223. *Studies in the Preparation of* B-*Nor-diterpenoids.*

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The 11-hydroxy-9,10-diketones obtained by oxidation of methyl abieta-5,7,13(14)-trien-15-oate and the enantiomer of methyl 10-hydroxy-9-oxopodocarpa-5,7,10,13(14)-tetraen-16-oate with chromic oxide are shown by infrared studies to have the 11α- and 11β-configuration respectively. A mechanism for the formation of the hydroxy-diketones is discussed. Benzilic acid rearrangement of the enantiomer of methyl 9,10-dioxo-11β-podocarpa-5,7,13(14)-trien-16-oate gave 1,2,3,4,10α,11-hexahydro-9β-hydroxy-1β,11α-dimethylfluorene-1α,9α-dicarboxylic acid, the stereochemistry of which was deduced from the reactions of its anhydride. Under similar conditions methyl 11-hydroxy-9,10-dioxopodocarpa-5,7,13(14)-trien-15-oate gave (−)-1,2,3,6,7,11b-hexahydro-4,11b-dimethyl-6,7-dioxodibenz[*b*,*d*]oxepin.

GIBBERELLIC ACID (I),[1] the plant-growth promoting substance obtained [2] from *Gibberella fujikuroi*, has been shown [3] to be a diterpenoid in which, in addition to other structural modifications, contraction of ring B of the pimarane skeleton (II) to the perhydrofluorene skeleton (III) has occurred with extrusion of one carbon atom as a carboxyl group.

This paper records attempts to contract ring B of some resin acid analogues * to compounds with a hydrofluorene skeleton. These attempts were only successful with the enantiomer [4,5] (IV; R = H, absolute configuration) of 11β-podocarpa-5,7,13(14)-trien-16-oic acid † in which rings A/B are *cis*-fused, inversion at position 12 in podocarpa-5,7,13(14)-trien-15-oic acid (deisopropyldehydroabietic acid) having been effected with

* The absolute configuration of gibberellic acid was unknown when this work was commenced.

† The nomenclature used is that of Klyne, *J.*, 1953, 3072. The names deisopropylallodehydroabietic acid [5] and 5-isodeoxypodocarpic acid enantiomer [6] have also been used for (IV; R = H).

[1] Cross, Grove, McCloskey, Mulholland, and Klyne, *Chem. and Ind.*, 1959, 1345; Edwards, Nicolson Apsimon, and Whalley, *Chem. and Ind.*, 1960, 624.
[2] Cross, *J.*, 1954, 4670.
[3] Birch, Rickards, and Smith, *Proc. Chem. Soc.*, 1958, 192.
[4] Fieser and Campbell, *J. Amer. Chem. Soc.*, 1938, **60**, 2631.
[5] Ohta and Ohmori, *Pharm. Bull.* (*Japan*), 1957, **5**, 91, 96.
[6] Wenkert and Chamberlin, *J. Amer. Chem. Soc.*, 1959, **81**, 688.

aluminium chloride in benzene. Only with *cis*-fusion of rings A/B was a 9,10-diketone obtained which could be subjected to ring contraction.

Oxidation of the ester (IV; R = Me) by chromic oxide gave the 9,10-diketo-ester [5] (V) which formed a quinoxaline derivative (cf. Ohta [7]) and, on benzilic acid rearrangement, smoothly gave the acid (VI; R = H). The best yields of the acid (VI; R = H) were obtained with boiling 10% sodium hydroxide.

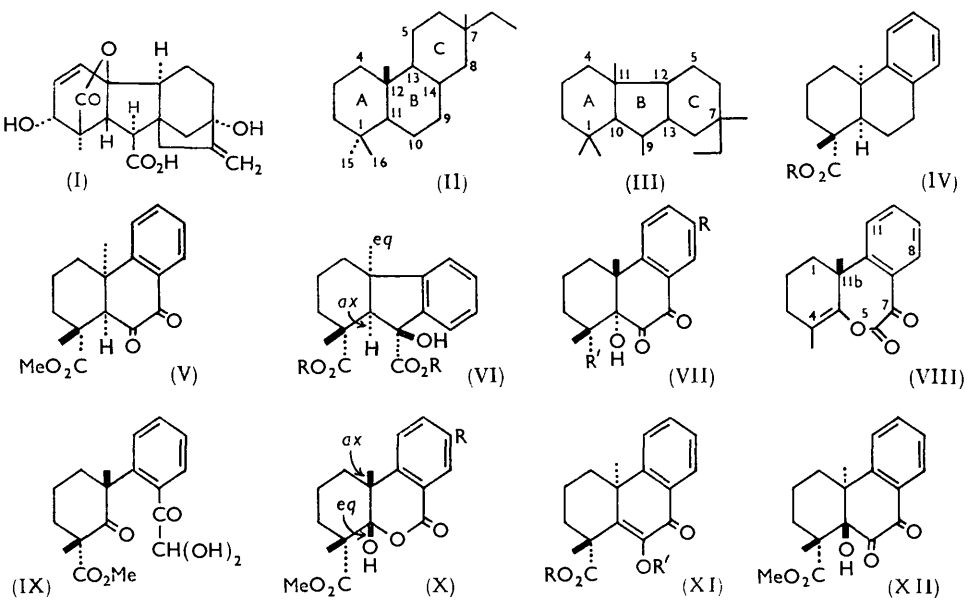
Wenkert and his co-workers [6,8] found that chromic oxide oxidised the A/B-*trans*-compounds, methyl abieta-5,7,13(14)-trien-15-oate (methyl dehydroabietate) and the nitrile of podocarpa-5,7,13(14)-trien-15-oic acid, to the corresponding 9-ketones only. By more vigorous oxidation Ohta and Ohmori [5] converted methyl podocarpa-5,7,13(14)-trien-15-oate into a hydroxy-9,10-diketone which they assumed to be the 11-hydroxy-compound. In the present study the formation of an 11-hydroxy-compound from methyl podocarpa-5,7,13(14)-trien-15-oate has been confirmed, and, in addition, the 11-hydroxy-9,10-dioxo-derivative (VII; R = Pr^i, R′ = CO_2Me) has been obtained from methyl abieta-5,7,13(14)-trien-15-oate. The 11-hydroxy-9,10-diketones are equivalent to *o*-(2-oxocyclohexyl)phenylglyoxals (open form) and under the conditions of the benzilic acid rearrangement do not undergo contraction of ring B; even in an atmosphere of nitrogen (although oxygen was not rigorously excluded from the reactants) the hydroxy-diketone (VII; R = H, R′ = CO_2Me) gave the oxepin derivative (VIII) and carbon dioxide, the latter being eliminated from the intermediate open-chain β-keto-ester (IX). The formation of compound (IX) from the monohydrate of the dione (VII; R = H, R′ = CO_2Me) may be regarded as a retroaldol reaction or, more generally, as a case of ring-chain tautomerism. The formation of the oxepin derivative (VIII), which liberated carbon monoxide on treatment with phosphoric acid, and the oxidation of the hydroxy-diketone (VII; R = H, R′ = CO_2Me) under more vigorous conditions to the acid (X; R = H; lactol form) confirm the structure of the hydroxy-diketone.

The α-oxidation of a methylene-ketone by chromic oxide may be considered (cf. refs. 6 and 8) to take place by a mechanism whereby disproportionation of the initially formed enol chromate to the α-ketol chromite is followed by liberation of the α-ketol. If it is assumed, similarly, that the oxidation of αβ-diketones to γ-hydroxy-αβ-diketones is dependent upon enolisation of the β-keto-group as the initial step, then the difference towards chromic oxide oxidation of diterpenoids with rings A/B *cis*- and *trans*-fused can be explained. Molecular models show there is no restriction on the enolisation of methyl 9,10-dioxopodocarpa-5,7,13(14)-trien-15-oate; but enolisation of the diketo-ester (V), in which the 12-methyl group is equatorial, brings about a conformational change in ring A and leads to 1,3-diaxial interaction between the 1-methoxycarbonyl and the 12-methyl group. This barrier to enolisation allows the isolation of the diketo-ester (V) as a stable oxidation product: however, once formed, the enol (XI; R = Me, R′ = H) is stabilized by hydrogen bonding with the 9-keto-group.

Like the enantiomer of the nitrile [8] of 9,10-dioxo-11β-podocarpa-5,7,13(14)-trien-16-oic acid the ester (V) gave no colour with ferric chloride. Hydrolysis of the ester (V) occurred with 5% aqueous ethanolic potassium hydroxide, and gave the enol (XI; R = R′ = H), which gave a red colour with ferric chloride. In alkaline solution, the ultraviolet spectra of this enol and the diketone (V) were identical. The infrared spectrum of the enol showed a band at 1634 $cm.^{-1}$ consistent with the presence of a conjugated ketone bonded to the adjacent hydroxyl group. This band appeared again at 1633 $cm.^{-1}$ in the methyl ester (XI; R = Me, R′ = H) but shifted to the normal conjugated-ketone position at 1655 $cm.^{-1}$ in the methyl ether (XI; R = R′ = Me). Some ketonisation of the enol ester (XI; R = Me, R′ = H) took place in carbon tetrachloride, as shown by the appearance of bands near 1725 and 1700 $cm.^{-1}$ in addition to the 1733 $cm.^{-1}$ (ester) and the 1633 $cm.^{-1}$ band.

[7] Ohta, *Pharm. Bull.* (*Japan*), 1957, **5**, 256.
[8] Wenkert and Jackson, *J. Amer. Chem. Soc.*, 1958, **80**, 211.

Oxidation of the enol-ester (XI; R = Me, R′ = H) by chromic oxide gave the enantiomer (XII) of methyl 11-hydroxy-9,10-dioxopodocarpa-5,7,13(14)-trien-16-oate. Oxidation presumably occurred at the β-face since both the 1-methoxycarbonyl and the 12-methyl group are α-axial, and the possibility of subsequent rearrangement to the A/B-*cis*-11α-hydroxy-compound is excluded by the infrared spectrum in solution [$\nu_{max.}$ 3600, 1736 (broad and intense) and 1695 cm.$^{-1}$] which showed no hydrogen bonding between the



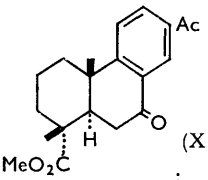
11-hydroxy-substituent and the 10-keto- or 1-methoxycarbonyl group. As expected for a compound with the 11α-configuration, the 11-hydroxy-diketone [9] (VII; R = H, R′ = Me), $\nu_{max.}$ 1731 and 1690 cm.$^{-1}$, also showed no intramolecular hydrogen bonding. Such bonding occurred in both the esters (VII; R = H and Pr^{i}, R′ = CO_2Me), $\nu_{max.}$ near 3300, 1736, 1695 cm.$^{-1}$ (broad and intense), and in the quinoxaline derivative of (VII; R = H, R′ = CO_2Me), $\nu_{max.}$ 1685 cm.$^{-1}$, between the 11-hydroxy- and the 1-methoxycarbonyl substituent, consistent with the 11α-configuration expected from attack at the less obstructed α-face. Further oxidation of the ester (VII; R = H, R′ = CO_2Me) with chromic oxide gave the acidic methyl 3-*o*-carboxyphenyl-1,3-dimethyl-2-oxocyclohexanecarboxylate [5,7] (lactol form; X; R = H) which was also obtained directly from methyl podocarpa-5,7,13(14)-trien-15-oate.

In addition to the ester (VII; R = Pr^{i}, R′ = CO_2Me) and the ketone [10] (XIII) which were isolated from the neutral fraction, oxidation of methyl abieta-5,7,13(14)-trien-15-oate by chromic oxide gave an acidic product (X; R = Ac). Both acids (X; R = H and Ac) were insoluble in sodium hydrogen carbonate, and the infrared spectra were consistent only with their formulation as lactols,[5] the more probable configuration of the 11-hydroxy-substituent being β(equatorial). There was no intramolecular hydrogen bonding with the 1-methoxycarbonyl group.

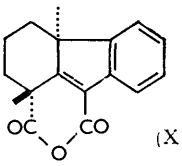
With acetic anhydride the acid (VI; R = H) gave a mixture of anhydrides (XIV) and (XV), which on alkaline hydrolysis gave the same product (XVI; R = R′ = H). Two centres, at positions 9 and 10, have been involved in the formation of the acid (VI; R = H), but of the four possible stereoisomeric structures for this acid, molecular models

[9] Hodges and Raphael, *J.*, 1960, 50.
[10] Ritchie, Sanderson, and McBurney, *J. Amer. Chem. Soc.*, 1954, **76**, 723; Zeiss and Tsutsui, *ibid.*, 1955, **77**, 6706.

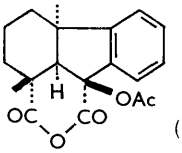
show that only three are capable of anhydride formation and of these only one, namely (VI; R = H), gives an acetoxy-anhydride in which the 10-hydrogen atom and the 9-acetoxy-group are *trans* and near-coplanar and therefore capable of ready elimination. Moreover, in form (VI; R = H) the 1-carboxylic acid and the 11-methyl group are



(XIII)



(XIV)



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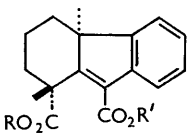
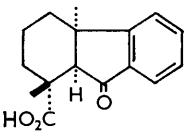
(XVI)





(XVII)

equatorial; there is a strong 1,3-diaxial interaction between these groups in structures where rings A/B are *trans*-fused.

The introduction of a 9,10-double bond in the acid (XVI; R = R′ = H) brings about a conformational change in ring A. The axial configuration of the 1-methoxycarbonyl group in the ester (XVI; R = R′ = Me) was confirmed by the formation of the half-ester (XVI; R = Me, R′ = H) under conditions which hydrolyse the equatorial ester substituent in methyl abieta-5,7,13(14)-trien-15-oate but leave the axial ester substituent of methyl 6-hydroxypodocarpa-5,7,13(14)-trien-16-oate unaffected.[11]

Lead tetra-acetate oxidises the acid (VI; R = H) to the hexahydrofluorenone[7] (XVII). Here again, as with the acid (VI; R = H), the more stable configuration at position 10 is that in which rings A/B are *cis*-fused.

The acids (VI; R = H) and (XVI; R = R′ = H) showed no plant-growth promoting properties when applied to the leaves of intact dwarf-pea seedlings.[12] The lactols (X; R = H and were likewise inactive.

Experimental

M. p.s (Kofler block) were corrected. Unless otherwise stated, ultraviolet absorption spectra and optical rotations were determined for EtOH solutions, and infrared spectra were obtained for Nujol " mulls." Light petroleum had b. p. 60—80°. Silica of 100—200 mesh size was used in chromatography.

Methyl 9,10-dioxo-11β-podocarpa-5,7,13(14)-trien-16-oate enantiomer (V), m. p. 137—138°, $[\alpha]_D^{22}$ −218° (*c* 0·4), was prepared by oxidation of methyl 11β-podocarpa-5,7,13(14)-trien-16-oate enantiomer[5] (IV; R = Me) with chromic oxide. The infrared spectrum of a dilute solution in carbon tetrachloride showed C=O bands at 1729 (ester and 10-ketone) and 1686 $cm.^{-1}$ (9-ketone).

The *quinoxaline derivative* formed a glass [after short-path distillation at 110—115° (bath)/8·3 × 10^{-5} mm.], m. p. 61—69° (Found: C, 77·3; H, 6·7; N, 7·6. $C_{24}H_{24}N_2O_2$ requires C, 77·4; H, 6·5; N, 7·5%). It gave an orange-red colour with concentrated sulphuric acid.

Action of Alkali on the Diketo-ester (V).—(A) *2·5N-Sodium hydroxide.* The ester (V) (1 g.) in 2·5N-sodium hydroxide (200 ml.) was heated under reflux for 3 hr. The cooled solution was acidified with concentrated hydrochloric acid (46 ml.) and extracted with ether. The ethereal extract was separated into acid and neutral fractions. Crystallisation of the acid fraction from methanol and then acetone gave 1,2,3,4,10α,11-*hexahydro*-9β-*hydroxy*-1β,11α-*dimethylfluorene*-1α,9α-*dicarboxylic acid* (VI; R = H) (738 mg., 74%) as prismatic needles, m. p. 179—180° (decomp.), $[\alpha]_D^{25}$ −30·6° (*c* 1·0) [Found, dried at 100°: C, 66·3; H, 7·2. $C_{17}H_{20}O_5,(CH_3)_2CO$ requires C, 66·3; H, 7·2%. Found, dried at 140°: C, 66·9; H, 6·6%; equiv., 154. $C_{17}H_{20}O_5$

[11] Sherwood and Short, *J.*, 1938, 1006.
[12] Moffatt and Radley, *J. Sci. Food Agric.*, 1960, 386.

requires C, 67·1; H, 6·6%; equiv. (dibasic), 152], $\lambda_{max.}$ 264, ~270—272 mμ (log ε 3·1, 3·0 respectively), $\nu_{max.}$ 3400 (broad, bonded OH), 3175—2630 (broad, OH of CO_2H), 1706 (CO of CO_2H), 1607 (aromatic ring), or (in CCl_4) 3535 (OH), 1700 cm.$^{-1}$ (CO of CO_2H).

Crystallisation from methanol gave the *methanol solvate* as prisms, m. p. 172—173° (loss of solvent) (Found, dried at 100°: C, 64·8; H, 7·3%; equiv., 163. $C_{17}H_{20}O_5,CH_3OH$ requires C, 64·3; H, 7·2%; equiv., 168).

The *methyl ester* (VI; R = Me), prepared with ethereal diazomethane, crystallised from ether in prismatic needles, m. p. 98—100° (Found: C, 69·1; H, 7·4; OMe, 17·4. $C_{19}H_{24}O_5$ requires C, 68·7; H, 7·3; 2OMe, 18·7%), $\nu_{max.}$ 3595 (OH), 1724 (ester CO), 1600 cm.$^{-1}$ (aromatic ring).

When the reaction was carried out with 30% sodium hydroxide for 20 hr. the yield of the acid (VI; R = H) fell to 53%.

(B) 5% *Aqueous-ethanolic potassium hydroxide.* The ester (V) (24 mg.) was heated under reflux for 2 hr. with potassium hydroxide (190 mg.) in ethanol (2 ml.) and water (2 ml.). An orange colour developed which reverted to yellow on cooling. The solution was acidified, and extracted with ether. The ether extract was washed with 2N-sodium carbonate and evaporated, giving a yellow intractable gum (1·5 mg.). Acidification of the sodium carbonate solution and extraction with ether gave, on recovery, a gum (19 mg.) which slowly crystallised from benzene–light petroleum in prisms (6 mg.), m. p. 94—105°, of 10-*hydroxy*-9-*oxopodocarpa*-5,7,10,13(14)-*tetraen*-16-*oic acid enantiomer* (XI; R = R′ = H), $\nu_{max.}$ 3200 (broad, OH), 2650 (OH of CO_2H); 1705 (carboxylic acid CO), 1634 (bonded, conjugated CO), 1599 cm.$^{-1}$ (aromatic ring), $\lambda_{max.}$ 260, 304 mμ (log ε 3·86, 3·87 respectively) changed to $\lambda_{max.}$ 241, 302 mμ (log ε 3·96, 3·53 respectively) on addition of 1 drop of 3N-sodium hydroxide. The same spectrum was obtained on addition of 3N-sodium hydroxide to the diketo-ester (V). Unlike the diketo-ester (V), the enol (XI; R = R′ = H) gave a red colour with ferric chloride and decolorized potassium permanganate in acetone.

The *methyl ester* (XI; R = Me, R′ = H), prepared with ethereal diazomethane, was an oil, b. p. 90° (bath)/2·3 × 10^{-4} mm. (Found: C, 71·7; H, 6·8. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%), $\nu_{max.}$ (film) 3380 (OH), 1730 (ester CO), 1635 (bonded conjugated CO), 1602, 1572 cm.$^{-1}$ (aromatic ring), $\nu_{max.}$ (in CCl_4, dilute solution) 3514 (weak, broad) 3392, 3339 (bonded OH), 1733 (ester CO), 1633 cm.$^{-1}$ (bonded conjugated CO), together with 1724, 1703 cm.$^{-1}$ (9,10-diketone CO), contributed by form (V).

Treatment of the ester (XI; R = Me, R′ = H) in methanol with ethereal diazomethane for 24 hr. gave, after recovery and short-path distillation at 110—120° (bath)/1·3 × 10^{-4} mm., the *methyl ether* (XI; R = R′ = Me) as an oil (Found: C, 72·6; H, 7·2; OMe, 18·7. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·1; 2OMe, 19·7%), $\nu_{max.}$ (film) 1738 (ester CO), 1655 (conjugated CO), 1619 (enol ether), 1603, 1577 cm.$^{-1}$ (aromatic ring), $\lambda_{max.}$ 260, 290 mμ (log ε 3·99, 3·98 respectively).

Only intractable products were obtained when the ester (V) was heated under reflux with 20% butanolic potassium hydroxide (1·5 hr.) or with sodium methoxide in methanol (3 hr.).

Oxidation of the Enol Ester (XI; R = Me; R′ = H).—The enol-ester (XI; R = Me, R′ = H) (25 mg.), in acetic acid (1 ml.) was treated dropwise with chromium trioxide (9 mg.) in acetic acid (1 ml.) and water (0·25 ml.). The mixture was heated at 60° for 2 hr. and kept at room temperature for 18 hr. When worked up as described below for methyl podocarpa-5,6,13(14)-trien-15-oate, gummy acidic (5 mg.) and yellow neutral (20 mg.) fractions were obtained. Chromatography of the neutral fraction on silica gel (1 g.), and elution with benzene–ether (19 : 1) gave a homogeneous product which crystallised from benzene–light petroleum in yellow needles of *methyl* 11-*hydroxy*-9,10-*dioxopodocarpa*-5,7,13(14)-*trien*-16-*oate enantiomer* (XII), m. p. 164—167° (15 mg.) (Found: C, 68·1; H, 6·3. $C_{18}H_{20}O_5$ requires C, 68·3; H, 6·4%), $\nu_{max.}$ 3425 (OH), 1736, 1695 (ester and 9,10-diketone C=O), 1595 cm.$^{-1}$ (aromatic ring), or (in $CHCl_3$) 3600 (OH), 1732 (ester and 10-ketone CO), 1699 (9-ketone C=O), 1599 cm.$^{-1}$ aromatic ring).

Anhydrides from the Acid (VI; R = H).—The acid (VI; R = H) (300 mg.) in acetic anhydride (6 ml.) was heated under reflux for 1½ hr. After removal of the solvent *in vacuo*, the residue was fractionally crystallised from acetone, giving (i) 2,3,4,11-*tetrahydro*-1β,11α-*dimethyl*-1H-*fluorene*-1α,9-*dicarboxylic anhydride* (XIV) (87 mg., 33%), needles (changing to rectangular plates above 170°), m. p. 208—209° (decomp.) (Found: C, 76·0; H, 6·0. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%), $\lambda_{max.}$ 240, ~270—272 mμ (log ε 3·85, 3·1 respectively), $\nu_{max.}$ 1786, 1763 (C=O of αβ-unsaturated 6-ring anhydride), 1640 (conjugated C=C), and 1607 cm.$^{-1}$ (aromatic ring); and (ii) 9β-*acetoxy*-1,2,3,4,10α,11-*hexahydro*-1β,11α-*dimethylfluorene*-1α,9α-*dicarboxylic*

anhydride (XV), prisms (64 mg., 19%), m. p. 163—165° (Found: C, 69·3; H, 6·1. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%), $\nu_{max.}$ 1816, 1764 (C=O of 6-ring anhydride), 1742, 1230 (OAc), 1615 cm.$^{-1}$ (aromatic ring). When the reaction time was extended to 2 hr., the anhydride (XIV) was isolated in 53% yield, but none of the acetoxy-anhydride (XV) was found.

Alkaline Hydrolysis of the Anhydride (XIV).—The anhydride (6 mg.) in N-sodium hydroxide (2 ml.) was shaken at room temperature for 20 hr. Acidification gave a precipitate which was filtered off and crystallised from dilute methanol, giving 2,3,4,11-*tetrahydro*-1β,11α-*dimethyl*-1H-*fluorene*-1α,9-*dicarboxylic acid* (XVI; R = R′ = H), needles (5 mg.), m. p. 210—212° (Found: C, 71·2; H, 6·3%; equiv., 128. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%; equiv., 143), $\lambda_{max.}$ 266 mμ (log ε 3·86), $\nu_{max.}$ 3285, 2655 (broad; OH of CO_2H), 1739, 1691 (CO of CO_2H), 1600 (conjugated C=C), 1590, 1574 cm.$^{-1}$ (aromatic ring). The acid was stable to 3N-sulphuric acid under reflux and to concentrated sulphuric acid at −10°.

The *methyl ester* (XVI; R = R′ = Me), prepared with diazomethane, formed needles, m. p. 118—119° (Found: C, 72·3; H, 6·9. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·1%).

Hydrolysis of the Ester (XVI; R = R′ = Me).—The ester (15 mg.) in 0·5N-ethanolic potassium hydroxide was heated under reflux for 2 hr. After dilution with water, the solution was extracted with ether, and the extract was separated into acidic (9 mg.) and neutral (6 mg.) fractions. The acid fraction was chromatographed on silica gel (1 g.) in ether and gave the homogeneous half-ester (XVI; R = Me, R′ = H) which crystallised from ether in needles (8 mg.), m. p. 135—139°, $\nu_{max.}$ 3460—2500 (broad, weak; OH of CO_2H), 1730 (ester CO), 1699 sh, 1684 (CO of CO_2H), 1598, 1575 cm.$^{-1}$ (aromatic ring).

Hydrolysis of Methyl Abieta-5,7,13(14)-*trien*-15-*oate*.—The ester (50 mg.) in 0·5N-ethanolic potassium hydroxide (20 ml.) was heated under reflux for 2 hr. After dilution with water the solution was extracted with ether and the extract was separated into acidic (10 mg.) and neutral (39 mg.) fractions. The acid fraction crystallised from hexane and was identified (infrared spectrum) as abieta-5,7,13(14)-trien-15-oic acid.

Alkaline Hydrolysis of the Anhydride (XV).—The anhydride (10 mg.), in 2N-sodium hydroxide (5 ml.), was heated under reflux for 2 hr. Acidification and recovery in ether gave the acid (XVI; R = R′ = H) (9 mg.), m. p. and mixed m. p. 208—209° (correct infrared spectrum). When the reaction was conducted at room temperature for 20 hr. in 0·1N-sodium hydroxide only starting material was recovered.

1,2,3,4,10α,11-*Hexahydro*-1β,11α-*dimethyl*-9-*oxofluorene*-1α-*carboxylic Acid* (XVII).—The acid (VI; R = H) (50 mg.) and lead tetra-acetate (82 mg., 1·1 equiv.) were heated in acetic acid (6 ml.) at 65—70° for 1 hr. The solution was diluted with water and extracted with ether. Chromatography of the recovered gum on silica gel (3 g.) in benzene–ether (9 : 1) gave 1,2,3,4,10α,11-hexahydro-1β,11α-dimethyl-9-oxofluorene-1α-carboxylic acid (XVII) (33 mg.) in needles, m. p. 129—130° (from ether–light petroleum) (Found: C, 74·4; H, 7·0. Calc. for $C_{16}H_{18}O_3$: C, 74·4; H, 7·0%), $\lambda_{max.}$ 248, 293 mμ (log ε 3·93, 3·28 respectively), $\nu_{max.}$ 3400—2500 (broad), 1716 (OH and CO of CO_2H), 1699 (conjugated CO in 5-ring), 1604 cm.$^{-1}$ (aromatic ring). Ohta [7] gives m. p. 130—131°, $\nu_{max.}$ 1695, 1686 cm.$^{-1}$.

Oxidation of Methyl Podocarpa-5,7,13(14)-*trien*-15-*oate by Chromic Oxide*.—The ester (1 g.) in acetic acid (10 ml.) at 60° was treated dropwise with chromic oxide (2 g.) in acetic acid (10 ml.) and water (2 ml.). The mixture was heated at 80° for 7·5 hr. and kept at room temperature for a further 18 hr. After addition of methanol and evaporation *in vacuo*, the residue was diluted with water (50 ml.) and extracted with ether. The ether extract was washed with 2N-sodium carbonate and evaporated, giving a mixture of yellow (A) and colourless (B) prisms. These were separated manually, since fractional crystallisation was difficult. The yellow prisms (A) (350 mg.) were crystallised from benzene and then benzene–light petroleum, giving *methyl* 11-*hydroxy*-9,10-*dioxopodocarpa*-5,7,13(14)-*trien*-15-*oate* (VII; R = H, R′ = CO_2Me) (270 mg., 23%), m. p. 223—226°, $[\alpha]_D^{22}$ +345° (*c* 0·7 in $CHCl_3$) (Found: C, 68·4; H, 6·4; OMe, 9·7. $C_{18}H_{20}O_5$ requires C, 68·3; H, 6·4; OMe, 9·9%), $\nu_{max.}$ 3315 (bonded OH), 1739, 1685 (bonded ester and 9,10-diketone C=O), 1598 cm.$^{-1}$ (aromatic ring), or (in CCl_4, dilute solution) 3297 (bonded OH), 1736 (10-ketone CO), 1694 cm.$^{-1}$ (bonded ester and 9-ketone C=O), $\lambda_{max.}$ 285, 442 mμ (log ε 3·83, 1·70 respectively). On addition of 2 drops of 3N-sodium hydroxide the maximum at 285 mμ rapidly decreased whilst the end-absorption below 250 mμ increased, until after 4 hr. no maximum could be detected between 220 and 310 mμ.

Ohta and Ohmori [5] give m. p. 201—203° for their oxidation product of methyl podocarpa-5,7,13(14)-trien-15-oate. The m. p. of the ester (VII; R = H, R′ = CO_2Me) was not depressed

on admixture with an authentic specimen kindly provided by Dr. Ohta, and the infrared spectra were identical for both solutions and the solid state. The difference in m. p. is ascribed to dimorphism.

The diketo-ester (VII; R = H, R′ = CO_2Me) was stable to hot dilute hydrochloric acid. The *quinoxaline derivative* formed plates, m. p. 188—189° (Found: C, 73·8; H, 6·2. $C_{24}H_{24}N_2O_3$ requires C, 74·2; H, 6·2%), $\nu_{max.}$ 3342 (bonded OH), 1685 cm.$^{-1}$ (bonded ester CO). It gave a yellow colour, which rapidly darkened, with concentrated sulphuric acid.

The colourless prisms (B) crystallised from methanol, to give the acid (X; R = H), m. p. 150—152°, identical (mixed m. p. and infrared spectra) with the material obtained from the acid fraction (below).

Acidification of the sodium carbonate extract followed by extraction with ether and recovery gave methyl 3-*o*-carboxyphenyl-1β,3β-dimethyl-2-oxocyclohexanecarboxylate (lactol form; X; R = H) (365 mg., 33%) as prisms, m. p. 150—152°, $[\alpha]_D^{27}$ −8·3° (*c* 0·9) (Found: C, 67·2; H, 6·8; OMe, 10·9. Calc. for $C_{17}H_{20}O_5$: C, 67·1; H, 6·6; OMe, 10·2%), $\nu_{max.}$ 3425 (OH), 1730 (ester and δ-lactone C=O), 1608 cm.$^{-1}$ (aromatic ring). Ohta and Ohmori [5] give m. p. 151—152°, $[\alpha]_D^{25}$ −8·4° (*c* 2·4).

Oxidation of the Diketo-ester (VII; R = H, R′ = CO_2Me).—The diketo-ester (VII; R = H) (12 mg.) in acetic acid (0·5 ml.) was treated with chromic oxide (9 mg.) in acetic acid (0·5 ml.) and water (0·15 ml.). Heating at 80° for 5·5 hr., and working up as in the previous experiment, gave a gum (10 mg.) which crystallised from methanol in prisms, m. p. 149—150·5°, of the acid (X; R = H). Only starting material was recovered when the reaction was performed at 60° for 7 hr.

Action of Alkali on the Diketo-ester (VII; R = H, R′ = CO_2Me).—The diketo-ester (VII; R = H, R′ = CO_2Me) (52 mg.) in 3N-sodium hydroxide (15 ml.) was heated under reflux for 1 hr., in a nitrogen atmosphere. The cooled solution was extracted with ether, acidified, and again extracted with ether, giving, on recovery, a gum (41 mg.) which crystallised from methanol in prisms (10 mg.), m. p. 221—222°, $[\alpha]_D^{24}$ −10·8° (*c* 0·4 in $CHCl_3$), of 1,2,3,6,7,11b-*hexahydro*-4,11b-*dimethyl*-6,7-*dioxodibenz*[b,d]*oxepin* (VIII) (Found: C, 75·0, 75·3; H, 6·3, 6·1. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%), $\lambda_{max.}$ 202, 260, 290 mμ (log ε 4·18, 4·03, 3·96 respectively), $\nu_{max.}$ 1803 (enol lactone CO), 1678 (conjugated CO), 1659 (C=C), 1600 cm.$^{-1}$ (aromatic ring). It liberated carbon monoxide when heated with phosphoric acid (detected by the production of molybdenum blue with phosphomolybdic acid [13]).

When barium hydroxide was used instead of sodium hydroxide for the hydrolysis of the ester a precipitate of barium carbonate was obtained.

Oxidation of Methyl Abieta-5,7,13(14)-trien-15-oate.—To the ester (1 g.) in acetic acid (10 ml.) at 80° was added dropwise chromic oxide (2 g.) in acetic acid (10 ml.) and water (2·5 ml.). The solution was heated at 80° for 5·5 hr. and kept at room temperature for 18 hr. The solution was worked up as in previous oxidations, and was separated into yellow gummy acidic (200 mg.) and yellow gummy neutral (722 mg.) fractions by extraction with N-sodium hydroxide.

The acid fraction crystallised from methanol, giving *methyl* 3-(4-*acetyl*-2-*carboxyphenyl*)-1β,3β-*dimethyl*-2-*oxocyclohexanecarboxylate* (lactol form; X; R = Ac) (128 mg.), prisms, m. p. 225—227° (changing to plates above 215°), $[\alpha]_D^{24}$ −59·0° (*c* 0·5 in $CHCl_3$) (Found: C, 66·2, 66·2; H, 6·6, 6·4. $C_{19}H_{22}O_6$ requires C, 65·9; H, 6·4%), $\nu_{max.}$ 3335 (OH), 1723 (ester and δ-lactone CO), 1691 (conjugated CO), 1609 cm.$^{-1}$ (aromatic ring), $\lambda_{max.}$ 225, 245, 291·5, 301 mμ (log ε 4·47, 4·03, 3·04, 3·02 respectively) changing to 215, 255, ~290—293 mμ (log ε 4·29, 4·09, 3·25 respectively) on addition of 2 drops of 3N-sodium hydroxide. It gave a positive iodoform reaction, a red colour with sodium nitroprusside, and on treatment with *o*-nitrobenzaldehyde a substituted indigo.[14]

The amorphous *dinitrophenylhydrazone*, m. p. 256—257° (decomp.), was precipitated from benzene with light petroleum (Found: C, 56·8; H, 5·5. $C_{25}H_{26}N_4O_9$ requires C, 57·0; H, 5·0%).

The neutral fraction was chromatographed on silica gel (20 g.), and the column was eluted with benzene. A yellow band (a) moved rapidly down the column and gave a yellow gum (125 mg.) on recovery. This was distilled at 110—120° (bath)/1·5 × 10^{-4} mm., giving *methyl* 11-*hydroxy*-9,10-*dioxoabieta*-5,7,13(14)-*trien*-15-*oate* (VII; R = Pr^i, R′ = CO_2Me) as a yellow oil (Found: C, 70·7; H, 7·7. $C_{21}H_{26}O_5$ requires C, 70·4; H, 7·3%), $\nu_{max.}$ (in CCl_4) 3320 (bonded OH), 1737 (10-ketone CO), 1699s cm.$^{-1}$ (bonded ester and 9-ketone CO), $\lambda_{max.}$ 258, 291, 450 mμ

[13] Feigl, "Spot Tests in Organic Analysis," Elsevier, Amsterdam, 5th edn., p. 327.
[14] Ref. 13, p. 224.

(log ε 3·61, 3·67, 1·41 respectively) changed to 250 mμ (log ε 3·77) on addition of 2 drops of 3N-sodium hydroxide.

Continued elution of the column with 50 ml. portions of benzene–ether gave two yellow gummy fractions (benzene–ether ratio and fraction weights in parentheses).

Fraction (b) (9 : 1, 430 mg.), on rechromatography on grade II neutral alumina (40 g.), and elution with benzene–ether in ultraviolet light, gave the following fractions: (i), a blue band (benzene; 144 mg.), intractable gum, (ii) a yellow band (9 : 1; 77 mg.), yellow intractable gum, (iii) (9 : 1; 59 mg.), a yellow gum which deposited colourless prisms of methyl 7-acetyl-1,2,3,4,9,10,11α,12-octahydro-1β,12β-dimethyl-9-oxophenanthrene-1α-carboxylate (XIII), m. p. 142—143°, $[\alpha]_D^{24}$ +30·8° (*c* 1·9 in $CHCl_3$) (Found: C, 73·5; H, 7·4. Calc. for $C_{20}H_{24}O_4$: C, 73·1; H, 7·4%), $\nu_{max.}$ 1723 (ester CO), 1684 (conjugated CO), 1603 cm.$^{-1}$ (aromatic ring) {Ritchie *et al.*[10] give m. p. 144—145°, $[\alpha]_D^{22}$ +30·8° (*c* 2·0 in $CHCl_3$)}, (iv) (3 : 1; 21 mg.), an intractable gum, (v) (1 : 1; 8 mg.) an intractable gum, and (vi) (ether; 8 mg.) a yellow gum depositing yellow prismatic needles, m. p. 135—141°, $\nu_{max.}$ 3300 (OH), 1738, 1691, 1654 (C=O), 1603, 1566 cm.$^{-1}$ (aromatic ring), $\lambda_{max.}$ 243, ~282—287 mμ (log $E_{1\,cm.}^{1\%}$ 2·68, 2·12 respectively).

Fraction (c) (4 : 1; 81 mg.), a yellow intractable gum, was rechromatographed on silica gel (5 g.) and eluted with 10 ml. portions of benzene–ether (19 : 1). After a series of intractable gums (35 mg.) had been eluted, fractions 10—15 crystallised from methanol in prisms (29 mg.), m. p. 140—142°, of the ketone (XIII) (infrared spectrum).

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