C, 57·6; H, 5·5%).

2-Isobutyryl-5-methylphenoxyacetic Acid.—The standard procedure applied to 2-hydroxy-4-methylisobutyrophenone gave the desired *phenoxyacetic acid* as prisms, m. p. 92°, from benzene (Found: C, 66·1; H, 6·7. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

Benzofurans (XXV; R = H).—For the preparation of these, the *o*-acylphenoxyacetic acids (0·4 mole) were heated with sodium acetate (100 g.) and acetic anhydride (300 ml.) at 160° for 1 hr., cooled, and poured into water (2 l.). The oils produced were collected into ether, washed with aqueous sodium hydrogen carbonate to remove acids, dried ($MgSO_4$), and recovered by evaporation of the solvent. The crude *benzofurans* (see Table) were then purified by distillation and/or crystallisation.

Benzofurans (XXV; R = H).

Substituents	B. p./mm.	n_D/° c	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
3-Isopropyl-5-methyl	82°/0·5	1·5335/15·5	$C_{12}H_{14}O$	82·8	7·8	82·7	8·1
3-Isopropyl-6-methyl	78°/0·4	1·5345/20·0	$C_{12}H_{14}O$	82·7	8·1	82·7	8·1
3-Isopropyl-4,6-dimethyl * ...	97°/1·0	1·5412/17·0	$C_{13}H_{16}O$	82·9	8·8	83·0	8·6
3-Isopropyl-5,6-dimethyl	98°/0·7	1·5378/20	$C_{13}H_{16}O$	82·8	8·9	83·0	8·6
5-Chloro-3-ethyl-4,6-dimethyl	Plates, m. p. 45°, from light petroleum		$C_{12}H_{13}ClO$	68·8	6·1	69·1	6·2

* Prisms, m. p. 30°, from light petroleum.

2-Formylbenzofurans (XXV; R = CHO).—(i) To freshly distilled phosphorus oxychloride (1 mol.) mixed with dimethylformamide (1 mol.) at 5° was added a solution of the benzofuran (1 mol.) in dimethylformamide. The mixture was kept at 85° (60° for methoxybenzofurans) for 1 hr., cooled, diluted with water, and neutralised with sodium hydrogen carbonate. 2 Hr. later, the product was isolated with ether and purified by distillation or crystallisation from aqueous alcohol.

[5] von Auwers, *Annalen*, 1920, **421**, 74.
[6] Dohme, Cox, and Miller, *J. Amer. Chem. Soc.*, 1926, 1692; Reichstein, Oppenauer, Grüssner, Hirt, Rhyner, and Glatthaar, *Helv. Chim. Acta*, 1935, **18**, 816.
[7] Tiwari and Singh, *J. Indian Chem. Soc.*, 1958, **35**, 749.

2-Formylbenzofurans (XXV; R = CHO).

No.	Substituents	B. p./mm. or m. p.	Yield (%) (i)	Yield (%) (ii)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
(1)	3,4,6-Trimethyl [8]		85	85					
(2)	3-Ethyl-4,6-dimethyl [8]		82	86					
(3)	3-Isopropyl-5-methyl	150°/2·0	34	36	$C_{13}H_{14}O_2$	77·2	7·1	77·2	7·0
(4)	3-Isopropyl-6-methyl	150°/3·0	83	81	$C_{13}H_{14}O_2$	77·4	7·1	77·2	7·0
(5)	3-Isopropyl-4,6-dimethyl.....	159°/3	84	86	$C_{14}H_{16}O_2$	77·7	7·5	77·8	7·4
(6)	3-Isopropyl-5,6-dimethyl * ...	122°	48	50	$C_{14}H_{16}O_2$	77·5	7·6	77·8	7·4
(7)	5-Chloro-3-ethyl-4,6-dimethyl	124°	42	43	$C_{13}H_{13}ClO_2$	65·7	5·3	66·0	5·5
(8)	3-Isopropyl-6-methoxy †	154°/1·0	78	80	$C_{13}H_{14}O_3$	71·4	6·4	71·5	6·5

* Pure specimens could be obtained only by hydrolysis of the semicarbazone, which separated from aqueous alcohol in flakes, m. p. 238° (Found: N, 15·1. $C_{15}H_{19}N_3O_2$ requires N, 15·4%).

† M. p. 30° (Found: OMe, 14·5. $C_{12}H_{11}O_2$·OMe requires OMe, 14·2%). Aluminium chloride was omitted from this preparation.

2-Formylbenzofuran 2,4-dinitrophenylhydrazones.

No.*	M. p.	Colour	Formula	Found (%)	Required (%)
3	218°	Red	$C_{19}H_{18}N_4O_5$	14·3	14·7
4	226	Red	$C_{19}H_{18}N_4O_5$	14·4	14·7
5	250	Scarlet	$C_{20}H_{20}N_4O_5$	14·0	14·1
6	294	Orange	$C_{20}H_{20}N_4O_5$	14·0	14·1
7	246	Red	$C_{19}H_{17}ClN_4O_5$	13·2	13·4
8	228	Maroon	$C_{19}H_{18}N_4O_6$	14·1	14·1

* See preceding Table.

These *aldehydes* (see Table) gave **2,4-*dinitrophenylhydrazones*** as tabulated.

(ii) A solution of the benzofuran (0·2 mole) in ether (400 ml.) containing hydrogen cyanide (18 ml.) and aluminium chloride (34 g.) was saturated with hydrogen chloride at 0°. Next day, volatile materials were allowed to escape and the residue was added to water (2 l.): when the vigorous reaction had subsided the water was boiled to complete the hydrolysis. A heavy oil separated and was taken up in ether, washed with aqueous sodium hydrogen carbonate, dried ($MgSO_4$), recovered by evaporation of the solvent, and purified by distillation or other appropriate method.

Azlactones (XXVI).—The 2-formylbenzofuran (0·2 mol.) was heated with hippuric acid (70 g.), sodium acetate (40 g.), and acetic anhydride (250 ml.) on the steam-bath for 2 hr. The cooled product was diluted with 50% alcohol (700 ml.) and kept overnight to complete the precipitation of the *azlactone*, which was then collected and crystallised from alcohol (see Table).

4-2′-Benzofurylmethylene-2-phenyloxazolin-5-ones (XXVI).

Substituents	M. p.	Habit	Formula	Found N (%)	Required N (%)
3-Isopropyl-6-methyl	176°	Yellow needles	$C_{22}H_{19}NO_3$	4·0	4·1
3-Isopropyl-4,6-dimethyl	228	Yellow prisms	$C_{23}H_{21}NO_3$	4·0	3·9
5-Chloro-3-ethyl-4,6-dimethyl	216	Yellow needles	$C_{22}H_{18}ClNO_3$	3·4	3·7
3-Isopropyl-6-methoxy.....	160	Golden needles	$C_{22}H_{19}NO_4$	3·6	3·9

Pyruvic Acids (XXVII).—The azlactone (0·09 mole) was boiled with 20% aqueous potassium hydroxide (300 ml.) until ammonia was no longer evolved, water being added intermittently to maintain the volume of fluid. The resulting solution, diluted with water (750 ml.) and acidified with concentrated hydrochloric acid, was warmed to 60° to coagulate the precipitate which had been formed. The solid was collected, washed with warm water, and crystallised from aqueous alcohol to give the *pyruvic acid* (see Table).

2′-Benzofurylpyruvic acids (XXVII).

Substituents	M. p.	Habit	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
3-Isopropyl-6-methyl	184°	Yellowish needles	$C_{15}H_{16}O_4$	69·3	6·3	69·2	6·2
3-Isopropyl-4,6-dimethyl	192	Yellowish needles	$C_{16}H_{18}O_4$	70·1	6·3	70·1	6·6
5-Chloro-3-ethyl-4,6-dimethyl	210	Pinkish needles	$C_{15}H_{15}ClO_4$	60·8	4·9	61·1	5·1
3-Isopropyl-6-methoxy	165	Yellowish plates	$C_{15}H_{16}O_5$	64·9	5·7	65·2	5·8

[8] Dean, Halewood, Mongkolsuk, Robertson, and Whalley, *J.*, 1953, 1250.

Hydrazides (XXVIII).—The finely powdered azlactone (0·02 mole), suspended in ether (150 ml.), was treated with hydrazine hydrate (0·028 mole) and stirred until the colour was completely discharged; the resulting solid was collected and purified from alcohol. All the *hydrazides* obtained thus (see Table) formed needles.

α-*Benzamido*-β-2-*benzofurylacrylohydrazides* (XXVIII).

Substituents	M. p.	Formula	Found N (%)	Required N (%)
3-Ethyl-4,6-dimethyl	198°	$C_{22}H_{23}N_3O_3$	11·0	11·1
3-Isopropyl-6-methyl	184	$C_{22}H_{23}N_3O_3$	11·2	11·1
3-Isopropyl-4,6-dimethyl	180	$C_{23}H_{25}N_3O_3$	10·6	10·7
5-Chloro-3-ethyl-4,6-dimethyl	212	$C_{22}H_{22}ClN_3O_3$	10·1	10·3
3-Isopropyl-6-methoxy	186	$C_{22}H_{23}N_3O_4$	10·8	10·7
4,6-Dimethoxy-3-methyl	230	$C_{21}H_{21}N_3O_5$	10·5	10·6

Oxadiazines (XXIX).—A solution of sodium nitrite in the minimum amount of water was added slowly to the hydrazide (XXVIII) in the smallest convenient quantity of acetic acid, the temperature being kept below 17°. After ½ hr., the yellow crystalline precipitate was washed with water, to give crude azides which were too unstable for characterisation. The azides were dried in air and extracted from a Soxhlet thimble with benzene. When concentrated and cooled, the benzene extracts deposited the *oxadiazines* (XXIX) (see Table) which usually formed needles when recrystallised from benzene.

4-2′-*Benzofuryl*-6-*phenyl*-1,3,5-*oxadiazin*-2-*ones* (XXIX).

Substituents	Colour	M. p.	Formula	Found N (%)	Required N (%)
3-Ethyl-4,6-dimethyl	Red	174°	$C_{22}H_{20}N_2O_3$	7·7	7·8
3-Isopropyl-6-methyl	Deep yellow	206	$C_{22}H_{20}N_2O_3$	7·6	7·8
3-Isopropyl-4,6-dimethyl	Yellow rods	226	$C_{23}H_{22}N_2O_3$	7·3	7·5
5-Chloro-3-ethyl-4,6-dimethyl	Orange-red	246	$C_{22}H_{19}ClN_2O_3$	6·8	7·1
3-Isopropyl-6-methoxy	Orange-yellow	208	$C_{22}H_{20}N_2O_4$	7·2	7·4
4,6-Dimethoxy-3-methyl	Red	226	$C_{21}H_{18}N_2O_5$	7·2	7·4

2-*Benzofurylacetic Acids* (XXV; R = $CH_2{\cdot}CO_2H$).—(i) Hydrogen peroxide (100-vol.; 20 ml.) was added to the pyruvic acid (0·062 mole) in 5% aqueous potassium hydroxide (20 ml.) at 0°. After 5 min. the mixture was diluted with iced water (1 l.) and acidified with dilute sulphuric acid to liberate the crude 2-benzofurylacetic acid which was crystallised from light petroleum or from aqueous alcohol (see Table).

(ii) A mixture of the oxadiazine (0·1 mole), acetic acid (400 ml.), and dilute hydrochloric acid (40 ml.) was boiled until dissolution was complete and the colour was discharged, whereafter dilution with water precipitated the benzofurylacetic and benzoic acids. The latter was leached out with water at 60°, leaving the crude benzofurylacetic acid which was recrystallised from light petroleum or aqueous alcohol.

2-*Benzofurylacetic acids*.

Substituents	M. p.	Yields * (%) (i)	(ii)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
3-Ethyl-4,6-dimethyl [8]		54	56					
3-Isopropyl-6-methyl	136°	55	55	$C_{14}H_{16}O_3$	72·2	6·6	72·4	6·9
3-Isopropyl-4,6-dimethyl	158	50	48	$C_{15}H_{18}O_3$	73·0	7·3	73·1	7·4
5-Chloro-3-ethyl-4,6-dimethyl	182	57	55	$C_{14}H_{15}ClO_3$	63·1	5·8	63·0	5·5
3-Isopropyl-6-methoxy	142	51	49	$C_{14}H_{16}O_4$	67·7	6·3	67·7	6·5
4,6-Dimethoxy-3-methyl [9]		50	52					

* Overall yields based on 2-formylbenzofurans.

3-*Isopropyl*-6-*methoxybenzofuran*-2-*carboxylic Acid*.—These reactions were carried out to ensure that 2-formyl-3-isopropyl-6-methoxybenzofuran, prepared as above, had the formyl group in the 2-position.[9]

(i) 2-Formyl-3-isopropyl-6-methoxybenzofuran (1 g.) in acetone (30 ml.) was oxidised by potassium permanganate (0·6 g.) in the least quantity of water. 18 Hr. later, the mixture was clarified by sulphur dioxide and diluted with water. The precipitate, taken up in ether and

[9] Birch and Robertson, *J.*, 1938, 306.

extracted thence into aqueous sodium hydrogen carbonate, was liberated by acidification and crystallised from acetic acid, giving the methoxybenzofuran-2-carboxylic acid in prisms, m. p. 180° (lit., m. p. 180°). (ii) The crude phenoxyacetate (1 g.) formed as an intermediate in the preparation of 2-isobutyryl-5-methoxyphenoxyacetic acid (see above) was heated with a solution from sodium (0·2 g.) in alcohol (10 ml.) on the steam-bath for 15 min. The product was isolated by dilution with water (20 ml.) and acidification, and when purified from glacial acetic acid gave the methoxybenzofuran-2-carboxylic acid in prisms, m. p. 180°, identical with a sample prepared by method (i).

3-Isopropyl-4,6-dimethylbenzofuran-3-carboxylic Acid.—Prepared by both the methods described for the 6-methoxybenzofuran-3-carboxylic acid analogue, *3-isopropyl-4,6-dimethylbenzofuran-2-carboxylic acid* separated from acetic acid in prisms, m. p. 232° (Found: C, 72·2; H, 6·8. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%).

β-(3-Isopropyl-4,6-dimethyl-2-benzofuryl)propionic Acid.—When effervescence ceased in a mixture of 2-formyl-3-isopropyl-4,6-dimethylbenzofuran (50 g.), malonic acid (50 g.), piperidine (1 ml.), and pyridine (150 ml.) held at 100°, a large excess of dilute hydrochloric acid was added. The reddish precipitate was collected, washed with water, and dried in air before being boiled with benzene (100 ml.) to extract impurities. The white residue crystallised from a large volume of benzene to give *β-(3-isopropyl-4,6-dimethyl-2-benzofuryl)acrylic acid* in needles (48 g.), m. p. 230° (decomp.), $\lambda_{max.}$ 248, 336 mμ (log ε 3·80, 4·52) (Found: C, 74·2; H, 7·0. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%). Suspended in 10 : 1 ether–methanol and treated with diazomethane until no more effervescence was noted, this acrylic acid furnished the *methyl ester*, which separated from aqueous methanol in needles, m. p. 45° (Found: OMe, 11·7. $C_{16}H_{17}O_2$·OMe requires OMe, 11·4%).

The acrylic acid (12 g.) in 0·1N-aqueous sodium hydroxide (500 ml.) containing Raney nickel (1·5 g.) was shaken with hydrogen (50 atm.) for 6 hr. The oil that separated when the filtrate was acidified solidified slowly and was then purified from light petroleum (b. p. 40—60°), giving the *propionic acid* in prisms (10 g.), m. p. 76°, $\lambda_{max.}$ 258, 296 mμ (log ε 4·16, 3·42). This substance retained the solvent tenaciously, and had to be melted before consistent analytical data could be obtained (Found: C, 74·0; H, 7·8. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%). The *methyl ester*, prepared by means of diazomethane, was an oil, b. p. 190°/1 mm. (Found: OMe, 11·3. $C_{16}H_{19}O_2$·OMe requires OMe, 11·3%), but the *hydrazide*, prepared from this ester and hydrazine hydrate, crystallised from aqueous methanol in plates, m. p. 141° (Found: N, 10·2. $C_{16}H_{22}N_2O_2$ requires N, 10·2%).

β-(3,4,6-Trimethyl-7-t-butyl-2-benzofuryl)propionic Acid (XXXI; R = Bu^t).—β-(3,4,6-Trimethyl-2-benzofuryl)propionic acid (2·5 g.) was mixed with sulphuric acid monohydrate (30 ml.) and t-butyl alcohol (0·75 g.) and left at −2° for 2 days. After the addition of crushed ice, ether extracted material part of which was soluble in aqueous sodium hydrogen carbonate and was identified as the starting material; the insoluble part, when isolated by means of dilute sodium hydroxide solution and crystallised from aqueous alcohol, afforded the *t-butylbenzofurylpropionic acid* in needles (0·8 g.), m. p. 163° (Found: C, 74·8; H, 8·4; O, 16·3. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·4; O, 16·6%).

β-(3-Isopropyl-5,6-dimethyl-2-benzofuryl)propionic Acid.—Obtained from 2-formyl-3-isopropyl-5,6-dimethylbenzofuran by the method given above for the 4,6-dimethyl isomer, *β-(3-isopropyl-5,6-dimethyl-2-benzofuryl)acrylic acid* formed needles, m. p. 236°, when crystallised from benzene (Found: C, 74·4; H, 7·0. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%): the *methyl ester* separated from aqueous methanol in prisms, m. p. 85° (Found: OMe, 11·4. $C_{16}H_{17}O_3$·OMe requires OMe, 11·4%).

Hydrogenation of the acrylic acid on Raney nickel afforded the *propionic acid* which formed rods, m. p. 120°, from light petroleum (b. p. 60—80°) (Found: C, 73·7; H, 7·8. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%). The methyl ester prepared by means of diazomethane was an oil which was converted into the *hydrazide*, plates, m. p. 130° (from aqueous methanol) (Found: N, 10·4. $C_{16}H_{22}N_2O_2$ requires N, 10·2%).

β-(3-Isopropyl-5-methyl-2-benzofuryl)propionic Acid.—By the method described for the analogues, 2-formyl-3-isopropyl-5-methylbenzofuran was converted into *β-(3-isopropyl-5-methyl-2-benzofuryl)acrylic acid* which crystallised from benzene in needles, m. p. 230° (Found: C, 73·7; H, 6·7. $C_{15}H_{16}O_3$ requires C, 73·8; H, 6·6%), and with diazomethane rapidly gave the *methyl ester*, crystallising from aqueous methanol in needles, m. p. 70° (Found: C, 74·3; H, 7·1. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%).

Hydrogenation of the acrylic acid furnished the *propionic acid* which separated from light petroleum (b. p. 40—60°) in cubes, m. p. 97° (Found: C, 73·2; H, 7·5. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%), and formed a *methyl ester* as needles, m. p. 28°, from light petroleum (b. p. 40—60°) (Found: C, 73·9; H, 7·7. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%).

β-(3-*Isopropyl*-6-*methoxy*-2-*benzofuryl*)*propionic Acid*.—By interaction with malonic acid in hot pyridine containing piperidine, 2-formyl-3-isopropyl-6-methoxybenzofuran (20 g.) was converted into β-(3-*isopropyl*-6-*methoxy*-2-*benzofuryl*)*acrylic acid*, which, when purified from benzene (charcoal), formed cream needles (19 g.), m. p. 198°, $\lambda_{max.}$ 252, 340 mμ (log ε 3·79, 4·79) (Found: C, 69·1; H, 6·3; OMe, 12·0. $C_{14}H_{13}O_3$·OMe requires C, 69·2; H, 6·2; OMe, 11·9%). Hydrogenation of this acrylic acid on Raney nickel afforded the *methoxybenzofurylpropionic acid* as cubes, m. p. 76—78°, $\lambda_{max.}$ 249, 256, 292 mμ (log ε 4·12, 4·12, 3·81), from light petroleum (b. p. 40—60°) (Found: C, 68·7; H, 7·2; OMe, 12·1. $C_{14}H_{15}O_3$·OMe requires C, 68·7; H, 6·9; OMe, 11·8%).

4,6,2′-*Trimethyl*-3-*methylenegris*-2′-*en*-4′-*one* (VIII; R = H).—β-(3,4,6-Trimethyl-2-benzofuryl)propionic acid (10 g.) (Part II) was added to phosphorus pentachloride (10 g.) in chloroform (75 ml.). After ¼ hr., the temperature was raised to 60° for ½ hr., and then the solvent was distilled off. Phosphorus oxychloride was removed by co-distillation with benzene, and the residual crude acid chloride was further purified by subjection to a vacuum at 50° for ½ hr. To the product in ether (125 ml.) was added the ethoxymagnesio-derivative (equiv. to 1·2 g. of magnesium) of t-butyl acetoacetate, and the mixture was heated under reflux for 3 hr. The resulting complex was decomposed by dilute acetic acid, and the organic layer, having been washed with sodium hydrogen carbonate solution and with water and dried ($MgSO_4$), was evaporated, leaving a crude dioxo-ester (XXX; R = CO_2Bu^t, R′ = Me) as a viscous oil with a pleasant odour and an intense red ferric reaction. This oil was warmed in toluene (150 ml.) containing toluene-*p*-sulphonic acid (0·5 g.) on the steam-bath until carbon dioxide was no longer evolved (about 3 hr.). When cool, the solution was diluted with ether, washed with aqueous sodium hydrogen carbonate and then water, dried ($MgSO_4$), and concentrated, finally under reduced pressure. The residue solidified and when purified first by chromatography from benzene on silica and then by crystallisation from light petroleum (b. p. 40—60°) supplied 5-(3,4,6-*trimethyl*-2-*benzofuryl*)*hexane*-2,4-*dione* (XXX; R = H, R′ = Me) in needles (4·4 g.), m. p. 83°, $\nu_{max.}$ 1639 cm.$^{-1}$ (broad: chelated carbonyl), with a red ferric reaction (Found: C, 74·7; H, 7·4. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·4%).

This diketone (2 g.), mixed at 5° with sulphuric acid monohydrate (15 ml.), was kept at −2° for 2 days, treated with crushed ice, and extracted with ether. Acidic materials were removed by means of 2N-sodium hydroxide, and the solution was then washed with water, dried ($MgSO_4$), and evaporated. The product solidified in contact with light petroleum (b. p. 60—80°) and when crystallised from this solvent afforded the *trimethyl*-3-*methylenegrisenone* in faintly yellow prisms (1·5 g.), m. p. 111°, insoluble in 2N-sodium hydroxide, devoid of a ferric reaction, and having $\nu_{max.}$ 1675 cm.$^{-1}$ (conj. ketone) [Found: C, 80·1; H, 7·2%; *M* (Rast), 215. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%; *M*, 254]. The 2,4-*dinitrophenylhydrazone* crystallised in orange needles, m. p. 208°, from ethyl acetate (Found: C, 63·5; H, 5·3; N, 12·8. $C_{23}H_{22}N_4O_5$ requires C, 63·6; H, 5·1; N, 12·9%).

When the crude dioxo-ester (5·0 g.) was treated directly with sulphuric acid monohydrate (15 ml.) at 5° (that is, with omission of the treatment with toluene-*p*-sulphonic acid), three products were formed. The neutral one was the desired grisen (0·25 g.), m. p. and mixed m. p. 111°; another, an acid insoluble in aqueous sodium hydrogen carbonate, was identified spectroscopically and by mixed m. p.s with the t-butylpropionic acid (XXXI; R = Bu^t); the third, an acid soluble in sodium hydrogen carbonate solution, was obtained in small yield only but is considered to be 4,6,2′-*trimethyl*-3-*methylene*-4′-*oxogris*-2′-*en*-3′-*carboxylic acid*: it separated from alcohol–light petroleum in needles, m. p. 150°, having an infrared spectrum closely similar to that of the 3-ethylidene homologue (Found: C, 72·6; H, 6·1%; *M*, 267. $C_{17}H_{17}O_2$·CO_2H requires C, 72·5; H, 6·1%; *M*, 298).

4,6,2′-*Trimethyl*-3-*ethylidenegris*-2′-*en*-4′-*one* (VIII; R = Me).—Prepared in the same way as the foregoing 3-methyl analogue but beginning with β-(3-ethyl-4,6-dimethyl-2-benzofuryl)-propionic acid (10 g.), 5-(3-*ethyl*-4,6-*dimethyl*-2-*benzofuryl*)*hexane*-2,4-*dione* (XXX; R = H, R′ = Et) was purified from benzene on silica and recrystallised from light petroleum (b. p. 40—60°) as plates (7·4 g.), m. p. 87° (Found: C, 75·6; H, 7·9. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·7%).

Cyclised by sulphuric acid monohydrate at −2° by the general method, the diketone (5 g.)

supplied the 3-ethylidenegrisenone which crystallised from light petroleum (b. p. 60—80°) in pale yellow prisms (1·2 g.), m. p. 106°, not depressed by admixture with specimens prepared by methods given in Part II.

Methyl 4,6,2′-*Trimethyl*-3-*methylene*-4′-*oxogris*-2′-*en*-3′-*carboxylate*.—The acid chloride from β-(3,4,6-trimethyl-2-benzofuryl)propionic acid (10 g.) interacted with the methoxymagnesio-derivative (20 g.) of methyl acetoacetate in boiling ether (200 ml.) during 3 hr. Isolated by evaporation of the ethereal layer obtained when dilute acetic acid was added, *methyl* α-*acetyl*-β-*oxo*-δ-(3,4,6-*trimethyl*-2-*benzofuryl*)*valerate* (XXX; R = CO_2Me, R′ = Me) crystallised from light petroleum (b. p. 40—60°) in pale yellow prisms (8 g.), m. p. 88° (Found: C, 68·9; H, 6·7. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7%). Treated with sulphuric acid monohydrate (10 ml.) at 2° for 12 hr., this ester (1 g.) cyclised giving a gum, that was isolated by the addition of ice followed by extraction into ether. Acidic materials were removed from the extract by means of 2N-sodium hydroxide, whereafter evaporation of the solvent left a solid which, purified from aqueous alcohol, gave the *methyl* 3-*methyleneoxogrisencarboxylate* in needles (0·5 g.), m. p. 151° (Found: C, 73·0; H, 6·7; OMe, 9·8. $C_{18}H_{17}O_3$·OMe requires C, 73·1; H, 6·5; OMe, 9·9%).

3-*Isopropylidene*-6-*methoxy*-2′-*methylgris*-2′-*en*-4′-*one* (XI; H for CO_2Me).—β-(3-Isopropyl-6-methoxy-2-benzofuryl)propionic acid (5·2 g.) was converted into the acid chloride, condensed with t-butyl acetoacetate, and de-esterified by the method described for the analogues. The resulting crude β-diketone could not be properly purified and was therefore treated at once with sulphuric acid monohydrate (25 ml.) at 2°. After 2 days, the product was isolated in the usual fashion and formed an oil which solidified in contact with light petroleum (b. p. 60—80°) and was purified from benzene on a silica column. Thus obtained, the *isopropylidenemethoxygrisenone* separated from benzene–light petroleum (b. p. 60—80°) in pyramids (1·3 g.), m. p. 120°, $\lambda_{max.}$ 220, 228, 261, 312 mμ (log ε 4·45, 4·47, 4·20, 4·07), $\nu_{max.}$ 1670 cm.$^{-1}$ (cyclohexenone C:O) (Found: C, 75·9; H, 7·2. $C_{18}H_{20}O_3$ requires C, 76·0; H, 7·0%). Crystallised from alcohol, the 2,4-*dinitrophenylhydrazone* appeared as needles, m. p. 248° (Found: N, 12·2. $C_{24}H_{24}N_4O_6$ requires N, 12·1%).

Methyl 3-*Isopropylidene*-5,6,2′-*trimethyl*-4′-*oxogris*-2′-*en*-3′-*carboxylate* (X).—Interaction of β-(3-isopropyl-5,6-dimethyl-2-benzofuryl)propionic acid (5·2 g.) with phosphorus pentachloride (4·2 g.) in chloroform (20 ml.) at 50° for 1 hr. gave an acid chloride which was partially purified by repeated distillation with benzene and when condensed with the methoxymagnesio-derivative (5 g.) of methyl acetoacetate in boiling ether for 1 hr. supplied a complex salt. This, when decomposed by dilute acetic acid, afforded an oil which, after purification on silica from light petroleum followed by crystallisation from the same solvent (b. p. 40—60°), gave *methyl* α-*acetyl*-δ-(3-*isopropyl*-5,6-*dimethyl*-2-*benzofuryl*)-β-*oxovalerate* in yellow needles (5 g.), m. p. 63°, $\lambda_{max.}$ 260, 284 mμ (log ε 4·20, 4·18), $\nu_{max.}$ 1706, 1563 cm.$^{-1}$ (Found: C, 70·5; H, 7·3; OMe, 8·6. $C_{20}H_{23}O_4$·OMe requires C, 70·4; H, 7·3; OMe, 8·7%).

In sulphuric acid monohydrate (12 ml.) at 2° (2 days) the foregoing ester (4·0 g.) cyclised and the product was isolated by the addition of crushed ice followed by extraction into ether. The neutral fraction, when crystallised from aqueous methanol, supplied the *isopropylidenetrimethyloxogrisencarboxylate* in yellowish rods (1·3 g.), m. p. 160°, $\lambda_{max.}$ 216, 233, 260, 268, 317, 330 mμ (log ε 4·43, 4·45, 4·24, 4·13, 4·03, 4·06), $\nu_{max.}$ 1736 (ester), 1672 cm.$^{-1}$ (conjugated C:O), devoid of a ferric reaction (Found: C, 74·2; H, 7·1; OMe, 8·9. $C_{20}H_{21}O_3$·OMe requires C, 74·1; H, 7·1; OMe, 9·1%). The 2,4-*dinitrophenylhydrazone* was deposited from ethyl acetate as orange needles, m. p. 250° (decomp.) (Found: N, 10·9. $C_{27}H_{28}N_4O_7$ requires N, 10·8%), and the *oxime* was obtained as needles, m. p. 210°, from aqueous alcohol (Found: N, 4·2. $C_{21}H_{25}NO_4$ requires N, 3·9%).

3-*Isopropylidene*-5,6,2′-*trimethylgris*-2′-*en*-4′-*one* (X; H for CO_2Me).—By the general method, the acid chloride of β-(3-isopropyl-5,6-dimethyl-2-benzofuryl)propionic acid was condensed with the methoxymagnesio-derivative of t-butyl acetoacetate and the product, heated with toluene-*p*-sulphonic acid in toluene, afforded a crude β-diketone which failed to crystallise after purification from benzene on a silica column. This diketone (2 g.) was mixed with sulphuric acid monohydrate (25 ml.) at 2° and kept for 2 days. Addition of ice gave a gum which was chromatographed on silica from benzene and then crystallised from light petroleum (b. p. 60—80°), to furnish the 5,6,2′-*trimethylgrisenone* as prisms (0·1 g.), m. p. 184° (Found: C, 80·5; H, 7·5. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·8%), $\lambda_{max.}$ 234, 259, 318, 331 mμ (log ε 4·51, 4·21, 4·06, 4·08), $\nu_{max.}$ 1672 cm.$^{-1}$. Its 2,4-*dinitrophenylhydrazone* crystallised from ethyl acetate in orange needles, m. p. 268° (Found: N, 11·9. $C_{25}H_{26}N_4O_5$ requires N, 12·1%).

Methyl 3-*Isopropylidene*-6-*methoxy*-2′-*methyl*-4′-*oxogris*-2′-*en*-3′-*carboxylate* (XI).—The acid chloride from β-(3-isopropyl-6-methoxy-2-benzofuryl)propionic acid (5·2 g.) was dissolved in ether (50 ml.) and added to the methoxymagnesio-derivative (6 g.) of methyl acetoacetate suspended in boiling ether (100 ml.). After 2 hr., the mixture was cooled, and dilute acetic acid was added. The organic layer was washed with water, dried ($MgSO_4$), and evaporated to an oil (6 g.) that crystallised from light petroleum (b. p. 40—60°) to give *methyl* α-*acetyl*-δ-(3-*isopropyl*-6-*methoxy*-2-*benzofuryl*)-β-*oxovalerate* in prisms (4 g.), m. p. 81°, having a red ferric reaction [Found: C, 66·6; H, 6·6; OMe, 17·2. $C_{18}H_{18}O_4(OMe)_2$ requires C, 66·7; H, 6·7; OMe, 17·2%]. After this dioxo-ester (1·0 g.) had been kept with sulphuric acid monohydrate (10 ml.) at 2° for 2 days, the neutral cyclisation product was isolated in the usual way and when crystallised from methanol afforded the *methyl* 6-*methoxyoxogrisencarboxylate* in pale yellow parallelepipeds (0·27 g.), m. p. 194°, $\lambda_{max.}$ 230, 262, 312, 324 mμ (log ε 4·31, 4·12, 3·93, 3·92), $\nu_{max.}$ 1742 (ester), 1678 cm.$^{-1}$ (unsaturated C:O) [Found: C, 70·1; H, 6·6; OMe, 18·0. $C_{18}H_{16}O_3(OMe)_2$ requires C, 70·2; H, 6·5; OMe, 18·1%]. The 2,4-*dinitrophenylhydrazone* was obtained as orange-red needles, m. p. 214°, from alcohol (Found: N, 10·6. $C_{26}H_{25}N_4O_8$ requires N, 10·8%).

Methyl 3-*Ethylidene*-4,6,2′-*trimethyl*-4′-*oxocoumaran*-2-*spiro*-1′-*cyclopent*-2′-*ene*-3′-*carboxylate* (I).—Prepared from the methoxymagnesio-derivative of methyl acetoacetate and the acid chloride (Part II) of 3-ethyl-4,6-dimethyl-2-benzofurylacetic acid by the standard sequence, this *spiran* was obtained as slightly yellow prisms, m. p. 92°, from light petroleum (b. p. 40—60°) (Found: C, 73·0; H, 6·5. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·5%), $\lambda_{max.}$ 229, 260, 269, 310, 321 mμ (log ε 4·49, 4·22, 4·16, 3·91, 3·94), $\nu_{max.}$ 1724 (ester), 1695 cm.$^{-1}$ (unsaturated C:O). The 2,4-*dinitrophenylhydrazone* crystallised from ethyl acetate in yellow needles, m. p. 235° (Found: N, 11·5. $C_{25}H_{24}N_4O_7$ requires N, 11·4%).

Attempted Preparations of Methyl 3-*Isopropylidene*-4,6,2′-*trimethyl*-4′-*oxogris*-2′-*en*-3-*carboxylate* (XII) *and of Methyl* 3-*Isopropylidene*-4,6,2′-*trimethyl*-4′-*oxobenzofuran*-2-*spiro*-1′-*cyclopent*-2′-*ene*-3′-*carboxylate* (XIII).—(i) β-(3-Isopropyl-4,6-dimethyl-2-benzofuryl)propionic acid was converted into the acid chloride and condensed with the methoxymagnesio-derivative of methyl acetoacetate as described for the analogues above. The resulting dioxo-ester formed a yellow oil with an intense ferric reaction but did not crystallise. Attempts to cyclise this ester to a grisen by sulphuric acid by the standard procedure failed to yield any neutral material or to affect the infrared spectrum appreciably. (ii) Taken through the sequence adumbrated in (i), 3-isopropyl-4,6-dimethyl-2-benzofurylacetic acid also failed to yield any neutral spiran. The use of other dehydrating agents and of higher temperatures (60°) led to no different result.

2,3,4,4*a*,6,6*a*-*Hexahydro*-6a*α*-*hydroxy*-4a*β*,6*β*,7,9-*tetramethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]-*pentalene* (IX—XIV).—The dark crystalline complex which separated during 2 days from a solution of 3-ethylidene-4,6,2′-trimethylgris-2′-en-4′-one (1·0 g.) in ether (50 ml.) containing osmium tetroxide (1 g.) and pyridine (2 ml.) was collected, washed with ether, and dried in air. When reduced by a stream of sulphur dioxide, the complex in 80% alcohol (120 ml.) containing charcoal (2 g.) was decomposed after about 40 min. and the mixture was then filtered. The filtrate, when concentrated under reduced pressure and diluted with water, gave a solid which was isolated with ether and crystallised from aqueous alcohol, affording the 4a*β*,6*β*,7,9-*tetramethyl*-5,11-*dioxapentalene* in diamond-shaped plates (0·53 g.), m. p. 151°, $\lambda_{max.}$ 286 mμ (log ε 3·48), with a negative ferric reaction and insoluble in 2N-sodium hydroxide but giving a red Zimmermann reaction (Found: C, 71·5; H, 7·6. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%). The 2,4-*dinitrophenylhydrazone* crystallised from ethyl acetate–methanol in yellow needles, m. p. 221° (Found: C, 59·8; H, 5·3; N, 11·5. $C_{24}H_{26}O_7N_4$ requires C, 59·7; H, 5·4; N, 11·6%).

2,3,4,4*a*,6,6*a*-*Hexahydro*-6a*α*-*methoxy*-4a*β*,6*β*,7,9-*tetramethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]-*pentalene* (XIV; OMe for OH).—The foregoing hydroxy-ketone (0·30 g.) in dimethylformamide (9 ml.) was shaken for 73 hr. with silver oxide (0·9 g.) and methyl iodide (6 ml.). The residues from filtration were washed with small quantities of (1 : 1) ether–dimethylformamide; these washings were combined with the filtrate which was then diluted with ether (60 ml.) and extracted with aqueous potassium cyanide to remove silver salts. After being washed with water and dried (Na_2SO_4), the ethereal solution was evaporated to an oil which, crystallised from methanol, afforded the 6a*α*-methoxy-5,11-dioxapentalene in prisms (0·10 g.), m. p. 128°. This compound was identified with the product (IV; H for CO_2Me) of ozonolysis of 3-ethylidene-4,6,2′-trimethylgris-2′-en-4′-one (III; H for CO_2Me) by spectroscopic and mixed-melting-point

methods: specimens from the two preparations also gave the same 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 211°.

*2,3,4,4a,6,6a-Hexahydro-6aα-hydroxy-4aβ,6α,7,9-tetramethyl-3-oxo-*1H-*5,11-dioxadibenzo*[a,d]-*pentalene* (XV).—The above 6aα-hydroxy-4aβ,6β,7,9-tetramethyldioxapentalene (200 mg.) was heated under reflux for 1 hr. with methanol (20 ml.) and N-sodium hydroxide (20 ml.). The cooled solution was diluted with water and extracted with ether (4 × 50 ml.): the extract, washed with water, dried (Na_2SO_4), and evaporated, afforded a solid. This solid supplied the *6aα-hydroxy-4aβ,6α,7,9-tetramethyldioxapentalene* as prisms (153 mg.), m. p. 178°, from aqueous alcohol (Found: C, 71·5; H, 7·4%). This compound had $\lambda_{max.}$ 280, 289 mμ (log ε 3·40, 3·44) and $\nu_{max.}$ 3440 cm.$^{-1}$ (OH) and 1705 cm.$^{-1}$ (C:O), gave a negative ferric reaction but a red Zimmermann reaction, and was converted into the *2,4-dinitrophenylhydrazone* which crystallised from alcohol–ethyl acetate in golden needles, m. p. 268° (decomp.) (Found: C, 59·7; H, 5·4; N, 11·4. $C_{24}H_{26}N_4O_7$ requires C, 59·7; H, 5·4; N, 11·6%).

Methylated by silver oxide and methyl iodide in dimethylformamide in the same way as the isomer above, this alcohol gave *2,3,4,4a,6,6a-hexahydro-6aα-methoxy-4aβ,6α,7,9-tetramethyl-3-oxo-*1H-*5,11-dioxadibenzo*[a,d]*pentalene* (XV; OMe for OH) as needles, m. p. 159°, from aqueous methanol (Found: C, 72·4; H, 7·9. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·7%), $\lambda_{max.}$ 1715 cm.$^{-1}$ (C:O), and formed a *2,4-dinitrophenylhydrazone* crystallising from alcohol–ethyl acetate in yellow needles, m. p. 224° (Found: N, 10·9; OMe, 6·2. $C_{24}H_{25}N_4O_6$·OMe requires N, 11·3; OMe, 6·2%).

*2,3,4,4a,6,6a-Hexahydro-6aα-hydroxy-4aβ,7,9-trimethyl-3-oxo-*1H-*5,11-dioxadibenzo*[a,d]*pentalene* (XXI).—Interaction of osmium tetroxide (1 g.), pyridine (1 ml.), and 4,6,2′-trimethyl-3-methylenegris-2′-en-4′-one (1·0 g.) in ether (200 ml.) furnished a dark crystalline complex which was decomposed as described above. The product was an oil that crystallised on addition of a little methanol and could then be purified from aqueous methanol, giving the *6aα-hydroxy-4aβ,7,9-trimethyldioxapentalene* in needles (0·41 g.), m. p. 141°, $\nu_{max.}$ 3440 (OH), 1724 cm.$^{-1}$ (C:O) (Found: C, 70·2; H, 7·0. $C_{17}H_{20}O_4$ requires C, 70·8; H, 7·0%). Kuhn–Roth estimations gave values of 13·9 (theor. for three *C*-Me groups, 15·0%). The semicarbazone separated from aqueous methanol in plates, m. p. 224° (Found: C, 62·2; H, 6·9; N, 11·5. $C_{18}H_{23}N_3O_4$ requires C, 62·6; H, 6·7; N, 12·2%).

This alcohol was unaffected by boiling 2N-aqueous-alcoholic sodium hydroxide after 1 hr., or by similar treatment with 4N-methanolic sodium methoxide.

*2,3,4,4a,6,6a-Hexahydro-6aα-hydroxy-9-methoxy-4aβ,6,6-trimethyl-3-oxo-*1H-*5,11-dioxadibenzo*[a,d]*pentalene* (XX).—When the adduct from osmium tetroxide (0·5 g.), pyridine (1 ml.), and 3-isopropylidene-6-methoxy-2′-methylgris-2′-en-4′-one (0·50 g.) was decomposed by sulphur dioxide in the usual way, there resulted a viscous oil which crystallised from ether–light petroleum (b. p. 40—60°) to give the *9-methoxy-4aβ,6,6-trimethyldioxapentalene* in tiny needles (0·31 g.), m. p. 163°, $\lambda_{max.}$ 284, 290 mμ (log ε 3·68, 3·61), $\nu_{max.}$ 3333 (OH), 1689 cm.$^{-1}$ (C:O) (Found: C, 67·9; H, 7·0; OMe, 9·7. $C_{17}H_{19}O_4$·OMe requires C, 67·9; H, 7·0; OMe, 9·7%). The *2,4-dinitrophenylhydrazone* separated from ethyl acetate in orange needles, m. p. 208°, $\lambda_{max.}$ 361 mμ (log ε 4·41) (Found: N, 11·0. $C_{24}H_{26}N_4O_8$ requires N, 11·2%).

This alcohol (100 mg.) was recovered after being heated with alcohol (10 ml.) and 2N-sodium hydroxide (4 ml.) for 1 hr.

*Ethyl 2,3,4,4a,6,6a-Hexahydro-6aα-hydroxy-4aβ,6β,7,9-tetramethyl-3-oxo-*1H-*5,11-dioxadibenzo*[a,d]*pentalene-4-carboxylate* (VII; CO_2Et for CO_2Me).—Osmium tetroxide (0·5 g.) in ether (40 ml.) containing pyridine (1 ml.) was added to ethyl 3-ethylidene-4,6,2′-trimethyl-4′-oxogris-2′-en-3′-carboxylate (0·65 g.) (Part II), also in ether (100 ml.); precipitation of the brown complex, if not complete in 2 days, was promoted by addition of light petroleum. The *adduct* formed chocolate-coloured needles (1·2 g.), m. p. ~187° (decomp.), from pyridine–light petroleum (Found: * H, 4·7; N, 3·8. $C_{21}H_{24}O_8Os,2C_5H_5N$ requires H, 4·5; N, 3·7%). This adduct had $\nu_{max.}$ 1737 (ester) and 1675 cm.$^{-1}$ (αβ-unsaturated C:O).

The adduct (1·2 g.) in 80% alcohol (120 ml.) containing charcoal (2·0 g.) was reduced by a stream of sulphur dioxide as described for the analogues above; it furnished a gum which crystallised when alcohol was added. The same product resulted when the adduct was reduced by hydrogen sulphide instead of sulphur dioxide; also when the adduct (0·4 g.) in 95% alcohol (75 ml.) was shaken with hydrogen in the presence of 5% palladium–charcoal (1·0 g.) for 1·5 hr., the mixture filtered, the filtrate concentrated, diluted with water, and extracted with ether, and

* Facilities for the determination of carbon in the presence of osmium were not available.

the extract concentrated to a gum (0·13 g.) which solidified when kept. Recrystallised from aqueous alcohol, these solids afforded the ethyl 6aα-hydroxy-4aβ,6β,7,9-tetramethyldioxapentalene as the *ethanol solvate* in thick needles, m. p. 106° (Found: C, 65·6; H, 7·7; OEt, 20·7. $C_{19}H_{21}O_5$·OEt,EtOH requires C, 65·7; H, 7·7; OEt, 21·4%), $\lambda_{max.}$ (in neutral alcohol) 229, 251, and 290 mμ (log ε 4·04, 3·98, 3·52), $\lambda_{max.}$ (in alkaline alcohol) 243 and 280 mμ (log ε 3·40, 4·12), $\nu_{max.}$ 3420, 3290 (OH) and 1641 cm.$^{-1}$ (bonded C:O). The alcohol of crystallisation could be removed efficiently only at 120°, giving a melt (Found: OMe, 12·8%) having infrared absorption bands at 1748 (ester) and 1720 cm.$^{-1}$ (ketone) in addition to those shown by the solvate. This melt could not be crystallised except from alcohol, in which the solvate was regenerated, or from methanol, which gave material containing variable amounts of methanol of crystallisation and having properties closely similar to those of the ethanol solvate.

The ethanol solvate behaved as a β-oxo-ester in giving a red ferric reaction but a negative Zimmermann reaction and in dissolving in dilute alkali. It afforded *ethyl 6aα-hydroxy-3-hydroxyimino-4aβ,6β,7,9-tetramethyl-5,11-dioxapentalene-4-carboxylate* which separated from aqueous alcohol in needles, m. p. 220° (decomp.), $\nu_{max.}$ 3450, 3370 (OH), 1724 cm.$^{-1}$ (ester) (Found: C, 64·9; H, 6·9; N, 3·7; OEt, 11·2. $C_{19}H_{22}NO_5$·OEt requires C, 64·8; H, 7·0; N, 3·6; OEt, 11·6%).

Methyl 2,3,4,4a,6,6a-*Hexahydro*-6aα-*hydroxy*-4aβ,6β,7,9-*tetramethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]*pentalene*-4-*carboxylate* (VII).—Prepared in the same way as the ethyl ester above from the appropriate grisenone (0·6 g.), this methyl ester crystallised from methanol as the *methanol solvate*, needles (0·4 g.), m. p. 148°, $\nu_{max.}$ 3460 (OH), 1630 cm.$^{-1}$ (bonded C:O) (Found: C, 63·8; H, 7·5; OMe, 12·7. $C_{19}H_{21}O_5$·OMe,MeOH requires C, 64·3; H, 7·2; OMe, 15·8%). When ethanol replaced methanol in these reactions, the product was the *ethanol solvate*, needles, m. p. 147° (not depressed on admixture with the methanol solvate) (Found: C, 64·8; H, 7·4; alkoxyl as OMe, 9·2. $C_{19}H_{21}O_5$·OMe,EtOH requires C, 65·0; H, 7·4; alkoxyl as OMe, 15·3%). Both solvates were soluble in dilute alkali and gave red ferric reactions. Kept *in vacuo* at 120°, the methanol solvate did not lose its crystalline habit but eventually afforded the solvent-free *methyl dioxapentalene-4-carboxylate* (Found: C, 66·8; H, 6·8; OMe, 8·0. $C_{19}H_{21}O_5$·OMe requires C, 66·7; H, 6·7; OMe, 8·6%). This solid had almost the same infrared absorption spectrum as the solvates, but when it had been melted a band at 1723 cm.$^{-1}$ (ester) developed.

The two solvates gave the same (solvent-free) *oxime*, which crystallised from aqueous alcohol in needles, m. p. 221°, $\nu_{max.}$ 3495, 3320 (OH), 1727 cm.$^{-1}$ (ester) (Found: C, 64·2; H, 6·7; N, 3·7; OMe, 8·1. $C_{19}H_{22}NO_5$·OMe requires C, 64·0; H, 6·7; N, 3·7; OMe, 8·3%).

4-*Acetyl*-2,3,4,4a,6,6a-*hexahydro*-6aα-*hydroxy*-4aβ,6β,7,9-*tetramethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]*pentalene* (XVI).—The adduct which separated from a solution of osmium tetroxide (1 g.), pyridine (2 ml.), and 2′-acetyl-3-ethylidene-4,6,2′-trimethylgris-2′-en-4′-one (1·24 g.) (Part II) in ether (200 ml.) was reduced by sulphur dioxide in 20% aqueous methanol. Recovered in the usual way, the oily product eventually solidified and crystallised from aqueous alcohols with varying amounts of alcohols of crystallisation. Crystallised from benzene–light petroleum (b. p. 60—80°), however, these solvates furnished the 4-*acetyl*-6aα-*hydroxy*-4aβ,6β,7,9-*tetramethyldioxapentalene* in needles (0·80 g.), m. p. 164°, with a red ferric reaction (Found: C, 69·5; H, 7·0. $C_{20}H_{24}O_5$ requires C, 69·8; H, 7·0%). This ketone had $\nu_{max.}$ 3401 (OH), 1695 and 1672 (both weak; C:O), and 1577 (strong; bonded C:O).

Ethyl 1,2,3,3a,5,5a-*Hexahydro*-5aα-*hydroxy*-3aβ,6,8-*trimethyl*-2-*oxo*-4,10-*dioxabenzo*[a]*cyclopenta*[d]*pentalene*-3-*carboxylate*.—When oxidised by osmium tetroxide as in the examples above, ethyl 3-methylene-4,6,2′-trimethyl-4′-oxocoumaran-2-spiro-1′-cyclopent-2′-ene-3′-carboxylate (0·60 g.) was converted into the *ethyl hydroxytrimethyldioxapentalene-3-carboxylate* which separated from aqueous alcohol in needles or plates (0·38 g.), m. p. 148°, $\lambda_{max.}$ 208, 226, 278, 288 mμ (log ε 4·62, 4·13, 3·48, 3·49), soluble in dilute alkali and having a red ferric reaction (Found: C, 65·5; H, 6·5; OEt, 11·3. $C_{17}H_{17}O_5$·OEt requires C, 65·9; H, 6·4; OEt, 13·0%). This compound had, in the crystalline state, $\nu_{max.}$ 3440 (OH) and 1650 cm.$^{-1}$ (bonded C:O), and in the fused state 3440 (OH) and 1727 cm.$^{-1}$ (ester).

The *oxime* crystallised from benzene–methanol in needles, m. p. 200° (decomp.), $\nu_{max.}$ 1736 cm.$^{-1}$ (ester) (Found: N, 3·6. $C_{19}H_{23}NO_6$ requires N, 3·9%).

Methyl 1,2,3,3a,5,5a-*Hexahydro*-5aα-*hydroxy*-3aβ,5β,6,8-*tetramethyl*-2-*oxo*-4,10-*dioxabenzo*[a]-*cyclopenta*[d]*pentalene*-3-*carboxylate* (VI).—By the method used in the foregoing example, methyl 3-ethylidene-4,6,2′-trimethyl-4′-oxocoumaran-2-spiro-1′-cyclopent-2′-ene-3′-carboxylate (0·6 g.) was oxidised to the *methyl hydroxytetramethyldioxapentalenecarboxylate* which, when purified

from methanol, formed needles or plates (0·3 g.), m. p. 152—154°, $\lambda_{max.}$ 212, 229, 280, 290 mμ (log ε 4·42, 4·12, 3·46, 3·48), $\nu_{max.}$ 3704 (OH), 1660 cm.$^{-1}$ (bonded C:O) (Found: C, 65·9; H, 6·6; OMe, 9·0. $C_{18}H_{19}O_5$·OMe requires C, 65·9; H, 6·4; OMe, 9·0%).

3aα-2′-Carboxyethyl-3α-carboxymethyl-1,3,3a,8b-tetrahydro-8bα-hydroxy-1,3β,6,8-tetramethyl-2,4-dioxacyclopenta[a]*indene* (XVII; R = OH).—The ethyl hydroxy-4aβ,6β,7,9-tetramethyldioxapentalenecarboxylate (VII) (1·0 g.) was heated under reflux with 2N-sodium hydroxide for ¾ hr. Insoluble material which had been formed was isolated with ether and crystallised from alcohol–light petroleum (b. p. 60—80°), giving the 4αβ,6α,7,9-tetramethyldioxapentalene (IX) in prisms (0·12 g.), m. p. and mixed m. p. 177°, and thence the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 268°. On acidification, the alkaline solution deposited a solid. This was collected into ether, washed with water, dried (Na_2SO_4), recovered by evaporation of the solvent, and purified from aqueous alcohol, giving the *3aα-2′-carboxyethyl-3α-carboxymethyldioxacyclopenta*[a]*indene* (XVII; R = OH) in hexagonal prisms (0·30 g.), m. p. 224° (decomp.), pK_a (potentiometric titration in water) 4·75 (one inflection) [Found: C, 62·5; H, 6·6%; equiv., 187. $C_{17}H_{22}O_3(CO_2H)_2$ requires C, 62·6; H, 6·6%; equiv., 182]. This acid gave negative results in tests with ferric chloride, sodium nitroprusside, Ehrlich's reagent, and Zimmermann's reagent. With diazomethane, it afforded the *dimethyl ester* crystallising from methanol and then light petroleum (b. p. 40—60°) in needles, m. p. 112°, $\nu_{max.}$ (in $CHCl_3$) 3410 (OH), 1733 cm.$^{-1}$ (ester), $\nu_{max.}$ (in Nujol) 3470, 1736, 1721 cm.$^{-1}$, $\lambda_{max.}$ 280, 286 mμ (log ε 3·42, 3·45) [Found: C, 64·4; H, 7·1; OMe, 15·6. $C_{19}H_{22}O_5(OMe)_2$ requires C, 64·3; H, 7·1; OMe, 15·8%].

When this diacid was kept at its m. p. until effervescence ceased, a glass was formed which, when crystallised from benzene, afforded a *lactone* in plates, m. p. 187°, $\nu_{max.}$ 1754, (δ-lactone), 1721 cm.$^{-1}$ (CO_2H) [Found: C, 65·5; H, 6·5%; equiv. (direct titration) 342, (back-titration) 173. $C_{18}H_{21}O_4$·CO_2H requires C, 65·9; H, 6·4%; equiv., 346].

Lactone (XVIII) *of 3α-Acetonyl-3aα-2′-carboxyethyl-1,3,3a,8b-tetrahydro-8bα-hydroxy-1,3β,6,8-tetramethyl-2,4-dioxacyclopenta*[a]*indene* (XVII; R = Me).—The 4-acetyl-6α-hydroxy-4aβ,6β,7,9-tetramethyldioxapentalene (XVI) (0·5 g.), when heated under reflux for 1 hr. with 2·5N-sodium hydroxide, gave a neutral and an acidic product. The former crystallised from light petroleum (b. p. 60—80°), giving the hydroxy-4aβ,6α,7,9-tetramethyldioxapentalene (IX) in plates, m. p. and mixed m. p. 177°, further identified spectroscopically. The latter formed a brownish oil which could not be satisfactorily purified. Slow distillation at 140°/0·1 mm. afforded the *lactone* as a glass, $\nu_{max.}$ 1761 (δ-lactone) and 1706 cm.$^{-1}$ (C:O) (no OH absorption) (Found: C, 69·5; H, 7·0. $C_{20}H_{24}O_5$ requires C, 69·8; H, 7·0%).

γ-Lactone (XIX) *of 3α,3aα-Biscarboxymethyl-1,3,3a,8b-tetrahydro-8bα-hydroxy-1,3β,6,8-tetramethyl-2,4-dioxacyclopenta*[a]*indene*.—The methyl 5aα-hydroxytetramethyldioxapentalenecarboxylate (VI) (1 g.) was heated under reflux in an atmosphere of nitrogen for 4 hr. with 10% aqueous potassium hydroxide (25 ml.). The cooled solution was acidified with concentrated hydrochloric acid, and the organic materials were isolated by repeated extraction with benzene. These extracts were dried ($MgSO_4$) and concentrated: the residue was taken up in 1 : 1 benzene–light petroleum and left. After 15 days, prisms had separated. A second crop was garnered after a further 8 days. A week later, a third crop had separated. The first two crops were recrystallised in a similar fashion, giving the *γ-lactone* in prisms (0·3 g.), m. p. 170°, $\lambda_{max.}$ 212, 280, 287 mμ (log ε 4·11, 3·36, 3·39), $\nu_{max.}$ 1779 (γ-lactone), 1695 cm.$^{-1}$ (CO_2H) [Found: C, 64·9; H, 6·1%; equiv. (direct titration) 335, (back-titration) 155. $C_{17}H_{19}O_4$·CO_2H requires C, 65·1; H, 6·1%; equiv., 332]. The third crop had infrared absorption consistent with the presence of this lactonic acid together with the parent hydroxy-diacid: when heated, it afforded further quantities of the pure lactone.

With diazomethane in ether, the lactonic acid furnished the *methyl ester* separating from benzene in cubes, m. p. 130° (Found: C, 65·9; H, 6·5; OMe, 9·2. $C_{18}H_{19}O_5$·OMe requires C, 65·9; H, 6·4; OMe, 9·0%), $\lambda_{max.}$ 286 mμ (log ε 3·49), $\nu_{max.}$ 1786 (γ-lactone) and 1738 cm.$^{-1}$ (ester).

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